Syntheses of Carbobicyclic Nucleosides

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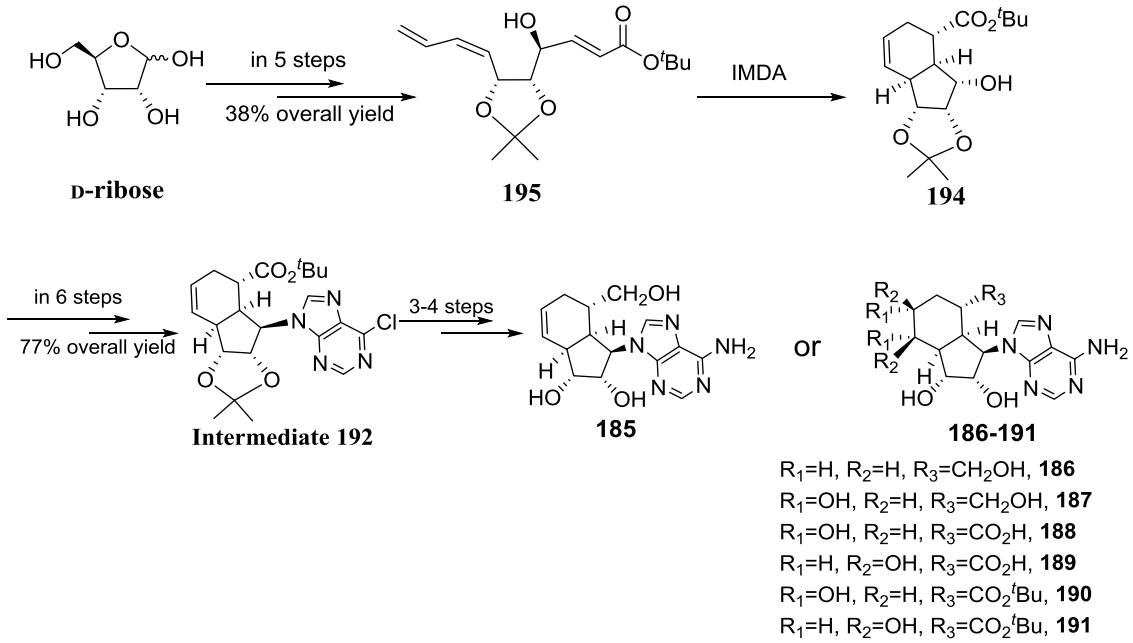
Table of Contents

Abstract

In this thesis, a review regarding the development of carbobicyclic nucleosides and conformationally locked carbobicyclic nucleosides by fusing different rings onto the five-member ring was presented.

The key intermediate **192** was synthesized from D-ribose in 12 steps with 27% overall yield, using an Intramolecular Diels-Alder reaction (IMDA) as the key step. By modification of the cyclohexene ring, seven carbobicyclic adenosine analogues **185-191** with a bicyclo[4.3.0]nonane framework were prepared successfully from intermediate **192** in 3 to 4 steps and their conformations were examined by X-ray crystallography.

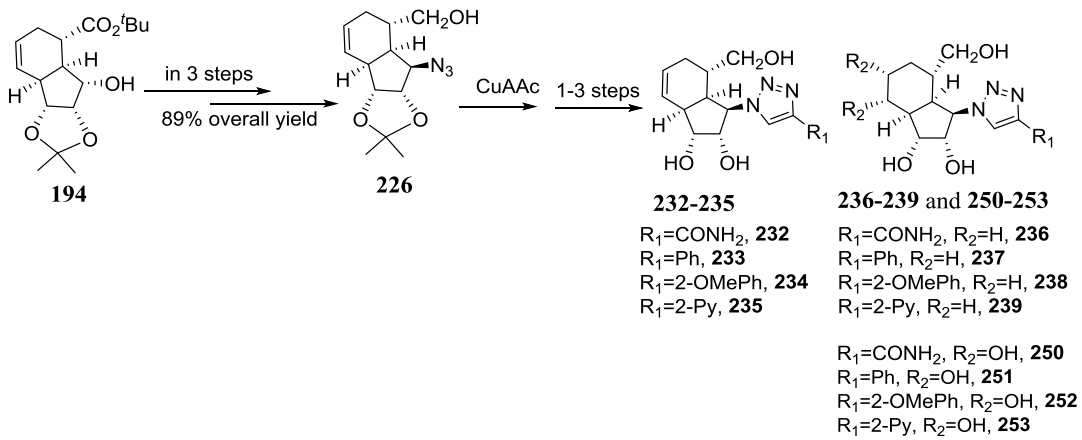


D-ribose **195** **194**

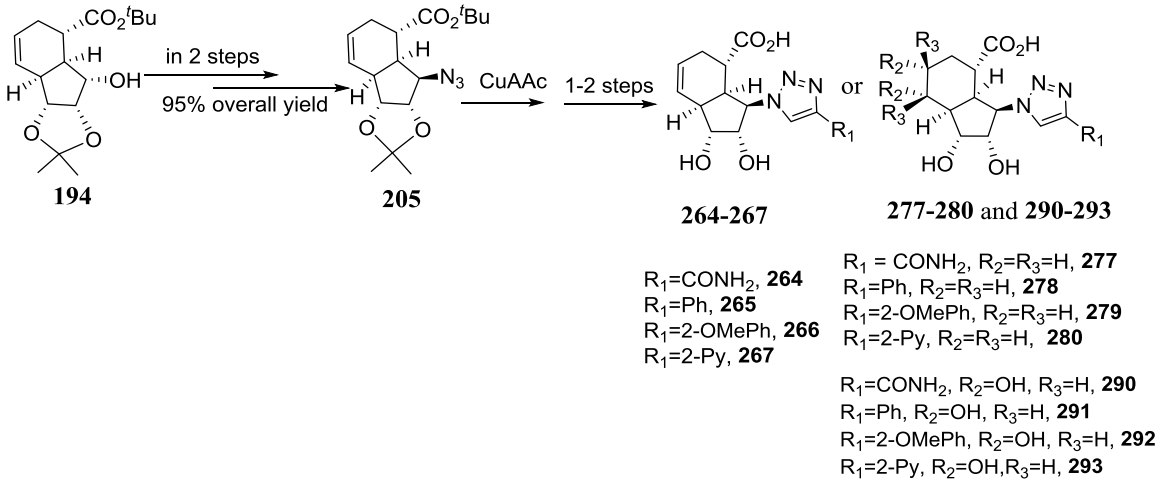
Intermediate 192 **185** **186-191**

R_1=H, R_2=H, R_3=CH_2OH, **186**
R_1=OH, R_2=H, R_3=CH_2OH, **187**
R_1=OH, R_2=H, R_3=CO_2H, **188**
R_1=H, R_2=OH, R_3=CO_2H, **189**
R_1=OH, R_2=H, R_3=$CO_2{}^tBu$, **190**
R_1=H, R_2=OH, R_3=$CO_2{}^tBu$, **191**

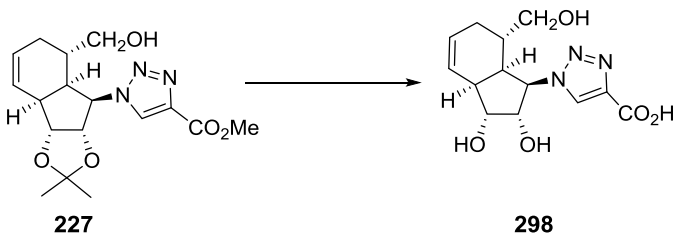
Twelve carbobicyclic ribavirin analogues **232-239** and **250-253** with a bicyclo[4.3.0]nonane framework were synthesized successfully by using a copper catalyzed azide-alkyne cycloaddition (Huigsen reaction) as the key step.

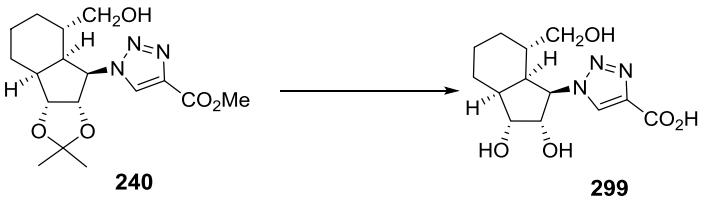


Another twelve ribavirin analogues bearing a carboxylate group (**264-267**, **277-280** and **290-293**) with a bicyclo[4.3.0]nonane framework were also obtained.

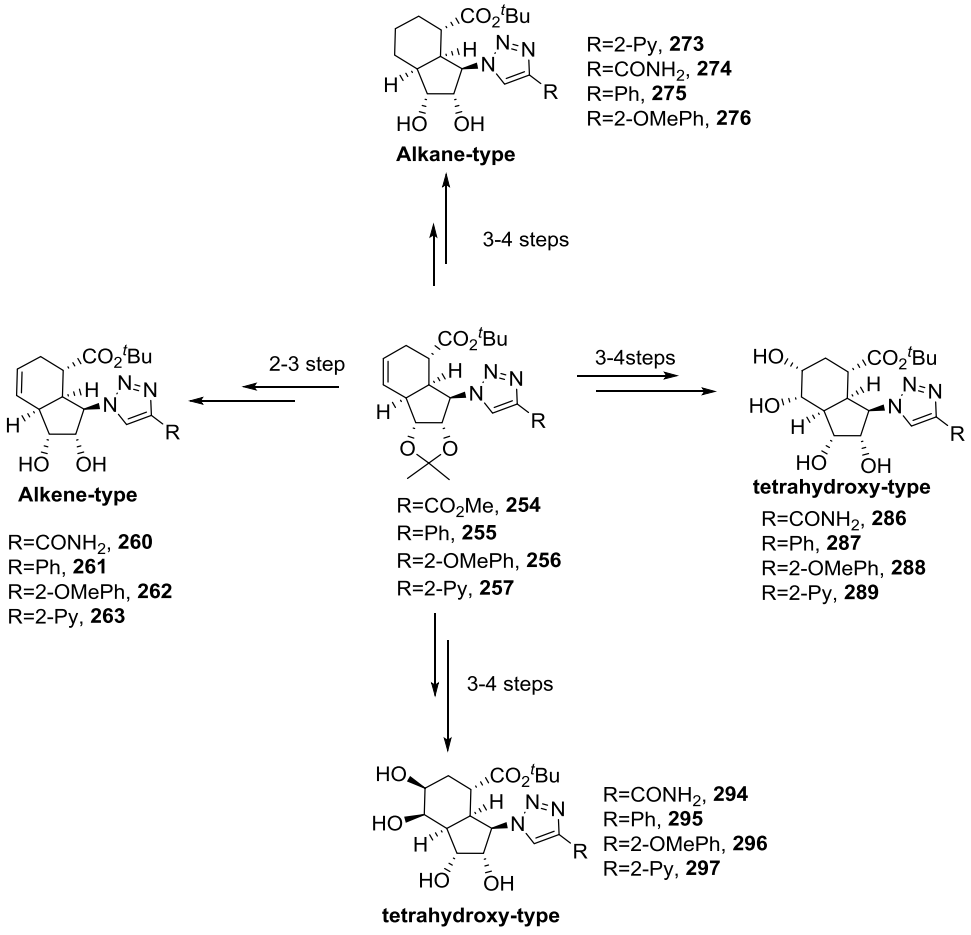


Furthermore, two more ribavirin analogues bearing a carboxylic acid in triazole (**298** and **299**) with a bicyclo[4.3.0]nonane framework were obtained.





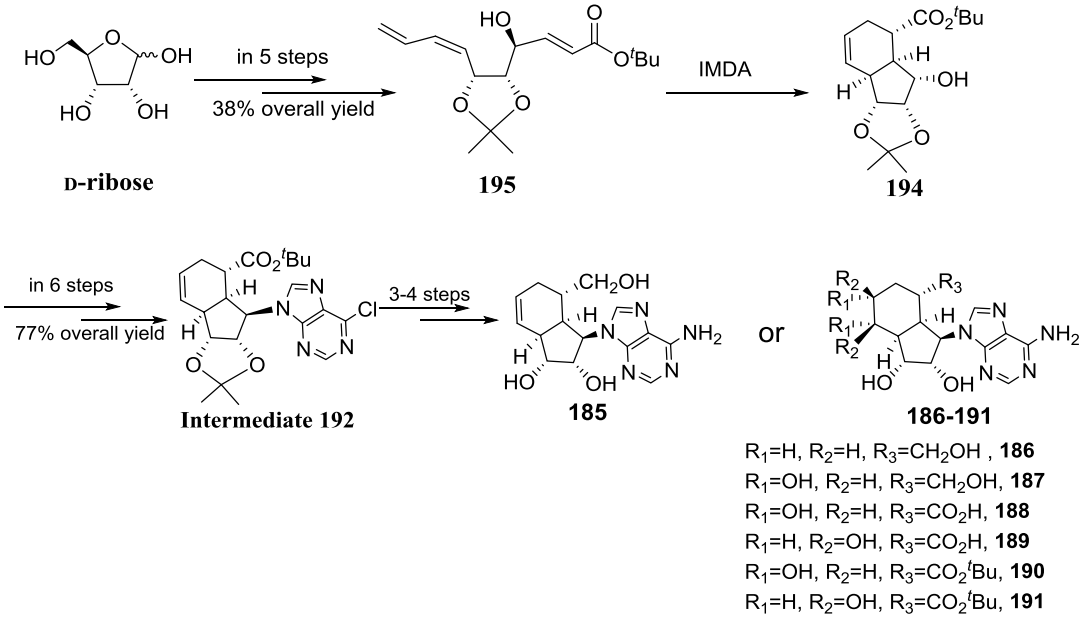
Finally, twelve ribavirin analogues bearing a *tert*-butyl carboxylate ester (**260-263**, **273-276, 286-289** and **290-293**) with a bicyclo[4.3.0]nonane framework were also obtained.



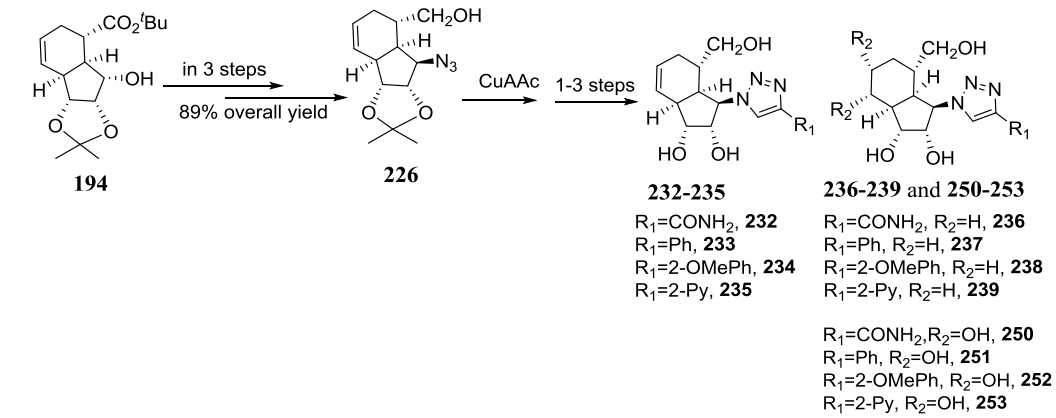
摘要

本文描述了碳環核苷的發展過程，同時也描述了將不同環融合在五元碳環上的方法來對碳環核苷的構象進行鎖定。

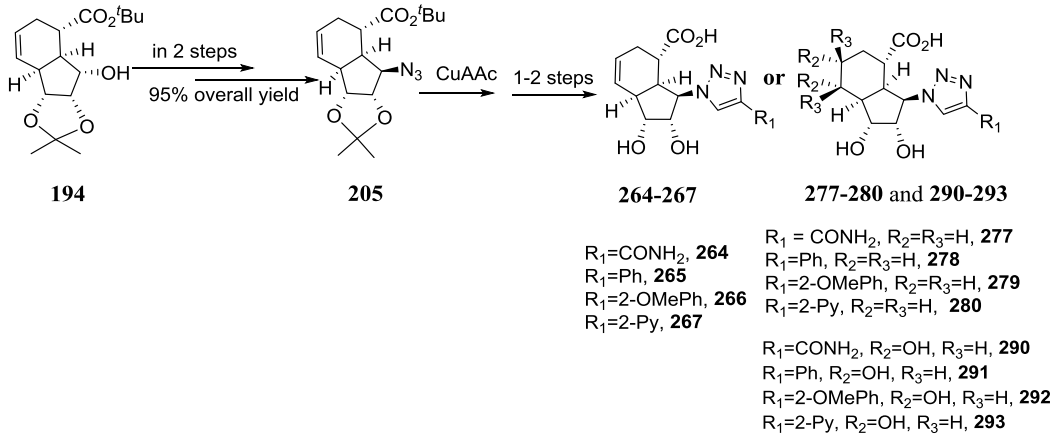
以 D-核糖為起始原料，經過 12 步反應並以分子內的 Diels-Alder 反應 (IMDA) 為關鍵步驟合成出了關鍵的中間體 **192**，它的總產率為 27%。通過對中間體 **192** 中的環己烯的結構進行修飾，經過 3-4 步反應成功合成出了 7 個具有雙環[4.3.0]壬烷結構的碳環核苷（**185-191**），它們的構型也通過其 X 光單晶結構圖來進行確定。



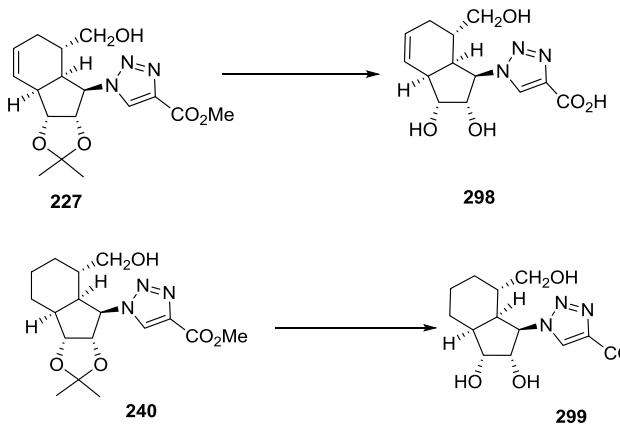
以一價銅催化端炔和疊氮化物的 Huisgen 環加成反應為關鍵步驟，成功地合成出了 12 個具有雙環[4.3.0]壬烷結構的碳環三唑核苷。



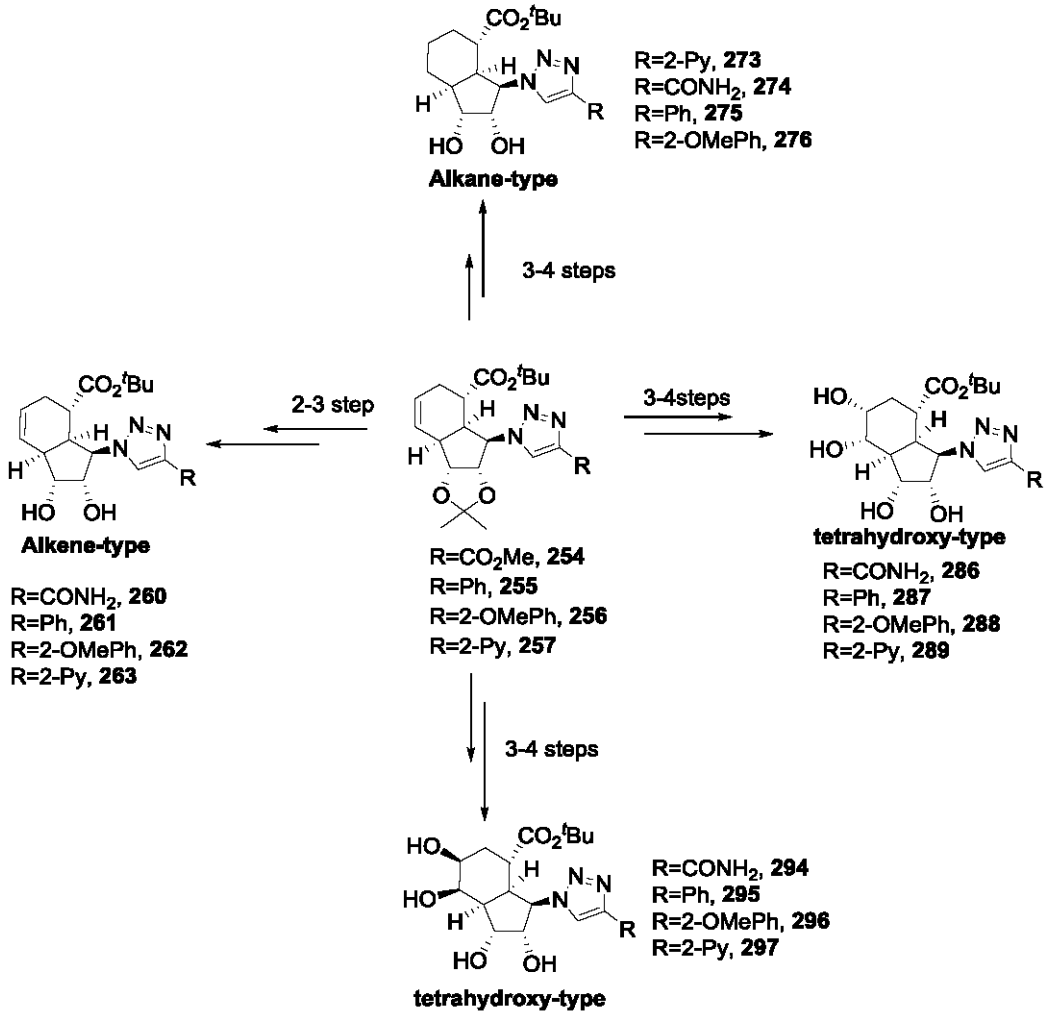
同時，我們也合成 12 個具有雙環[4.3.0]壬烷結構的碳環三唑核苷羧酸。



另外，我們也合成出了兩個在三唑環上含有羧酸的碳環三唑核苷（298 和 299）。



最後，我們還合成出了 16 個含有大基團叔丁基羧酸酯的碳環三唑核苷(260-263, 273-276, 286-289 和 294-297)。



Abbreviation

[α]	specific rotation	Hz	hertz
Å	angstrom (s)	IMDA	intramolecular Diels-Alder
Ac	acetyl	IR	infrared
Anal.	analytical	*J*	coupling constant (in NMR)
BORSM	based on recovered starting material	KHMDS	potassium hexamethyldisilazide
br	broad (spectral)	KO^{t}Bu	potassium tertbutoxide
^{n}Bu	*n*-butyl	$LiAlH_4$	lithium aluminium hydride
^{t}Bu	*tert*-butyl	LiHMDS	lithium hexamethyldisilazide
℃	degree Celsius	$LiBH_4$	lithium borohydride
ca.	circa/approximately	M	moles per liter
cat.	catalytic	m	multiplet (spectral), milli-
COSY	correlated Spectroscopy	Me	methyl
ROESY	correlated Spectroscopy	MHz	megahertz
NOESY	correlated Spectroscopy	min	minute
(±)-CSA	(±)-10-camphorsulfonic acid	mp	melting point
δ	chemical shift in parts per million downfield from tetramethylsilane (spectral)	Ms	methanesulfonyl
		MeONa	sodium methoxide
		MeOPh	4-methoxylphenyl
d	day (s) or doublet (spectral)	MS	molecular sieves or mass spectrum
2-D	two dimesion	*m/z*	mass-to-charge ratio
DEPT	distortionless Enhancement by Polarization Transfer	n	nano
		NaHMDS	sodium hexamethyldisilazide
DMF	dimethylformamide		
DEAD	diethyl azodicarboxylate	NaO^{t}Bu	sodium tertbutoxide
DIAD	diisopropyl azodicarboxylate	NMO	4-methylmorpholine *N*-oxide
DIBAL-H	diisobutylaluminum hydride		
DMSO	dimethyl sulfoxide	NMR	nuclear magnetic resonance
E1	unimolecular elimination	Nu	nucleophile
ESI	electrospray Ionization	NOESY	nuclear overhauser effect spectroscopy
Et	ethyl		
EtONa	sodium ethoxide	Ph	phenyl
Et_2O	diethyl ether	ppm	parts per million (in NMR)
FT	fourier transform	$PhI(OAc)_2$	iodobenzene diacetate
g	gram	Py	pyridine
Δ	heat	Pd/C	Pd-on-charcoal
h	hour	^{i}PrONa	sodium isopropoxide
HRMS	high-resolution mass spectrum		

PBu_3	tributylphosphine	S_N2	bimolecular nucleophilic substitution
PPh_3	triphenylphosphine		
q	quartet (spectral)	t	triplet (spectral)
quin	quintet (spectral)	Tf	trifluoromethanesufonyl
R_f	retention factor	Tf_2O	trifluoromethanesulfonic anhydride
rt	room temperature		
ROESY	rotational frame nuclear overhauser effect spectroscopy	TFA	trifluoroacetic acid
		THF	tetrahydrofuran
		TLC	thin layer chromatography
s	singlet (spectral)	TS	transition state
sat.	saturated	v	volume

Chapter 1

Introduction

1.1 General Background

In 1909, Levene P. A. and Jacobs W. A. used the term "nucleoside" to describe carbohydrate derivatives of purines and pyrimidines.[1] These compounds have a simple structures as shown in Figure 1. Nucleosides are glycosylamines that consist of a nucleobase bonding to a ribose or deoxyribose (at the *N*-9 position for purine, or the *N*-1 position for pyrimidine) via a β-D-glycosidic bond.

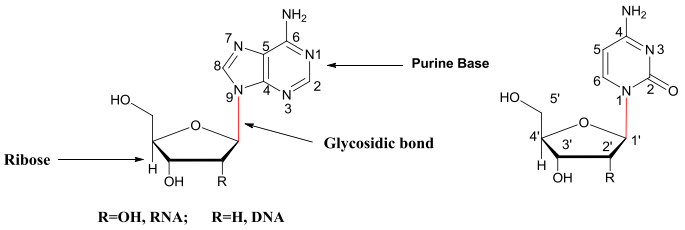
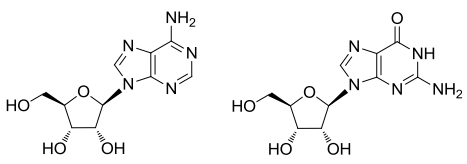
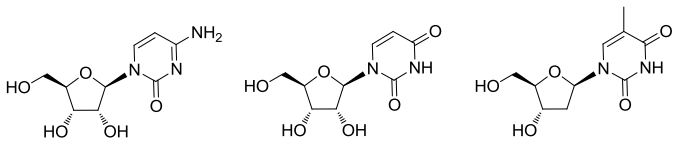


Figure 1

There are five basic nucleosides including adenosine, guanine, cytosine, thymidine and uracil in natural nucleosides as shown in Figure 2. They are the fundamental building blocks of DNA and RNA, which are related to the expression of genetic sequences and corresponding codes for protein synthesis.



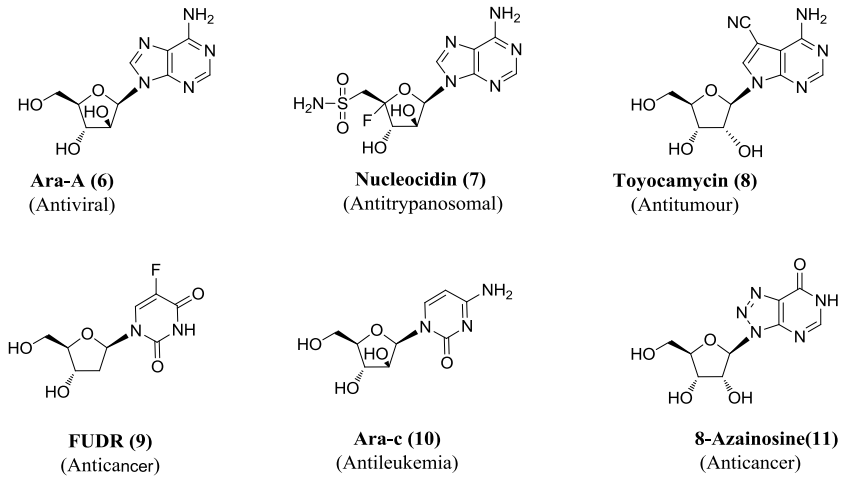
Adenosine (1) **Guanosine (2)**



Cytidine (3) **Thymidine (4)** **Uracil (5)**

Figure 2

During the 1950s and 1960s, the conventional synthetic methodology in the chemistry of nucleosides and nucleotides was developed rapidly,[2] and resulted in the availability of natural and synthetic nucleosides. Many methodologies have proved to be valuable tools for elucidating the biosynthetic pathways of nucleosides and produced a large number of compounds with anticancer and antiviral activities[3] as shown in Figure 3.



Ara-A (6) (Antiviral)

Nucleocidin (7) (Antitrypanosomal)

Toyocamycin (8) (Antitumour)

FUDR (9) (Anticancer)

Ara-c (10) (Antileukemia)

8-Azainosine(11) (Anticancer)

Figure 3

In the early 1980s, with the emergency of Human Immunodeficiency Virus (HIV) that was the main causative agent of Acquired Immunodeficiency Syndrome (AIDS), many valuable nucleoside mimetics were used as chemotherapeutic agents. AZT

(Zidovudine),[4a] the first drug licensed for the treatment of HIV infection which can inhibit HIV-1 reverse transcription, was synthesized firstly at Detroit Institute of Cancer Research in 1964. There are four more licensed nucleoside analogues, namely DDC (Zalcitabine), DDI (Didanosine), D_4T (Stavudine) and 3TC^{TM} for such theropeutic use (Figure 4).[4]

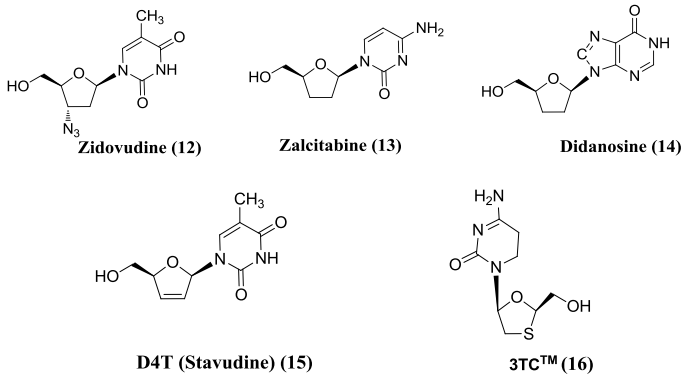


Figure 4

1.2 Conformation of Nucleosides

In solution, the ribose ring in the nucleosides keeps puckering, which result in two main structural conformations, envelope (*E*) and twist (*T*). The conformation of furanose rings of nucleosides was described by Altona with the concept of pseudorotation. Pseudorotation is a set of intramolecular movements of attached groups on a highly symmetric molecule, resulting in a molecule which could not be discriminated from the original one. The puckering was determined by the pseudorotation phase angle P which was used to describe which atoms are displaced

out of the plane and the direction of displacement. The puckering was also determined by the maximum torsional angle τ_{max} that was used to describe the degree of displacement or pucker. [5-6]

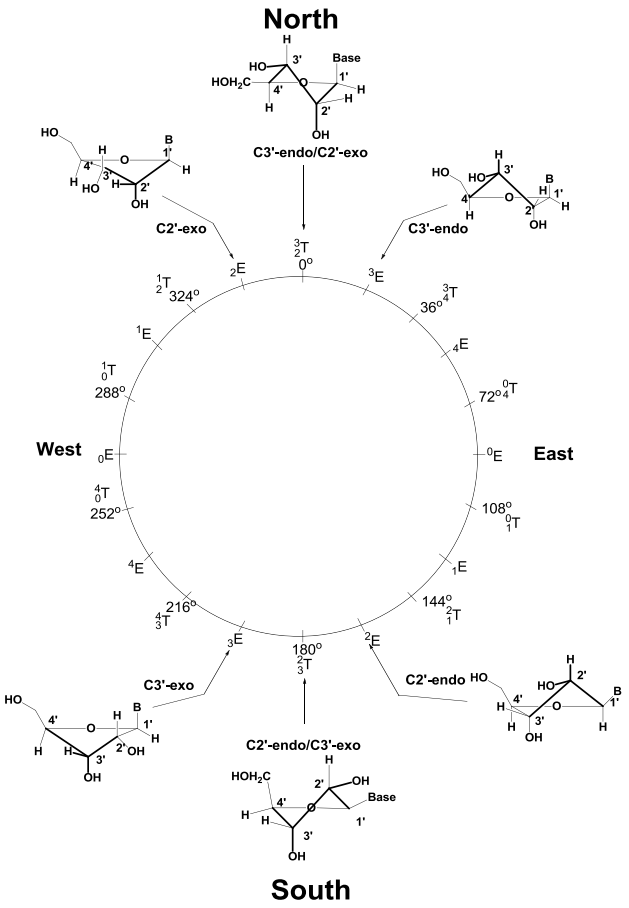


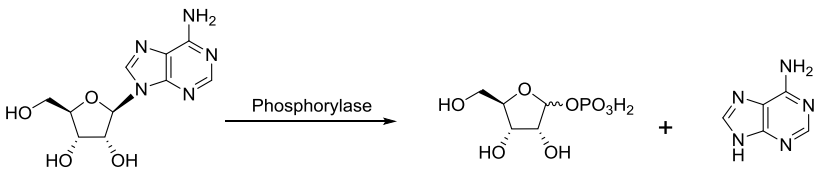
Figure 5

The conformational preference of the sugar ring is influenced by both steric effects and the gauche effect. [6] As shown in Figure 5, the *endo* and *exo* are used to describe the displaced atom above or below the plane of other atoms in the sugar ring, respectively. The psuedorotation cycle can be divided into 20 distinct twist and envelope conformations when the pseudorotation phase angle P varies from 0^o to 360^o.

The phase angle P = 0^{o} corresponds to an absolute North conformation with a symmetrical twist form $^{3}T_{2}$, while its South antipode $^{2}T_{3}$ is represented by P = 180^{o}. For a typical North conformation, P can range between 342 ^{o} and 18 ^{o} ($_{2}E \rightarrow {}^{3}T_{2} \rightarrow {}^{3}E$) and for a typical South conformation P fluctuates between 162 ^{o} and 198 ^{o} ($^{2}E \rightarrow {}^{2}T_{3} \rightarrow {}_{3}E$). Altona found that most nucleosides are existed in either North (*N*) conformations or South (*S*) conformations by the study of more than 178 X-ray crystal structures of different nucleosides.

1.3 Carbocyclic Nucleosides

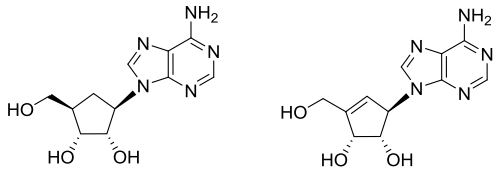
In the first section, we have presented that nucleosides can be used as anti-viral and anti-cancer drugs. However, they have a main drawback that these nucleosides are highly sensitive to nucleoside phosphorylases, which can hydrolyze the glycosidic bond and lead to the loss of their biological activity (Scheme 1).



Scheme 1

Carbocyclic nucleosides are analogues of natural nucleosides in which the oxygen is replaced by a methylene group in the sugar portion of conventional nucleosides.[7-8] This modification makes carbocyclic nucleosides resistant toward

phosphorylases because of the loss of the glycosidic bond. [9-12]



Aristeromycin (**19**) Neplanocin A(**20**)

Figure 6

Two nucleosides, aristeromycin (**19**)[13] and neplanocin A (**20**),[14] were found in natural world (Figure 6). In 1966, Shealy and his coworkers[15] first prepared aristeromycin from norbornadiene. Two years later, it was isolated from a metabolite of *Streptomyces cirtricolor*[13], while neplanocin A was first isolated from the culture broth of *Ampullariella regulars* in 1981[14,16]. These two naturally occurring nucleosides exhibit significant antitumor and antiviral activities. In particular, they show prominent broad-spectrum antiviral activity, which has been correlated with the potent inhibitory effect on S-adenosyl-L-homocysteine (SAH) hydrolase.[17-22]

Aristeromycin and neplanocin A are potent SAH inhibitors, but their utility in therapy has been restricted because of their high toxicity.[23-26] Therefore, modifications of these two naturally nucleosides have generated many carbocyclic nucleosides that keep the inhibitory activity against SAH hydrolase and exhibit less toxicity. [27-35] Recently, many research groups are also interested in modifying aristeromycin and neplanocin A, which lead to the syntheses of a number of novel

carbocyclic nucleosides with good biological activity and extremely low toxicity (Figure 7).[36-50]

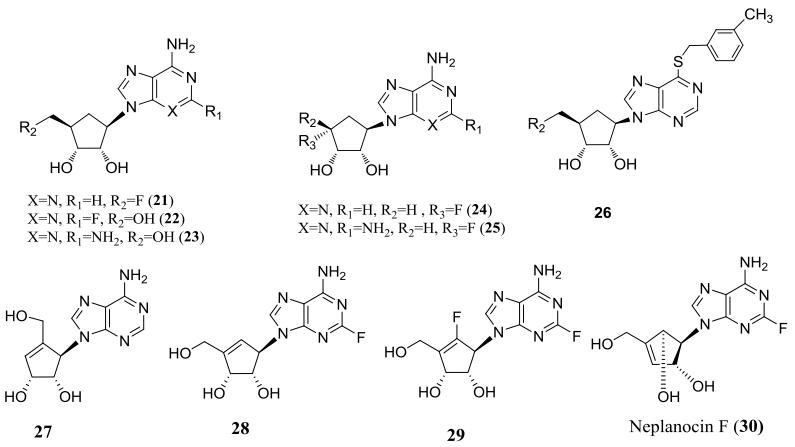


Figure 7

In 1988, Vice and his coworkers first reported the synthesis of (±)-carbovir (**31**), which exhibits potent anti-HIV activity and low cytotoxicity.[51] However, the unacceptable properties, such as limited aqueous solubility, poor oral bioavailability and inefficient penetration into central nervous system, have hindered its further development into an anti-HIV drug.[52-54] For the purpose of improving its preclinical application, plenty of prodrugs of carbovir were synthesized and charaterized, for example, abacavir (**32**) which is a 6-cyclopropylamino substituted analogue was known as the clinically useful drug (Figure 8).

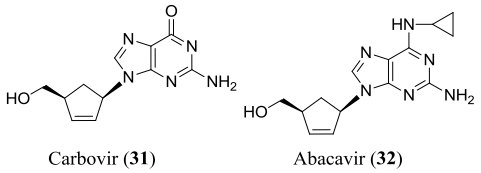


Figure 8

Recently, many research groups are also interested in modifying carbovir and abacavir, which lead to the syntheses of a number of novel carbocyclic nucleosides with good biological activity and extremely low toxicity,[55-62] and some of them are listed in Figure 9.

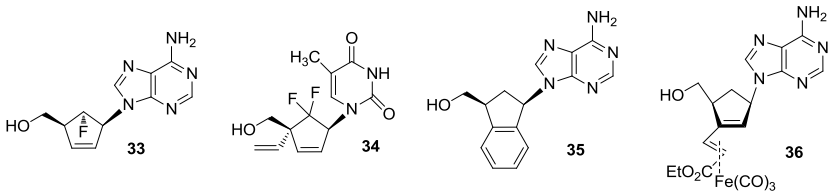
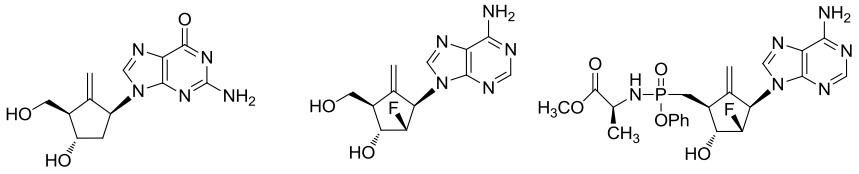


Figure 9

Novel carbocyclic nucleoside analogue, entecavir, is an approved anti-viral drug used to treat heptatitis B virus (HBV). [63] However, entecavir would become clinically ineffective when it was used continuously resulting mutation and producing synergistic effect with lamivudine-resistant mutatant.[64] That's why the use of currently approved anti-HBV drugs was constrained by viral mutation.[65]



entecavir (**37**) FMCA (**38**) FMCAP (**39**)

Figure 10

2'-β-Fluoro-6'-methylene carbocyclic adenosine (FMCA, **38**) and its phosphoramidate prodrug (FMCAP, **39**) (Figure 10) found by Chu and his

collaborators[67] in 2014 were endowed with anti-HBV effect in both wild type strain and the drug-resistance mutant.[66] Further study found that FMCA (EC_{50} = 0.67 μM) and FMCAP (EC_{50} = 0.054 μM) can maintain their anti-HBV efficiency *in vitro* against the entecavir-resistant triple mutant (L180M+M204V+S202G), while entecavir lost its function by 150-fold against the mutant as compared with the wild type.

1.4 Conformationally Locked Carbocyclic Nucleosides

The replacement of the furanose oxygen to a methylene unit makes the carbocyclic nucleoside resistant to phosphorylase due to the absence of glycosidic bond. However, the modification of nucleoside results in significant change in its conformation. As illusrated before, the sugar moiety should exist in either a South or a North type so as to give the best effects. However, the carbocyclic nucleosides generally are inclined to take an unrepresentative C'1-*exo* conformation due to the steric bulk of the heterocyclic base, which prefers to adopt the equatorial orientation (Figure 11).

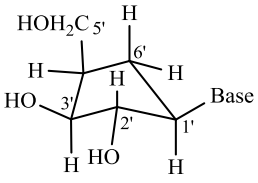
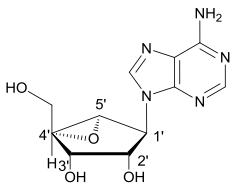


Figure 11

Fortunately, scientists found that the carbocyclic nucleosides could be locked in a certain conformation by fusing a ring to the cyclopentane ring. Now the conformations of locked carbocyclic nucleosides are closer to the original North-type conformation (C2'-*exo* or C3'-*endo*) or South-type conformation (C2'-*endo* or C3'-*exo*). The carbocyclic nucleosides locked by fusing different rings are presented in the following sections.

1.4.1 Synthesis of Conformationally Locked Carbocyclic Nucleosides by Fusing a Oxirane Ring

In the early of 1980s, the natural occurring carbocyclic nucleoside, neplanocin C (Figure 12) was isolated from *Ampullariela regularis*, which is the first example of conformationally locked carbocyclic nucleosides with an oxirane ring fused on 4'-5' position of cyclopentane ring.[68] From the analysis of its X-ray crystallography,[69] the bicyclo[3.1.0] system of neplanocin C adopted a predominant Northern conformation.

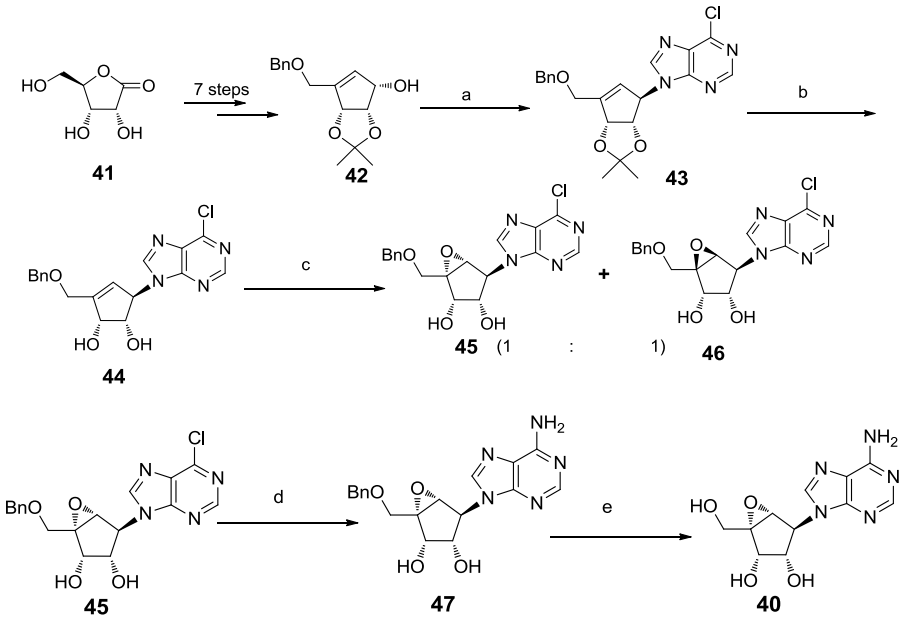


Neplanocin C (40)

Figure 12

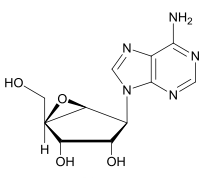
In 2000, Comin and his coworkers[70] finished the first synthesis of neplanocin C. The synthesis started from cyclopentenol **42**, which was prepared from

D-ribonolactone in 7 steps according to literature.[71] Cyclopentenol **42** was then coupled with 6-chloropurine by Mitsunobu reaction to give carbanucleoside **43** (Scheme 2). Deprotection of the isopropylidene group in carbanucleoside **43** afforded diol **44** in 40% overall yield from cyclopentenol **42**.



Scheme 2 Reagents and conditions: (a) DIAD, PPh_3, 6-chloropurine, THF, rt, 1 h; (b) 60%AcOH, 50 °C, 24 h, 40% from **41**; (c) *m*-CPBA, CH_2Cl_2, 0 °C to rt, 10 d; (d) NH_3/MeOH, 70 °C, 5 h, 75%; (e) H_2, 10% Pd/C, MeOH, 3 atm, 88%.

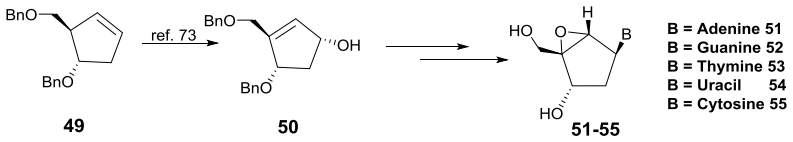
Then, the epoxidation of diol **44** with *m*-CPBA afforded epoxide **45** and its diastereomer **46** in a 1:1 ratio, which were fractionated by column chromatography. Treatment of epoxide **45** with methanolic ammonia furnished purine derivative **47**, which was subsequently subjected to catalytic hydrogenation to yield neplanocin C.



48

Figure 13

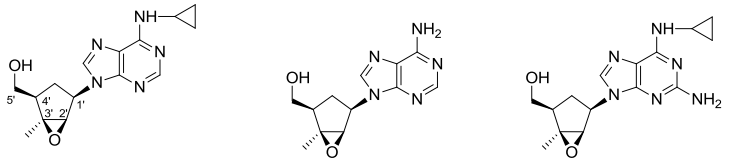
Diastereomer **46** obtained during the epoxidation of diol **44**, was converted into carbanucleoside **48** (Figure 13) in a comparable overall yield according to the procedure for the synthesis of **40** from epoxide **45**.



49 **50** **51-55**

Scheme 3

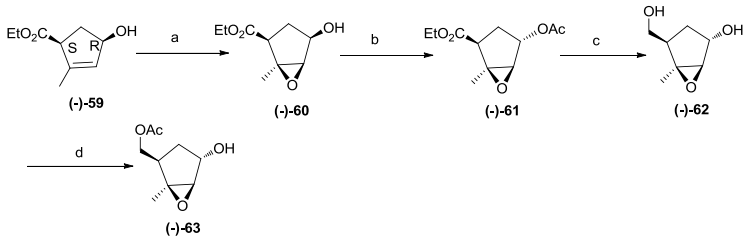
Two years later, Comin and coworkers[72] synthesized all purine and pyrimidine 2'-deoxyneplanocin C analogues from the readily available chiral template (3R, 4S)-4-phenylmethoxy-3-[(phenylmethoxy)methyl]-cyclopent-1-ene(**49**)[74] (Scheme 3). Unfortunately, only the target purines **51** and **52** were obtained because of the extremely facile intramolecular ring opening of the epoxide in compounds with pyrimidine bases (thymine and uracil).



56 **57** **58**

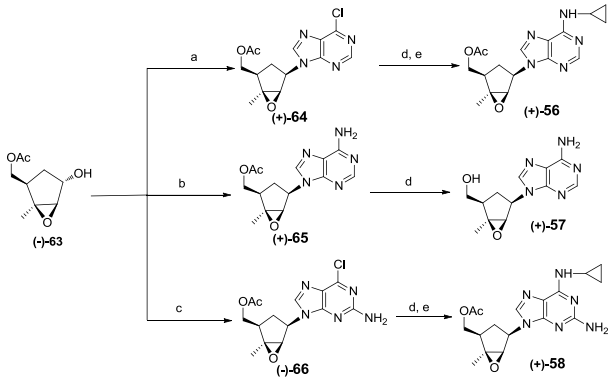
Figure 14

Furthermore, Aubin reported the chemoenzymatic synthesis of conformationally locked carbocyclic nucleosides with a β-oxirane ring fused onto the 2'-3' position of cyclopentane ring[75] (Figure 14).



Scheme 4. Reagents and Conditions: (a) *m*-CPBA, CH_2Cl_2, 86%; (b) Ph_3P, DIAD, AcOH, THF, 94%; (c) $LiAlH_4$, ether, 84%; (d) RML (*Rhysomucor meihei lipase*), vinyl acetate.

The hydroxyl-directed epoxidation of cyclopentene (-)-**59** with *m*-CPBA gave rise to β-epoxide (-)-**60**, which was then converted into (-)-**63** by a sequence of reactions involving Mitsunobu reaction, deprotection and acetylation (Scheme 4).



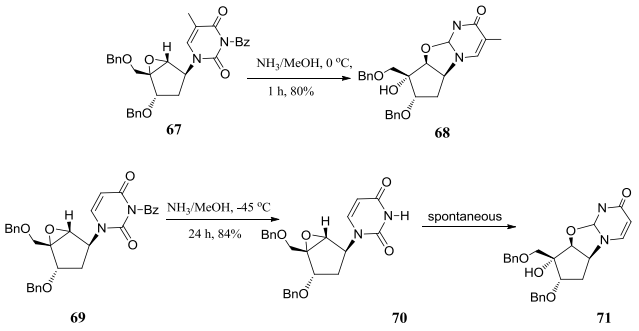
Scheme 5. Reagents and Conditions: (a) Ph_3P, DIAD, 6-chloropurine, THF, 78%; (b) Ph_3P, DIAD, adennine, THF, 63%; (c) Ph_3P, DIAD, 2-amino-6-chloropurine, THF; (d) 7M ammonina in MeOH; (e) cyclopropylamine-THF (1:5), 50 ^oC, 12 h.

With the desired β-epoxide (-)-**63** in hand, the synthesis of the target carbacyclic nucleosides **56-58** were depicted in Scheme 5.

1.4.2 Synthesis of Conformationally Locked Carbocyclic Nucleosides by Fusing a Thiirane Ring

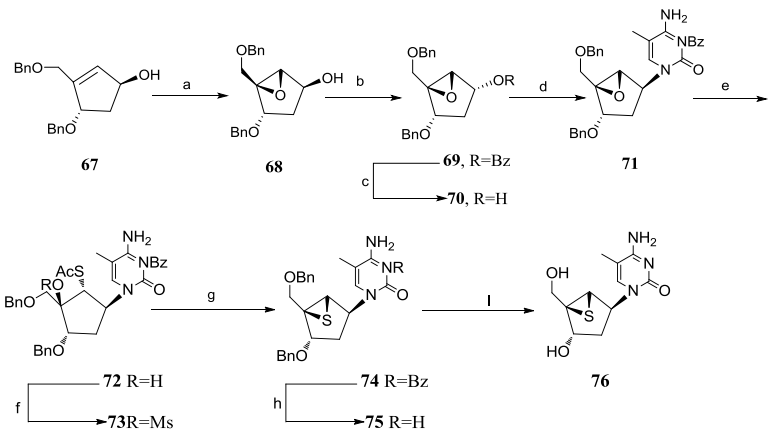
When Comin prepared 2'-deoxyneplanocin C analogues, they found that the analogues with pyrimidine bases (thymine and uracil) could not be obtained

successfully, because these epoxides would suffer ring opening when the epoxy group is adjacent to pyrimidine base[72] (Scheme 6).



Scheme 6

For the above reason, they tried to use a thiirane group to fix nucleoside conformation. Therefore Elhalem chose compound **76** as a molecular target.[76]



Scheme 7. Reagents and Conditions: (a) *m*-CPBA, CH_2Cl_2, rt, 3 h, 85%; (b) DEAD, PPh_3, $PhCO_2H$, toluene, rt, 28 h, 53%; (c) 7M NH_3 in MeOH, seal tube, 40 °C, 13 h, 90%; (d) DEAD, PPh_3, THF, ^{3}N-benzoyl thymine, -45 °C, 2 h, then rt 16 h, 60%; (e) $KSCOCH_3$, DMF, 60 °C, 2 h, 60%; (f) MsCl, 4-DMAP, Py, rt, 10 h, 78%. (g) $NaHCO_3$, EtOH/H_2O/THF, reflux, 7 h, 48%; (h) 7M NH_3 in MeOH, seal tube, 0 °C, 2 h, 100%; (i) 1.0M BCl_3, CH_2Cl_2, -78 °C, 2 h, 100%.

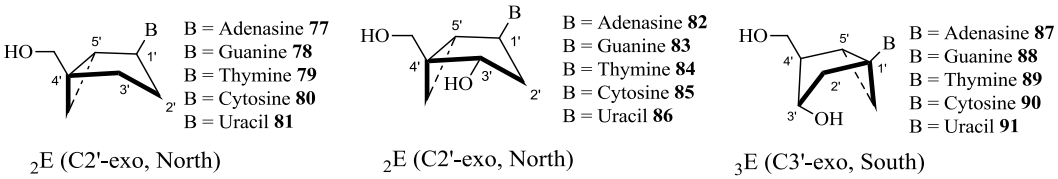
As shown in Scheme 7, the synthesis of target molecular **76** was completed by using (1*S*,4*S*)-4-phenylmethoxy-3-[(phenylmethoxy)methyl]-cyclopent-2-en-1-ol (**67**) as a chiral advanced synthetic intermediate, which can be synthesized according to

literature.[76]

With alkene **67** in hand, it was reacted with *m*-CPBA to yield β-epoxide **68** as a single isomer because of the presence of a β free hydroxyl group (Henbest rule).[77] The β-hydroxyl group was then inverted into α-hydroxyl group by Mitsunobu esterification followed by deprotection of ester, which was coupled with ^{3}*N*-benzoylthymine to give the desired *N*-alkylated product **71**. The reaction between the precursor of carbonucleoside and potassium thioacetate gave rise to the sulfur-contained derivative **72**, which was then activated with mesyl chloride to afford mesylate **73**. The final product **76** was obtained by S_N2 reaction and then deprotection.[78]

1.4.3 Synthesis of Conformationally Locked Carbocyclic Nucleosides by Fusing a Cyclopropane Ring

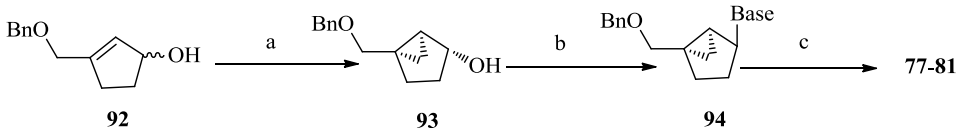
Since the novel structure of neplanocin C exhibits the typical Northern conformation and shows good biological activity, many carbocyclic analogs were synthesized successfully. Among these compounds, 1',5'-methano (**82-86**) and 4',5'-methano (**87-91**) are the most systematically and extensively studied (Figure 15)[79].



$_2$E (C2'-exo, North) $_2$E (C2'-exo, North) $_3$E (C3'-exo, South)

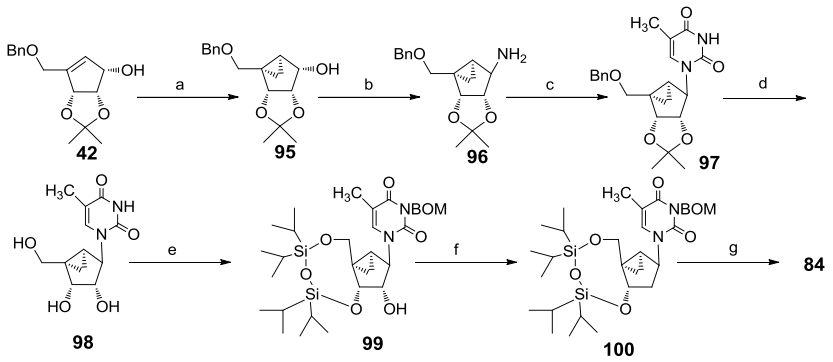
Figure 15

It was reported that carbobicyclic nucleoside **77** adopted a typical Northern conformation and exhibited moderate anti-HIV activity while its enantiomer showed no antiviral activity. The syntheses of nucleosides **77**-**81** began with cyclopentanol **92**. Treatment of cyclopentanol **92** with chloroiodomethane and samarium(II) afforded carbobicyclic **93**, which was then coupled with different bases and deprotected under catalytic hydrogenation conditions to give the desired products **77**-**81** (Scheme 8). [80-81]



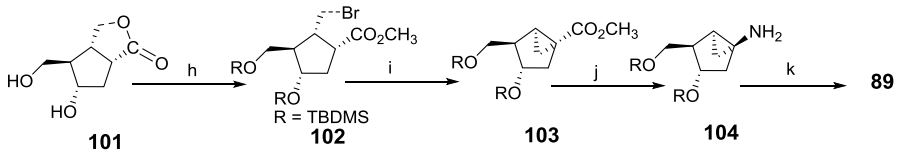
Scheme 8. Reagents and Conditions: (a) CH_2ICl, Sm, $HgCl_2$; (b) diad, PPh_3, Base; (c) Base derivation and deprotection.

After Rodriguez reported the synthesis of dideoxynucleosides **77**-**81**, Altamann also finished the synthesis of 4'5'-and 1'5'-methano-2'-deoxy carbocyclic thymidines **84** and **89** (Scheme 9 and 10).[82]



Scheme 9. Reagents and conditions: (a) Zn/Cu, CH_2I_2; (b) (i)TsCl, Et_3N, DMAP; (ii) NaN_3; (iii) H_2, Lindar's catalyst; (c) Base construction; (d) (i) HCl; (ii) H_2 Pd/C; (e) $TIPDSCl_2$, Im; (ii) BOM-Cl,DBU; (f) (i) $CH_3C_6H_4OC(S)Cl$, DMAP, Et_3N; (ii) Bu_3SnH, AIBN; (g) (i)TBAF; (ii) H_2, Pd/C; (iii) NaOMe.

As shown in Scheme 9, the ring fused compound **95** was obtained from allylic alcohol **42** by Simmons-Smith cyclopropanation. After the hydroxyl group in compound **95** was transformed into the corresponding amine **96**, the heterocyclic base was constructed under standard condition to afford nucleoside **97**. Finally, the target compound **84** was obtained by protection and followed by Barton-McCombie deoxygenation and subsequent deprotection.



Scheme 10. Reagents and conditions: (h) (i) TMSBr, ZnBr; (ii) *N*-methyl acetamide; (i) ^tBuOK, *t*-BuOH; (j) (i) KOH; (ii) DPPA, Et_3N; (iii) H_2, Pd/C; (k) Base construction and deprotection.

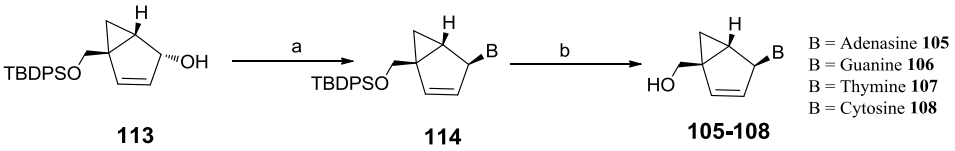
On the other hand, for the synthesis of **89** with the bicyclic lactone **101** as starting material, it was treated with TMSBr and *N*-TBDMS respectively to furnish compound **102** (Scheme 10). The three-membered ring was formed smoothly under basic conditions to give **103**, which was converted into target **89** via sequential deprotection,

Curtius rearrangement, deprotection and base construction.

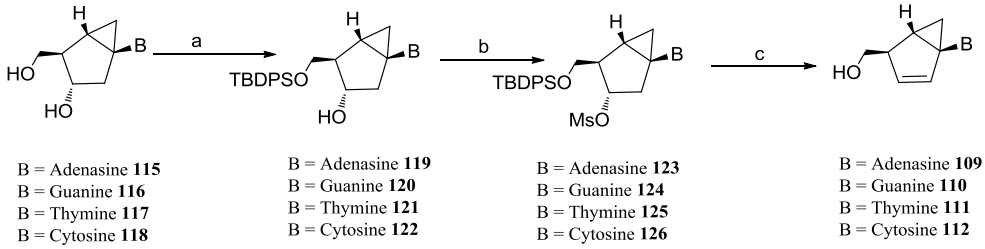
In the series of Northern 2'-deoxy nucleosides **77**-**81** prepared by Siddiqui and Marquez, the adenosine analogue **77** exhibited good antiviral activity against HCMV and EBV.[83] In order to explore the full potential of this class of nucleosides, four more nucleosides (**82**, **83**, **85** and **86**) built on the Northern bicyclo[3.1.0]hexane system were synthesized using a convergent approach.[84] Furthermore, a series of nucleosides (**87**, **88**, **90** and **91**) built on the Southern bicyclo[3.1.0]hexane pseudo-sugar ring were also synthesized using a convergent approach.[85]

Marquez and his coworkers found that chemically synthesized 5'-triphosphates of bicyclo[3,1,0] of North conformation[82] (**82**, **83**, **85** and **86**) were readily incorporated by HIV-1 RT and other polymerases. All these nucleosides were ineffective anti-HIV agents because of inefficient cellular phosphorylation. On the other hand, the conformational constraint in South conformation resulted in that these nucleosides (**87**, **88**, **90** and **91**) were not phosphorylated by cellular kinases, although they can be recognized excellently by the more tolerant, viral HSV-1 kinase.

Marquez V. E. and his coworkers incorporated the main plane feature of D4T (Figure 4) into these nucleosides of North conformation (**82**-**85**) and South conformation (**87**-**90**), producing a series of nucleosides (**105**-**112**) [86] as shown in Scheme 11 and Scheme 12.



Scheme 11 Reagents and conditions: (a) DIAD, PPh_3, Base, THF, 0 ^oC to rt; (b) $Et_3N.3HF$, MeCN, heat.



Scheme 12 Reagents and conditions: (a) TBDPSCl,Imidazole, DMF or TBDPSCl, DMAP and Pyridine; (b) MsCl, Pyridine; (c) (i) DBU, PhMe or DMF, Base; (ii) TBAF, THF.

In 2005, Herdewijn and coworkers reported the synthesis of L-deoxythreosyl phosphonate nucleosides (Figure 16). Nucleosides **127** and **128** were proved effective against HIV-1 and HIV-2 with EC_{50} values of 2.53 and 6.59 μM[87]. Therefore Marquez and his coworkers synthesized L-deoxythreosyl phosphonate nucleosides with bicyclo[3.1.0]hexane system **129**.[88] Moon and his coworkers also finished the syntheses of L-bicyclo[3.1.0]hexenyl carbanucleosides **130**-**132**.[89]

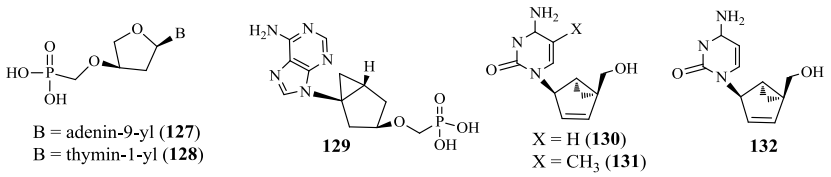


Figure 16

Other nucleosides with a bicyclo[3.1.0]hexane system were synthesized successfully as shown in Figure 17.[90-94]

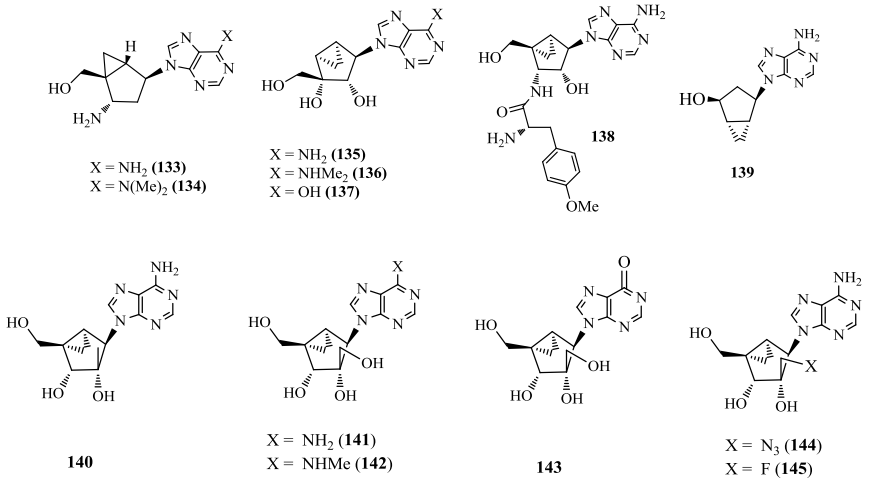
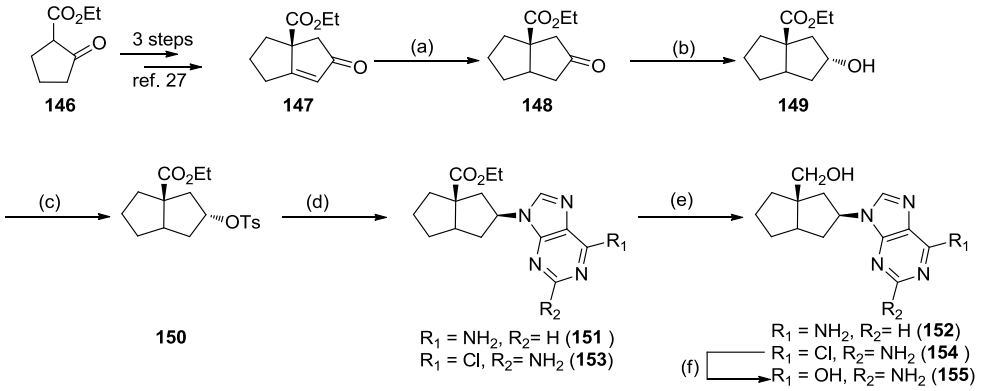


Figure 17

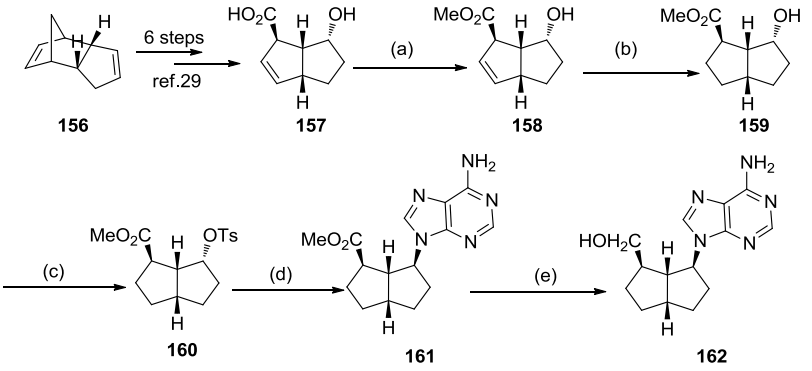
1.4.4 Synthesis of Conformationally Locked Carbocyclic Nucleosides by Fusing a Cyclopetane Ring

In the previous sections, the carbocyclic nucleosides can be locked by fusing a cyclopropane ring to improve their conformation. In addition to this method, carbocyclic nucleosides could also be locked by fusing a cyclopentane ring. In 1995, Chao and Nair[95] reported the synthesis of novel carbocyclic dideoxyonucleoside with a bicyclo[3.3.0]octane system. Syntheses of this class of nucleosides started from enone **147**, which was prepared from ethyl-2- oxocyclopentan-1-carboxylate (**146**) in three steps according to literature.[96] Tosylate **150** was then obtained from enone **147** via sequential hydrogenation, reduction and tosylation. Condensation of tosylate **150** with adenine in the presence of potassium carbonate and 18-crown-6 gave rise to adenosine analogue **151** or **153**, which was converted into dideoxyonucleosides **152** and **155**, respectively (Scheme 13).



Scheme 13. Reagents and conditions: (a) H_2, 5% Pd/C, 40 psi, EtOH, rt; (b) $NaBH_4$, $CeCl_3$, MeOH; (c) TsCl, Py; (d) Adenine, K_2CO_3, 18-crown-6, DMF; 2-amino-6-chloropurine, K_2CO_3, 18-crown-6, DMF; (e) DIBAL-H, THF; (f) 1M NaOH, reflux

In 1997, Chao and Nair [97] reported the second type of dideoxyonucleoside. Syntheses of these nucleosides started from hydroxyacid **157**, which can be prepared from dicyclopentadiene (**156**) in six steps according to literature.[98]

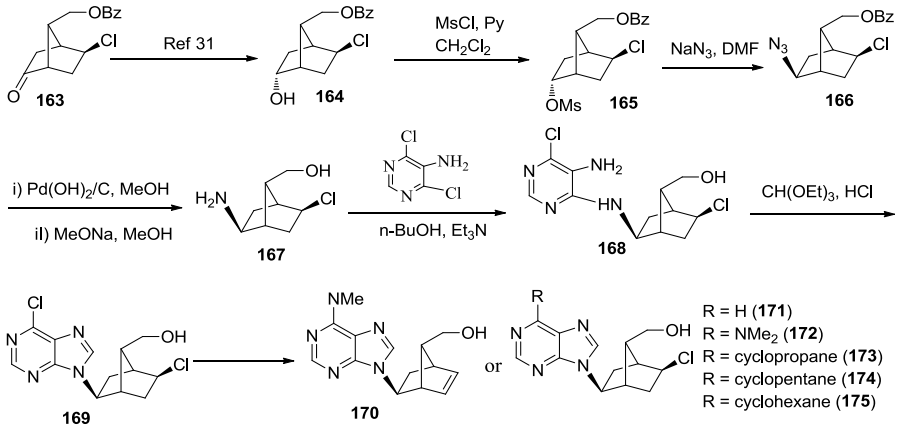


Scheme 14. Reagents and conditions: (a) CH_2N_2, MeOH; (b) H_2, 5% Pd/C, 40 psi, EtOH; (c) p-TsCl, Py; (d) Adenine, K_2CO_3, 18-crown-6, DMF; (e) DIBAL-H, THF.

Tosylate **160** was then obtained from hydroxyacid **157** via sequential esterification, hydrogenation and tosylation. Condensation of tosylate **160** with adenine afforded adenosine analogue **161**, which was then reduced to dideoxyonucleoside **162** (Scheme 14).

1.4.5 Synthesis of Carbocyclic Nucleosides with a Bicyclo[2.3.1]heptane System

In 2014, Tănase and his coworkers[99] reported the synthesis of new conformation locked nucleosides with a bicyclo[2.2.1]heptane system (Scheme 15).



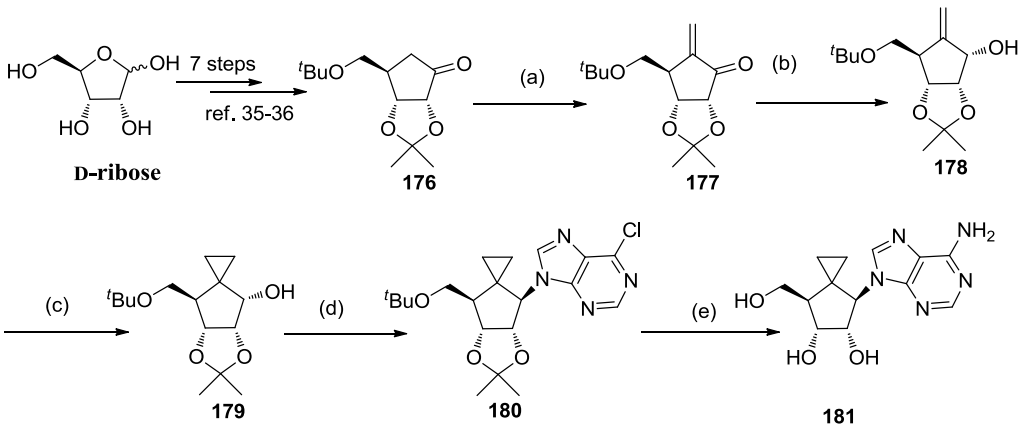
Scheme 15

Syntheses of these nucleosides started from the optically active intermediate **164**, which was obtained by reduction of ketone **163** with sodium borohydride.[100] The hydroxyl group in **164** was activated to mesylate **165**, which was converted into azide **166** by S_N2 reaction with sodium azide in DMF. Amine **167** was prepared from azide **166** by reduction and then deprotection. In order to obtain purine **169**, amine **167** was reacted with 4,6-dichloropyrimidine-5-amine and was then treated with triethylorthoformate in the presence of concentrated hydrochloric acid. Finally, a series of nucleosides **171-175** was obtained from purine **169** and nucleoside **170** was produced via a secondary dehydrochlorination reaction (Scheme 15).

1.4.6 Synthesis of Spirocarbicyclic Nucleosides

Since Kittaka and his coworkers[101] reported the conformation locked nucleosides with a spiro ring incorporated to furanose ring in 1999. Many research groups have reported this kind of nucleosides.[102] In 2011, Chu reported the synthesis of carbocyclic nucleoside **181** locked by a spiro ring with biological activity against heptatitis C virus.[103]

The synthesis of nucleoside started with cyclopentanone **176**, which was prepared from D-ribose in seven steps.[104-105] The reaction between Eshenmoser's salt[106] and enolate of the ketone **176** afforded the ammonium salt, which was subsequently subjected to Hoffmann elimination,[107] eventually installing an exocyclic methylene group at 6-position of **176**. Exocyclic enone **177** was then converted into alcohol **178** by Luche reduction in 90% yield. The key spiro-intermediate **179** was prepared from alcohol **178** by Simmons-Smith cyclopropanation.[108] With spiro-alcohol **179** in hand, it was coupled with 6-chloropurine by Mitsunobu reaction to yield purine **180**, which was converted into the target molecular **181** by amination and then deprotection (Scheme 16).



Scheme 16. Reagents and conditions: (a) (i) LDA, THF; (ii) Eschenmoser's salt; (iii) CH_3I, rt then 10% $NaHCO_3$; (b) $NaBH_4$, $CeCl_3$, MeOH; (c) Et_2Zn, CH_2I_2, Et_2O; (d) 6-chloropurine, PPh_3, DIAD, THF; (e) (i) NH_3, MeOH; (ii) TFA, H_2O.

In the same year, Oh and his coworkers[109] reported the synthesis of carbocyclic nucleoside **182** locked by a spiro ring. Li[110] also reported the synthesis of carbocyclic nucleoside **183** locked by a spiro ring (Figure 18).

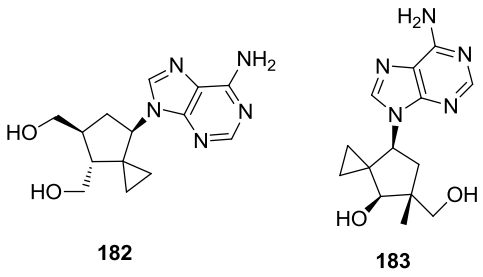


Figure 18

Chapter 2

Results and Discussion

2.1 Synthetic Targets and Retrosynthetic Analyses

As shown in the previous chapter, only carbobicyclic nucleosides with a bicyclo[3.1.0]hexane and a bicyclo[3.3.0]octane system were reported. Recently, carbobicyclic nucleosides with a bicyclo[4.3.0] nonane system were reported by our group.[111] However, the conformations of these nucleosides are C1'-*exo* conformations (Figure 19), which possess weak biological activity.

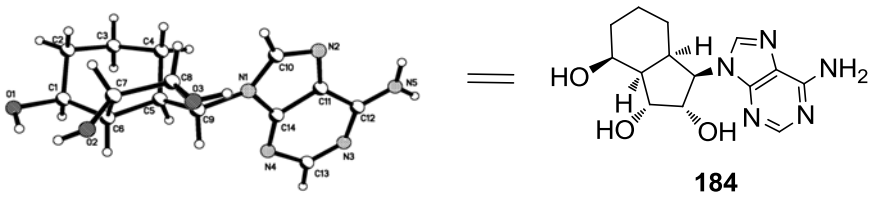


Figure 19

In order to obtain carbobicyclic nucleosides with a North-type conformation (C3'-*endo* or C2'-*exo*) or a South-type conformation (C2'-*endo* or C3'-*exo*), alkene-type adenosine analogue **185**, alkane-type adenosine analogue **186**, penta-hydroxy-type adenosine analogue **187** and tetrahydroxy-type adenosine analogues **188-191** containing a bicyclo[4.3.0]nonane system were synthesized continuously (Figure 20).

Retrosynthetic analysis of adenosine analogue **185** showed that it could be obtained from cycloadduct **194** which should be synthesized from D-ribose, using an Intramolecular Diels-Alder reaction as the key step. By modifications of the cyclohexene ring in intermediate **192**, the other kinds of adenosine analogues **186-191** with a bicyclo[4.3.0]nonane framework would be synthesized.

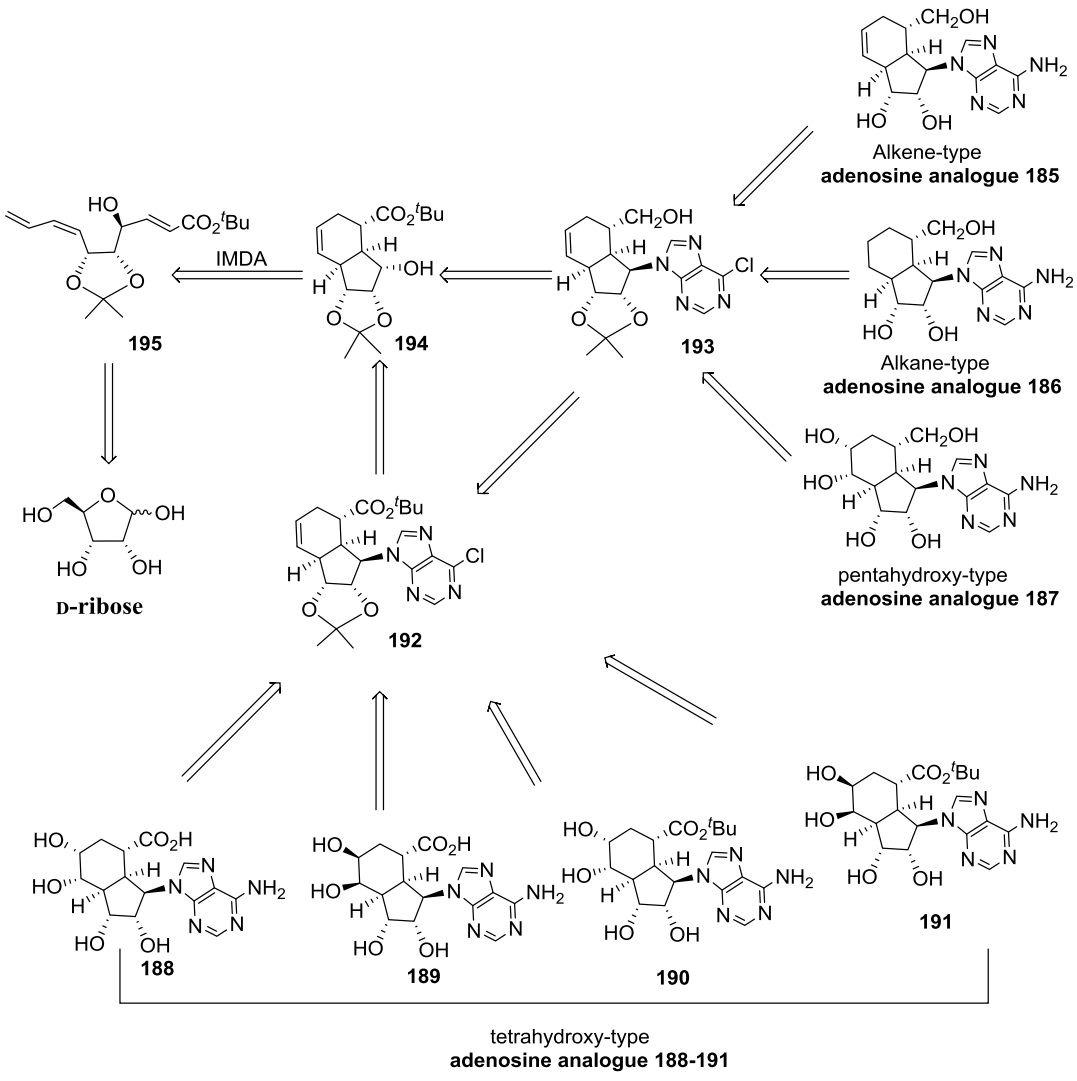
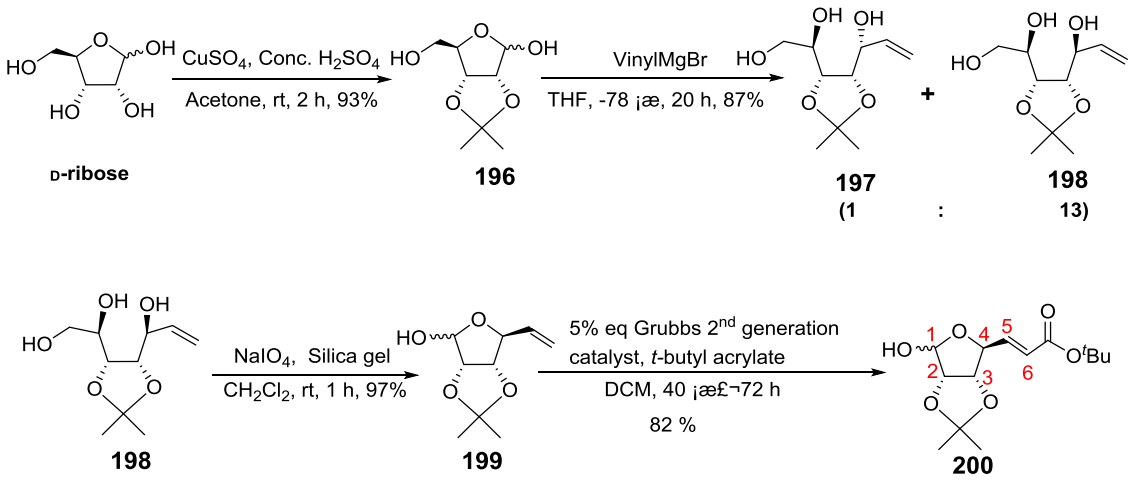


Figure 20

2.2 Construction of Bicyclic Carbocycle via Intramolecular Diels Alder (IMDA) Reaction

2.2.1 Synthesis of the Triene Precursor

Starting from D-ribose, the 2,3-hydroxyl groups were selectively protected by an isopropylidene group by reacting with acetone to furnish acetonide **196** in 93% yield. Then, the vinylation of acetonide **196** gave alkene **198** in a good yield (Scheme 17),[112] which was then subjected to glycol cleavage to give lactol **199** in an excellent yield.



Scheme 17

Lactol **199** reacted with *tert*-butyl acrylate in the presence of the second generation Grubbs catalyst to afford *trans*-ester **200** exclusively. The ^{1}H NMR spectrum of ester **200** ($J_{5,6}$ = 15.7 Hz) indicated a *trans* relationship, hence the thermodynamic product was favored. From the 2D-ROESY spectrum of lactol **200**,

there were ROE correlations between H^1 and H^2, H^1 and H^3 for the major product (Figure 21), indicating that H^1 was *syn* to H^2 and H^3 in the major lactol **200**. Therefore, their ratio of **200α/200β** was 8.3/1.

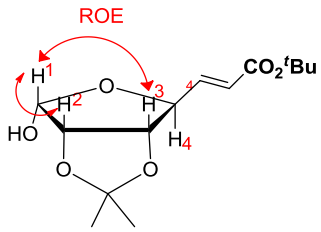
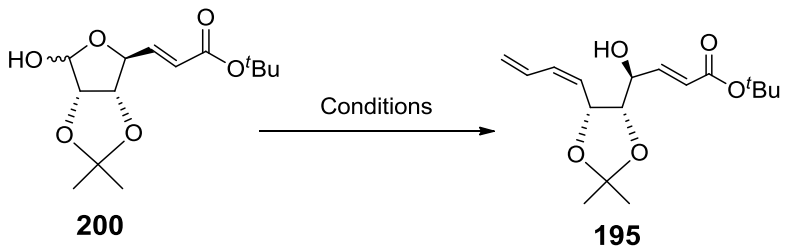


Figure 21

The triene **195** could be obtained from lactol **200** by Wittig Reaction under different conditions (Scheme 18) and the results are summarized in Table 1.



Scheme 18

Table 1. Wittig reaction of lactol **200** with allyltriphenylphosphonium bromide.

Entry	**Conditions**	Yield of **195**
1	**200**, LiHMDS, THF, 0 ℃ to rt, 1 h	No reaction
2	**200**, KO^{t}Bu, THF, 0 ℃ to rt, 1 h	No reaction
3	**200**, NaHMDS, THF, 0 ℃ to rt, 1 h	35%

4	**200**, KHMDS, THF, 0 ℃ to rt, 1 h	38%
5	**200**, NaH, THF, 0 ℃ to rt, 1 h	39%
6	**200**, NaH+DMSO, THF , 0 ℃ to rt, 1 h	59%, 64% (BORSM)
7	**200**, EtONa, THF, 0 ℃ to rt, 1 h	48%
8	**200**, MeONa, THF, 0 ℃ to rt, 1 h	40%
9	**200**, ^{t}BuOH+NaH, THF , 0 ℃ to rt, 1 h	20%
10	**200**, ^{i}PrOH+NaH, THF, 0 ℃ to rt, 1 h	24%

When using lithium LiHMDS (Entry 1) or KO^{t}Bu (Entry 2), no triene was obtained. Using KHMDS, NaHMDS, NaH, EtONa and MeONa, triene Z-**195** was obtained in low yield. Even using ^{i}PrONa and NaO^{t}Bu prepared *in situ*, the yield did not improve. When using NaH with DMSO as base, the yield of triene Z-**195** was increased to 59% (64%, BORSM), probably due to the reaction between DMSO and NaH, resulting in the formation of a dimsyl anion (sodium methylsulfinylmethanide), which was a milder base (Figure 22). Increasing the amount of DMSO from 3 eq to 42 eq, the yield of Z-**195** increased to 64% from 35%, because all the NaH can be converted into sodium methylsulfinylmethanide.

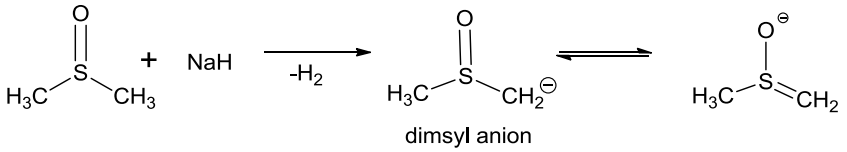
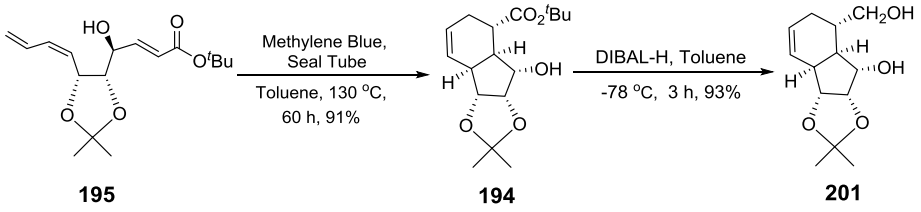


Figure 22

For this Wittig reaction, triene **195** was only obtained in a fair yield, probably due to the existence of the α,β-unsaturated carboxylic ester group in the structure of ester

200, resulting in the formation of Michael addition products.

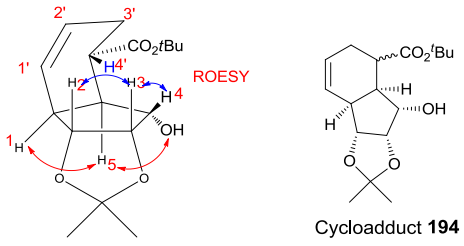
2.2.2 Synthesis of the Bicyclo[4.3.0]nonane



195 **194** **201**

Scheme 19

With triene Z-**195** in hand, an intramolecular Diel-Alder reaction was carried out in high dilution to afford cycloadduct **194** in an excellent yield (Scheme 19). In order to confirm its stereochemistry, 2D-ROESY experiment were carried out. From the 2D-ROESY NMR spectrum of cycloadduct **194** (Figure 23), there were ROE correlations between H^2 and H^3, H^3 and H^4, showing that H^2, H^3 and H^4 were *syn* to each other in β face of the cyclopentane ring. The ROE correlations between OH and H^5, H^5 and H^1, indicated that OH, H^1 and H^5 were *syn* to each other and were located in α face of the cyclopentane ring. However, the stereochemistry of carboxylic ester could not be confirmed, because we did not find the correlations between $H^{4'}$ and H^4, or $H^{4'}$ and H^3, or $H^{4'}$ and H^2.



Cycloadduct **194**

Figure 23

In order to confirm further its absolute stereochemistry, cycloadduct **194** was reduced to crystalline primary alcohol **201**. The X-ray crystallography for primary alcohol **201** was performed. Its absolute stereochemistry is shown in Figure 24.

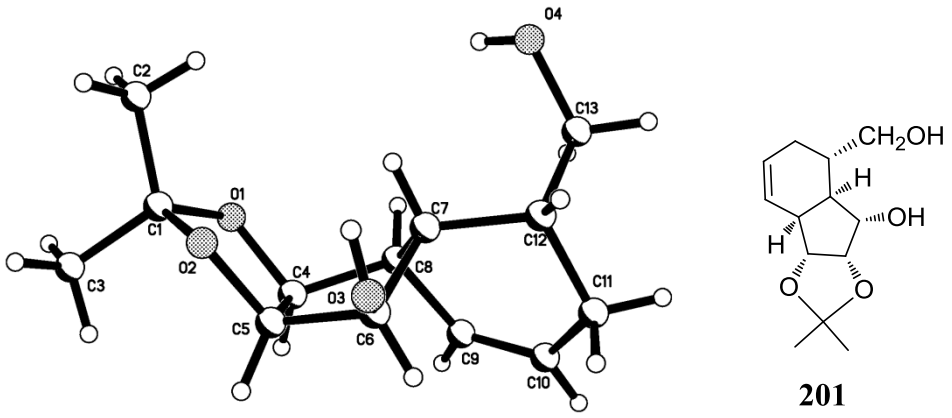
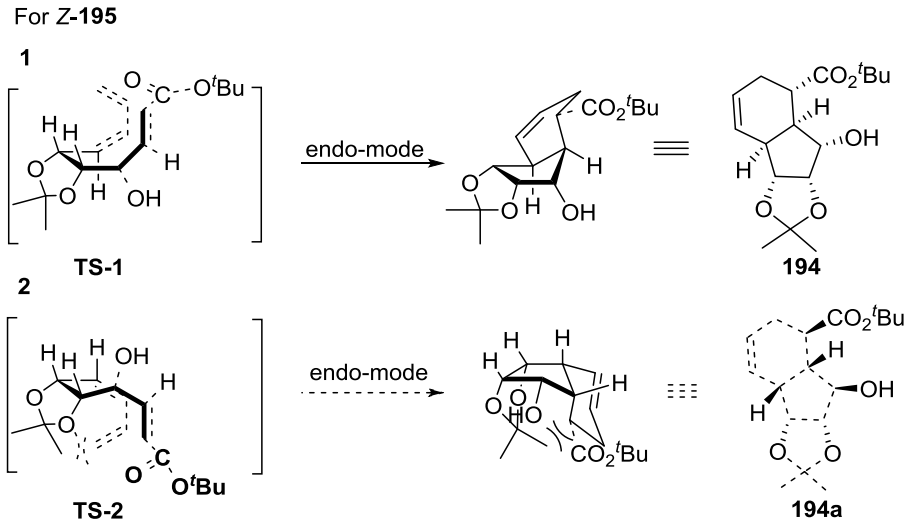


Figure 24

The high stereoselectivity of the cycloaddition giving **194** might be explained by considering transition states of the cyclization as shown in Figure 25.



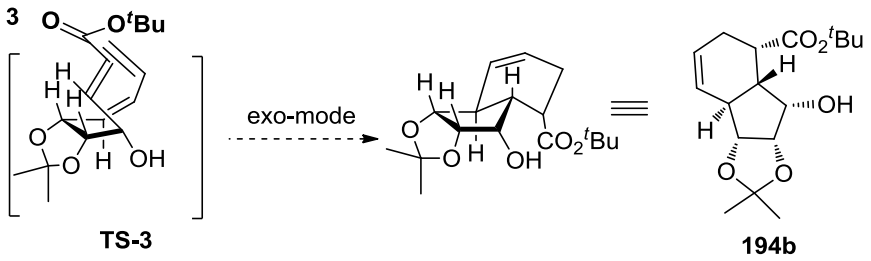


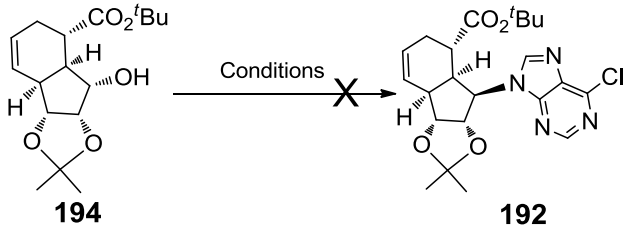
Figure 25

As shown in Figure 25, there are two possible transition states TS-1 and TS-2 for *endo* mode. TS-1 was favored because of the steric and secondary orbital effects, which resulted in the formation of cycloadduct **194**. However, for TS-2, there was steric repulsion between the isopropylidene, the newly formed six member ring and the *tert*-butyl ester, thus disfavoring the formation of cycloadduct **194a**. In the *exo* mode of cycloaddition, TS-3 is an unfavorable because it is highly.

2.3 Synthesis of the Target Nucleosides

2.3.1 Synthesis of the Purine by Coupling Reaction

With the cycloadduct **194** in hand, its direct coupling with the nucleobase with it via Mitsunobu reaction was carried out (Scheme 20) and the results are summarized in Table 2.



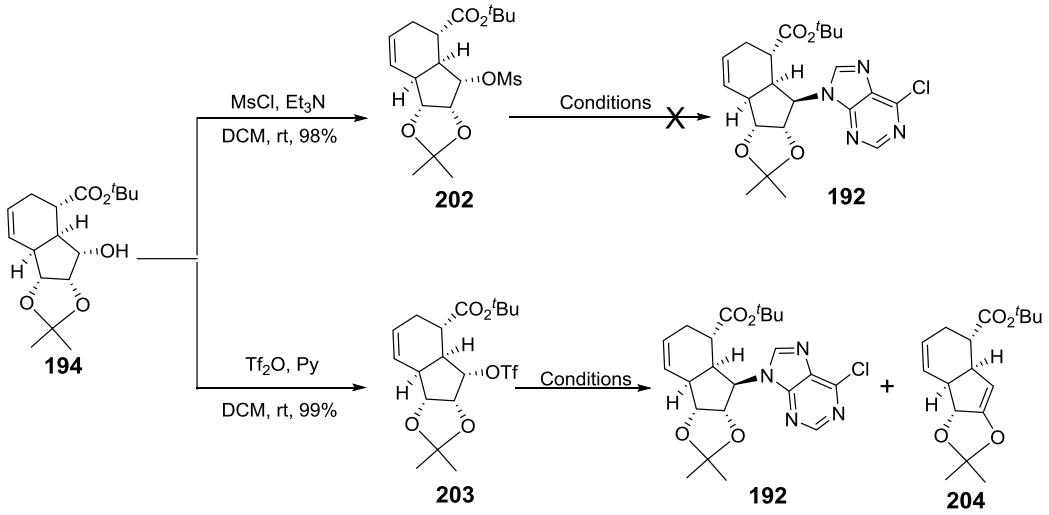
Scheme 20

Table 2. Mitsunobu reaction of cycloadduct **194** with 6-chloropurine

Entry	Conditions	Results
1	DIAD, PPh_3, 6-chloropurine, THF, rt, 24 h	No reaction
2	(i) DIAD, PPh_3, 1 h (ii) 6-chloropurine , rt, 24 h	No reaction
3	DEAD, PPh_3, 6-chloropurine, THF, rt, 24 h	No reaction
4	(i) DEAD, PPh_3, 1 h (ii) 6-chloropurine, rt, 24 h	No reaction
5	DIAD, PBu_3, 6-chloropurine, THF, rt, 24 h	Complex
6	(i) DIAD, PBu_3, 1 h (ii) 6-chloropurine, rt, 24 h	Complex
7	DEAD, PBu_3, 6-chloropurine, THF, rt, 24 h	Complex
8	(i) DEAD, PBu_3, 1 h (ii) 6-chloropurine, rt, 24 h	Complex
9	$PhI(OAc)_2$, DEAD, PPh_3, 6-chloropurine, THF, rt, 2 d	No reaction
10	$PhI(OAc)_2$, DIAD, PPh_3, 6-chloropurine, THF, rt, 2 d	No reaction

Treatment of cycloadduct **194** with the combination of DEAD and PPh_3, or DIAD and PPh_3, no reaction was observed (Entry 1-4). Even when the reaction mixture

was heated to reflux, there were no changes. Presumably, the complex formed by reacting DIAD or DEAD with PPh_3 was so bulky that its approach to the hydroxyl group was difficult. Form Entry 5-8, when using the combination of DIAD and PBu_3, or DEAD and PBu_3, no desired product was obtained although the starting material was completely consumed. Maybe the intermediate formed was quite stable so that nucleophilic attack became difficult. We further investigated on the Mitsunobu reaction according to the catalytic method[113] (Entry 9-10). When DEAD was used as the catalyst, there was no reaction. Replacement DEAD with DIAD, the result was the same.



Scheme 21

As the Mitsunobu reaction failed to generate purine **192**, cycloadduct **194** was firstly activated by the reaction with mesyl chloride (MsCl), producing mesylate **202**, which was then reacted with 6-chloropurine (Scheme 21). However, no reaction was observed, which was checked by TLC (Table 3).

Table 3. The reaction of mesylate **202** with 6-chloropurine

Entry	**Condition**	**Results**
1	K_2CO_3, 6-Chloropurine, 18-Crown-6, DMF, rt to 100 ^oC	No reaction
2	Cs_2CO_3, 6-Chloropurine, 18-Crown-6, DMF, rt to 100 ^oC	No reaction
3	NaH, 6-Chloropurine, 18-Crown-6, THF，80 to 100 ^oC	No reaction

Since no desired purine **192** was obtained by reacting mesylate **202** with 6-chloropurine, maybe the reactivity of mesylate **202** was not also strong enough. Therefore cycloadduct **194** was converted into a more reactive compound, the triflate **203**, and examined its displacement with 6-chloropurine. The results are summarized in Table 4.

Table 4. The reaction of triflate **203** with 6-chloropurine

Entry	Conditions	Results
1	K_2CO_3, 6-Chloropurine, 18-Crown-6, DMF, rt to 100 ℃	**192**: 13% **204**: 32%
2	Cs_2CO_3, 6-Chloropurine, 18-Crown-6, DMF, rt to 100 ℃	**192**: 17% **204**: 46%
3	NaH, 6-Chloropurine, 18-Crown-6, THF，80 to 100 ℃	**192**: 14% **204**: 40%
4	K_2CO_3, 6-Chloropurine, 18-Crown-6, DMF, rt to 100 ℃	**192**: 15% **204**: 37%

5	NaH, 6-Chloropurine, 18-Crown-6, THF, 80 to 100 ℃	**192**: 14% **204**: 43%

As shown in Table 4, when using K_2CO_3 as base (Entry 1), the desired purine **192** was obtained. Besides, we also obtained elimination product diene **204** as the major product. For this reaction, deprotonation of 6-chloropurine by K_2CO_3 produced 6-chloropurine anion firstly. Since crown ether can capture K^+, the addition of 18-Crown-6 can enhance the nucleophilicity of the 6-chloropurine anion (Figure 26). The 6-chloropurine anion was then used as a nucleophile to attack the triflate **203**, affording the desired purine **192** in 13% yield (Entry 1).

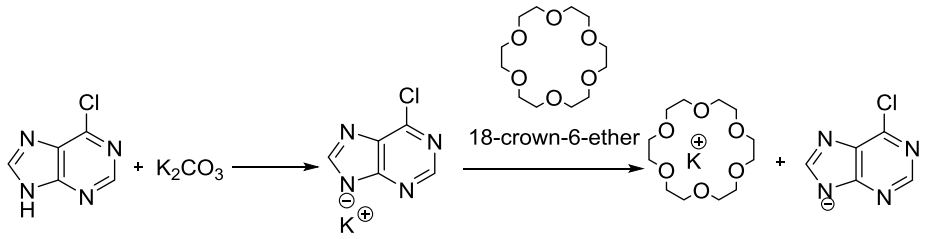


Figure 26

The poor yield of purine **192** can be explained in Figure **27**. When the bulky 6-chloropurine anion as nucleophile attacked the C1, the steric hindrance from the six-membered ring and *tert*-butyl carboxylic ester in β face of the cyclopentane ring resulted in the low yield of purine **192**. Furthermore 6-chloropurine anion can also be a base, which led to the formation of diene **204** by E2 reaction. Since 6-chloropurine anion can be either a nucleophile or base, and the competition between S_N2 and E2 resulted in the formation of elimination product, diene **204** as the major

product.

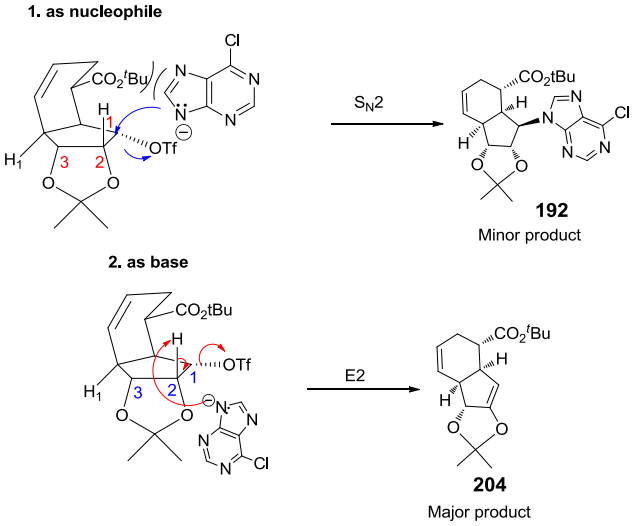


Figure 27

Furthermore, there is an equilibrium between two resonance structures for 6-chloropurine anion between A and B (Figure 28), resonance form B can also be used as a nucleophile, which is the other reason for the low yield of purine **192**.

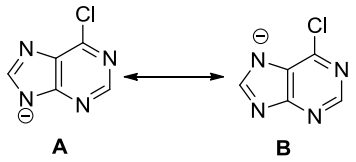
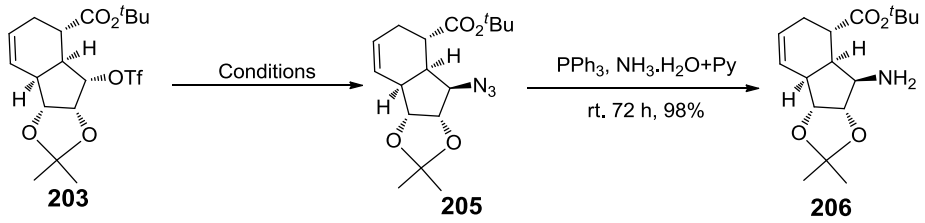


Figure 28

In order to optimize the conditions, different bases were investigated. However, both Cs_2CO_3 and NaH gave disappointing results.

2.3.2 Synthesis of the Purine via Linear Methods

Although the purine **192** was obtained by convergent method successfully, the yield was so poor that we had to synthesize it by the linear method.



Scheme 22

Firstly, azide **205** was obtained by reacting triflate **203** with an azide salt (Scheme 22). The results are summarized in Table 5.

Treatment of triflate **203** with NaN_3 in DMF at 50 ^oC afforded azide **205** in 68% (Entry 1). From the IR spectra, there was a peak at 2111 cm^{-1} which corresponded to the asymmetric stretching vibration of the azide group and suggested the azide **205** was synthesized successfully. Due to its poor yield, we had to optimize the reaction conditions. The displacement in DMSO, caused the yield to increase to 75% and the amount of diene **204** was also increased (Entry **2**). When the reaction was carried out at room temperature and the yield was improved (Entry **1** and Entry **6**). By the addition of 3Å MS, the yield of azide **205** was improved further (Entry **5** and Entry **9**). For both LiN_3/DMF and NaN_3/DMSO system, we found that when the 6 reactions were carried out at room temperature in the longer reaction time, the better yields were obtained.

With azide **205** in hand, it was reduced to its corresponding amine **206** by triphenyl phosphine in 98% yield. It should be noted that the reaction mixture must be filtered first by a thin pad of silica gel so that the product would not be trapped by

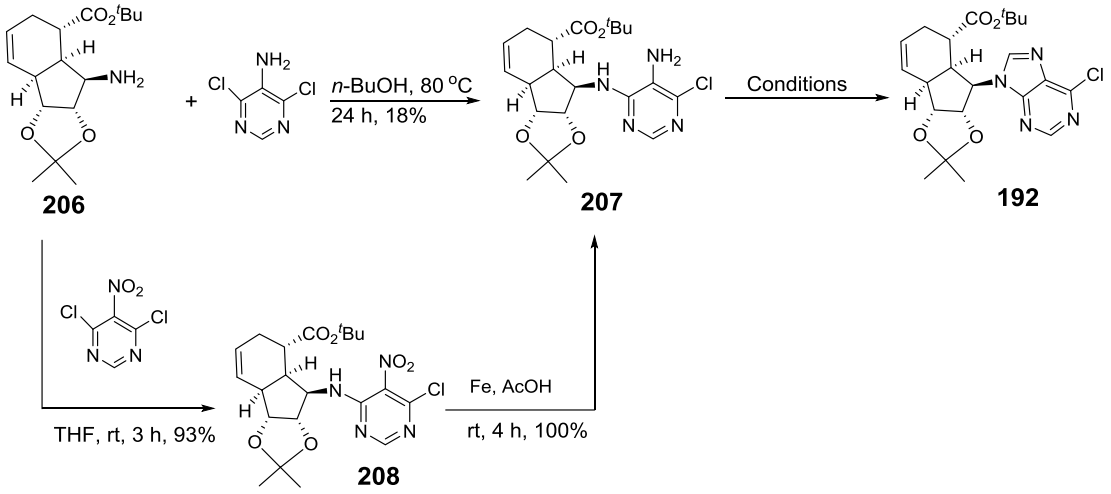
the solid residue after the completion of this reaction, or it would result in a lower yield of amine **206** (in Scheme 22).

Table 5. The reaction of triflate **203** with azide salts.

Entry	Condition	Results(205)
1	NaN_3, DMF, 50 ^oC, 24 h	68% (diene **204**, 10%)
2	NaN_3, DMSO, 50 ^oC, 24 h	75% (diene **204**, 17%)
3	NaN_3, DMF, 3Å MS, rt, 24 h	82% (diene **204**, 7%)
4	NaN_3, DMSO, rt, 36 h	85% (diene **204**, 13%)
5	NaN_3, DMSO, 3Å MS, rt, 36 h	89% (diene **204**, 8%)
6	LiN_3, DMSO, 3Å MS, rt, 120 h	47% (diene **204**, 11%)
7	LiN_3, DMF, 50 ^oC, rt, 24 h	77% (diene **204**, 9%)
8	LiN_3, DMF, rt, 120 h	87% (diene **204**, 6%)
9	LiN_3, DMF, 3Å MS, rt, 120 h	95% (diene **204**, 4%)

The amine **206** was then converted into pyrimidine **207** by reacting with 5-amino-4,6-dichloropyrimidine in *n*-BuOH. However, the yield was poor because the electrophilicity of 5-amino-4,6-dichloropyrimidine was relatively low. In order to improve its reactivity, we used a stronger electrophile, 5-nitro-4,6-dichloro-pyrimidine and then pyrimidine **208** was prepared in 93% yield (Scheme 23). Based on several trials, this reaction should be carried out at room temperature, because the pyrimidine **208** might decompose under the heating conditions. Reduction of the nitro group using iron in acetic acid, afforded pyrimidine **207** quantitatively. In the ^1H NMR, the proton in the pyrimidine ring of the pyrimidine **208** appeared at 8.44 ppm, 8.03 ppm in the pyrimidine **207**. The apparently different electron effects

between the nitro group (electron-withdrawing group) and the amine group (an electron- donating group) in the pyrimidine ring resulted in the distinct change in chemical shift for this proton in the pyrimidine ring.



Scheme 23

The purine **192** was prepared from pyrimidine **207** by the conditions shown in Table 6. When using (±)camphorsulfonic acid ((±)CSA) as catalyst, a mixture of the intermediate and purine **192** was obtained, which could not be separated (Entry 1) probably due to insufficient amount of catalyst used. Therefore, we increased the amount of (±)CSA. However, many intermediates were present in the mixture. We suspected that the acidity was not strong enough, thus we tried concentrated sulfuric acid as catalyst. To our disappointment, the result did not improve. In order to obtain purine **192**, we continued to try concentrated hydrochloric acid and obtained the desired pruine **192** in 93%. However, the reaction was not reproducible. When we used TFA, purine **192** was obtained in an excellent yield

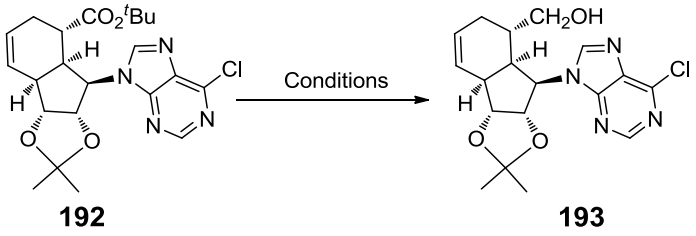
finally and the reaction was reproducible.

Table 6. Reaction of pyrimidine **207** with triethyl orthoformate

Entry	Condition	Results (192)
1	(±)CSA, $CH(OEt)_3$, rt, 7 d	Mixture(not separble)
2	Conc.H_2SO_4, $CH(OEt)_3$, rt, 7 d	Mixture(not separble)
3	Conc.HCl, $CH(OEt)_3$, rt, 6 d	93%
4	(i) TFA, $CH(OEt)_3$, rt, 60 h (ii) 60 ^oC 12 h	92%

2.3.3 Synthesis of the Alkene-type Target Nucleosides

With purine **192** in hand, the reduction of it was carried out to give primary alcohol **193** (Scheme 24), the results are summarized in Table **7**.



192 **193**

Scheme 24

Treatment of purine **192** with lithium borohydride in toluene at -78 ^oC, no reaction was observed from TLC (Entry 1). We reckoned that the reaction temperature was so low that the reaction did not proceed. When the reaction mixture was warmed to room temperature from -78 ^oC, there was no any change in TLC and

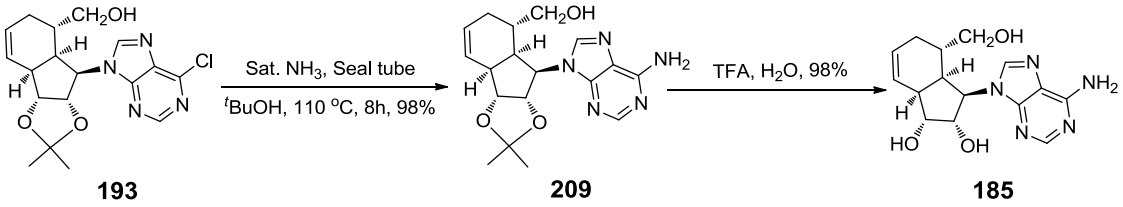
the starting material was recovered (Entry 2). Since $LiBH_4$ was not strong enough, we tried $LiAlH_4$, a stronger reducing reagent. Unfortunately, the starting material decomposed because of the high reactivity of $LiAlH_4$ (Entry 3). Therefore, we had to choose a milder one, diisobutylaluminium hydride (DIBAL-H), to reduce purine **192**. To our delight, the desired primary alcohol **193** was obtained in 72%. Besides, the intermediate aldehyde was also obtained, which suggested the reducing reagent was not added enough (Entry 4). When increasing the amount of DIBAL-H to 2.5 eq, the amount of aldehyde was decreased but the yield of primary alcohol **193** was also decreased. When increasing the amount of DIBAL-H to 3.0 eq, no aldehyde was observed and the yield of our product was decreased to 58%.

Table 7. Reduction of purine **192** to alcohol **193**

Entry	Condition	Results (193)
1	$LiBH_4$, Toluene, -78 ^oC, 3 h	No reaction
2	$LiBH_4$, Toluene, 0 ^oC, 16 h	No reaction
3	$LiAlH_4$, Toluene, 0 ^oC, 16 h	Decomposed
4	2.1 eq DIBAL-H, Toluene, -78 ^oC, 3 h	72%
5	2.5 eq DIBAL-H, DCM, -78 ^oC to rt, 8 h	69%
6	3.0 eq DIBAL-H, Toluene, -78 ^oC to rt, 8 h	58%
7	(i) 2.0 eq DIBAL-H, Toluene, -78 ^oC to rt, 8 h (ii) 0.5 eq $NaBH_4$, MeOH, rt, 10 min	97%

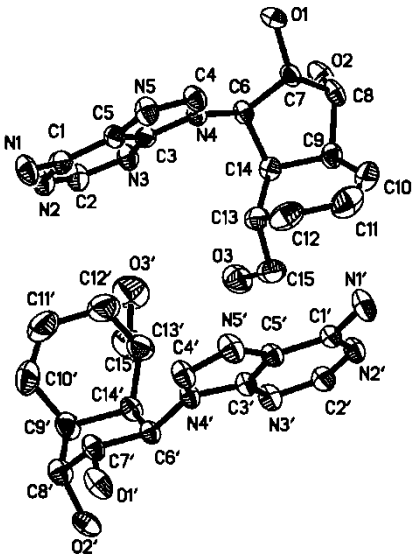
The problem was that the intermediate aldehyde was not be converted into alcohol **193** thoroughly when the amount of DIBAL-H was not enough. However,

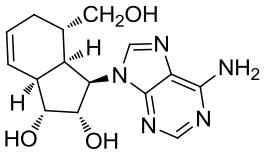
when the amount of DIBAL-H was increased, the intermediate aldehyde could be consumed but the yield of alcohol **193** was also decreased. Finally, we adopted a different approach to solve this problem. Firstly, 2 eq DIBAL-H was added to the solution of purine **192**, and then methanol and sodium borohydride were added to the above reaction mixture at room temperature after all the starting material was transformed into the intermediate or alcohol **193** (checked by TLC). Fortunately, all the aldehyde was converted into alcohol **193** effectively and the yield of our product increased to 97%.



Scheme 25

The chloride in the alcohol **193** was then replaced by an amino group using saturated NH_3 in *t*-BuOH and purine **209** was obtained in an excellent yield. Deprotection of purine **209** with aq. TFA give the alkene-type adenosine analogue **185** in 98% yield (Scheme 25). The absolute stereochemistry of our target, alkene-type adenosine analogue **185** was confirmed by X-ray crystallography (Figure 29).





Alkene-type adenosine analogue **185**

Figure 29

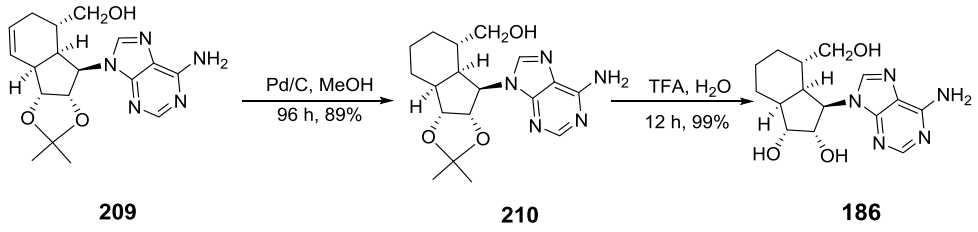
As shown in Figure 29, we clearly observe that the conformation of alkene-type adenosine analogue **185** is C3'-*exo*, which belongs to the South-type conformation and is more similar to the conformation of conventional nucleosides.

2.3.4 Synthesis of the Alkane-type Nucleosides

In the previous section, we synthesized alkene-type adenosine analogue **185** successfully, which possesses the South-type conformation. As the cyclohexene ring locked the conformation of the carbocyclic adenosine analogue successfully, this intrigued us to wonder whether its conformation would be changed or not when the cyclohexene ring was hydrogenated to a cyclohexane ring.

Based on the above idea, the C=C bond in alcohol **193** was hydrogenated with a catalytic amount of 10% Pd-on-charcoal. However, a mixture was obtained, which

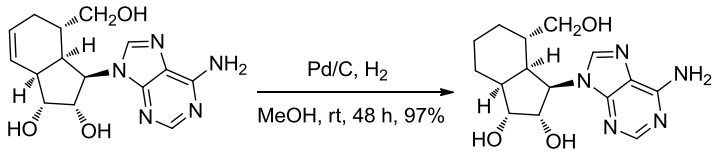
could not be separated because the chloride atom in the ring of purine was prone to be hydrogenolyized.



209 **210** **186**

Scheme 26

Therefore, the hydrogenation of C=C bond in purine **209** was carried out at room temperature and the purine **210** was obtained in 89% yield. The structure of **210** was verified by ^{1}H NMR and ^{13}C DEPT experiments. In the ^{1}H NMR spectrum of purine **210**, two alkene protons in 5.67 and 5.41 ppm disappeared and four alkane protons appeared between 1.50-1.80 ppm. Besides, two more CH_2 peaks appeared in the DEPT135 spectrum of purine **210**. Then deprotection of the isopropylidene group with aq. TFA in H_2O afforded alkane-type adenosine analogue **186** in 99% yield (Scheme 26).



185 **186**

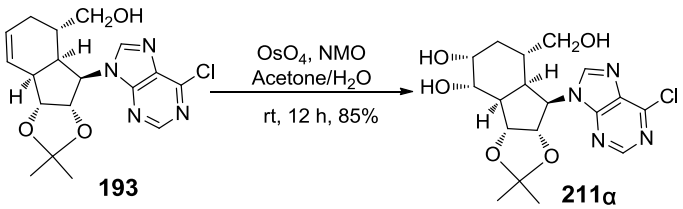
Scheme 27

Because of the long reaction time for purine **209** during hydrogenation, we also tried to hydrogenate the free alkene-type adenosine analogue directly (Scheme 27) and the alkane-type adenosine analogue **186** was obtained in 99% at room

temperature after 48 h.

2.3.5 Synthesis of Pentahydroxy-type Nucleosides

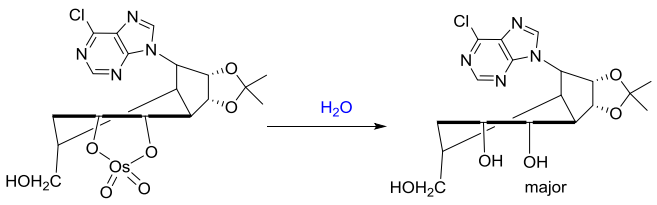
In the previous section, we synthesized the alkene-type adenosine analogue **185** and the alkane-type adenosine analogue **186** successfully. We also wondered if the introduction of two hydroxyl groups could lead to any influence on its conformation.



Scheme 28

Based on the above thought, dihydroxylation of the alcohol **193** with osmium tetraoxide produced triol **211** (Scheme 28), which were separable isomers and their ratio was 20/1. The major one was **211α**, whose absolute stereochemistry could be confirmed by X-ray crystallography of its final product, adenosine analogue **187** at the latter stage. Its formation is rationalised in Figure 30.

Routine 1



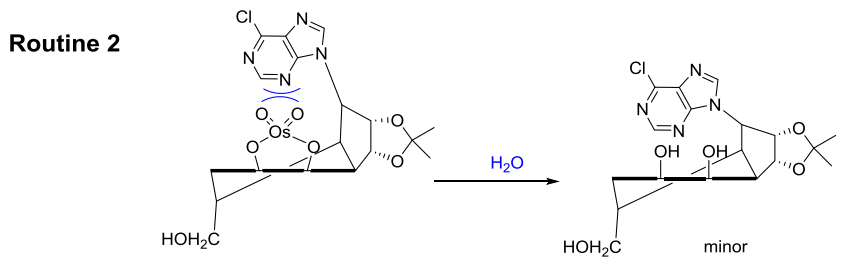
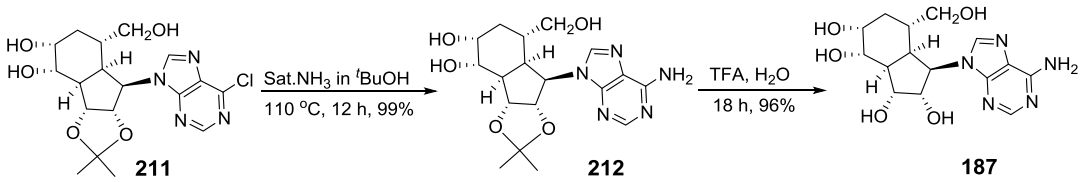


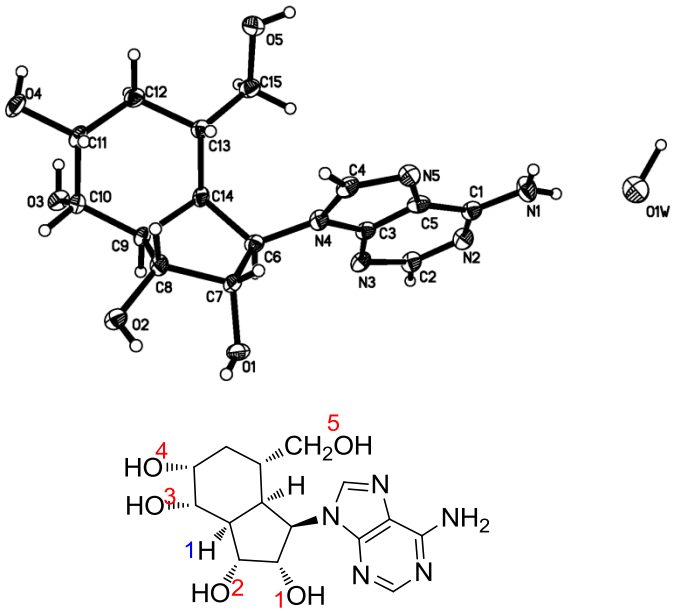
Figure 30

The first step for the dihydroxylation was that the osmium tetraoxide cycloadded to the C=C bond. When osmium tetraoxide cycloadded to the C=C under the plane (routine 1), the major product triol **211α** was obtained. When the tetraoxide cycloadded to the C=C above the plane, steric repulsion from the nucleobase and five-member ring in β face resulted in the formation of product triol **211β** in minority.



Scheme 29

Then, the chloride group in the alcohol **211** was replaced by an amino group using saturated NH_3 in *t*-BuOH and purine **212** was obtained in an excellent yield. Finally, deprotection of the isopropylidene group by aq. TFA furnished alkane-type adenosine analogue **187** in 96% yield (Scheme 29). The absolute stereochemistry of our target, the pentahydroxy-type adenosine analogue **187** was confirmed by X-ray crystallography (Figure 31).



pentahydroxy-type adenosine analogue **187**

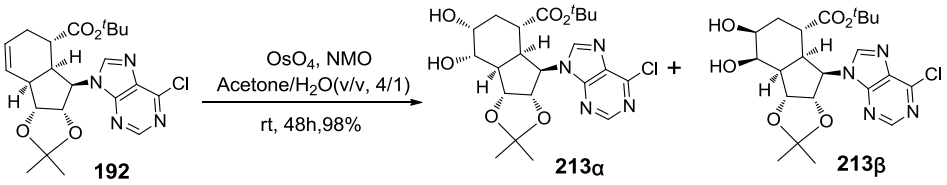
Figure 31

As shown in Figure 31, 3-OH can be seen as an axial hydroxyl group and 4-OH an equatorial hydroxyl group. They are *syn* to each other and are on the same side with H^1. The conformation of pentahydroxy-type adenosine analogue **187** is C4'-*exo*, which belongs to neither South-type conformation nor North-type conformation. C4'-*exo* is a novel conformation which has not been reported in carbacyclic nucleosides up to now. For natural nucleosides, examples were rarely reported.

2.3.6 Synthesis of Target Nucleosides Bearing Carboxylic Group

In the previous sections, we had synthesized three kinds of adenosine analogues

successfully, the alkene-type (C3'-*exo* South-type conformation), alkane-type and pentahydroxy-type (C4'-*exo*, novel conformation) adenosine analogues. Since two hydroxyl groups were introduced to the cyclohexane ring, resulting in great influence on their conformations, which intrigued us to wonder whether there would be distinct changes for their conformations or not for adenosine analogues bearing a carboxylic group.



Scheme 13

On the basis of the above idea, the dihydroxylation of purine **192** with osmium tetraoxide afforded diol **213** (Scheme 13), which was separable isomers and the ratio was 1.8/1. The minor one was **213β**, which was confirmed by 2D-NOESY experiments (Figure 32).

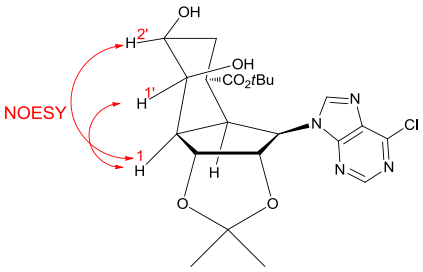


Figure 32

From the 2D-NOESY NMR spectrum of diol **213β** (a minor product), there were NOE correlations between H^1 and $H^{1'}$, H^1 and $H^{2'}$, showing that these two hydroxyl

group are located in β face of cyclohexane ring.

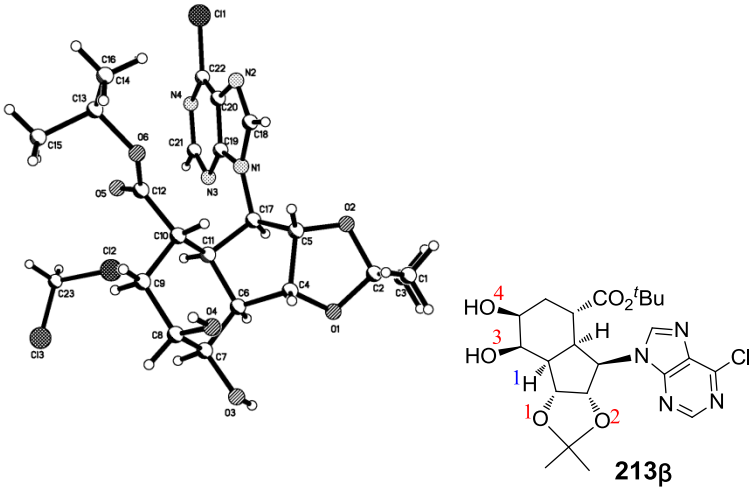


Figure 33

The absolute stereochemistry of diol **213β** was further corroborated by X-ray crystallography. As shown in Figure 33, we clearly observe that 3-OH is an equatorial hydroxyl group and 4-OH is an axial hydroxyl group. They are *syn* to each other and are on opposite side with H^1. The conformation of adenosine analogue **213β** bearing carboxylate group is C5'-*endo*, which belongs to neither the South-type conformation, nor the North-type conformation. C5'-*endo* is also a novel conformation, which has not been reported in the literature. Even in natural nucleosides, the example of C5'-*endo* conformation is also very rare.

When the bulky carboxylate was retained in the cyclohexane ring, we found that the ratio of β/α was increased to 1/1.8 (diol **213**) from 1/20 (triol **211**). It can be explained by the directing group effects from the bulky *tert*-butyl carboxylate group

in Figure 34.

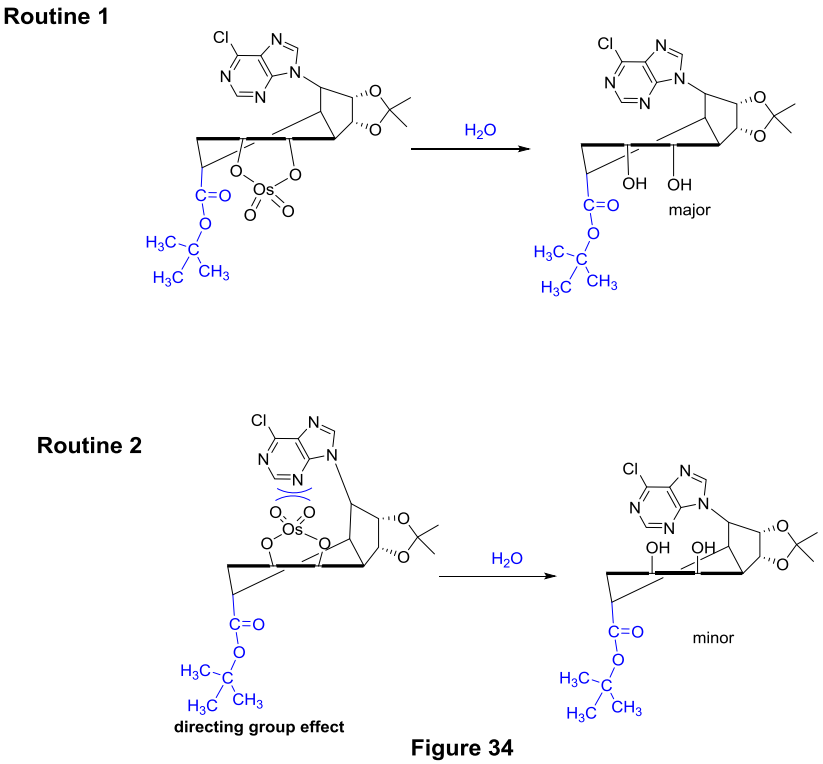
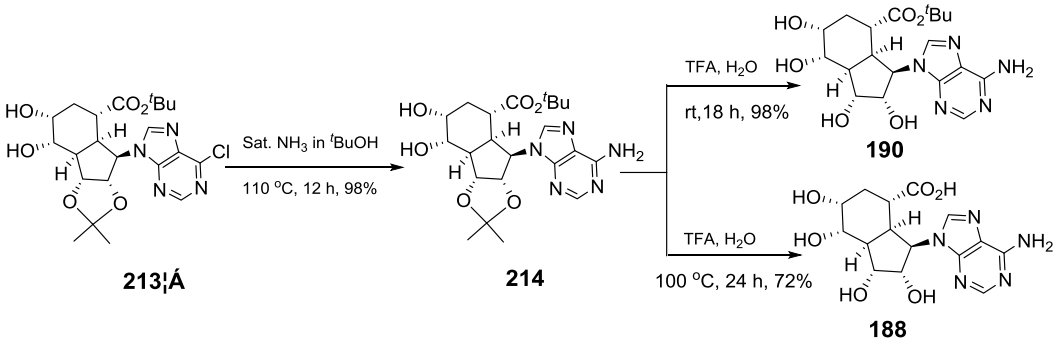


Figure 34

The first step for dihydroxylation was that the osmium tetraoxide cycloadded to the C=C bond. When osmium tetraoxide cycloadded to the C=C under the plane, the existence of the *tert*-butyl carboxylate in α face of the cyclohexane ring resulted in the formation triol **213α** as a major product. When the osmium tetraoxide cycloadded to the C=C above the plane, greater steric hindrance exerted from the nucleobase and five-membered ring in β face on osmium tetraoxide resulted in the formation of product triol **213β** in minority.

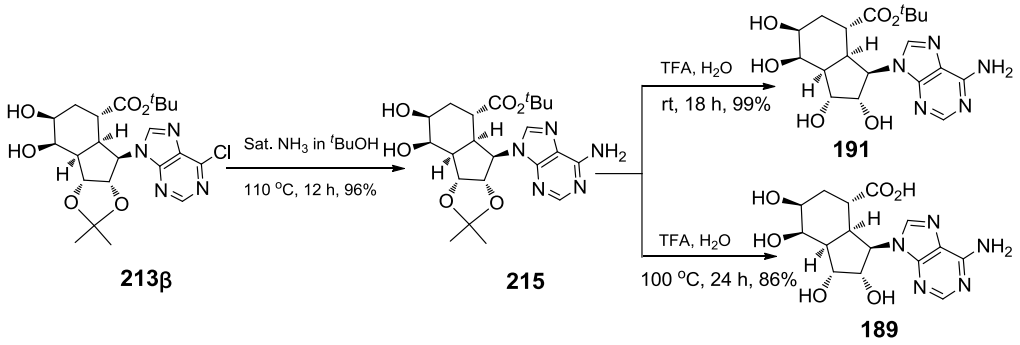
The chloride group in diol **213α** was then replaced by an amino group using saturated NH_3 in *t*-BuOH and purine **214** was obtained in an excellent yield. Since

the *tert*-butyl carboxylate was more stable under aq. TFA condition, comparing with the isopropylidene group in purine **214**, the adenosine analogue **190** bearing a bulky *tert*-butyl carboxylate group in the cyclohexane ring was obtained successfully in 98% yield by selective deprotection of the isopropylidene group (Scheme 30).



Scheme 30

To our delight, when the mixture of purine **214** in aq. TFA was refluxed for 24 h, the adenosine analogue **188** bearing a carboxylic acid group in the cyclohexane ring was obtained successfully in 72% yield.



Scheme 31

The chloride group in diol **213β** was also converted to an amino group using saturated NH_3 in *t*-BuOH and purine **215** was obtained in an excellent yield. As shown in Scheme 31, adenosine analogue **191** and adenosine analogue **189** were

obtained in good yields from diol **213β**.

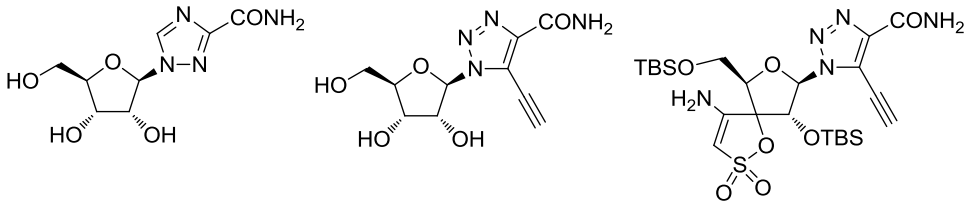
To summarize this part, alkene-type adenosine analogue **185**, alkane-type adenosine analogue **186**, pentahyroxy-type adenosine analogue **187** and tetrahyroxy-type adenosine analogues **188-191** were synthesized successfully from D-ribose, which could be subjected to different biological tests at the latter stage.

2.4 Synthesis of Ribavirin Analogues by Click Chemistry

In the past decades, nucleosides and carbonucleosides had played a major role in the treatment of viral infectious diseases such as AIDS and hepatitis.[114] In the previous sections, seven carbobicyclic nucleosides with a bicyclo[4.3.0]nonane system were synthesized successfully. We also have an interest in preparing a series of other kinds of carbocyclic nucleosides, triazole carbanucleoside analogues of ribavirin.

Ribavirin **(216)** (Figure 35) was the first triazole nucleoside and it was widely used to cure severe respiratory syncytial virus (RSV) infection, hepatitis C infection and other viral infections.[115] It has been approved by the FDA for therapy against Hepatitis C Virus (HCV) and is currently being used clinically worldwide.[116] The discovery of ribavirin[115a] in 1972 created a new template to design and synthesize novel triazole nucleosides[117] and some of them showed a very promising biological

potential. For instance, the group of Zeidler reported that ETCAR (**217)** exhibited cytostatic activity,[118] while TASO (**218)** showed anti-HIV activity.[119]



Ribavirin (216) **ETCAR (217)** **TASO (218)**

Figure 35

Carbocyclic nucleosides have potent metabolic stability because they are ineffective for phosphorylase and hydrolase enzymes by cleaving the glycosidic bond of natural nucleosides. Because of this, 1,2,3-triazole carbanucleosides are drawing more attention and great efforts by some research groups[120] have led to interesting biological agents. For example (Figure 36), Compound **219** showed a moderate antiviral activity against HIV-1 (IC_{50} 43.8 μM).[121] Compound **220** showed potent antiviral activity against vaccinia virus (EC_{50} 0.4 μM), but moderate activity against cowpox virus (EC_{50} 39 μM) and severe acute respiratory syndrome coronavirus (SARCoV) (EC_{50} 47 μM).[122] Meanwhile, Compound **221** exihibited a specific inhibitory potential against Varicella Zoster Virus (TK+VZV).[123] Recently, González-González[124] has reported the synthesis of novel 1,2,3-triazole carbocyclic nucleoside (**222**) using Corey lactone as key precursor, but there is no report for its biological activity.

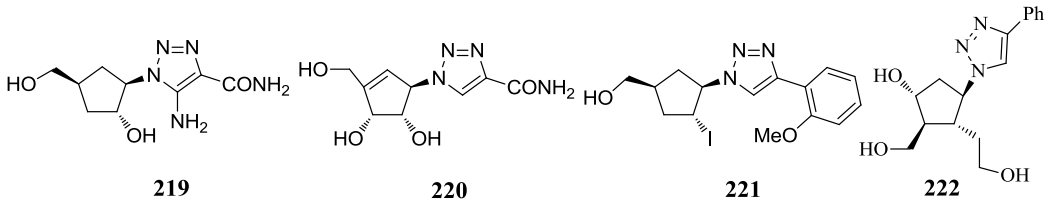


Figure 36

Click Chemistry proposed by Sharpless has emerged as a fast and efficient approach to simplify compound synthesis.[125] The Huisgen 1,3-dipolar cycloaddition[126] between a terminal alkyne and an azide furnished a large number of 1,2,3-triazoles in a fast, reproducible and quantitative way. This reaction is also termed the copper(I) catalyzed azide alkyne cycloaddition (CuAAC). In most cases, both 1,4-disubstitued regioisomer and 1,5-disubstitued regioisomer were obtained by this reaction under thermal condition[127] (Figure 37). This cycloaddition only afforded 1,4-isomer[128] in regard to the discovery of copper(I) catalysts in 2002.

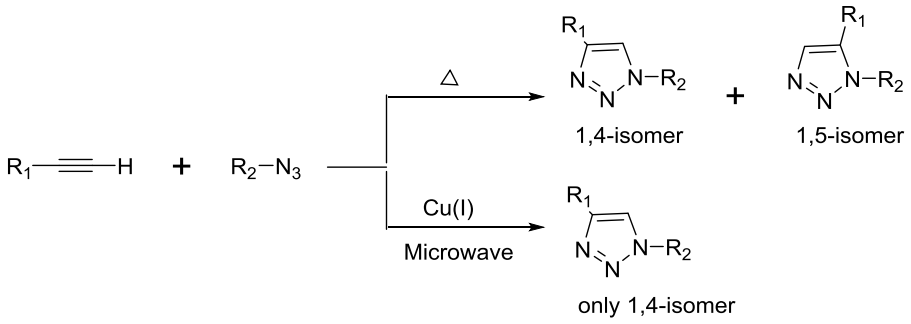
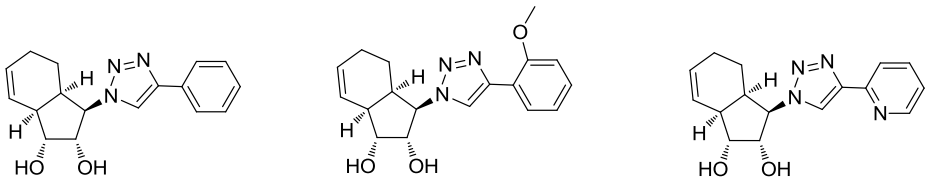


Figure 37

In our group, ten novel 1,2,3-triazole carbonucleosides with a bicyclo[4.3.0]-nonane system were synthesized successfully using CuAAC as the key step.[129] After

the test of their biological activity, three of them (**223**-**225**) showed *in vitro* antiviral activity against Coxsackie B3 virus (Figure 38). However, they also exhibited a high level of cytotoxicity.



223 **224** **225**

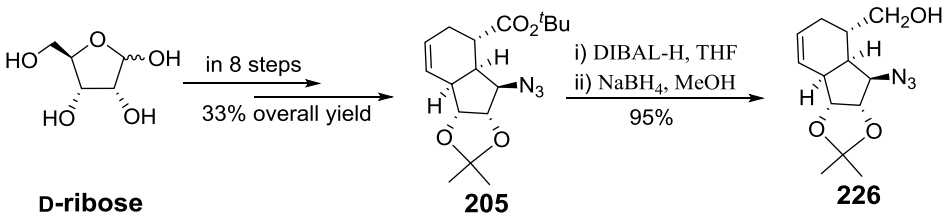
Figure 38

Therefore, I would like to modify the cyclohexene ring and alkene-type, alkane-type, pentahydroxy-type and tetrahydroxy-type ribavirin analogues would be prepared to reduce their toxicity.

2.4.1 Synthesis of Ribavirin Analogues

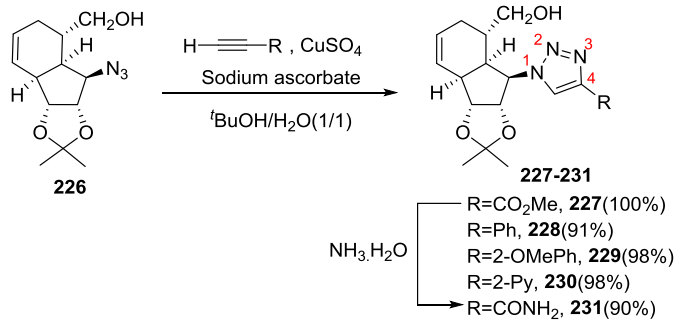
2.4.1.1 Synthesis of Alkene-type Ribavirin Analogues

In the previous section, azide **205** was successfully synthesized from D-ribose in 8 steps with 33% overall yield, which was then reduced by DIBAL-H and then $NaBH_4$ to yield azide **226** in an excellent yield (Scheme 32).



Scheme 32

With azide **226** in hand, it was subjected to CuAAC with four different acetylenes and four 1,2,3-triazoles were obtained in excellent yields (Scheme 33).



Scheme 33

All obtained triazoles **227**-2**31** were 1,4-disubstitued regioisomers and no 1,5-disubstitued regioisomers were obtained, which were confirmed by X-ray crystallography of their final products. The regiochemistry and stereochemistry of triazoles **227**-2**31** can be explained according to the following mechanism (Figure 39).

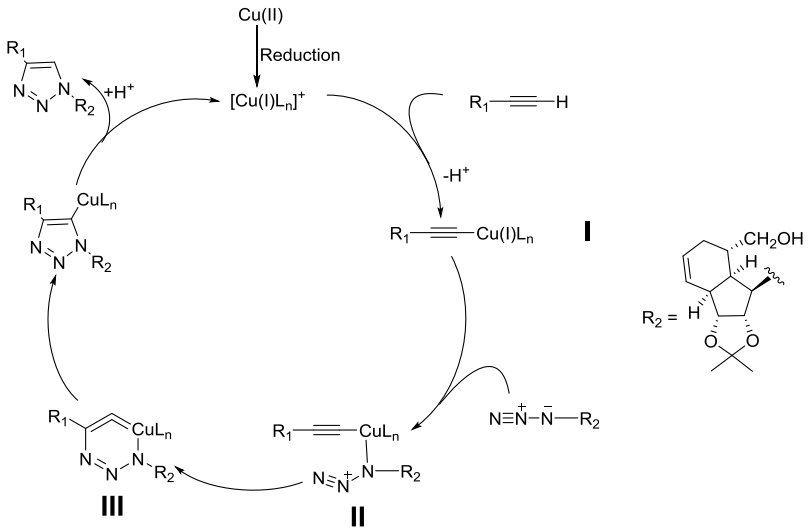
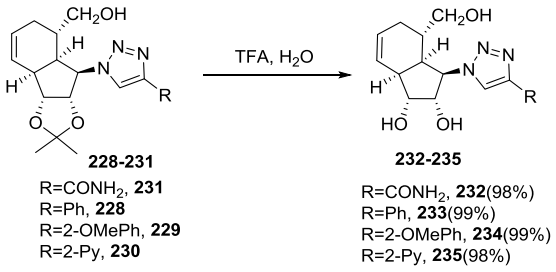


Figure 39

As shown in Figure 39, the copper(I) species were *in situ* generated by reduction of copper sulfate with sodium ascorbate, which was then formed a Cu(I) acetylide via initial π-complex. Then the σ-acetylide Cu(I) complex (**I**) was yielded by sequential deprotonation. The density functional theory calculations proposed by Fokin and Sharpless revealed that the copper catalyzed reaction would proceed in a stepwise mechanism over a concerted mechanism, resulting in the formation of 1,4-disubstitued regioisomer.[130]



228-231
R=$CONH_2$, **231**
R=Ph, **228**
R=2-OMePh, **229**
R=2-Py, **230**

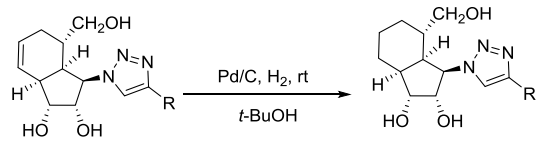
232-235
R=$CONH_2$, **232**(98%)
R=Ph, **233**(99%)
R=2-OMePh, **234**(99%)
R=2-Py, **235**(98%)

Scheme 34

The ester group of triazole **227** was converted into amide group by reacting with 7M ammonia solution in methanol and the amide **231** was obtained in an excellent yield. By deprotection of triazoles **228**-2**31** with TFA in CH_2Cl_2/H_2O (v/v, 1/ 8), triazoles **232**-**235** were obtained in 82%-93% yields (Scheme 34). By adding more water, the yield could be improved. After several trials, we found that no side-product trifluroroacetate was obtained and this reaction was cleaner and more efficient when only water was used as solvent under acidic condition.

2.4.1.2 Synthesis of Alkane-type Ribavirin Analogues

In the previous section, we synthesized alkene-type ribavirin analogues **232-235** successfully in excellent yields, this intrigued us to wonder if there would be a conformational change when the cyclohexene ring was saturated to the cyclohexane ring.



232-235

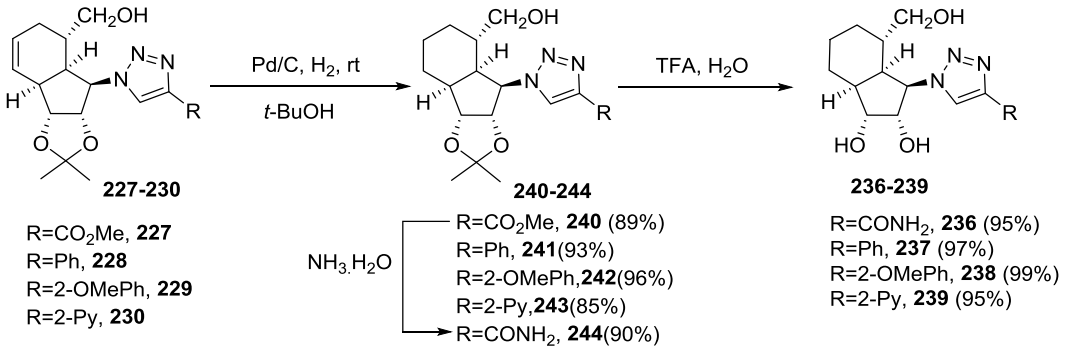
R=$CONH_2$, **232**(98%)
R=Ph, **233**(99%)
R=2-OMePh, **234**(99%)
R=2-Py,**235**(98%)

236-239

R=$CONH_2$, **236**
R=Ph, **237**
R=2-OMePh, **238**
R=2-Py, **239**

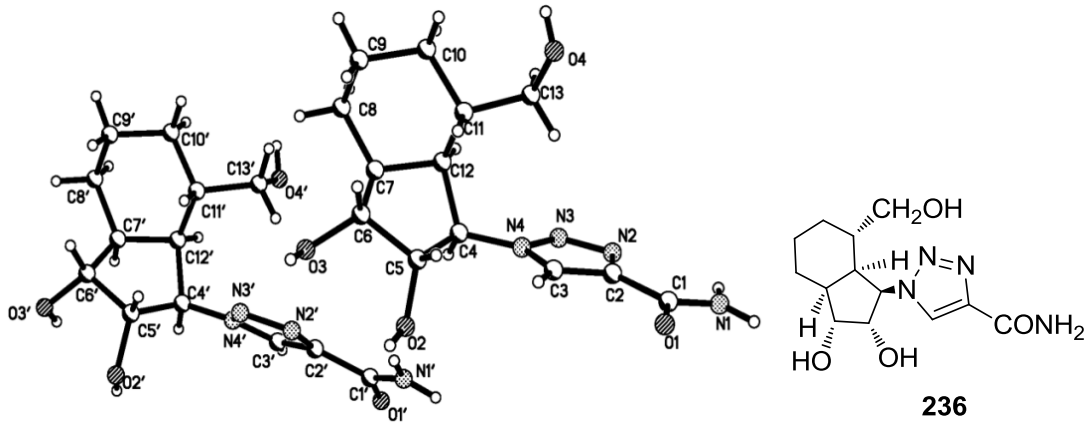
Scheme 35

With final products triazoles **232-235** in hand, these compounds were hydrogenated directly with a catalytic amount of 10% Pd-on-charcoal. However, a complex mixture was obtained (Scheme 35).



Scheme 36

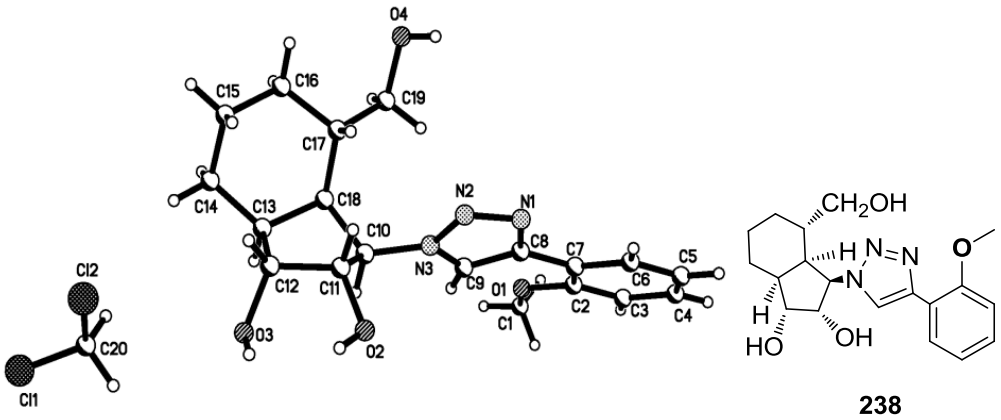
Triazoles **227-230** were then hydrogenated with a catalytic amount of 10% Pd-on-charcoal under the atmosphere of H_2, to give triazoles **240-243** in excellent yields (Scheme 36). It should be noted that the hydrogenation for triazole **227** would lead to the deprotection of the isopropylidene group under a long reaction time (more than 16 h). After the completion of hydrogenation, we tested the pH value for the reaction mixture and found the pH was about 4, a weak acidic condition. Comparing with other triazoles, the hydrogenation of triazole **230** needed a longer reaction time to consume all the starting material and its yield was a little lower, probably because the N lone pair electrons can coordinate with metal Pd easily, which results in the competition with H_2 for the active site.



236

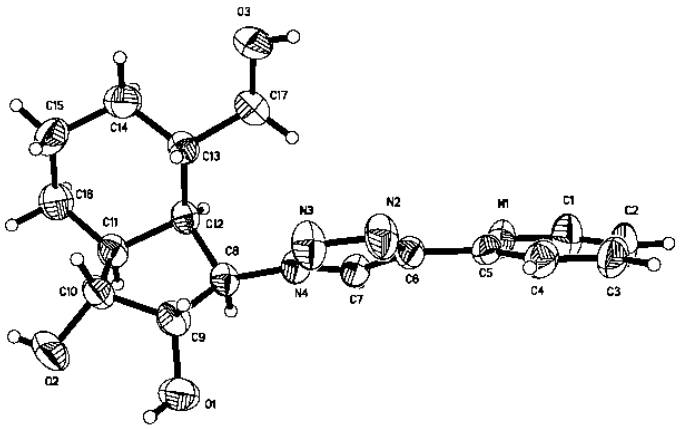
Figure 40

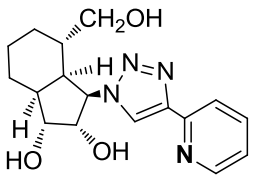
The ester group of triazole **240** was converted into amide group by reacting with 7M ammonia solution in methanol and the amide **244** was obtained in an excellent yield. The isopropylidene group in triazoles **241-244** was hydrolysed with aq.TFA and alkane-type triazoles **236-239** were obtained in excellent yields. Their absolute stereochemistries and conformations were confirmed by X-ray crystallography.



238

Figure 41





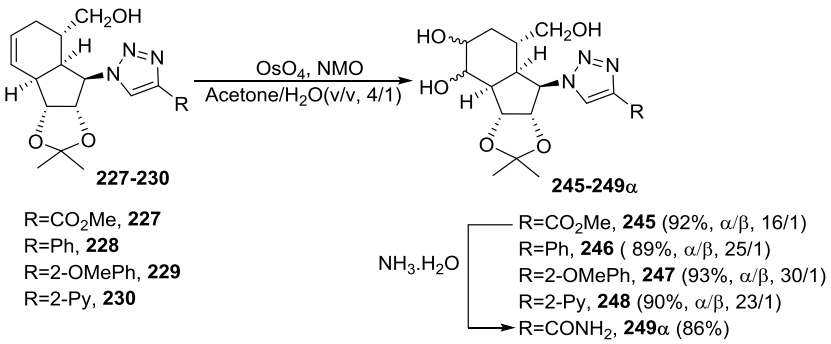
239

Figure 42

As shown in Figure 40-42, we clearly observe that the conformation of triazole **236** and triazole **239** are C5'-*endo* conformations, which are novel structures. However, the conformation of triazole **238** is C1'-*exo* conformation, which might induce insignificant biological activity.

2.4.1.3 Synthesis of Polyhydroxy-type Ribavirin Analogues

In the previous sections, we had synthesized four alkene-type ribavirin analogues **232-235** and four alkane-type ribavirin analogues **236-239** successfully, the conformations of alkane-type have C5'-*endo* conformation or C1'-*exo* conformation. The diversity of their conformations intrigued us to synthesize a series of pentahydroxy-type ribavirin analogues.



Scheme 37

The dihydroxylation of triazoles **227-230** by osmium tetraoxide produced triols **245-248** (Scheme 37), which were separable isomers and their ratios varied from 16/1 to 25/1. The high selectivity of dihydroxylation for triazoles **227-230** might be rationalised in Figure 43.

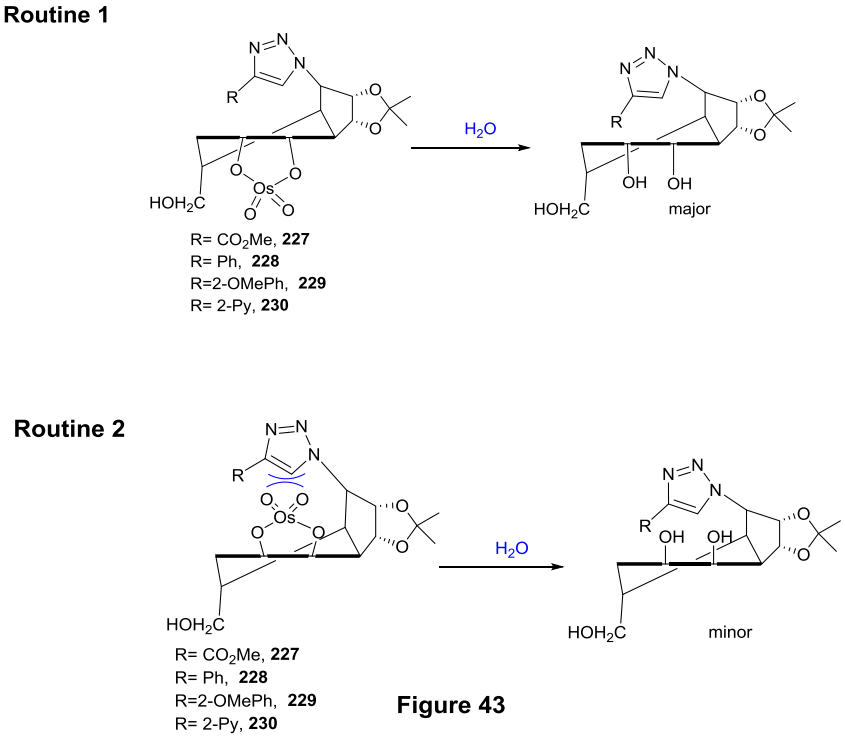


Figure 43

As shown in Figure 43, when osmium tetraoxide cycloadded to the C=C bond

under the plane (Routine 1), the major product triols **245α-248α** were obtained. When the tetraoxide cycloadded to the C=C bond above the plane, the steric hindrance from the triazole and five-member ring in β face with osmium tetraoxide resulted in the formation of product triols **245α-248α** in minority. When R group was MeOPh, which was the biggest one in the four different groups, the selectivity of triazole **229** was the best (α/β, 30/1). When R group was CO_2Me, which was the smallest one in the four different groups, the selectivity of triazole **247** was the worst (α/β, 16/1). The bulkiness of Ph group is close to Py group, so their ratios of α/β are close to each other (25/1, 23/1).

Taking the triol **247** as an example, the major one was **247α**, whose absolute stereochemistry was confirmed by X-ray crystallography in Figure 44.

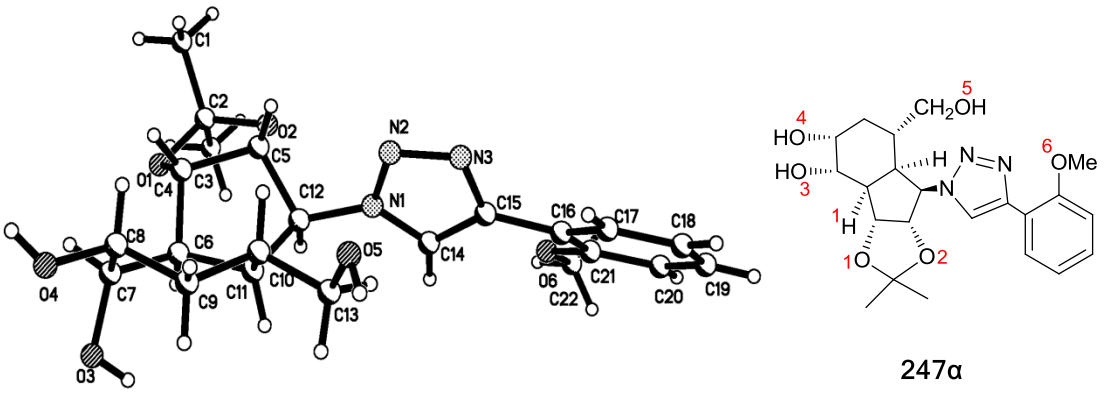
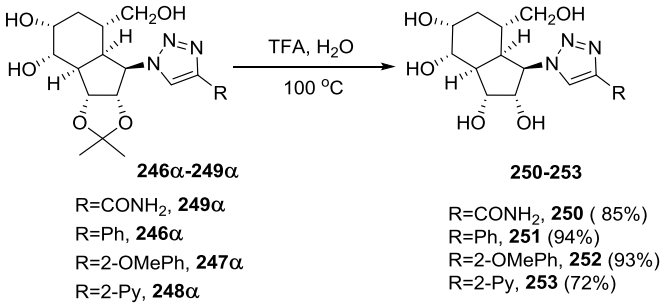


Figure 44

As shown in Figure 23, we clearly observe that 3-OH is an axial hydroxyl group and 4-OH is an equatorial hydroxyl group, thus are *syn* to each other and then are son

the same side with H^1. The conformation of triol **247**α is C5'-*endo*, which belong to neither South-type conformation nor North-type conformation.



246α-249α

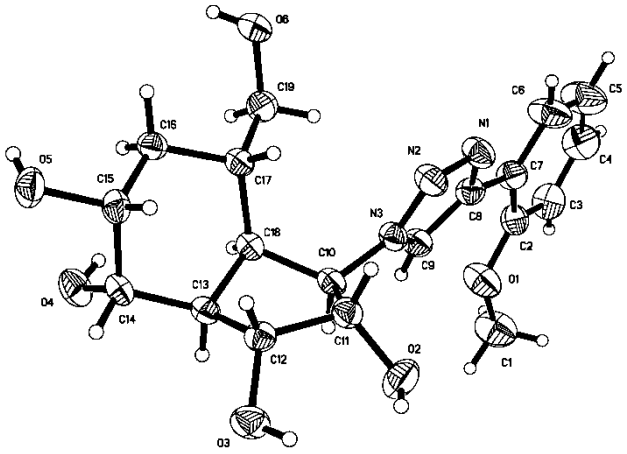
R=$CONH_2$, **249α**
R=Ph, **246α**
R=2-OMePh, **247α**
R=2-Py, **248α**

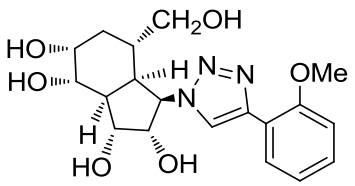
250-253

R=$CONH_2$, **250** (85%)
R=Ph, **251** (94%)
R=2-OMePh, **252** (93%)
R=2-Py, **253** (72%)

Scheme 38

The ester group of triazole **245α** was converted into amide group by reacting with 7M ammonia solution in methanol and amide **249α** was obtained in an excellent yield. Finally, deprotection of the isopropylidene group by aq. TFA furnished pentahydroxy -type ribavirin analogues **250-253** in a good yield (Scheme 38). The absolute stereochemistry of our target, the pentahydroxy-type ribavirin analogue **252** was confirmed by X-ray crystallography in Figure 45.





252

Figure 45

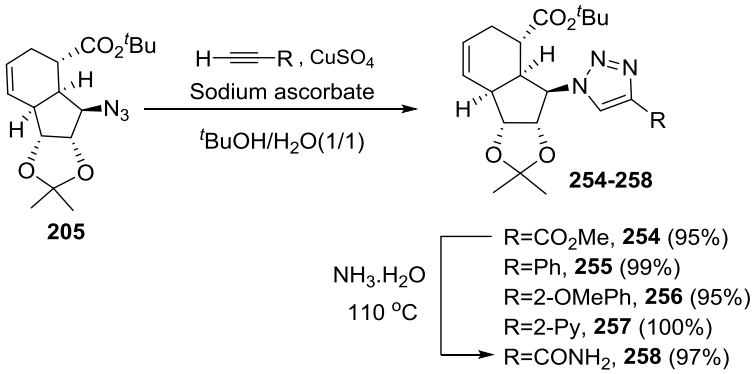
As shown in Figure 45, we clearly observe that the conformation of triol **252** is also a C5'-*endo*, a novel conformation which is same with that of triazole **247**α.

2.4.2 Synthesis of Ribavirin Analogues Bearing Carboxylate Group

Since the alkene-type ribavirin analogues **232-235**, alkane-type ribavirin analogues **236-239** and pentahydroxy-type ribavirin analogues **250-253** were synthesized successfully in the previous sections. However, we found that they could not dissolve in water readily. Therefore, we would prepare some ribavirin analogues bearing carboxylic acid, which could be converted into carboxylate salts by reacting with sodium hydroxide in order to enhance their solubility in water. Besides, we would synthesize some ribavirin analogues with bulky carboxylic ester in the cyclohexane ring to investigate the effect on their conformation.

2.4.2.1 Synthesis of Alkene-type Ribavirin Analogues Bearing Carboxylate Group

With azide **205** in hand, it was subjected to CuAAC with four different acetylenes and four 1,2,3-triazoles were obtained in excellent yields (Scheme 39).



Scheme 39

All obtained triazoles **254-257** were 1,4-disubstitued regioisomer and no 1,5-disubstitued regioisomer were obtained, which can be confirmed by X-ray crystallography of triazole **255**.

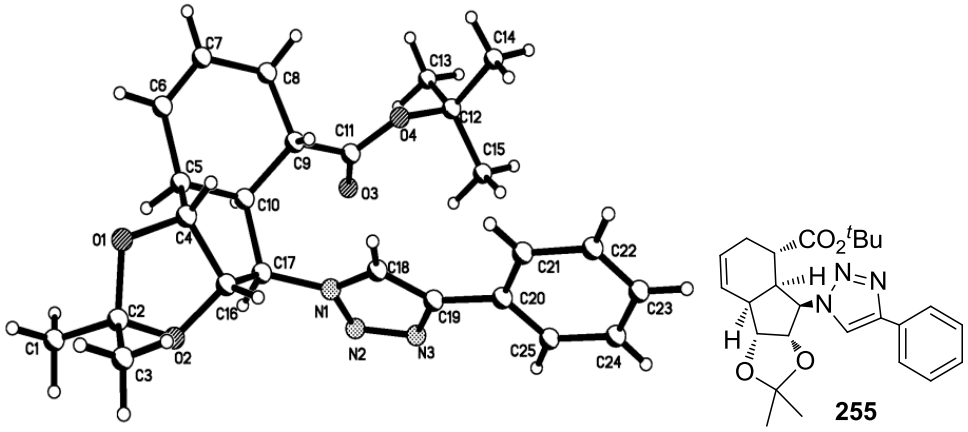
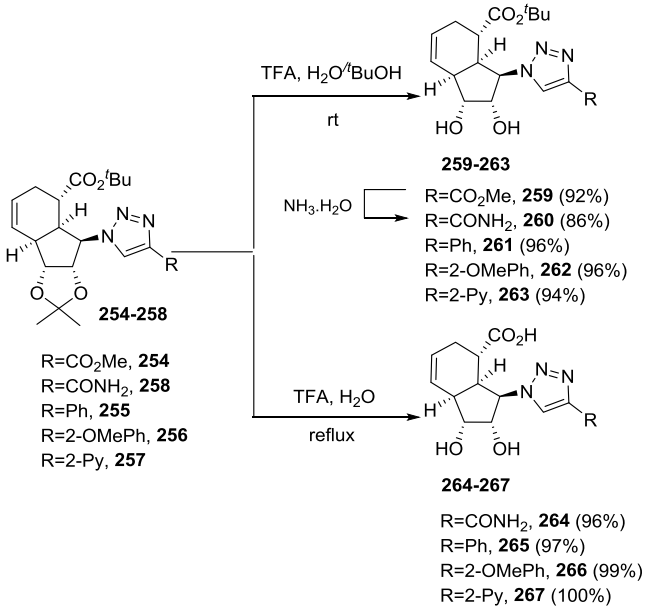


Figure 46

As shown in Figure 46, we clearly observe that triazole **255** is 1,4-disubstitued regioisomer and its conformation is a C4'-*exo*, a novel conformation which belongs to neither South type nor North type.

The ester group of triazole **254** was converted into amide group by reacting with 7M ammonia solution in methanol at room temperature for 12 h. However, no reaction was observed (checked by TLC). The reaction mixture was then heated to 110 ^{o}C in a seal tube and stirred for 12 h. To our delight, amide **258** was obtained in excellent yield.

Since the *tert*-butyl carboxylate is more stable than the isopropylidene group in purine **214** under acidic conditions using aq. TFA, ribavirin analogues **260-263** bearing a bulky group in the cyclohexane ring were obtained successfully in excellent yields by selective deprotection of the isopropylidene group with aq. TFA at room temperature (Scheme 40).



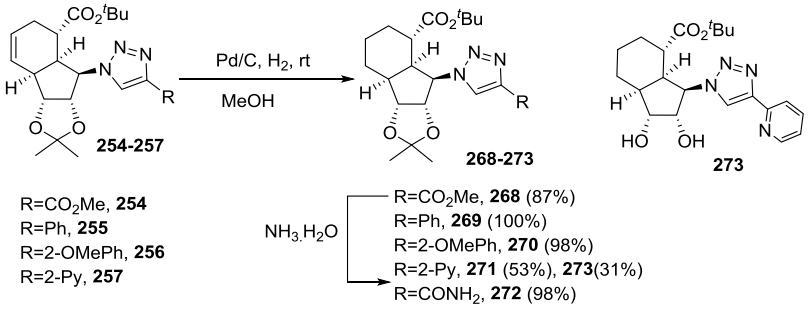
Scheme 40

Luckily, when the mixture of triazoles **255-258** under aq. TFA conditions were

refluxed for 24 h, the ribavirin analogues **264-267** bearing a carboxylic acid group in the cyclohexane ring were obtained successfully in excellent yields respectively.

2.4.2.2 Synthesis of Alkane-type Ribavirin Analogues Bearing Carboxylate Group

Since a series of alkene-type ribavirin analogues **259**-2**67** were obtained successfully. With the same idea, we would synthesize alkane-type ribavirin analogues with bulky group or carboxylic acid in cyclohexane ring.

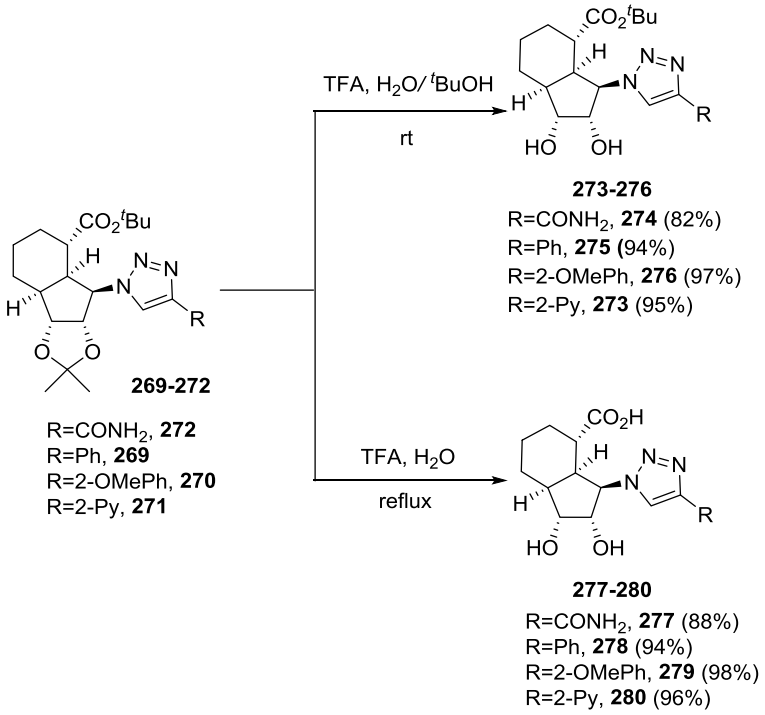


Scheme 41

With triazoles **254**-**257** in hand, they were subjected to hydrogenation with a catalytic amount of 10% Pd-on-charcoal and triazoles **268**-**272** were obtained in excellent yields (Scheme 41). It should be noted that the hydrogenation of triazole **257** needed a longer reaction time to consume all the starting material and its yield was a little lower than other triazoles, probably because the N lone pair electrons could coordinate with metal Pd tightly, which resulted in the competition with H_2 for

the active site.

The ester group of triazole **268** was converted into amide group by reacting with 7M ammonia solution in methanol at room temperature for 12 h. However, no reaction was observed from TLC. The reaction mixture was then heated to 110 ^{o}C in a seal tube and stirred for 12 h. Luckily, amide **272** was obtained in an excellent yield.



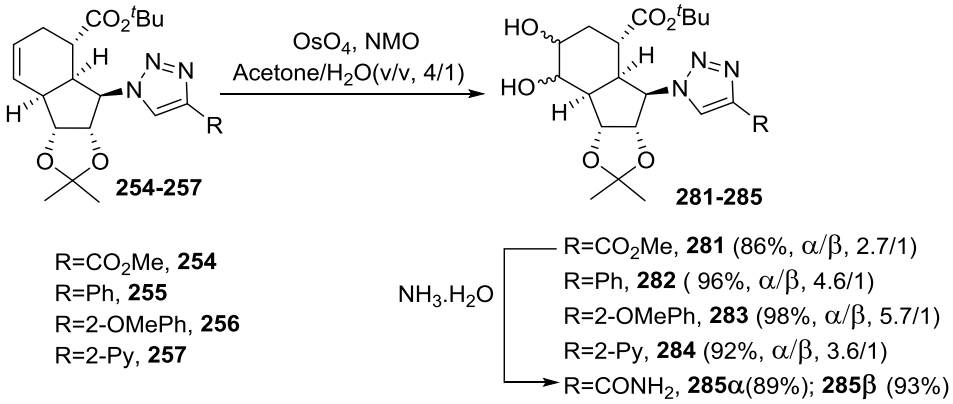
Scheme 42

Finally, selective deprotection of triazoles **269-272** with TFA in H_2O/*t*-BuOH at room temperature furnished tetrahydroxy-type ribavirin analogues **273-276** bearing a carboxylate group in the cyclohexane ring in excellent yields (Scheme 42). When triazoles **269-272** under aq. TFA condition were refluxed for 24 h, the ribavirin

analogues **277-280** bearing a carboxylic acid group in the cyclohexane ring were obtained successfully in good yields respectively.

2.4.2.3 Synthesis of Polyhydroxy-type Ribavirin Analogues Bearing Carboxylate Group

In the previous sections, we synthesized alkene-type ribavirin analogues and alkane-type ribavirin analogues successfully. From their X-ray crystallography, many kinds of conformations (C1'-*exo*, C4'-*exo* and C5'-*endo* conformation) were obtained. Therefore, we also wondered whether its conformation would be changed or not when two hydroxyl groups were introduced to the cyclohexane ring in the presence of bulky *tert*-butyl group or carboxylic acid.



Scheme 43

With triazoles **254-257** in hand, these compounds were subjected to dihydroxylation with osmium tetraoxide respectively and diols **281-284** were obtained

in excellent yields (Scheme 43), which were separable isomers and their ratio varied from 2.7/1 to 5.7/1. Taking diol **284** as an example, the minor one was **284β**, whose stereochemistry was confirmed by its ^{1}H NMR and 2D-NOESY spectrum in Figure 47.

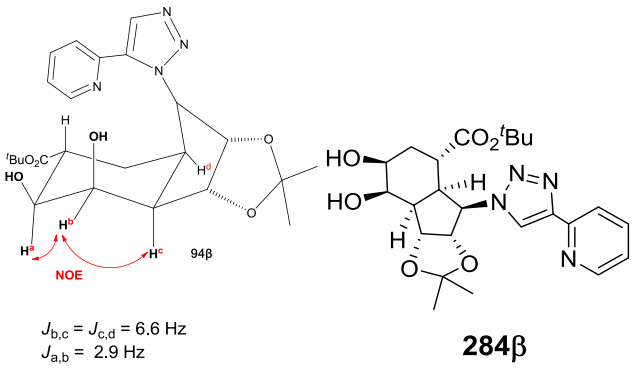


Figure 47

From its ^{1}H NMR of diol **284β** (a minor product), the coupling constant for $J_{b,c}$ was 6.6 Hz, which fell into the range of axial-equatorial coupling. The H^c was an axial proton, indicating that H^b was an equatorial proton. Because the coupling constant for $J_{b,c}$ was 2.9 Hz and H^b was *syn* to H^a, the stereochemistry for diol **284** can be confirmed as shown in Figure 47. From its 2D-NOESY NMR, there were NOE correlations between H^c and H^b, H^b and H^a, indicating that these three hydroxyl groups were *syn* to each other. Furthermore, the position of H^c was confirmed, so the stereochemistry of diol **284β** can be confirmed as shown in Figure 47, which was in accord with the analysis result of its ^{1}H NMR spectrum.

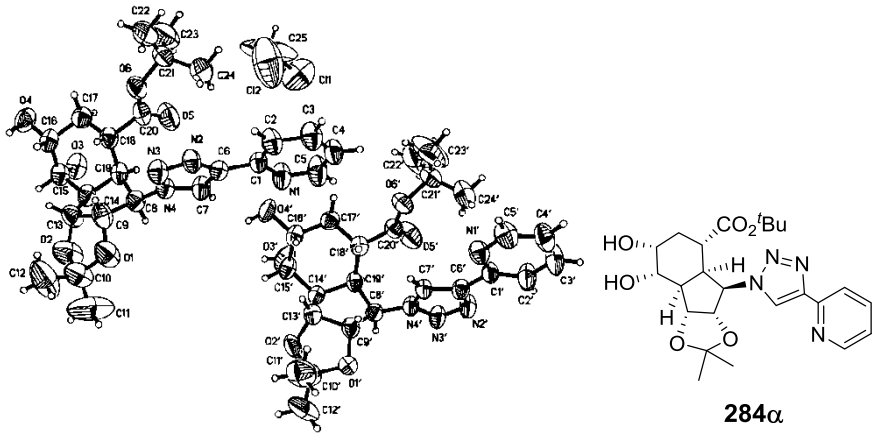
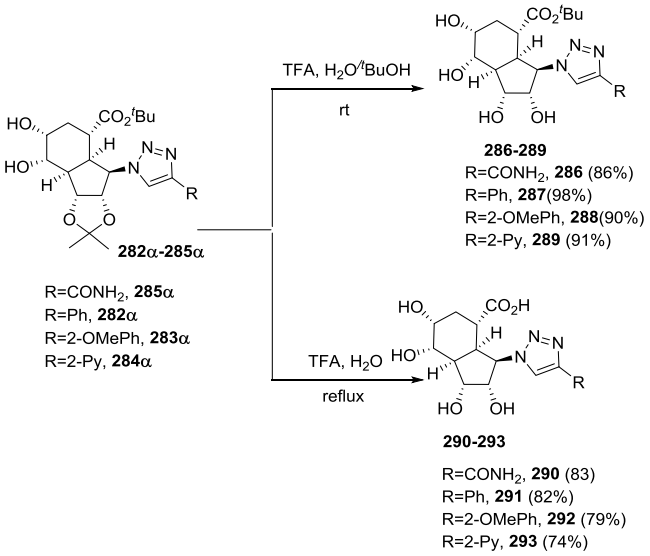


Figure 48

The major one was **284α**, whose stereochemistry were confirmed by X-ray crystallography. As shown in Figure 48, we clearly observed that the conformation of triol **284**α was C5'-*endo*, which belongs to neither South-type conformation nor North-type conformation.

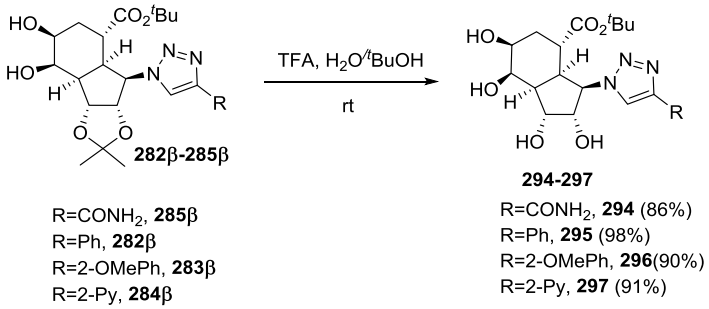
When the bulky carboxylate ester was retained in the cyclohexane ring, we found that the ratio of β was increased, attributable to the directing group effects of *tert*-butyl carboxylic ester discussed in the previous section.



Scheme 44

The ester group of triazole **281α** was converted into amide group by reacting with 7M ammonia solution in methanol at 110 ^{o}C for 12 h in a good yield. Finally, selective deprotection of triazoles **282α-285α** with TFA in H_2O/*t*-BuOH at room temperature furnished tetrahydroxy-type ribavirin analogues **286-289** bearing a carboxylate ester in the cyclohexane ring in excellent yields (Scheme 44). When triazoles **282α-285α** under aq. TFA condition were refluxed for 24 h, the ribavirin analogues **290-293** bearing a carboxylic acid group in the cyclohexane ring were obtained successfully in good yields respectively.

The ester group of triazole **281β** was converted into amide group by reacting with 7M ammonia solution in methanol at 110 ^{o}C for 12 h in a good yield (Scheme 43). Since diols **282β-285β** were minor products, we would only plan to synthesize ribavirin analogues bearing a bulky *tert*-butyl carboxylic ester group.



R=$CONH_2$, **285β**
R=Ph, **282β**
R=2-OMePh, **283β**
R=2-Py, **284β**

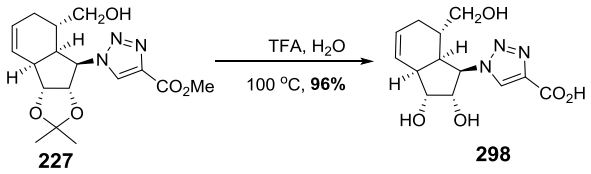
R=$CONH_2$, **294** (86%)
R=Ph, **295** (98%)
R=2-OMePh, **296**(90%)
R=2-Py, **297** (91%)

Scheme 45

Therefore, selective deprotection of the isopropylidene group by TFA in H_2O/*t*-BuOH at room temperature yielded tetrahydroxy-type ribavirin analogues **294-297** in excellent yields (Scheme 45).

2.4.3 Synthesis of Ribavirin Analogues Bearing Carboxylate Group in Triazole

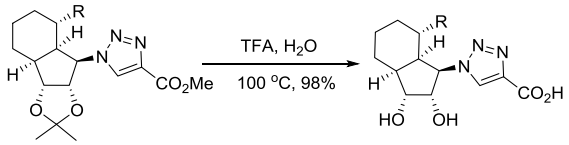
In the previous section, we synthesized two more ribavirin analogues bearing a carboxylic acid in the cyclohexane ring, we would plan to prepare some ribavirin analogues bearing a carboxylic acid in the triazole.



227 **298**

Scheme 46

With triazole **227** in hand, it was subjected to deprotection of the isopropylidene group and the carboxylic ester group by aq. TFA, affording carboxylic acid **298** in an excellent yield.



240 **299**

Scheme 47

With triazole **240** in hand, it was subjected to deprotection of the isopropylidene group and carboxylic ester group by aq. TFA, generating carboxylic acid **299** in an excellent yield (Scheme 47).

To summarize this part, 42 ribavirin analogues were successfully synthesized from D-ribose, which would be subjected to different biological tests at a latter stage as well.

2.5 Analyses of X-ray Crystallography

Crystals of **213β**, **238**, **255** and **284α** suitable for X-ray analyses were obtained by the slow diffusion of *n*-hexane into dichloromethane at room temperature. Crystals of **236**, **239**, **247α** and **252** suitable for X-ray analyses were obtained by slowly evaporating their methanol solution at room temperature. Crystals of **185** suitable for X-ray analyses was obtained by slowly evaporating its $MeOH/CHCl_3$ (v/v, 1/3) solution at room temperature. Crystals of **187** suitable for X-ray analyses was obtained by slowly evaporating its aqueous solution at room temperature.

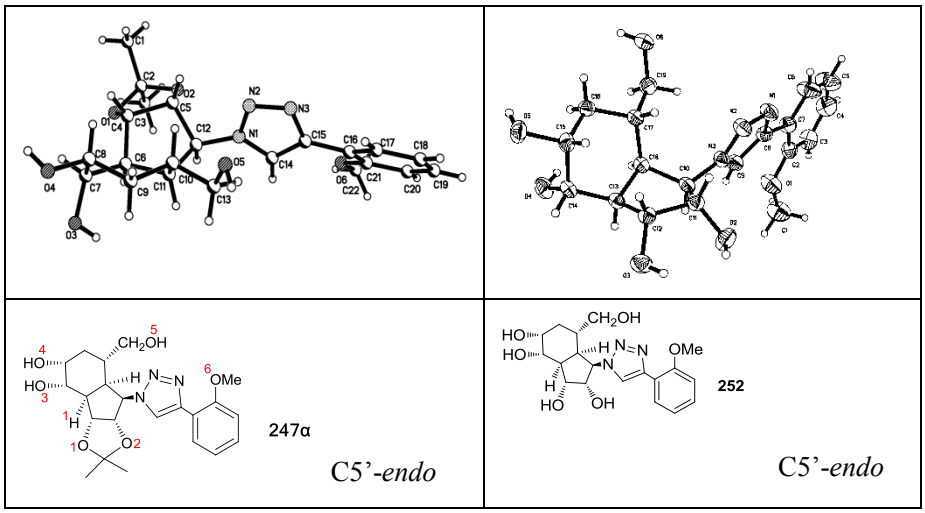


Figure 49

From the Figure 49, the conformation of trihydroxy-type triazole **247α** was C5'-*endo*. After deprotection of the isopropylidene group, its conformation was also C5'-*endo*, indicating that the isopropylidene group had little influence on its conformation.

Comparing the conformation of triazole **252** (Figure 49) with nucleoside **187** (Figure 50), their structures are similar except the heterocyclic bases, while their conformations are different. Because the purine group in nucleobase **187** is a plane structure, but the OCH_3 group out of the plane of phenyl group in the triazole **252** is close to the five-member ring, which results in their different conformations because of their repulsion strains.

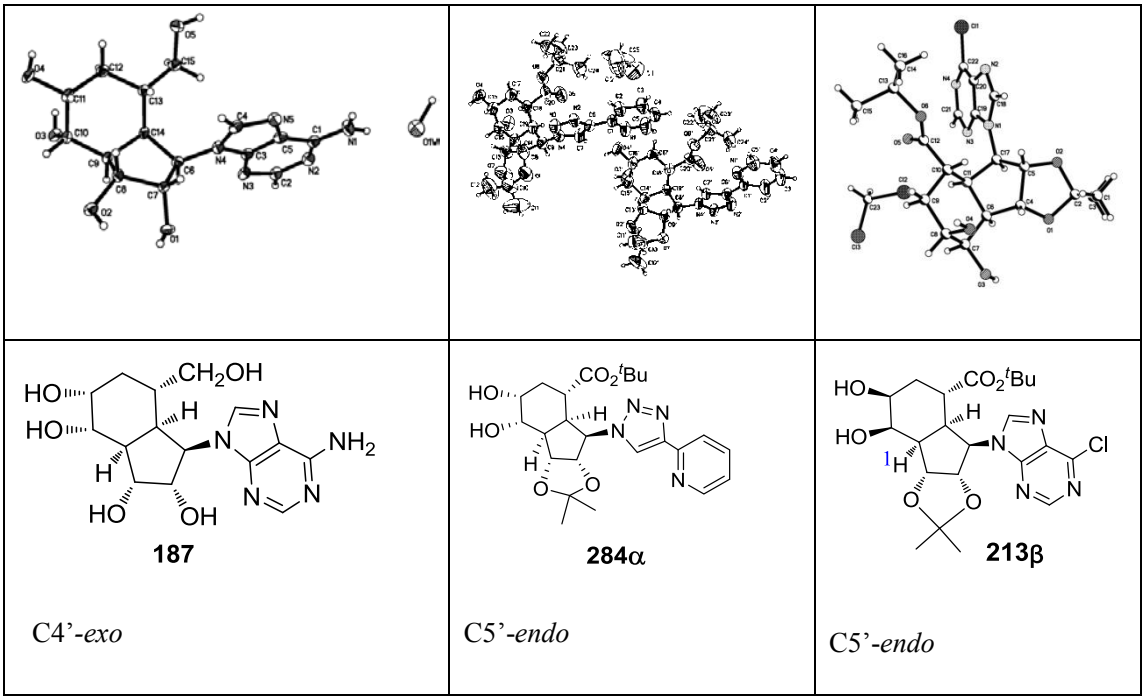


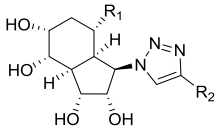
Figure 50

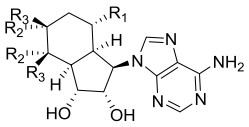
Comparing the conformation of triazole **284α** with nucleoside **187** (Figure 50), their heterocyclic bases (the purine and the triazole) are in the plane, but the bulky *tert*-butyl carboxylate in the cyclohexane ring results in the different conformation. From the structure of **284α** and **213β**, two heterocycle bases are plane structure and they have the same bulky *tert*-butyl carboxylate. And the only difference is the

position of dihydroxyl group, while their conformations are not changed, indicating that the direction of dihydroxyl group has no effects on their conformation.

From the analyses between their conformations and structures, we can speculate the conformations of polyhydroxy-type adenosine analogues and ribavirin analogues, which are listed as follow.

C4'-*exo*





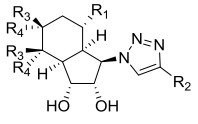
R_1 = CH_2OH, R_2=$CONH_2$, **250**
R_1 =CH_2OH, R_2=Ph, **251**
R_1 =CH_2OH, R_2=2-Py, **253**
R_1 = CO_2H, R_2=$CONH_2$, **290**
R_1 =CO_2H, R_2=Ph, **291**
R_1=CO_2H, R_2=2-Py, **293**

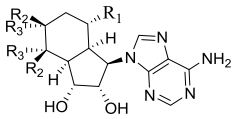
R_1=CO_2H, R_2=OH, R_3=H, **188**
R1=CO_2H, R_2=H, R_3=OH, **189**

Figure 51

As shown in Figure 51, ribavirin analogues **250**, **251**, **253**, **290**, **291**, **293** and adenosine analogues **188** and **189** belong to C4'-*exo* (novel conformation).

C5'-*endo*



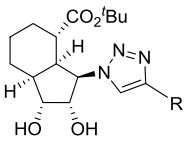


R_1 =COOH, R_2=2-OMePh, R_3=H, R_4=OH, **292**
R_1= $CO_2{}^tBu$, R_2=$CONH_2$, R_3=OH, R_4=H, **294**
R_1= $CO_2{}^tBu$, R_2=$CONH_2$, R_3=H, R_4=OH, **286**
R_1 =$CO_2{}^tBu$, R_2=Ph, R_3=OH, R_4=H, **295**
R_1 =$CO_2{}^tBu$, R_2=Ph, R_3=H, R_4=H, **287**
R_1 =$CO_2{}^tBu$, R_2=2-Py, R_3=OH, R_4=H, **297**
R_1 =$CO_2{}^tBu$, R_2=2-Py, R_3=H, R_4=OH, **289**

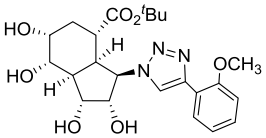
R_1=$CO_2{}^tBu$, R_2=H, R_3=OH, **190**
R_1=$CO_2{}^tBu$, R_2=OH, R_3=H, **191**

Figure 52

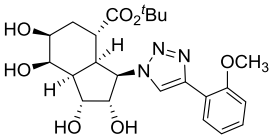
As shown in Figure 52, ribavirin analogues **286**, **287**, **289**, **292**, **294**, **295**, **297** and adenosine analogues **190** and **191** belong to C5'-*endo* (novel conformation).



R=$CONH_2$, **274**
R=Ph, **275**
R=2-OMePh, **276**
R=2-Py, **273**



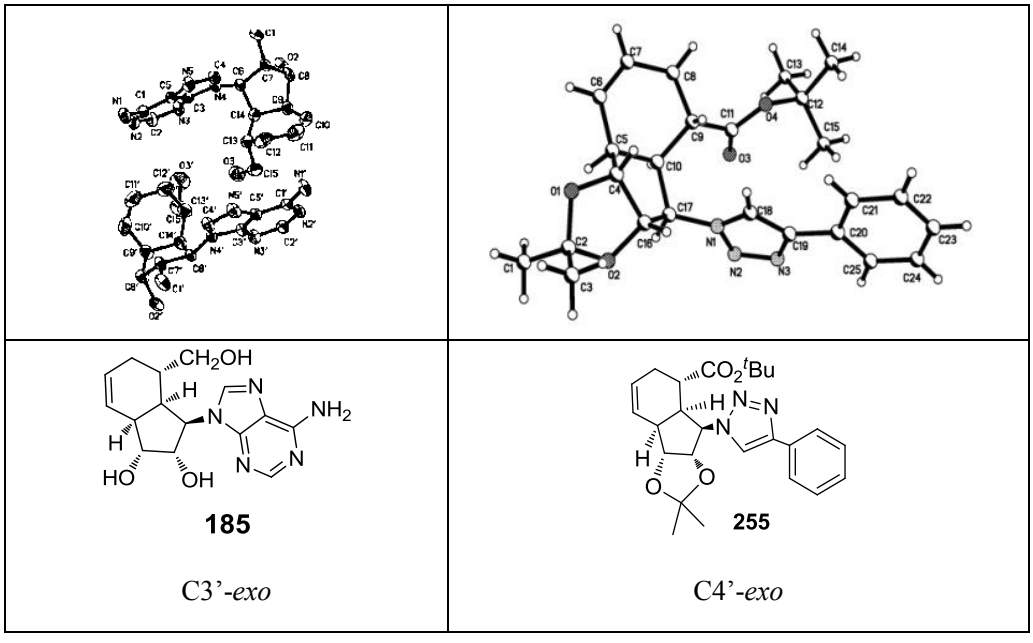
288



296

Figure 53

However, the conformations of ribavirin analogues **273**-**276**, **288** and **296** cannot be confirmed (Figure 53), which would be confirmed by X-ray crystallography at a later stage as well.



185

C3'-*exo*

255

C4'-*exo*

Figure 54

As shown in Figure 54, the adenosine analogue **185** is C3'-*exo* (South-type conformation), which is closer to the conformation of conventional nucleosides. Comparing the conformation of adenosine analogue with ribavirin analogue **255** (Figure 54), their structures are same except bulky *tert*-butyl carboxylate in the cyclohexane ring. Since the bulky *tert*-butyl carboxylate has repulsion with triazole plane, resulting in the changes from C3'-*exo* to C4'-*exo* for their conformations.

From the analyses between their conformations and structures, we can speculate the conformations of alkene-type adenosine analogues and ribavirin analogues, which are listed as follow.

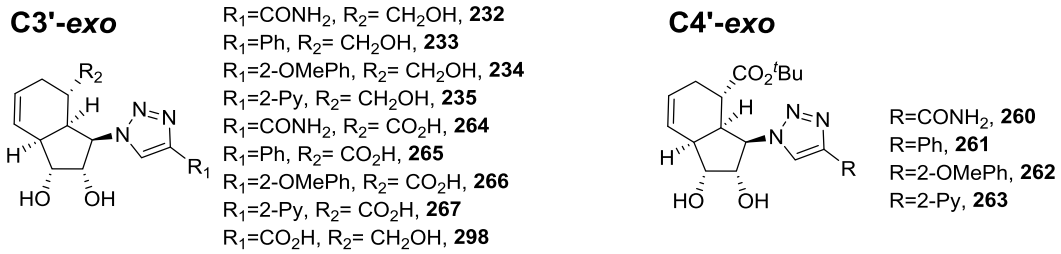


Figure 55

As shown in Figure 55, ribavirin analogues **232-235**, **264-267** and **298** belong to C3'-*exo* (South-type conformation), while ribavirin analogues **260-263** belong to C4'-*exo* conformation (novel conformation).

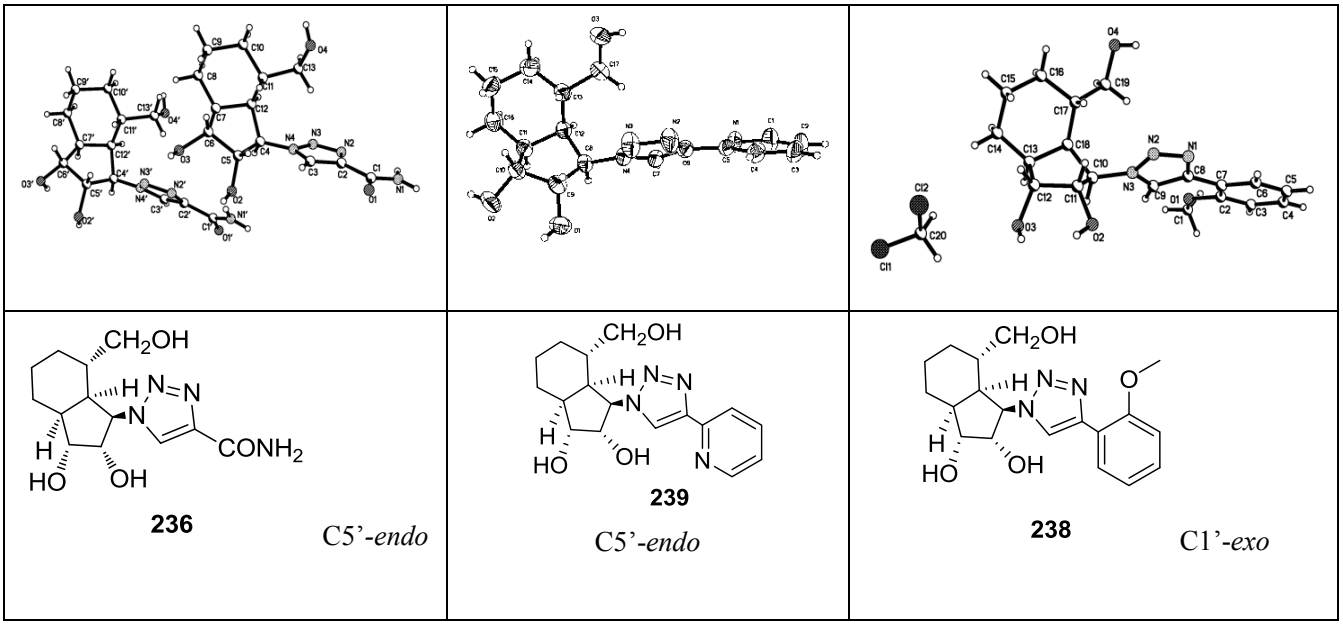


Figure 56

Comparing the conformation of alkane-type ribavirin analogues **236**, **238** and **239** (Figure 56), the conformations of ribavirin analogues **236**, **239** are C5'-*endo*, while the conformation of ribavirin analogues **238** is C1'-*exo*. I reckon that the heterocyclic bases in ribavirin analogues **236** and **239** have little effect on the five-member ring, while the existence of the methoxyl group of phenyl ring in ribavirin analogue **238** results in the formation of C1'-*exo* conformation.

From the analyses between their conformations and structures, we can also speculate the conformations of alkane-type adenosine analogues and ribavirin analogues, which were listed as follow.

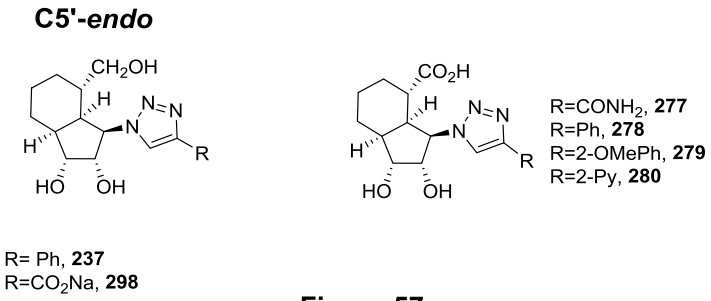


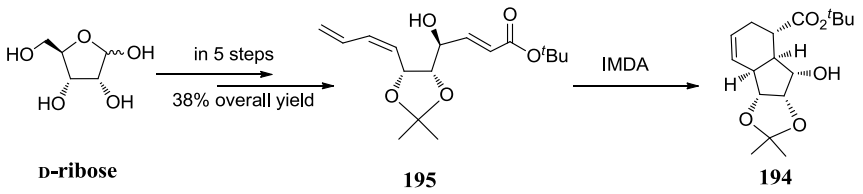
Figure 57

As shown in Figure 57, ribavirin analogues **237**, **298** and **277-280** belong to C5'-*endo* (novel conformation).

Chapter 3

Conclusion

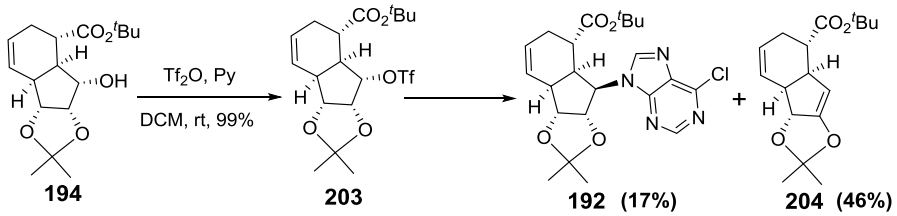
The triene **195** was successfully synthesized from the D-ribose in 5 steps with 38% overall yield, from which cycloadduct **195** was then subjected to cyclization and cycloadduct **194** was obtained using intramolecular Diels-Alder reaction (IMDA) as the key step (Scheme 48).



D-ribose **195** **194**

Scheme 48

The hydroxyl group in cycloadduct **194** was activated to triflate **203**, which was then converted into purine **192** by a convergent method. However, the yield of purine **192** was 17% because of the major production of **204** (46%) (Scheme 49).

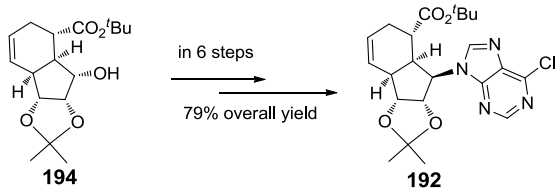


194 **203** **192** (17%) **204** (46%)

Scheme 49

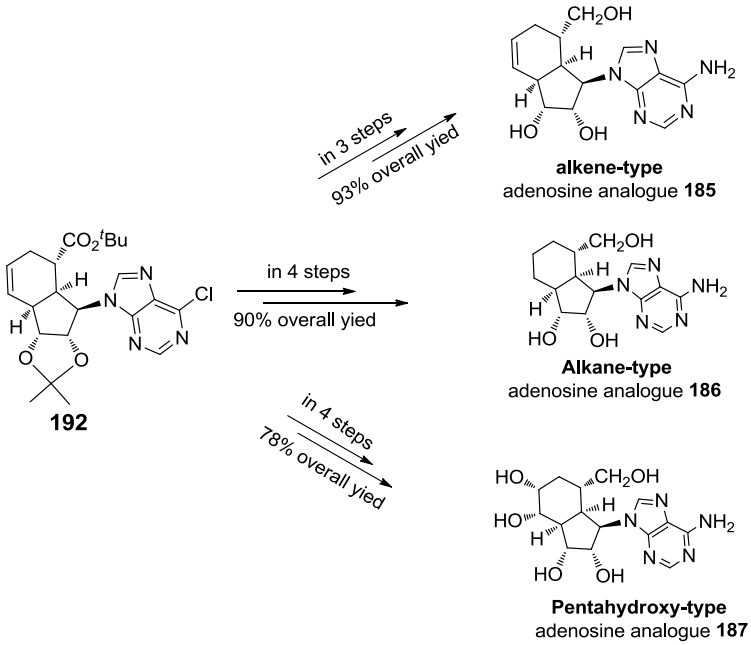
Because the yield of purine **192** was poor by the convergent method, we had

to prepare it by a linear method as shown in Scheme 50



Scheme 50

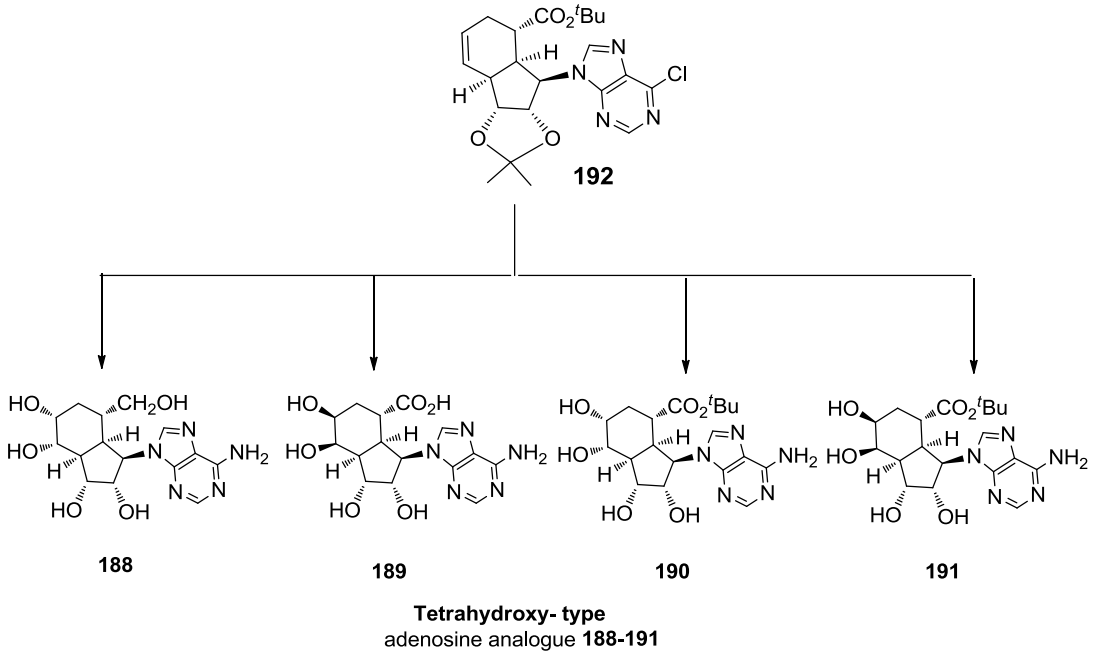
The alkene-type adenosine analogue **185** with a bicyclo[4.3.0]nonane framework was prepared from purine **192** by sequential reduction, amination and deprotection. By modification of the cyclohexene ring, alkane-type adenosine analogue **186** and pentahydroxy-type adenosine analogue **187** were synthesized from purine **192** in 4 steps with 90% and 78% overall yield, respectively.



Scheme 51

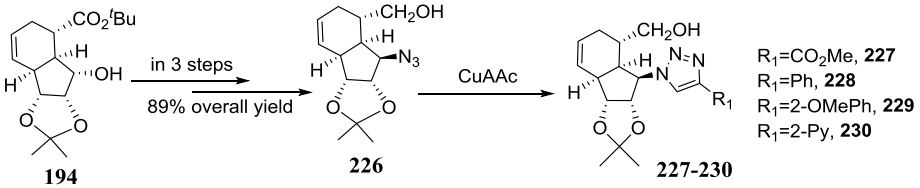
Besides, we also synthesized four tetrahydroxy-type adenosine bearing a

carboxylate group (**188**-**191**) (Scheme 52).

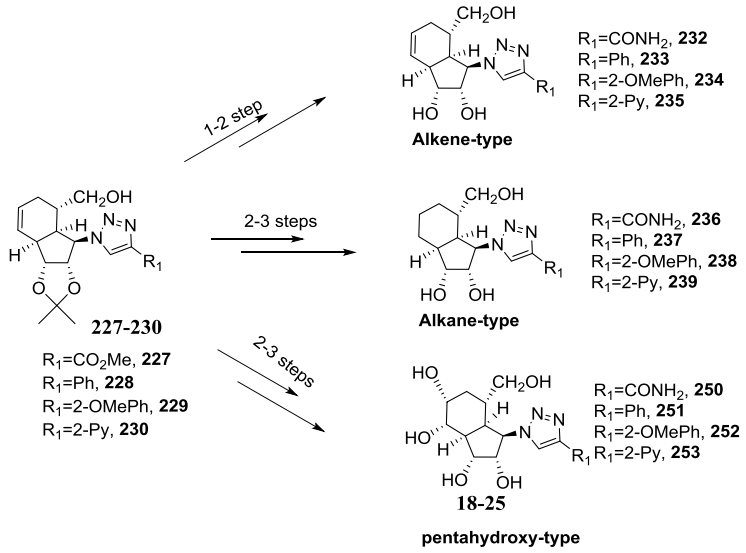


Scheme 52

Twelve novel ribavirin analogues including alkene-type ribavirin analogues (**232**-**235**) with a bicyclo[4.3.0]nonane framework, alkane-type ribavirin analogues (**236**-**239**) and pentahydroxy-type ribavirin analogues (**250**-**253**) were synthesized from D-ribose using a copper catalyzed azide-alkyne cyclization (Huigsen reaction) as the key step (Scheme 53-54).

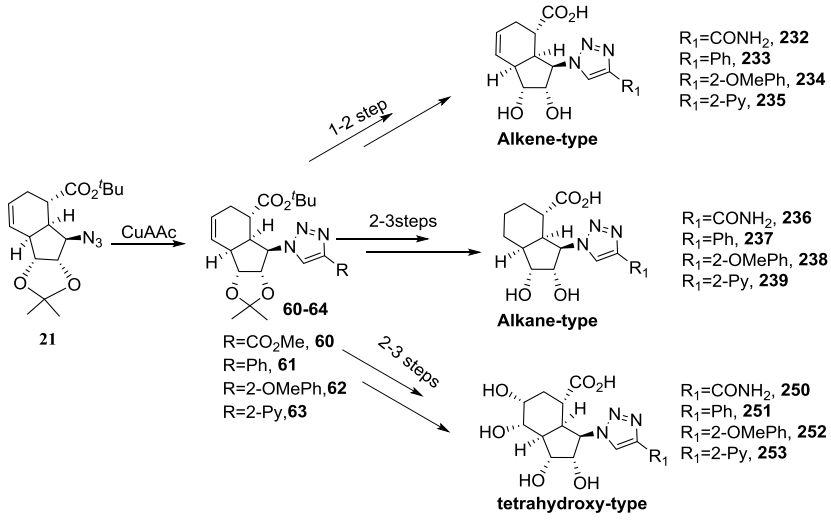


Scheme 53



Scheme 54

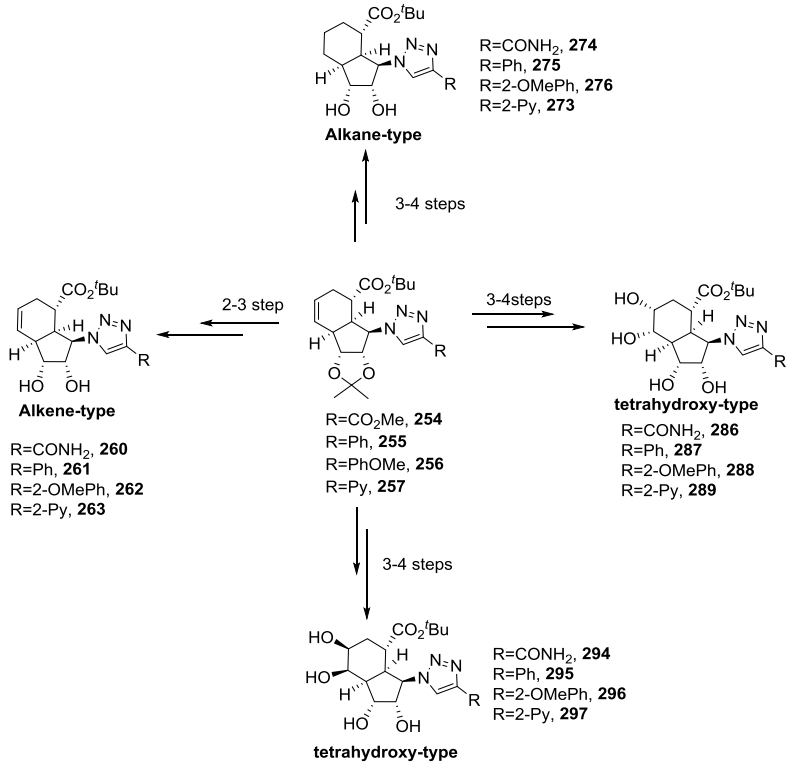
Another twelve ribavirin analogues bearing a carboxylic acid (**264-267**, **277-280**, **290-293**) with a bicyclo [4.3.0]nonane framework were also obtained to increase the solubility in water (Scheme 55).



Scheme 55

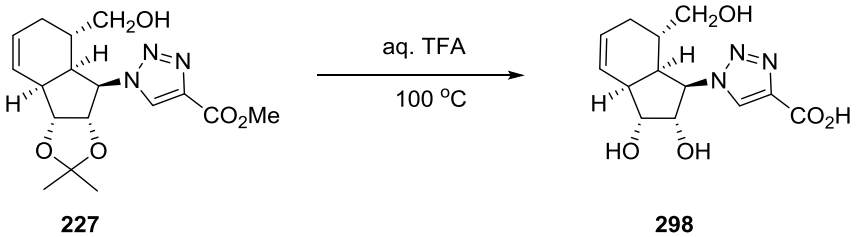
Besides, twelve ribavirin analogues bearing a bulky *tert*-butyl carboxylate group

(**260-263**, **273-276**, **286-289**, **294-297**) with a bicyclo[4.3.0]nonane framework were also prepared successfully (Scheme 56).

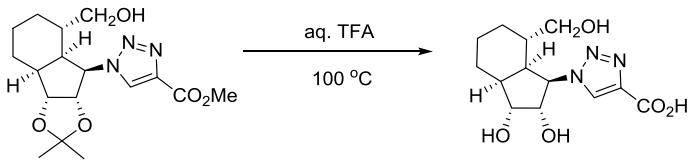


Scheme 56

Finally, two ribavirin analogues bearing a carboxylic acid in triazole were obtained (Scheme 57).



227 **298**

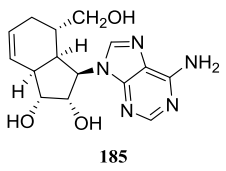


240 **299**

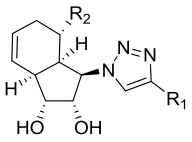
Scheme 57

Analyses of their structures via NMR spectroscopy or X-ray crystallography, the conformations of the adenosine analogues were speculated as following,

(a) C3'-*exo* conformation (South-type conformation) as shown in Figure 58



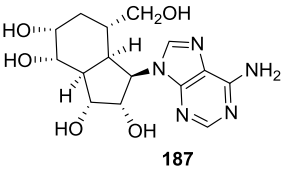
185



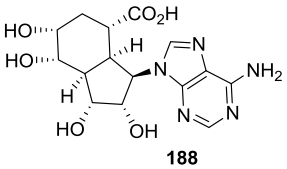
R_1=$CONH_2$, R_2= CH_2OH, **232**
R_1=Ph, R_2= CH_2OH, **233**
R_1=2-OMePh, R_2= CH_2OH, **234**
R_1=2-Py, R_2= CH_2OH, **235**
R_1=$CONH_2$, R_2= CO_2H, **264**
R_1=Ph, R_2= CO_2H, **265**
R_1=2-OMePh, R_2= CO_2H, **266**
R_1=2-Py, R_2= CO_2H, **267**
R_1=CO_2H, R_2= CH_2OH, **298**

Figure 58

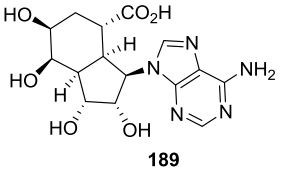
(b) C4'-*exo* conformation (novel conformation) as shown in Figure 59



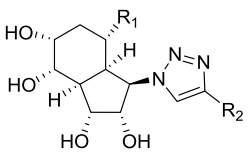
187



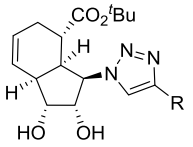
188



189



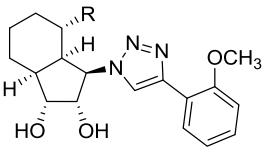
R_1 = CH_2OH, R_2=$CONH_2$, **250**
R_1 =CH_2OH, R_2=Ph, **251**
R_1 =CH_2OH, R_2=2-Py, **253**
R_1 = CO_2H, R_2=$CONH_2$, **290**
R_1 =CO_2H, R_2=Ph, **291**
R_1=CO_2H, R_2=2-Py, **293**



R=$CONH_2$, **260**
R=Ph, **261**
R=2-OMePh, **262**
R=2-Py, **263**

Figure 59

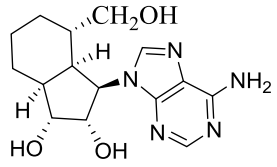
(c) C1'-*exo* conformation (novel conformation) as shown in Figure 60



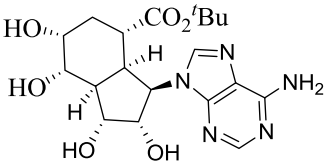
R= CH_2OH, **238**
R= CO_2H, **279**

Figure 60

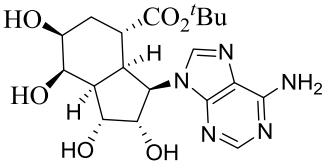
(d) C5'-*endo* conformation (novel conformation) as shown in Figure 61



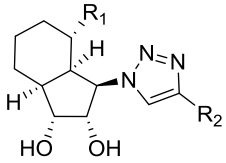
186



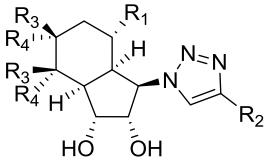
190



191



R_1=CH_2OH, R_2=$CONH_2$, **236**
R_1=CH_2OH, R_2=Ph, **237**
R_1=CH_2OH, R_2=2-Py, **239**
R_1=CH_2OH, R_2=CO_2H, **299**
R_1=CO_2H, R_2=$CONH_2$, **277**
R_1=CO_2H, R_2=Ph, **278**
R_1=CO_2H, R_2=2-Py, **280**



R_1 = CO_2H, R_2=$CONH_2$, R_3=H, R_4=OH, **290**
R_1 =CO_2H, R_2=Ph, R_3=H, R_4=OH, **291**
R_1=CO_2H, R_2=2-Py, R_3=H, R_4=OH, **293**
R_1= $CO_2{}^t$Bu, R_2=$CONH_2$, R_3=OH, R_4=H, **294**
R_1= $CO_2{}^t$Bu, R_2=$CONH_2$, R_3=H, R_4=OH, **286**
R_1 =$CO_2{}^t$Bu, R_2=Ph, R_3=OH, R_4=H, **295**
R_1 =$CO_2{}^t$Bu, R_2=Ph, R_3=H, R_4=H, **287**
R_1 =$CO_2{}^t$Bu, R_2=2-Py, R_3=OH, R_4=H, **297**
R_1 =$CO_2{}^t$Bu, R_2=2-Py, R_3=H, R_4=OH, **289**

Figure 61

Experimental Detail

Nuclear magnetic resonance (NMR) spectra were measured with Bruker Avance III 400 NMR spectrometer at 400.13 MHz (^{1}H) or at 100.61 MHz (^{13}C) as mentioned, in $CDCl_3$ solutions, unless stated otherwise. All chemical shifts were recorded in ppm relative to tetramethylsilane ($\delta = 0.0$). Spin-spin coupling constants (*J* value) recorded in Hz were measured directly from the spectra. MS and HRMS were measured on a ThermoFinnigan MAT 95 KL at the Department of Chemistry or Bruker 9.4 Tesla Fourier Transform Ion Cyclotron Resonance Mass spectrometer (Bruker 9.4T FT-ICR-MS) at the Faculty of Science, The Chinese University of Hong Kong, Hong Kong, China. All reactions were monitored by analytical thin-layer chromatography (TLC) on Merck aluminium-precoated plates of silica gel 60 F254 with detection by spraying with 5% (w/v) dodecamolybdophosphoric acid in ethanol and subsequent heating. E. Merck silica gel 60 (230-400 mesh) was used for flash column chromatography. All reagents and solvents were general reagent grade unless otherwise stated. Pyridine was distilled from barium oxide and stored in the presence of potassium hydroxide pellets. DMF was dried by magnesium sulfate, filtered and the filtrate was then distilled under reduced pressure. DMSO was dried by anhydrous magnesium sulfate, filtered and then the filtrate was dried by calcium hydride and distilled under reduced pressure. Acetone was dried by anhydrous $CaSO_4$ and filtered. THF and toluene were freshly distilled from Na/benzophenone ketyl under nitrogen. Dichloromethane was freshly distilled from P_2O_5 under

nitrogen. Other reagents were purchased from commercial suppliers and were used without purification.

General procedure for copper catalyzed azide-alkyne cycloaddition. To a 0.25M solution of azide (1 eq.) and alkyne (1.5 eq.) in the mixture of *t*-BuOH/ H_2O (v/v, 1/1) was added sodium ascorbate (0.05 eq., 1.0M) and $CuSO_4 \cdot 5H_2O$ (0.1 eq., 0.3M). The mixture was heated and stirred at 70 ^oC until all the starting material was consumed, which was checked by TLC. The reaction mixture was filtered through a pad of anhydrous $MgSO_4$/silica gel and washed with EtOAc. The filtrate was concentrated under reduced pressure, and the residue was fractionated by flash column chromatography to afford the triazole products.

General procedure for deprotection of the isopropylidene. To a solution of alkyl ether in H_2O (50 mL) was added TFA (0.5 mL) and the reaction mixture was stirred at room temperature until all the starting material consumed, which was checked by TLC. The solvent was removed under reduced pressure and the residue was fractionated by flash column chromatography to afford the corresponding compounds.

General procedure for hydrogenation of alkene. To a solution of alkene in MeOH (10 mL) was added 10% Pd-on-charcoal (5% of alkene in weight) and the mixture was activated with an atmosphere of H_2 (balloon) three times followed by stirring under the same H_2 atmosphere at room temperature. After the consumption of starting material, the mixture was filtered and washed with MeOH. The filtrate

was concentrated under reduced pressure and the residue was fractionated by flash column chromatography to afford the corresponding compounds.

General procedure for dihydroxylation of alkene. NMO (3 eq.) was added to a 0.1M solution of alkene (1 eq.) in acetone/H_2O (v/v, 4/1) with a catalytic amount of osmium tetraoxide (0.04 eq., 10 mg/mL *t*-butanol solution) at room temperature. The mixture was stirred until all the starting material was consumed, which was checked by TLC. The reaction mixture was then diluted with EtOAc and quenched with saturated $Na_2S_2O_3$ solution. The resultant mixture was extracted with $CHCl_3$/MeOH (v/v, 4/1) (6 × 15 mL). The combined extracts were washed with brine, dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was fractionated by flash column chromatography to afford the diols.

Adenosine analogue 185. Following the general procedure for deprotection of the isopropylidene, purine **209** (52 mg, 0.15 mmole) was converted into adenosine analogue **185** in 10 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 3:1) to afford adenosine analogue **185** (45.2 mg, 98%) as a white solid: mp 234-236 ^oC; $[\alpha]_D^{20}$ +32.9 (*c* 0.92, MeOH); R_f 0.37 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3390, 1682, 1652, 1482, 1442, 1421, 1336, 1309, 1206, 1140 cm^{-1}; ^1H NMR (400 MHz, CD_3OD:D_2O 1:1) δ 1.22-1.28 (1H, m), 1.37-1.43 (1H, m), 1.66-1.71 (1H, m), 2.69 (1H, d, *J* = 7.3 Hz), 3.03-3.08 (1H, m), 3.15-3.24 (2H, m), 4.09 (1H, d, *J* = 3.8 Hz), 5.02-5.08 (2H, m), 5.68-5.75 (2H, m),

8.19 (1H, s), 8.31 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.0 (CH_2), 34.2 (CH), 35.7 (CH), 41.5 (CH), 61.8 (CH), 65.0 (CH_2), 74.0 (CH), 76.5 (CH), 119.6 (C), 127.2 (CH), 127.5 (CH), 141.4 (CH), 151.0 (C), 153.6 (CH), 156.6 (C); MS (ESI) *m/z* (relative intensity) 340 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{15}H_{19}N_5O_3$ [M+Na]$^+$ 340.1380, found 340.1381.

Adenosine analogue 186. Following the general procedure for hydrogenation of alkene, adenosine analogue **185** (36.3 mg, 0.11 mmole) was converted into adenosine analogue **186** in 48 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 3:1) to afford adenosine analogue **186** (35.4 mg, 97%) as a white solid: mp 162-164 ^{o}C; $[\alpha]_D^{20}$ -48.1 (*c* 1.10, MeOH); R_f 0.35 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3338, 3219, 2930, 2862, 1648, 1603, 1575, 1481, 1418, 1333, 1308, 1204, 1135 cm^{-1}; ^{1}H NMR (400 MHz, $CHCl_3$:CD_3OD 1:1) δ 0.92-1.02 (1H, m), 1.39-1.46 (1H, m), 1.46-1.55 (1H, m), 1.57-1.62 (2H, m), 1.79-1.83 (1H, m), 1.87-1.92 (1H, m), 2.26-2.34 (2H, m), 2.36-2.44 (2H, m), 4.10 (1H, t, *J* = 6.8 Hz), 4.84 (1H, dd, *J* = 8.9, 7.2 Hz), 5.00-5.03 (1H, m), 8.20 (1H, s), 8.34 (1H, s); ^{13}C NMR (100 MHz, $CHCl_3$:CD_3OD 1:1) δ 20.7 (CH_2), 26.3 (CH_2), 29.0 (CH_2), 37.6 (CH), 38.6 (CH), 44.6 (CH), 65.2 (CH), 65.4 (CH_2), 71.0 (CH), 72.1 (CH), 119.9 (C), 140.9 (CH), 151.1 (C), 152.8 (CH), 156.3 (C); MS (ESI) *m/z* (relative intensity) 320 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{15}H_{21}N_5O_3$ [M+Na]$^+$ 320.1717, found 320.1717.

Adenosine analogue 187. Following the general procedure for deprotection of the isopropylidene, pyrimidine **212** (63.7 mg, 0.16 mmole) was converted into adenosine analogue **187** in 18 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH:30% aq.NH_3, 3:1:0.2) to afford adenosine analogue **187** (54.9 mg, 96%) as a white solid: mp 203-205 ^oC; $[\alpha]_D^{20}$ -57.7 (*c* 0.625, H_2O); R_f 0.32 ($CHCl_3$:MeOH:$NH_3.H_2O$, 3:1:0.2); IR (thin film) 3537, 3323, 3161, 3078, 2900, 1678, 1618, 1573, 1489, 1423, 1339, 1322, 1255, 1221, 1112, 1089, 1076, 1016 cm^{-1}; ^1H NMR (400 MHz, D_2O) δ 1.38 (1H, q, *J* = 11.8 Hz), 1.55-1.63 (4H, m), 1.64-1.70 (1H, m), 2.06 (1H, d, *J* = 10.2 Hz), 2.25-2.31 (2H, m), 2.44-2.47 (1H, m), 3.81 (1H, d, *J* = 10.8 Hz), 4.07-4.10 (2H, m), 4.69-4.71 (1H, m), 4.88-4.91 (1H, m), 8.02 (1H, s), 8.27 (1H, s); ^{13}C NMR (100 MHz, D_2O) δ 29.0 (CH_2), 33.3 (CH), 35.8 (CH), 51.3 (CH), 62.4 (CH), 63.6 (CH_2), 67.3 (CH), 68.5 (CH), 68.8 (CH), 69.7 (CH), 118.4 (C), 139.6 (CH), 149.3 (C), 152.4 (CH), 155.2 (C)；MS (ESI) *m/z* (relative intensity) 374 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{15}H_{21}N_5O_5$ $[M+Na]^+$ 374.1435, found 374.1435.

Adenosine analogue 188. Following the general procedure for deprotection of the isopropylidene, purine **214** (42.7 mg, 0.09 mmole) was converted into adenosine analogue **188** at 100 ^oC in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 1:3) to afford adenosine analogue **188** (24.3 mg, 72%) as a white solid: mp 190-193 ^oC; $[\alpha]_D^{20}$ -14.5 (*c* 0.94, DMF); R_f 0.33 ($CHCl_3$:MeOH, 1:3); IR (thin film) 3368, 2924, 1663, 1652, 1568, 1487, 1417, 1392,

1331, 1304, 1255, 1122, 1086 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.66 (1H, q, *J* = 12.2 Hz), 1.76-1.79 (1H, m), 2.20-2.27 (1H, m), 2.49-2.54 (1H, m), 2.93-2.99 (1H, m), 3.86-3.88 (1H, m), 4.10 (1H, s), 4.15 (1H, t, *J* = 8.1 Hz), 4.87-4.93 (2H, m), 8.18 (1H, s), 8.19 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 32.2 (CH_2), 37.4 (CH), 45.0 (CH), 52.2 (CH), 64.7 (CH), 69.09 (CH), 69.10 (CH), 69.8 (CH), 71.5 (CH), 119.8 (C), 141.6 (CH), 151.1 (C), 153.1 (CH), 156.6 (C), 180.8 (C)；MS (ESI) *m/z* (relative intensity) 366 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{15}H_{19}N_5O_6$ $[M+H]^+$ 366.1408, found 366.1408.

Adenosine analogue 189. Following the general procedure for deprotection of the isopropylidene, purine **215** (36 mg, 0.08 mmole) was converted into adenosine analogue **189** at 100 ^{o}C in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 1:3) to afford adenosine analogue **189** (25.4 mg, 89%) as a white solid: mp 194-197 ^{o}C; $[\alpha]_D^{20}$ -66.4 (*c* 0.32, DMF); R_f 0.33 ($CHCl_3$:MeOH, 1:3); IR (thin film) 3401, 2961, 2924, 2516, 2224, 1690, 1654, 1578, 1501, 1385, 1339, 1236, 1117, 1073, 1020 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.47-1.53 (1H, m), 1.98-2.03 (1H, m), 2.53-2.58 (1H, m), 2.75-2.78 (1H, m), 3.03-3.09 (1H, m), 3.88-3.90 (1H, m), 3.98 (1H, s), 4.66-4.69 (1H, m), 4.90 (1H, s), 4.98 (1H, s), 8.23 (1H, s), 8.35 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 35.3 (CH_2), 36.8 (CH), 49.3 (CH), 49.5 (CH), 49.9 (CH), 69.3 (CH), 69.9 (CH), 70.5 (CH), 71.9 (CH), 119.9 (C), 143.9 (CH), 146.8 (C), 151.5 (CH), 152.8 (C), 178.4 (C)；MS (ESI) *m/z* (relative intensity) 366 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{15}H_{19}N_5O_6$

$[M+H]^+$ 366.1408, found 366.1413.

Adenosine analogue 190. Following the general procedure for deprotection of the isopropylidene, purine **214** (62.5 mg, 0.14 mmole) was converted into adenosine analogue **190** in 18 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:2) to afford adenosine analogue **190** (55.9 mg, 98%) as a white solid: mp 257-261 ^oC; $[\alpha]_D^{20}$ -13.9 (*c* 0.98, MeOH); R_f 0.37 ($CHCl_3$:MeOH, 5:2); IR (thin film) 3430, 3401, 2916, 1705, 1647, 1574, 1420, 1203, 1141, 1115, 1088, 1058 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 0.99 (9H, s) 1.64-1.73 (1H, m), 1.73-1.77 (1H, m), 2.53-2.57 (2H, m), 2.58-2.62 (1H, m), 2.97-3.04 (1H, m), 3.83-3.86 (1H, m), 4.10 (1H, s), 4.13-4.15 (1H, m), 4.59 (1H, s), 4.81 (1H, t, *J* = 7.4 Hz), 8.15 (1H, s), 8.20 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 27.7 (CH_3), 32.1 (CH_2), 36.5 (CH), 42.7 (CH), 49.8 (CH), 52.1 (CH), 68.7 (CH), 69.6 (CH), 70.2 (CH), 71.8 (CH), 81.5 (C), 120.4 (C), 142.4 (CH), 151.4 (C), 153.4 (CH), 157.0 (C), 174.3 (C)； MS (ESI) *m/z* (relative intensity) 444 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{27}N_5O_6$ $[M+Na]^+$ 444.1854, found 444.1855.

Adenosine analogue 191. Following the general procedure for deprotection of the isopropylidene, purine **215** (56.6 mg, 0.12 mmole) was converted into adenosine analogue **191** in 18 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:2) to afford adenosine analogue **191** (51.2 mg,

99%) as a white solid: mp 257-260 ^{o}C; $[\alpha]_{D}^{20}$ -40.4 (*c* 0.70, MeOH); R_f 0.40 ($CHCl_3$:MeOH, 5:2); IR (thin film) 3306, 3127, 2974, 1709, 1660, 1604, 1576, 1364, 1269, 1208, 1152, 1066 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:3) δ 0.98 (9H, s), 1.42 (1H, t, *J* = 12.7 Hz), 1.95-2.00 (1H, m), 2.52-2.57 (1H, m), 2.74 (1H, br s), 3.02 (1H, dt, *J* = 11.1, 7.6 Hz), 3.86-3.88 (1H, m), 3.97 (1H, s), 4.64-4.66 (1H, m), 4.82-4.87 (2H, m), 8.21 (1H, s), 8.26 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:3) δ 27.7 (CH_3), 35.5 (CH_2), 37.5 (CH), 38.9 (CH), 63.8 (CH), 69.1 (CH), 69.9 (CH), 70.4 (CH), 72.0 (CH), 81.3 (C), 81.4 (CH), 120.1 (C), 141.5 (CH), 151.4 (C), 153.3 (CH), 156.8 (C), 175.3 (C)；MS (ESI) *m/z* (relative intensity) 444 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{27}N_5O_6$ $[M+Na]^+$ 444.1854, found 444.1854.

Purine 192. To a solution of pyrimidine **207** (138 mg, 0.32 mmole) in triethyl orthoformate (3.6 mL) was added TFA (1.5 mL). The mixture was stirred at room temperature for 60 h, and then heated at 60 ^{o}C for 12 h. After the starting material was consumed, the reaction mixture was cooled to room temperature and quenched with saturated $NaHCO_3$ solution and the aqueous phase was extracted with EtOAc (3 × 20mL). The combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was fractionated by flash column chromatography (hexane:EtOAc, 2:1) to afford purine **192** (141.2 mg, 92% yield) as a white solid: mp 65-66 ^{o}C; $[\alpha]_{D}^{20}$ +38.8 (*c* 1.07, $CHCl_3$); R_f 0.37 (hexane:EtOAc, 2:1); IR (thin film) 2982, 2359, 2339, 1716, 1591, 1557, 1370, 1336, 1199, 1149, 1068 cm^{-1}; ^{1}H NMR

(400 MHz) δ 1.00 (9H, s), 1.29 (3H, s), 1.49 (3H, s), 1.70-1.89 (2H, m), 2.48-2.50 (1H, m), 2.91 (1H, s), 3.23-3.30 (1H, m), 4.57-4.60 (1H, m), 5.07-5.10 (1H, m), 5.51 (1H, br s), 5.70 (1H, d, J = 8.6 Hz), 5.87 (1H, d, J = 9.7 Hz), 8.08 (1H, s), 8.72 (1H, s); ^{13}C NMR (100 MHz) δ 25.1 (CH_3), 27.46 (CH_3), 27.54 (CH_2), 27.8 (CH_3), 38.8 (CH), 41.8 (CH), 43.0 (CH), 64.8 (CH), 81.0 (C), 81.1 (CH), 84.0 (CH), 113.5 (C), 126.1 (CH), 126.2 (CH), 131.8 (C), 145.4 (CH), 151.2 (C), 151.9 (CH), 152.6 (C), 173.2 (C); MS (ESI) *m/z* (relative intensity) 447 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{22}H_{27}ClN_4O_4$ [M+Na]$^+$ 447.1794, found 447.1793.

Alcohol 193. To a stirred solution of purine **192** (140.1 mg, 0.31 mmole) in dry toluene (7 mL) at -78 ^{o}C was added DIBAL-H solution (0.52 mL, 1.2 M in toluene) over 1.5 h. MeOH (2 mL) and $NaBH_4$ (5.9 mg, 0.16 mmole) were then added to the above solution and the mixture was stirred at room temperature for 10 min. Removal of the solvent under reduced pressure was followed by flash column chromatography (hexane:EtOAc, 1:2) of the residue to furnish alcohol **193** (118.1 mg, 97% yield) as a white solid: mp 70-71 ^{o}C; $[\alpha]_D^{20}$ +20.2 (*c* 1.00, $CHCl_3$); R_f 0.30 (hexane:EtOAc, 2:3); IR (thin film) 3746, 3384, 2918, 2359, 2339, 1590, 1558, 1396, 1337, 1207, 1159, 1054 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.15-0.21 (1H, m), 1.29 (3H, s), 1.42 (1H, s), 1.47 (3H, s), 1.88-1.90 (1H, m), 2.79-2.81 (1H, m), 3.15-3.19 (2H, m), 3.33 (2H, ddd, J = 18.0, 10.5, 7.5 Hz), 4.83 (1H, d, J = 5.7 Hz), 4.99 (1H, d, J = 5.6 Hz), 5.22 (1H, d, J = 7.6 Hz), 5.40-5.44 (1H, m), 5.65 (1H, dd, J = 10.2, 1.5 Hz), 7.93 (1H, s), 8.65 (1H, s); ^{13}C NMR (100 MHz) δ 23.5 (CH_2), 24.1 (CH_3), 26.5 (CH_3), 32.6

(CH), 38.7 (CH), 42.7 (CH), 64.7 (CH), 66.1 (CH_2), 84.9 (CH), 85.6 (CH), 111.1 (C), 125.5 (CH), 128.7 (C), 130.3 (CH), 144.8 (CH), 151.1 (C), 152.0 (CH), 152.6 (C)；MS (ESI) *m/z* (relative intensity) 377 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{21}ClN_4O_3$ $[M+Na]^+$ 377.1375, found 377.1375.

Cycloadduct 194. Methylene blue (*ca.* 1 mg) was added to a solution of triene **195** (480 mg, 1.55 mmole) in toluene (500 mL) in a seal tube. The solution was degassed and heated to 130 ^oC and stirred for 60 h. The solution was filtered through a pad of silica gel and washed with Et_2O. The filtrate was concentrated under reduced pressure and the residue was fractionated by flash column chromatography (hexane:Et_2O, 2:1) to afford the cycloadduct **194** (436.8 mg, 91% yield) as a colorless oil: $[\alpha]_D^{20}$ +33.4 (*c* 1.00, $CHCl_3$); R_f 0.40 (hexane:Et_2O, 1:1); IR (thin film) 3436, 2979, 2933, 1726, 1456, 1369, 1251, 1210, 1155, 1118, 1062, 1041 cm^{-1}; ^1H NMR (400 MHz, C_6D_6) δ 1.16 (3H, s), 1.33 (9H, s), 1.39 (3H, s), 1.99-2.08 (1H, m), 2.37 (1H, d, *J* = 10.8 Hz), 2.47-2.53 (1H, m), 2.70-2.75 (1H, m), 2.81-2.83 (1H, m), 2.97-2.99 (1H, m), 3.66 (1H, dt, *J* = 15.6, 5.2 Hz), 4.06 (1H, d, *J* = 5.7 Hz), 4.18 (1H, *t*, *J* = 5.6 Hz), 5.24-5.27 (1H, m), 5.42-5.47 (1H, m)；^{13}C NMR (100 MHz, C_6D_6) δ 23.1 (CH_2), 24.3 (CH_3), 26.3 (CH_3), 28.0 (CH_3), 37.5 (CH), 40.2 (CH), 42.7 (CH), 73.7 (CH), 78.3 (CH), 79.7 (C), 83.4 (CH), 110.6 (C), 126.4 (C), 126.9 (C), 173.8 (C)；MS (ESI) *m/z* (relative intensity) 333 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{26}O_5$ $[M+Na]^+$ 333.1672, found 333.1673.

Triene 195. To a stirred solution of dimethyl sulfoxide (6.94 mL, 97.69 mmole) in anhydrous THF (100 mL) was added NaH (186.1 mg, 4.65 mmole, 60% in mineral oil) at room temperature under N_2. The reaction mixture was stirred at room temperature for 5 h and then cooled to 0 ^oC. Allyltriphenyl phosphonium bromide (1.33 g, 3.49 mmole) was added and the reaction mixture was stirred at 0 ^oC for an extra 20 min. Then a solution of ester **200** (666 mg, 2.33 mmole) in anhydrous THF (10 mL) was added dropwise to the above solution. Upon complete addition, the reaction mixture was stirred at 0 ^oC for further 1.5 h and was then quenched with saturated NH_4Cl solution. The aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$ and filtered. Removal of the solvent under reduced pressure was followed by flash column chromatography (hexane:EtOAc, 4:1) of the residue to yield triene **195** (426 mg, 59% yield; 64% yield BORSM) as a colorless oil: $[\alpha]_D^{20}$ -93.9 (*c* 1.00, $CHCl_3$); R_f 0.40 (hexane:EtOAc, 3:1); IR (thin film) 3435, 3307, 2981, 2931, 1714, 1698, 1657, 1383, 1370, 1310, 1256, 1217, 1153, 1053 cm^{-1}; ^1H NMR (400 MHz) δ 1.34 (3H, s), 1.44 (9H, s), 1.46 (3H, s), 2.42 (1H, d, *J* = 5.1 Hz), 4.05 (1H, *t*, *J*= 6.9 Hz), 4.25-4.30 (1H, m), 5.23 (1H, d, *J*= 10.1 Hz), 5.29 (1H, d, *J*= 16.8 Hz), 5.57 (1H, t, *J*= 10.0 Hz), 5.97 (1H, dd, *J*= 15.8, 1.8 Hz), 6.21 (1H, t, *J*= 11.1 Hz), 6.63 (1H, dt, *J* = 16.8, 10.4 Hz), 6.91 (1H, dd, *J* = 15.7, 4.3 Hz); ^{13}C NMR (100 MHz) δ 25.3 (CH_3), 27.7 (CH_3), 28.2 (CH_3), 69.7 (CH), 73.7 (CH), 80.52 (C), 80.54 (CH), 109.3 (C), 121.0 (CH_2), 123.5 (CH), 126.3 (CH), 131.2 (CH), 133.4 (CH), 145.7 (CH), 165.8 (C); MS (ESI) *m/z* (relative intensity) 333 ($[M+Na]^+$, 100); HRMS (ESI) calcd for

$C_{17}H_{26}O_5$ $[M+Na]^+$ 333.1672, found 333.1675.

Ester 200. A solution of the lactol **199** (0.81 g, 4.33 mmole), *t*-butyl acrylate (6.28 mL, 43.23 mmole) and second generation Grubbs catalyst (184.7 mg, 0.22 mmole) in CH_2Cl_2 (24 mL) was heated at 40 °C for 72 h. The solvent was evaporated and the residue was fractionated by flash column chromatography (hexane:Et_2O, 100:1; to hexane:EtOAc, 2:1) to afford ester **200** (1.02 g, 82% yield) as a mixture of diastereoisomers (100/18 by ^{1}H NMR) as a colorless oil: $[\alpha]_D^{20}$ -20.2 (*c* 1.01, $CHCl_3$); R_f 0.43 (hexane:EtOAc, 2:1); IR (thin film) 3443, 2981, 2939, 2359, 1715, 1652, 1456, 1370, 1308, 1255, 1212, 1157, 1072 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.31 (3H, s, *major*), 1.37 (3H, s, *minor*), 1.45 (9H, s, *major*), 1.46 (9H, s, *minor*), 1.48 (3H, s, *major*), 1.56 (3H, s, *minor*), 3.66 (1H, d, *J* = 3.0 Hz, *major*), 4.02 (1H, d, *J* = 10.4 Hz, *minor*), 4.58 (1H, dd, *J* = 6.4, 3.9 Hz, *minor*), 4.62-4.65 (1H, m, *minor*), 4.63 (1H, d, *J* = 5.8 Hz, *major*), 4.67-4.69 (1H, m, *minor*), 4.72 (1H, dd, *J* = 5.9, 1.2 Hz, *major*), 4.74-4.76 (1H, m, *major*), 5.31 (1H, dd, *J* = 10.4, 3.9 Hz, *minor*), 5.51 (1H, d, *J* = 2.7 Hz, *major*), 5.95 (1H, dd, *J* = 15.8, 1.5 Hz, *major*), 6.04 (1H, dd, *J* = 15.7, 2.0 Hz, *minor*), 6.72 (1H, dd, *J* = 15.7, 4.2 Hz, *minor*), 6.90 (1H, dd, *J* = 15.7, 6.5 Hz, *major*); ^{13}C NMR (100 MHz) δ 25.07 (CH_3), 25.10 (CH_3), 26.29 (CH_3), 26.62 (CH_3), 28.17 (CH_3), 28.18 (CH_3), 79.00 (CH), 79.42 (CH), 80.97 (C), 81.05 (C), 83.48 (CH), 84.36 (CH), 86.01 (CH), 86.41 (CH), 96.71 (CH), 103.28 (CH), 112.87 (C), 114.66 (C), 124.30 (CH), 124.41 (CH), 142.34 (CH), 145.45 (CH), 165.29 (C), 165.64 (C); MS (ESI) *m/z* (relative intensity) 309 ($[M+Na]^+$, 100); HRMS (ESI) calcd for

$C_{14}H_{22}O_6$ $[M+Na]^+$ 309.1309, found 309.1306.

Alcohol 201. To a stirred solution of cycloadduct **194** (83 mg, 0.27 mmole) in dry toluene (6 mL) was added diisobutylaluminium hydride (DIBAL-H) solution (0.47 mL, 1.2M in toluene) at -78 ^oC dropwise. The mixture was stirred for 2.5 h and quenched with saturated NH_4Cl solution at 0 ^oC. The mixture was filtered through a thin pad of celite and washed with EtOAc until no more product was detected, which was checked by TLC. The filtrate was concentrated under reduced pressure and the residue was fractionated by flash column chromatography (hexane:EtOAc, 1:3) to give alcohol **201** (60 mg, 93% yield) as a white solid: mp 119-122 ^oC; $[\alpha]_D^{20}$ +7.8 (*c* 1.28, $CHCl_3$); R_f 0.23 (hexane:EtOAc, 1:3); IR (thin film) 3401, 3014, 2987, 2918, 1648, 1440, 1382, 1274, 1252, 1209, 1163, 1106, 1058 cm^{-1}; ^1H NMR (400 MHz) δ 1.31 (3H, s), 1.46 (3H, s), 2.01-2.05 (1H, m), 2.12-2.21 (3H, m), 2.43-2.44 (2H, m), 2.56 (1H, br s), 3.52 (1H, d, *J*= 6.8 Hz), 3.78 (1H, dd, *J*= 9.3, 5.5 Hz), 4.37 (1H, d, *J*= 5.6 Hz), 4.47 (1H, *t*, *J*= 5.6 Hz), 5.40 (1H, d, *J*= 10.1 Hz), 5.57-5.60 (1H, m); ^{13}C NMR (100 MHz) δ 22.8 (CH_2), 24.2 (CH_3), 26.1 (CH_3), 33.0 (CH), 38.8 (CH), 41.6 (CH), 65.6 (CH_2), 73.5 (CH), 78.4(CH), 83.3 (CH), 110.5 (C), 125.6(CH), 127.3 (CH)；MS (ESI) *m/z* (relative intensity) 263 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{20}O_4$ $[M+Na]^+$ 263.1254, found 263.1259.

Mesylate 202. To a stirred solution of cycloadduct **194** (77 mg, 0.25 mmole) and triethylamine (0.14 mL, 0.99 mmole) in dry CH_2Cl_2 (8 mL) at 0 ^oC was added

methanesulfonyl chloride (0.04 mL, 0.50 mmole). The reaction mixture was stirred at room temperature for 2 h and quenched with saturated $NaHCO_3$ solution (3 mL). The aqueous phase was extracted with EtOAc (3 × 10 mL) and the combined organic extracts were washed with brine, dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was fractionated by flash column chromatography (hexane:EtOAc, 4:1) to afford mesylate **202** (94.4 mg, 98% yield) as a colorless oil: $[\alpha]_D^{20}$ +9.2 (*c* 0.95, $CHCl_3$); R_f 0.22 (hexane:EtOAc, 4:1); IR (thin film) 2979, 2936, 1726, 1457, 1366, 1343, 1258, 1211, 1172, 1162, 1045, 1019 cm^{-1}; ^1H NMR (400 MHz) δ 1.31 (3H, s), 1.42 (9H, s), 1.49 (3H, s), 2.23-2.29 (1H, m), 2.50-2.54 (1H, m), 2.67 (1H, br s), 2.80 (1H, d, *J* = 6.2 Hz), 2.95-2.99 (1H, m), 3.11 (3H, s), 4.38 (1H, d, *J* = 5.4 Hz), 4.58 (1H, dd, *J*= 10.7, 5.0 Hz), 5.30 (1H, t, *J* = 5.3 Hz), 5.45 (1H, d, *J* = 10.2 Hz), 5.67-5.70 (1H, m)；^{13}C NMR (100 MHz) δ 22.4 (CH_2), 24.5 (CH_3), 26.2 (CH_3), 28.1 (CH_3), 36.5 (CH), 38.7 (CH), 38.86 (CH_3), 38.91 (CH), 76.9 (CH), 80.9 (C), 83.2 (CH), 111.6 (C), 125.3 (CH), 127.2 (CH), 173.1 (C)； MS (ESI) *m/z* (relative intensity) 411 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{28}O_7S$ $[M+Na]^+$ 411.1448, found 411.1449.

Triflate 203. To a stirred solution of cycloadduct **194** (210 mg, 0.68 mmole) and pyridine (0.26 mL, 3.25 mmole) in dry CH_2Cl_2 (10 mL) was added trifluoromethanesulfonic anhydride (0.27 mL, 1.62 mmole) at 0 ^oC. The reaction mixture was stirred at room temperature for 1 h and was quenched with saturated $NaHCO_3$ solution. The aqueous phase was extracted with EtOAc (3 × 15 mL) and

the combined extracts were concentrated under reduced pressure. The residue was fractionated by flash column chromatography (hexane:Et_2O, 4:1) to afford triflate **203** (295 mg, 99% yield) as a colorless oil: $[\alpha]_D^{20}$ +1.5 (*c* 1.30, $CHCl_3$); R_f 0.30 (hexane:Et_2O, 4:1); IR (thin film) 2981, 2938, 1729, 1416, 1385, 1372, 1246, 1211, 1148, 1047 cm^{-1}; ^1H NMR (400 MHz) δ 1.34 (3H, s), 1.45 (9H, s), 1.52 (3H, s), 2.17-2.26 (1H, m), 2.56-2.60 (1H, m), 2.77-2.78 (1H, m), 3.07-3.12 (1H, m), 4.42 (1H, d, *J* = 5.5 Hz), 4.65 (1H, t, *J* = 5.4 Hz), 4.74 (1H, dd, *J* = 9.8, 5.2 Hz), 5.50 (1H, d, *J* = 10.0 Hz), 5.71-5.74 (1H, m); ^{13}C NMR (100 MHz) δ 22.7 (CH_2), 24.6 (CH_3), 26.1 (CH_3), 28.1 (CH_3), 36.8 (CH), 39.0 (CH), 39.7 (CH), 77.0 (CH), 81.4 (C), 83.2 (CH), 87.5 (CH), 112.5 (C), 125.1 (CH), 127.2 (C), 172.5 (C); MS (ESI) *m/z* (relative intensity) 465 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{25}F_3O_7S$ $[M+Na]^+$ 465.1165, found 465.1161.

Azide 205. Triflate **203** (235 mg, 0.53 mmole) was dissolved in dry DMF (1 mL) and 3**Å** Molecular Sieves (*ca.* 30 mg) was added to the above solution followed by stirring at room temperature for 0.5 h. LiN_3 (260 mg, 5.31 mmole) was then added and the reaction mixture was stirred for an extra 120 h. The mixture was quenched with H_2O and the aqueous phase was extracted by Et_2O (3 × 20 mL). The combined organic extracts were dried over anhydrous $MgSO_4$ and filtered. The filtrate was concentrated under reduced pressure and the residue was fractionated by flash column chromatography (hexane:Et_2O, 10:1) to yield azide **205** (169.2 mg, 95% yield) as a colorless oil: $[\alpha]_D^{20}$ +6.4 (*c* 1.05, $CHCl_3$); R_f 0.47 (hexane:Et_2O, 3:1); IR (thin film)

2980, 2935, 2359, 2111, 1725, 1368, 1258, 1209, 1150, 1070 cm^{-1}; ^1H NMR (400 MHz) δ 1.28 (3H, s), 1.46 (9H, s), 1.52 (3H, s), 2.00-2.08 (1H, m), 2.16 ((1H, dt, *J* = 16.3, 5.0 Hz), 2.31 ((1H, dt, *J* = 17.0, 5.0 Hz), 2. 67 (1H, br), 2.90 ((1H, dt, *J* = 11.2, 6.9 Hz), 4.04 (1H, t, *J* = 6.3 Hz), 4.30 (1H, dd, *J* = 7.0, 4.8 Hz), 4.50 (1H, t, *J* = 6.5 Hz), 5.74-5.75 (1H, m), 5.81-5.84 (1H, m); ^{13}C NMR (100 MHz) δ 25.1 (CH_2), 27.4 (CH_3), 28.0 (CH_3), 28.5 (CH_2), 40.0 (CH), 42.9 (CH), 43.1 (CH), 70.3 (CH), 80.6 (C), 84.1 (CH), 84.2 (CH), 113.5 (C), 126.0 (CH), 126.4 (CH), 174.8 (C); MS (ESI) *m/z* (relative intensity) 358 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{25}N_3O_4$ $[M+Na]^+$ 358.1737, found 333.1738.

Amine 206. To a solution of azide **205** (151 mg, 0.45 mmole) in pyridine (5.4 mL) and aqueous ammonia (30%, 3.6 mL) was added triphenylphosphine (354 mg, 1.35 mmole). The mixture was stirred at room temperature for 72 h under N_2. The mixture was then filtered through a pad of silica gel and washed by Et_2O. The filtrate was concentrated under reduced pressure, and the residue was fractionated by flash column chromatography (hexane:Et_2O, 2:1) to afford amine **206** (136.5 mg, 98% yield) as a pale yellow solid: mp 81.6-81.9 ^oC; $[\alpha]_D^{20}$ +100.4 (*c* 1.02, $CHCl_3$); R_f 0.23 (Hexane:Et_2O, 1:1); IR (thin film) 2979, 2934, 2359, 2339, 1721, 1368, 1305, 1273, 1208, 1151, 1058 cm^{-1}; ^1H NMR (400 MHz) δ 1.23 (3H, s), 1.25 (2H, br s), 1.40 (9H, s), 1.45 (3H, s), 1.98 (1H, qq, *J* = 9.8, 2.0 Hz), 2.1 (1H, td, *J* = 9.9, 5.2 Hz), 2.26 (1H, dt, *J* = 16.9, 5.2 Hz), 2.61-2.62 (1H, m), 2.67 (1H, td, *J* = 11.1, 6.9 Hz), 3.49 (1H, t, *J* = 6.0 Hz), 4.28 (1H, ddd, *J* = 14.8, 7.2, 4.4 Hz), 5.67-5.72 (1H, m), 5.81-5.85 (1H, m);

^{13}C NMR (100 MHz) δ 25.1 (CH_3), 27.4 (CH_3), 28.0 (CH_3), 28.6 (CH_2), 39.9 (CH), 43.6 (CH), 44.0 (CH), 61.4 (CH), 80.1 (C), 85.0 (CH), 87.0 (CH), 112.8 (C), 125.7 (CH), 127.5 (CH), 176.1 (C)； MS (ESI) *m/z* (relative intensity) 310 ($[M+H]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{27}NO_4$ $[M+H]^+$ 310.2013, found 310.2011.

Pyrimidine 207. To a solution of pyrimidine **208** (148 mg, 0.32 mmole) in AcOH (3.52 mL) was added iron powder (143 mg, 2.54 mmole) and the mixture was stirred at room temperature for 4 h. The mixture was then filtered through a pad of silica gel and washed by Et_2O. The filtrate was concentrated and fractionated by flash column chromatography (hexane:Et_2O, 1:2) to afford pyrimidine **207** (138.5 mg, 100% yield) as a white solid: mp 85-87 ^{o}C; $[\alpha]_D^{20}$ +49.7 (*c* 1.00, $CHCl_3$); R_f 0.23 (hexane:Et_2O, 1:2); IR (thin film) 3380, 2979, 2359, 2340, 1716, 1576, 1456, 1418, 1369, 1274, 1210, 1156, 1058 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.18 (9H, s), 1.32 (3H, s), 1.54 (3H, s), 2.12-2.22 (2H, m), 2.25-2.31 (1H, m), 2.80 (1H, br), 3.06 (1H, dt, *J* = 9.6, 6.9 Hz), 3.52 (2H, br s), 4.40 (1H, dd, *J* = 6.8, 3.9 Hz), 4.61 (1H, t, *J* = 6.4 Hz), 4.75 (1H, dd, *J* = 13.9, 6.4 Hz), 5.40 (1H, d, *J* = 8.0 Hz), 5.78-5.81 (1H, m), 5.89-5.91 (1H, m), 8.03 (1H, s)； ^{13}C NMR (100 MHz) δ 24.8 (CH_3), 27.1 (CH_3), 27.7 (CH_3), 28.0 (CH_2), 40.9 (CH), 41.2 (CH), 43.0 (CH), 60.8 (CH), 81.2 (C), 83.8 (CH), 84.1 (CH), 113.3 (C), 122.4(C), 126.2 (CH), 127.6 (CH), 142.4(C), 149.1(CH), 153.9(C), 175.4 (C)； MS (ESI) *m/z* (relative intensity) 437 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{29}ClN_4O_4$ $[M+Na]^+$ 437.1950, found 437.1950.

Pyrimidine 207 from amine 206. To a solution of amine **206** (13 mg, 0.04 mmole) in *n*-BuOH (0.2 mL) was added triethylamine (0.03 mL, 1.00 mmole) and 5-amino-4,6- dichloropyrimidine (10.7 mg, 0.63 mmole) and the mixture was stirred at 100 ^{o}C for 72 h. The solvent was removed under reduced pressure and the residue was fractionated by flash column chromatography (hexane:Et_2O, 1:2) to afford pyrimidine **207** (3.3 mg, 18% yield) as a white solid.

Pyrimidine 208. To a solution of amine **206** (129 mg, 0.42 mmole) in THF (0.6 mL) was added $NaHCO_3$ (143 mg, 0.17 mmole) and 4,6-dichloro-5-nitropyrimidine (324 mg, 0.17 mmole) and the mixture was stirred at room temperature for 3 h. The mixture was then filtered through a pad of silica gel and washed by Et_2O. The filtrate was concentrated and fractionated by flash column chromatography (hexane:Et_2O, 4:1) to afford pyrimidine **208** (181 mg, 93% yield) as a pale yellow solid: mp 54-55 ^{o}C; $[\alpha]_D^{20}$ +158.3 (*c* 1.10, $CHCl_3$); R_f 0.27 (hexane:Et_2O, 3:1); IR (thin film) 3401, 3358, 2980, 2933, 2359, 1726, 1582, 1522, 1490, 1370, 1337, 1211, 1154, 1060 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.30 (3H, s), 1.37 (9H, s), 1.51 (3H, s), 2.22-2.34 (2H, m), 2.56 (1H, dd, *J* = 12.4, 6.5 Hz), 2.79-2.80 (1H, m), 3.19 (1H, dd, *J* = 13.1, 6.5 Hz), 4.49 (1H, dd, *J* = 6.2, 2.8 Hz), 4.53 (1H, dd, *J* = 6.3, 1.6 Hz), 4.87-4.91 (1H, m), 5.86-5.89 (1H, m), 5.91-5.95 (1H, m), 7.80 (1H, d, *J* = 8.4 Hz), 8.45 (1H, s)； ^{13}C NMR (100 MHz) δ 24.5 (CH_3), 26.2 (CH_2), 26.8 (CH_3), 28.0 (CH_3), 38.1 (CH), 38.5 (CH), 43.1 (CH), 61.4 (CH), 81.1 (C), 84.4 (CH), 84.9 (CH), 111.9 (C), 127.2 (C), 127.7 (CH), 127.8 (CH), 155.3(C), 156.0(C), 158.2(CH), 174.1 (C)； MS (ESI) *m/z*

(relative intensity) 467 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{21}H_{27}ClN_4O_6$ [M+Na]$^+$ 467.1692, found 467.1696.

Purine 209. Alcohol **193** (70 mg, 0.19 mmole) was dissolved in a saturated ammonia solution in *t*-BuOH (7 mL) in a sealed tube and stirred at 110 ^oC for 14 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford purine **209** (65.1 mg, 98% yield) as a white solid: mp 124-128 ^oC; $[\alpha]_D^{20}$ +15.2 (*c* 1.01, MeOH); R_f 0.29 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3326, 2916, 2360, 2341, 1597, 1474, 1415, 1209, 1058 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 0.20-0.26 (1H, m), 1.33 (3H, s), 1.44 (1H, s), 1.49 (3H, s), 1.99-2.01 (1H, m), 2.74-2.75 (1H, m), 3.10-3.14 (1H, m), 3.26 (1H, dd, *J* = 10.6, 7.7 Hz), 3.29-3.32 (1H, m), 4.91-4.92 (1H, m), 5.09-5.12 (1H, m), 5.41-5.42 (1H, m), 5.67 (1H, d, *J* = 10.0 Hz), 7.87 (1H, s), 8.19 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.0 (CH_2), 24.3 (CH_3), 26.8 (CH_3), 33.9 (CH), 39.8 (CH), 43.8 (CH), 65.2 (CH), 66.5 (CH_2), 86.4 (CH), 86.9 (CH), 111.7 (C), 118.8 (C), 126.8 (CH), 129.1 (CH), 142.2 (CH), 151.7 (C), 153.8 (CH), 157.4 (C); MS (ESI) *m/z* (relative intensity) 380 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{18}H_{25}N_5O_3$ [M+Na]$^+$ 380.1693, found 380.1696.

Purine 210. Following the general procedure for hydrogenation of alkene, purine **209** (43.3 mg, 0.12 mmole) was converted into purine **210** in 96 h. The

residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford purine **210** (38.8 mg, 89%) as a white solid: mp 128-132 ^oC; $[\alpha]_D^{20}$ 65.7 (*c* 1.10, MeOH); R_f 0.29 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3327, 3194, 2986, 2930, 2860, 1646, 1600, 1574, 1477, 1415, 1375, 1330, 1302, 1251, 1210, 1158, 1056 cm^{-1}; ^1H NMR (400 MHz) δ 1.01-1.05 (1H, m), 1.36 (1H, s), 1.50 (1H, s), 1.54-1.57 (4H, m), 1.75-1.78 (1H, m), 2.44-2.46 (1H, m), 2.60-2.68 (2H, m), 2.68-2.72 (1H, m), 3.57 (2H, s), 4.70 (1H, t, *J* = 6.2 Hz), 4.84 (1H, t, *J* = 6.2 Hz), 5.46 (1H, s), 6.56 (2H, s), 7.98 (1H, s), 8.23 (1H, s); ^{13}C NMR (100 MHz) δ 20.3 (CH_2), 25.1 (CH_3), 25.8 (CH_2), 27.3 (CH_3), 28.1 (CH_2), 37.3 (CH), 43.0 (CH), 43.4 (CH), 64.9 (CH_2), 65.2 (CH), 81.0 (CH), 81.2 (CH), 113.8 (C), 119.7 (C), 139.4 (CH), 150.7 (C), 152.8 (CH), 155.7 (C)； MS (ESI) *m/z* (relative intensity) 382 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{25}N_5O_3$ $[M+Na]^+$ 382.1850, found 382.1852.

Triol 211. Following the general procedure for dihydroxylation of alkene, alcohol **193** (150 mg, 0.40 mmole) was converted into triol **211** in 12 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford triol **211** (139.0 mg, 85%) as a white solid: mp 178-180 ^oC; $[\alpha]_D^{20}$ -45.8 (*c* 2.10, MeOH); R_f 0.27 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3392, 2981, 2930, 1592, 1564, 1438, 1399, 1384, 1341, 1208, 1157, 1061 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.30-1.34 (1H, m), 1.37 (3H, s), 1.46-1.48 (1H, m), 1.51 (3H, s), 1.86-1.87 (1H, m), 2.61-2.64 (2H, m), 2.67-2.70 (1H, m), 2.86-2.92 (1H, m), 3.75-3.78 (1H, m), 3.91 (1H, dd, 5.2, 2.7 Hz), 4.88-4.90 (1H, s), 5.05 (1H, t, *J* = 6.2 Hz), 5.73 (1H, br s), 8.76 (1H,

s), 8.77 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.1 (CH_3), 27.4 (CH_3), 31.6 (CH_2), 37.0 (CH), 42.4 (CH), 51.2 (CH), 66.0 (CH_2), 66.9 (CH), 68.8 (CH), 70.1 (CH), 81.4 (CH), 81.5 (CH), 114.6 (C), 132.5 (C), 147.3 (CH), 151.7 (C), 153.1 (CH), 153.8 (C)；MS (ESI) *m/z* (relative intensity) 433 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{23}ClN_4O_5$ $[M+Na]^+$ 433.1249, found 433.1245.

Purine 212. Triol **211** (82.5 mg, 0.20 mmole) was dissolved in a saturated ammonia in *t*-BuOH (7 mL) in a sealed tube and stirred at 110 ^oC for 12 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 3:1) to afford purine **212** (77.9 mg, 99% yield) as a white solid: mp 201-202 ^oC; $[\alpha]_D^{20}$ -38.7 (*c* 1.25, MeOH); R_f 0.22 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3400, 2989, 2932, 1648, 1603, 1577, 1480, 1418, 1382, 1305, 1268, 1210, 1157, 1060 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.37 (3H, s), 1.38-1.41 (1H, m), 1.45-1.47 (1H, m), 1.50 (3H, s), 1.86 (1H, s), 2.60-2.64 (2H, m), 2.67-2.69 (1H, m), 2.76-2.82 (1H, m), 3.78-3.80 (1H, m), 3.94-3.96 (1H, m), 4.83-4.87 (1H, m), 4.92-4.93 (1H, m), 8.22 (1H, s), 8.37 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.1 (CH_3), 27.4 (CH_3), 31.5 (CH_2), 36.9 (CH), 42.2 (CH), 49.9 (CH), 51.2 (CH_3), 65.9 (CH_2), 68.9 (CH), 70.2 (CH), 81.5 (CH), 81.8 (CH), 111.5 (C), 120.3 (CH), 141.3 (C), 151.3 (C), 154.0 (CH), 157.4 (C)；MS (ESI) *m/z* (relative intensity) 414 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{25}N_5O_5$ $[M+Na]^+$ 414.1748, found 414.1749.

Diol 213α and 213β. Following the general procedure for dihydroxylation of alkene, purine **192** (134.0 mg, 0.40 mmole) was converted into diol **213** in 48 h. The residue was then fractionated by flash column chromatography (hex:EtOAc, 1:5) to afford first diol **213α** (90.8 mg, 63%) as a colorless oil and then diol **213β** (50.5 mg, 35%) as a white solid.

Data for **diol 213α**: $[\alpha]_D^{20}$ -12.7 (*c* 1.36, $CHCl_3$); R_f 0.30 (hex:EtOAc, 1:5); IR (thin film) 3401, 2982, 2934, 1720, 1592, 1561, 1400, 1370, 1339, 1259, 1208, 1152, 1069 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 0.96 (9H, s), 1.28 (1H, s), 1.34 (3H, s), 1.52 (3H, s), 1.64 (1H, q, *J* = 12.1 Hz), 1.73 (1H, dt, *J* = 12.0, 4.0 Hz), 2.70 (1H, t, *J* = 7.6 Hz), 3.20-3.26 (1H, m), 3.85-3.88 (1H, m), 4.06 (1H, t, *J* = 2.7 Hz), 4.72 (1H, t, *J* = 7.5 Hz), 5.12 (1H, t, *J* = 6.6 Hz), 8.65-8.77 (2H, m); ^{13}C NMR (100 MHz, CD_3OD) δ 25.3 (CH_3), 27.6 (CH_3), 27.7 (CH_3), 31.8 (CH_2), 42.9 (CH), 52.1 (CH), 68.7 (CH), 69.6 (CH), 79.4 (CH), 80.1 (CH), 80.7 (CH), 81.0 (CH), 81.8 (C), 115.8 (C), 132.7 (C), 145.9 (CH), 151.5 (C), 152.9 (CH), 153.8 (C), 173.9 (C)； MS (ESI) *m/z* (relative intensity) 503 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}ClN_4O_6$ $[M+Na]^+$ 503.1668, found 503.1663.

Data for **diol 213β**: mp 230-233 °C; $[\alpha]_D^{20}$ -12.9 (*c* 1.10, $CHCl_3$); R_f 0.22 (hex:EtOAc, 1:5); IR (thin film) 3392, 2981, 2931, 1722, 1716, 1593, 1563, 1371, 1339, 1259, 1208, 1151, 1068 cm-1; ^1H NMR (400 MHz, CD_3OD) δ 0.96 (9H, s), 1.27-1.39 (4H, m), 1.49 (3H, s), 1.99-2.02 (1H, m), 2.77-2.82 (2H, m), 3.16-3.22 (1H, m), 3.80 (1H, dd, *J* = 6.6, 2.6 Hz), 4.02 (1H, s), 5.00-5.04 (1H, m), 5.39-5.42 (1H, m),

8.78 (1H, s), 8.85 (1H, br s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.1 (CH_3), 26.3 (CH_3), 26.5 (CH_3), 34.7 (CH_2), 35.9 (CH), 46.9 (CH), 68.0 (CH), 68.1 (CH), 78.1 (CH), 78.5 (CH), 78.7 (CH), 78.9 (CH), 80.4 (C), 113.6 (C), 131.3 (C), 146.2 (CH), 150.0 (CH), 152.7 (C), 174.0 (C)；MS (ESI) *m/z* (relative intensity) 503 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}ClN_4O_6$ $[M+Na]^+$ 503.1668, found 503.1668.

Purine 214. Diol **213α** (95 mg, 0.20 mmole) was dissolved in a saturated ammonia in *t*-BuOH (7 mL) in a sealed tube and stirred at 110 °C for 12 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford purine **214** (89.3 mg, 98% yield) as a white solid: mp 186-188 °C; $[\alpha]_D^{20}$ -15.1 (*c* 1.61, MeOH); R_f 0.32 ($CHCl_3$:MeOH, 8:1); IR (thin film) 3337, 2981, 2925, 1702, 1647, 1370, 1332, 1304, 1269, 1210, 1155, 1068 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 0.83-1.00 (10H, m), 1.33 (3H, s), 1.51 (3H, s), 1.67-1.72 (2H, m), 2.52-2.68 (2H, m), 3.18-3.24 (1H, m), 3.85-3.87 (1H, m), 4.05 (1H, s), 4.69 (1H, t, *J* = 7.5 Hz), 4.98 (1H, t, *J* = 6.5 Hz), 8.23 (1H, s), 8.35 (1H, br s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.3 (CH_3), 27.6 (CH_3), 27.7 (CH_3), 32.0 (CH_2), 43.0 (CH), 52.2 (CH), 58.3 (CH), 64.4 (CH), 68.7 (CH), 69.6 (CH), 79.5 (CH), 80.2 (CH), 81.7 (C), 115.6 (C), 120.4 (C), 140.7 (CH), 151.3 (CH), 153.6 (CH), 157.3 (C), 174.0 (C)；MS (ESI) *m/z* (relative intensity) 484 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{31}N_5O_6$ $[M+Na]^+$ 484.2167, found 484.2166.

Purine 215. Diol **213β** (83 mg, 0.17 mmole) was dissolved in a saturated ammonia in *t*-BuOH (7 mL) in a sealed tube and stirred at 110 ^{o}C for 12 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford purine **215** (78.9 mg, 99% yield) as a white solid: mp 197-200 ^{o}C; $[\alpha]_D^{20}$ -53.4 (*c* 1.05, MeOH); R_f 0.37 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3338, 3216, 2982, 2932, 1711, 1646, 1603, 1478, 1419, 1370, 1334, 1304, 1258, 1211, 1156, 1074 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.00 (9H, s), 1.34 (3H, s), 1.35-1.41 (1H, m), 1.48 (3H, s), 1.98-2.03 (1H, m), 2.70 (1H, br s), 2.76-2.80 (1H, m), 3.14-3.20 (1H, m), 3.81 (1H, dd, *J* = 6.7, 2.9 Hz), 4.03 (1H, s), 4.85-4.89 (1H, m), 5.37-5.40 (1H, m), 5.51 (1H, br s), 8.24 (1H, s), 8.45 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.5 (CH_3), 27.8 (CH_3), 27.9 (CH_3), 36.2 (CH_2), 37.5 (CH), 44.9 (CH), 61.5 (CH), 65.1 (CH), 69.4 (CH), 69.6 (CH), 79.5 (CH), 79.8 (CH), 80.8 (CH), 81.6 (C), 114.9 (C), 141.1 (C), 151.5 (C), 153.6 (CH), 157.3 (C), 175.3 (C)；MS (ESI) *m/z* (relative intensity) 484 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{31}N_5O_6$ $[M+Na]^+$ 484.2167, found 484.2169.

Alcohol 226. To a stirred solution of azide **205** (234 mg, 0.70 mmole) in dry toluene (20mL) at -78 ^{o}C was added DIBAL-H solution (1.22 mL, 1.2M in toluene) over 1.5 h. Then MeOH (2 mL) and $NaBH_4$ (5.9 mg, 0.16 mmole) were added to the above solution and the mixture was stirred at room temperature for 10 min.

Removal of the solvent under reduced pressure was followed by flash column chromatography (hexane:EtOAc, 1:3) of the residue to furnish alcohol **226** (175.8 mg, 95% yield) as colorless oil: $[\alpha]_D^{20}$ +62.4 (*c* 0.87, $CHCl_3$); R_f 0.37 (hexane:EtOAc, 2:1); IR (thin film) 3400, 2987, 2917, 2103, 1375, 1263, 1210, 1160, 1057, 1034 cm^{-1}; ^1H NMR (400 MHz) δ 1.30 (3H, s), 1.47 (3H, s), 1.84-1.88 (1H, m), 1.98-2.00 (2H, m), 2.36-2.41 (1H, m), 2.60 (1H, br s), 2.67-2.71 (1H, m), 3.53-3.61 (2H, m), 3.99-4.00 (1H, m), 4.49 (1H, d, *J* = 5.9 Hz), 4.58 (1H, d, *J* = 6.0 Hz), 5.59-5.61 (1H, m) , 5.70-5.74 (1H, m); ^{13}C NMR (100 MHz) δ 24.5 (CH_3), 26.0 (CH_2), 26.8 (CH_3), 34.4 (CH), 39.6 (CH), 42.6 (CH), 66.8 (CH_2), 71.3 (CH), 84.7(CH), 85.3 (CH), 111.3 (C), 125.5(CH), 127.8 (CH)；MS (ESI) *m/z* (relative intensity) 288 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{19}N_3O_3$ $[M+Na]^+$ 288.1319, found 288.1313.

Triazole 227. Following the general procedure for copper catalyzed azide-alkyne cycloaddition, alcohol **226** (98.5 mg, 0.37 mmole) was converted into triazole **227** in 2 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **227** (129.7 mg, 100%) as a white solid: mp 158-161 ^oC; $[\alpha]_D^{20}$ +6.5 (*c* 1.90, $CHCl_3$); R_f 0.20 (hexane:EtOAc, 1:1); IR (thin film) 3400, 2990, 2917, 1733, 1437, 1383, 1212, 1159, 1049 cm^{-1}; ^1H NMR (400 MHz) δ 0.49-0.56 (1H, m), 1.31 (3H, s), 1.48 (3H, s), 1.52-1.57 (1H, m), 1.90-1.93 (1H, m), 2.53 (1H, br s), 3.19 (1H, td, *J* = 7.7, 3.7 Hz), 3.29 (1H, dd, *J* = 10.6, 6.5 Hz), 3.36 (1H, dd, *J* = 10.6, 7.6 Hz), 3.90 (3H, s), 4.80 (1H, d, *J*= 5.7 Hz), 5.06 (1H, d, *J* = 6.0 Hz), 5.09 (1H, d, *J* = 7.5 Hz), 5.43-5.47 (1H, m), 5.61 (1H, dd, *J*

= 10.2, 1.8 Hz), 8.06 (1H, s); ^{13}C NMR (100 MHz) δ 23.7 (CH_2), 24.3 (CH_3), 26.7 (CH_3), 33.1 (CH), 39.3 (CH), 42.9 (CH), 52.3 (CH_3), 66.0 (CH_2), 70.3 (CH), 84.3 (CH), 85.7 (CH), 111.4 (C), 125.4 (CH), 128.1 (CH), 128.7 (CH), 139.4 (C), 161.2 (C)；MS (ESI) *m/z* (relative intensity) 372 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{23}N_3O_5$ [M+Na]$^+$ 372.1530, found 372.1531.

Triazole **228.** Following the general procedure for copper catalyzed azide-alkyne cycloaddition, alcohol **226** (84.9 mg, 0.32 mmole) was converted into triazole **228** in 25 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **228** (107 mg, 91%) as a colorless oil; $[\alpha]_D^{20}$ -9.4 (*c* 1.60, $CHCl_3$); R_f 0.40 (hexane:EtOAc, 1:1); IR (thin film) 3435, 3401, 3306, 3272, 2981, 2917, 1646, 1457, 1383, 1211, 1052, 1028 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.69-0.76 (1H, m), 1.35 (3H, s), 1.52 (3H, s), 1.55-1.61 (1H, m), 1.91-1.94 (1H, m), 2.68 (1H, br s), 2.82-2.83 (1H, m), 3.19 (1H, td, *J* = 7.7, 4.4 Hz), 3.26 (1H, dd, *J* = 10.7, 6.4 Hz), 3.36 (1H, dd, *J* = 10.7, 7.2 Hz), 4.82-4.83 (1H, m), 5.08 (1H, dd, *J* = 7.4, 1.8 Hz), 5.14 (1H, dd, *J* = 5.9, 1.7 Hz), 5.48-5.52 (1H, m), 5.67 (1H, dd, *J* = 10.1, 2.1 Hz), 7.29-7.33 (1H, m), 7.40 (2H, t, *J* = 17.3 Hz), 7.78 (2H, d, *J* = 7.2 Hz), 7.74 (1H, s); ^{13}C NMR (100 MHz) δ 24.0 (CH_2), 24.4 (CH_3), 26.9 (CH_3), 33.5 (CH), 39.6 (CH), 43.2 (CH), 65.9 (CH_2), 69.9 (CH), 84.2 (CH), 85.8 (CH), 111.4 (C), 120.8 (CH), 125.5 (CH), 125.8 (CH), 128.0 (CH), 128.4 (CH), 129.0 (CH), 130.3 (C), 147.3 (C)；MS (ESI) *m/z* (relative intensity) 390 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{21}H_{25}N_3O_3$ [M+Na]$^+$ 390.1788, found 390.1783.

Triazole **229.** Following the general procedure for copper catalyzed azide-alkyne cycloaddition, alcohol **226** (84 mg, 0.32 mmole) was converted into triazole **229** in 21 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **229** (123.3 mg, 98%) as a colorless oil: $[\alpha]_D^{20}$ -16.2 (*c* 1.01, $CHCl_3$); R_f 0.30 (hexane:EtOAc, 1:1); IR (thin film) 3435, 3401, 3307, 2981, 2917, 1608, 1490, 1444, 1383, 1249, 1211, 1052, 1027 cm^{-1}; ^1H NMR (400 MHz) δ 0.65-0.72 (1H, m), 1.34 (3H, s), 1.52 (3H, s), 1.54-1.56 (1H, m), 1.93-1.95 (1H, m), 2.70 (1H, br s), 2.81-2.82 (1H, m), 3.18 (1H, td, *J*= 7.8, 4.1 Hz), 3.25 (1H, dd, *J* = 10.6, 6.5 Hz), 3.36 (1H, dd, *J* = 10.6, 7.2 Hz), 3.89 (3H, s), 4.82 (1H, d, *J* = 5.5 Hz), 5.08-5.10 (1H, m), 5.16-5.5.17 (1H, m), 5.46-5.49 (1H, m), 5.65(1H, dd, *J* = 10.1, 1.8 Hz), 6.94 (1H, d, *J* = 8.2 Hz), 7.04 (1H, t, *J* = 7.5 Hz), 7.28-7.30 (1H, m), 7.97 (1H, s) , 8.26 (1H, dd, *J* = 7.6, 1.4 Hz); ^{13}C NMR (100 MHz) δ 23.9 (CH_2), 24.5 (CH_3), 26.9 (CH_3), 33.4 (CH), 39.4 (CH), 43.2 (CH), 55.5 (CH_3), 66.0 (CH_2), 69.7 (CH), 84.3 (CH), 85.9 (CH), 110.9 (CH), 111.2 (C), 119.2 (C), 121.1 (CH), 124.2 (CH), 125.3 (CH), 127.7 (CH), 127.9 (CH), 129.1 (CH), 142.7 (C), 155.7 (C)；MS (ESI) *m/z* (relative intensity) 420 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{27}N_3O_4$ $[M+Na]^+$ 420.1894, found 420.1895.

Triazole **230.** Following the general procedure for copper catalyzed azide-alkyne cycloaddition, alcohol **226** (114 mg, 0.43 mmole) was converted into triazole **230** in 28 h. The residue was then fractionated by flash column

chromatography (Chloroform:Acetone, 3:2) to afford triazole **230** (155.1 mg, 98%) as a white solid: mp 135-139 ^{o}C; $[\alpha]_{D}^{20}$ -4.5 (*c* 1.48, $CHCl_3$); R_f 0.33 (Chloroform:Acetone, 3:2); IR (thin film) 3400, 2989, 2917, 1602, 1423, 1382, 1211, 1159, 1052 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.66-0.73 (1H, m), 1.32 (3H, s), 1.50 (3H, s), 1.52-1.57 (1H, m), 1.93-1.95 (1H, m), 2.80-2.81 (1H, m), 3.17-3.22 (1H, m), 3.28 (1H, dd, *J* = 10.6, 6.5 Hz), 3.37 (1H, dd, *J* = 10.6, 7.4 Hz), 4.82-4.83 (1H,m), 5.09-5.11 (1H, m), 5.13-5.15 (1H, m), 5.43-5.48 (1H, m), 5.65(1H, dd, *J* = 10.1, 2.1 Hz), 7.20 (1H, ddd, *J* = 6.0, 5.0, 1.0 Hz), 7.75 (1H, td, *J* = 7.7, 1.7 Hz), 8.12-8.14 (2H, m), 8.50-8.51 (1H, m); ^{13}C NMR (100 MHz) δ 23.9 (CH_2), 24.4 (CH_3), 26.8 (CH_3), 33.5 (CH), 39.6 (CH), 43.2 (CH), 65.9 (CH_2), 70.0 (CH), 84.3 (CH), 85.8 (CH), 111.2 (C), 120.5 (CH), 123.1 (CH), 123.3 (CH), 125.6 (CH), 127.9 (CH), 137.3(CH), 147.6 (C), 149.3 (CH), 150.0 (C)；MS (ESI) *m/z* (relative intensity) 391 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{20}H_{24}N_4O_3$ $[M+Na]^+$ 391.1741, found 391.1743.

Triazole 231. Triazole **227** (64 mg, 0.18 mmole) was dissolved in ammonia solution (7 mL, 0.7M in MeOH) and stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford triazole **231** (55.1 mg, 90% yield) as a white solid: mp 246-248 ^{o}C; $[\alpha]_{D}^{20}$ +19.4 (*c* 1.40, MeOH); R_f 0.37 ($CHCl_3$: acetone, 2:3); IR (thin film) 3503, 3406, 3085, 1654, 1630, 1376, 1213, 1076, 1064, 1051 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:1) δ 0.37-0.45 (1H, m), 1.34 (3H, s), 1.48-1.53 (4H, m), 1.91-1.96 (1H, m), 2.76-2.78 (1H, m), 3.16 (1H, td, *J* = 7.8, 2.7

Hz), 3.29-3.31 (2H, m), 4.86 (1H, d, *J* = 5.6 Hz), 5.10 (1H, s), 5.12 (1H, d, *J* = 2.8 Hz), 5.39-5.43 (1H, m), 5.61 (1H, dd, *J* = 10.2, 1.7 Hz), 8.22 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:1) δ 23.7 (CH_2), 24.4 (CH_3), 26.8 (CH_3), 33.6 (CH), 39.6 (CH), 43.4 (CH), 66.0 (CH_2), 71.0 (CH), 85.2 (CH), 86.6 (CH), 111.7 (C), 126.0 (CH), 128.1 (CH), 128.2 (CH), 142.7 (C), 163.8 (C)；MS (ESI) *m/z* (relative intensity) 357 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{16}H_{22}N_4O_4$ $[M+Na]^+$ 357.1533, found 357.1527.

Triazole 232. Following the general procedure for deprotection of the isopropylidene, triazole **231** (56.0 mg, 0.09 mmole) was converted into triazole **232** at 100 ^oC in 12 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 3:1) to afford triazole **232** (48.3 mg, 98%) as a white solid: mp 232-234 ^oC; $[\alpha]_D^{20}$ +19.8 (*c* 1.00, MeOH); R_f 0.33 ($CHCl_3$: MeOH, 3:1); IR (thin film) 3369, 2915, 1663, 1648, 1405, 1309, 1221, 1109, 1029 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.34-1.37 (1H, m), 1.60-1.65 (1H, m), 1.69-1.73 (1H, m), 2.665-2.67 (1H, m), 3.04-3.10 (1H, m), 3.15-3.19 (1H, m), 3.23 (1H, dd, *J* = 10.6, 6.9 Hz), 4.01-4.04 (1H, m), 4.83 (1H, dd, *J* = 9.2, 4.0 Hz), 5.20 (1H, t, *J*= 9.7 Hz), 5.68-5.74 (2H, m), 8.46 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.7 (CH_2), 35.1 (CH), 37.0 (CH), 42.5 (CH), 65.5 (CH_2), 68.6 (CH), 75.5 (CH), 77.2 (CH), 127.6 (CH), 127.9 (CH), 128.8 (CH), 143.3 (C), 164.8 (C)；MS (ESI) *m/z* (relative intensity) 317 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{18}N_4O_4$ $[M+Na]^+$ 317.1220, found 317.1225.

Triazole 233. Following the general procedure for deprotection of the isopropylidene, triazole **228** (66 mg, 0.18 mmole) was converted into triazole **233** at 100 ^{o}C in 12 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford triazole **233** (58.2 mg, 99%) as a white solid: mp 195-196 ^{o}C; $[\alpha]_D^{20}$ +11.8 (*c* 1.05, MeOH); R_f 0.33 ($CHCl_3$: MeOH, 8:1); IR (thin film) 3368, 2915, 1646, 1385, 1157, 1049, cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.43-1.44 (1H, m), 1.68-1.77 (2H, m), 2.67-2.69 (1H, m), 3.05-3.11 (1H, m), 3.19 (1H, dd, *J* = 10.5, 7.7 Hz), 3.25 (1H, dd, *J* = 10.6, 6.7 Hz), 4.04-4.05 (1H, m), 4.92 (1H, dd, *J* = 9.2, 4.0 Hz), 5.21 (1H, t, *J* = 9.5 Hz), 5.68-5.74 (2H, m), 7.34 (1H, t, *J* = 7.4 Hz), 7.43 (2H, t, *J* = 7.4 Hz), 7.83 (2H, t, *J* = 7.3 Hz), 8.42 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.7 (CH_2), 35.0 (CH), 37.0 (CH), 42.5 (CH), 65.5 (CH_2), 68.5 (CH), 75.3 (CH), 77.3 (CH), 123.8 (CH), 126.7 (CH), 127.6 (CH), 127.9 (CH), 130.0 (C), 131.7 (C), 148.4 (C)； MS (ESI) *m/z* (relative intensity) 350 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{21}N_3O_3$ $[M+Na]^+$ 350.1475, found 350.1470.

Triazole 234. Following the general procedure for deprotection of the isopropylidene, triazole **229** (64.2 mg, 0.16 mmole) was converted into triazole **234** at 100 ^{o}C in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford triazole **234** (57.2 mg, 99%) as a white solid: mp 68-71 ^{o}C; $[\alpha]_D^{20}$ +5.3 (*c* 1.35, CH_3Cl); R_f 0.35 ($CHCl_3$: MeOH, 8:1); IR (thin film) 3351, 2916, 2597, 1852, 1607, 1584, 1490, 1336, 1249, 1109, 1071, 1048, cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.43-1.44 (1H, m), 1.66-1.76 (2H, m), 2.66-2.68 (1H, m),

3.06-3.12 (1H, m), 3.18 (1H, dd, *J* = 10.4, 7.7 Hz), 3.25 (1H, dd, *J* = 10.6, 6.8 Hz), 3.91 (3H, s), 4.05-4.06 (1H, m), 4.93 (1H, dd, *J* = 9.0, 4.0 Hz), 5.19-5.24 (1H, m), 5.66-5.72 (2H, m), 7.02 (1H, d, *J* = 7.4 Hz), 7.06 (1H, d, *J* = 8.0 Hz), 7.30-7.34 (1H, m), 8.10 (1H, dd, *J* = 7.7, 1.4 Hz), 8.35 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.7 (CH_2), 34.9 (CH), 37.0 (CH), 42.4 (CH), 55.9 (CH), 65.5 (CH_2), 68.2 (CH), 75.5 (CH), 77.3 (CH), 112.2 (CH), 120.0 (C), 121.8 (CH), 126.5 (CH), 127.5 (CH), 127.9 (CH), 128.1 (C), 130.4 (CH), 143.8 (C), 157.3 (C)； MS (ESI) *m/z* (relative intensity) 380 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{23}N_3O_4$ $[M+Na]^+$ 380.1581, found 380.1577.

Triazole 235. Following the general procedure for deprotection of the isopropylidene, triazole **230** (67 mg, 0.18 mmole) was converted into triazole **235** at 100 ^{o}C in 12 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford triazole **235** (58.5 mg, 98%) as a white solid: mp 177-179 ^{o}C; $[\alpha]_D^{20}$ +7.2 (*c* 1.35, MeOH); R_f 0.30 ($CHCl_3$: MeOH, 8:1); IR (thin film) 3369, 2916, 2550, 1803, 1647, 1569, 1425, 1265, 1201, 1113, 1041 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.44-1.45 (1H, m), 1.70 (2H, br s), 2.69 (1H, d, *J* = 7.5 Hz), 3.07-3.13 (1H, m), 3.16-3.21 (1H, m), 3.25 (1H, dd, *J* = 10.7, 6.8 Hz), 4.06-4.07 (1H, m), 5.26 (1H, t, *J* = 9.4 Hz), 5.62-5.73 (2H, m), 7.35-7.38 (1H, m), 7.89-7.93 (1H, m), 8.07 (1H, d, *J* = 7.8 Hz), 8.53 (1H, s), 8.54-8.58 (1H, m); ^{13}C NMR (100 MHz, CD_3OD) δ 24.7 (CH_2), 35.0 (CH), 37.0 (CH), 42.5 (CH), 65.5 (CH_2), 68.6 (CH), 75.5 (CH), 77.3 (CH), 121.6 (CH), 124.5 (CH), 125.5 (CH), 127.6 (CH), 127.9 (CH),

138.9 (CH), 148.2 (C), 150.4 (CH), 150.9 (C)； MS (ESI) *m/z* (relative intensity) 351 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{20}N_4O_3$ [M+Na]$^+$ 351.1428, found 351.1432.

Triazole 236. Following the general procedure for deprotection of the isopropylidene, triazole **244** (59 mg, 0.18 mmole) was converted into triazole **236** at 100 ^oC in 24 h. The residue was washed by cold methanol to afford triazole **236** (49.4 mg, 95%) as a white solid: mp 261-262 ^oC; $[\alpha]_D^{20}$ -35.9 (*c* 1.25, DMF); IR (thin film) 3408, 2923, 2869, 1651, 1622, 1553, 1416, 1366, 1300, 1133, 1078, 1050, 1001 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.93-1.00 (1H, m), 1.23-1.34 (2H, m), 1.38-1.48 (3H, m), 1.58-1.66 (1H, m), 2.01-2.07 (1H, m), 2.24-2.30 (1H, m), 2.32-2.41 (2H, m), 3.86 (1H, q, *J* = 5.7 Hz), 4.19 (1H, t, *J* = 4.9 Hz), 4.73 (1H, d, *J* = 5.0 Hz), 4.75-4.78 (1H, m), 4.83 (1H, t, *J* = 8.0 Hz), 4.97 (1H, d, *J* = 6.4 Hz), 7.47 (1H, s), 7.85 (1H, s), 8.68 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.5 (CH_2), 25.1 (CH_2), 26.7 (CH_2), 35.2 (CH), 38.1 (CH), 43.1 (CH), 63.4 (CH_2), 69.5 (CH), 71.2 (CH), 73.3 (CH), 127.3 (CH), 142.7 (C), 161.6 (C)； MS (ESI) *m/z* (relative intensity) 319 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{13}H_{20}N_4O_4$ [M+Na]$^+$ 319.1377, found 319.1377.

Triazole 237. Following the general procedure for deprotection of the isopropylidene, triazole **241** (48.3 mg, 0.13 mmole) was converted into triazole **237** at 100 ^oC in 12 h. The residue was then fractionated by flash column chromatography

($CHCl_3$:MeOH, 10:1) to afford triazole **237** (41.8 mg, 97%) as a white solid: mp 238-239 ^oC; $[\alpha]_D^{20}$ -67.4 (*c* 0.75, MeOH); R_f 0.31 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3338, 3077, 2914, 2855, 1634, 1485, 1457, 1330, 1212, 1084, 1046, 1035 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.05-1.14 (1H, m), 1.44-1.52 (2H, m), 1.54-1.58 (1H, m), 1.60-1.66 (2H, m), 1.79-1.86 (1H, m), 2.24 (1H, quintet, *J* = 6.1 Hz), 2.41-2.47 (1H, m), 2.55 (1H, dd, *J* = 10.7, 7.0 Hz), 2.62 (1H, dd, *J* = 10.7, 4.1 Hz), 4.10 (1H, t, *J* = 6.5 Hz), 4.93 (1H, t, *J* = 7.9 Hz), 4.99-5.03 (1H, m), 7.33-7.37 (1H, m), 7.42-7.46 (1H, m), 7.84-7.86 (1H, m), 8.46 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 21.0 (CH_2), 26.4 (CH_2), 28.3 (CH_2), 37.2 (CH), 40.1 (CH), 45.0 (CH), 65.6 (CH_2), 71.4 (CH), 72.9 (CH), 74.8 (CH), 123.5 (CH), 126.7 (CH), 129.4 (CH), 130.0 (CH), 131.7 (C), 148.8 (C)；MS (ESI) *m/z* (relative intensity) 352 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{23}N_3O_3$ $[M+Na]^+$ 352.1632, found 352.1633.

Triazole 238. Following the general procedure for deprotection of the isopropylidene, triazole **242** (30 mg, 0.08 mmole) was converted into triazole **238** at 100 ^oC in 12 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford triazole **238** (26.5 mg, 99%) as a white solid: mp 197-200 ^oC; $[\alpha]_D^{20}$ -65.1 (*c* 1.10, MeOH); R_f 0.20 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3307, 2922, 2858, 1607, 1583, 1548, 1490, 1445, 1290, 1249, 1121, 1076, 1047, 1024 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.04-1.12 (1H, m), 1.46-1.51 (3H, m), 1.57-1.61 (2H, m), 1.79-1.83 (1H, m), 2.21-2.24 (1H, m), 2.45 (1H, q, *J* = 7.9 Hz), 2.55 (1H, dd, *J* = 10.4, 7.1 Hz), 2.63 (1H, dd, *J* = 10.7, 3.9 Hz), 3.95 (3H, s), 4.11 (1H, t, *J* = 6.4

Hz), 4.91-4.95 (1H, m), 5.05 (1H, t, *J* = 7.1 Hz), 7.04 (1H, t, *J* = 7.5 Hz), 7.09 (1H, d, *J* = 8.1 Hz), 7.34 (1H, t, *J* = 7.2 Hz), 8.12 (1H, d, *J* = 7.7 Hz), 8.41 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 20.9 (CH_2), 26.4 (CH_2), 28.2 (CH_2), 37.1 (CH), 40.2 (CH), 44.9 (CH), 55.9 (CH_3), 65.6 (CH_2), 71.2 (CH), 73.0 (CH), 74.8 (CH), 112.3 (CH), 120.1 (C), 121.8 (CH), 126.5 (CH), 128.1 (CH), 130.4 (CH), 144.2 (C), 157.4 (C)；MS (ESI) *m/z* (relative intensity) 382 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{25}N_3O_4$ $[M+Na]^+$ 382.1737, found 382.1732.

Triazole 239. Following the general procedure for deprotection of the isopropylidene, triazole **243** (80 mg, 0.22 mmole) was converted into triazole **239** at 100 ^{o}C in 18 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford triazole **239** (67.8 mg, 95%) as a white solid: mp 215-217 ^{o}C; $[\alpha]_D^{20}$ -74.7 (*c* 1.00, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3369, 2927, 2860, 1641, 1600, 1571, 1474, 1449, 1424, 1233, 1086, 1043 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 1.05-1.13 (1H, m), 1.40-1.48 (2H, m), 1.51-1.55 (1H, m), 1.57-1.64 (2H, m), 1.77-1.84 (1H, m), 2.21-2.27 (1H, m), 2.43-2.49 (1H, m), 2.52-2.56 (1H, m), 2.62 (1H, dd, *J* = 10.8, 3.9 Hz), 4.10 (1H, t, *J* = 6.1 Hz), 4.94-5.02 (2H, m), 7.36 (1H, t, *J* = 6.1 Hz), 7.90 (1H, t, *J* = 7.7 Hz), 8.08 (1H, d, *J* = 7.9 Hz), 8.51 (1H, s), 8.56-8.57 (1H, m); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 20.8 (CH_2), 26.3 (CH_2), 28.1 (CH_2), 37.1 (CH), 40.0 (CH), 44.8 (CH), 65.5 (CH_2), 71.3 (CH), 72.8 (CH), 74.6 (CH), 121.6 (CH), 124.4 (CH), 125.1 (CH), 138.8 (CH), 148.3 (C), 150.2 (CH), 150.8 (C)；MS (ESI) *m/z* (relative intensity) 353

([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{22}N_4O_3$ [M+Na]$^+$ 353.1584, found 353.1587.

Triazole 240 and **triazole 240a.** Following the general procedure for hydrogenation of alkene, triazole **227** (82.3 mg, 0.24 mmole) was converted into triazole **240** in 30 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1; to Chloroform:Acetone, 1:1) to afford first triazole **240** (11.6 mg, 14%) as a white solid and then triazole **240a** (57.9 mg, 79%) as a white solid.

Following the general procedure for hydrogenation of alkene, triazole **227** (61.2 mg, 0.18 mmole) was converted into triazole **240** in 6 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **240** (54.8 mg, 89%) as a white solid.

Data for triazole **240**: mp 156-157 ^oC; $[\alpha]_D^{20}$ -47.7 (*c* 1.23, $CHCl_3$); R_f 0.20 (hexane:EtOAc, 1:2); IR (thin film) 3401, 2981, 2930, 2862, 1731, 1437, 1383, 1210, 1161, 1042 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.54-0.59 (1H, m), 1.12-1.19 (1H, m), 1.29-1.38 (5H, m), 1.50 (3H, s), 1.52-1.60 (2H, m), 1.63-1.70 (1H, m), 1.82-1.88 (2H, m), 2.31-2.33 (1H, m), 2.80 (1H, q, *J* = 6.9 Hz), 3.05 (1H, dd, *J* = 10.4, 6.2 Hz), 3.17 (1H, dd, *J* = 10.3, 6.4 Hz), 3.94 (3H, s), 4.71 (1H, dd, *J* = 6.3, 2.3 Hz), 4.85 (1H, dd, *J* = 7.3, 2.8 Hz), 5.44 (1H, dd, *J* = 6.3, 2.9 Hz), 8.21 (1H, s); ^{13}C NMR (100 MHz) δ 19.9 (CH_2), 24.5 (CH_3), 24.8 (CH_2), 25.1 (CH_2), 26.9 (CH_3), 35.5 (CH), 42.0 (CH),

43.3 (CH), 52.4 (CH_3), 65.4 (CH_2), 70.9 (CH), 83.4 (CH), 83.9 (CH), 112.0 (C), 129.2 (CH), 139.9 (C), 161.2 (C)； MS (ESI) *m/z* (relative intensity) 374 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{25}N_3O_5$ $[M+Na]^+$ 374.1686, found 374.1687.

Data for triazole **240a**: mp 190-194 ^oC; $[\alpha]_D^{20}$ -59.4 (*c* 1.95, MeOH); R_f 0.27 ($CHCl_3$:Acetone, 1:2); IR (thin film) 3400, 3116, 2917, 2858, 1720, 1235, 1042 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 1.03-1.12 (1H, m), 1.38-1.47 (2H, m), 1.53-1.61 (3H, m), 1.74-1.79 (1H, m), 2.18-2.24 (1H, m), 2.43-2.48 (1H, m), 2.49-2.53 (1H, m), 2.59 (1H, dd, *J* = 10.8, 4.1 Hz), 3.03 (1H, s), 4.07 (1H, t, *J* = 6.0 Hz), 4.91-4.99 (2H, m), 8.62 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 20.7 (CH_2), 26.1 (CH_2), 27.9 (CH_2), 36.8 (CH), 39.8 (CH), 44.7 (CH), 52.5 (CH_3), 65.4 (CH_2), 71.3 (CH), 72.8.3 (CH), 74.6 (CH), 130.6 (CH), 140.2 (C), 162.2 (C)；MS (ESI) *m/z* (relative intensity) 334 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{14}H_{21}N_3O_5$ $[M+Na]^+$ 334.1373, found 334.1374.

Triazole 241. Following the general procedure for hydrogenation of alkene, triazole **228** (82 mg, 0.22 mmole) was converted into triazole **241** in 10 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **241** (76.7 mg, 93%) as a white solid: mp 190-191 ^oC; $[\alpha]_D^{20}$ -67.8 (*c* 1.05, $CHCl_3$); R_f 0.40 (hexane:EtOAc, 1:1); IR (thin film) 3527, 2917, 2854, 1457, 1449, 1381, 1374, 1209, 1155, 1075, 1059, 1049, 1029 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 0.63-0.66 (1H, m), 1.21-1.26 (1H, m), 1.42-1.50 (5H, m), 1.60 (3H, s), 1.64-1.69 (1H, m), 1.78-1.84 (2H, m), 2.39-2.45 (1H, m), 2.82-2.87 (1H, m),

3.11 (1H, dd, J = 10.4, 6.8 Hz), 3.22 (1H, dd, J = 10.6, 6.4 Hz), 4.81-4.83 (1H, m), 5.00-5.02 (1H, m), 5.62-5.64 (1H, m), 7.41-7.45 (1H, m), 7.50-7.53 (2H, m), 7.90 (2H, d, J = 7.4 Hz), 8.39 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 20.4 (CH_2), 24.6 (CH_3), 25.4 (CH_2), 25.9 (CH_2), 27.0 (CH_3), 35.9 (CH), 42.2 (CH), 43.7 (CH), 65.1 (CH_2), 71.3 (CH), 84.1 (CH), 84.9 (CH), 112.4 (C), 123.2 (CH), 126.4 (CH), 129.1 (CH), 129.6 (CH), 130.8 (C), 148.5 (C)； MS (ESI) *m/z* (relative intensity) 392 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{27}N_3O_3$ $[M+Na]^+$ 392.1945, found 392.1944.

Triazole 242. Following the general procedure for hydrogenation of alkene, **200** (42 mg, 0.11 mmole) was converted into triazole **242** in 10 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **242** (40.5 mg, 96%) as a white solid: mp 73-74 ^{o}C; $[\alpha]_D^{20}$ -63.9 (*c* 1.20, $CHCl_3$); R_f 0.37 (hexane:EtOAc, 1:1); IR (thin film) 3401, 2981, 2931, 2867, 1491, 1464, 1381, 1249, 1210, 1160, 1069, 1049, 1028 cm^{-1}; ^{1}H NMR (400 MHz) δ 0.66-0.73 (1H, m), 1.08-1.16 (1H, m), 1.33-1.37 (5H, m), 1.51 (3H, s), 1.55-1.60 (1H, m), 1.62-1.67 (1H, m), 1.76-1.85 (1H, m), 2.29-2.35 (2H, m), 2.76 (1H, q, J = 6.8 Hz), 3.00 (1H, dd, J = 10.6, 6.3 Hz), 3.14 (1H, dd, J = 10.6, 6.0 Hz), 4.71 (1H, dd, J = 6.4, 2.9 Hz), 4.86 (1H, dd, J = 7.3, 3.1 Hz), 5.52 (1H, dd, J = 6.4, 3.1 Hz), 6.96 (1H, d, J = 8.3 Hz), 7.06 (1H, t, J = 7.5 Hz), 7.30 (1H, t, J = 7.4 Hz), 8.11 (1H, s), 8.31 (1H, d, J = 7.7 Hz); ^{13}C NMR (100 MHz) δ 20.0 (CH_2), 24.6 (CH_3), 25.1 (CH_2), 25.4 (CH_2), 27.0 (CH_3), 35.8 (CH), 41.9 (CH), 43.3 (CH), 55.6 (CH_3), 65.4 (CH_2), 70.3 (CH),

83.5 (CH), 83.8 (CH), 111.0 (CH), 111.8 (C), 119.2 (C), 121.2 (CH), 124.8 (CH), 127.8 (CH), 129.2 (CH), 143.1 (C), 155.8 (C)； MS (ESI) *m/z* (relative intensity) 422 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}N_3O_4$ $[M+Na]^+$ 422.2050, found 422.2051.

Triazole 243. Following the general procedure for hydrogenation of alkene, triazole **230** (98 mg, 0.27 mmole) was converted into triazole **243** in 10 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 20:1) to afford triazole **243** (84 mg, 85%) as a white solid: mp 186-188 ^oC; $[\alpha]_D^{20}$ -68.6 (*c* 1.37, $CHCl_3$); R_f 0.22 ($CHCl_3$:MeOH, 20:1); IR (thin film) 3392, 2988, 2930, 2866, 1603, 1572, 1473, 1449, 1423, 1382, 1209, 1159, 1049 cm^{-1}; ^1H NMR (400 MHz) δ 0.61-0.63 (1H, m), 1.06-1.11 (1H, m), 1.17-1.30 (5H, m), 1.46 (3H, s), 1.49-1.54 (1H, m), 1.57-1.59 (1H, m), 1.65-1.70 (1H, m), 2.28-2.29 (1H, m), 2.77 (1H, q, *J* = 6.8 Hz), 2.96-3.01 (1H, m), 3.11-3.15 (1H, m), 3.66 (1H, s), 4.68 (1H, dd, *J* = 6.2, 2.4 Hz), 4.87 (1H, dd, *J* = 7.1, 2.7 Hz), 5.46 (1H, dd, *J* = 6.3, 2.8 Hz), 7.16-7.18 (1H, m), 7.72 (1H, td, *J* = 7.8, 1.4 Hz), 8.10 (1H, d, *J* = 7.9 Hz), 8.26 (1H, s), 8.47 (1H, d, *J* = 4.2 Hz); ^{13}C NMR (100 MHz) δ 19.9 (CH_2), 24.4 (CH_3), 25.0 (CH_2), 25.2 (CH_2), 26.9 (CH_3), 35.6 (CH), 41.9 (CH), 43.2 (CH), 65.0 (CH_2), 70.4 (CH), 83.3 (CH), 83.9 (CH), 111.7 (C), 120.5 (CH), 123.0 (CH), 123.8 (CH), 137.2 (CH), 147.9 (C), 149.2 (CH), 150.0 (C)； MS (ESI) *m/z* (relative intensity) 393 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{20}H_{26}N_4O_3$ $[M+Na]^+$ 393.1897, found 393.1900.

Triazole 244. Triazole **240** (80 mg, 0.23 mmole) was dissolved in the ammonia solution (10 mL, 0.7 M in MeOH) and stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **244** (69.7 mg, 91% yield) as a white solid: mp >280 ^oC; $[\alpha]_D^{20}$ -53.0 (*c* 1.05, DMSO); R_f 0.38 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3511, 3430, 3216, 3083, 2925, 2915, 1641, 1423, 1384, 1303, 1258, 1210, 1152, 1081, 1053, 1033 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.30-0.34 (1H, m), 1.03-1.07 (1H, m), 1.23-1.27 (2H, m), 1.28 (3H, s), 1.42 (3H, s), 1.45-1.50 (1H, m), 1.54-1.57 (2H, m), 2.17-2.23 (1H, m), 2.58 (1H, q, *J* = 6.5 Hz), 2.75-2.80 (1H, m), 2.84-2.89 (1H, m), 4.48 (1H, d, *J* = 4.5 Hz), 4.64 (1H, d, *J* = 4.4 Hz), 4.96 (1H, dd, *J* = 7.2, 2.8 Hz), 5.42 (1H, dd, *J* = 6.1, 3.0 Hz), 7.50 (1H, s), 7.88 (1H, s), 8.66 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.3 (CH_2), 24.40 (CH_3), 24.41 (CH_2), 24.9 (CH_2), 26.8 (CH_3), 34.6 (CH), 42.2 (CH), 63.2 (CH_2), 69.6 (CH), 82.6 (CH), 83.2 (CH), 111.0 (C), 127.9 (CH), 143.0 (C), 161.5 (C)；MS (ESI) *m/z* (relative intensity) 359 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{16}H_{24}N_4O_4$ $[M+Na]^+$ 359.1690, found 359.1693.

Triazole 245. Following the general procedure for dihydroxylation of alkene, triazole **227** (70 mg, 0.20 mmole) was converted into diol triazole **245** in 18 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 15:1) to afford first triazole **245α** (70.7 mg, 87%) as a white solid: mp 130-133 ^oC; $[\alpha]_D^{20}$ -57.4 (*c* 2.20, MeOH); R_f 0.36 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3400, 2930, 1729,

1550, 1437, 1383, 1261, 1213, 1160, 1045 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 0.49-0.53 (1H, m), 1.35 (3H, s), 1.42-1.47 (1H, m), 1.50 (3H, s), 1.67-1.68 (1H, m), 2.48 (1H, t, *J* = 8.8 Hz), 3.00-3.02 (1H, m), 3.20 (1H, dd, *J* = 10.3, 5.0 Hz), 3.27-3.29 (1H, m), 3.66-3.67 (1H, m), 3.85-3.88 (1H, m), 3.93 (3H, s), 5.01 (1H, d, *J* = 6.0 Hz), 5.40 (1H, d, *J* = 6.2 Hz), 8.71 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 24.5 (CH_3), 27.0 (CH_3), 31.9 (CH_2), 34.8 (CH), 43.0 (CH), 48.8 (CH), 52.7 (CH_3), 67.4 (CH_2), 68.7 (CH), 69.3 (CH), 71.9 (CH), 84.0 (CH), 84.4 (CH), 112.6 (C), 131.3 (CH), 140.5 (C), 162.2 (C)； MS (ESI) *m/z* (relative intensity) 406 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{25}N_3O_7$ $[M+Na]^+$ 406.1585, found 406.1588.

Triazole 246. Following the general procedure for dihydroxylation of alkene, triazole **228** (60 mg, 0.16 mmole) was converted into diol triazole **246** in 13 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford first triazole **246α** (56.4 mg, 86%) as a white solid: mp 209-210 ^{o}C; $[\alpha]_D^{20}$ -84.0 (*c* 1.30, MeOH); R_f 0.38 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3401, 3307, 3234, 2930, 2726, 2512, 2279, 2083, 1855, 1647, 1429, 1385, 1213, 993 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 0.52-0.55 (1H, m), 1.36 (3H, s), 1.44 (1H, dt, *J* = 14.7, 4.7 Hz), 1.51 (3H, s), 1.72-1.75 (1H, m), 2.46 (1H, t, *J* = 9.1 Hz), 3.04 (1H, td, *J* = 7.6, 3.1 Hz), 3.28-3.30 (1H, m), 3.35-3.40 (1H, m), 3.65-3.67 (1H, m), 3.95 (1H, dd, *J* = 10.3, 2.8 Hz), 4.94 (1H, d, *J* = 7.6 Hz), 5.03 (1H, d, *J* = 6.0 Hz), 5.41 (1H, d, *J* = 6.0 Hz), 7.31-7.35 (1H, m), 7.42 (1H, t, *J* = 7.5 Hz), 7.80 (1H, d, *J* = 7.44 Hz), 8.32 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 24.5 (CH_3), 26.9 (CH_3), 31.7

(CH_2), 34.1 (CH), 42.7 (CH), 48.3 (CH), 67.5 (CH_2), 68.4 (CH), 68.9 (CH), 71.3 (CH), 84.0 (CH), 84.4 (CH), 112.0 (C), 123.6 (CH), 126.4 (CH), 129.3 (CH), 129.7 (CH), 130.8 (C), 148.6 (C)； MS (ESI) *m/z* (relative intensity) 424 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{27}N_3O_5$ $[M+Na]^+$ 424.1843, found 424.1849.

Triazole 247. Following the general procedure for dihydroxylation of alkene, triazole **229** (92 mg, 0.23 mmole) was converted into diol triazole **247** in 12 h. The residue was then fractionated by flash column chromatography (Chloroform:acetone, 2:3) to afford first triazole **247α** (89.9 mg, 90%) as a white solid: mp 238-239 ^oC; $[\alpha]_D^{20}$ -83.3 (*c* 0.72, MeOH); R_f 0.33 ($CHCl_3$:Acetone, 2:3); IR (thin film) 3401, 3307, 3118, 2915, 2726, 2103, 1803, 1594, 1385, 1165, 1053 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 0.58-0.62 (1H, m), 1.27-1.33 (4H, m), 1.45 (3H, s), 1.58-1.63 (1H, m), 2.31-2.36 (1H, m), 2.79-2.84 (2H, m), 2.95-2.97 (1H, m), 3.52-3.57 (1H, m), 3.76-3.78 (1H, m), 3.91 (3H, s), 4.49 (1H, d, *J* = 3.44 Hz), 4.52-4.56 (2H, m), 4.88 (1H, dd, *J* = 6.5, 2.9 Hz), 5.00 (1H, dd, *J* = 7.3, 3.3 Hz), 5.41 (1H, dd, *J* = 6.5, 3.3 Hz), 7.05 (1H, t, *J* = 7.4 Hz), 7.12 (1H, d, *J* = 8.2 Hz), 7.31-7.36 (1H, m), 8.16 (1H, dd, *J* = 7.7, 1.5 Hz), 8.53 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.4 (CH_3), 26.8 (CH_3), 30.4 (CH_2), 34.1 (CH), 41.2 (CH), 47.8 (CH), 55.6 (CH_3), 65.0 (CH_2), 67.2 (CH), 67.8 (CH), 69.0 (CH), 81.6 (CH), 82.3 (CH), 110.9 (CH), 111.6 (C), 119.0 (CH), 120.7 (CH), 125.5 (CH), 126.6 (CH), 129.1 (CH), 141.8 (C), 155.5 (C)； MS (ESI) *m/z* (relative intensity) 454 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}N_3O_6$ $[M+Na]^+$ 454.1949, found 454.1950.

Triazole 248. Following the general procedure for dihydroxylation of alkene, triazole **230** (57 mg, 0.15 mmole) was converted into diol triazole **248** in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford first triazole **248α** (58.6 mg, 86%) as a white solid: mp 128-132 ^oC; $[\alpha]_D^{20}$ -92.7 (*c* 1.30, MeOH); R_f 0.26 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3369, 2981, 2930, 1601, 1571, 1425, 1383, 1269, 1209, 1158, 1045 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 0.52-0.58 (1H, m), 1.32 (3H, s), 1.41 (1H, dt, *J* =14.6, 5.3 Hz), 1.47 (3H, s), 1.71-1.75 (1H, m), 2.43-2.48 (1H, m), 3.01 (1H, td, *J* = 7.7, 4.0 Hz), 3.21 (1H, dd, *J* = 10.7, 5.3 Hz), 3.26-3.29 (1H, m), 3.62-3.66 (1H, m), 3.91 (1H, dd, *J* = 10.0, 3.1 Hz), 4.98-5.01 (2H, m), 5.41 (1H, dd, *J* = 6.2, 2.1 Hz), 7.33 (1H, ddd, *J* = 7.5, 5.0, 7.5 Hz), 7.87 (1H, td, *J* = 7.8, 1.7 Hz), 5.03 (1H, d, *J* = 7.9 Hz), 8.50 (1H, s) , 8.54 (1H, d, *J* = 4.6 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 24.5 (CH_3), 27.0 (CH_3), 32.0 (CH_2), 34.9 (CH), 43.1 (CH), 46.3 (CH), 67.6 (CH_2), 68.8 (CH), 69.4 (CH), 71.7 (CH), 84.2 (CH), 84.6 (CH), 112.5 (C), 121.6 (CH), 124.6 (CH), 125.9 (CH), 138.9 (CH), 148.7 (C), 150.5 (CH), 150.8 (C)；MS (ESI) *m/z* (relative intensity) 425 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{20}H_{26}N_4O_5$ $[M+Na]^+$ 425.1795, found 425.1795.

Triazole 249. Triazole **245** (52 mg, 0.14 mmole) was dissolved in ammonia solution (7 mL, 0.7M in MeOH) and stirred at room temperature for 12 h. The solvent was removed under reduced pressure and the residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **249** (43.0 mg, 86%

yield) as a white solid: mp >280 ^{o}C; $[\alpha]_{D}^{20}$ -73.7 (*c* 1.20, DMF); R_f 0.30 ($CHCl_3$:MeOH, 5:1); IR (thin film) 3426, 3196, 3124, 2992, 2931, 1654, 1614, 1418, 1385, 1299, 1260, 1211, 1071, 1044 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 0.51 (1H, d, *J* = 12.9 Hz), 1.28 (3H, s), 1.30-1.33 (1H, m), 1.43 (3H, s), 1.53 (1H, q, *J* = 5.5 Hz), 2.28-2.31 (1H, m), 2.74-2.79 (1H, m), 2.86-2.91 (1H, m), 3.49-3.51 (1H, m), 3.62-3.65 (1H, m), 4.50 (1H, d, *J* = 3.0 Hz), 4.53-4.55 (2H, m), 4.83 (1H, dd, *J* = 6.1, 2.5 Hz), 4.95 (1H, dd, *J* = 7.0, 3.0 Hz), 5.35 (1H, dd, *J* = 6.2, 3.1 Hz), 7.51 (1H, s), 7.89 (1H, s), 8.63 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.5 (CH_3), 26.8 (CH_3), 30.4 (CH_2), 34.1 (CH), 41.2 (CH), 47.9 (CH), 64.9 (CH_2), 67.1 (CH), 67.8 (CH), 69.4 (CH), 81.5 (CH), 82.1 (CH), 111.1 (C), 128.0 (CH), 143.0 (C), 161.6 (C)；MS (ESI) *m/z* (relative intensity) 391 ([M+Na]$^{+}$, 100); HRMS (ESI) calcd for $C_{16}H_{24}N_4O_6$ [M+Na]$^{+}$ 391.1588, found 391.1587.

Triazole 250. Following the general procedure for deprotection of the isopropylidene, triazole **249** (37.6 mg, 0.10 mmole) was converted into triazole **250** at room temperature in 36 h. The residue was washen by cold methanol to afford triazole **250** (28.4 mg, 92%) as a white solid: mp 162-165 ^{o}C; $[\alpha]_{D}^{20}$ -46.9 (*c* 1.15, DMF); IR (thin film) 3459, 3317, 3091, 2938, 2870, 1650, 1616, 1424, 1362, 1347, 1292, 1078, 1050, 1014 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6:D_2O 3:1) δ 1.27-1.38 (2H, m), 1.45-1.48 (1H, m), 2.11-2.14 (1H, m), 2.20-2.29 (2H, m), 2.29-2.33 (1H, m), 3.59-3.61 (1H, m), 3.77 (1H, s), 3.91 (1H, t, *J* = 6.7 Hz), 4.67-4.71 (1H, m), 4.78-4.82 (1H, m), 8.51 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 30.7 (CH_2), 35.2 (CH), 35.8

(CH), 50.7 (CH), 63.7 (CH_2), 67.1 (CH), 68.6 (CH), 69.0 (CH), 69.3 (CH), 72.1 (CH), 127.3 (CH), 142.7 (C), 161.6 (C)； MS (ESI) *m/z* (relative intensity) 351 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{20}N_4O_6$ $[M+Na]^+$ 351.1275, found 351.1277.

Triazole 251. Following the general procedure for deprotection of the isopropylidene, triazole **246** (46 mg, 0.11 mmole) was converted into triazole **251** at 100 ^oC in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 3:1) to afford triazole **251** (38.9 mg, 94%) as a white solid: mp 149-155 ^oC; $[\alpha]_D^{20}$ -58.3 (*c* 0.82, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3369, 2917, 1669, 1647, 1459, 1425, 1384, 1236, 1203, 1124, 1074, 1059, 1025 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.50-1.63 (2H, m), 1.66-1.70 (1H, m), 2.45-2.50 (1H, m), 2.61-2.67 (3H, m), 3.80-3.83 (1H, m), 4.01 (1H, dd, *J* = 5.1, 2.8 Hz), 4.20 (1H, t, *J* = 6.4 Hz), 4.92-5.01 (2H, m), 7.34 (1H, t, *J* = 7.4 Hz), 7.43 (2H, t, *J* = 7.6 Hz), 7.84 (2H, d, *J* = 7.4 Hz), 8.46 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 31.8 (CH_2), 36.6 (CH), 38.0 (CH), 51.6 (CH), 66.0 (CH_2), 69.0 (CH), 70.5 (CH), 70.8 (CH), 71.6 (CH), 74.2 (CH), 123.6 (CH), 126.7 (CH), 129.4 (CH), 130.0 (CH), 131.6 (C), 148.8 (C)； MS (ESI) *m/z* (relative intensity) 384 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{23}N_3O_5$ $[M+Na]^+$ 384.1530, found 384.1532.

Triazole 252. Following the general procedure for deprotection of the isopropylidene, triazole **247** (36 mg, 0.08 mmole) was converted into triazole **252** at 100 ^oC in 12 h. The residue was then fractionated by flash column chromatography

($CHCl_3$:MeOH, 3:1) to afford triazole **252** (30.4 mg, 93%) as a white solid: mp 153-156 ^oC; $[\alpha]_D^{20}$ -63.2 (*c* 0.48, MeOH); R_f 0.37 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3391, 3307, 2930, 2540, 1628, 1490, 1465, 1385, 1309, 1249, 1161, 1073, 1021 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.51-1.56 (1H, m), 1.57-1.67 (2H, m), 2.44-2.48 (1H, m), 2.62-2.71 (3H, m), 3.80-3.83 (1H, m), 3.96 (3H, s), 3.99-4.01 (1H, m), 4.93-4.95 (1H, m), 5.02 (1H, t, *J* = 7.1 Hz), 7.04 (1H, t, *J* = 7.5 Hz), 7.11 (1H, d, *J* = 8.3 Hz), 7.33-7.37 (1H, m), 8.10 (1H, d, *J* = 7.7 Hz), 8.42 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 31.9 (CH_2), 36.5 (CH), 38.3 (CH), 51.3 (CH), 55.9 (CH_3), 66.2 (CH_2), 69.1 (CH), 70.5 (CH), 70.7 (CH), 71.9 (CH), 74.5 (CH), 112.3 (CH), 120.1 (CH), 121.8 (CH), 126.7 (CH), 128.1 (CH), 130.5 (CH), 144.2 (C), 157.5 (C)；MS (ESI) *m/z* (relative intensity) 414 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{25}N_3O_6$ $[M+Na]^+$ 414.1636, found 414.1637.

Triazole 253. Following the general procedure for deprotection of the isopropylidene, triazole **248** (46 mg, 0.11 mmole) was converted into triazole **253** at 100 ^oC in 12 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 3:1) to afford triazole **253** (40.9 mg, 72%) as a white solid: mp 153-156 ^oC; $[\alpha]_D^{20}$ -49.2 (*c* 1.00, MeOH); R_f 0.27 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3392, 2917, 1684, 1370, 1205, 1124, 1049 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.51-1.58 (2H, m), 1.69-1.71 (1H, m), 2.50-2.54 (1H, m), 2.62-2.71 (3H, m), 3.85-3.86 (1H, m), 4.05 (1H, br s), 4.24-4.27 (1H, m), 5.00-5.07 (2H, m), 7.34-7.37 (1H, m), 7.87-7.90 (1H, m), 8.05 (1H, d, *J* = 7.8 Hz), 8.57 (1H, d, *J* = 4.0 Hz), 8.60

(1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 31.8 (CH_2), 36.5 (CH), 38.0 (CH), 51.4 (CH), 65.9 (CH_2), 69.0 (CH), 70.5 (CH), 70.8 (CH), 71.7 (CH), 74.3 (CH), 121.7 (CH), 124.6 (CH), 125.5 (CH), 138.9 (CH), 148.4 (C), 150.4 (CH), 150.7 (C)；MS (ESI) *m/z* (relative intensity) 385 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{24}N_4O_5$ $[M+Na]^+$ 385.1482, found 385.1483.

Triazole **254.** Following the general procedure for copper catalyzed azide-alkyne cycloaddition, azide **205** (85.6 mg, 0.26 mmole) was converted into triazole **254** in 2 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 2:1) to afford triazole **254** (107.1 mg, 95%) as a white solid: mp 159-160 ^{o}C; $[\alpha]_D^{20}$ +32.4 (*c* 1.85, $CHCl_3$); R_f 0.35 (hexane:EtOAc, 2:1); IR (thin film) 3138, 2981, 2935, 1725, 1437, 1382, 1369, 1234, 1211, 1152, 1068, 1041 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 1.23 (9H, s), 1.32 (3H, s), 1.51 (3H, s), 1.82-1.90 (1H, m), 1.98 (1H, dt, *J* = 17.8, 5.4 Hz), 2.57 (1H, td, *J* = 9.7, 6.0 Hz), 2.90 (1H, br s), 3.19 (1H, dt, *J* = 10.7, 7.3 Hz), 3.91 (3H, s), 4.57 (1H, dd, *J* = 6.8, 4.7 Hz), 5.18 (1H, t, *J* = 6.5 Hz), 5.44 (1H, t, *J* = 6.5 Hz), 5.72-5.75 (1H, m), 5.86-5.89 (1H, m), 8.49 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 24.9 (CH_3), 27.3 (CH_3), 27.4 (CH_2), 27.9 (CH_3), 38.3 (CH), 41.9 (CH), 43.6 (CH), 52.2 (CH_3), 69.4 (CH), 81.1 (C), 82.9 (CH), 84.2 (CH), 113.2 (C), 126.1 (CH), 126.2 (CH), 129.5 (CH), 139.5 (C), 161.1 (C), 173.2 (C)；MS (ESI) *m/z* (relative intensity) 442 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{29}N_3O_6$ $[M+Na]^+$ 442.1949, found 442.1952.

Triazole 255. Following the general procedure for copper catalyzed azide-alkyne cycloaddition, azide **205** (84.4 mg, 0.25 mmole) was converted into triazole **255** in 25 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 4:1) to afford triazole **255** (110 mg, 99%) as a white solid: mp 147-148 ^{o}C; $[\alpha]_D^{20}$ +18.8 (*c* 1.80, $CHCl_3$); R_f 0.33 (hexane:EtOAc, 4:1); IR (thin film) 3030, 2980, 2932, 1724, 1483, 1438, 1382, 1369, 1246, 1211, 1152, 1066 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.23 (9H, s), 1.31 (3H, s), 1.53 (3H, s), 1.85-1.89 (2H, m), 2.54-2.60 (1H, m), 2.86-2.91 (1H, m), 3.22-3.29 (1H, m), 4.61 (1H, dd, *J* = 6.6, 4.4 Hz), 5.07 (1H, dd, *J* = 7.2, 4.8 Hz), 5.38 (1H, dd, *J* = 6.6, 4.9 Hz), 5.68-5.73 (1H, m), 5.85-5.89 (1H, m), 7.27-7.31 (1H, m), 7.36-7.40 (1H, m), 7.74 (1H, s), 7.77-7.79 (2H, m); ^{13}C NMR (100 MHz) δ 24.9 (CH_3), 27.3 (CH_3), 27.3 (CH_2), 27.8 (CH_3), 38.4 (CH), 41.9 (CH), 43.8 (CH), 68.8 (CH), 80.8 (C), 83.2 (CH), 84.4 (CH), 112.9 (C), 121.6 (CH), 125.7 (CH), 126.1 (CH), 126.3 (C), 128.0 (CH), 128.8 (CH), 130.6 (C), 147.2 (C), 173.3 (C)； MS (ESI) *m/z* (relative intensity) 460 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{25}H_{31}N_3O_4$ $[M+Na]^+$ 460.2207, found 460.2206.

Triazole 256. Following the general procedure for copper catalyzed azide-alkyne cycloaddition, azide **205** (87 mg, 0.26 mmole) was converted into triazole **256** in 28 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 1:1) to afford triazole **256** (115.2 mg, 95%) as a white solid: mp 153-157 ^{o}C; $[\alpha]_D^{20}$ +33.2 (*c* 1.55, $CHCl_3$); R_f 0.28 (hexane:EtOAc, 4:1);

IR (thin film) 2979, 2933, 2839, 1724, 1490, 1458, 1381, 1369, 1249, 1212, 1152, 1067 cm^{-1}; ^1H NMR (400 MHz) δ 1.25 (9H, s), 1.32 (3H, s), 1.55 (3H, s), 1.72-1.80 (1H, m), 1.86-1.94 (1H, m), 2.56 (1H, td, *J* = 8.6, 6.5 Hz), 2.89 (1H, br s), 3.25-3.31 (1H, m), 3.92 (3H, m), 4.66 (1H, dd, *J* = 6.5, 4.3 Hz), 5.09 (1H, dd, *J* = 7.3, 4.2 Hz), 5.36 (1H, dd, *J* = 6.5, 4.3 Hz), 5.67-5.71 (1H, m), 5.85-5.89 (1H, m), 6.95 (1H, d, *J* = 8.2 Hz), 7.02-7.06 (1H, m), 7.26-7.30 (1H, m), 8.02 (1H, s), 8.30 (1H, dd, *J* = 7.7, 1.6 Hz); ^{13}C NMR (100 MHz) δ 25.0 (CH_3), 27.0 (CH_2), 27.4 (CH_3), 27.9 (CH_3), 38.4 (CH), 41.9 (CH), 44.0 (CH), 55.4 (CH_3), 68.6 (CH), 80.8 (C), 83.6 (CH), 84.8 (CH), 110.8 (CH), 112.7 (C), 119.5 (C), 121.0 (CH), 124.9 (CH), 126.2 (CH), 126.5 (CH), 127.6 (CH), 128.8 (CH), 142.6 (C), 155.7 (C), 173.4 (C)；MS (ESI) *m/z* (relative intensity) 490 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{26}H_{33}N_3O_5$ $[M+Na]^+$ 490.2312, found 490.2312.

Triazole 257. Following the general procedure for copper catalyzed azide-alkyne cycloaddition, azide **205** (130 mg, 0.39 mmole) was converted into triazole **257** in 31 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 2:1) to afford triazole **257** (169.7 mg, 100%) as a white solid: mp 153-155 ^oC; $[\alpha]_D^{20}$ +27.1 (*c* 1.50, $CHCl_3$); R_f 0.37 (hexane:EtOAc, 4:3); IR (thin film) 2980, 2931, 1724, 1604, 1473, 1457, 1382, 1369, 1249, 1209, 1153, 1065 cm^{-1}; ^1H NMR (400 MHz) δ 1.24 (9H, s), 1.31 (3H, s), 1.52 (3H, s), 1.58-1.64 (1H, m), 1.87-1.94 (1H, m), 2.60 (1H, q, *J* = 7.4 Hz), 2.90 (1H, br s), 3.29 (1H, q, *J* = 7.9 Hz), 4.65 (1H, dd, *J* = 6.3, 3.8 Hz), 5.10 (1H, dd, *J* = 7.2, 4.2 Hz), 5.31 (1H, dd, *J*

= 6.1, 4.5 Hz), 5.64-5.66 (1H, m), 5.82-5.84 (1H, m), 7.18-7.21 (1H, m), 7.72-7.76 (1H, m), 8.11 (1H, s), 8.13 (1H, s), 8.55 (1H, d, J = 4.6 Hz); ^{13}C NMR (100 MHz) δ 24.9 (CH_3), 26.6 (CH_2), 27.3 (CH_3), 27.9 (CH_3), 38.2 (CH), 41.4 (CH), 43.7 (CH), 69.1 (CH), 80.8 (C), 83.5 (CH), 84.7 (CH), 112.6(C), 120.3 (CH), 122.9 (CH), 123.9 (CH), 126.3 (CH), 126.4 (CH), 137.1 (CH), 147.7 (C), 149.3 (CH), 150.2 (C), 173.3 (C)；MS (ESI) *m/z* (relative intensity) 461 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{24}H_{30}N_4O_4$ [M+Na]$^+$ 461.2159, found 461.2158.

Triazole 258. In a sealed tube, triazole **254** (68 mg, 0.16 mmole) was dissolved in the ammonia solution (5 mL, 0.7M in MeOH) and stirred at 110 ^{o}C in 12 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 20:1) to afford triazole **258** (63.7 mg, 97% yield) as a white solid: mp 208-210 ^{o}C; $[\alpha]_D^{20}$ +34.2 (*c* 0.80, $CHCl_3$); R_f 0.32 ($CHCl_3$:MeOH, 20:1); IR (thin film) 3401, 3192, 2981, 2934, 1723, 1660, 1608, 1369, 1297, 1252, 1212, 1153, 1068 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.26 (9H, s), 1.30 (3H, s), 1.51 (3H, s), 1.72 (1H, dt, J = 17.9, 5.4 Hz), 1.86-1.93 (1H, m), 2.49-2.55 (1H, m), 2.89 (1H, br s), 3.22-3.28 (1H,m), 4.60 (1H, dd, J = 6.6, 4.1 Hz), 5.06 (1H, dd, J = 7.1, 4.9 Hz), 5.30 (1H, dd, J = 6.3, 5.2 Hz), 5.66-5.69 (1H, m), 5.82-5.84 (1H, m), 6.20 (1H, s), 7.13 (1H, s), 8.11 (1H, s); ^{13}C NMR (100 MHz) δ 24.9 (CH_3), 27.0 (CH_2), 27.3 (CH_3), 27.9 (CH_3), 38.3 (CH), 41.7 (CH), 43.6 (CH), 69.4 (CH), 81.0 (C), 83.1 (CH), 84.4 (CH), 113.1 (C), 126.2 (CH), 126.3 (CH), 127.7

(CH), 142.3 (C), 162.2 (C), 173.1 (C)；MS (ESI) *m/z* (relative intensity) 427 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{20}H_{28}N_4O_5$ [M+Na]$^+$ 427.1952, found 427.1957.

Triazole 259. Following the general procedure for deprotection of the isopropylidene, triazole **254** (70 mg, 0.17 mmole) was converted into triazole **259** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 15:1) to afford triazole **259** (58.2 mg, 92%) as a white solid: mp 169-171 ^oC; $[\alpha]_D^{20}$ +62.2 (*c* 0.90, MeOH); R_f 0.30 ($CHCl_3$:MeOH, 2:1); IR (thin film) 3369, 3140, 2916, 1726, 1705, 1544, 1528, 1436, 1367, 1234, 1155, 1111, 1047, 1021 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.22 (9H, s), 1.82-1.89 (1H, m), 2.19-2.24 (1H, m), 2.25-2.31 (1H, m), 2.79-2.81 (1H, m), 3.13-3.21 (1H, m), 3.91 (3H, s), 4.02 (1H, t, *J* = 5.3 Hz), 4.52-4.53 (1H, m), 5.19 (1H, t, *J* = 8.0 Hz), 5.83-5.86 (1H, m), 5.90-5.92 (1H, m), 8.56 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.1 (CH_3), 29.2 (CH_2), 38.1 (CH), 40.7 (CH), 44.2 (CH), 52.5 (CH_3), 68.7 (CH), 75.3 (CH), 76.2 (CH), 81.8 (C), 126.6 (CH), 128.7 (CH), 131.9 (CH), 139.9 (C), 162.4 (C), 175.2 (C)；MS (ESI) *m/z* (relative intensity) 402 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{18}H_{25}N_3O_6$ [M+Na]$^+$ 402.1636, found 442.1637.

Triazole 260. Triazole **259** (51 mg, 0.13 mmole) was dissolved in the ammonia solution (7 mL, 0.7M in MeOH) and stirred at 100 ^oC in 15 h. The solvent was

removed under reduced pressure and the residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford triazole **260** (42 mg, 86% yield) as a white solid: mp 286-289 ^oC; $[\alpha]_D^{20}$ +78.6 (*c* 1.15, DMSO); R_f 0.23 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3419, 3317, 3091, 1716, 1648, 1615, 1367, 1305, 1156, 1092, 1046 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.16 (9H, s), 1.73-1.79 (1H, m), 2.04-2.10 (1H, m), 2.10-2.16 (1H, m), 2.65-2.66 (1H, m), 3.00 (1H, q, *J* = 9.4 Hz), 3.85 (1H, s), 4.32 (1H, br s), 5.05 (1H, s), 5.09 (1H, t, *J* = 8.2 Hz), 5.12(1H, br s), 5.75-5.79 (1H, m), 5.83-5.85 (1H, m), 7.41 (1H, s), 7.79 (1H, s), 8.55 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.4 (CH_3), 27.5 (CH_2), 36.1 (CH), 38.8 (CH), 42.5 (CH), 66.5 (CH), 73.9 (CH), 74.5 (CH), 79.8 (C), 125.1 (CH), 128.2 (CH), 128.3 (CH), 142.3 (C), 161.7 (C), 173.0 (C)；MS (ESI) *m/z* (relative intensity) 387 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{24}N_4O_5$ $[M+Na]^+$ 387.1639, found 387.1632.

Triazole 261. Following the general procedure for deprotection of the isopropylidene, triazole **255** (69 mg, 0.16 mmole) was converted into triazole **261** using *t*-BuOH/H_2O (v/v, 1/5) instead of H_2O (50 mL) at room temperature in 48 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 20:1) to afford triazole **261** (60.4 mg, 96%) as a white solid: mp 211-212 ^oC; $[\alpha]_D^{20}$ +57.8 (*c* 1.32, MeOH); R_f 0.27 ($CHCl_3$:MeOH, 20:1); IR (thin film) 3339, 3135, 2977, 2929, 2841, 1717, 1461, 1439, 1390, 1368, 1297, 1244, 1154, 1115, 1057 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 3:1) δ 1.15 (9H, s), 1.84-1.92 (1H, m), 2.23 (1H, dt,

J = 16.7, 5.3 Hz), 2.35 (1H, td, *J* = 10.6, 5.0 Hz), 2.81-2.84 (1H, m), 3.17-3.24 (1H, m), 4.08 (1H, t, *J* = 5.5 Hz), 4.53 (1H, dd, *J* = 6.5, 5.4 Hz), 5.14 (1H, dd, *J* = 8.7, 7.0 Hz), 5.81-5.85 (1H, m), 5.91 (1H, dt, *J* = 9.9, 2.6 Hz), 7.31 (1H, t, *J* = 7.4 Hz), 7.41 (1H, t, *J* = 7.6 Hz), 7.78 (1H, d, *J* = 7.4 Hz), 8.16 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 3:1) δ 28.1 (CH_3), 28.9 (CH_2), 37.8 (CH), 40.4 (CH), 43.6 (CH), 68.1 (CH), 75.4 (CH), 81.6 (C), 124.0 (CH), 126.35 (CH), 126.39 (CH), 128.4 (CH), 129.0 (CH), 129.7 (CH), 131.2 (C), 147.8 (C), 175.1 (C)； MS (ESI) *m/z* (relative intensity) 420 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{22}H_{27}N_3O_4$ [M+Na]$^+$ 420.1894, found 420.1899.

Triazole 262. Following the general procedure for deprotection of the isopropylidene, triazole **256** (69 mg, 0.15 mmole) was converted into triazole **262** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 15:1) to afford triazole **262** (60.6 mg, 96%) as a white solid: mp 83-85 ^oC; $[\alpha]_D^{20}$ +39.1 (*c* 0.80, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 15:1); IR (thin film) 3369, 2974, 2930, 1717, 1491, 1367, 1290, 1249, 1151, 1074, 1047, 1028 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.13 (9H, s), 1.83-1.90 (1H, m), 2.22 (1H, dt, *J* = 16.7, 5.3 Hz), 2.32 (1H, td, *J* = 10.7, 4.9 Hz), 2.81-2.85 (1H, m), 3.21 (1H, q, *J* = 9.3 Hz), 3.94 (3H, s), 4.13 (1H, t, *J* = 5.7 Hz), 4.49 (1H, t, *J* = 5.6 Hz), 5.17 (1H, dd, *J* = 8.9, 6.3 Hz), 5.83-5.87 (1H, m), 5.94 (1H, dt, *J* = 9.9, 2.5 Hz), 7.04 (1H, t, *J* = 7.5 Hz), 7.09 (1H, d, *J* = 8.3 Hz), 7.31-7.35 (1H, m), 8.11 (1H, dd, *J* = 7.7, 1.6 Hz), 8.26 (1H, s); ^{13}C NMR (100 MHz,

CD_3OD) δ 28.0 (CH_3), 29.3 (CH_2), 38.3 (CH), 40.8 (CH), 43.9 (CH), 55.9 (CH_3), 68.2 (CH), 76.1 (CH), 76.7 (CH), 81.7 (C), 112.3 (CH), 120.2 (C), 121.8 (CH), 126.6 (CH), 127.5 (CH), 128.0 (CH), 128.9 (CH), 130.4 (CH), 143.5 (C), 157.3 (C), 175.5 (C); MS (ESI) *m/z* (relative intensity) 450 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{23}H_{29}N_3O_5$ $[M+Na]^+$ 450.1999, found 450.1996.

Triazole 263. Following the general procedure for deprotection of the isopropylidene, triazole **257** (78 mg, 0.18 mmole) was converted into triazole **263** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 15:1) to afford triazole **263** (66.8 mg, 94%) as a white solid: mp 145-147 ^oC; $[\alpha]_D^{20}$ +48.6 (*c* 1.45, MeOH); R_f 0.27 ($CHCl_3$:MeOH, 15:1); IR (thin film) 3351, 3029, 2975, 2930, 1718, 1601, 1571, 1474, 1368, 1294, 1250, 1151, 1112 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.14 (9H, s), 1.83-1.92 (1H, m), 2.22 (1H, dt, *J* = 16.7, 5.3 Hz), 2.34 (1H, td, *J* = 10.6, 4.9 Hz), 2.82-2.86 (1H, m), 3.19-3.26 (1H, m), 4.09 (1H, t, *J* = 5.5 Hz), 4.55 (1H, dd, *J* = 6.8, 5.3 Hz), 5.22 (1H, dd, *J* = 7.1, 8.8 Hz), 5.82-5.87 (1H, m), 5.93 (1H, dt, *J* = 10.0, 2.7 Hz), 7.33-7.36 (1H, m), 7.90 (1H, td, *J* = 7.8, 1.6 Hz), 8.07 (1H, d, *J* = 8.0 Hz), 8.42 (1H, s), 8.57 (1H, d, *J* = 4.5 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 28.1 (CH_3), 29.2 (CH_2), 38.2 (CH), 40.8 (CH), 44.1 (CH), 68.5 (CH), 75.7 (CH), 76.5 (CH), 81.6 (C), 121.4 (C), 124.4 (CH), 126.4 (CH), 126.6 (CH), 128.8 (CH), 138.8 (CH), 148.0 (C), 150.5 (CH), 151.1 (C), 175.3 (C); MS (ESI) *m/z* (relative intensity) 421 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{26}N_4O_4$ $[M+Na]^+$

421.1826, found 421.1825.

Triazole 264. Following the general procedure for deprotection of the isopropylidene, triazole **258** (38.6 mg, 0.10 mmole) was converted into triazole **264** at 100 ^{o}C in 36 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH:AcOH, 2:1:0.2) to afford triazole **264** (28.2 mg, 96%) as a white solid: mp 94-97 ^{o}C; $[\alpha]_D^{20}$ +59.4 (*c* 0.60, DMF); R_f 0.23 ($CHCl_3$:MeOH:AcOH, 2:1:0.2); IR (thin film) 3425, 3215, 1701, 1676, 1403, 1274, 1201, 1139, 1052 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.91-1.97 (1H, m), 2.19-2.24 (1H, m), 2.30-2.35 (1H, m), 2.81-2.87 (1H, br s), 3.22 (1H, q, *J* = 9.4 Hz), 4.05 (1H, t, *J* = 4.7 Hz), 4.62 (1H, t, *J* = 5.7 Hz), 5.18 (1H, t, *J* = 7.6 Hz), 5.82-5.86 (1H, m), 5.92 (1H, d, *J* = 9.9 Hz), 8.45 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.9 (CH_2), 39.0 (CH), 39.8 (CH), 44.3 (CH), 68.8 (CH), 75.1 (CH), 76.2 (CH), 126.7 (CH), 128.6 (CH), 129.7 (C), 131.6 (CH), 163.8 (C), 177.8 (C)； MS (ESI) *m/z* (relative intensity) 331 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{13}H_{16}N_4O_5$ [M+Na]$^+$ 331.1013, found 331.1016.

Triazole 265. Following the general procedure for deprotection of the isopropylidene, triazole **255** (43.9 mg, 0.10 mmole) was converted into triazole **265** at 100 ^{o}C in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1; to $CHCl_3$:MeOH, 5:1) to afford triazole **265** (33.2 mg, 97%) as a white solid: mp 234-236 ^{o}C; $[\alpha]_D^{20}$ +51.7 (*c* 0.65, MeOH); R_f 0.20 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3389, 3085, 2923, 1648, 1437, 1208, 1197, 1169, 1098, 1076,

1041 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.93-2.00 (1H, m), 2.21 (1H, dt, *J* = 16.9, 5.1 Hz), 2.27-2.33 (1H, m), 2.83-2.84 (1H, m), 3.24-3.29 (1H, m), 4.10 (1H, t, *J* = 5.4 Hz), 4.63 (1H, dd, *J* = 6.9, 5.1 Hz), 5.18 (1H, dd, *J* = 8.8, 7.1 Hz), 5.82-5.87 (1H, m), 5.90-5.93 (1H, m), 7.31-7.35 (1H, m), 7.42 (2H, t, *J* = 7.5 Hz), 7.82 (1H, d, *J* = 7.2 Hz), 8.30 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.9 (CH_2), 39.1 (CH), 40.3 (CH), 44.1 (CH), 68.6 (CH), 75.6 (CH), 76.6 (CH), 124.5 (CH), 126.8 (CH), 127.0 (CH), 128.6 (CH), 129.2 (CH), 129.9 (CH), 131.8 (C), 148.1 (C), 179.2 (C)； MS (ESI) *m/z* (relative intensity) 364 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{19}N_3O_4$ $[M+Na]^+$ 364.1268, found 364.1269.

Triazole 266. Following the general procedure for deprotection of the isopropylidene, triazole **256** (40 mg, 0.09 mmole) was converted into triazole **266** at 100 ^oC in 20 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1; to $CHCl_3$:MeOH, 4:1) to afford triazole **266** (31.5 mg, 99%) as a white solid: mp 163-165 ^oC; $[\alpha]_D^{20}$ +36.7 (*c* 1.05, MeOH); R_f 0.27 ($CHCl_3$:MeOH, 9:1); IR (thin film) 3401, 3293, 3153, 2946, 2839, 2679, 2531, 2376, 1684, 1491, 1406, 1250, 1209, 1113 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.92-2.00 (1H, m), 2.21 (1H, dt, *J* = 16.9, 5.1 Hz), 2.35 (1H, td, *J* = 9.8, 5.0 Hz), 2.83-2.84 (1H, m), 3.24-3.26 (1H, m), 3.94 (3H, s), 4.11 (1H, t, *J* = 5.5 Hz), 4.62 (1H, dd, *J* = 6.6, 5.2 Hz), 5.17 (1H, dd, *J* = 8.9, 6.9 Hz), 5.82-5.87 (1H, m), 5.91-5.93 (1H, m), 7.01-7.55 (1H, m), 7.08 (1H, d, *J* = 8.2 Hz), 7.30-7.35 (1H, m), 8.09 (1H, dd, *J* = 7.7, 1.6 Hz), 8.27 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.8 (CH_2), 39.0 (CH), 39.9 (CH), 44.0 (CH), 55.9 (CH_3), 68.4

(CH), 75.7 (CH), 76.7 (CH), 112.3 (CH), 120.3 (C), 121.7 (CH), 126.8 (CH), 127.4 (CH), 128.1 (CH), 128.7 (CH), 130.3 (CH), 143.6 (C), 157.4 (C), 178.4 (C); MS (ESI) *m/z* (relative intensity) 394 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{19}H_{21}N_3O_5$ [M+Na]$^+$ 394.1373, found 394.1372.

Triazole 267. Following the general procedure for deprotection of the isopropylidene, triazole **257** (58.8 mg, 0.13 mmole) was converted into triazole **267** at 100 ^{o}C in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **267** (45.8 mg, 100%) as a white solid: mp 189-195 ^{o}C; $[\alpha]_D^{20}$ +39.6 (*c* 1.15, MeOH); R_f 0.23 ($CHCl_3$:MeOH, 3:1); IR (thin film) 3401, 3234, 2838, 2592, 2376, 2171, 1959, 1684, 1602, 1574, 1384, 1182 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.92-1.98 (1H, m), 2.17-2.23 (1H, m), 2.25-2.29 (1H, m), 2.84 (1H, br s), 3.26-3.28 (1H, m), 4.12 (1H, t, *J* = 5.3 Hz), 4.65 (1H, t, *J* = 5.4 Hz), 5.23 (1H, t, *J* = 7.6 Hz), 5.82-5.86 (1H, m), 5.90-5.92 (1H, m), 7.34-7.37 (1H, m), 7.88-7.92 (1H, m), 8.04 (1H, d, *J* = 7.8 Hz), 8.42 (1H, s), 8.56 (1H, d, *J* = 3.4 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 29.0 (CH_2), 39.2 (CH), 40.5 (CH), 44.1 (CH), 68.8 (CH), 75.6 (CH), 76.6 (CH), 121.7 (CH), 124.5 (CH), 126.5 (CH), 127.1 (CH), 128.6 (CH), 139.0 (CH), 147.8 (C), 150.3 (CH), 151.0 (C), 179.4 (C); MS (ESI) *m/z* (relative intensity) 365 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{18}N_4O_4$ [M+Na]$^+$ 365.1220, found 365.1228.

Triazole 268 and triazole 268a. Following the general procedure for

hydrogenation of alkene, triazole **254** (94.2 mg, 0.22 mmole) was converted into triazole **268** in 32 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 2:1; to Chloroform:Acetone, 2:1) to afford first triazole **268** (17 mg, 18%) as a white solid and then triazole **268a** (61.7 mg, 72%) as a white solid.

Following the general procedure for hydrogenation of alkene, triazole **254** (51.7 mg, 0.12 mmole) was converted into triazole **268** in 6 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 2:1) to afford triazole **268** (45.2 mg, 87%) as a white solid.

Data for triazole **268**: mp 180-183 ^{o}C; $[\alpha]_D^{20}$ -30.0 (*c* 1.33, $CHCl_3$); R_f 0.37 (hexane:EtOAc, 2:1); IR (thin film) 3123, 2979, 2929, 2857, 1724, 1541, 1456, 1437, 1371, 1263, 1235, 1209, 1149, 1096, 1068, 1037 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.21 (9H, s), 1.31 (3H, s), 1.44-1.48 (1H, m), 1.51 (3H, s), 1.52-1.58 (1H, m), 1.61-1.66 (2H, m), 1.69-1.73 (1H, m), 1.86-1.90 (1H, m), 2.36 (1H, td, *J* = 11.1, 4.0 Hz), 2.47-2.49 (1H, m), 3.02 (1H, dt, *J* = 10.6, 6.7 Hz), 3.91 (3H, s), 4.68 (1H, d, *J* = 7.1 Hz), 4.87 (1H, t, *J* = 6.1 Hz), 5.56 (1H, dd, *J* = 7.4, 5.6 Hz), 8.06 (1H, s); ^{13}C NMR (100 MHz) δ 20.5 (CH_2), 24.7 (CH_2), 24.9 (CH_3), 27.2 (CH_3), 27.9 (CH_3), 29.1 (CH_2), 41.3 (CH), 43.3 (CH), 44.5 (CH), 52.2 (CH_3), 69.9 (CH), 80.4 (C), 80.9 (CH), 82.5 (CH), 113.9 (C), 129.6 (CH), 139.6 (C), 161.2 (C), 173.4 (C)； MS (ESI) *m/z* (relative intensity) 444 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{31}N_3O_6$ $[M+Na]^+$ 444.2105, found 394.2109.

Data for triazole **268a**: mp 200.1-200.4 ^{o}C; $[\alpha]_D^{20}$ -30.2 (*c* 0.65, MeOH); R_f 0.22

($CHCl_3$:acetone, 2:1); IR (thin film) 3393, 3120, 2916, 1723, 1539, 1378, 1338, 1264, 1231, 1150, 1086, 1074, 1048, 1033 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 1.07-1.13 (1H, m), 1.16 (9H, s), 1.42-1.52 (1H, m), 1.53-1.61 (1H, m), 1.62-1.68 (1H, m), 1.89-1.95 (2H, m), 2.26-2.33 (2H, m), 2.77 (1H, dT, *J* = 11.6, 6.8 Hz), 3.89 (3H, s), 4.06-4.10 (1H, m), 4.85 (2H, dt, *J* = 11.4, 7.3 Hz), 8.34 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 20.7 (CH_2), 24.8 (CH_2), 27.9 (CH_3), 30.4 (CH_2), 39.6 (CH), 42.0 (CH), 43.7 (CH), 52.4 (CH_3), 70.1 (CH), 71.2 (CH), 73.4 (CH), 81.2 (C), 130.6 (CH), 139.4 (CH), 161.9 (C), 174.8 (C)； MS (ESI) *m/z* (relative intensity) 404 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{18}N_4O_4$ $[M+Na]^+$ 404.1792, found 404.1792.

Triazole 269. Following the general procedure for hydrogenation of alkene, triazole **255** (87 mg, 0.20 mmole) was converted into triazole **269** in 10 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 4:1) to afford triazole **269** (87.3 mg, 100%) as a white solid: mp 156-157 ^oC; $[\alpha]_D^{20}$ -39.6 (*c* 1.15, $CHCl_3$); R_f 0.27 (hexane:EtOAc, 4:1); IR (thin film) 3401, 2917, 2860, 1719, 1628, 1449, 1384, 1209, 1153, 1053 cm^{-1}; ^1H NMR (400 MHz) δ 1.18 (9H, s), 1.20-1.27 (1H, m), 1.33 (3H, s), 1.43-1.50 (1H, m), 1.52 (3H, s), 1.55-1.67 (2H, m), 1.68-1.71 (1H, m), 1.87-1.92 (1H, m), 2.42 (1H, td, *J* = 10.9, 4.0 Hz), 2.46-2.50 (1H, m), 3.05 (1H, dt, *J* = 10.4, 6.8 Hz), 4.70 (1H, t, *J* = 7.0 Hz), 4.89 (1H, dd, *J* = 6.6, 5.5 Hz), 5.59 (1H, dd, *J* = 7.4, 5.3 Hz), 7.28-7.31 (1H, m), 7.37-7.40 (2H, m), 7.76 (1H, s), 7.77-7.79 (2H, m); ^{13}C NMR (100 MHz) δ 20.5 (CH_2), 24.8 (CH_2), 24.9 (CH_3), 27.3

(CH_3), 27.9 (CH_3), 29.0 (CH_2), 41.5 (CH), 43.4 (CH), 44.4 (CH), 69.4 (CH), 80.6 (CH), 80.7 (C), 82.8 (CH), 113.6 (C), 121.8 (CH), 125.9 (CH), 128.1 (CH), 128.8 (CH), 130.7 (C), 147.4 (C), 173.6 (C)；MS (ESI) *m/z* (relative intensity) 462 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{25}H_{33}N_3O_4$ $[M+Na]^+$ 462.2363, found 462.2366.

Triazole 270. Following the general procedure for hydrogenation of alkene, triazole **256** (63 mg, 0.13 mmole) was converted into triazole **270** in 4 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 4:1) to afford triazole **270** (63.2 mg, 100%) as a white solid: mp 160-161 ^oC; $[\alpha]_D^{20}$ -43.4 (*c* 1.43, $CHCl_3$); R_f 0.24 (hexane:EtOAc, 4:1); IR (thin film) 3400, 2979, 2930, 2860, 1723, 1491, 1458, 1382, 1369, 1249, 1153, 1049 cm^{-1}; ^1H NMR (400 MHz) δ 1.15-1.23 (10H, m), 1.32 (3H, s), 1.52 (3H, s), 1.54-1.59 (2H, m), 1.60-1.62 (1H, m), 1.86-1.90 (1H, m), 2.40-2.47 (2H, m), 3.06 (1H, dt, *J* = 9.8, 6.9 Hz), 3.91 (3H, s), 4.70 (1H, t, *J* = 6.7 Hz), 4.90 (1H, dd, *J* = 6.8, 5.0 Hz), 5.57 (1H, dd, *J* = 7.2, 4.9 Hz), 6.94-7.31 (1H, d, *J* = 8.2 Hz), 7.01-7.05 (1H, m), 7.25-7.29 (1H, m), 8.05 (1H, s), 8.29 (1H, dd, *J* = 7.7, 1.6 Hz); ^{13}C NMR (100 MHz) δ 20.5 (CH_2), 24.7 (CH_2), 24.8 (CH_3), 27.2 (CH_3), 27.9 (CH_3), 28.7 (CH_2), 41.3 (CH), 43.4 (CH), 44.1 (CH), 55.4 (CH_3), 69.2 (CH), 80.5 (C), 81.0 (CH), 83.1 (CH), 110.8 (CH), 113.2 (C), 119.5 (CH), 120.9 (CH), 125.1 (CH), 127.6 (CH), 128.8 (CH), 142.7 (C), 155.8 (C), 173.5 (C)；MS (ESI) *m/z* (relative intensity) 492 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{26}H_{35}N_3O_5$ $[M+Na]^+$ 492.2469, found 492.2465.

Triazole 271 and **triazole 271a.** Following the general procedure for hydrogenation of alkene, triazole **257** (113.3 mg, 0.26 mmole) was converted into triazole **271** in 72 h. The residue was then fractionated by flash column chromatography (hexane:EtOAc, 2:1; to Chloroform:Acetone, 2:1) to afford first triazole **271** (60.3 mg, 53%) as a white solid and triazole **273** (31.9 mg, 31%) as a white solid.

Data for triazole **271**: mp 148-151 ^{o}C; $[\alpha]_{D}^{20}$ -49.3 (*c* 1.00, $CHCl_3$); R_f 0.30 (hexane:EtOAc, 2:1); IR (thin film) 2980, 2933, 2860, 1721, 1604, 1473, 1456, 1425, 1382, 1369, 1273, 1255, 1208, 1153, 1051 cm^{-1}; ^{1}H NMR (400 MHz) δ 1.18 (9H, s), 1.20-1.24 (2H, m), 1.32 (3H, s), 1.44-1.47 (1H, m), 1.52 (3H, s), 1.55-1.59 (2H, m), 1.84-1.87 (1H, m), 2.42 (2H, td, *J* = 10.1, 3.6 Hz), 2.46-2.50 (1H, m), 3.05-3.11 (1H, m), 4.70 (1H, t, *J* = 6.6 Hz), 4.90-4.93 (1H, m), 5.55 (1H, dd, *J* = 7.1, 5.2 Hz), 7.20-7.26 (1H, m), 7.74-7.78 (1H, m), 8.13 (1H, d, *J* = 7.9 Hz), 8.22 (1H, s), 8.56 (1H, d, *J* = 4.6 Hz); ^{13}C NMR (100 MHz) δ 20.5 (CH_2), 24.8 (CH_3), 24.9 (CH_2), 27.2 (CH_3), 27.9 (CH_3), 28.6 (CH_2), 41.3 (CH), 43.3 (CH), 43.9 (CH), 69.6 (CH), 80.6 (C), 81.1 (CH), 82.9 (CH), 113.4 (C), 120.3 (CH), 122.9 (CH), 124.3 (CH), 137.3 (CH), 147.6 (C), 149.1 (CH), 150.1 (C), 173.4 (C)； MS (ESI) *m/z* (relative intensity) 463 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{24}H_{32}N_4O_4$ $[M+Na]^+$ 463.2316, found 463.2318.

Data for triazole **273**: mp 200-201 ^{o}C; $[\alpha]_{D}^{20}$ -40.8 (*c* 1.20, MeOH); R_f 0.25

($CHCl_3$:acetone, 2:1); IR (thin film) 3118, 2913, 2849, 1723, 1594, 1570, 1455, 1420, 1365, 1251, 1202, 1148, 1073, 1048 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 1.09 (9H, s), 1.13-1.20 (1H, m), 1.48-1.54 (1H, m), 1.57-1.62 (1H, m), 1.64-1.68 (1H, m), 1.91-1.92 (1H, m), 1.94-1.98 (1H, m), 2.29-2.41 (2H, m), 2.84 (1H, dt, *J* = 11.7, 7.1 Hz), 4.12 (1H, t, *J* = 8.1 Hz), 4.86-4.89 (1H, m), 4.96 (1H, t, *J* = 7.3 Hz), 7.32-7.35 (1H, m), 7.85-7.90 (1H, m), 8.05 (1H, d, *J* = 8.0 Hz), 8.39 (1H, s), 8.55 (1H, d, *J* = 4.8 Hz); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 21.1 (CH_2), 25.2 (CH_2), 28.0 (CH_3), 30.9 (CH_2), 40.1 (CH), 42.6 (CH), 44.1 (CH), 70.6 (CH), 71.5 (CH), 74.1 (CH), 81.3 (C), 121.2 (CH), 124.2 (CH), 125.6 (CH), 138.7 (CH), 147.9 (C), 150.2 (CH), 150.9 (C), 175.3 (C)； MS (ESI) *m/z* (relative intensity) 423 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{21}H_{28}N_4O_4$ $[M+Na]^+$ 423.2003, found 423.2006.

Triazole 272. In a sealed tube, triazole **254** (33 mg, 0.08 mmole) was dissolved in the ammonia solution (5 mL, 0.7M in MeOH) and stirred at 110 ^oC in 15 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 20:1) to afford triazole **272** (31.2 mg, 98% yield) as a white solid: mp 213-214 ^oC; $[\alpha]_D^{20}$ -37.7 (*c* 1.45, $CHCl_3$); R_f 0.43 ($CHCl_3$:MeOH, 20:1); IR (thin film) 3392, 3196, 2981, 2935, 2859, 1720, 1672, 1637, 1453, 1382, 1370, 1296, 1278, 1260, 1209, 1153, 1097, 1066, 1050 cm^{-1}; ^1H NMR (400 MHz) δ 1.15-1.18 (1H, m), 1.20 (9H, s), 1.30 (3H, s), 1.40-1.45 (1H, m), 1.49 (3H, s), 1.53-1.56 (1H, m), 1.59-1.65 (2H, m), 1.83-1.86 (1H, m), 2.34

(1H, td, J = 10.7, 3.6 Hz), 2.46-2.47 (1H, m), 3.03 (1H, dt, J = 10.2, 6.7 Hz), 4.67 (1H, t, J = 6.9 Hz), 4.89 (1H, t, J = 6.0 Hz), 5.48-5.52 (1H, m), 6.19 (1H, br s), 7.12 (1H, s), 8.13 (1H, s); ^{13}C NMR (100 MHz) δ 20.5 (CH_2), 24.8 (CH_2), 24.9 (CH_3), 27.2 (CH_3), 27.9 (CH_3), 29.0 (CH_2), 41.4 (CH), 43.2 (CH), 44.3 (CH), 69.8 (CH), 80.5 (CH), 80.7 (C), 82.6 (CH), 113.8 (C), 127.8 (CH), 142.4 (C), 162.2 (C), 173.2 (C)； MS (ESI) *m/z* (relative intensity) 429 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{20}H_{30}N_4O_5$ [M+Na]$^+$ 429.2108, found 429.2104.

Triazole 273. Following the general procedure for deprotection of the isopropylidene, triazole **271** (29.8 mg, 0.17 mmole) was converted into triazole **273** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:acetone, 2:1) to afford triazole **273** (25.7 mg, 95%) as a white solid. The data for triazole **273** was described before.

Triazole 274. Following the general procedure for deprotection of the isopropylidene, triazole **272** (59.6 mg, 0.15 mmole) was converted into triazole **274** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford triazole **274** (44.1 mg, 82%) as a white solid: mp 235-237 ^{o}C; $[\alpha]_D^{20}$ -22.5 (*c* 0.43, MeOD); R_f 0.17 ($CHCl_3$:MeOH, 10:1); IR (thin film) 3435, 3243, 3094, 2980, 2948, 2930, 2863, 2569, 2546, 2411, 2359, 1713, 1675, 1650, 1543, 1436, 1368,

1295, 1154, 1098, 1055 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.19 (9H, s), 1.29 (1H, s), 1.48-1.54 (1H, m), 1.57-1.68 (2H, m), 1.90-1.96 (2H, m), 2.30-2.37 (2H, m), 2.77-2.83 (1H, m), 4.10 (1H, t, *J* = 8.1 Hz), 4.79-4.82 (1H, m), 4.92-4.96 (1H, m), 8.39 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 21.3 (CH_2), 25.4 (CH_2), 28.1 (CH_3), 31.1 (CH), 40.3 (CH), 42.7 (CH), 44.4 (CH), 70.8 (CH), 71.7 (CH), 74.3 (CH), 81.5 (C), 129.1 (CH), 143.3 (C), 164.8 (C), 175.4 (C)； MS (ESI) *m/z* (relative intensity) 389 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{26}N_4O_5$ $[M+Na]^+$ 389.1795, found 389.1790.

Triazole 275. Following the general procedure for deprotection of the isopropylidene, triazole **269** (43 mg, 0.10 mmole) was converted into triazole **275** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 15:1) to afford triazole **275** (36.7 mg, 94%) as a white solid: mp 217-218 ^oC; $[\alpha]_D^{20}$ -33.8 (*c* 0.67, MeOH); R_f 0.23 ($CHCl_3$:MeOH, 20:1); IR (thin film) 3415, 2974, 2940, 1726, 1459, 1392, 1367, 1283, 1255, 1226, 1201, 1152, 1083, 1050 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 2:3) δ 1.0 (9H, s), 1.15-1.20 (1H, m), 1.43-1.54 (1H, m), 1.54-1.63 (1H, m), 1.64-1.68 (1H, m), 1.92-1.95 (2H, m), 2.30-2.32 (1H, m), 2.32-2.39 (1H, m), 2.78-2.85 (1H, m), 4.11 (1H, t, *J* = 7.6 Hz), 4.84-4.90 (2H, m), 7.30 (1H, t, *J* = 7.3 Hz), 7.39 (2H, t, *J* = 7.5 Hz), 7.75 (2H, d, *J* = 7.5 Hz), 8.11 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 20.8 (CH_2), 24.9 (CH_2), 28.0 (CH_3), 30.6 (CH_2), 39.8 (CH), 42.3 (CH), 43.8 (CH), 70.3 (CH), 71.0 (CH), 73.8 (CH), 81.3 (CH),

123.3 (CH), 126.2 (CH), 128.9 (CH), 129.5 (CH), 131.1 (C), 147.8 (C), 175.1 (C); MS (ESI) *m/z* (relative intensity) 422 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}N_3O_4$ $[M+Na]^+$ 422.2050, found 422.2051.

Triazole 276. Following the general procedure for deprotection of the isopropylidene, triazole **270** (39.5 mg, 0.08 mmole) was converted into triazole **276** using *t*-BuOH/H_2O (v/v, 1/10) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 15:1) to afford triazole **276** (35.0 mg, 97%) as a white solid: mp 175-176 ^oC; $[\alpha]_D^{20}$ -40.1 (*c* 0.96, MeOH); R_f 0.30 ($CHCl_3$:MeOH, 15:1); IR (thin film) 3426, 2933, 1728, 1490, 1461, 1454, 1392, 1368, 1341, 1285, 1249, 1153, 1073, 1048 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.09 (9H, s), 1.11-1.15 (1H, m), 1.50-1.65 (4H, m), 1.91-1.94 (2H, m), 2.32-2.36 (1H, m), 2.39 (1H, td, *J* = 12.1, 3.6 Hz), 2.80-2.86 (1H, m), 3.94 (3H, s), 4.13 (1H, t, *J* = 8.1 Hz), 4.85-4.89 (1H, m), 4.95 (1H, t, *J* = 7.2 Hz), 7.02 (1H, t, *J* = 7.5 Hz), 7.07 (1H, d, *J* = 8.3 Hz), 7.30-7.33 (1H, m), 8.10 (1H, d, *J* = 7.6 Hz), 8.30 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 18.4 (CH_2), 21.2 (CH_2), 25.3 (CH_3), 31.1 (CH_2), 40.3 (CH), 42.7 (CH), 44.2 (CH), 55.9 (CH_3), 71.0 (CH), 71.3 (CH), 74.5 (CH), 81.3 (CH), 112.2 (CH), 120.2 (C), 121.7 (CH), 126.9 (CH), 127.9 (CH), 130.2 (CH), 143.7 (C), 157.3 (C), 175.5 (C); MS (ESI) *m/z* (relative intensity) 452 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{23}H_{31}N_3O_5$ $[M+Na]^+$ 452.2156, found 452.2158.

Triazole 277. Following the general procedure for deprotection of the isopropylidene, triazole **272** (29 mg, 0.07 mmole) was converted into triazole **277** at 100 ^{o}C for 24 h. The residue was then washed by cold methanol to afford triazole **277** (19.5 mg, 88%) as a white solid: mp >280 ^{o}C; $[\alpha]_D^{20}$ -32.2 (*c* 0.30, DMF); R_f 0.15 ($CHCl_3$:MeOH, 2:1); IR (thin film) 3421, 1715, 1656, 1594, 1430, 1294, 1177, 1099, 1014 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.03-1.08 (1H, m), 1.45-1.50 (3H, m), 1.75-1.77 (2H, m), 2.13 (1H, s), 2.29 (1H, t, *J* = 10.1 Hz), 2.60-2.64 (1H, m), 3.93 (1H, t, *J* = 7.1 Hz), 4.63-4.67 (1H, m), 4.76-4.93 (3H, m), 7.38 (1H, s), 7.75 (1H, s), 8.53 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 19.9 (CH_2), 24.2 (CH_2), 29.3 (CH_2), 39.0 (CH), 39.8 (CH), 42.8 (CH), 69.0 (CH), 69.9 (CH), 72.6 (CH), 127.6 (CH), 142.3 (C), 161.8 (C), 175.5 (C)；MS (ESI) *m/z* (relative intensity) 333 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{13}H_{18}N_4O_5$ $[M+Na]^+$ 333.1169, found 333.1170.

Triazole 278. Following the general procedure for deprotection of the isopropylidene, triazole **269** (42 mg, 0.10 mmole) was converted into triazole **278** at 100 ^{o}C in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 6:1) to afford triazole **278** (30.7 mg, 94%) as a white solid: mp 288-291 ^{o}C; $[\alpha]_D^{20}$ -39.8 (*c* 0.70, MeOH); R_f 0.47 ($CHCl_3$:MeOH, 6:1); IR (thin film) 3369, 3111, 3080, 2929, 2869, 1663, 1558, 1440, 1412, 1365, 1257, 1206, 1182, 1086, 1051 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.17-1.27 (1H, m), 1.51-1.57 (1H, m), 1.58-1.67 (2H, m), 1.92-1.95 (2H, m), 2.28-2.34 (1H, m), 2.35-2.38 (1H, m), 2.88 (1H, dt, *J* = 11.6, 6.9 Hz), 4.15 (1H, t, *J* = 7.9 Hz), 4.87-4.90 (1H, m), 4.94-4.96 (1H, m),

7.33 (1H, t, J = 7.4 Hz), 7.42 (2H, t, J = 7.5 Hz), 7.82 (2H, d, J = 7.3 Hz), 8.32 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 21.5 (CH_2), 25.5 (CH_2), 31.0 (CH_2), 41.5 (CH), 43.0 (CH), 44.5 (CH), 71.1 (CH), 71.8 (CH), 74.3 (CH), 123.9 (CH), 126.8 (CH), 129.2 (CH), 129.9 (CH), 148.3 (C), 179.8 (C); MS (ESI) *m/z* (relative intensity) 366 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{21}N_3O_4$ $[M+Na]^+$ 366.1424, found 366.1427.

Triazole 279. Following the general procedure for deprotection of the isopropylidene group from alkyl ether, triazole **270** (32 mg, 0.07 mmole) was converted into triazole **279** at 100 ^oC in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 10:1) to afford triazole **279** (25.7 mg, 98%) as a white solid: mp 202-203 ^oC; $[\alpha]_D^{20}$ -53.0 (*c* 1.12, MeOH); R_f 0.25 ($CHCl_3$:MeOH, 15:1); IR (thin film) 3306, 2917, 2850, 1701, 1490, 1446, 1289, 1249, 1184, 1122, 1075, 1048, 1022 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.16-1.26 (1H, m), 1.53-1.60 (2H, m), 1.64-1.67 (1H, m), 1.94-1.97 (2H, m), 2.30-2.34 (1H, m), 2.45 (1H, td, J = 12.0, 3.7 Hz), 2.83-2.89 (1H, m), 3.95 (3H, s), 4.16 (1H, dd, J = 8.4, 6.8 Hz), 4.93-4.94 (2H, m), 7.02 (1H, t, J = 7.5 Hz), 7.08 (1H, d, J = 8.3 Hz), 7.30-7.34 (1H, m), 8.09 (1H, dd, J = 7.6, 1.3 Hz), 8.30 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 21.3 (CH_2), 25.3 (CH_2), 30.9 (CH_2), 41.3 (CH), 42.1 (CH), 44.3 (CH), 55.9 (CH_3), 70.9 (CH), 71.5 (CH), 74.2 (CH), 112.2 (CH), 120.4 (C), 121.7 (CH), 126.9 (CH), 128.1 (CH), 130.2 (CH), 143.8 (C), 157.4 (C), 178.2 (C); MS (ESI) *m/z* (relative intensity) 396 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{23}N_3O_5$ $[M+Na]^+$

396.1530, found 396.1531.

Triazole 280. Following the general procedure for deprotection of the isopropylidene, triazole **271** (41.5 mg, 0.09 mmole) was converted into triazole **280** at 100 ^{o}C in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 6:1) to afford triazole **280** (31.2 mg, 96%) as a white solid: mp 278-271 ^{o}C; $[\alpha]_D^{20}$ -18.5 (*c* 1.45, DMF); R_f 0.30 ($CHCl_3$:MeOH, 6:1); IR (thin film) 3394, 2938, 2870, 1680, 1606, 1572, 1477, 1450, 1429, 1204, 1137, 1087 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.15-1.25 (1H, m), 1.43-1.56 (1H, m), 1.56-1.64 (2H, m), 1.89-1.92 (2H, m), 2.28-2.33 (2H, m), 2.87-2.93 (1H, m), 4.17-4.21 (1H, m), 4.96-5.03 (2H, m), 7.33-7.36 (1H, m), 7.87-7.91 (1H, m), 8.01 (1H, d, *J* = 7.9 Hz), 8.45 (1H, s), 8.57 (1H, d, *J* = 4.4 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 21.4 (CH_2), 25.3 (CH_2), 30.9 (CH_2), 41.6 (CH), 43.0 (CH), 44.4 (CH), 71.2 (CH), 71.8 (CH), 74.3 (CH), 121.8 (CH), 124.4 (CH), 126.0 (CH), 139.0 (CH), 147.8 (C), 150.4 (CH), 150.9 (C), 180.0 (C)；MS (ESI) *m/z* (relative intensity) 367 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{20}N_4O_4$ $[M+Na]^+$ 367.1377, found 367.1377.

Triazole 281α and triazole 281β. Following the general procedure for dihydroxylation of alkene, triazole **254** (190 mg, 0.45 mmole) was converted into diol triazole **281** in 48 h. The residue was then fractionated by flash column chromatography (hex:EtOAc, 1:4) to afford first triazole **281α**(130 mg, 63%) as a white solid and then triazole **281β** (46.8 mg, 23%) as a white solid.

Data for triazole **281α**: mp 144.1-144.7 °C; $[\alpha]_D^{20}$ -28.3 (*c* 2.25, MeOH); R_f 0.36 (hexane:EtOAc, 1:3); IR (thin film) 3401, 3139, 2980, 2931, 1719, 1439, 1371, 1211, 1156, 1068 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.21 (9H, s), 1.33 (3H, s), 1.51 (3H, s), 1.54-1.59 (1H, m), 1.69 (1H, q, *J* = 11.6 Hz), 2.59 (1H, td, *J* = 11.2, 4.3 Hz), 2.65 (1H, td, *J* = 6.7, 4.1 Hz), 3.23 (1H, dt, *J* = 10.9, 6.6 Hz), 3.86 (1H, dt, *J* = 10.6, 3.2 Hz), 3.91 (3H, s), 4.00 (1H, t, *J* = 3.2 Hz), 4.74 (1H, t, *J* = 7.2 Hz), 5.10 (1H, t, *J* = 6.3 Hz), 5.51-5.55 (1H, m), 8.62 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.1 (CH_3), 27.4 (CH_3), 28.0 (CH_3), 31.8 (CH_2), 41.7 (CH), 42.6 (CH), 51.8 (CH), 52.6 (CH_3), 68.6 (CH), 69.5 (CH), 70.4 (CH), 80.5 (C), 81.8 (CH), 82.8 (CH), 115.3 (C), 131.2 (CH), 140.4 (C), 162.3 (C), 174.0 (C)；MS (ESI) *m/z* (relative intensity) 476 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{25}H_{33}N_3O_6$ $[M+Na]^+$ 476.2003, found 476.2003.

Data for triazole **281β**: mp 267-270 °C; $[\alpha]_D^{20}$ -66.5 (*c* 1.45, MeOH:$CHCl_3$ 5:1); R_f 0.26 (hexane:EtOAc, 1:4); IR (thin film) 3351, 3123, 2979, 2931, 1722, 1711, 1541, 1455, 1438, 1368, 1260, 1233, 1211, 1157, 1069, 1036 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.19 (9H, s), 1.33 (3H, s), 1.51 (3H, s), 1.34-1.40 (1H, m), 2.03 (1H, dt, *J* = 13.8, 4.0 Hz), 2.73-2.77 (1H, m), 2.77-2.81 (1H, m), 3.09-3.15 (1H, m), 3.77 (1H, dd, *J* = 6.5, 2.6 Hz), 3.91 (3H, s), 4.00 (1H, br s), 5.04 (1H, t, *J* = 7.1 Hz), 5.34-5.37 (1H, m), 5.54 (1H, t, *J* = 7.6 Hz), 8.63 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.4 (CH_3), 27.8 (CH_3), 28.0 (CH_3), 36.0 (CH_2), 36.9 (CH), 45.5 (CH), 48.6 (CH), 52.5 (CH_3), 69.4 (CH), 69.5 (CH), 70.7 (CH), 79.9 (CH), 81.8 (CH), 82.2 (C), 114.9 (C), 131.1 (CH), 140.3 (C), 162.4 (C), 175.3 (C)；MS (ESI) *m/z* (relative intensity) 476

([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{25}H_{33}N_3O_6$ [M+Na]$^+$ 476.2003, found 476.2007.

Triazole 282α and triazole **282β.** Following the general procedure for dihydroxylation of alkene, triazole **255** (160 mg, 0.37 mmole) was converted into diol triazole **282** in 36 h. The residue was then fractionated by flash column chromatography (hex:EtOAc, 1:4) to afford first triazole **282α** (135.5 mg, 79%) as a white solid and then triazole **282β** (29.4 mg, 17%) as a white solid.

Data for triazole **282α**: mp 228-229 ^{o}C; $[\alpha]_D^{20}$ -48.3 (*c* 0.70, MeOH); R_f 0.30 (hexane:EtOAc, 1:3); IR (thin film) 3410, 2980, 2934, 1715, 1484, 1458, 1382, 1370, 1272, 1250, 1209, 1155, 1068 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.11 (9H, s), 1.28 (3H, s), 1.29-1.32 (1H, m), 1.46 (3H, s), 1.57 (1H, q, *J* = 11.3 Hz), 2.51-2.53 (1H, m), 2.58 (1H, td, *J* = 10.7, 4.0 Hz), 3.05-3.10 (1H, m), 3.72-3.76 (1H, m), 3.79 (1H, br s), 4.63 (1H, d, *J* = 5.0 Hz), 4.67 (1H, d, *J* = 3.5 Hz), 4.74 (1H, t, *J* = 7.0 Hz), 5.01 (1H, t, *J* = 6.2 Hz), 5.47 (1H, t, *J* = 6.7 Hz), 7.33 (1H, t, *J* = 7.3 Hz), 7.45 (2H, t, *J* = 7.6 Hz), 7.80 (2H, d, *J* = 7.7 Hz), 8.59 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 24.8 (CH_3), 26.9 (CH_3), 27.4 (CH_3), 30.9 (CH_2), 40.9 (CH), 50.1 (CH), 66.6 (CH), 67.8 (CH), 68.0 (CH), 78.9 (CH), 79.2 (CH), 79.3 (C), 81.3 (CH), 112.8 (C), 122.5 (CH), 125.1 (CH), 127.8 (CH), 128.9 (CH), 130.8 (C), 146.1 (C), 172.2 (C); MS (ESI) *m/z* (relative intensity) 494 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{25}H_{33}N_3O_6$ [M+Na]$^+$ 494.2262, found 494.2262.

Data for triazole **282β**: mp 228-229 ^{o}C; $[\alpha]_D^{20}$ -70.8 (*c* 0.75, MeOH); R_f 0.17

(hexane:EtOAc, 1:3); IR (thin film) 3401, 2980, 2930, 1712, 1461, 1369, 1258, 1210, 1158, 1071, 1028 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:1) δ 1.11 (9H, s), 1.33 (3H, s), 1.34-1.40 (1H, m), 1.50 (3H, s), 2.05 (1H, dt, *J* = 13.8, 4.1 Hz), 2.74 (1H, q, *J* = 6.6 Hz), 2.80 (1H, td, *J* = 12.2, 3.8 Hz), 3.15 (1H, dt, *J* = 11.3, 6.8 Hz), 3.78 (1H, dd, *J* = 6.7, 2.9 Hz), 4.00 (1H, br s), 4.94 (1H, t, *J* = 6.9 Hz), 5.31-5.35 (1H, m), 5.55 (1H, t, *J* = 7.5 Hz), 7.30 (1H, t, *J* = 7.3 Hz), 7.39 (2H, t, *J* = 7.5 Hz), 7.74 (2H, d, *J* = 7.4 Hz), 8.11 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:1) δ 25.2 (CH_3), 27.6 (CH_3), 27.9 (CH_3), 35.1 (CH_2), 36.5 (CH), 44.8 (CH), 48.1 (CH), 68.6 (CH), 68.9 (CH), 69.8 (CH), 79.2 (CH), 81.5 (C), 81.9 (CH), 114.4 (C), 122.6 (CH), 126.1 (CH), 128.8 (CH), 129.4 (CH), 130.8 (C), 147.9 (C), 174.7 (C)；MS (ESI) *m/z* (relative intensity) 494 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{25}H_{33}N_3O_6$ $[M+Na]^+$ 494.2262, found 494.2264.

Triazole 283α and **triazole 283β.** Following the general procedure for dihydroxylation of alkene, triazole **256**(178 mg, 0.38 mmole) was converted into diol triazole **283** in 36 h. The residue was then fractionated by flash column chromatography (hex:EtOAc, 1:4) to afford first triazole **283α** (159.6 mg, 84%) as a white solid and then triazole **283β** (27.6 mg, 14%) as a white solid.

Data for triazole **283α**: mp 119-121 ^oC; $[\alpha]_D^{20}$ -51.9 (*c* 1.80, MeOH); R_f 0.36 (hexane:EtOAc, 1:4); IR (thin film) 3436, 2980, 2936, 1720, 1551, 1491, 1456, 1382, 1370, 1250, 1210, 1156, 1067, 1027 cm^{-1}; ^1H NMR (400 MHz, DMSO-d_6) δ 1.10 (9H, s), 1.27 (3H, s), 1.28-1.38 (1H, m), 1.45 (3H, s), 1.54 (1H, q, *J* = 11.3 Hz), 2.45-2.48

(1H, m), 2.57 (1H, td, *J* = 10.6, 4.0 Hz), 3.02-3.08 (1H, m), 3.71-3.78 (1H, m), 3.79 (3H, s), 4.60 (1H, d, *J* = 5.0 Hz), 4.64 (1H, d, *J* = 3.6 Hz), 4.73 (1H, t, *J* = 6.9 Hz), 5.06 (1H, t, *J* = 6.2 Hz), 5.46 (1H, t, *J* = 6.8 Hz), 7.02 (1H, t, *J* = 7.4 Hz), 7.11 (2H, d, *J* = 8.2 Hz), 7.28-7.32 (1H, m), 8.09-8.11 (1H, m), 8.45 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.1 (CH_3), 27.5 (CH_3), 28.0 (CH_3), 31.9 (CH_2), 41.7 (CH), 42.5 (CH), 51.6 (CH), 55.9 (CH_3), 68.7 (CH), 69.6 (CH), 70.0 (CH), 80.9 (C), 81.7 (CH), 83.3 (CH), 112.2 (CH), 114.9 (C), 120.0 (C), 121.7 (CH), 126.7 (CH), 128.0 (CH), 130.4 (CH), 144.0 (C), 157.3 (C), 174.2 (C)；MS (ESI) *m/z* (relative intensity) 524 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{26}H_{35}N_3O_7$ $[M+Na]^+$ 524.2367, found 524.2369.

Data for triazole **283β**: mp 224-225 ^{o}C; $[\alpha]_D^{20}$ -52.6 (*c* 1.35, $CHCl_3$); R_f 0.21 (hexane:EtOAc, 1:4); IR (thin film) 3401, 2980, 2930, 1714, 1490, 1456, 1369, 1250, 1212, 1157, 1122, 1071, 1027 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 2:1) δ 1.10 (9H, s), 1.33 (3H, s), 1.34-1.39 (1H, m), 1.50 (3H, s), 2.05 (1H, dt, *J* = 13.9, 4.0 Hz), 2.73 (1H, q, *J* = 6.4Hz), 2.80 (1H, td, *J* = 12.0, 3.7 Hz), 3.12 (1H, dt, *J* = 11.3, 6.7 Hz), 3.77 (1H, dt, *J* = 6.5, 3.0 Hz), 3.93 (3H, s), 4.00 (1H, br s), 4.93 (1H, t, *J* = 6.9 Hz), 5.33 (1H, t, *J* = 6.5 Hz), 5.55 (1H, t, *J* = 7.4 Hz), 6.97-6.99 (1H, m), 6.99-7.02 (1H, m), 7.26-7.30 (1H, m), 8.08 (1H, dd, *J* = 7.6, 1.3 Hz), 8.21 (1H, br s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 2:1) δ 25.2 (CH_3), 27.6 (CH_3), 27.8 (CH_3), 35.0 (CH_2), 36.4 (CH), 44.8 (CH), 48.1 (CH), 55.6 (CH_3), 68.6 (CH), 68.8 (CH), 69.5 (CH), 79.2 (CH), 81.4 (C), 81.9 (CH), 111.4 (CH), 114.3 (C), 119.3 (C), 121.3 (CH), 125.4 (CH), 127.5 (CH), 129.6 (CH), 143.3 (C), 156.3 (C), 174.5 (C)；MS (ESI) *m/z* (relative intensity)

524 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{26}H_{35}N_3O_7$ [M+Na]$^+$ 524.2367, found 524.2370.

Triazole 284α and triazole 284β. Following the general procedure for dihydroxylation of alkene, triazole **257** (220 mg, 0.50 mmole) was converted into diol triazole **284** in 72 h. The residue was then fractionated by flash column chromatography (hex:EtOAc, 1:4) to afford first triazole **284α** (170.7 mg, 72%) as a white solid and then triazole **284β** (47.4 mg, 20%) as a white solid.

Data for triazole **284α**: mp 111-112 ^{o}C; $[\alpha]_D^{20}$ -50.8 (*c* 1.70, MeOH); R_f 0.27 (hexane:EtOAc, 1:4); IR (thin film) 3394, 2980, 2917, 1716, 1602, 1457, 1370, 1247, 1211, 1155, 1112, 1069 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.16 (9H, s), 1.34 (3H, s), 1.49-1.52 (1H, m), 1.52 (3H, s), 1.73 (1H, q, *J* = 11.4 Hz), 2.60-2.66 (1H, m), 2.66-2.69 (1H, m), 3.27-3.31 (1H, m), 3.84-3.87 (1H, m), 4.02 (1H, br s), 4.78 (1H, t, *J* = 6.9 Hz), 5.12 (1H, t, *J* = 6.1 Hz), 5.53-5.57 (1H, m), 7.34-7.37 (1H, m), 7.89-7.91 (1H, m), 8.04 (1H, d, *J* = 7.9 Hz), 8.48 (1H, s), 8.57 (1H, d, *J* = 4.3 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 25.1 (CH_3), 27.5 (CH_3), 28.1 (CH_3), 31.9 (CH_2), 41.7 (CH), 42.6 (CH), 51.7 (CH), 68.7 (CH), 69.6 (CH), 70.3 (CH), 80.9 (CH), 81.7 (CH), 83.1 (C), 115.0 (C), 121.4 (CH), 124.5 (CH), 125.7 (CH), 138.8 (CH), 148.5 (C), 150.5 (CH), 151.0 (C), 174.1 (C)； MS (ESI) *m/z* (relative intensity) 495 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{24}H_{32}N_4O_6$ [M+Na]$^+$ 495.2214, found 495.2212.

Data for triazole **284β**: mp 276-279 ^{o}C; $[\alpha]_D^{20}$ -69.3 (*c* 0.98, MeOH); R_f 0.15 (hexane:EtOAc, 1:4); IR (thin film) 3401, 2981, 2931, 1725, 1604, 1472, 1458, 1426,

1369, 1257, 121112,09, 1151, 1078, 1038 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.12 (9H, s), 1.34 (3H, s), 1.36-1.42 (1H, m), 1.51 (3H, s), 2.04 (1H, dt, *J* = 13.7, 4.2 Hz), 2.77 (1H, t, *J* = 6.6 Hz), 2.82 (1H, td, *J* = 12.2, 3.9 Hz), 3.17 (1H, dt, *J* = 11.4, 6.6 Hz), 3.79 (1H, dd, *J* = 6.6, 2.9 Hz), 4.15 (1H, br s), 5.06 (1H, t, *J* = 7.1 Hz), 5.36-5.39 (1H, m), 5.58 (1H, t, *J* = 7.6 Hz), 7.34-7.37 (1H, m), 7.88-7.92 (1H, m), 8.05 (1H, d, *J* = 7.9 Hz), 8.50 (1H, s), 8.57 (1H, d, *J* = 4.2 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 25.4 (CH_3), 27.8 (CH_3), 28.0 (CH_3), 36.1 (CH_2), 37.1 (CH), 45.6 (CH), 48.8 (CH), 69.4 (CH), 69.6 (CH), 70.6 (CH), 79.9 (CH), 81.6 (C), 82.4 (CH), 114.8 (C), 121.4 (CH), 124.4 (CH), 125.6 (CH), 138.8 (CH), 148.4 (C), 150.5 (CH), 151.1 (C), 174.3 (C)；MS (ESI) *m/z* (relative intensity) 495 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{24}H_{32}N_4O_6$ $[M+Na]^+$ 495.2214, found 495.2215.

Triazole 285α. In a sealed tube, triazole **281α**(130 mg, 0.29 mmole) was dissolved in the ammonia solution (20 mL, 0.7M in MeOH) and stirred at 90 ^oC in 12 h. The reaction mixture was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **285α** (111.9 mg, 89% yield) as a white solid: mp 227-230 ^oC; $[\alpha]_D^{20}$ -25.2 (*c* 1.34, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 5:1); IR (thin film) 3271, 2975, 2979, 2913, 1726, 1646, 1608, 1370, 1294, 1266, 1254, 1208, 1155, 1062, 1042 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.23 (9H, s), 1.33 (3H, s), 1.51 (3H, s), 1.71 (1H, q, *J* = 11.5 Hz), 2.56-2.62 (1H, m), 2.62-2.67 (1H, m), 3.25 (1H, , td, *J* = 10.4, 6.6 Hz), 3.83-3.86 (1H,

m), 3.96-4.01 (1H, m), 4.75 (1H, t, J = 7.1 Hz), 5.09 (1H, t, J = 6.2 Hz), 5.51 (1H, t, J = 6.7 Hz), 8.45 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 25.1 (CH_3), 27.5 (CH_3), 28.1 (CH_3), 31.8 (CH_2), 41.7 (CH), 42.5 (CH), 51.7 (CH), 68.7 (CH), 69.6 (CH), 70.3 (CH), 80.7 (CH), 81.7 (C), 83.0 (CH), 115.1 (C), 129.1 (CH), 143.6 (C), 164.5 (C), 174.0 (C)；MS (ESI) *m/z* (relative intensity) 461 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{20}H_{30}N_4O_7$ [M+Na]$^+$ 461.2007, found 461.2004.

Triazole 285β. In a sealed tube, triazole **281β** (59 mg, 0.13 mmole) was dissolved in the ammonia solution (5 mL, 0.7M in MeOH) and stirred at 110 ^{o}C in 12 h. The reaction mixture turned brown and was allowed to cool to room temperature. The tube was opened and the solvent was removed under reduced pressure. The residue was fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **285β** (52.7 mg, 93% yield) as a white solid: mp > 280 ^{o}C; $[\alpha]_D^{20}$ -64.7 (*c* 0.99, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 5:1); IR (thin film) 1958, 1723, 1650, 1596, 1454, 1417, 1367, 1295, 1254, 1204, 1141, 1084, 1054, 1019 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$:CD_3OD 1:2) δ 1.20 (9H, s), 1.33 (3H, s), 1.34-1.41 (1H, m), 1.49 (3H, s), 1.99-2.02 (1H, m), 2.72-2.75 (1H, m), 2.75-2.81 (1H, m), 3.13 (1H, , dt, J = 11.1, 6.7 Hz), 3.77 (1H, dd, J = 6.4, 2.9 Hz), 3.99 (1H, br s), 5.00 (1H, t, J = 7.0 Hz), 5.32-5.35 (1H, m), 5.51 (1H, t, J = 7.4 Hz), 8.41 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:2) δ 25.3 (CH_3), 27.7 (CH_3), 28.0 (CH_3), 35.5 (CH_2), 36.8 (CH), 45.1 (CH), 48.5 (CH), 69.0 (CH), 69.3 (CH), 70.4 (CH), 79.7 (CH), 81.7 (C), 82.2 (CH), 114.6 (C), 128.7 (CH), 143.2 (C), 164.3 (C), 175.0 (C)；MS (ESI) *m/z* (relative intensity) 461

([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{20}H_{30}N_4O_7$ [M+Na]$^+$ 461.2007, found 461.2009.

Triazole 286. Following the general procedure for deprotection of the isopropylidene, triazole **285α** (83 mg, 0.19 mmole) was converted into triazole **286** using *t*-BuOH/H_2O (v/v, 1/10; 50 mL) instead of H_2O (50 mL) at room temperature in 36 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 4:1) to afford triazole **286** (64.9 mg, 86%) as a white solid: mp 237-240 ^oC; $[\alpha]_D^{20}$ -10.2 (*c* 0.73, DMF); R_f 0.28 ($CHCl_3$:MeOH, 4:1); IR (thin film) 3410, 3357, 3177, 2981, 2932, 1706, 1666, 1614, 1370, 1299, 1205, 1158, 1082, 1048, 1027, 1004 cm^{-1}; ^{1}H NMR (400 MHz, DMSO-d_6) δ 1.11 (9H, s), 1.48-1.55 (1H, m), 2.26-2.29 (1H, m), 2.43-2.7 (1H, m), 2.67-2.73 (1H, m), 3.17 (1H, s), 3.68 (1H, d, *J* = 7.9 Hz), 3.81 (1H, s), 3.87 (1H, t, *J* = 7.5 Hz), 4.48 (1H, s), 4.62 (1H, 2m), 4.81 (1H, t, *J* = 7.5 Hz), 4.87 (1H, s), 4.96 (1H, s), 7.37 (1H, s), 7.75 (1H, s), 8.55 (1H, s); ^{13}C NMR (100 MHz, DMSO-d_6) δ 27.4 (CH_3), 31.3 (CH_2), 34.9 (CH), 40.2 (CH), 51.5 (CH), 66.6 (CH), 67.8 (CH), 68.2 (CH), 69.2 (CH), 71.9 (CH), 79.3 (C), 127.4 (CH), 142.5 (C), 161.7 (C), 172.4 (C)；MS (ESI) *m/z* (relative intensity) 421 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{17}H_{26}N_4O_7$ [M+Na]$^+$ 421.1694, found 421.1695.

Triazole 287. Following the general procedure for deprotection of the isopropylidene, triazole **282α** (52 mg, 0.11 mmole) was converted into triazole **287** using *t*-BuOH/H_2O (v/v, 1/10; 50 mL) instead of H_2O (50 mL) at room temperature in

24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **287** (46.6 mg, 98%) as a white solid: mp 232-233 ^oC; $[\alpha]_D^{20}$ -24.6 (*c* 0.95, MeOH); R_f 0.35 ($CHCl_3$:MeOH, 5:1); IR (thin film) 3392, 3138, 2972, 2929, 1708, 1461, 1392, 1369, 1247, 1156, 1079, 1049 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.12 (9H, s), 1.70 (1H, q, *J* = 12.1 Hz), 1.81-1.84 (1H, m), 2.51-2.56 (1H, m), 2.56-2.63 (1H, m), 3.00-3.07 (1H, m), 3.85-3.88 (1H, m), 4.07 (1H, d, *J* = 3.1 Hz), 4.09 (1H, d, *J* = 9.0 Hz), 4.81-4.85 (1H, m), 4.93 (1H, t, *J* = 7.4 Hz), 7.33 (1H, t, *J* = 7.4 Hz), 7.42 (2H, t, *J* = 7.5 Hz), 7.80 (2H, d, *J* = 7.4 Hz), 8.35 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.1 (CH_3), 32.3 (CH_2), 36.8 (CH), 42.4 (CH), 52.6 (CH), 68.7 (CH), 69.7 (CH), 70.3 (CH), 70.9 (CH), 73.7 (CH), 81.7 (C), 124.0 (CH), 126.6 (CH), 129.3 (CH), 129.9 (CH), 131.8 (C), 148.3 (C), 174.4 (C)；MS (ESI) *m/z* (relative intensity) 454 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}N_3O_6$ $[M+Na]^+$ 454.1949, found 454.1945.

Triazole 288. Following the general procedure for deprotection of the isopropylidene, triazole **283α** (83 mg, 0.17 mmole) was converted into triazole **288** using *t*-BuOH/H_2O (v/v, 1/1; 50 mL) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford triazole **288** (68.8 mg, 90%) as a white solid: mp 123-126 ^oC; $[\alpha]_D^{20}$ -31.2 (*c* 1.50, MeOH); R_f 0.23 ($CHCl_3$:MeOH, 8:1); IR (thin film) 3391, 2976, 2932, 1716, 1608, 1491, 1456, 1368, 1290, 1251, 1155, 1082, 1049, 1025 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.10 (9H, s), 1.7 (1H, q, *J* = 12.1 Hz), 1.82 (1H,

dt, J = 12.2, 4.2 Hz), 2.52-2.58 (1H, m), 2.62 (1H, dd, J = 12.4, 3.9 Hz), 3.03 (1H, dt, J = 11.9, 7.2 Hz), 3.85-3.89 (1H, m), 3.95 (3H, s), 4.07-4.12 (2H, m), 4.83-4.87 (1H, m), 4.94 (1H, t, J = 7.3 Hz), 7.00-7.04 (1H, m), 7.08 (1H, d, J = 8.2 Hz), 7.32 (1H, td, J = 8.7, 1.6 Hz), 8.08 (1H, dd, J = 7.7, 1.6 Hz), 8.32 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.0 (CH_3), 32.3 (CH_2), 36.8 (CH), 42.4 (CH), 52.4 (CH), 55.9 (CH_3), 68.7 (CH), 69.7 (CH), 70.4 (CH), 70.6 (CH), 73.8 (CH), 81.6 (C), 112.2 (CH), 120.2 (C), 121.7 (CH), 127.0 (CH), 127.9 (CH), 130.3 (CH), 143.7 (C), 157.3 (C), 174.4 (C)；MS (ESI) *m/z* (relative intensity) 484 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{23}H_{31}N_3O_7$ $[M+Na]^+$ 484.2054, found 484.2058.

Triazole 289. Following the general procedure for deprotection of the isopropylidene, triazole **284α** (70 mg, 0.16 mmole) was converted into triazole **289** using *t*-BuOH/H_2O (v/v, 1/2; 50 mL) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **289** (61.6 mg, 91%) as a white solid: mp 207-209 ^{o}C; $[\alpha]_D^{20}$ -25.6 (*c* 1.45, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 5:1); IR (thin film) 3368, 2980, 2930, 1710, 1679, 1604, 1427, 1369, 1252, 1205, 1154, 1084, 1050 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.70 (1H, q, J = 12.1 Hz), 1.82-1.85 (1H, m), 2.54-2.56 (1H, m), 2.56-2.63 (1H, m), 3.01-3.07 (1H, m), 3.87-3.90 (1H, m), 4.09 (1H, s), 4.10-4.13 (1H, m), 4.85-4.86 (1H, m), 4.99 (1H, t, J = 7.4 Hz), 7.33-7.36 (1H, m), 7.87-7.91 (1H, m), 8.04 (1H, d, J = 8.0 Hz), 8.46 (1H, s), 8.57 (1H, d, J = 4.5 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 28.0 (CH_3), 32.3 (CH_2), 36.8 (CH), 42.3 (CH), 52.5 (CH),

68.7 (CH), 69.7 (CH), 70.3 (CH), 70.9 (CH), 73.6 (CH), 81.6 (C), 121.4 (CH), 124.4 (CH), 125.9 (CH), 138.8 (CH), 148.2 (C), 150.5 (CH), 151.1 (C), 174.3 (C)；MS (ESI) *m/z* (relative intensity) 455 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{21}H_{28}N_4O_6$ [M+Na]$^+$ 455.1901, found 455.1892.

Triazole 290. Following the general procedure for deprotection of the isopropylidene, triazole **285α** (28 mg, 0.06 mmole) was converted into triazole **290** at 100 ^{o}C in 48 h. The residue was washed by cold acetone to afford triazole **290** (18.1 mg, 83%) as a white solid: mp >280 ^{o}C; $[\alpha]_D^{20}$ -26.7 (*c* 1.05, MeOH); IR (thin film) 3397, 1677, 1559, 1542, 1432, 1407, 1201, 1137, 1085, 1054 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.74 (1H, q, *J* = 11.8 Hz), 1.83-1.86 (1H, m), 2.52-2.55 (1H, m), 2.55-2.62 (1H, m), 3.00-3.06 (1H, m), 3.87 (1H, d, *J* = 10.1 Hz), 4.07 (1H, s), 4.11 (1H, t, *J* = 7.8 Hz), 4.79-4.90 (2H, m), 8.49 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 32.0 (CH_2), 37.7 (CH), 41.5 (CH), 52.6 (CH), 68.7 (CH), 69.7 (CH), 70.2 (CH), 71.0 (CH), 73.2 (CH), 116.8 (C), 131.1 (CH), 163.2 (C), 177.0 (C)；MS (ESI) *m/z* (relative intensity) 365 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{13}H_{18}N_4O_7$ [M+Na]$^+$ 365.1068, found 365.1069.

Triazole 291. Following the general procedure for deprotection of the isopropylidene, triazole **282α** (64 mg, 0.14 mmole) was converted into triazole **291** at 100 ^{o}C in 48 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH:AcOH, 4:1:0.2) to afford triazole **291** (41.8 mg, 82%) as a white solid:

mp >280 ^{o}C; $[\alpha]_D^{20}$ -38.4 (*c* 0.50, DMF); R_f 0.26 ($CHCl_3$:MeOH:AcOH, 4:1:0.2); IR (thin film) 3422, 3117, 2933, 1657, 1564, 1410, 1342, 1275, 1108, 1077, 1047 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD:D_2O:AcOH 2:1:0.1) δ 1.73-1.75 (2H, m), 2.28-2.31 (1H, m), 2.51-2.52 (1H, m), 3.10-3.14 (1H, m), 3.84-3.88 (1H, m), 4.03 (1H, s), 4.22 (1H, t, *J* = 6.8 Hz), 4.90-4.94 (1H, m), 4.96-5.00 (1H, m), 7.33-7.36 (1H, m), 7.44 (1H, t, *J* = 7.2 Hz), 7.81 (1H, d, *J* = 7.5 Hz), 8.29 (1H, s); ^{13}C NMR (100 MHz, CD_3OD:D_2O: AcOH 2:1:0.1) δ 32.3 (CH_2), 39.0 (CH), 49.8 (CH), 51.1 (CH), 69.0 (CH), 70.1 (CH), 70.6 (CH), 71.2 (CH), 74.4 (CH), 124.1 (CH), 126.8 (C), 129.3 (CH), 129.9 (CH), 131.5 (C), 148.2 (C), 180.6 (C)；MS (ESI) *m/z* (relative intensity) 398 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{18}H_{21}N_3O_6$ $[M+Na]^+$ 398.1323, found 398.1328.

Triazole 292. Following the general procedure for deprotection of the isopropylidene, triazole **283α** (41.3 mg, 0.08 mmole) was converted into triazole **292** at 100 ^{o}C in 33 h. The residue was then fractionated by flash column chromategraphy ($CHCl_3$:MeOH, 2:1) to afford triazole **292** (26.4 mg, 79%) as a white solid: mp 228-231 ^{o}C; $[\alpha]_D^{20}$ -58.8 (*c* 1.00, MeOH); R_f 0.20 ($CHCl_3$:MeOH, 2:1); IR (thin film) 3400, 2930, 2936, 1642, 1569, 1491, 1456, 1399, 1290, 1251, 1121, 1080, 1025 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.48-1.52 (1H, m), 1.74-1.81 (1H, m), 2.21-2.26 (1H, m), 2.49 (1H, q, *J* = 6.6 Hz), 3.25-3.30 (1H, m), 3.79-3.81 (1H, m), 3.94-3.96 (4H, m), 4.32 (1H, t, *J* = 5.7 Hz), 4.94-4.98 (1H, m), 5.07 (1H, t, *J* = 6.3 Hz), 7.02 (1H, t, *J* = 7.5 Hz), 7.07 (1H, d, *J* = 8.3 Hz), 7.31 (1H, t, *J* = 7.6 Hz), 8.09 (1H, d, *J* = 7.5 Hz), 8.34 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 32.0 (CH_2), 40.6

(CH), 49.9 (CH), 50.1 (CH), 55.9 (CH_3), 69.3 (CH), 70.4 (CH), 71.1 (CH), 72.6 (CH), 76.0 (CH), 112.2 (CH), 120.4 (C), 121.7 (CH), 127.6 (CH), 128.2 (CH), 130.2 (CH), 143.8 (C), 157.5 (C), 182.3 (C)；MS (ESI) *m/z* (relative intensity) 428 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{19}H_{23}N_3O_7$ $[M+Na]^+$ 428.1428, found 494.1421.

Triazole 293. Following the general procedure for deprotection of the isopropylidene, triazole **284α** (138 mg, 0.29 mmole) was converted into triazole **293** at 100 ^oC in 72 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 2:3) to afford triazole **293** (81.3 mg, 74%) as a white solid: mp >280 ^oC; $[\alpha]_D^{20}$ -37.6 (*c* 1.00, MeOH); R_f 0.40 ($CHCl_3$:MeOH, 2:3); IR (thin film) 3430, 3412, 2918, 1638, 1571, 1399, 1364, 1310, 1251, 1121, 1084, 1058, 1005 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.60-1.66 (1H, m), 1.74-1.82 (1H, m), 2.18-2.24 (1H, m), 2.48-2.53 (1H, m), 3.24 (1H, q, *J* = 7.7 Hz), 3.80-3.82 (1H, m), 3.96-3.97 (1H, m), 4.26 (1H, t, *J* = 5.8 Hz), 4.95-5.02 (2H, m), 7.32-7.35 (1H, m), 7.88 (1H, t, *J* = 7.7 Hz), 8.02 (1H, d, *J* = 7.9 Hz), 8.44 (1H, s), 8.56 (1H, d, *J* = 4.1 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 32.5 (CH_2), 40.1 (CH), 43.5 (CH), 50.8 (CH), 69.3 (CH), 70.4 (CH), 71.4 (CH), 72.1 (CH), 75.4 (CH), 121.8 (CH), 124.2 (CH), 126.3 (CH), 138.7 (CH), 148.0 (C), 150.4 (CH), 151.3 (C), 182.3 (C)； MS (ESI) *m/z* (relative intensity) 399 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{20}N_4O_6$ $[M+Na]^+$ 399.1275, found 399.1277.

Triazole 294. Following the general procedure for deprotection of the

isopropylidene, triazole **285β** (45.7 mg, 0.10 mmole) was converted into triazole **294** using *t*-BuOH/H_2O (v/v, 1/10; 50 mL) instead of H_2O (50 mL) at room temperature in 40 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 4:1) to afford triazole **294** (35.4 mg, 93%) as a white solid: mp 236-240 ^oC; $[\alpha]_D^{20}$ -47.7 (*c* 0.90, MeOH); R_f 0.28 ($CHCl_3$:MeOH, 4:1); IR (thin film) 3410, 2977, 1706, 1665, 1638, 1397, 1370, 1350, 1156, 1108, 1081 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$:CD_3OD 1:3) δ 1.19 (9H, s), 1.43 (1H, , t, *J* = 12.3 Hz), 1.99-2.03 (1H, m), 2.47-2.52 (1H, m), 2.74 (1H, td, *J* = 12.1, 3.6 Hz), 2.95-3.02 (1H, m), 3.83-3.86 (1H, m), 3.96 (1H, br s), 4.59-4.62 (1H, m), 4.82-4.86 (1H, m), 4.96 (1H, t, *J* = 8.2 Hz), 8.36 (1H, s); ^{13}C NMR (100 MHz, $CDCl_3$:CD_3OD 1:3) δ 28.0 (CH_3), 35.2 (CH_2), 37.1 (CH), 39.0 (CH), 49.9 (CH), 68.9 (CH), 69.3 (CH), 70.19 (CH), 70.23 (CH), 73.8 (CH), 81.5 (C), 128.6 (CH), 142.9 (C), 164.3 (C), 175.3 (C)；MS (ESI) *m/z* (relative intensity) 421 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{26}N_4O_7$ $[M+Na]^+$ 421.1694, found 421.1690.

Triazole 295. Following the general procedure for deprotection of the isopropylidene, triazole **282β** (39 mg, 0.08 mmole) was converted into triazole **295** using *t*-BuOH/H_2O (v/v, 1/8; 50 mL) instead of H_2O (50 mL) at room temperature in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 8:1) to afford triazole **295** (34.3 mg, 96%) as a white solid: mp 232-234 ^oC; $[\alpha]_D^{20}$ -59.5 (*c* 0.80, MeOH); R_f 0.32 ($CHCl_3$:MeOH, 8:1); IR (thin film) 3408, 3136, 2972, 2930, 1724, 1717, 1637, 1446, 1390, 1367, 1257, 1152, 1110, 1077,

1017 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.11 (9H, s), 1.40-1.48 (1H, m), 2.04 (1H, td, *J* = 13.8, 4.3 Hz), 2.51-2.56 (1H, m), 2.84 (1H, td, *J* = 12.1, 4.2 Hz), 2.98-3.04 (1H, m), 3.87 (1H, dd, *J* = 6.2, 2.7 Hz), 3.97-3.98 (1H, m), 4.65 (1H, t, *J* = 5.9 Hz), 4.88-4.92 (1H, m), 4.97-5.01 (1H, m), 7.33 (1H, t, *J* = 7.4 Hz), 7.42 (2H, t, *J* = 7.5 Hz), 7.81 (2H, d, *J* = 7.5 Hz), 8.36 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.1 (CH_3), 35.8 (CH_2), 37.5 (CH), 39.4 (CH), 49.0 (CH), 69.37 (CH), 69.44 (CH), 70.4 (CH), 70.7 (CH), 74.0 (CH), 81.6 (C), 123.7 (CH), 126.6 (CH), 129.2 (CH), 129.9 (CH), 131.8 (C), 148.2 (C), 175.8 (C)；MS (ESI) *m/z* (relative intensity) 454 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{22}H_{29}N_3O_6$ $[M+Na]^+$ 454.1949, found 454.1948.

Triazole 296. Following the general procedure for deprotection of the isopropylidene, triazole **283β** (37 mg, 0.07 mmole) was converted into triazole **296** using *t*-BuOH/H_2O (v/v, 1/4; 50 mL) instead of H_2O (50 mL) at room temperature in 24 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **296** (32.3 mg, 95%) as a white solid: mp 176-179 ^oC; $[\alpha]_D^{20}$ -56.0 (*c* 0.85, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 5:1); IR (thin film) 3369, 2974, 2930, 1721, 1490, 1456, 1367, 1290, 1250, 1152, 1122, 1072, 1021 cm^{-1}; ^1H NMR (400 MHz, CD_3OD) δ 1.09 (9H, s), 1.41-1.48 (1H, m), 2.03 (1H, dt, *J* = 13.8, 4.2 Hz), 2.51-2.56 (1H, m), 2.84 (1H, td, *J* = 12.1, 4.1 Hz), 2.98-3.04 (1H, m), 3.87-3.88 (1H, m), 3.96 (4H, br s), 4.66 (1H, t, *J* = 5.9 Hz), 4.89-4.91 (1H, m), 4.99 (1H, t, *J* = 8.1 Hz), 7.03 (1H, t, *J* = 7.5 Hz), 7.09 (1H, d, *J* = 8.3 Hz), 7.32 (1H, t, *J* =

7.7 Hz), 8.09 (1H, d, J = 7.6 Hz), 8.33 (1H, s); ^{13}C NMR (100 MHz, CD_3OD) δ 28.0 (CH_3), 35.7 (CH_2), 37.6 (CH), 39.4 (CH), 48.9 (CH), 55.9 (CH_3), 69.2 (CH), 69.4 (CH), 70.6 (CH), 70.7 (CH), 74.2 (CH), 81.5 (C), 112.3 (CH), 120.3 (C), 121.8 (CH), 126.5 (CH), 128.0 (CH), 130.2 (CH), 143.7 (C), 157.3 (C), 175.8 (C)； MS (ESI) *m/z* (relative intensity) 484 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{23}H_{31}N_3O_7$ [M+Na]$^+$ 484.2054, found 484.2051.

Triazole 297. Following the general procedure for deprotection of the isopropylidene, triazole **284β** (41 mg, 0.09 mmole) was converted into triazole **297** using *t*-BuOH/H_2O (v/v, 1/5; 50 mL) instead of H_2O (50 mL) at room temperature in 20 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 5:1) to afford triazole **297** (36.4 mg, 97%) as a white solid: mp 139-143 ^{o}C; $[\alpha]_D^{20}$ -59.6 (*c* 1.00, MeOH); R_f 0.33 ($CHCl_3$:MeOH, 5:1); IR (thin film) 3392, 2977, 2917, 1720, 1602, 1474, 1425, 1368, 1254, 1205, 1152, 1073, 1019 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD) δ 1.10 (9H, s), 1.41-1.49 (1H, m), 2.03 (1H, dt, J = 13.8, 4.4 Hz), 2.54 (1H, dt, J = 8.0, 5.7 Hz), 2.83 (1H, td, J = 12.1, 4.3 Hz), 3.04 (1H, dt, J = 11.4, 7.9 Hz), 3.88 (1H, dd, J = 6.2, 3.0 Hz), 3.97 (1H, q, J = 3.3 Hz), 4.65 (1H, t, J = 5.8 Hz), 4.93 (1H, dd, J = 9.1, 6.7 Hz), 5.03-5.07 (1H, m), 7.33-7.37 (1H, m), 7.90 (1H, td, J = 7.7, 1.6 Hz), 8.06 (1H, d, J = 7.9 Hz), 8.49 (1H, s), 8.57 (1H, d, J = 4.6 Hz); ^{13}C NMR (100 MHz, CD_3OD) δ 28.0 (CH_3), 35.6 (CH_2), 37.6 (CH), 39.4 (CH), 48.99 (CH), 69.3 (CH), 69.5 (CH), 70.61 (CH), 70.64 (CH), 74.2 (CH), 81.5 (C), 121.3 (CH), 124.4 (CH), 125.5 (CH), 138.8 (CH), 148.1 (C), 150.4 (CH), 151.2 (C),

175.7 (C)； MS (ESI) *m/z* (relative intensity) 455 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{21}H_{28}N_4O_6$ [M+Na]$^+$ 455.1901, found 455.1905.

Triazole 298. Following the general procedure for deprotection of the isopropylidene, triazole **227** (41 mg, 0.12 mmole) was converted into triazole **298** at 100 ^{o}C in 36 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH:AcOH, 2:1:0.2) to afford triazole **298** (33.3 mg, 96%) as a white solid: mp 56-58 ^{o}C; $[\alpha]_D^{20}$ +28.2 (*c* 1.80, DMF); R_f 0.22 ($CHCl_3$:MeOH:AcOH 2:1:0.2); IR (thin film) 3401, 2930, 1574, 1414, 1297, 1240, 1176, 1113, 1054 cm^{-1}; ^{1}H NMR (400 MHz, CD_3OD:D_2O:AcOH 1:1:0.1) δ 1.38 (1H, s), 1.50 (1H, d, *J* = 18.2 Hz), 1.65 (1H, d, *J* = 17.6 Hz), 2.65-2.69 (1H, m), 3.02-3.07 (1H, m), 3.15-3.24 (2H, m), 4.09 (1H, s), 4.87-4.89 (1H, m), 5.19 (1H, t, *J* = 9.6 Hz), 5.67-5.70 (2H, m), 8.29 (1H, s); ^{13}C NMR (100 MHz, CD_3OD:D_2O:AcOH 1:1:0.1) δ 24.5 (CH_2), 34.5 (CH), 36.5 (CH), 42.0 (CH), 65.2 (CH_2), 68.0 (CH), 75.1 (CH), 76.9 (CH), 127.1 (CH), 127.9 (CH), 128.6 (CH), 146.2 (C), 181.6 (C)； MS (ESI) *m/z* (relative intensity) 318 ([M+Na]$^+$, 100); HRMS (ESI) calcd for $C_{13}H_{17}N_3O_5$ [M+Na]$^+$ 318.1060, found 318.1069.

Triazole 299. Following the general procedure for deprotection of the isopropylidene group from alkyl ether, triazole **240** (60.5 mg, 0.17 mmole) was converted into triazole **299** at 100 ^{o}C in 36 h. The residue was then fractionated by flash column chromatography ($CHCl_3$:MeOH, 1:3) to afford triazole **299** (50.2 mg, 98%) as a white solid: mp > 280 ^{o}C; $[\alpha]_D^{20}$ -78.9 (*c* 0.77, DMF/H_2O, v/v, 10/1); R_f 0.24

($CHCl_3$:MeOH: AcOH, 2:1:0.2); IR (thin film) 3367, 2934, 2892, 2857, 1587, 1562, 1450, 1415, 1355, 1293, 1249, 1100, 1059 cm^{-1}; ^1H NMR (400 MHz, CD_3OD:D_2O 1:1) δ 0.99-1.05 (1H, m), 1.34-1.42 (2H, m), 1.54-1.56 (2H, m), 1.61-1.65 (1H, m), 1.74-1.76 (1H, m), 2.24-2.26 (1H, m), 2.34-2.37 (2H, m), 2.41-2.45 (1H, m), 4.12-4.14 (1H, m), 4.96-4.98 (2H, m), 8.35 (1H, s); ^{13}C NMR (100 MHz, CD_3OD:D_2O 1:1) δ 20.4 (CH_2), 26.0 (CH_2), 28.3 (CH_2), 36.8 (CH), 39.5 (CH), 44.4 (CH), 65.2 (CH_2), 70.6 (CH), 72.1 (CH), 73.9 (CH), 128.3 (CH), 146.2 (C), 168.0 (C); MS (ESI) *m/z* (relative intensity) 320 ($[M+Na]^+$, 100); HRMS (ESI) calcd for $C_{17}H_{25}N_3O_5$ $[M+Na]^+$ 320.1217, found 320.1217.

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Appendix

I X-ray crystallographic structures

II NMR spectra

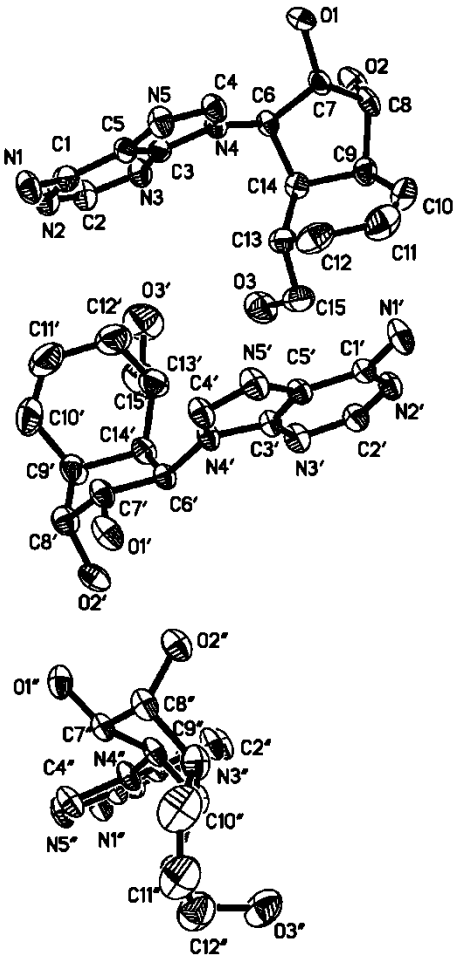
NMR spectra were measured in $CDCl_3$ solutions, unless stated otherwise.

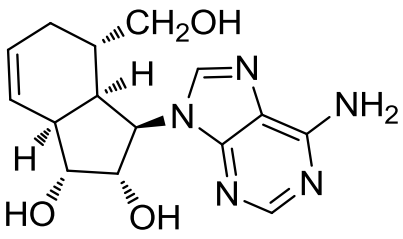
X-ray crystallographic data and structure of adenosine analogue 185

Table 1. Crystal data and structure refinement for p.

Identification code	LFL A17
Empirical formula	C15 H19 N5 O3
Formula weight	317.35
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 14.9903(19) A alpha = 90 deg. b = 8.7994(11) A beta = 109.284(3) deg. c = 18.716(2) A gamma = 90 deg.
Volume	2330.2(5) A^3
Z, Calculated density	6, 1.357 Mg/m^3
Absorption coefficient	0.098 mm^-1
F(000)	1008
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	1.44 to 25.25 deg.
Limiting indices	-17<=h<=17, -10<=k<=10, -22<=l<=22
Reflections collected / unique	27684 / 8353 [R(int) = 0.0925]
Completeness to theta = 25.25	99.9 %
Absorption correction	multi-scan
Max. and min. transmission	0.7185 and 0.5669

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	8353 / 1 / 622
Goodness-of-fit on F^2	1.042
Final R indices [I>2sigma(I)]	R1 = 0.0647, wR2 = 0.1569
R indices (all data)	R1 = 0.0972, wR2 = 0.1768
Absolute structure parameter	0.8(15)
Largest diff. peak and hole	0.409 and -0.326 e.A^-3





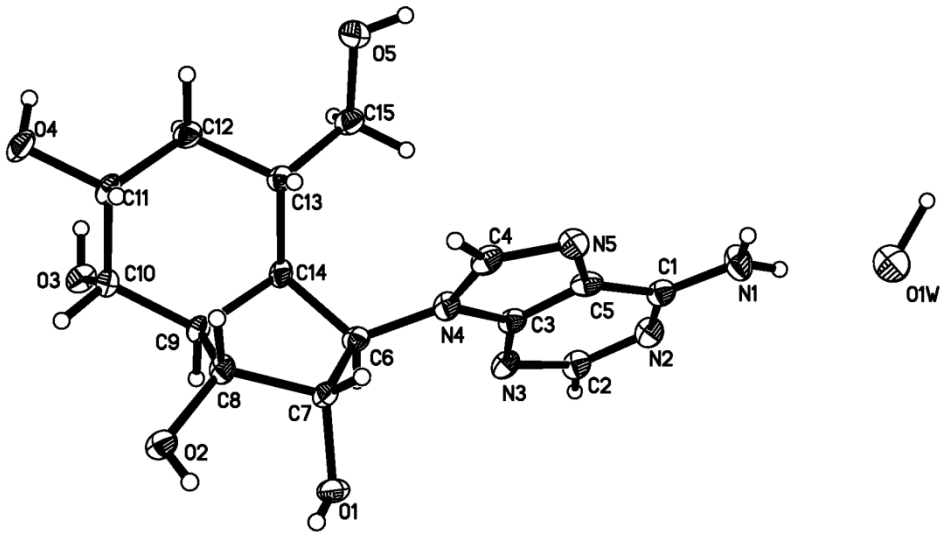
185

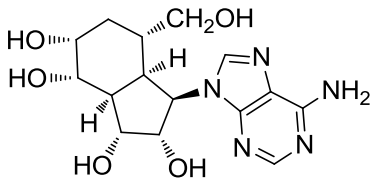
X-ray crystallographic data and structure of adenosine analogue187

Table 1. Crystal data and structure refinement for p.

Identification code	LFL A25
Empirical formula	C15 H23 N5 O6
Formula weight	369.38
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 6.949(2) A alpha = 90 deg. b = 8.295(2) A beta = 90 deg. c = 27.041(8) A gamma = 90 deg.
Volume	1558.7(8) A^3
Z, Calculated density	4, 1.574 Mg/m^3
Absorption coefficient	0.123 mm^-1
F(000)	784
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	2.57 to 25.23 deg.
Limiting indices	-8<=h<=8, -4<=k<=9, -32<=l<=32
Reflections collected / unique	11425 / 2780 [R(int) = 0.0615]
Completeness to theta = 25.23	99.8 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.4700

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2780 / 0 / 243
Goodness-of-fit on F^2	1.070
Final R indices [I>2sigma(I)]	R1 = 0.0609, wR2 = 0.1558
R indices (all data)	R1 = 0.0870, wR2 = 0.1753
Absolute structure parameter	-1(2)
Largest diff. peak and hole	0.346 and -0.551 e.A^-3





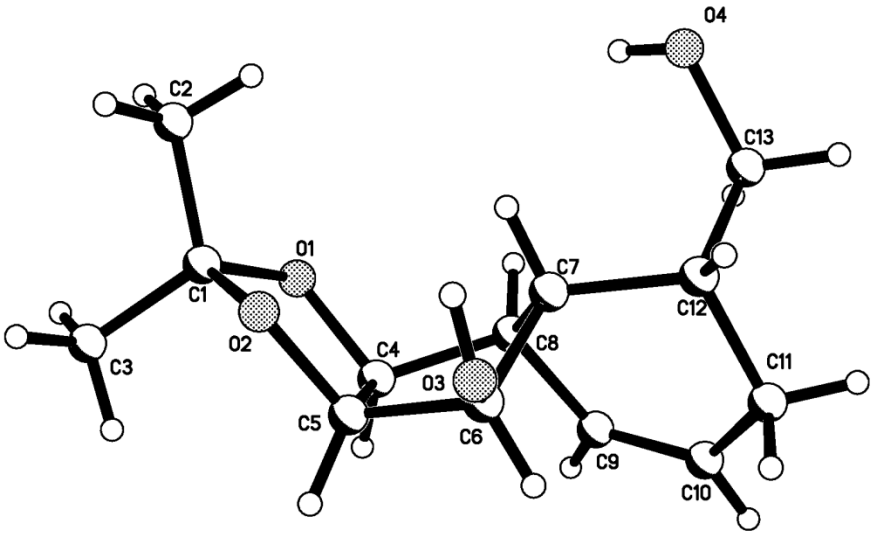
187

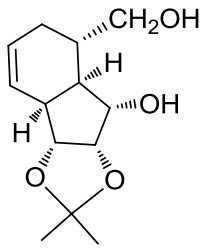
X-ray crystallographic data and structure of cycloadduct 201

Table 1. Crystal data and structure refinement for p.

Identification code	LFL A08
Empirical formula	C13 H20 O4
Formula weight	240.29
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 5.9125(6) A alpha = 90 deg. b = 11.7320(12) A beta = 90 deg. c = 18.4633(18) A gamma = 90 deg.
Volume	1280.7(2) A^3
Z, Calculated density	4, 1.246 Mg/m^3
Absorption coefficient	0.091 mm^-1
F(000)	520
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	2.06 to 25.25 deg.
Limiting indices	-7<=h<=6, -14<=k<=14, -22<=l<=22
Reflections collected / unique	9513 / 2280 [R(int) = 0.0801]
Completeness to theta = 25.25	99.2 %
Absorption correction	multi-scan

Max. and min. transmission	0.6963 and 0.4830
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2280 / 0 / 154
Goodness-of-fit on F^2	1.079
Final R indices [I>2sigma(I)]	R1 = 0.0587, wR2 = 0.1567
R indices (all data)	R1 = 0.0644, wR2 = 0.1633
Absolute structure parameter	0.3(18)
Largest diff. peak and hole	0.288 and -0.335 e.A^-3





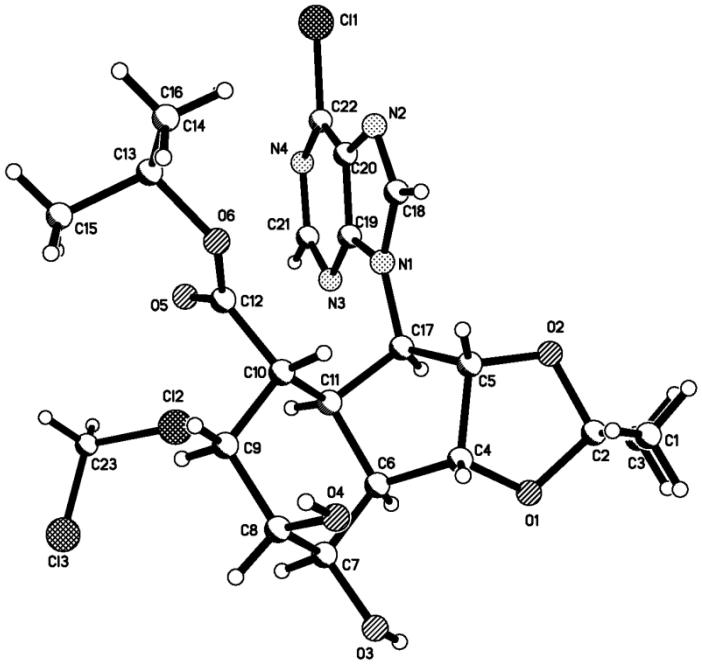
201

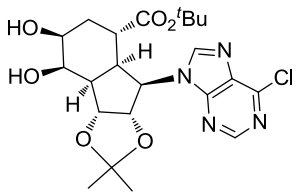
X-ray crystallographic data and structure of diol 213β

Table 1. Crystal data and structure refinement for p.

Identification code	LFL A36b
Empirical formula	C22.50 H30 Cl2 N4 O6
Formula weight	523.41
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 10.0311(3) A alpha = 90 deg. b = 14.0245(4) A beta = 90 deg. c = 19.9833(7) A gamma = 90 deg.
Volume	2811.27(15) A^3
Z, Calculated density	4, 1.237 Mg/m^3
Absorption coefficient	0.271 mm^-1
F(000)	1100
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	1.77 to 25.25 deg.
Limiting indices	-11<=h<=12, -10<=k<=16, -23<=l<=23
Reflections collected / unique	17742 / 5079 [R(int) = 0.0273]
Completeness to theta = 25.25	100.0 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.6734

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5079 / 0 / 325
Goodness-of-fit on F^2	1.049
Final R indices [I>2sigma(I)]	R1 = 0.0741, wR2 = 0.2238
R indices (all data)	R1 = 0.0846, wR2 = 0.2395
Absolute structure parameter	0.02(14)
Largest diff. peak and hole	0.992 and -0.431 e.A^-3





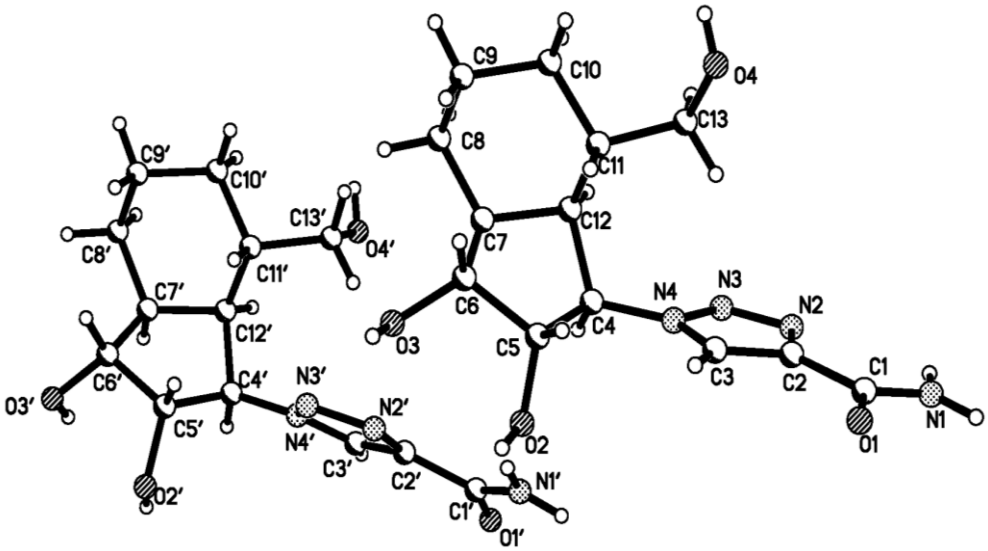
213β

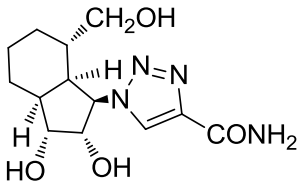
X-ray crystallographic data and structure of triazole 236

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA46
Empirical formula	C13 H20 N4 O4
Formula weight	296.33
Temperature	293(2) K
Wavelength	1.54178 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 8.6891(12) A alpha = 90 deg. b = 10.4088(15) A beta = 98.217(6) deg. c = 15.725(2) A gamma = 90 deg.
Volume	1407.6(3) A^3
Z, Calculated density	4, 1.398 Mg/m^3
Absorption coefficient	0.878 mm^-1
F(000)	632
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	2.84 to 69.55 deg.
Limiting indices	-10<=h<=10, -12<=k<=12, -18<=l<=18
Reflections collected / unique	31415 / 5173 [R(int) = 0.0755]
Completeness to theta = 69.55	98.1 %
Absorption correction	multi-scan
Max. and min. transmission	0.7531 and 0.2991

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	5173 / 1 / 379
Goodness-of-fit on F^2	1.062
Final R indices [I>2sigma(I)]	R1 = 0.0596, wR2 = 0.1588
R indices (all data)	R1 = 0.0658, wR2 = 0.1674
Absolute structure parameter	0.2(3)
Largest diff. peak and hole	0.310 and -0.348 e.A^-3





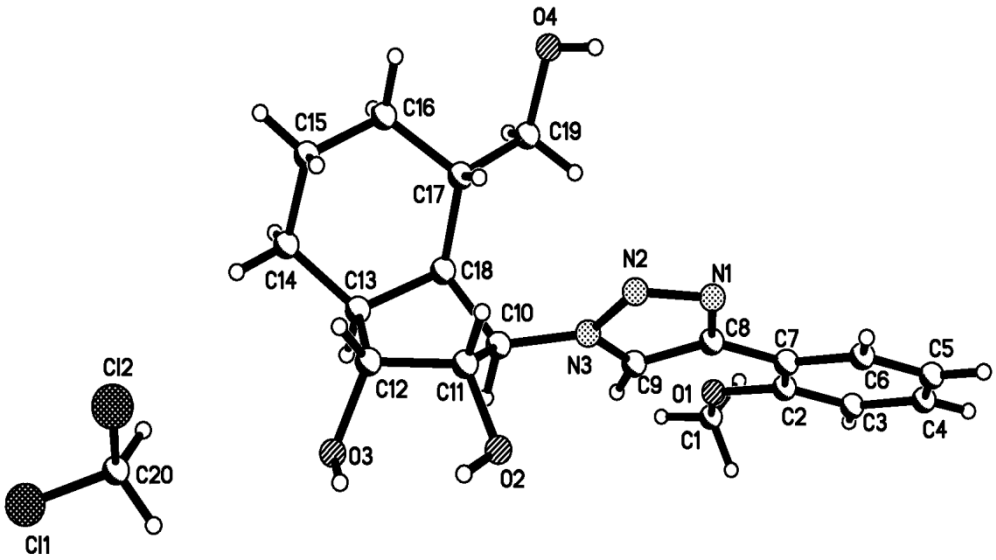
236

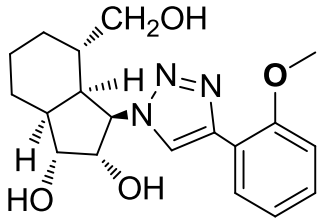
X-ray crystallographic data and structure of triazole 238

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA36
Empirical formula	C20 H27 C12 N3 O4
Formula weight	444.35
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, C2
Unit cell dimensions	a = 14.637(6) A alpha = 90 deg. b = 9.780(4) A beta = 106.821(11) deg. c = 15.990(6) A gamma = 90 deg.
Volume	2191.0(15) A^3
Z, Calculated density	4, 1.347 Mg/m^3
Absorption coefficient	0.327 mm^-1
F(000)	936
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	1.33 to 25.24 deg.
Limiting indices	-17<=h<=15, -11<=k<=11, -19<=l<=19
Reflections collected / unique	12836 / 3921 [R(int) = 0.0297]
Completeness to theta = 25.24	99.3 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.6863

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3921 / 1 / 262
Goodness-of-fit on F^2	1.052
Final R indices [I>2sigma(I)]	R1 = 0.0648, wR2 = 0.1921
R indices (all data)	R1 = 0.0797, wR2 = 0.2116
Absolute structure parameter	0.10(18)
Largest diff. peak and hole	0.567 and -0.454 e.A^-3





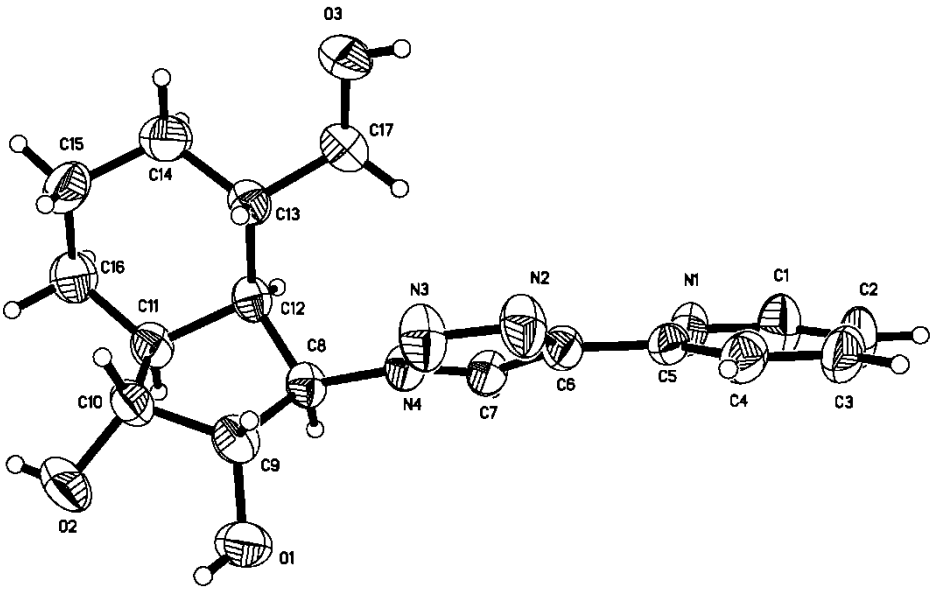
238

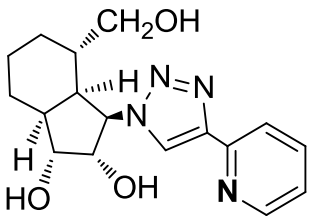
X-ray crystallographic data and structure of triazole 239

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA37
Empirical formula	C17 H22 N4 O3
Formula weight	330.39
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 5.5943(5) A alpha = 90 deg. b = 20.8936(19) A beta = 96.665(6) deg. c = 7.2329(7) A gamma = 90 deg.
Volume	839.70(13) A^3
Z, Calculated density	2, 1.307 Mg/m^3
Absorption coefficient	0.092 mm^-1
F(000)	352
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	1.95 to 25.24 deg.
Limiting indices	-6<=h<=6, -23<=k<=25, -8<=l<=8
Reflections collected / unique	8301 / 2903 [R(int) = 0.0212]
Completeness to theta = 25.24	99.6 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.6346

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	2903 / 1 / 217
Goodness-of-fit on F^2	1.036
Final R indices [I>2sigma(I)]	R1 = 0.0379, wR2 = 0.0947
R indices (all data)	R1 = 0.0431, wR2 = 0.0983
Absolute structure parameter	-0.7(13)
Largest diff. peak and hole	0.242 and -0.232 e.A^-3





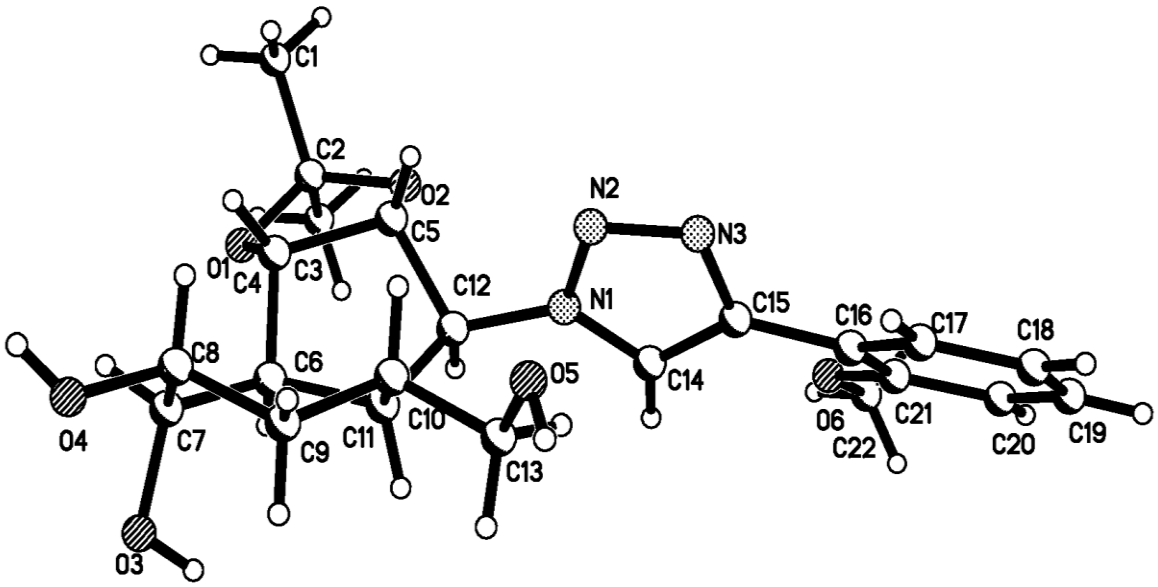
239

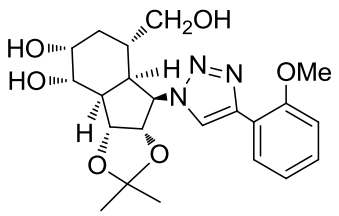
X-ray crystallographic data and structure of triazole 247

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA15a
Empirical formula	C22 H29 N3 O6
Formula weight	431.48
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 6.0384(6) A alpha = 90 deg. b = 9.8906(11) A beta = 92.301(2) deg. c = 17.9993(19) A gamma = 90 deg.
Volume	1074.1(2) A^3
Z, Calculated density	2, 1.334 Mg/m^3
Absorption coefficient	0.098 mm^-1
F(000)	460
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	1.13 to 25.24 deg.
Limiting indices	-7<=h<=4, -11<=k<=11, -21<=l<=21
Reflections collected / unique	12003 / 3853 [R(int) = 0.0310]
Completeness to theta = 25.24	99.3 %
Absorption correction	multi-scan
Max. and min. transmission	0.9713 and 0.6849

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3853 / 1 / 280
Goodness-of-fit on F^2	1.082
Final R indices [I>2sigma(I)]	R1 = 0.0372, wR2 = 0.0902
R indices (all data)	R1 = 0.0479, wR2 = 0.1032
Absolute structure parameter	0.3(10)
Largest diff. peak and hole	0.206 and -0.352 e.A^-3





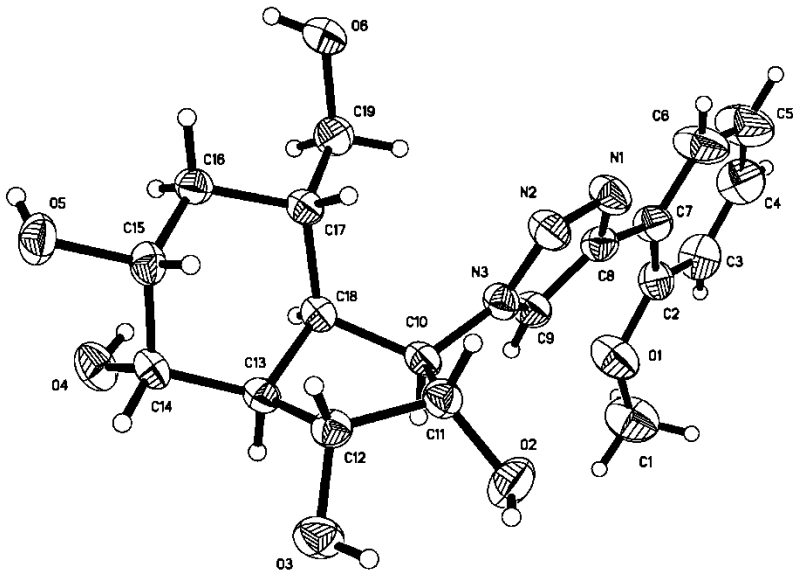
247

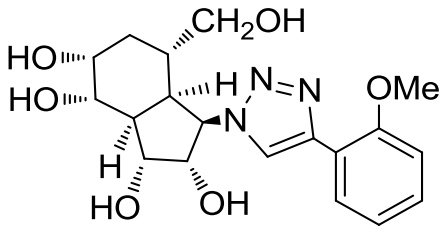
X-ray crystallographic data and structure of triazole 252

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA23
Empirical formula	C19 H25 N3 O6
Formula weight	391.42
Temperature	296(2) K
Wavelength	0.71073 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2(1)
Unit cell dimensions	a = 7.1679(2) A alpha = 90 deg. b = 8.2681(2) A beta = 90 deg. c = 30.0628(9) A gamma = 90 deg.
Volume	1781.67(8) A^3
Z, Calculated density	4, 1.459 Mg/m^3
Absorption coefficient	0.110 mm^-1
F(000)	832
Crystal size	0.50 x 0.40 x 0.30 mm
Theta range for data collection	1.35 to 25.25 deg.
Limiting indices	-8<=h<=8, -9<=k<=8, -32<=l<=36
Reflections collected / unique	15752 / 3192 [R(int) = 0.0208]
Completeness to theta = 25.25	98.9 %
Absorption correction	multi-scan
Max. and min. transmission	0.7456 and 0.6967

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	3192 / 0 / 253
Goodness-of-fit on F^2	1.099
Final R indices [I>2sigma(I)]	R1 = 0.0385, wR2 = 0.1149
R indices (all data)	R1 = 0.0407, wR2 = 0.1220
Absolute structure parameter	-0.4(11)
Largest diff. peak and hole	0.333 and -0.382 e.A^-3





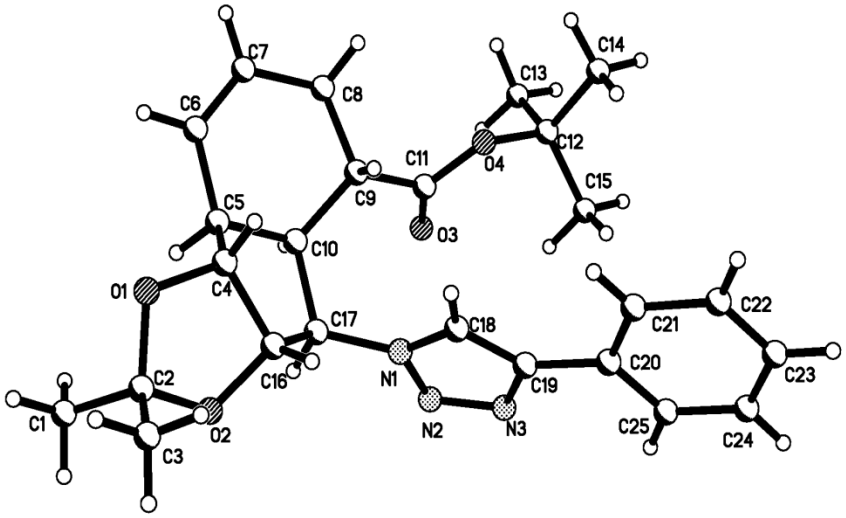
252

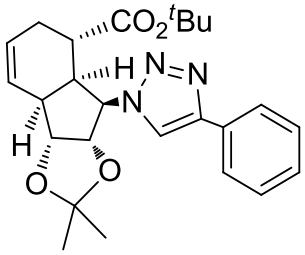
X-ray crystallographic data and structure of triazole 255

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA14
Empirical formula	C25 H31 N3 O4
Formula weight	437.53
Temperature	296(2) K
Wavelength	1.54178 A
Crystal system, space group	Orthorhombic, P2(1)2(1)2
Unit cell dimensions	a = 17.3645(7) A alpha = 90 deg. b = 24.6126(9) A beta = 90 deg. c = 5.6727(2) A gamma = 90 deg.
Volume	2424.43(16) A^3
Z, Calculated density	4, 1.199 Mg/m^3
Absorption coefficient	0.660 mm^-1
F(000)	936
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	3.11 to 68.83 deg.
Limiting indices	-20<=h<=20, -29<=k<=29, -6<=l<=5
Reflections collected / unique	33651 / 4464 [R(int) = 0.1103]
Completeness to theta = 68.83	99.7 %
Absorption correction	multi-scan
Max. and min. transmission	0.7531 and 0.1823

Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	4464 / 0 / 290
Goodness-of-fit on F^2	1.006
Final R indices [I>2sigma(I)]	R1 = 0.0502, wR2 = 0.1176
R indices (all data)	R1 = 0.0951, wR2 = 0.1436
Absolute structure parameter	0.3(3)
Extinction coefficient	0.0074(5)
Largest diff. peak and hole	0.138 and -0.140 e.A^-3





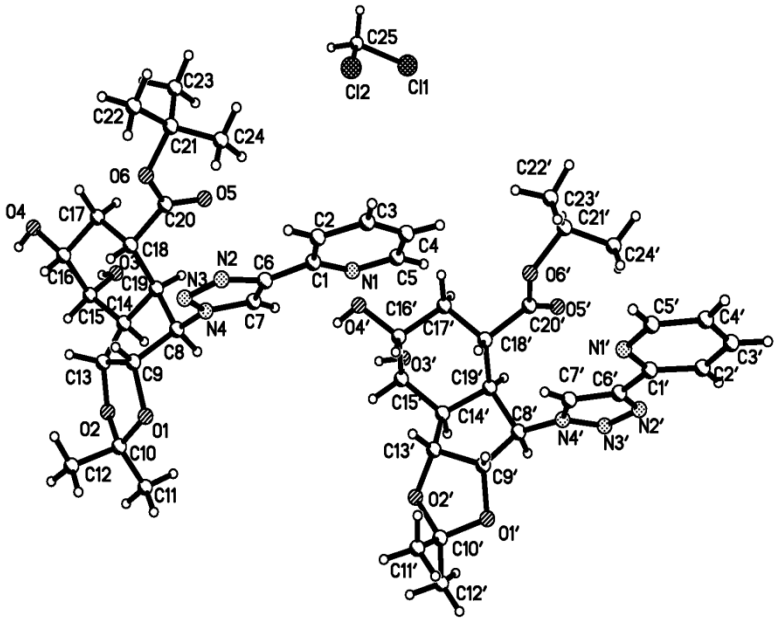
255

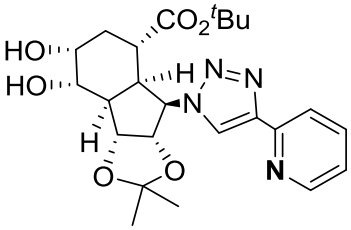
X-ray crystallographic data and structure of triazole 284α

Table 1. Crystal data and structure refinement for p.

Identification code	LFL AA31a
Empirical formula	C24.25 H32.50 Cl0.50 N4 O6
Formula weight	493.77
Temperature	296(2) K
Wavelength	1.54178 A
Crystal system, space group	Monoclinic, P2(1)
Unit cell dimensions	a = 12.6694(4) A alpha = 90 deg. b = 10.9853(3) A beta = 102.6290(15) deg. c = 21.3354(6) A gamma = 90 deg.
Volume	2897.56(15) A^3
Z, Calculated density	4, 1.132 Mg/m^3
Absorption coefficient	1.082 mm^-1
F(000)	1050
Crystal size	0.40 x 0.30 x 0.20 mm
Theta range for data collection	3.58 to 68.53 deg.
Limiting indices	-15<=h<=15, -13<=k<=11, -25<=l<=25
Reflections collected / unique	46682 / 10314 [R(int) = 0.0800]
Completeness to theta = 68.53	99.5 %
Absorption correction	multi-scan
Max. and min. transmission	0.7531 and 0.1787

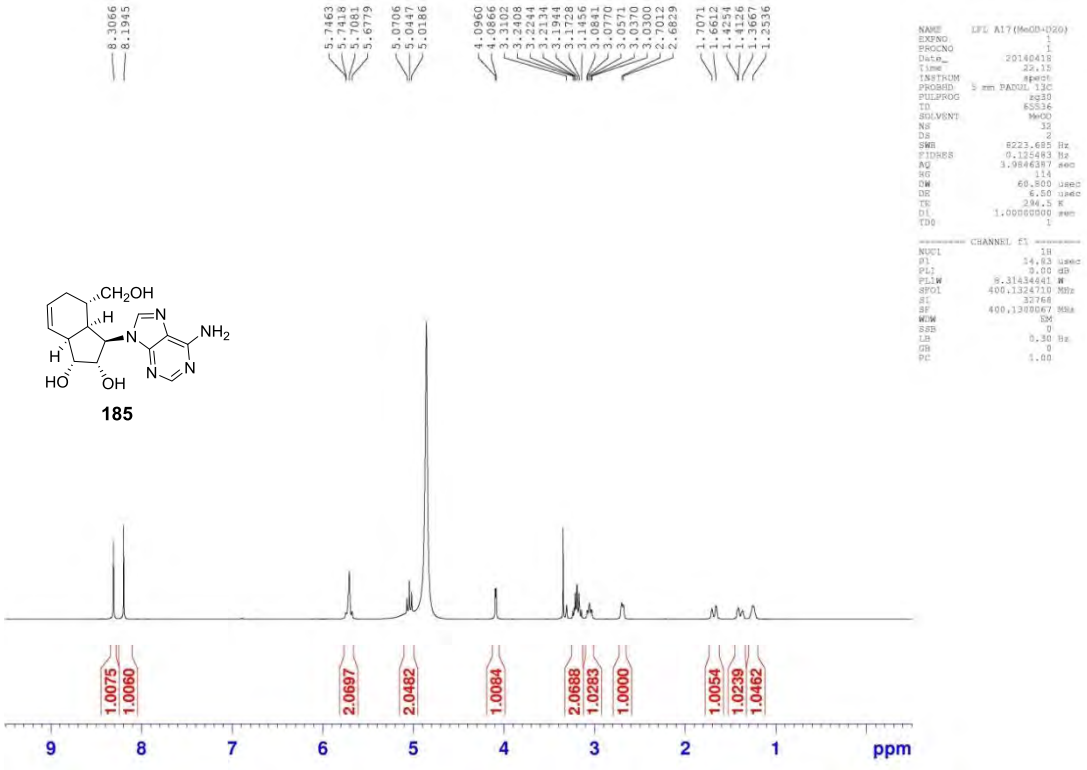
Refinement method	Full-matrix least-squares on F^2
Data / restraints / parameters	10314 / 1 / 641
Goodness-of-fit on F^2	1.004
Final R indices [I>2sigma(I)]	R1 = 0.0733, wR2 = 0.1992
R indices (all data)	R1 = 0.0990, wR2 = 0.2198
Absolute structure parameter	0.07(8)
Extinction coefficient	0.0020(4)
Largest diff. peak and hole	0.477 and -0.262 e.A^-3



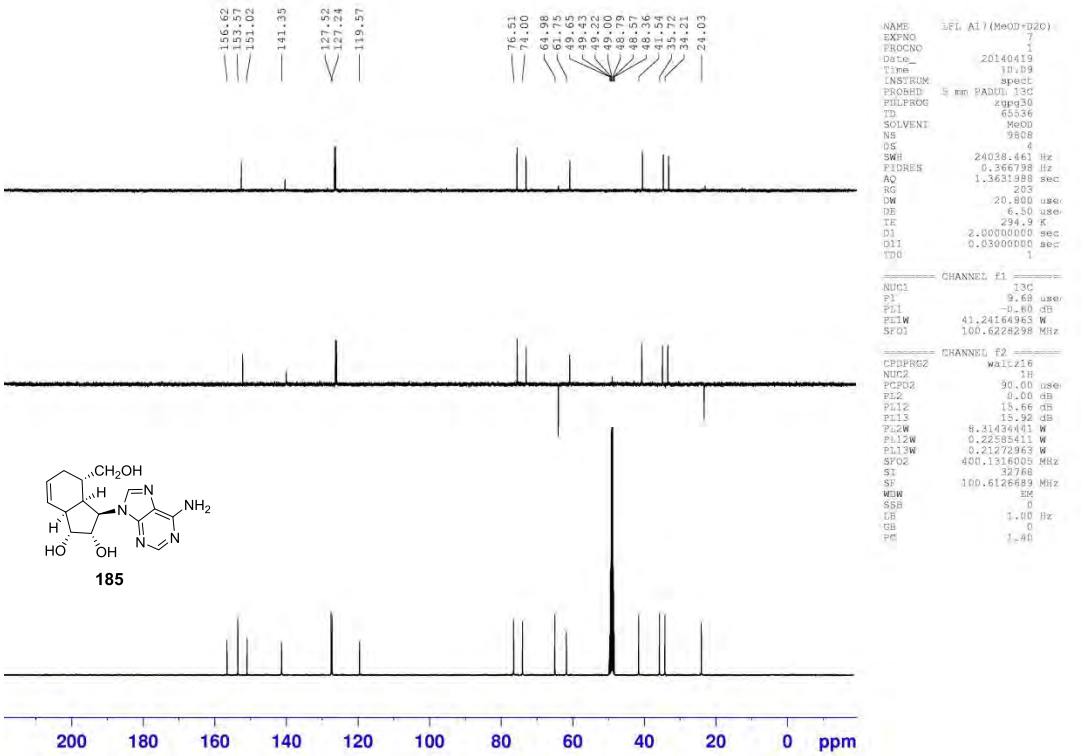


284α

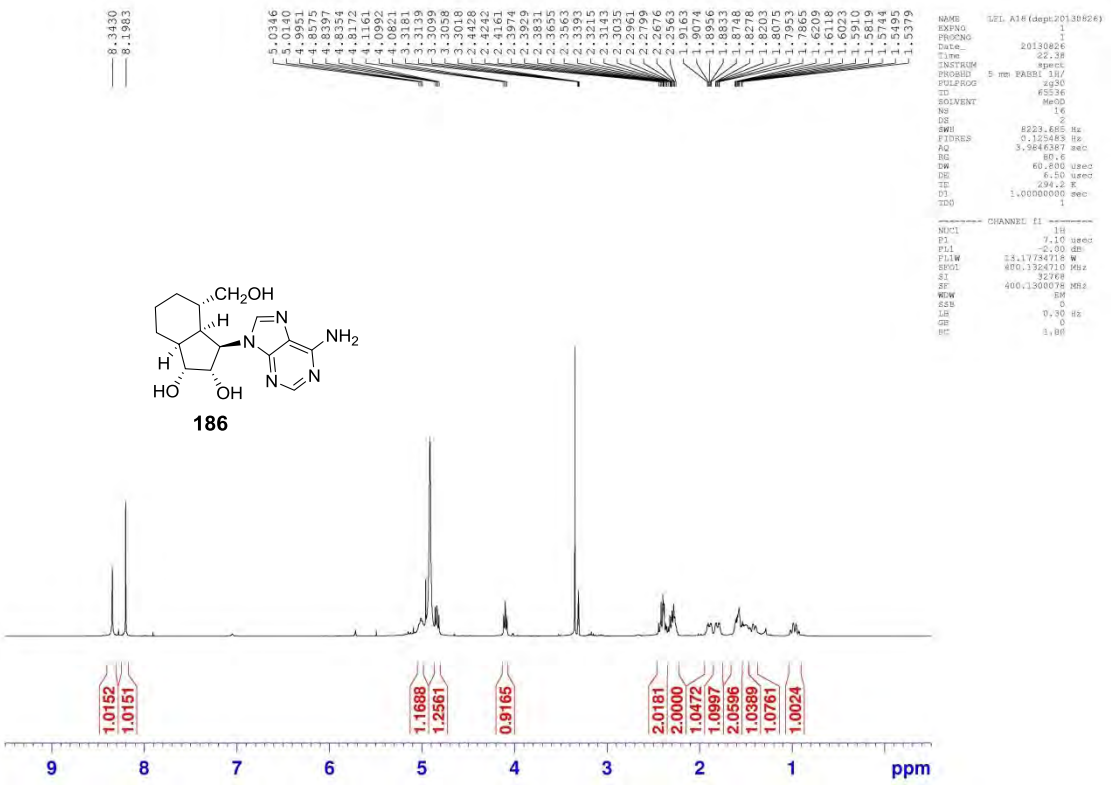
^{1}H NMR (Solvent: CD_3OD:D_2O 1:1)



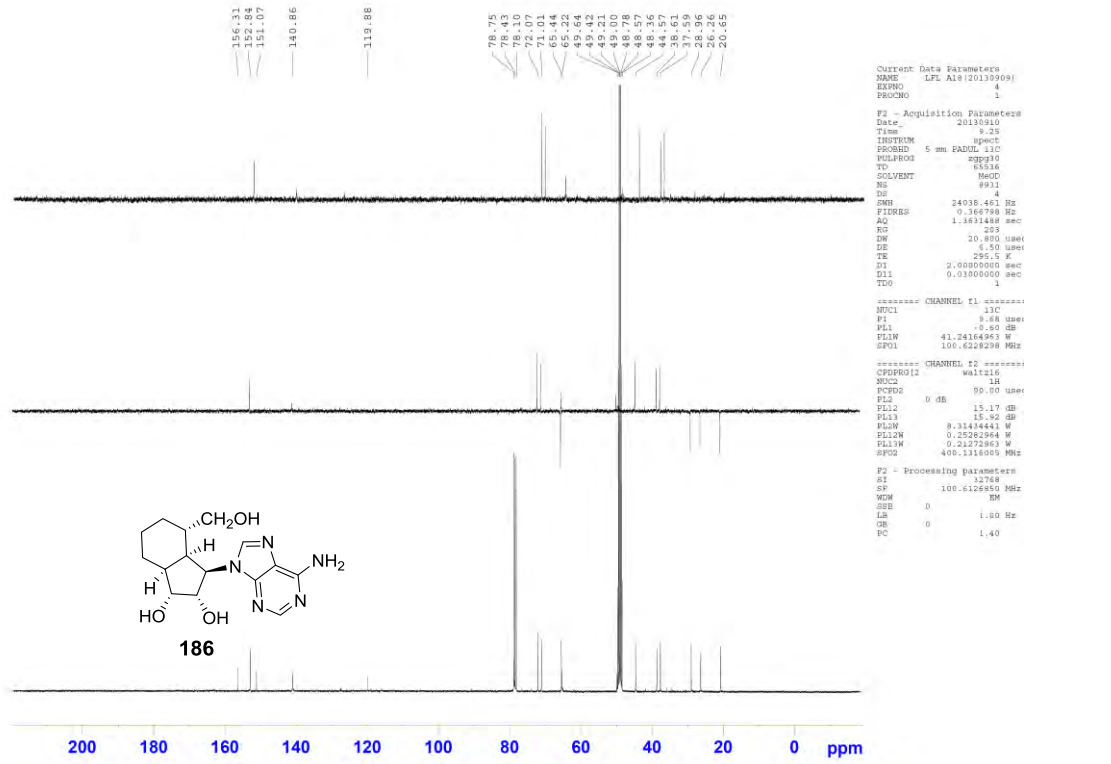
^{13}C NMR (Solvent: CD_3OD:D_2O 1:1)



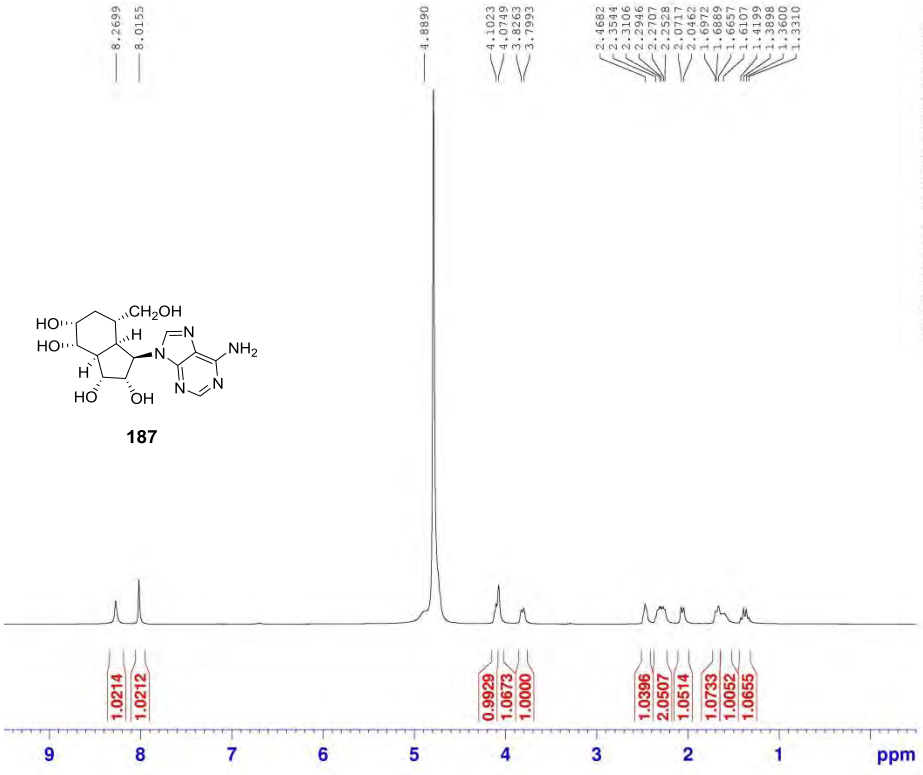
^{1}H NMR (Solvent: $CHCl_3$:CD_3OD 1:1)



^{13}C NMR (Solvent: $CHCl_3$:CD_3OD 1:1)

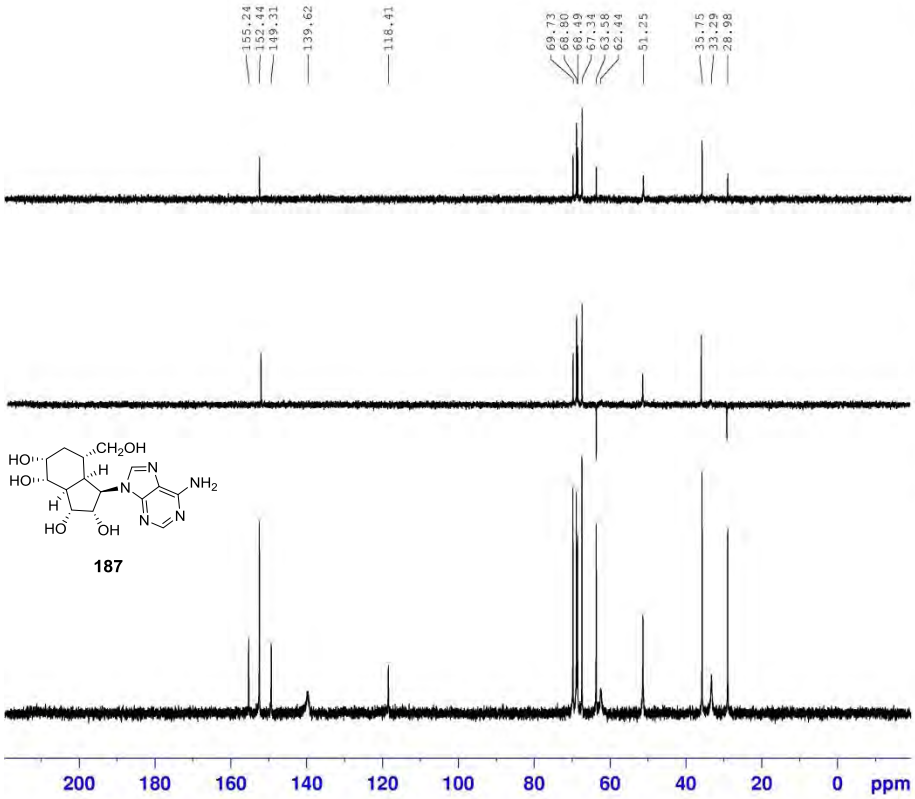


^{1}H NMR (Solvent: D_2O)



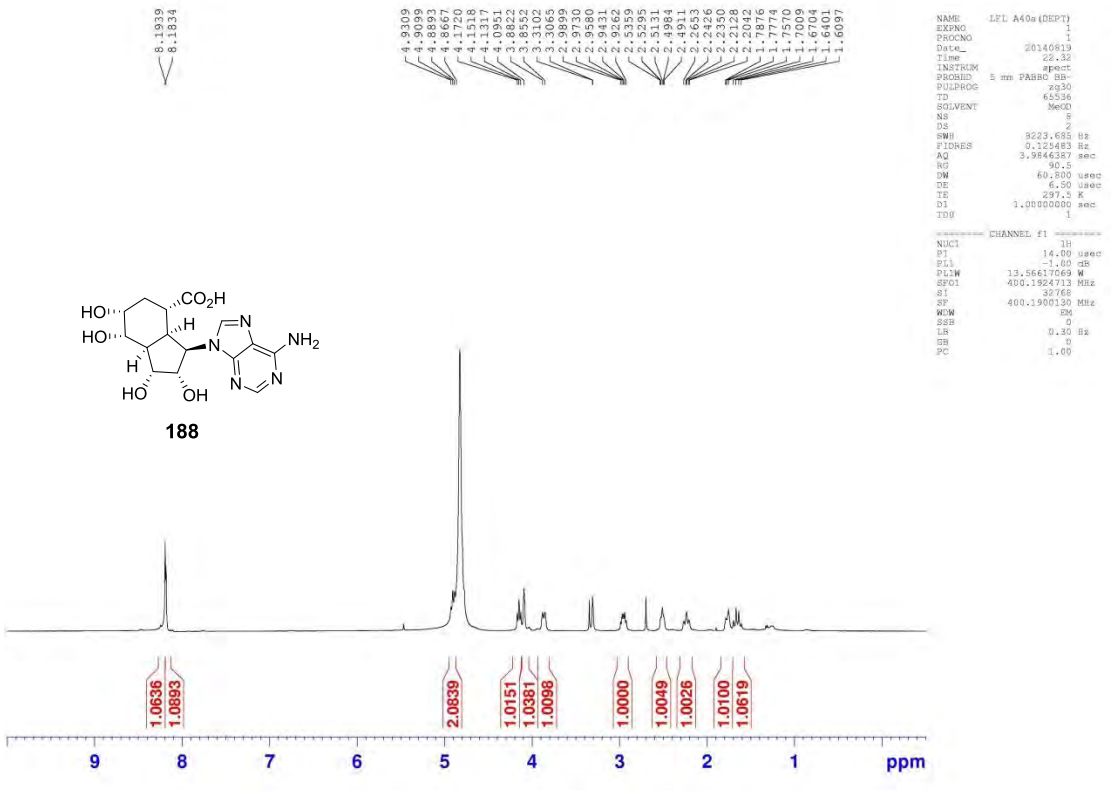
187

^{13}C NMR (Solvent: D_2O)

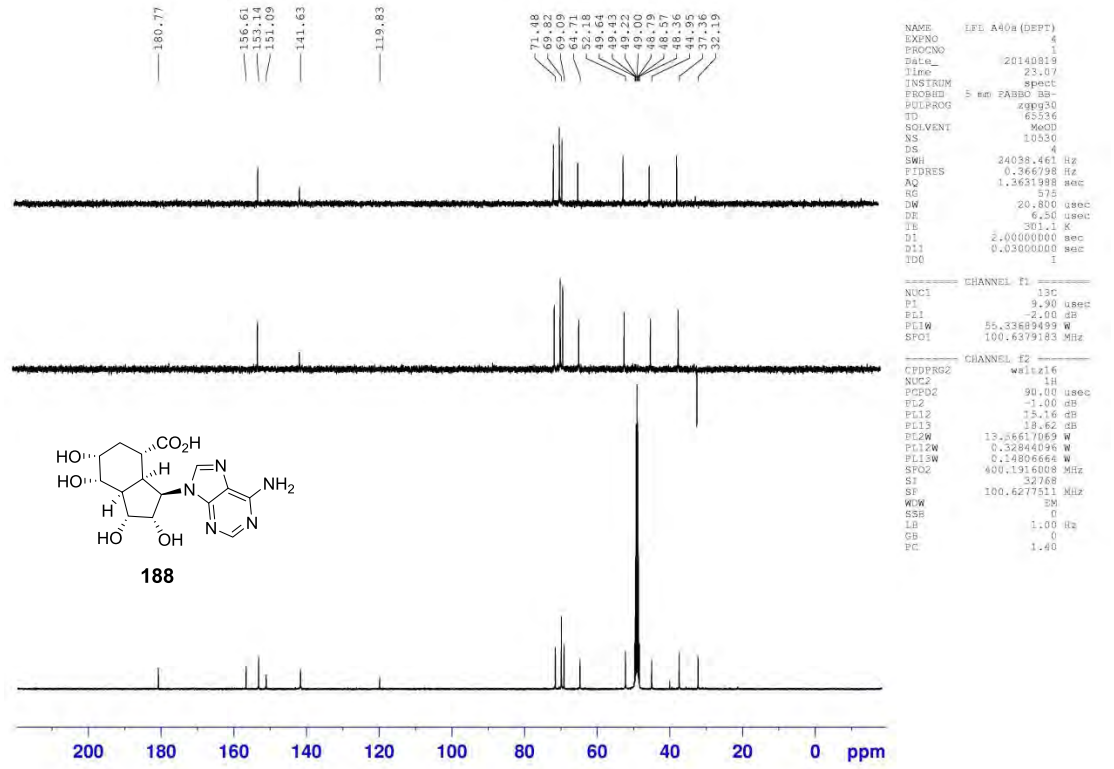


187

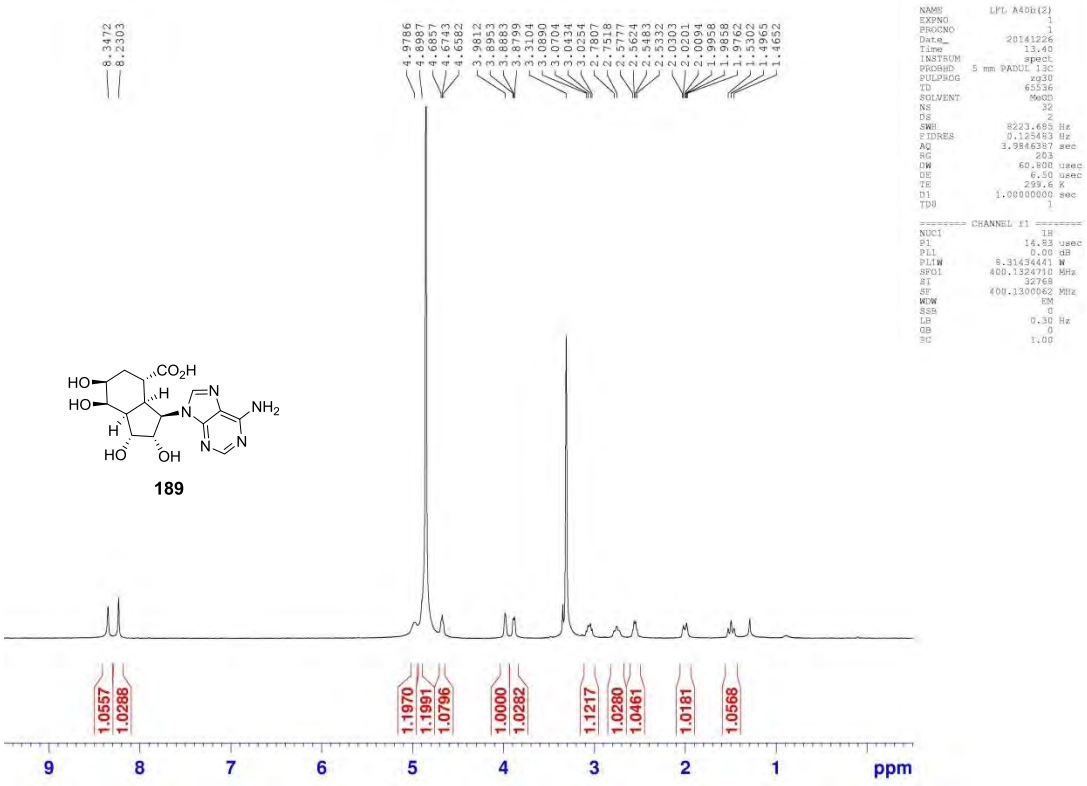
^{1}H NMR (Solvent: CD_3OD)



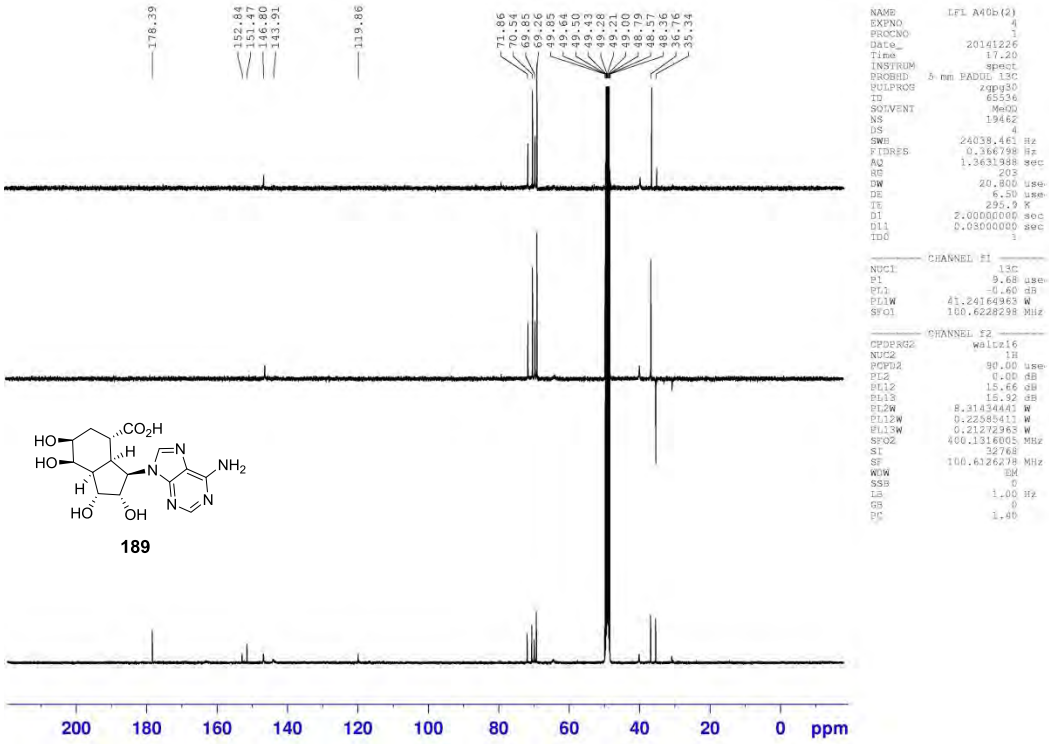
^{13}C NMR (Solvent: CD_3OD)



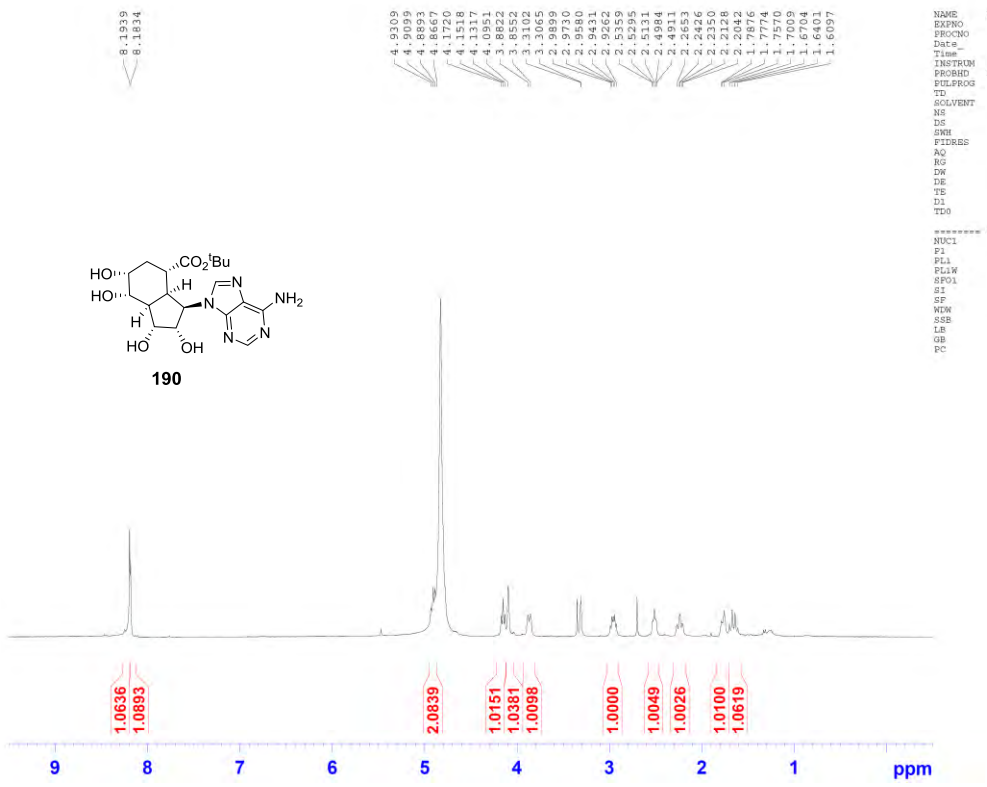
^{1}H NMR (Solvent: CD_3OD)



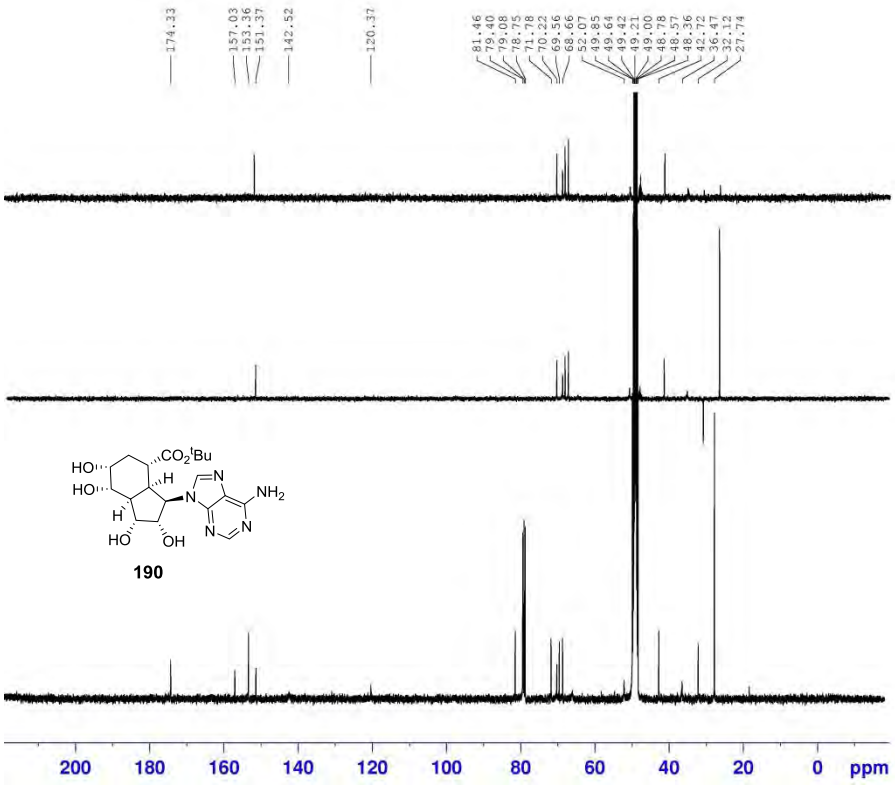
^{13}C NMR (Solvent: CD_3OD)



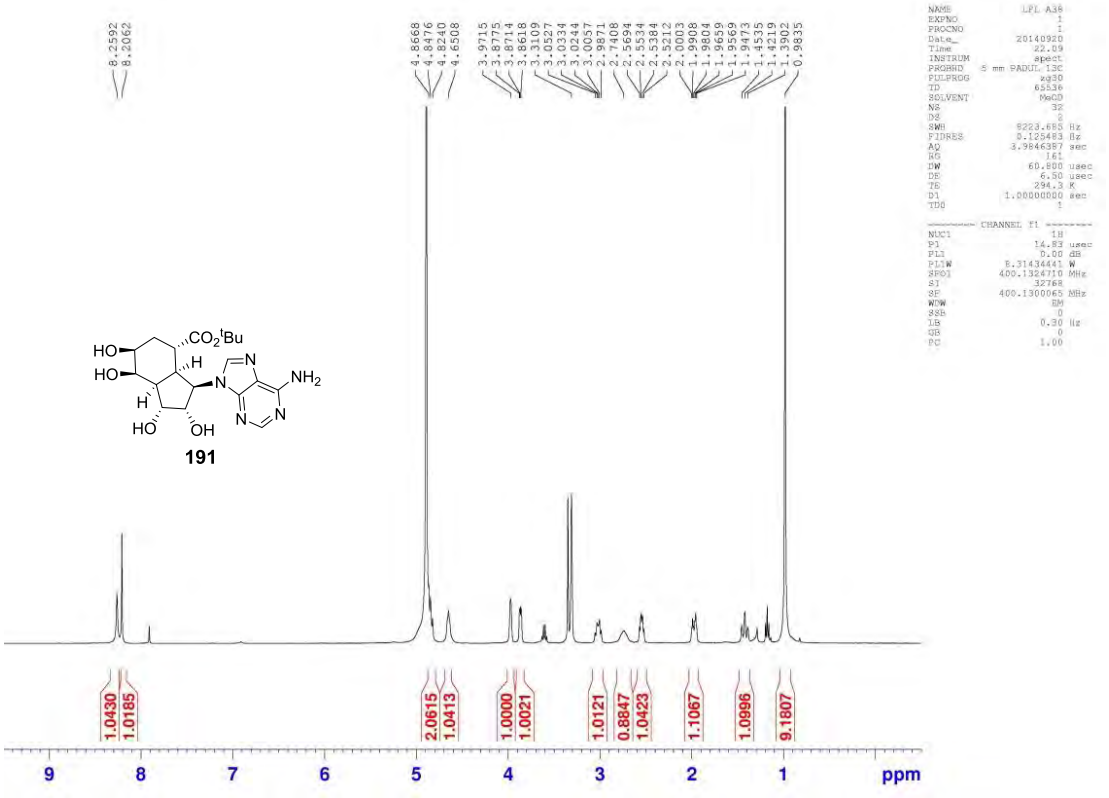
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



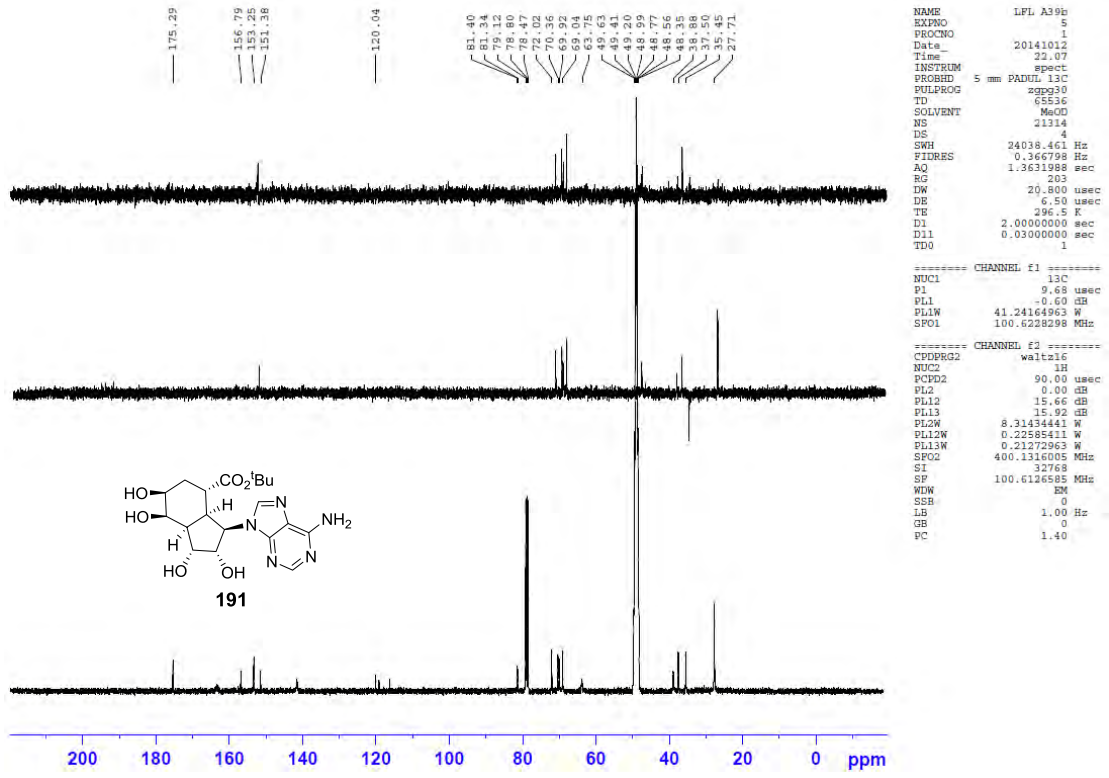
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



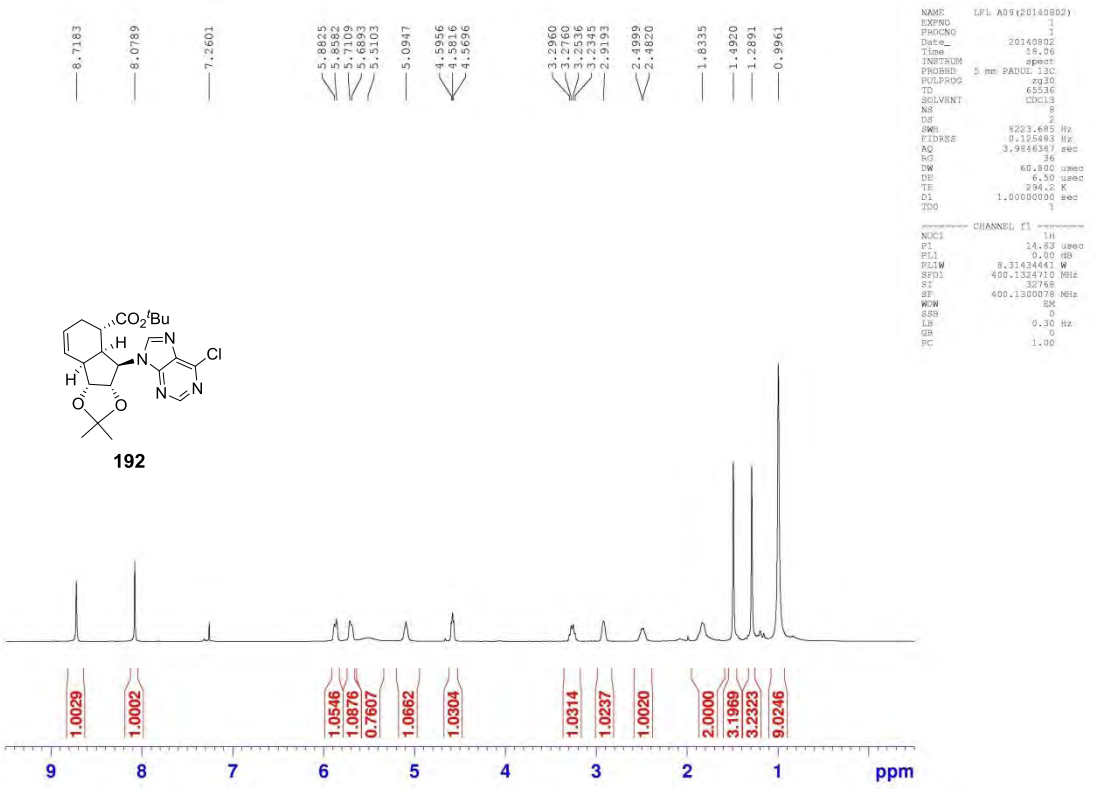
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:3)



^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:3)

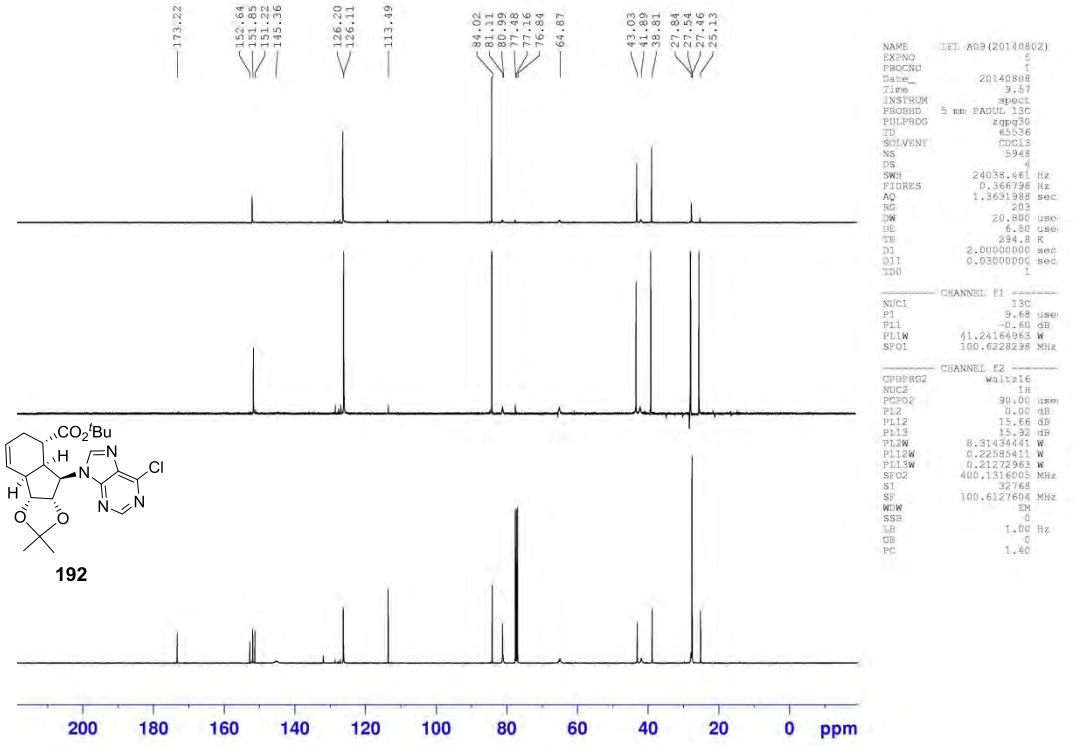


^{1}H NMR



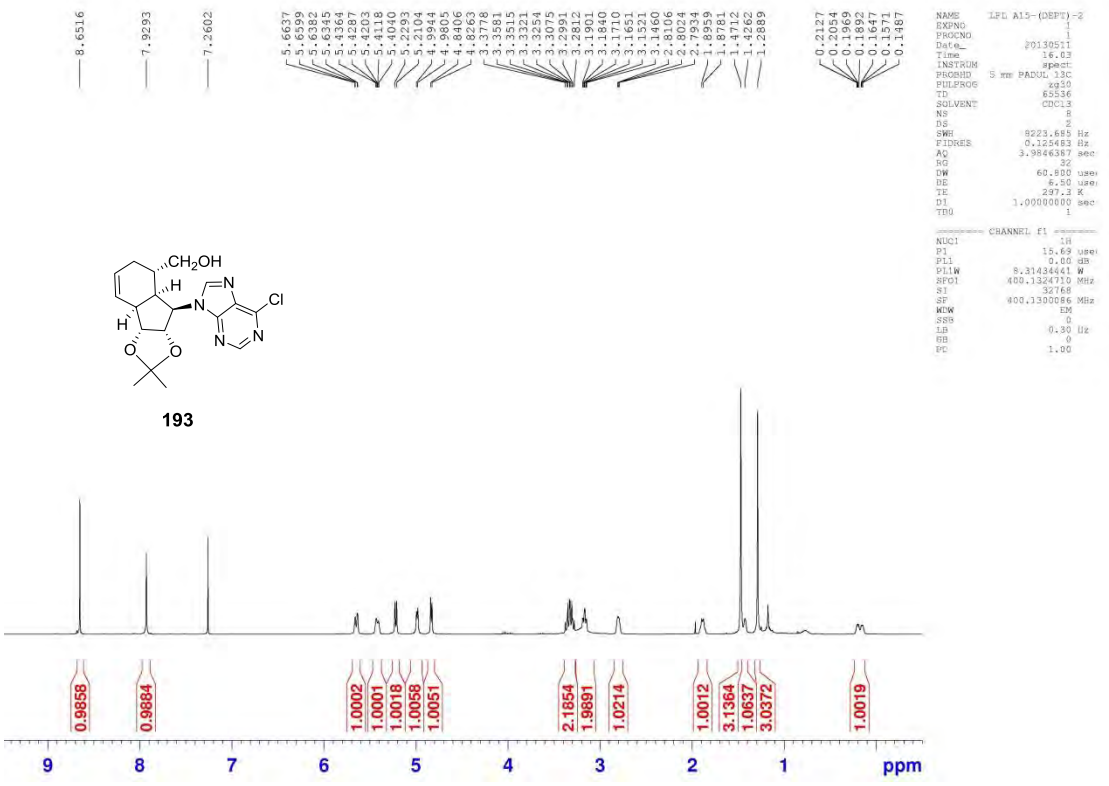
192

^{13}C NMR

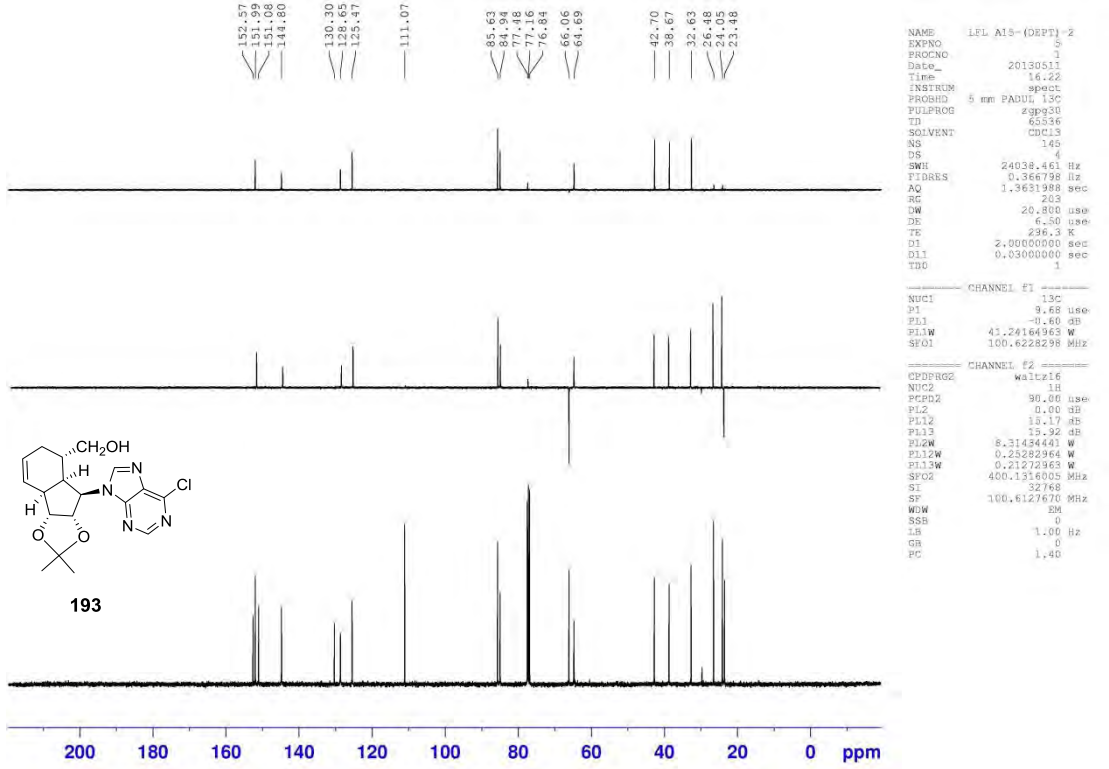


192

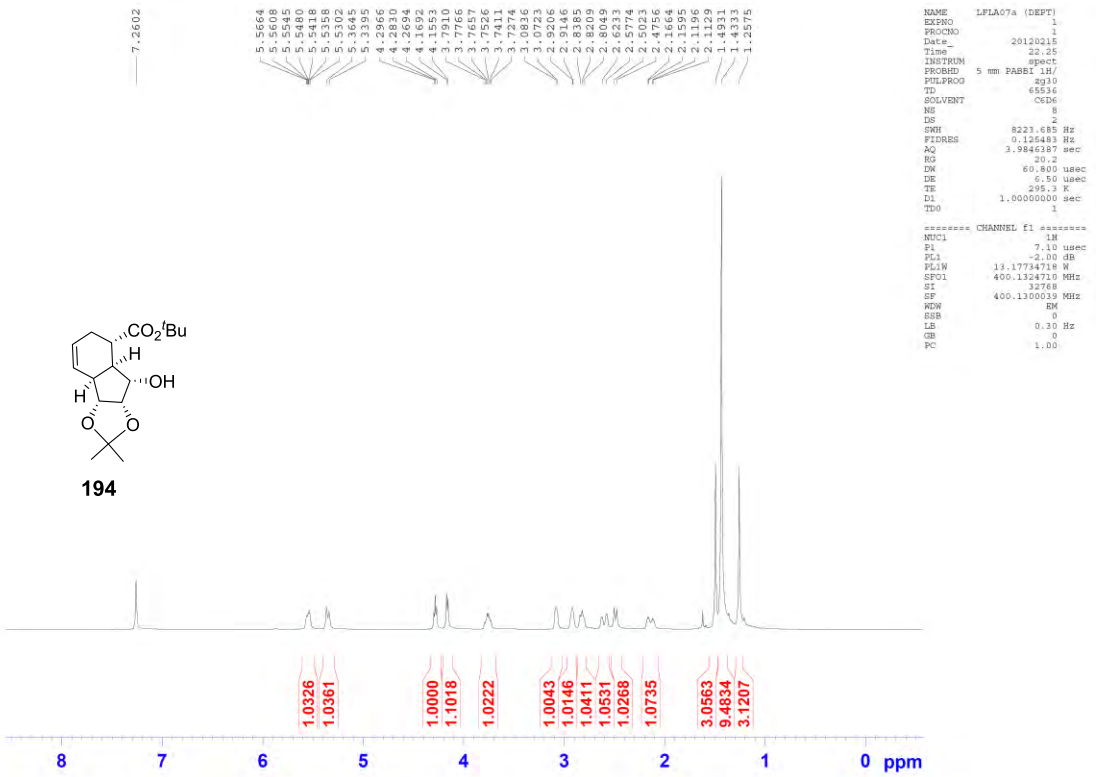
^{1}H NMR



^{13}C NMR

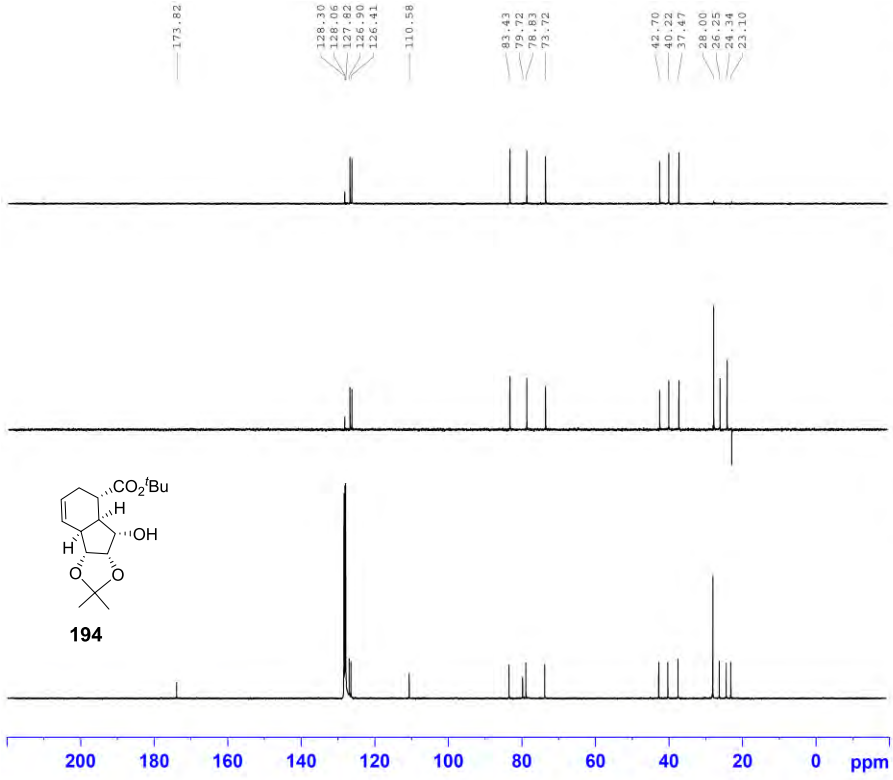


^{1}H NMR (Solvent: C_6D_6)



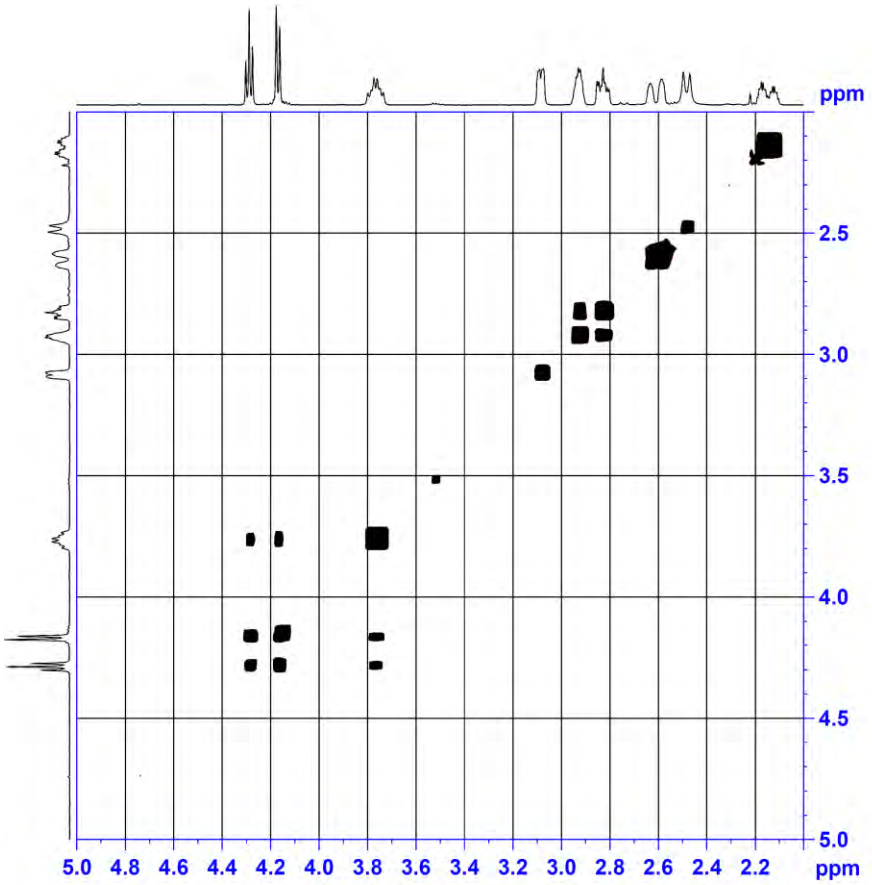

```
NAME          LFLA07a (DEPT)
EXPNO                      1
PROCNO                     1
Date_               20120215
Time                   22.25
INSTRUM                spect
PROBHD   5 mm PABBI 1H/
PULPROG                zg30
TD                    65536
SOLVENT                C6D6
NS                        8
DS                        2
SWH                8223.685 Hz
FIDRES             0.125483 Hz
AQ                 3.9846387 sec
RG                      20.2
DW                  60.800 usec
DE                   6.50 usec
TE                  295.3 K
D1                 1.00000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      1H
P1                   7.10 usec
PL1                  -2.00 dB
PL1W            13.17734718 W
SFO1           400.1324710 MHz
SI                      32768
SF              400.1300039 MHz
WDW                      EM
SSB                       0
LB                   0.30 Hz
GB                        0
PC                     1.00
```

^{13}C NMR (Solvent: C_6D_6)

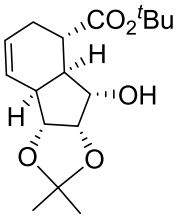



```
NAME          LFLA07a (DEPT)
EXPNO                      2
PROCNO                     1
Date_               20120215
Time                   22.32
INSTRUM                spect
PROBHD   5 mm PABBI 1H/
PULPROG              zgpg30
TD                    65536
SOLVENT                C6D6
NS                      204
DS                        4
SWH               24038.461 Hz
FIDRES             0.366798 Hz
AQ                 1.3631988 sec
RG                      203
DW                  20.800 usec
DE                   6.50 usec
TE                  295.5 K
D1                 2.00000000 sec
D11                0.03000000 sec
TD0                       1

======== CHANNEL f1 ========
NUC1                      13C
P1                   14.50 usec
PL1                  -4.00 dB
PL1W            90.22689819 W
SFO1           100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2                waltz16
NUC2                      1H
PCPD2                90.00 usec
PL2                  -2.00 dB
PL12                 20.06 dB
PL13                 22.00 dB
PL2W            13.17734718 W
PL12W            0.08200268 W
PL13W            0.05245997 W
SFO2           400.1316005 MHz
SI                      32768
SF              100.6127429 MHz
WDW                      EM
SSB                       0
LB                   1.00 Hz
GB                        0
PC                     1.40
```

ROESY (Solvent: C_6D_6)

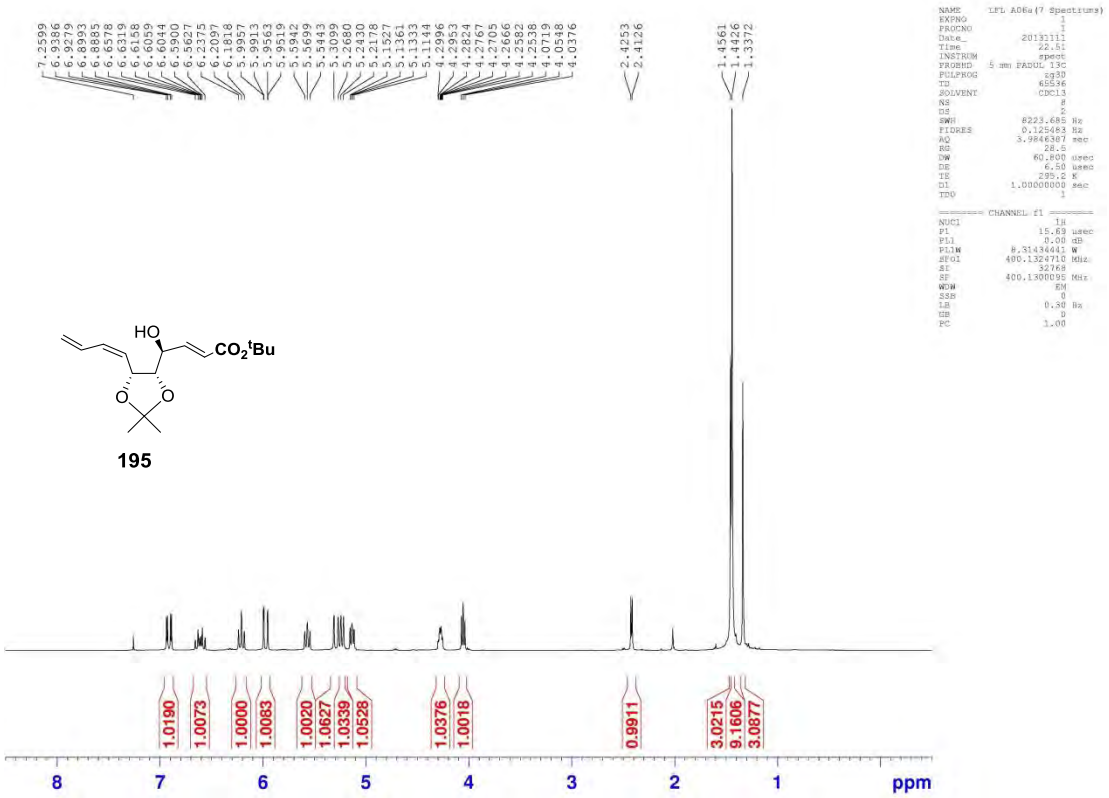



```
NAME        LFL A07a(ROESY)
EXPNO                     5
PROCNO                    1
Date_              20141122
Time                 17.03
INSTRUM              spect
PROBHD    5 mm PADUL 13C
PULPROG           roesyph
TD                   2048
SOLVENT              C6D6
NS                     12
DS                      4
SWH             4084.967 Hz
FIDRES          1.994613 Hz
AQ              0.2507252 sec
RG                     64
DW               122.400 usec
DE                 6.50 usec
TE                300.0 K
D0             0.00010878 sec
D1             2.00000000 sec
D12            0.00002000 sec
IN0            0.00024445 sec

======== CHANNEL f1 ========
NUC1                   1H
P1                  14.83 usec
P15             300000.00 usec
PL1                 0.00 dB
PL11               15.66 dB
PL1W          8.31434441 W
PL11W         0.22585411 W
SFO1         400.1318419 MHz
ND0                    1
TD                   203
SFO1           400.1318 MHz
FIDRES        20.152540 Hz
SW              10.224 ppm
FnMODE       States-TPPI
SI                  1024
SF           400.1300000 MHz
WDW                QSINE
SSB                    2
LB                  0.00 Hz
GB                     0
PC                  1.00
SI                  1024
MC2          States-TPPI
SF           400.1300000 MHz
WDW                QSINE
SSB                    2
LB                  0.00 Hz
GB                     0
```

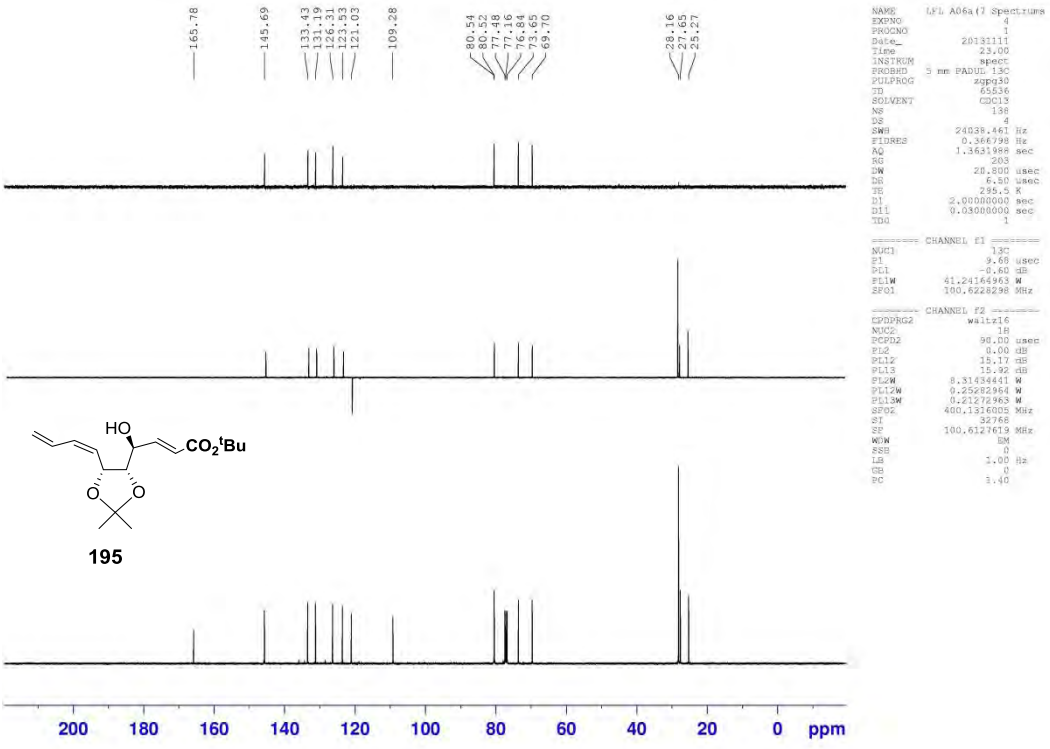


194

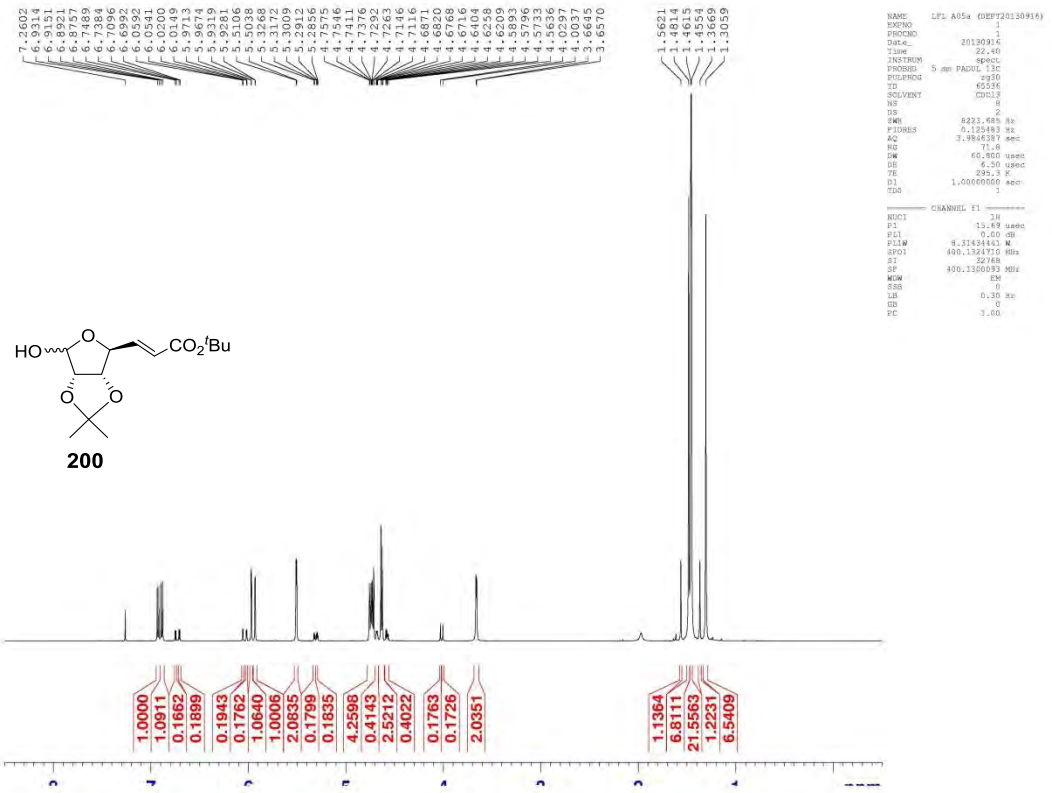
^{1}H NMR



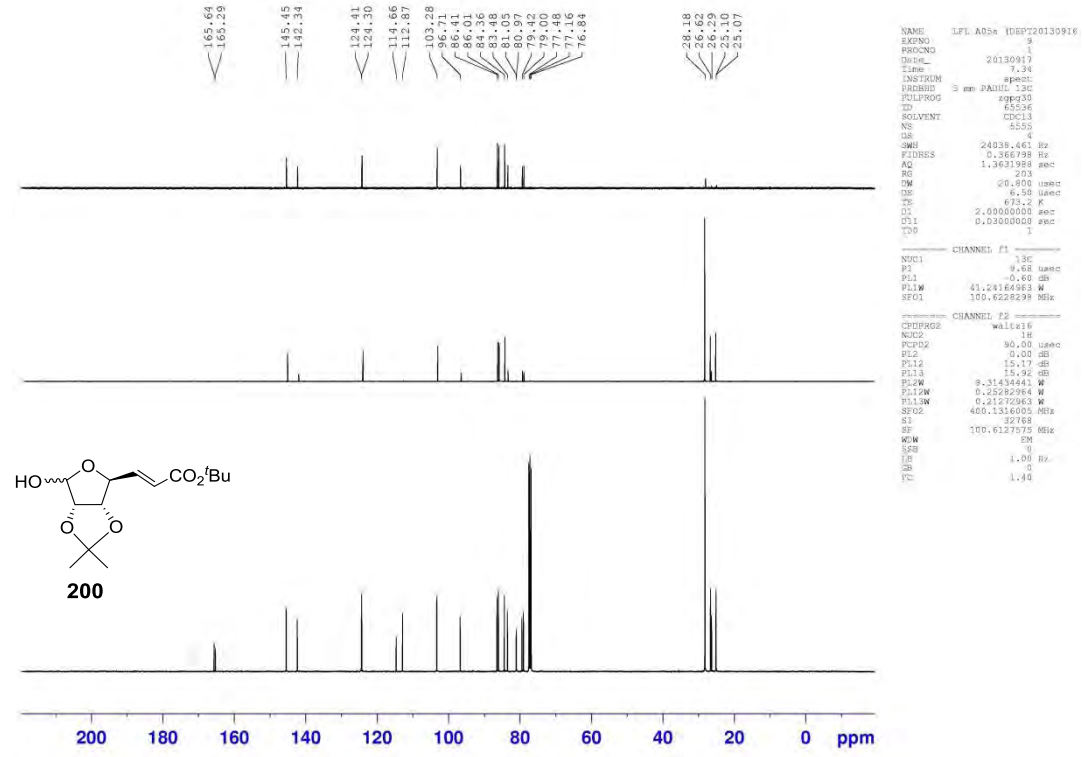
^{13}C NMR



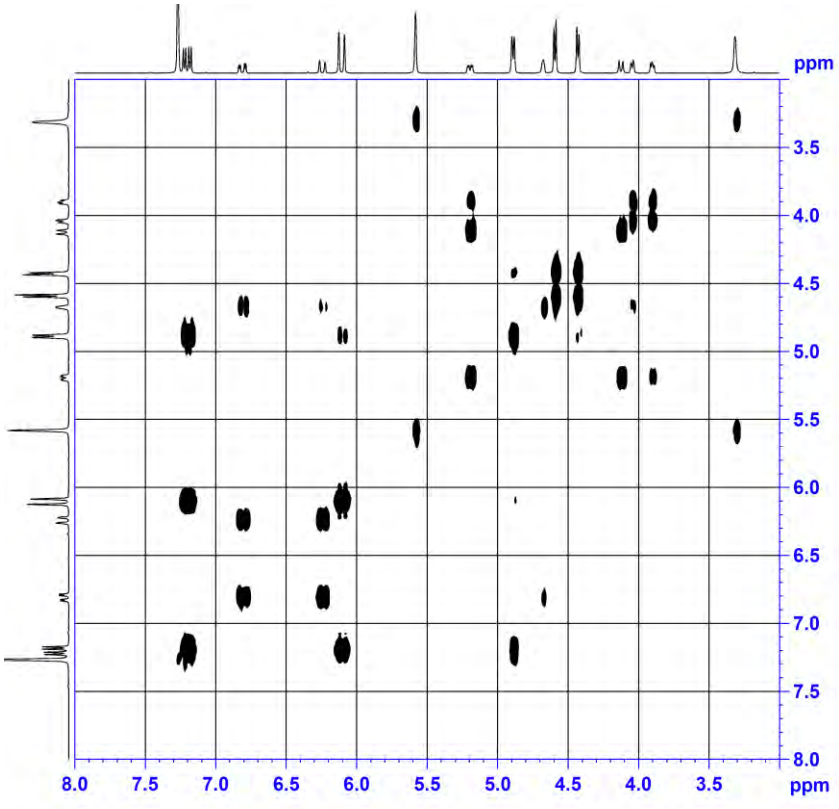
^{1}H NMR



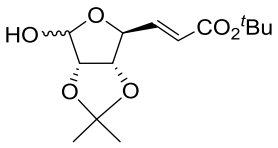
^{13}C NMR



^{1}H-^{1}H COSY

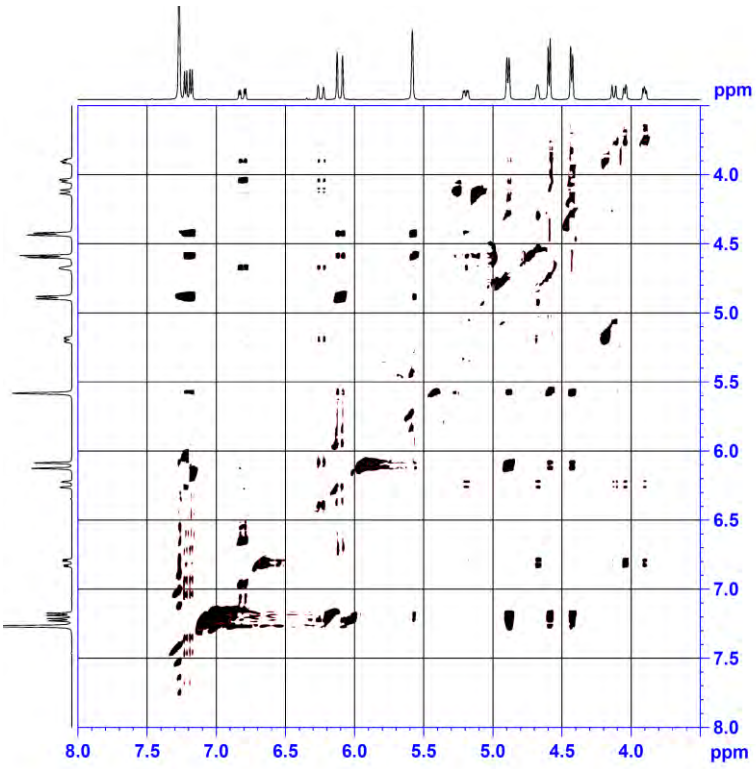



```
NAME          LFL A05a(ROE)
EXPNO                     4
PROCNO                    1
Date_              20141116
Time_                 14.46
INSTRUM               spect
PROBHD   5 mm PADUL 13C
PULPROG        cosygpmfqf
TD                     2048
SOLVENT               C6D6
NS                       4
DS                       8
SWH              5341.880 Hz
FIDRES           2.608340 Hz
AQ               0.1917428 sec
RG                     203
DW                  93.600 usec
DE                   6.50 usec
TE                  296.8 K
D0               0.00000300 sec
D1               2.00000000 sec
D13              0.00000400 sec
D16              0.00020000 sec
IN0              0.00018720 sec

======== CHANNEL f1 ========
NUC1                    1H
P1                   14.83 usec
PL1                   0.00 dB
PL1W             8.31434441 W
SFO1           400.1324057 MHz

====== GRADIENT CHANNEL =====
GPNAM1              SINE.100
GPNAM2              SINE.100
GPNAM3              SINE.100
GPZ1                 16.00 %
GPZ2                 12.00 %
GPZ3                 40.00 %
P16                1000.00 usec
ND0                       1
TD                      128
SFO1             400.1324 MHz
FIDRES          41.733440 Hz
SW                13.350 ppm
FnMODE                   QF
SI                     1024
SF             400.1300000 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
PC                     1.40
SI                     1024
MC2                      QF
SF             400.1300000 MHz
WDW                    SINE
SSB                       0
LB                     0.00 Hz
GB                        0
```

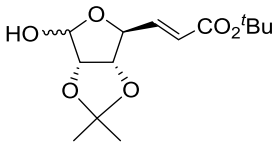


200

ROESY

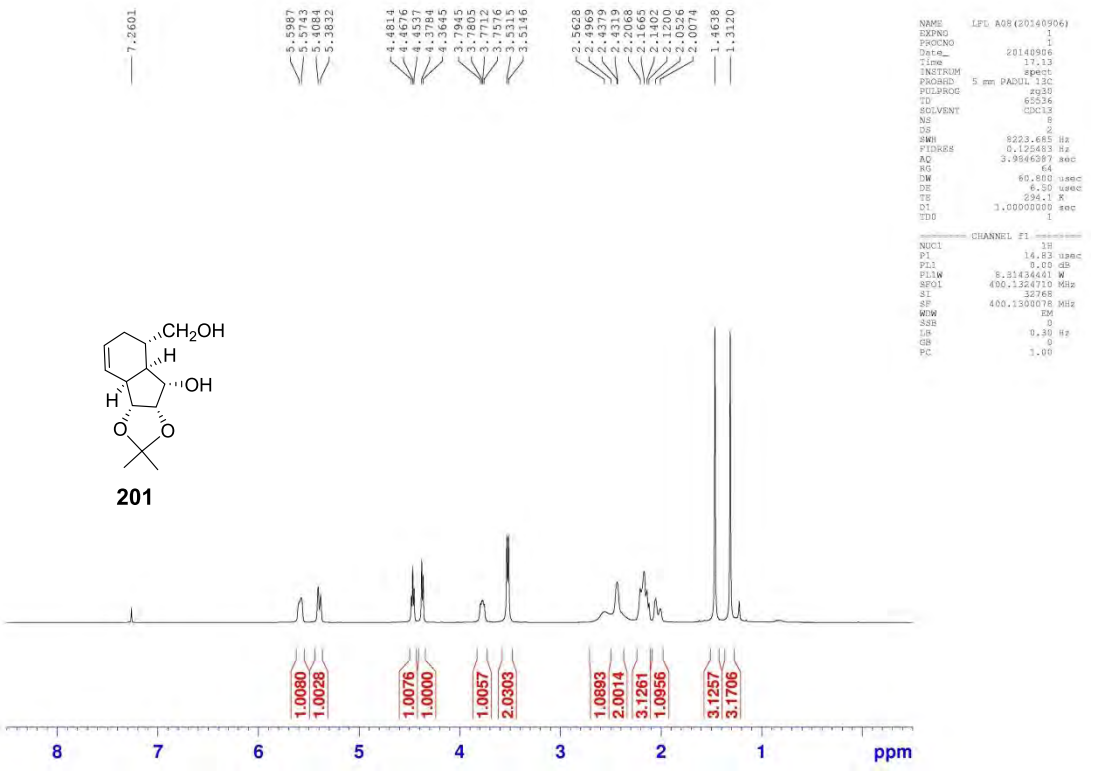


NAME	LFL A05a(ROE)
EXPNO	2
PROCNO	1
Date_	20141115
Time	20.59
INSTRUM	spect
PROBHD	5 mm PADUL 13C
PULPROG	roesyph
TD	2048
SOLVENT	C6D6
NS	16
DS	4
SWH	4084.967 Hz
FIDRES	1.994613 Hz
AQ	0.2507252 sec
RG	114
DW	122.400 usec
DE	6.50 usec
TE	297.7 K
D0	0.00010878 sec
D1	2.00000000 sec
D12	0.00002000 sec
IN0	0.00024445 sec
========	CHANNEL f1 ========
NUC1	1H
P1	14.83 usec
P15	300000.00 usec
PL1	0.00 dB
PL11	15.66 dB
PL1W	8.31434441 W
PL11W	0.22585411 W
SFO1	400.1318419 MHz
ND0	1
TD	178
SFO1	400.1318 MHz
FIDRES	22.982954 Hz
SW	10.224 ppm
FnMODE	States-TPPI
SI	1024
SF	400.1300000 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0
PC	1.00
SI	1024
MC2	States-TPPI
SF	400.1300000 MHz
WDW	QSINE
SSB	2
LB	0.00 Hz
GB	0

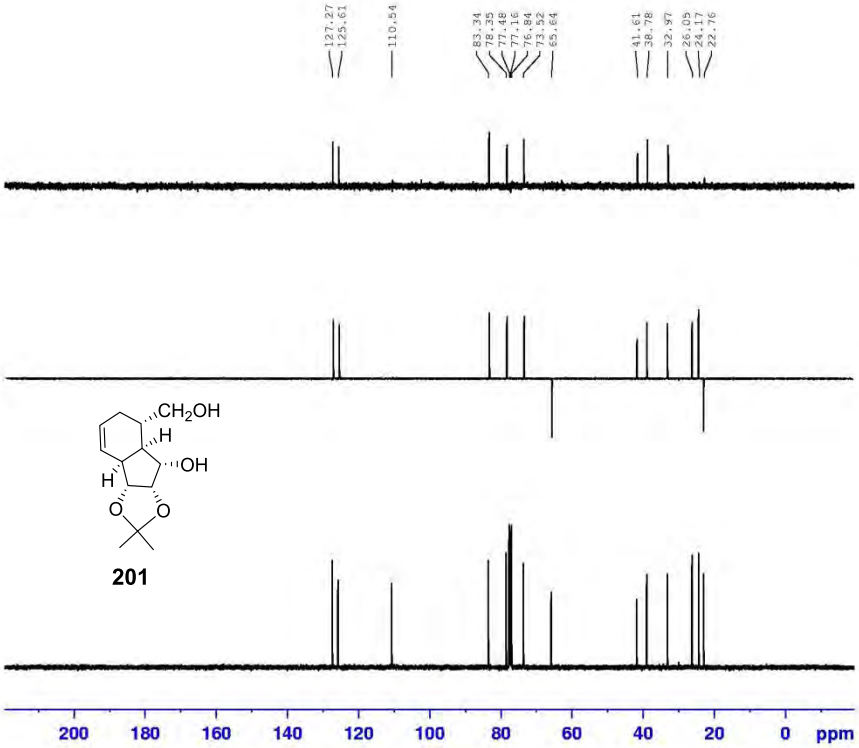


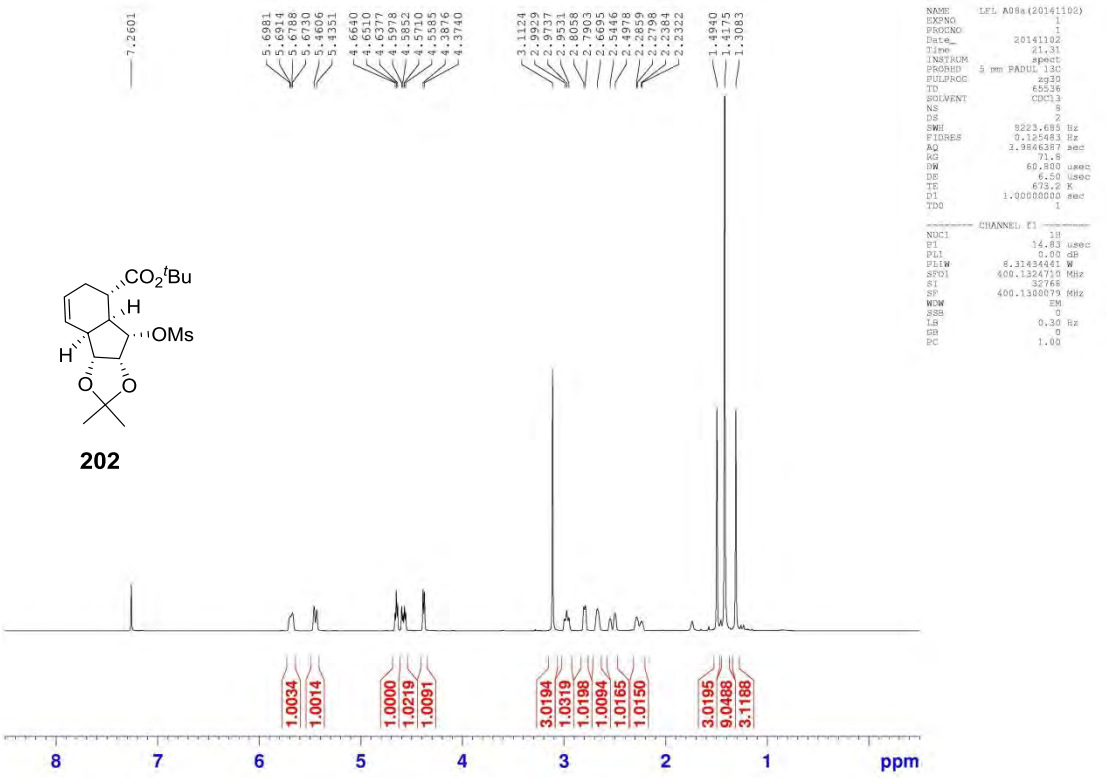
200

^{1}H NMR



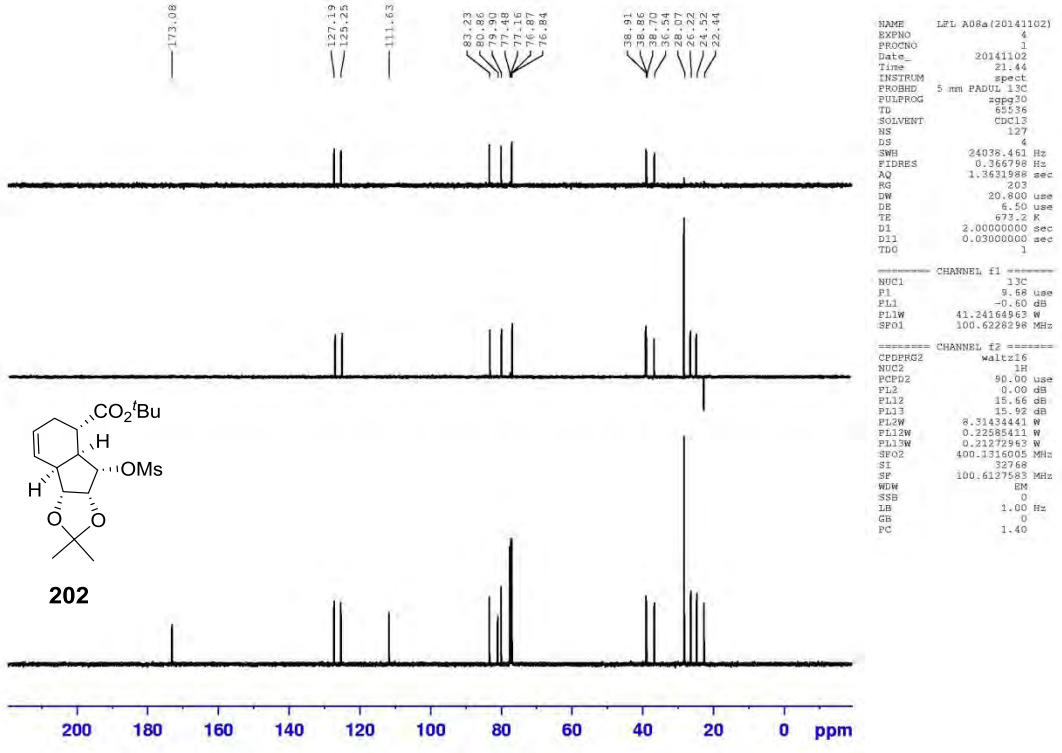
^{13}C NMR



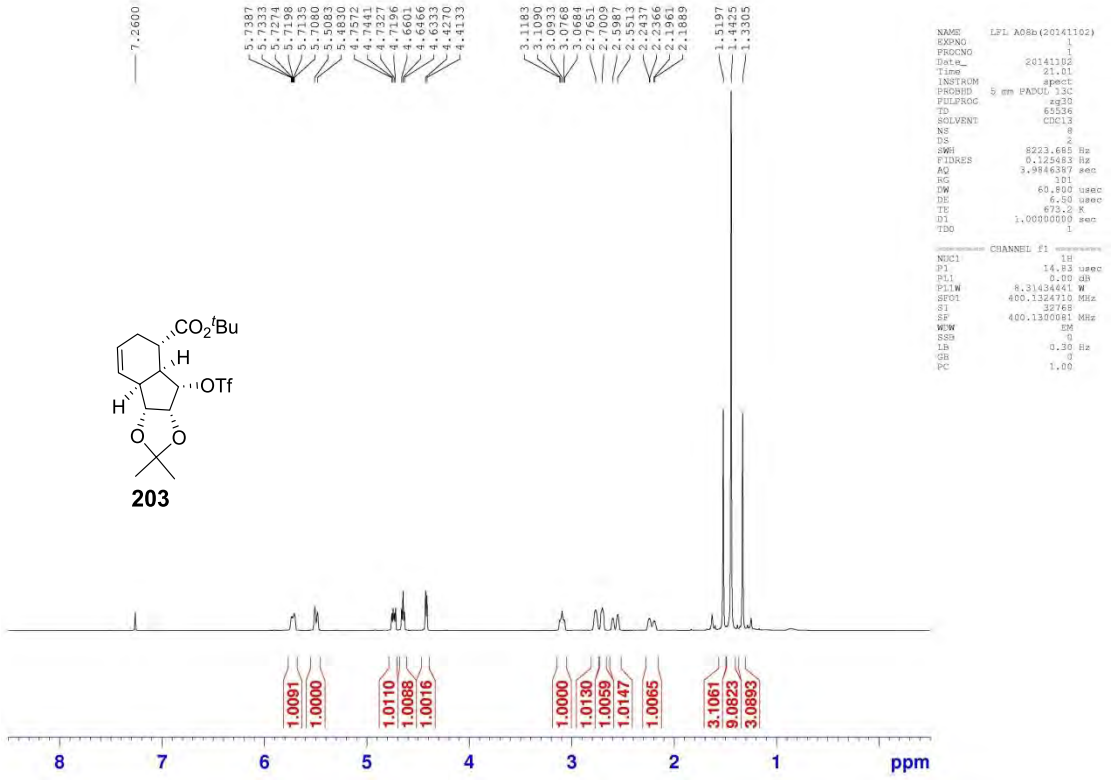


^{1}H NMR

^{13}C NMR

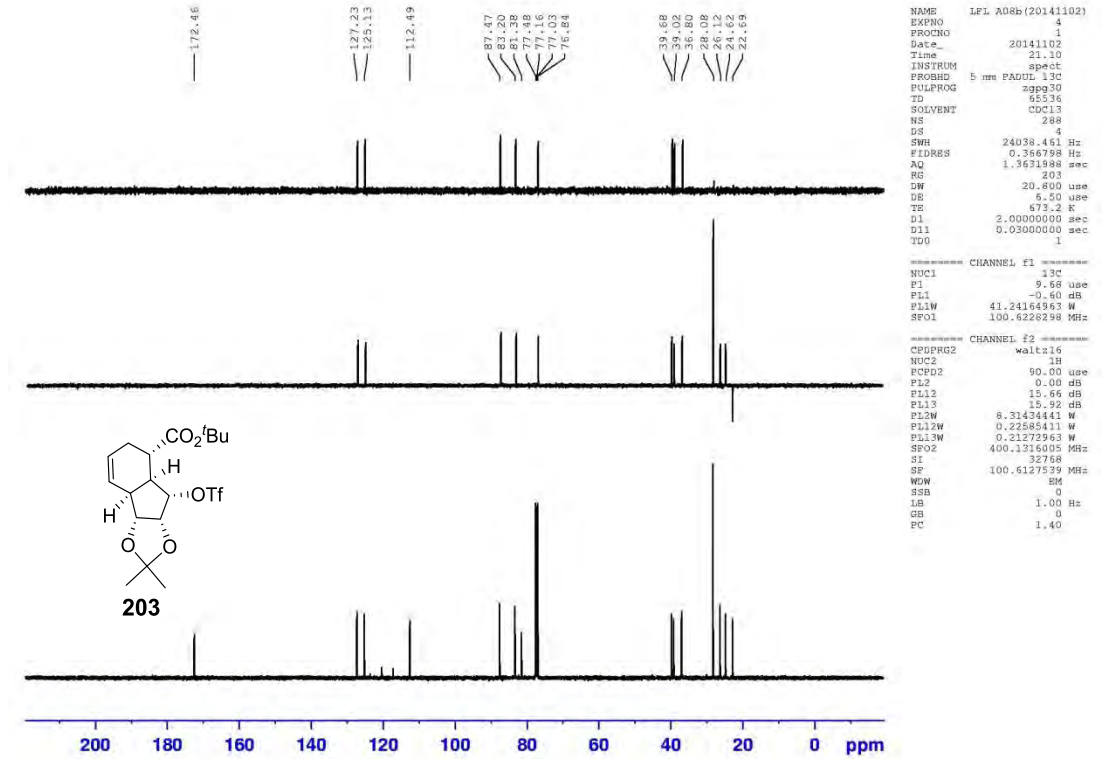


^{1}H NMR



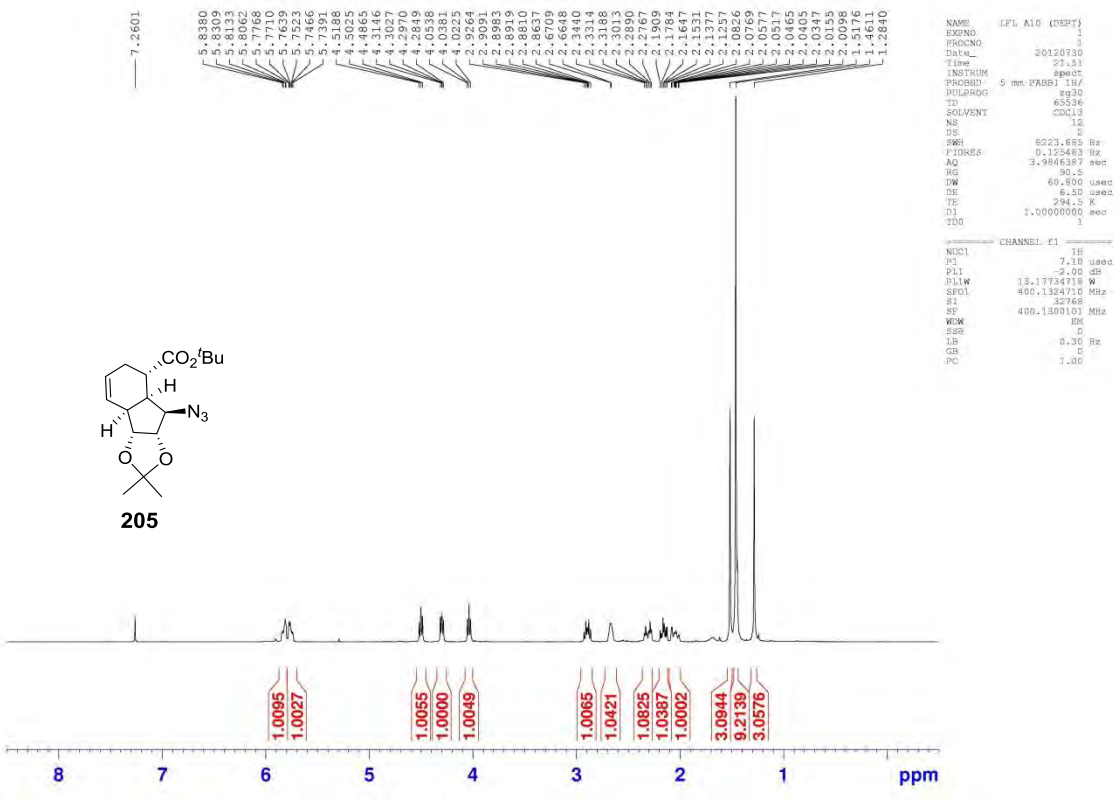
NAME LFL A08b(20141102)
EXPNO 1
PROCNO 1
Date_ 20141102
Time 21.01
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 8
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9846387 sec
RG 101
DW 60.800 usec
DE 6.50 usec
TE 673.2 K
D1 1.00000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 1H
P1 14.83 usec
PL1 0.00 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz
SI 32768
SF 400.1300081 MHz
WDW EM
SSB 0
LB 0.30 Hz
GB 0
PC 1.00

^{13}C NMR

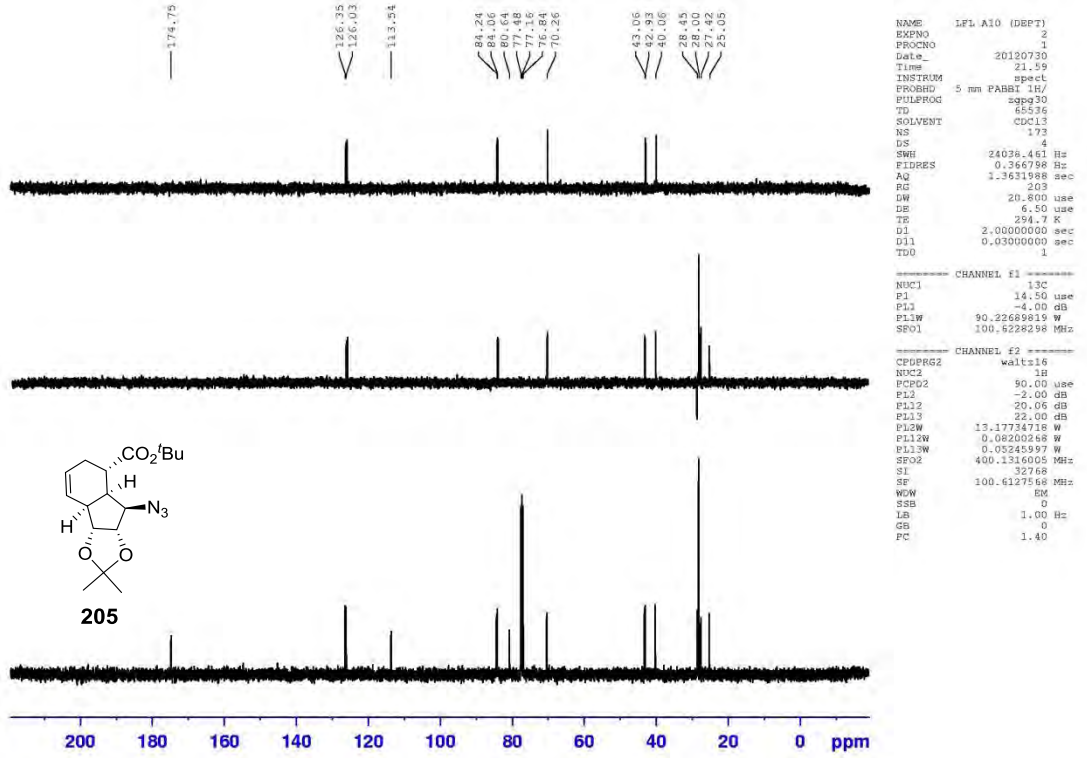


NAME LFL A08b(20141102)
EXPNO 4
PROCNO 1
Date_ 20141102
Time 21.10
INSTRUM spect
PROBHD 5 mm PADUL 13C
PULPROG zgpg30
TD 65536
SOLVENT CDCl3
NS 288
DS 4
SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631988 sec
RG 203
DW 20.800 use
DE 6.50 use
TE 673.2 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1
======== CHANNEL f1 ========
NUC1 13C
P1 9.68 use
PL1 -0.60 dB
PL1W 41.24164963 W
SFO1 100.6228298 MHz
======== CHANNEL f2 ========
CPDPRG2 waltz16
NUC2 1H
PCPD2 90.00 use
PL2 0.00 dB
PL12 15.66 dB
PL13 15.92 dB
PL2W 8.31434441 W
PL12W 0.22585411 W
PL13W 0.21272963 W
SFO2 400.1316005 MHz
SI 32768
SF 100.6127539 MHz
WDW EM
SSB 0
LB 1.00 Hz
GB 0
PC 1.40

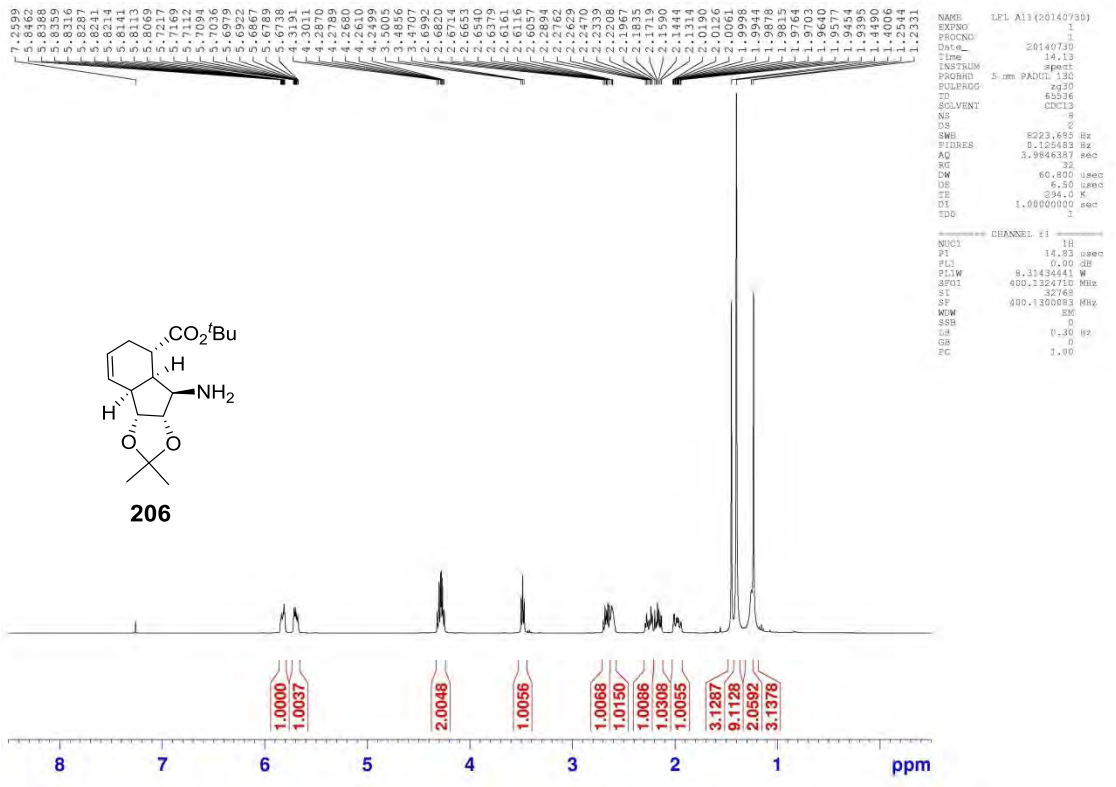
^{1}H NMR



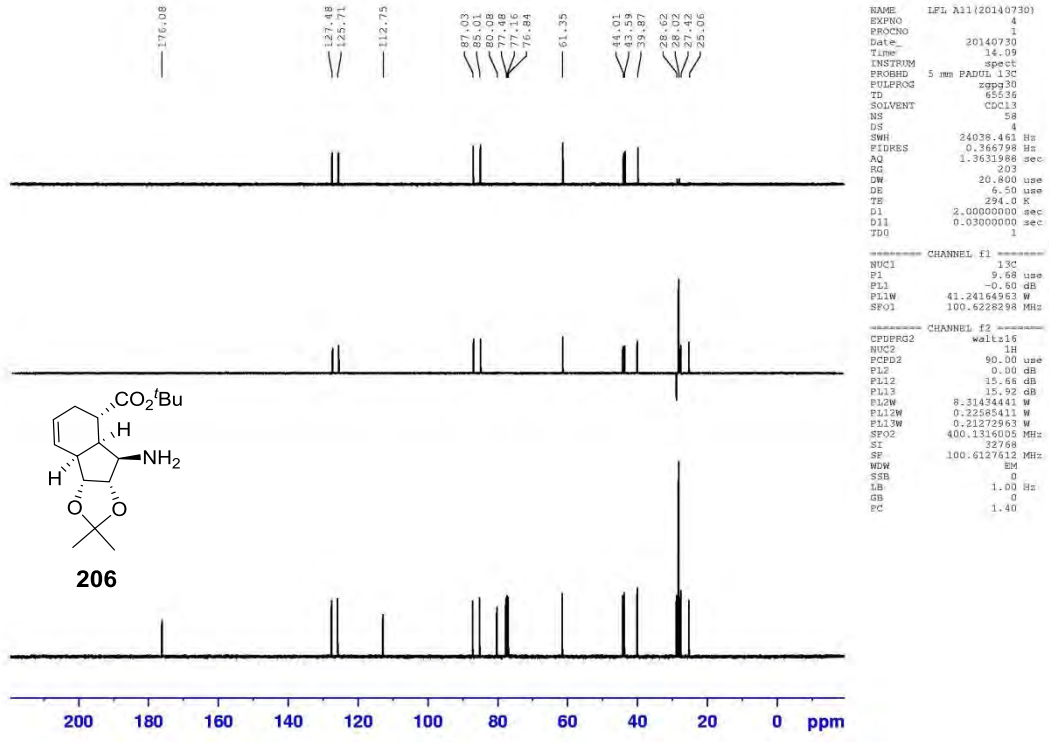
^{13}C NMR



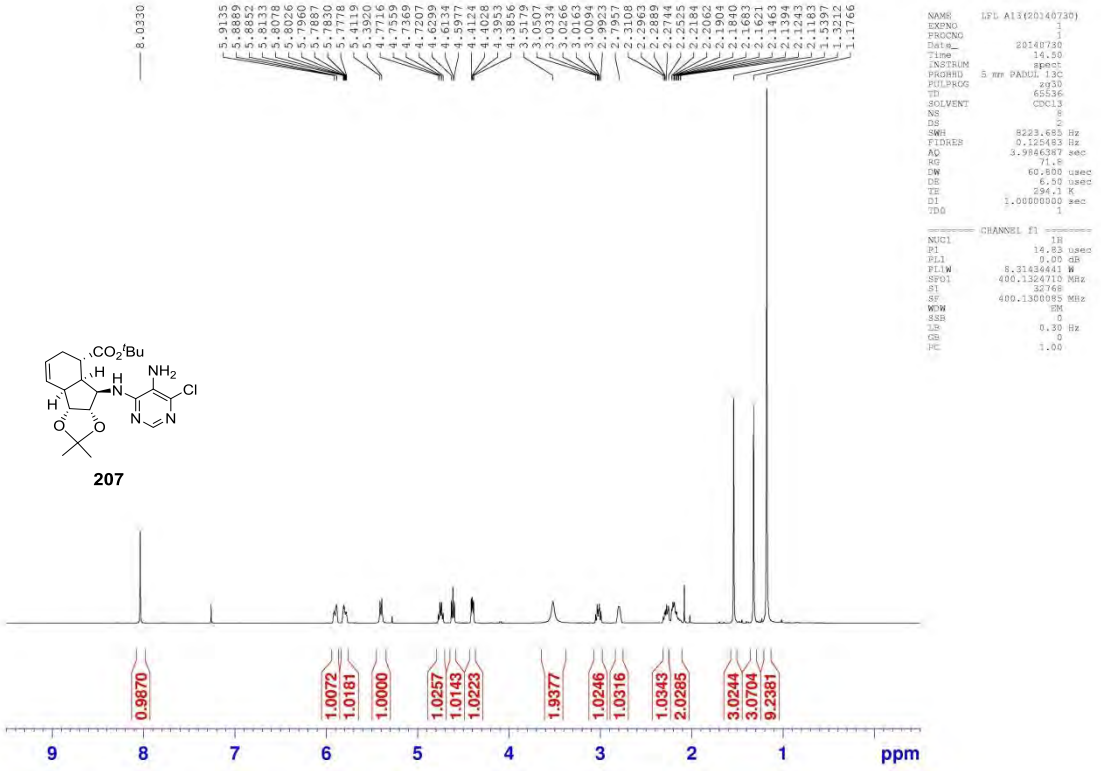
^{1}H NMR



^{13}C NMR

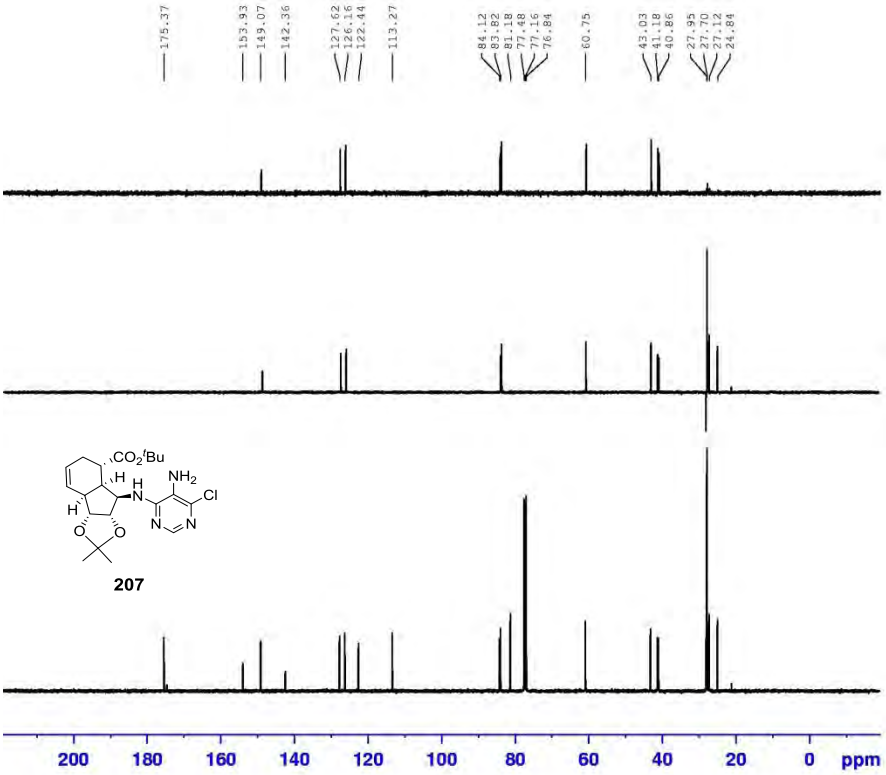


^{1}H NMR



207

^{13}C NMR



207

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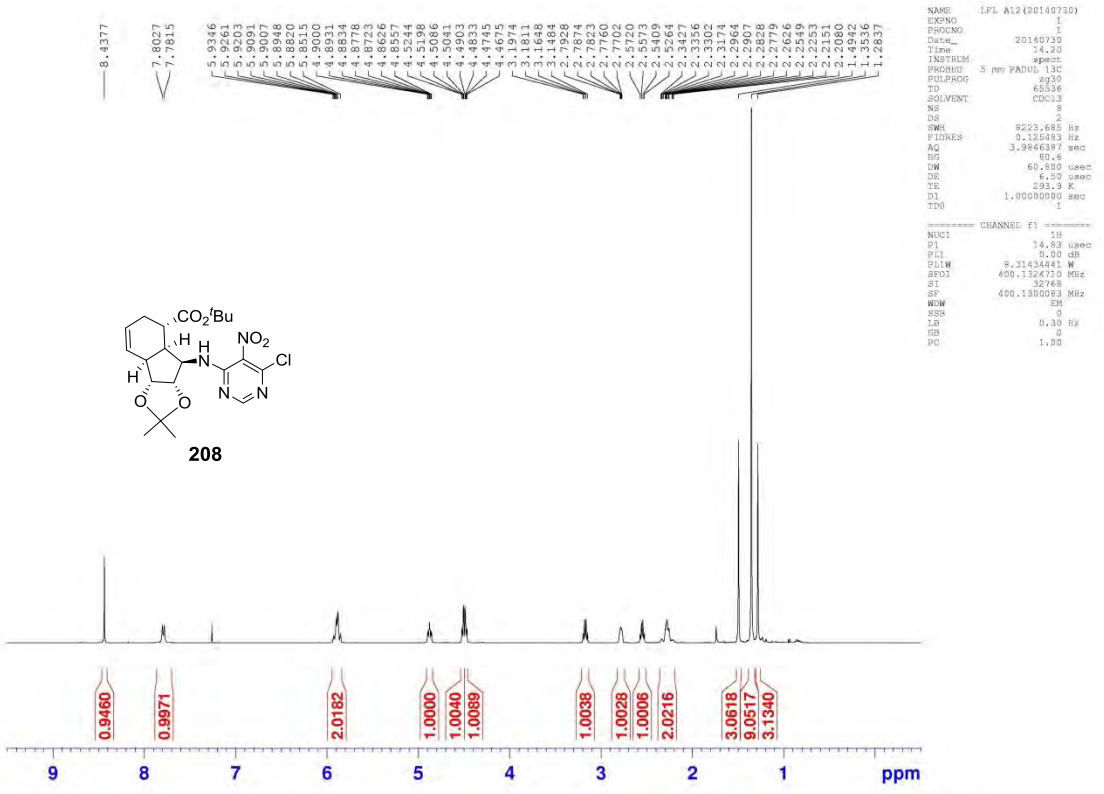

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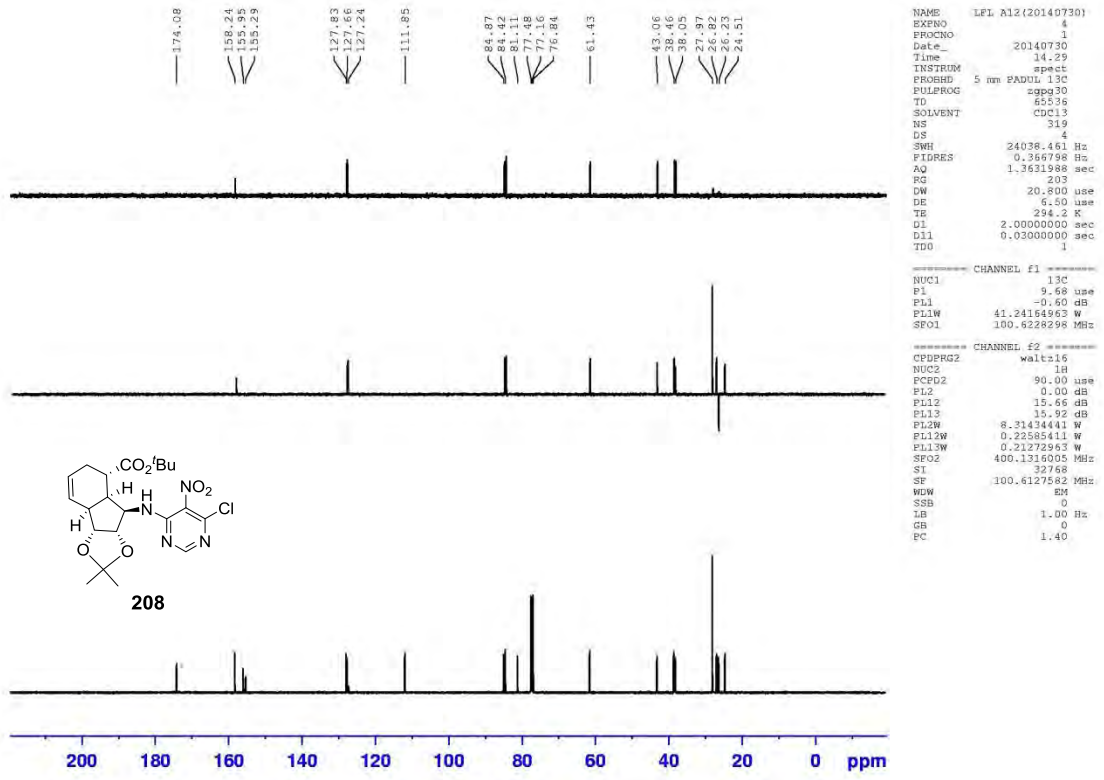
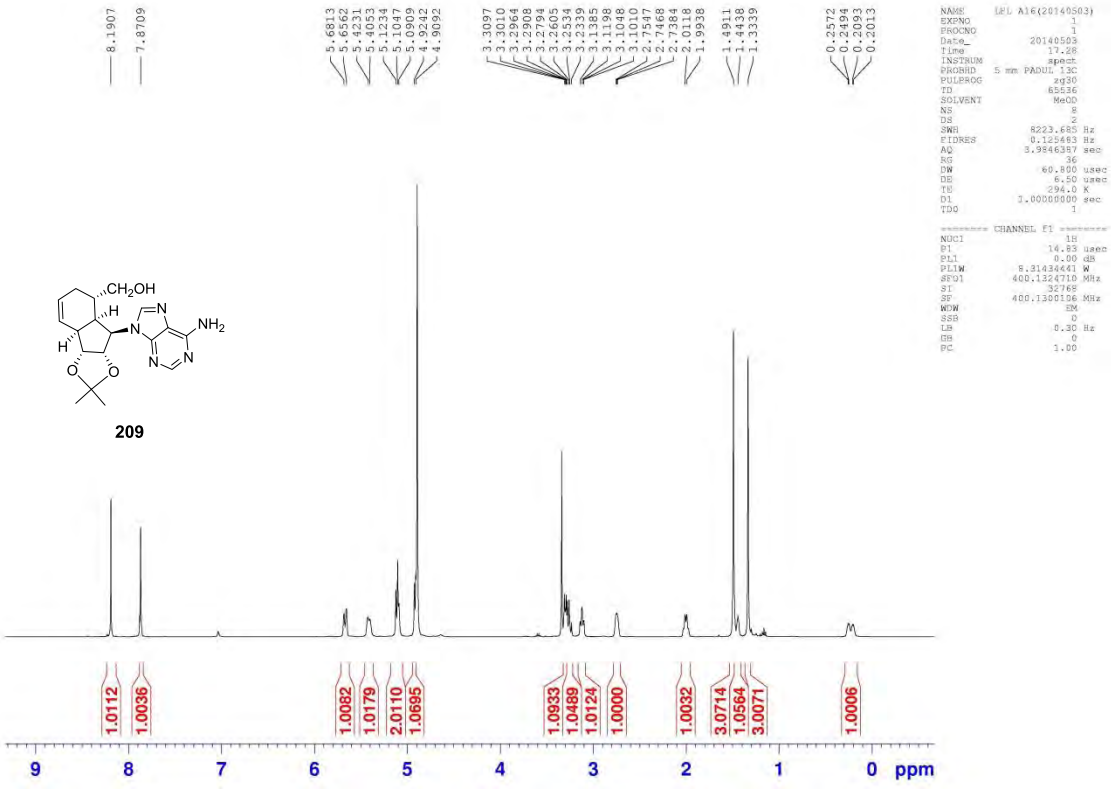
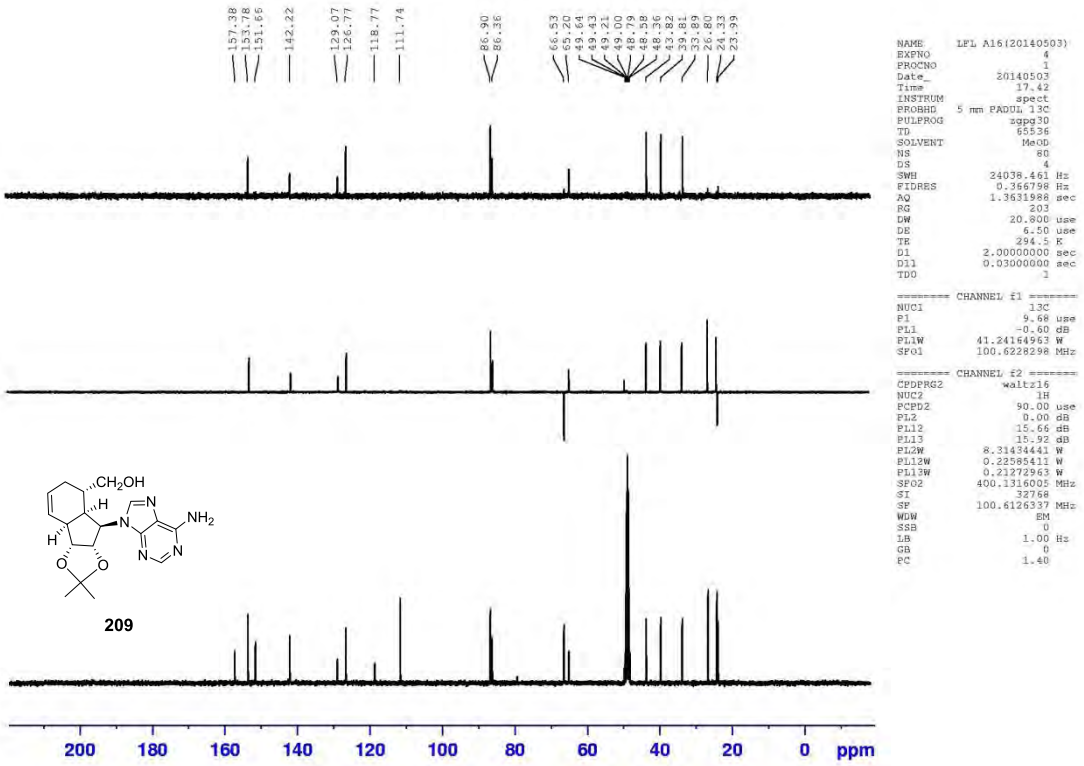


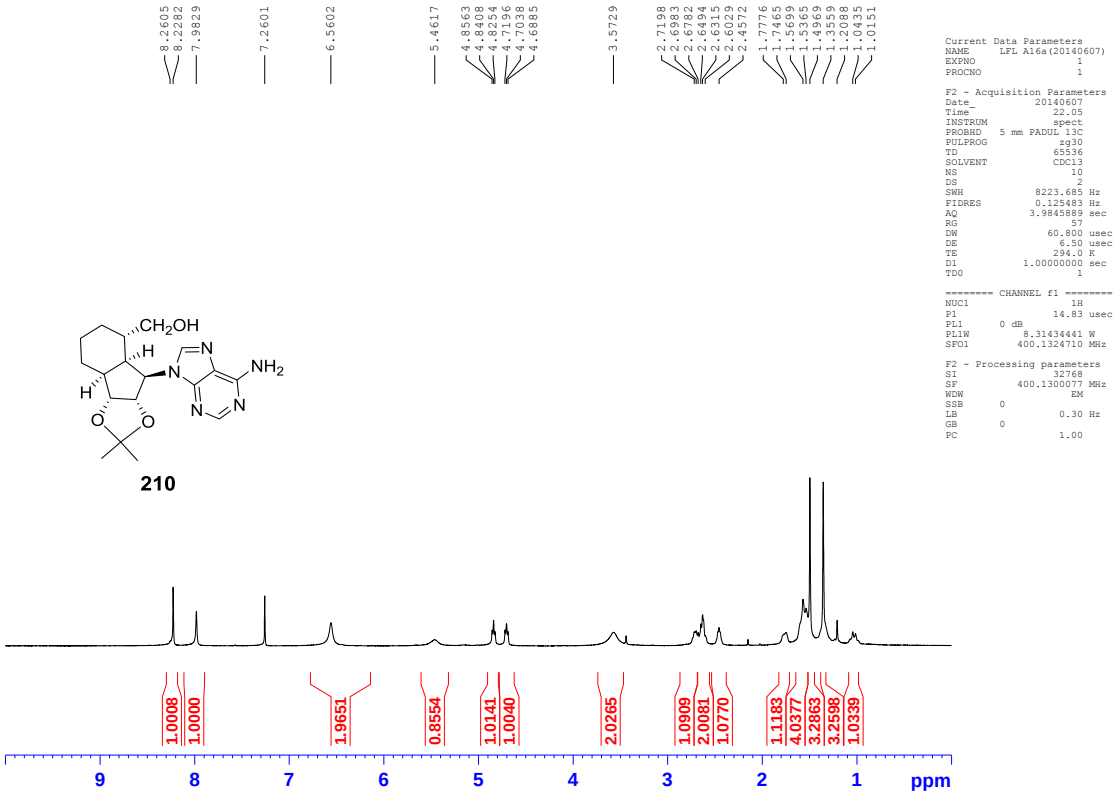
^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)



^{1}H NMR (Solvent: CD_3OD)



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EXPNO 1
PROCNO 1

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Time_ 22.05
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PULPROG zg30
TD 65536
SOLVENT CDCl3
NS 10
DS 2
SWH 8223.685 Hz
FIDRES 0.125483 Hz
AQ 3.9845889 sec
RG 57
DW 60.800 usec
DE 6.50 usec
TE 294.0 K
D1 1.00000000 sec
TD0 1

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P1 14.83 usec
PL1 0 dB
PL1W 8.31434441 W
SFO1 400.1324710 MHz

F2 - Processing parameters
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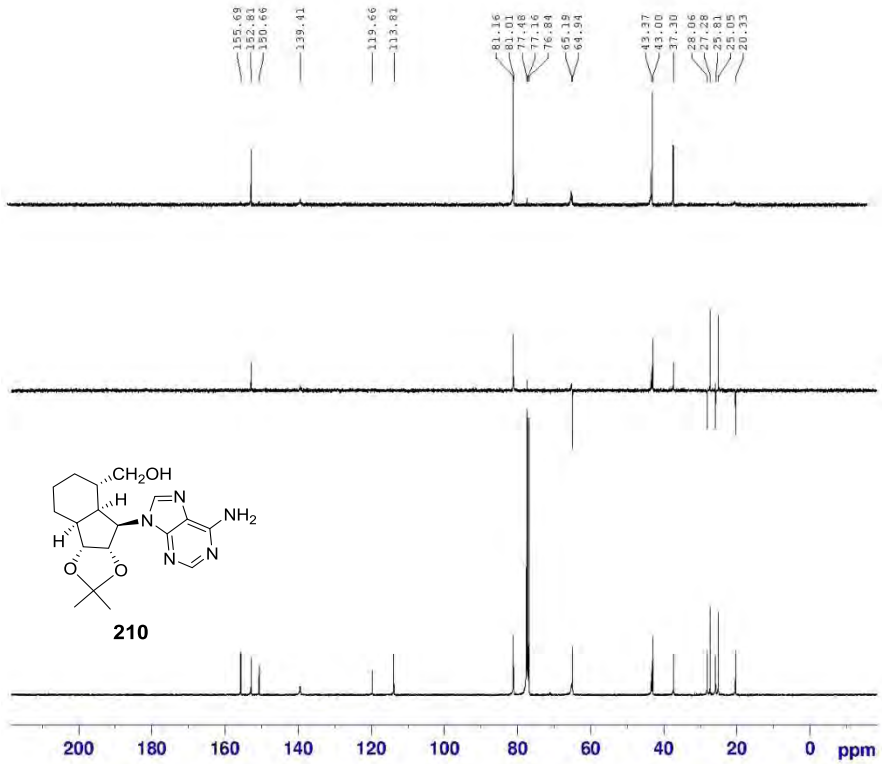
210

^{13}C NMR (Solvent: CD_3OD)



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PROCNO 1

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SOLVENT CDCl3
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SWH 24038.461 Hz
FIDRES 0.366798 Hz
AQ 1.3631488 sec
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DW 20.800 usec
DE 6.50 usec
TE 294.5 K
D1 2.00000000 sec
D11 0.03000000 sec
TD0 1

======== CHANNEL f1 ========
NUC1 13C
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PL1 0.60 dB
PL1W 41.24164963 W
SFO1 100.6228298 MHz

======== CHANNEL f2 ========
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NUC2 1H
PCPD2 90.00 usec
PL2 0 dB
PL12 15.66 dB
PL13 15.92 dB
PL2W 8.31434441 W
PL12W 0.22585411 W
PL13W 0.21272963 W
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F2 - Processing parameters
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210

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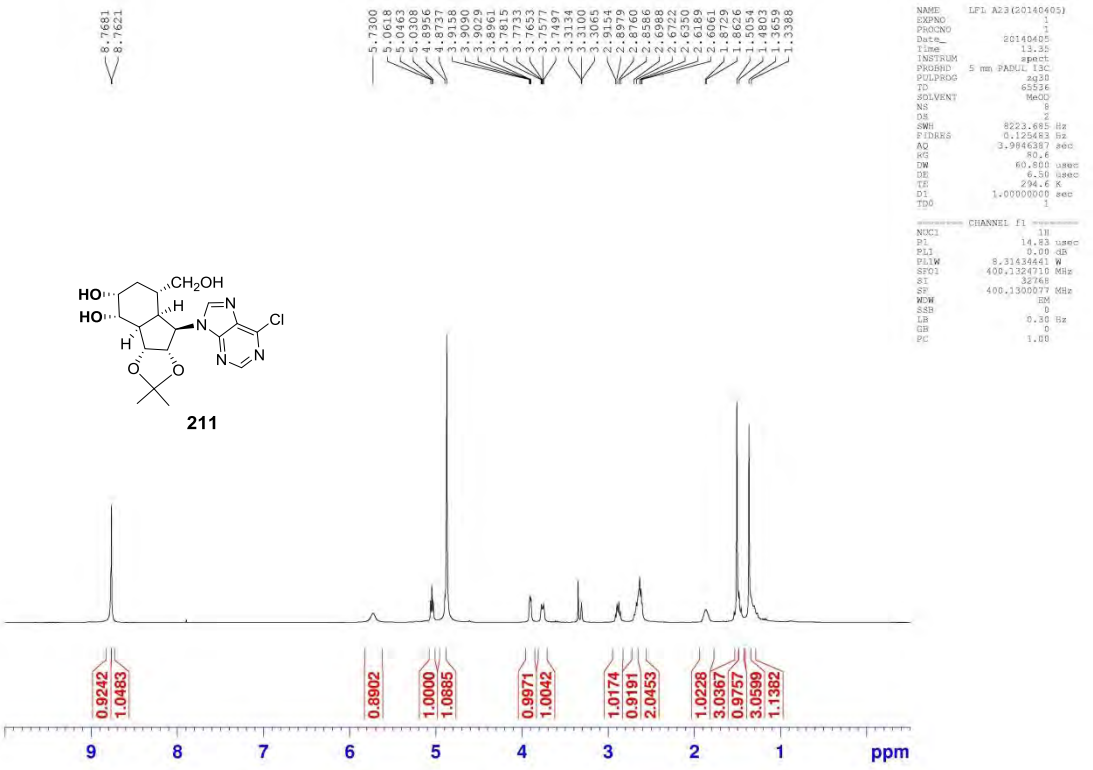
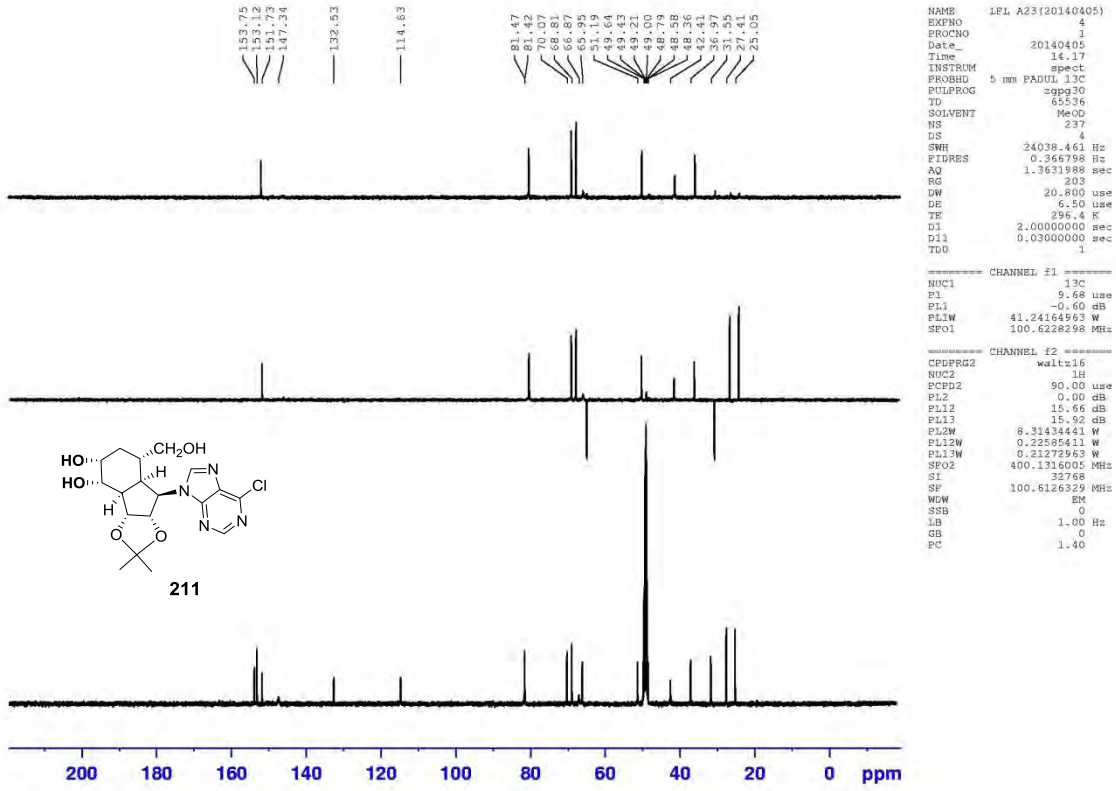
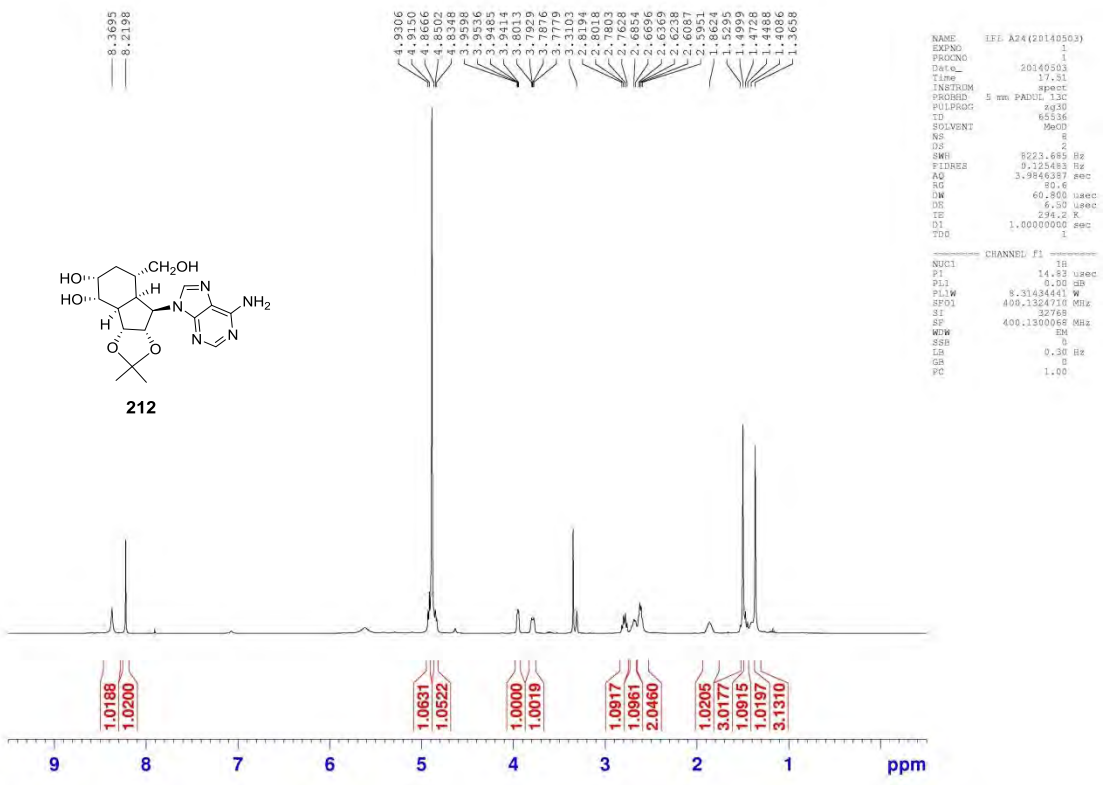


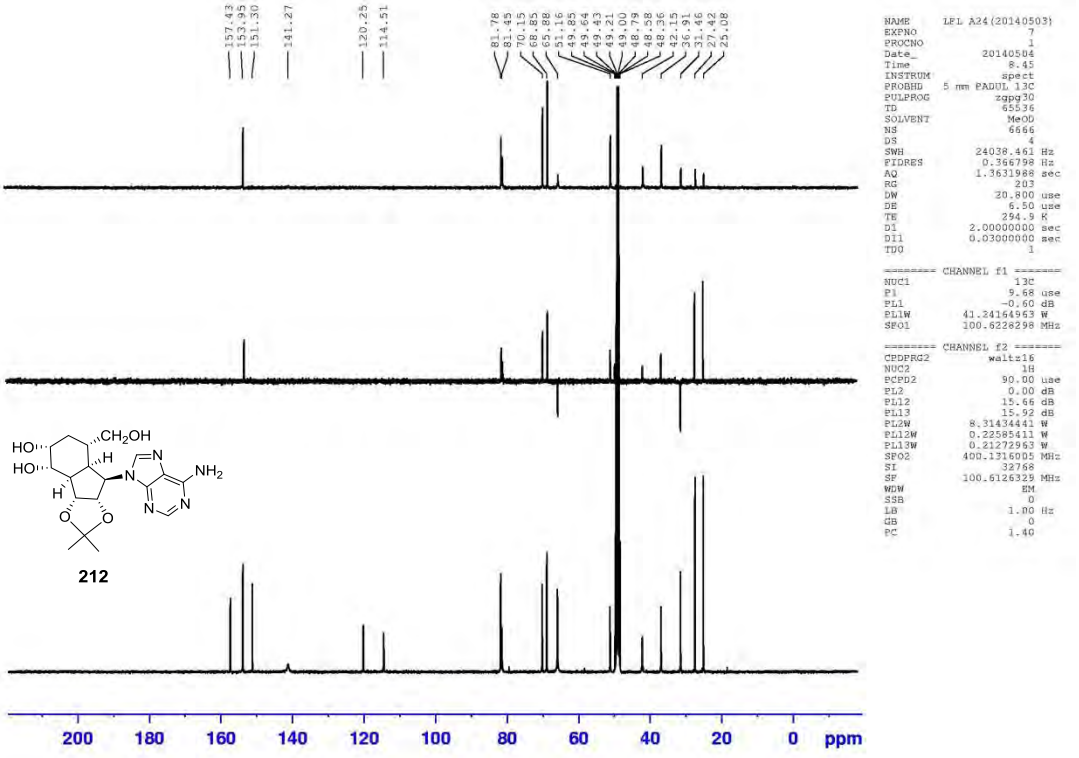
^{13}C NMR (Solvent: CD_3OD)



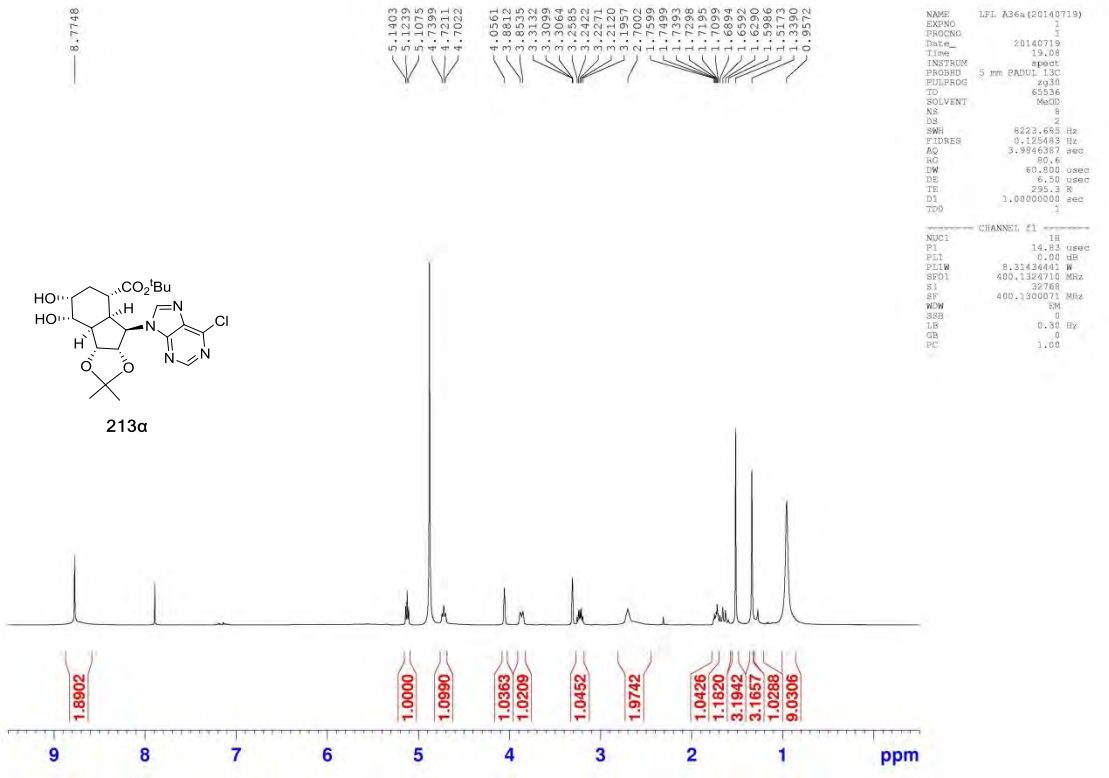
^{1}H NMR (Solvent: CD_3OD)



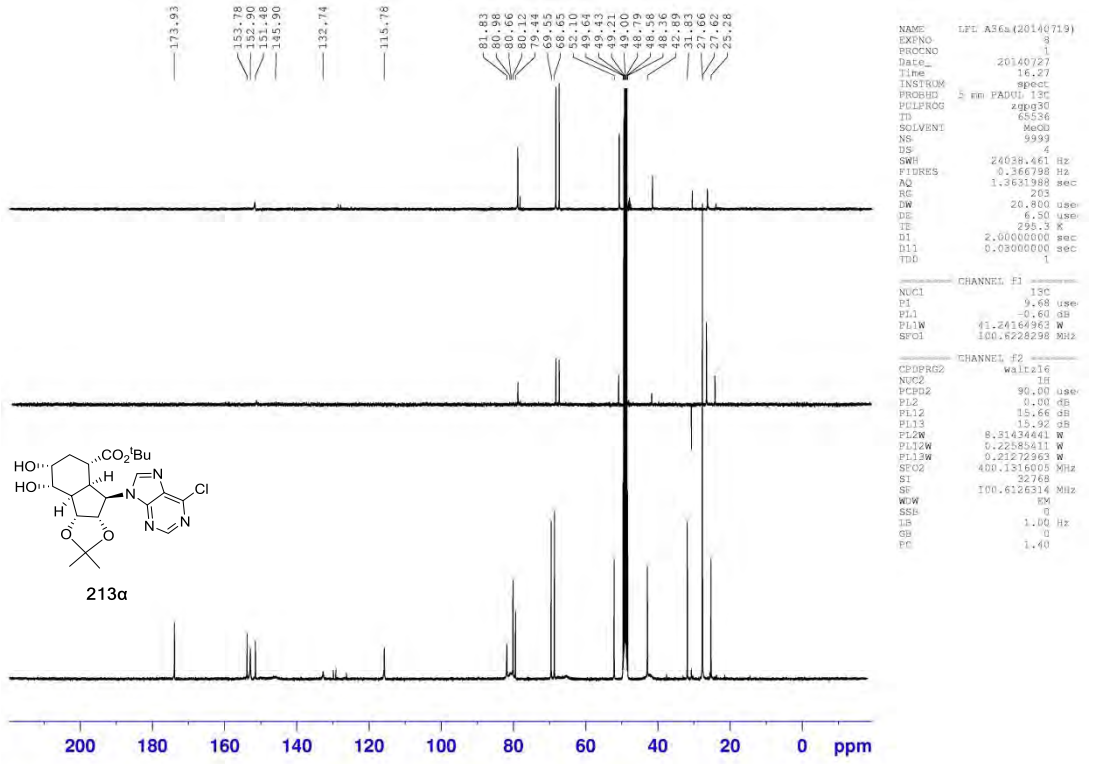
^{13}C NMR (Solvent: CD_3OD)



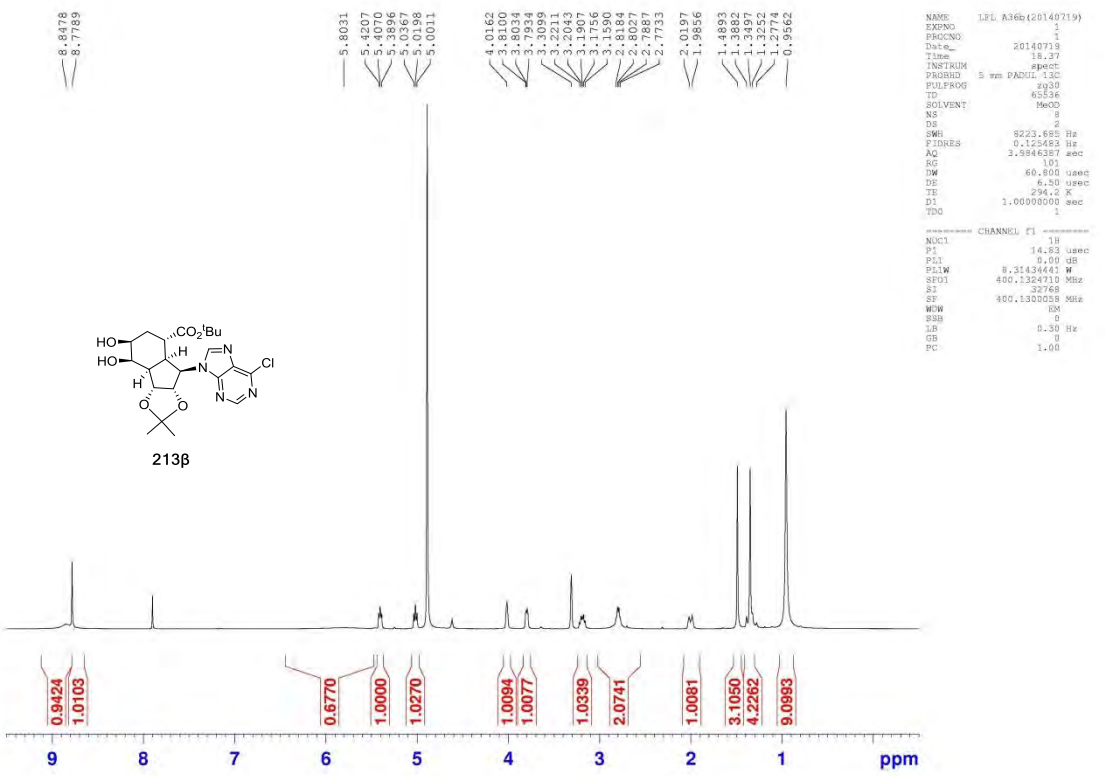
^{1}H NMR (Solvent: CD_3OD)



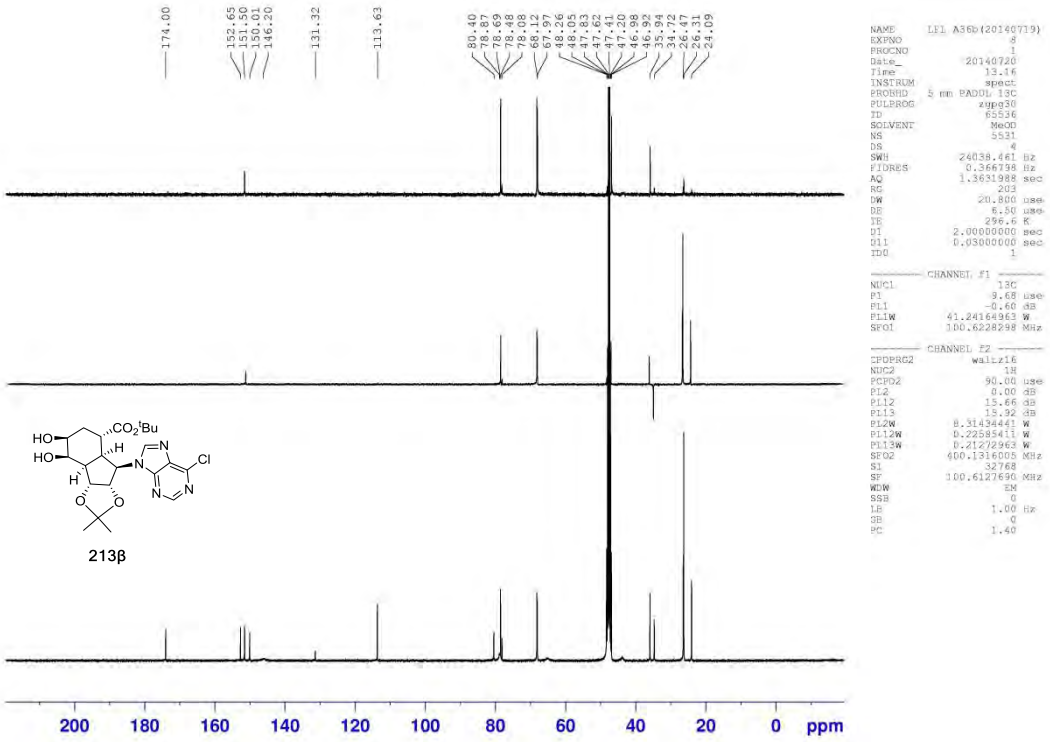
^{13}C NMR (Solvent: CD_3OD)



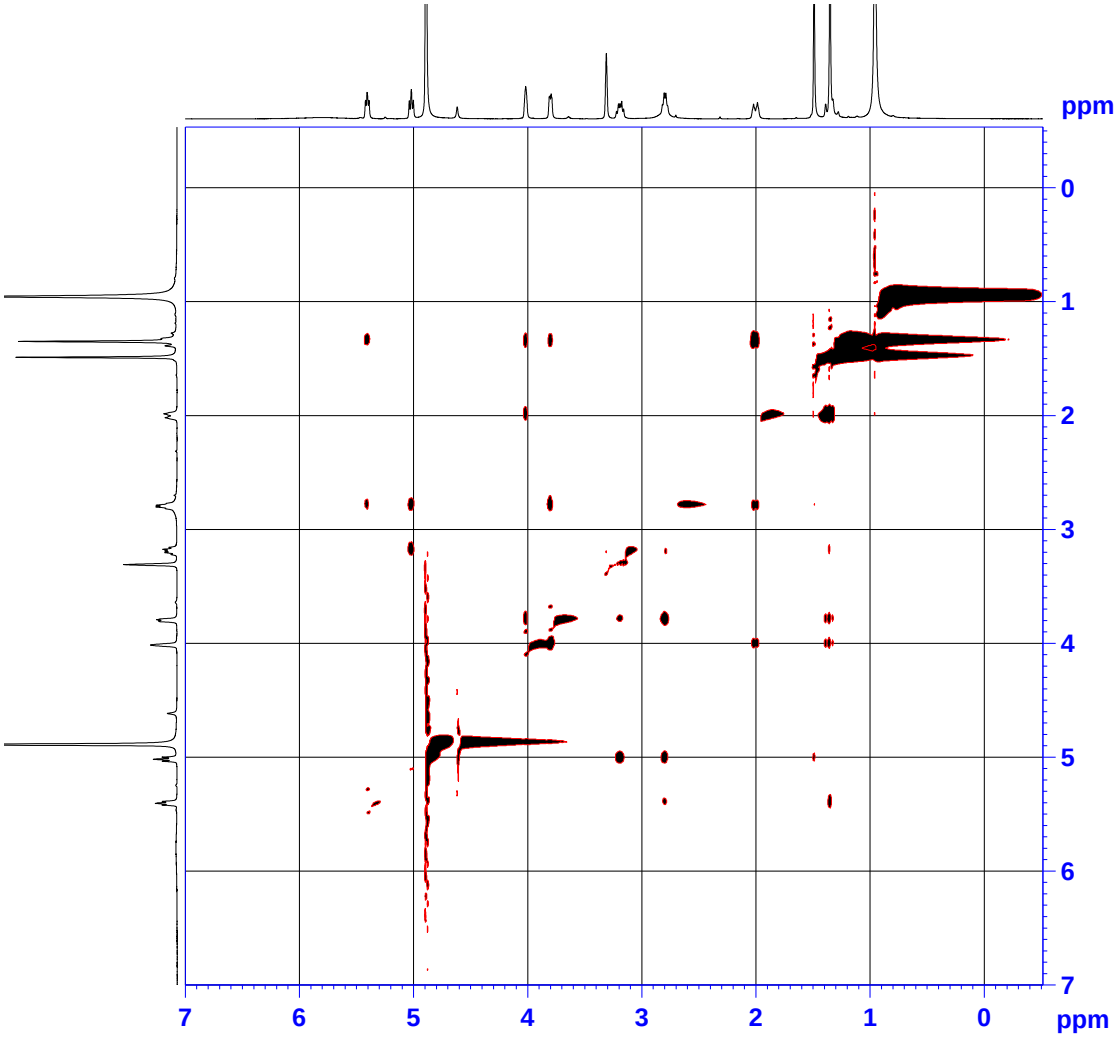
^{1}H NMR (Solvent: CD_3OD)

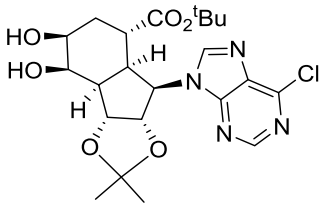


^{13}C NMR (Solvent: CD_3OD)



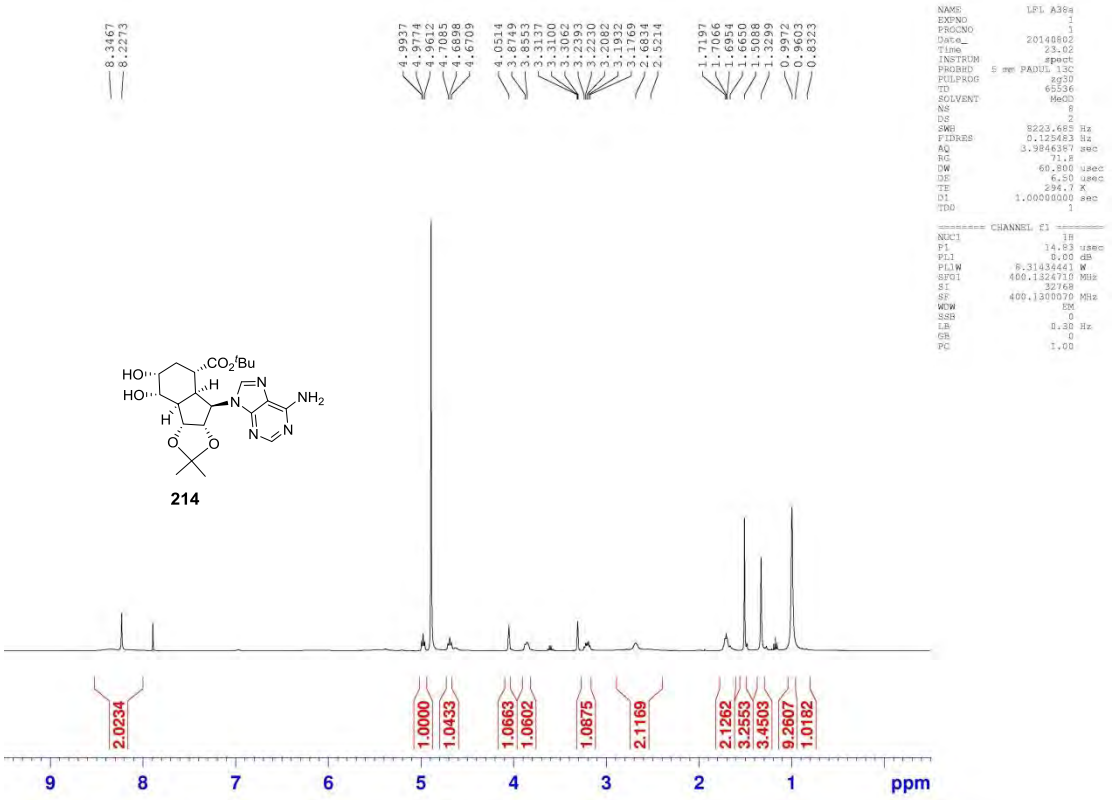
ROESY (Solvent: CD_3OD)



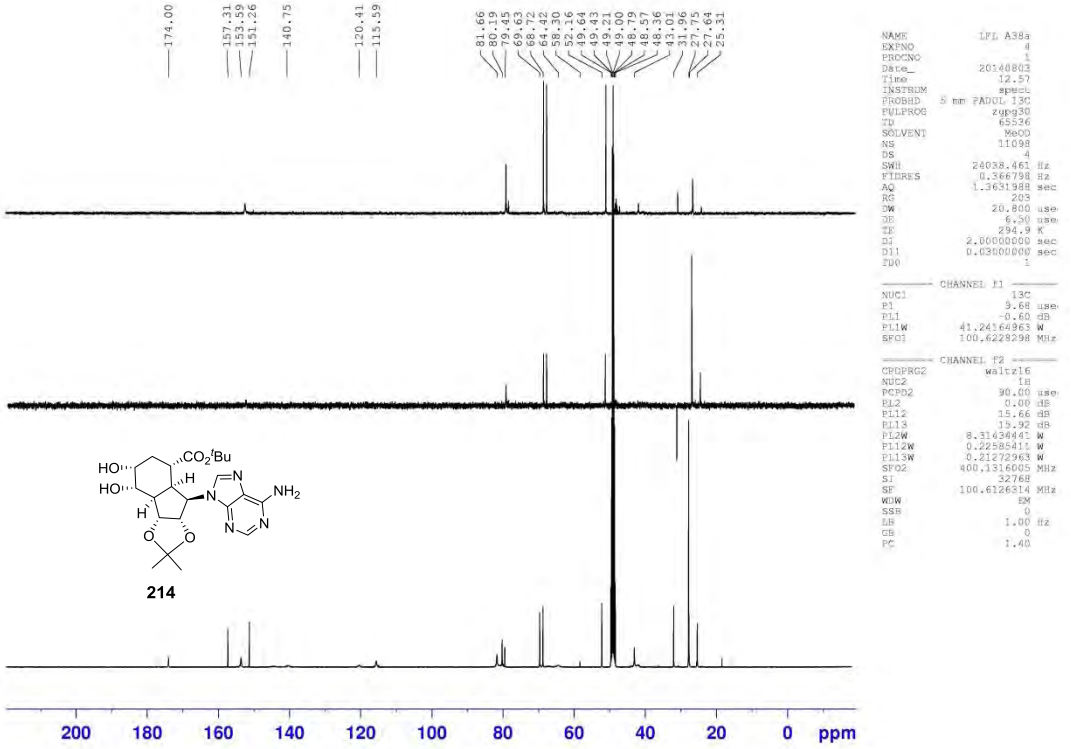


213β

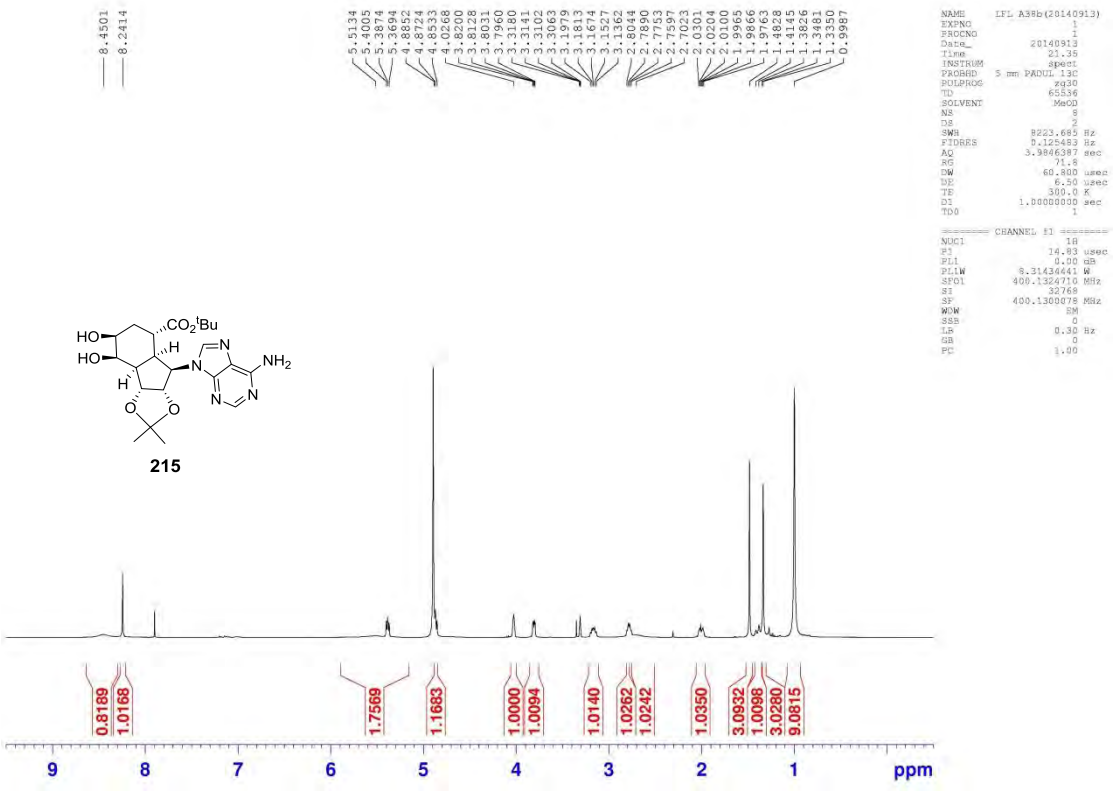
^{1}H NMR (Solvent: CD_3OD)



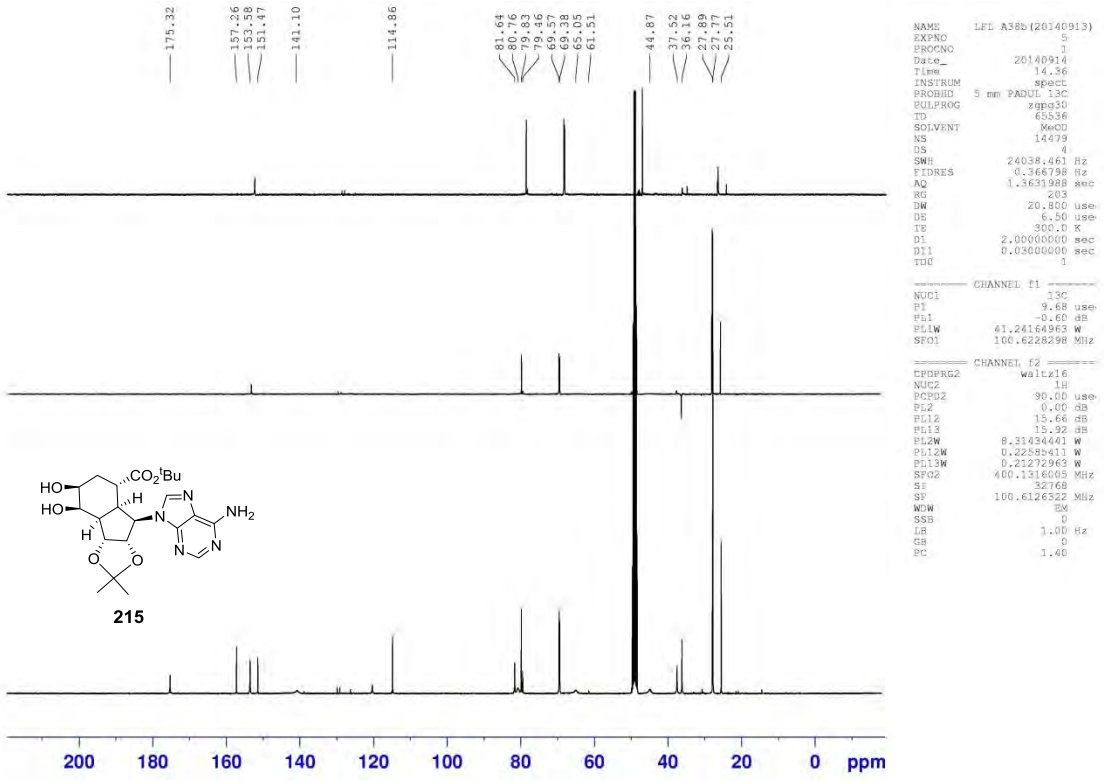
^{13}C NMR (Solvent: CD_3OD)



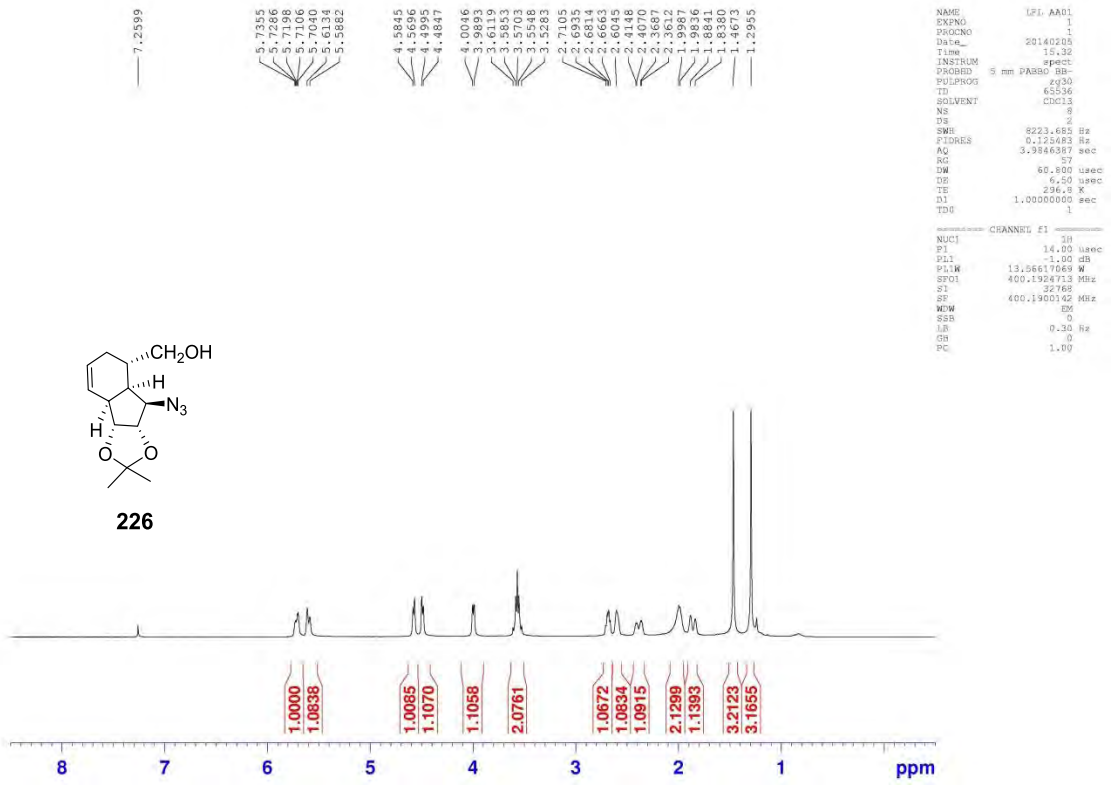
^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)



^{1}H NMR



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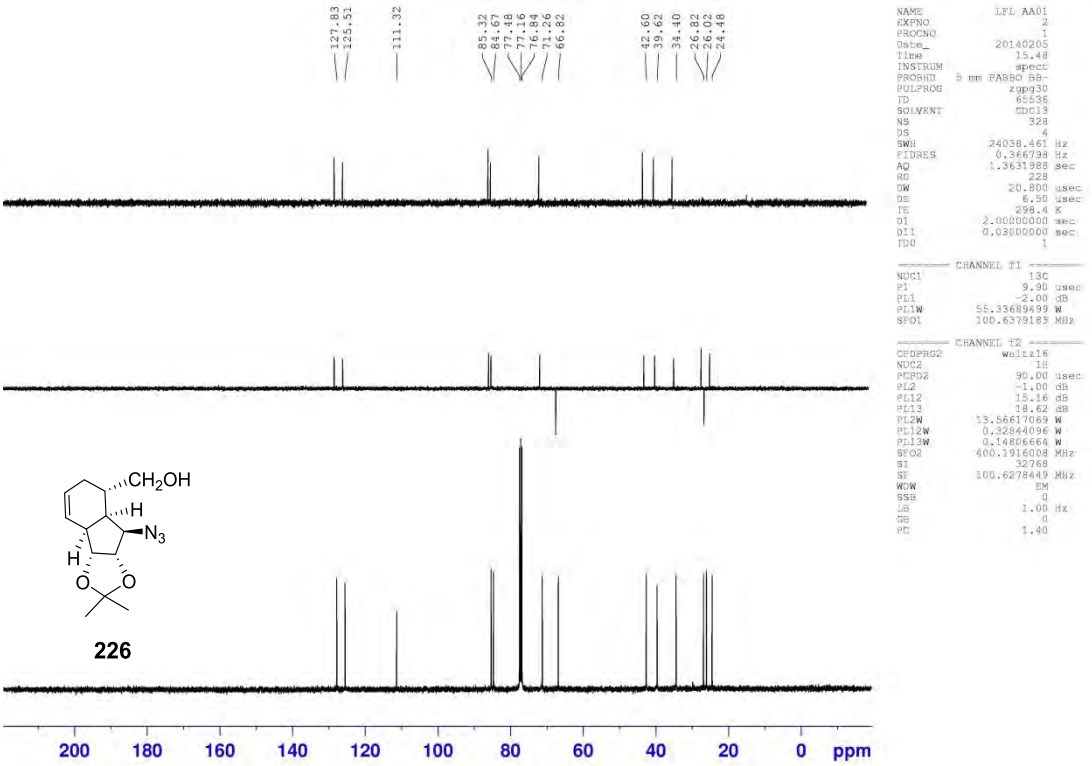
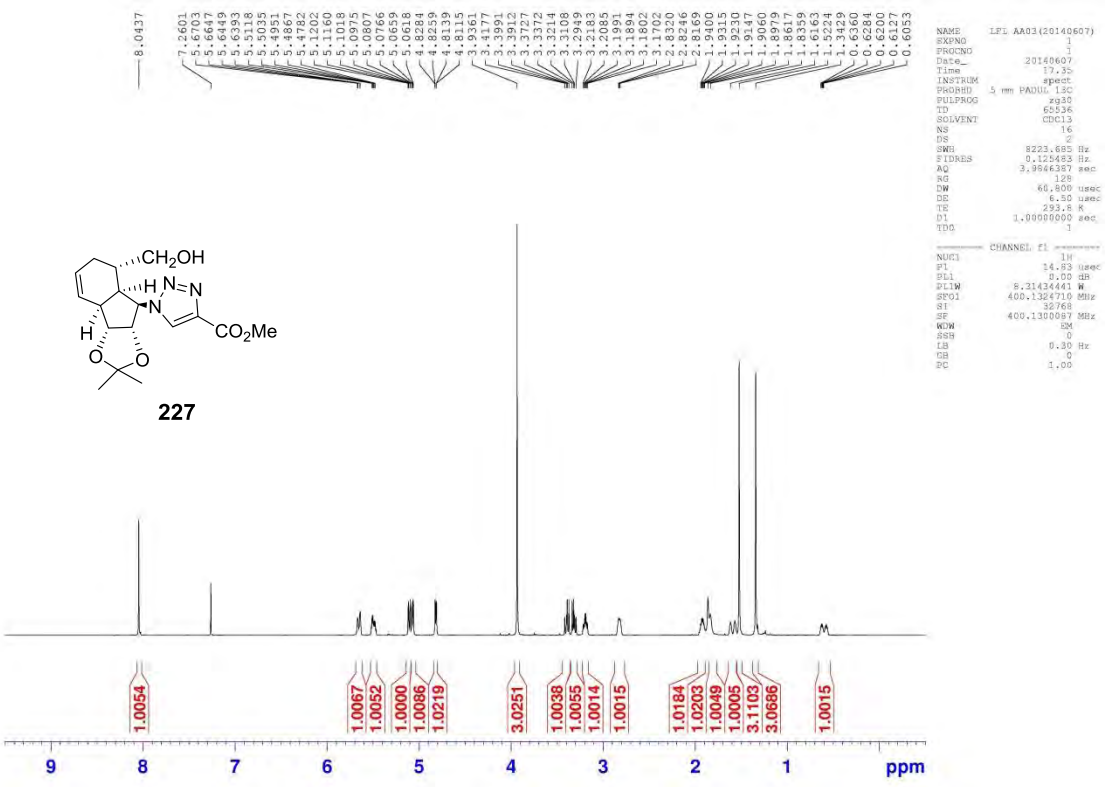


^{1}H NMR



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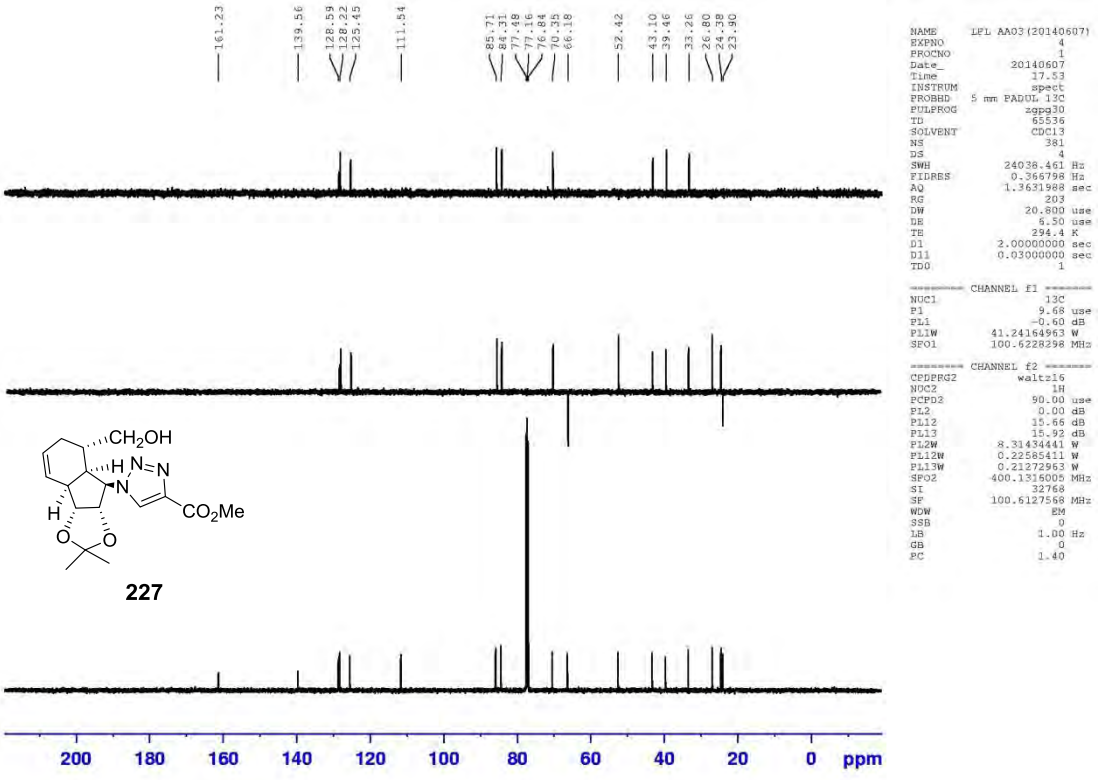

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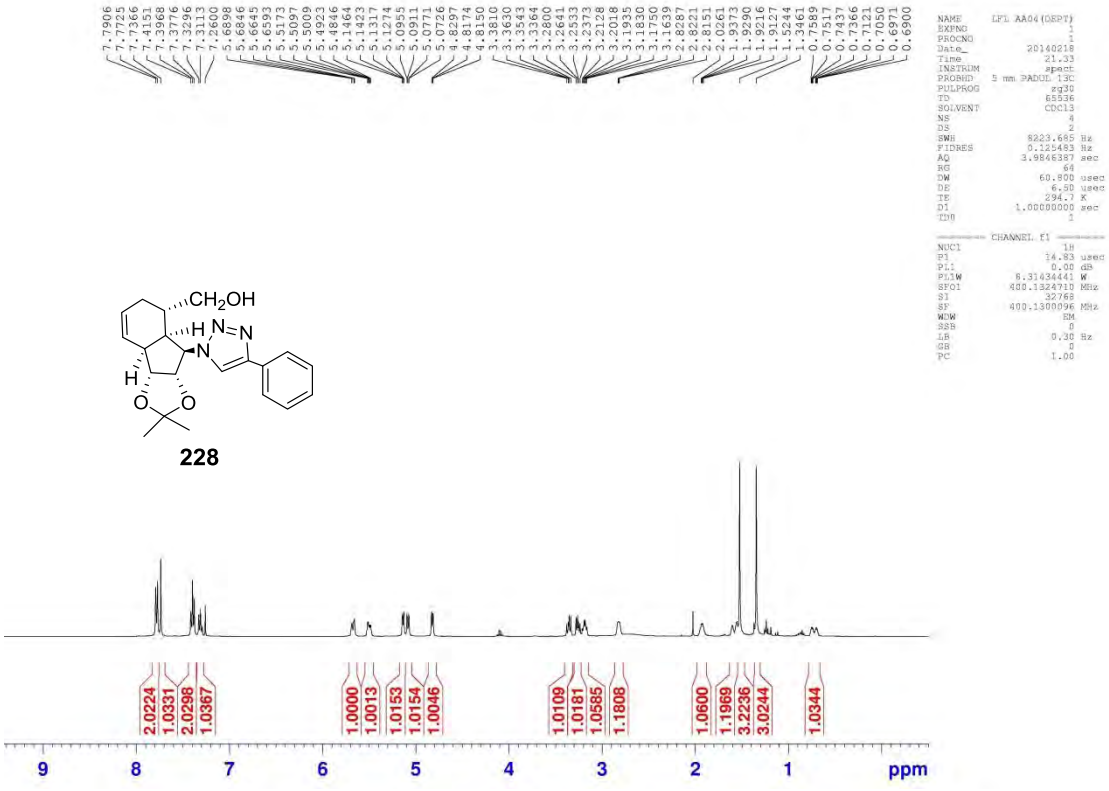

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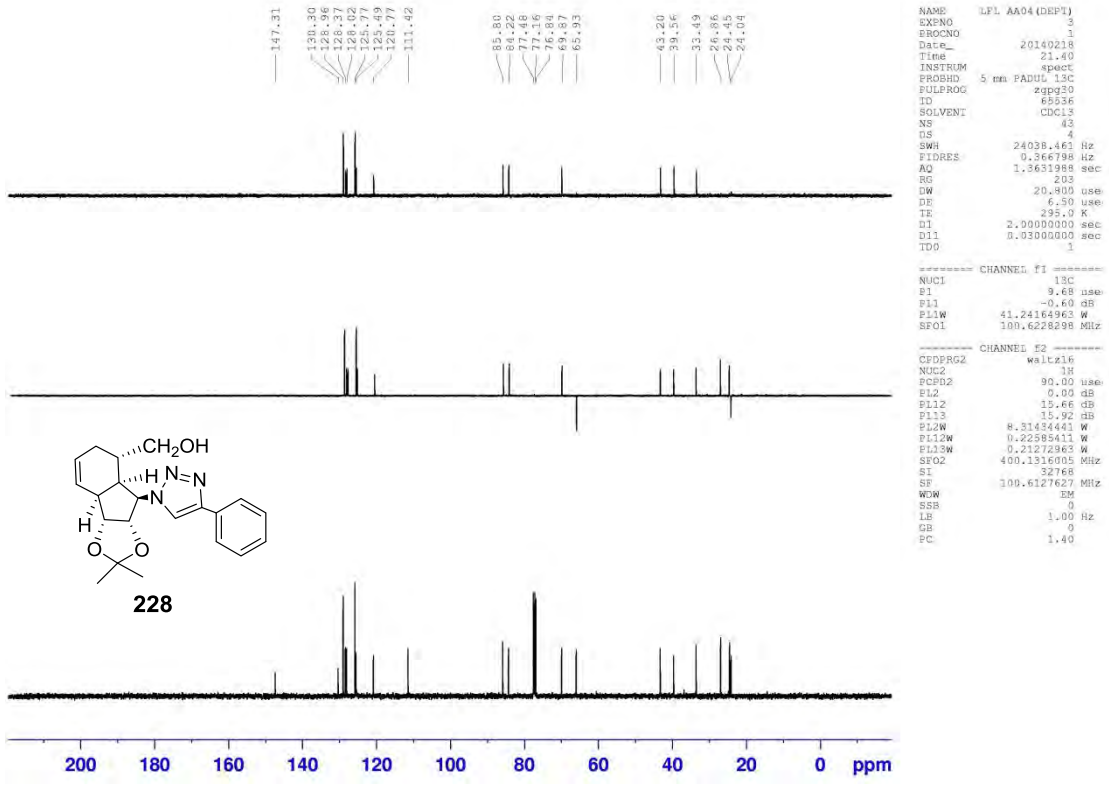
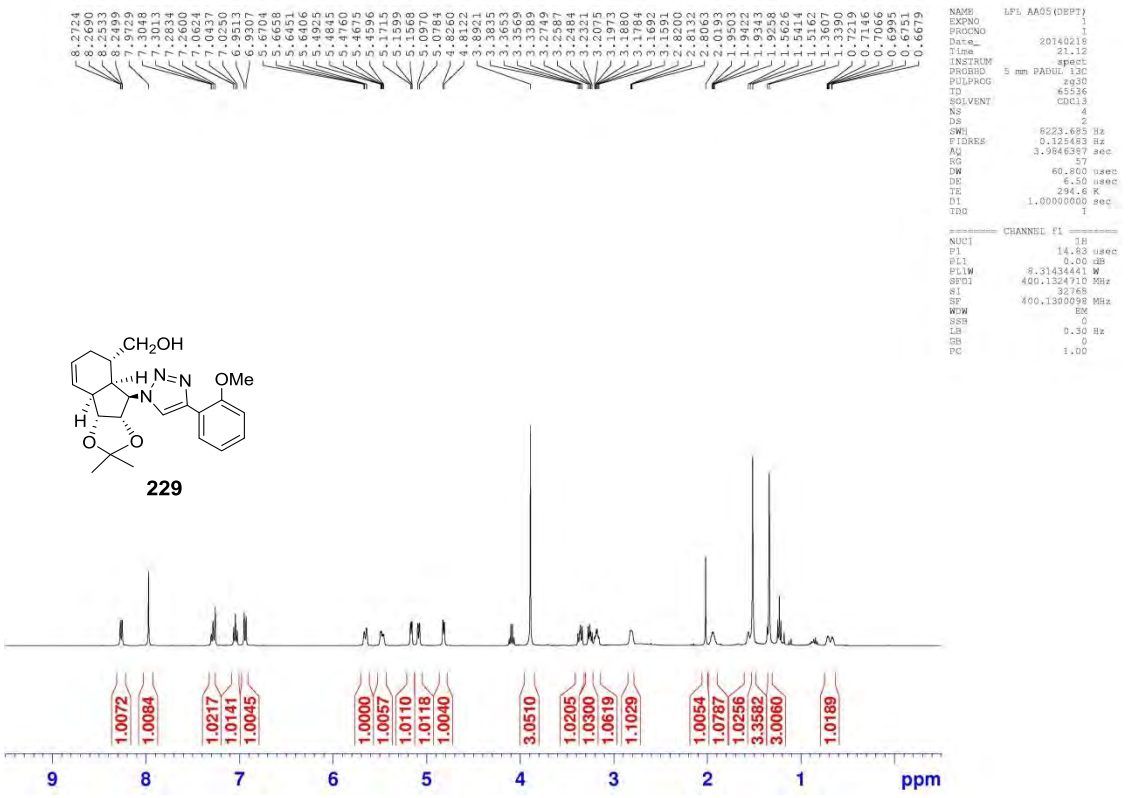
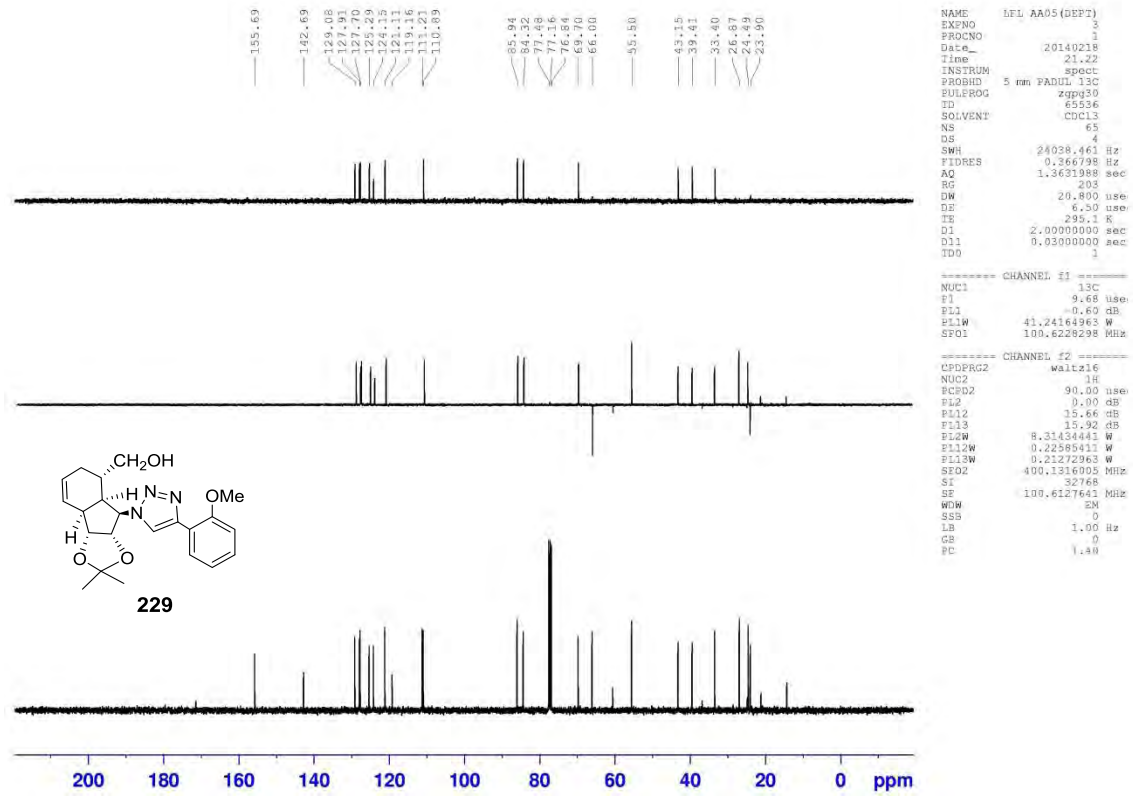


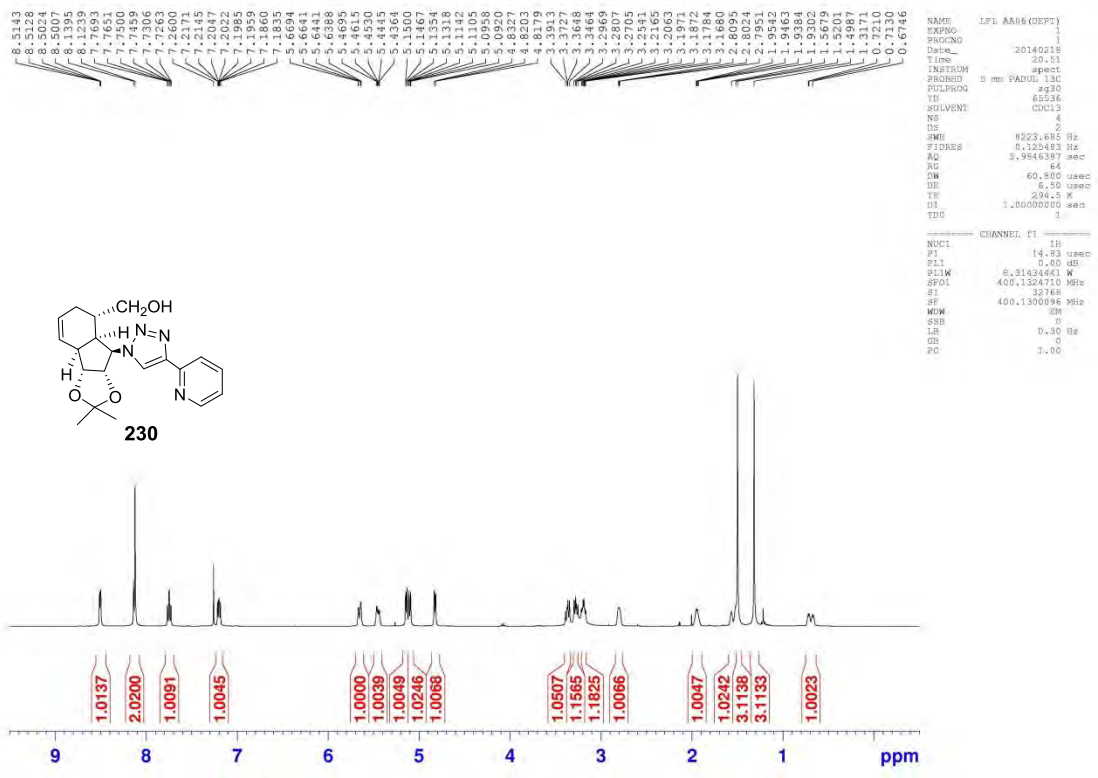
^{1}H NMR



^{13}C NMR



^{1}H NMR



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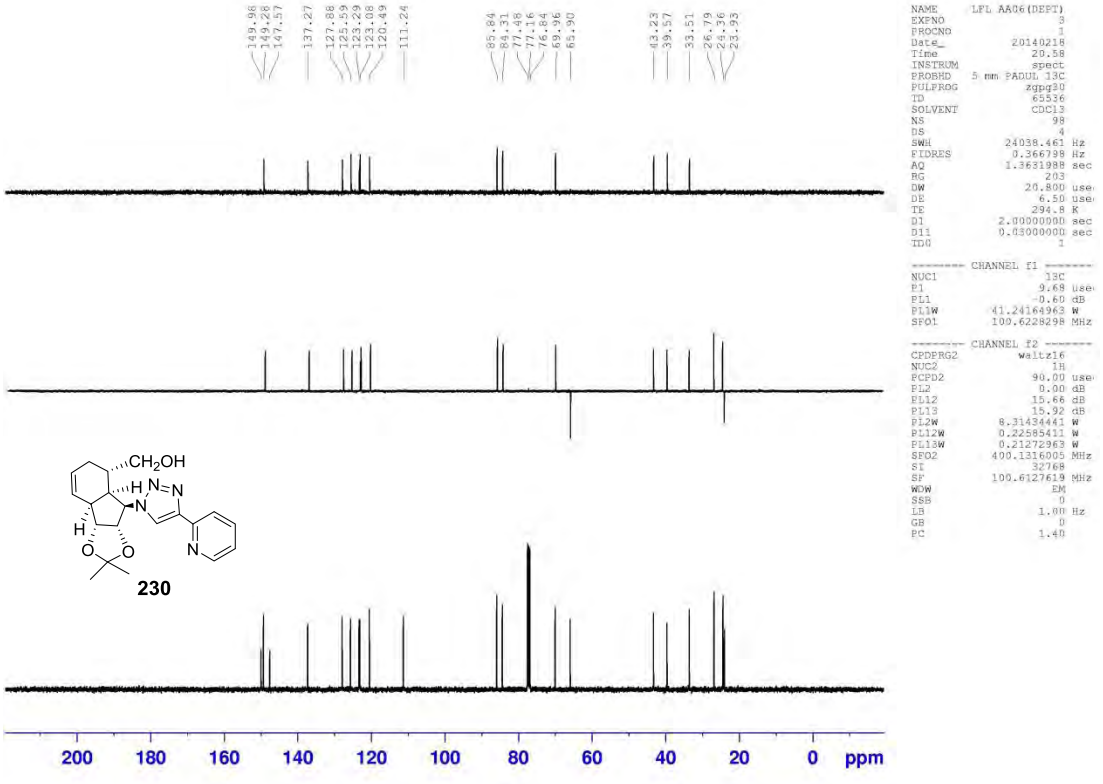
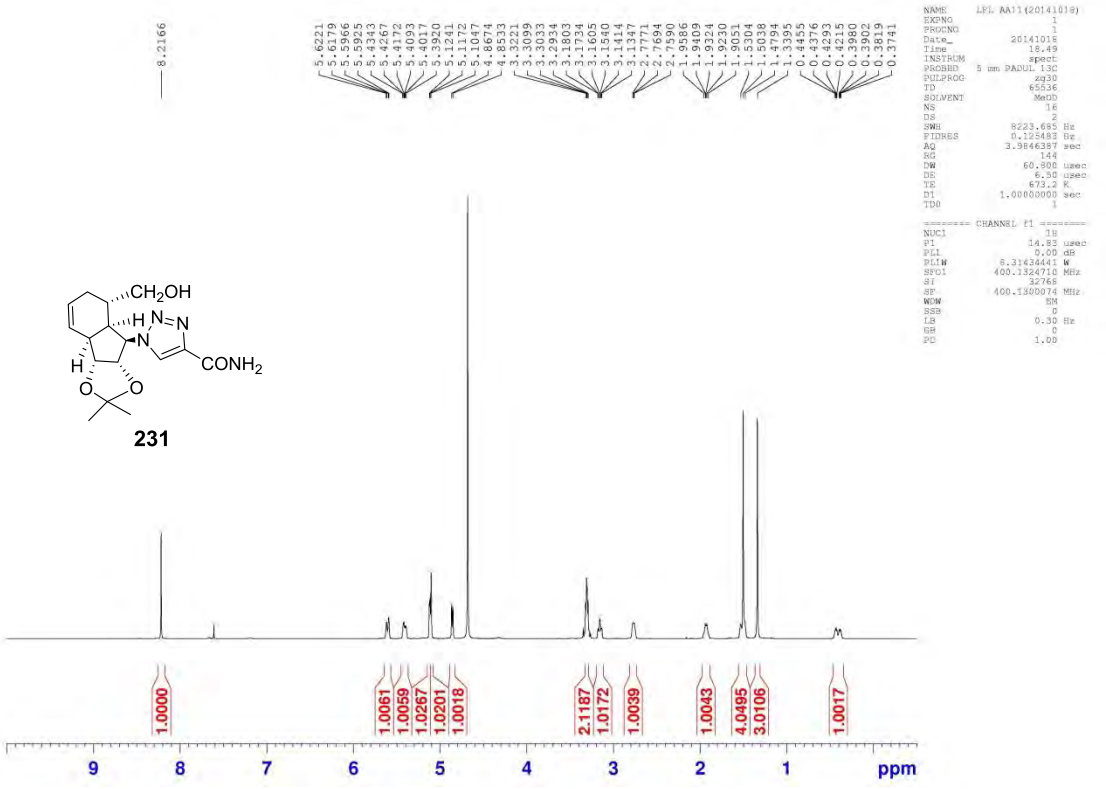
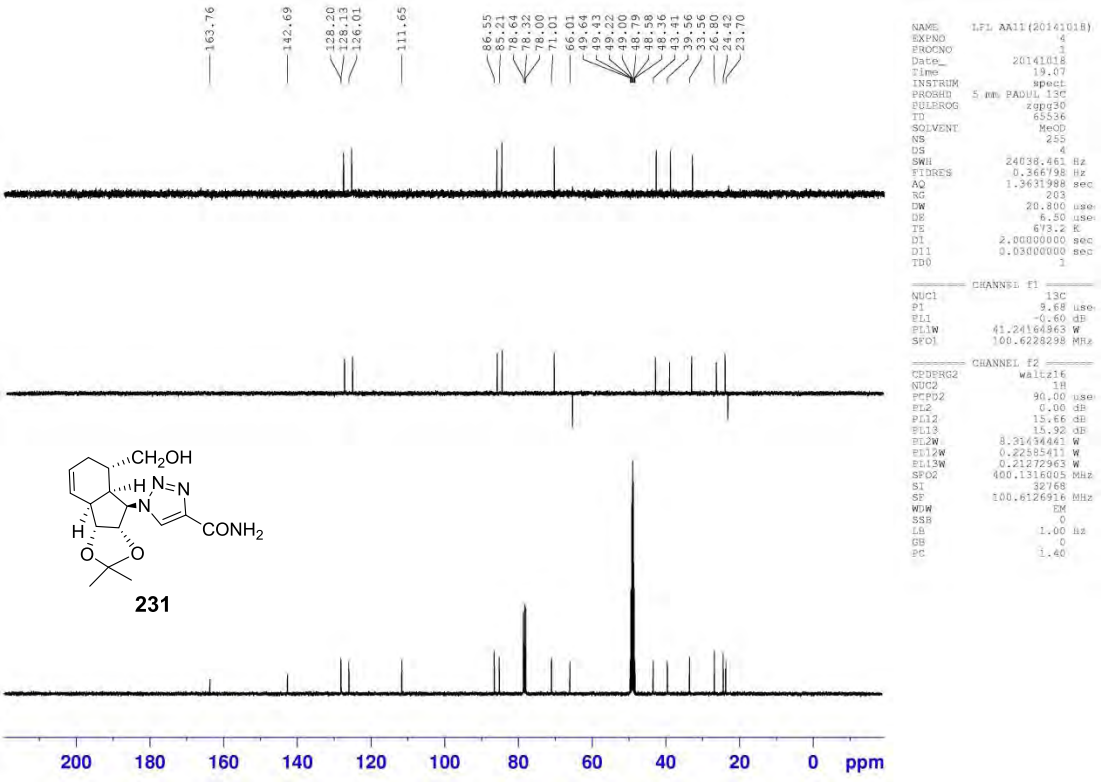


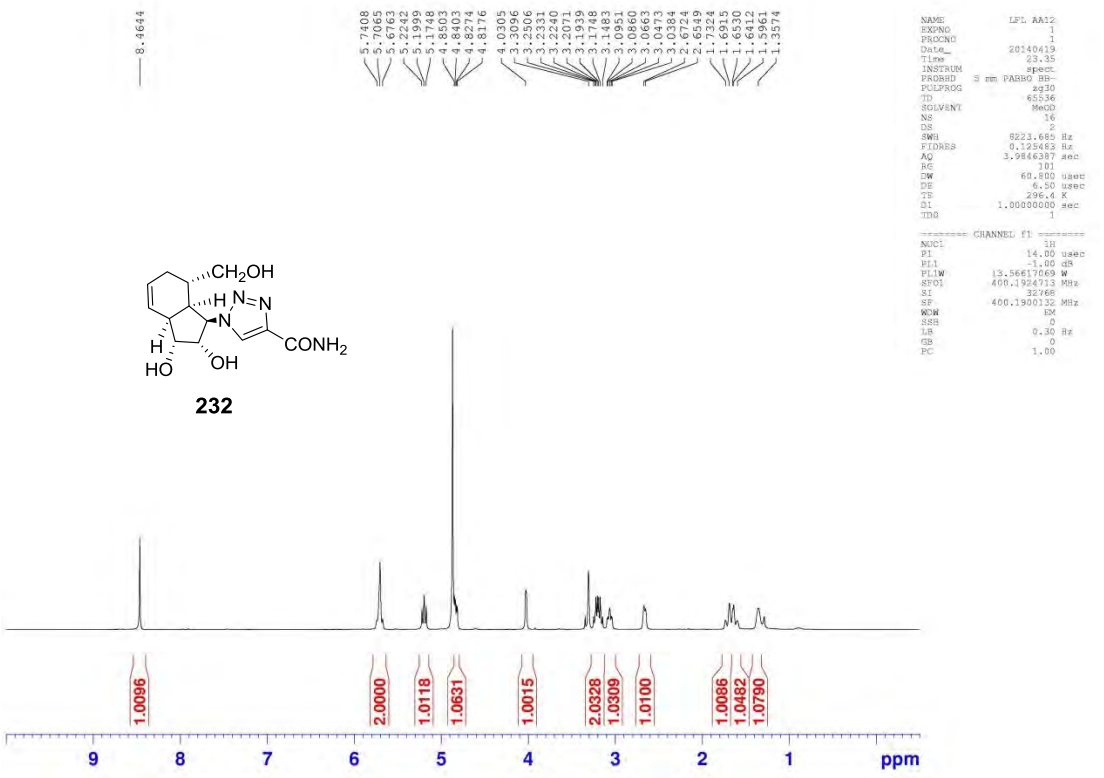
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:1)



^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:1)



^{1}H NMR (Solvent: CD_3OD)



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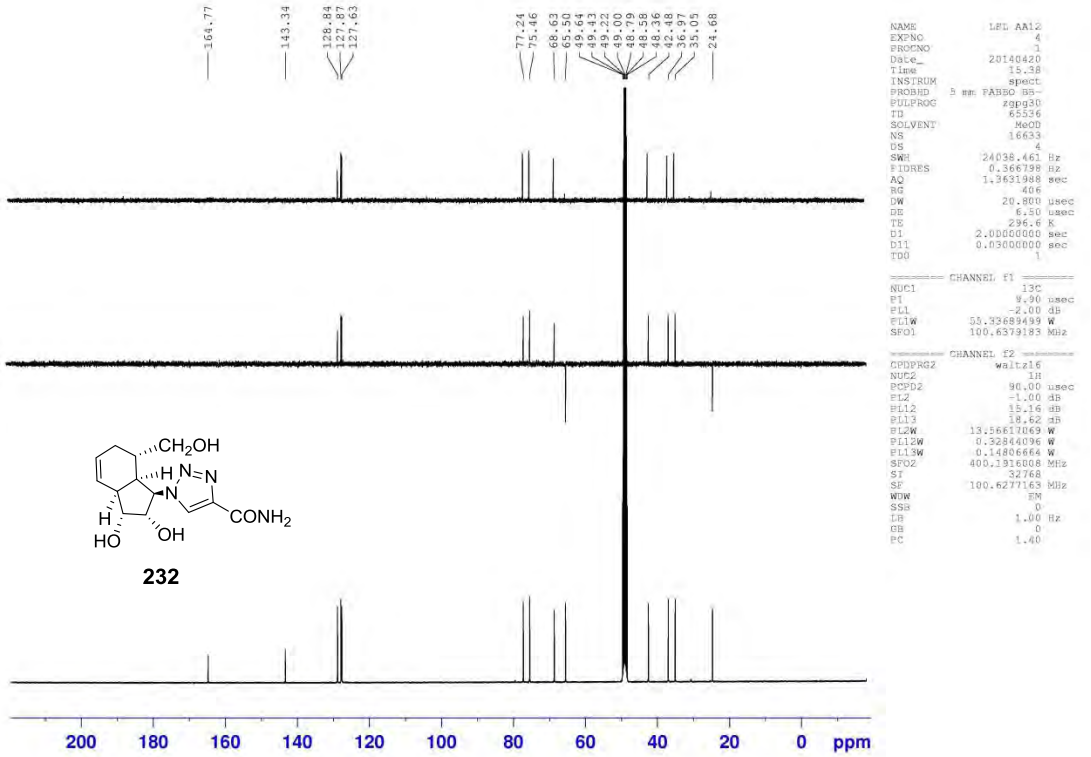
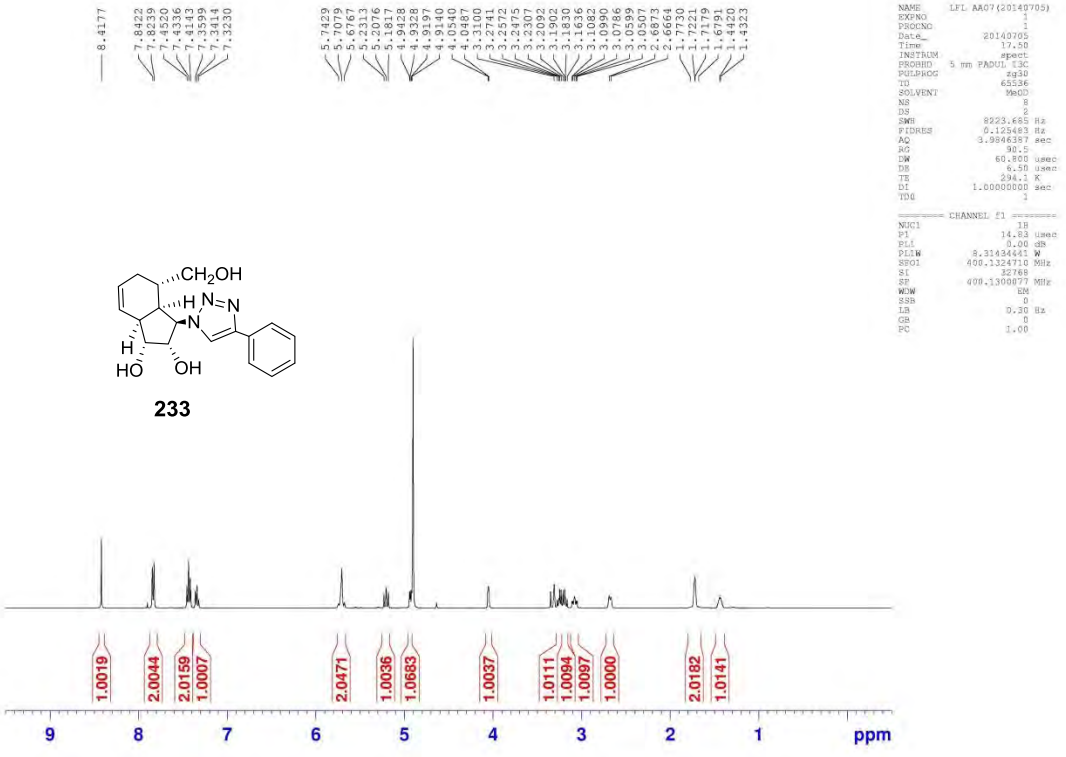
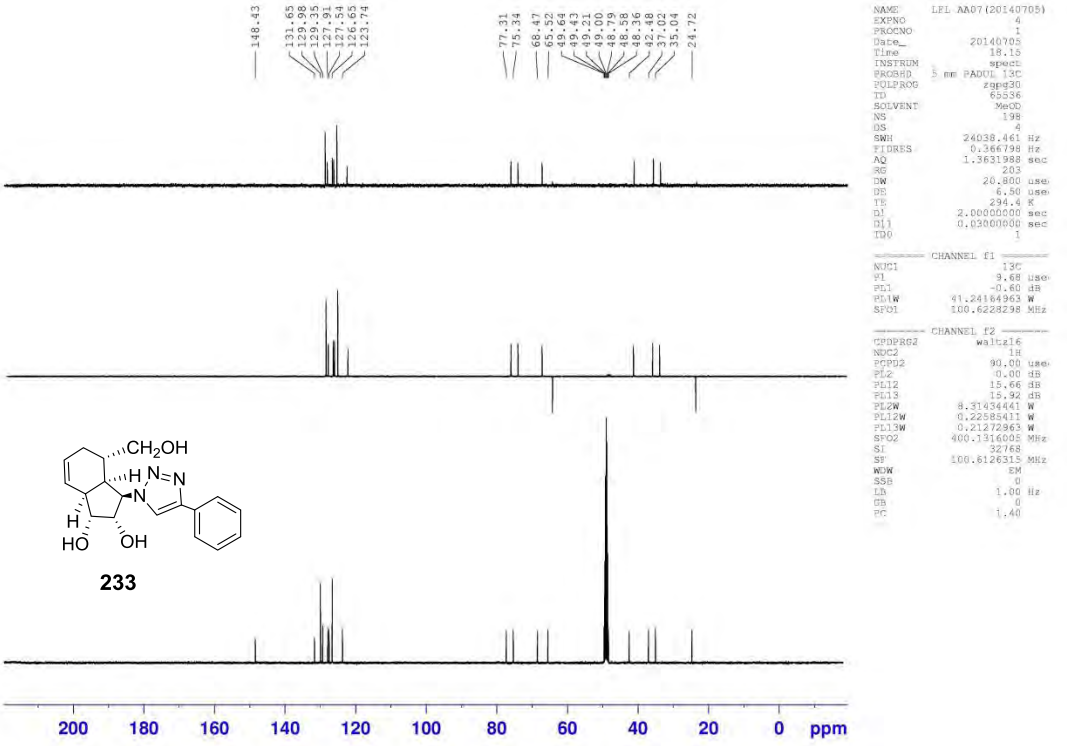


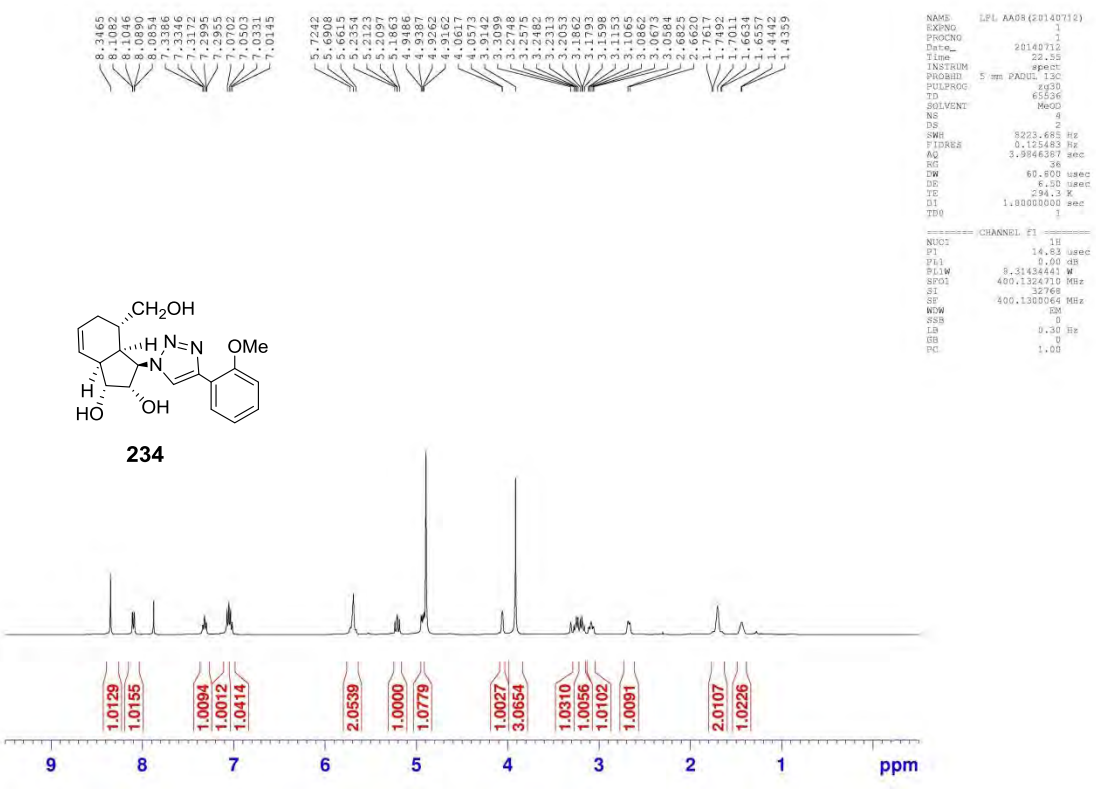
^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)



^{1}H NMR (Solvent: CD_3OD)



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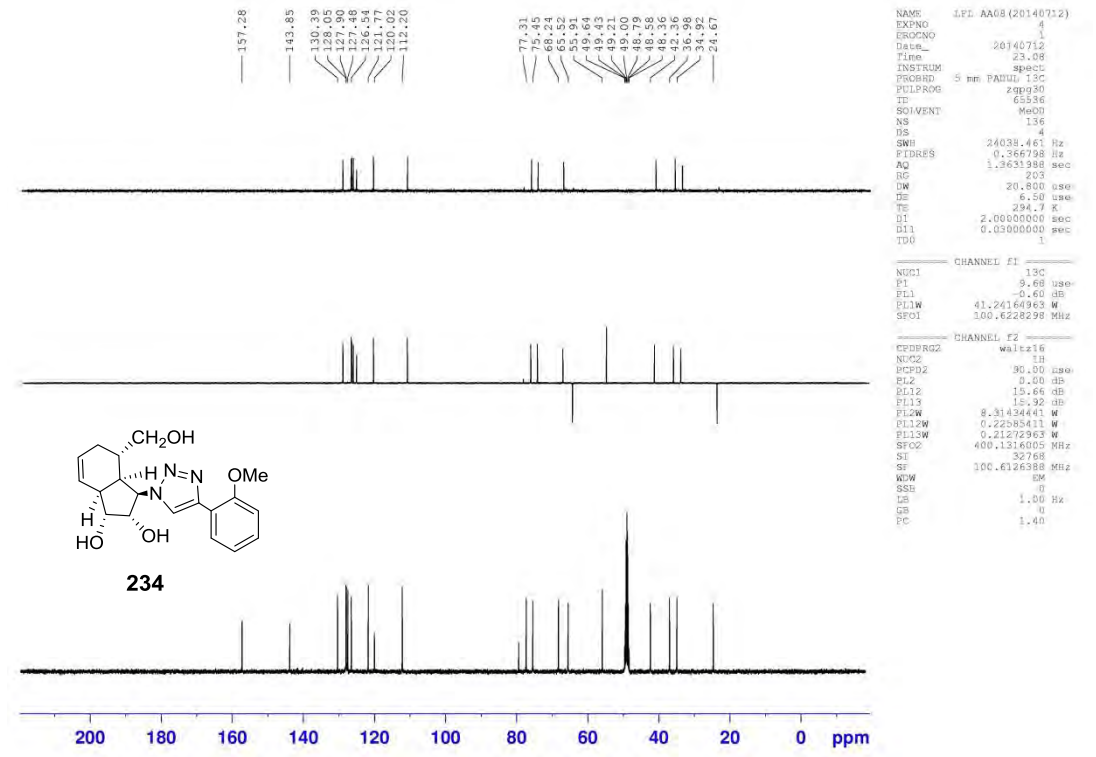
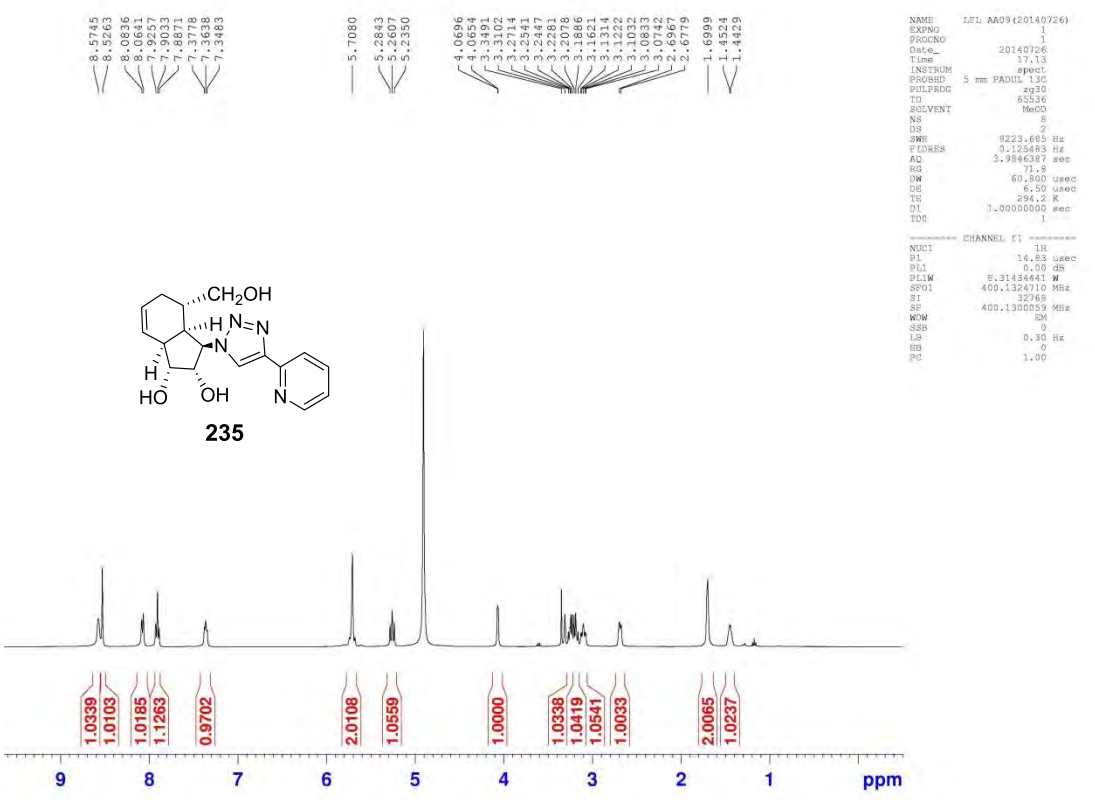
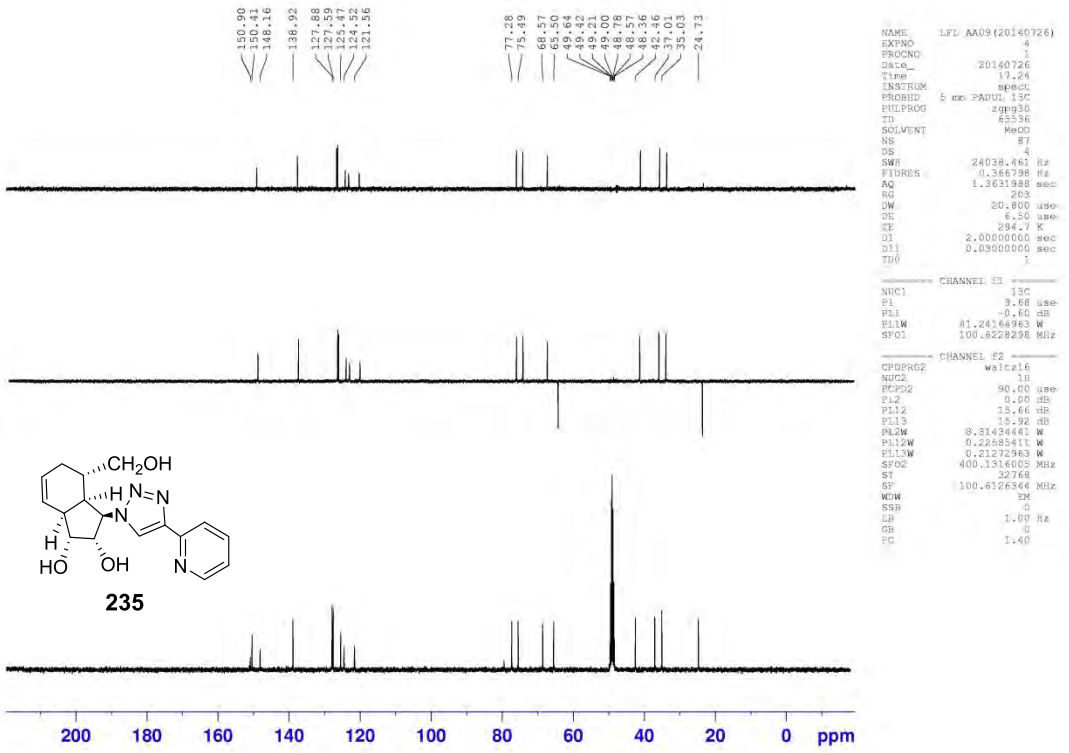


^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)



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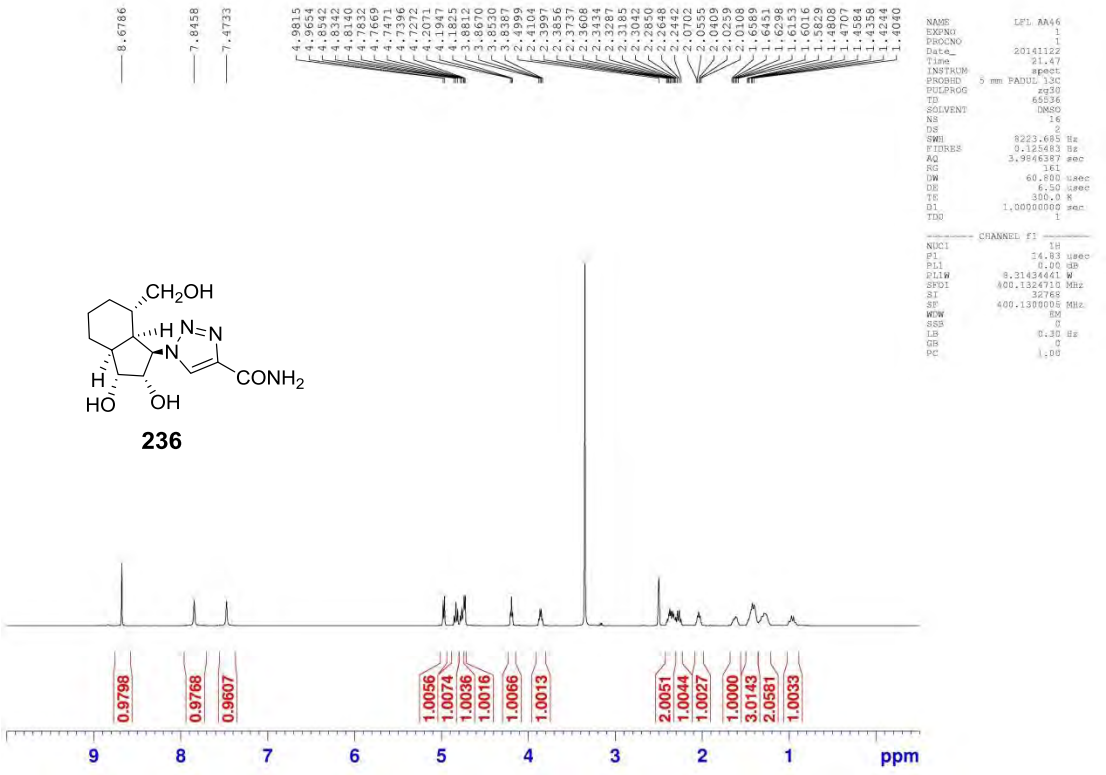
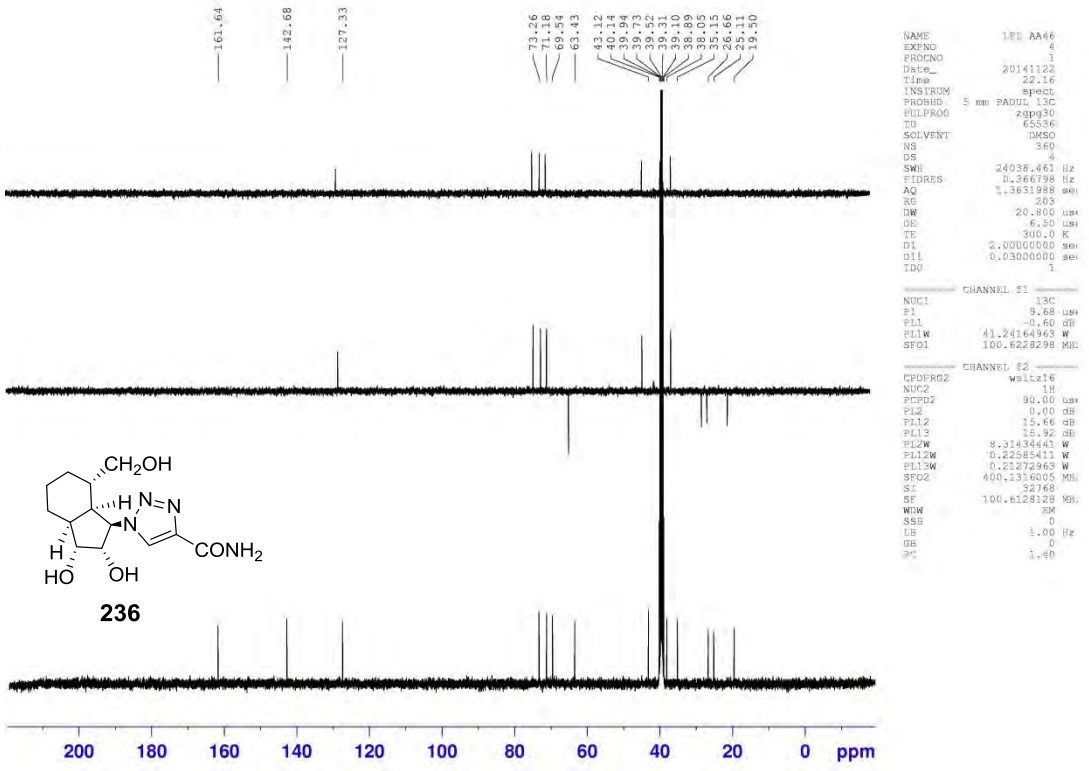
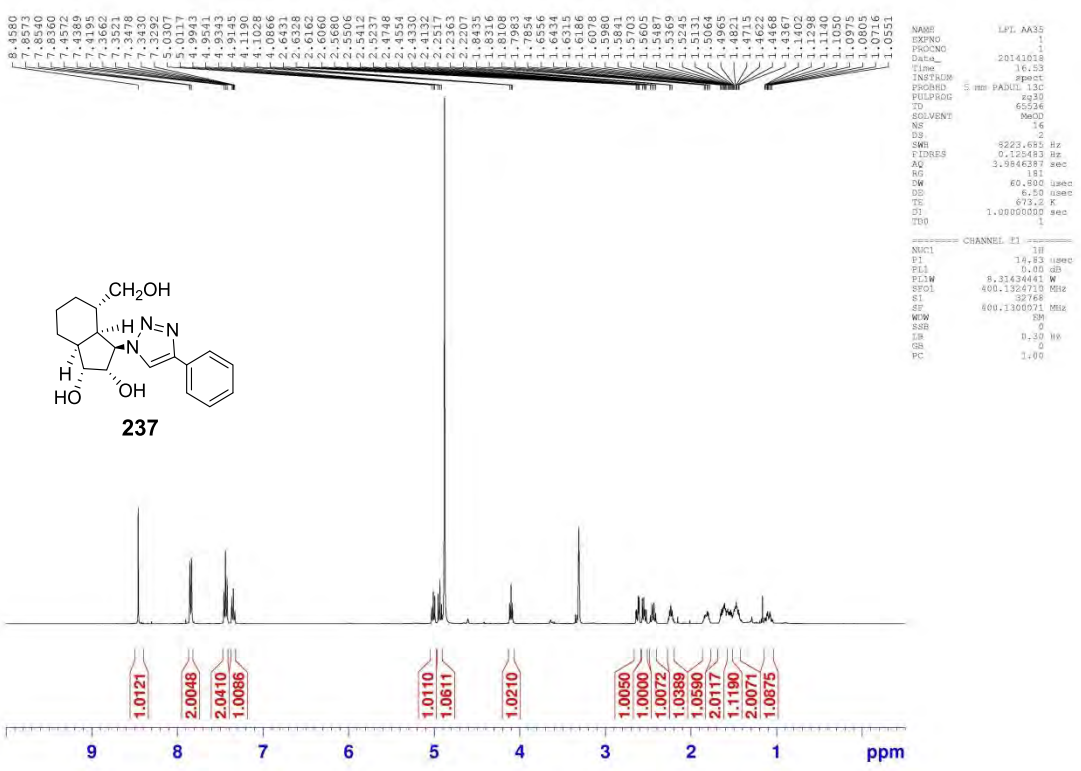


^{13}C NMR (Solvent: DMSO-d_6)



^{1}H NMR (Solvent: CD_3OD)



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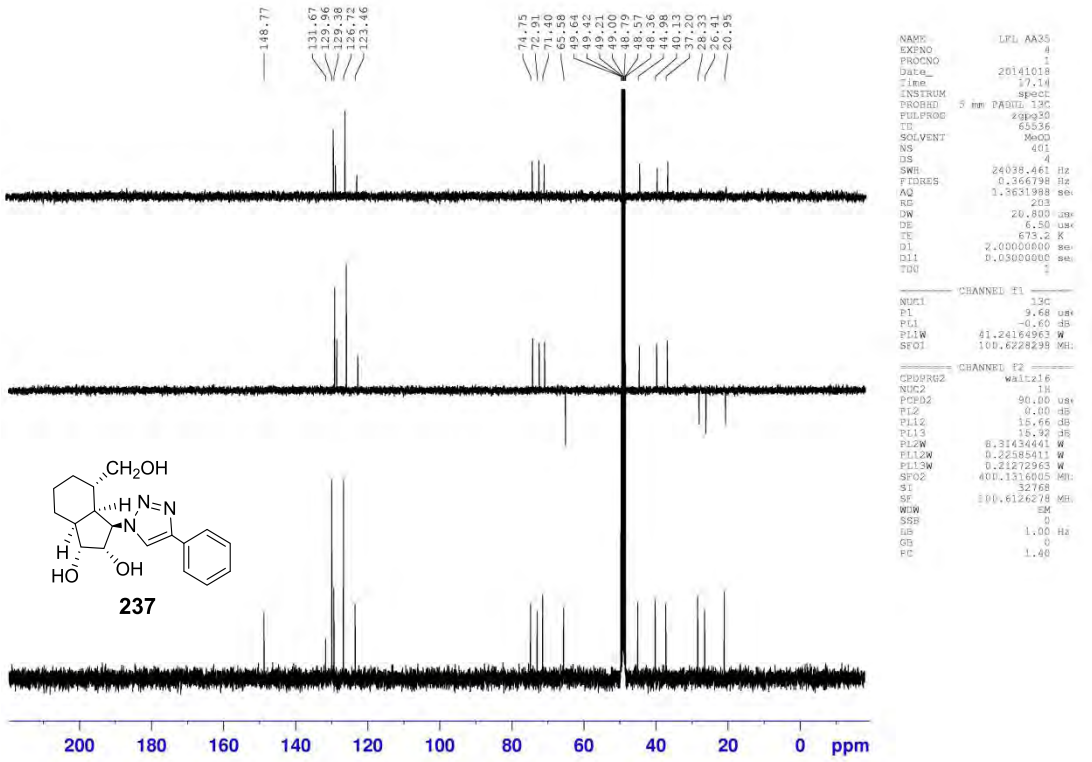

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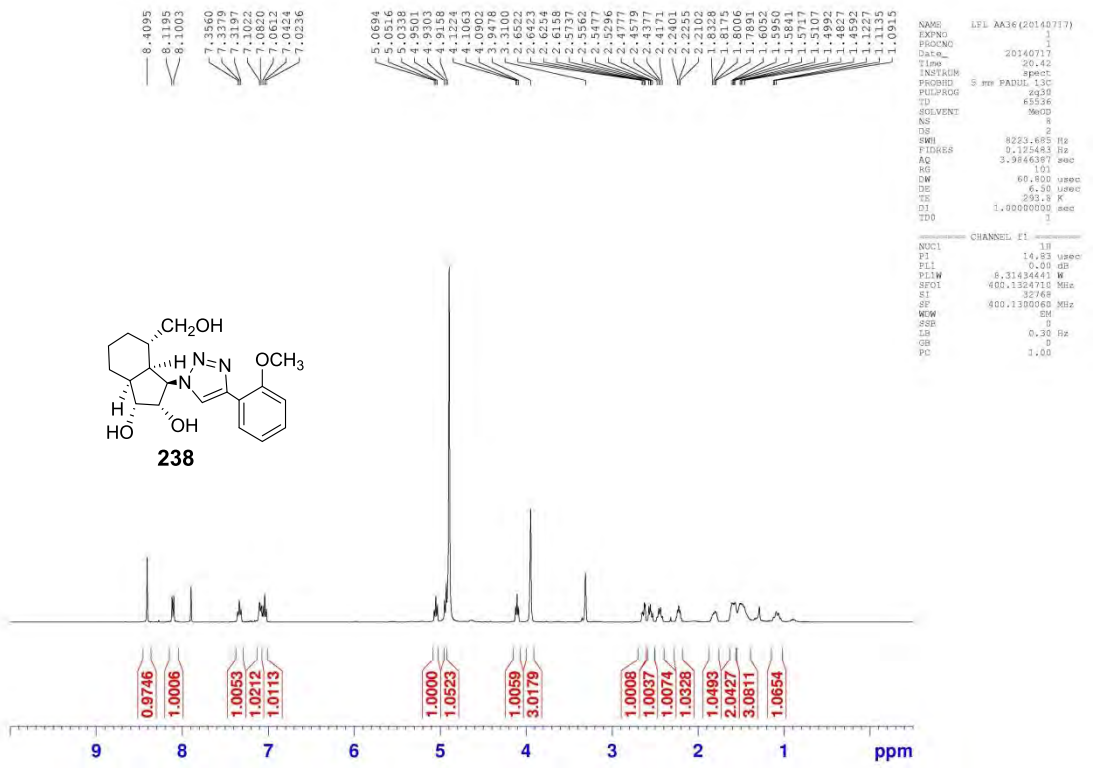
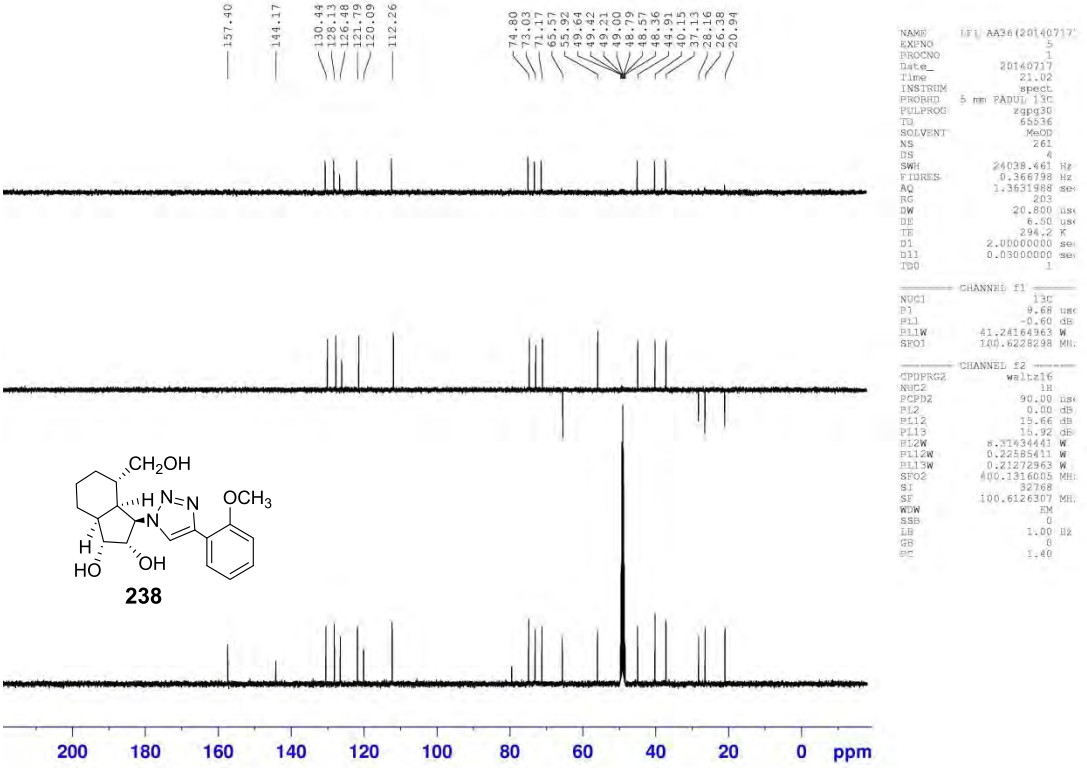
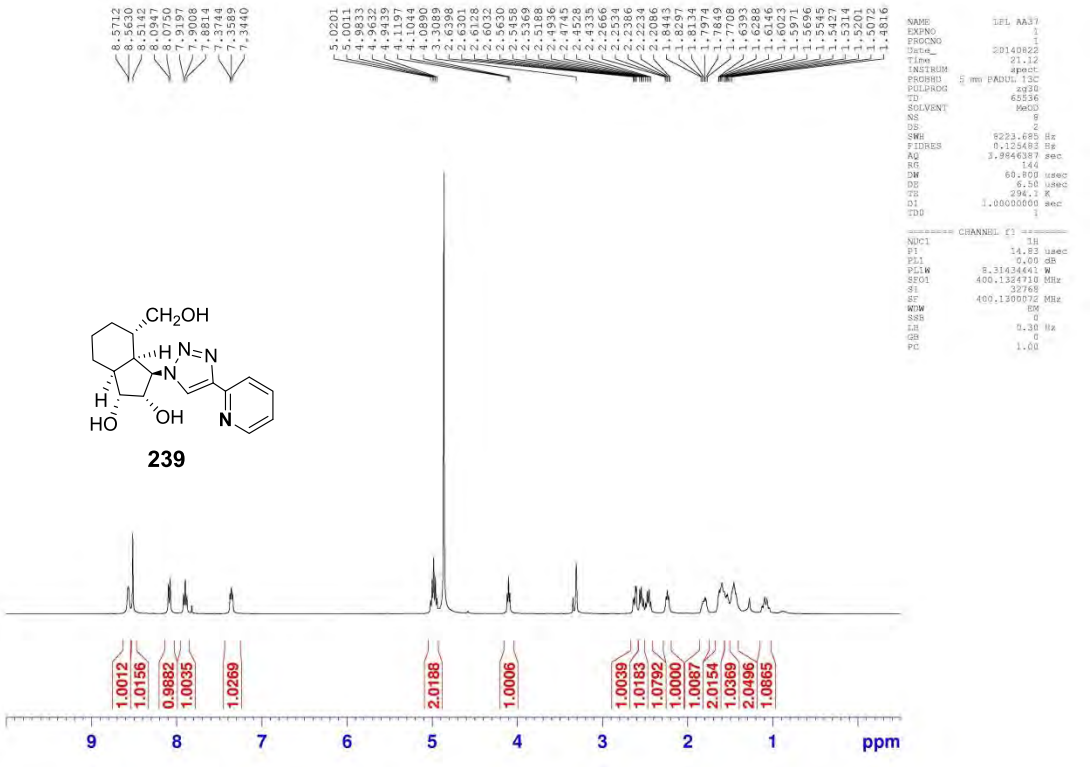


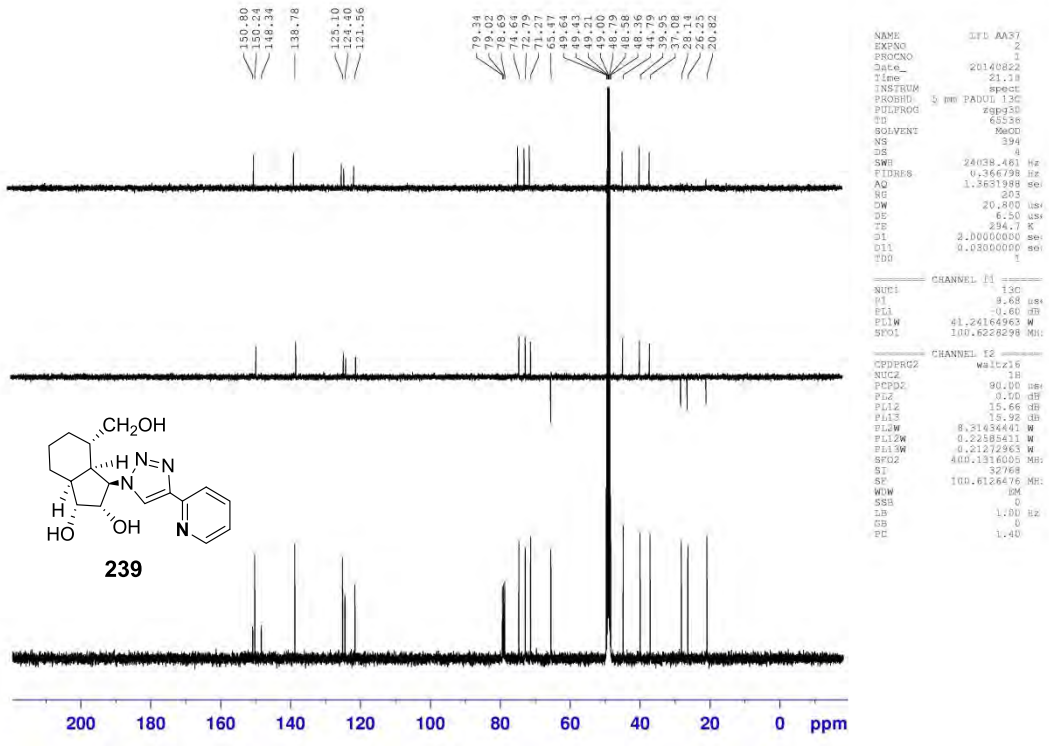
^{13}C NMR (Solvent: CD_3OD)



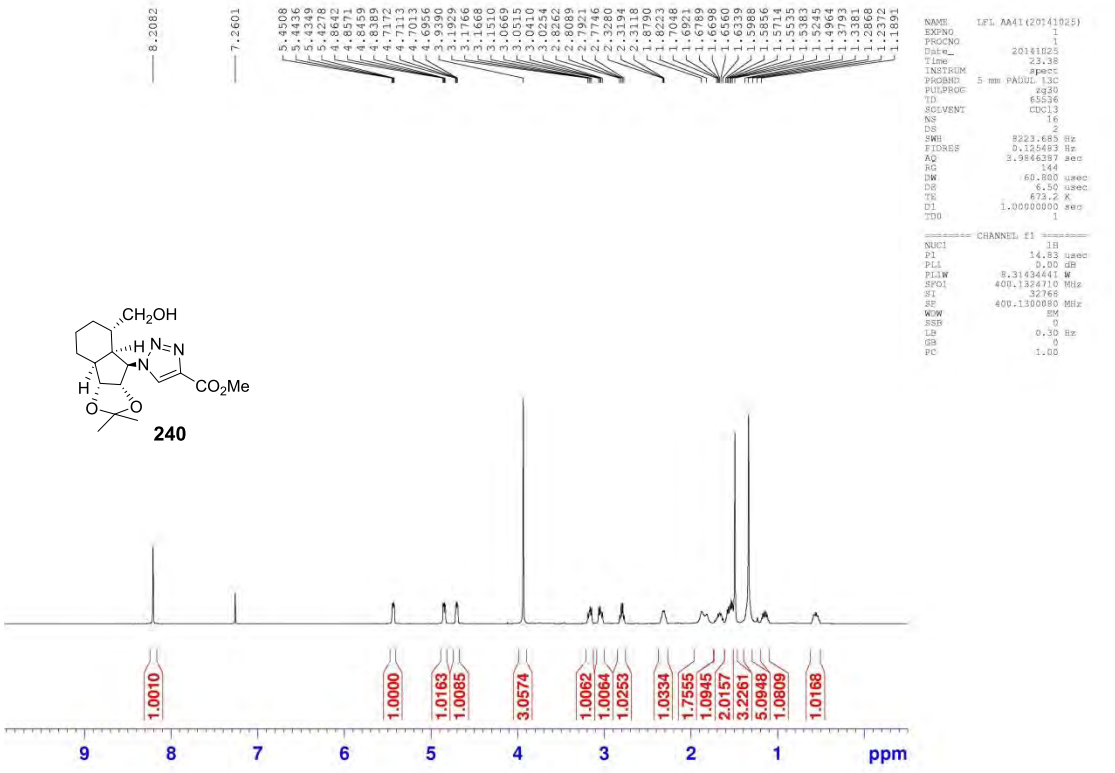
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



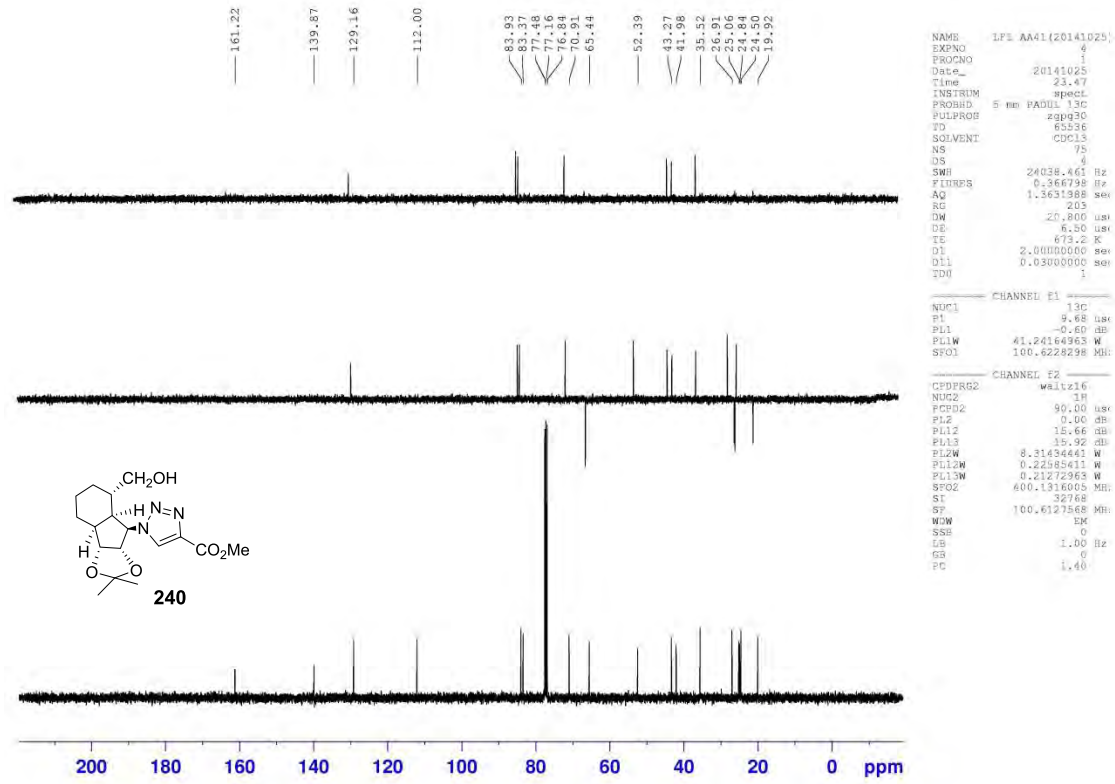
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



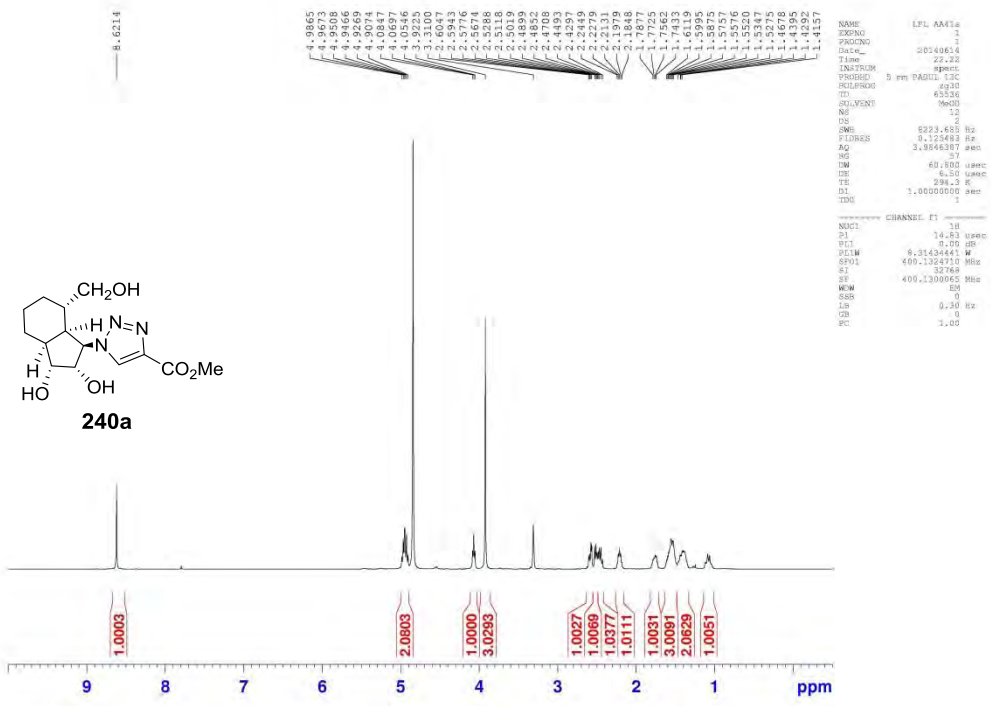
^{1}H NMR (Solvent:)



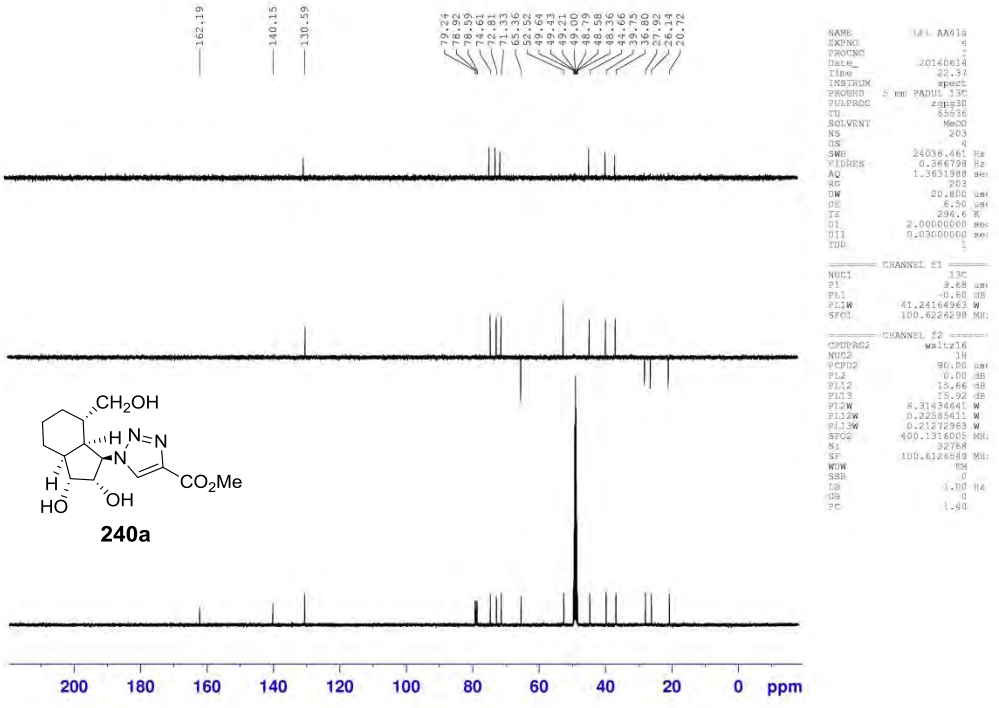
^{13}C NMR



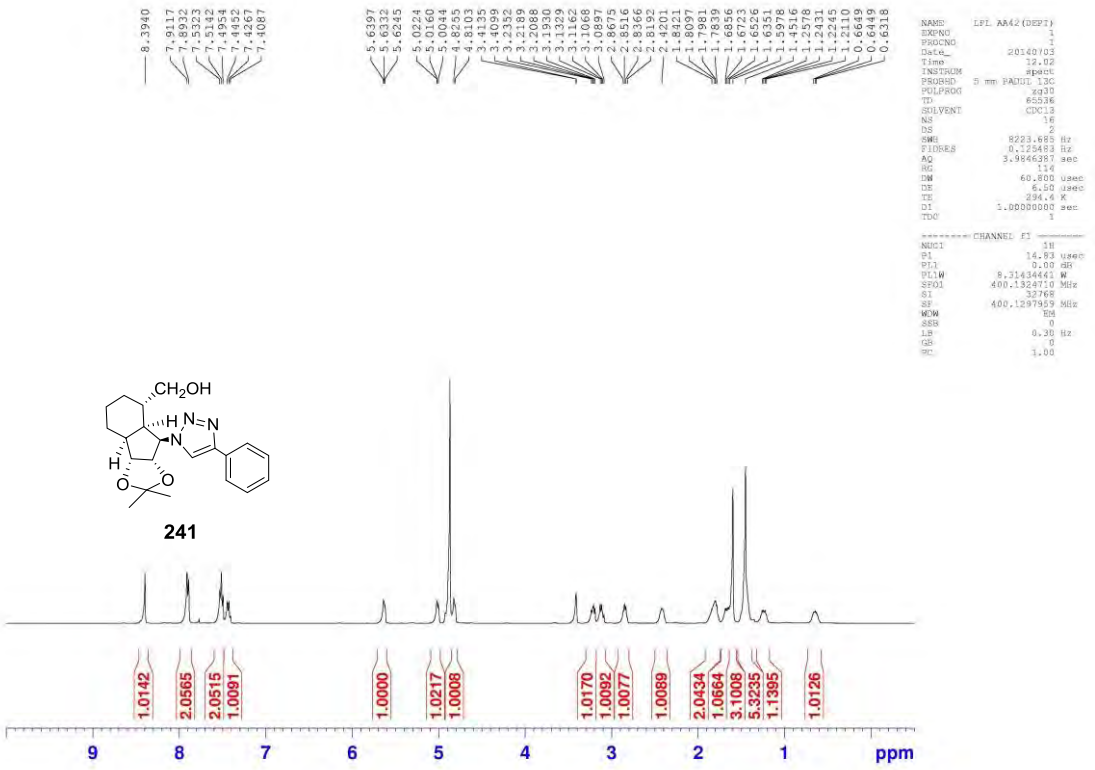
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



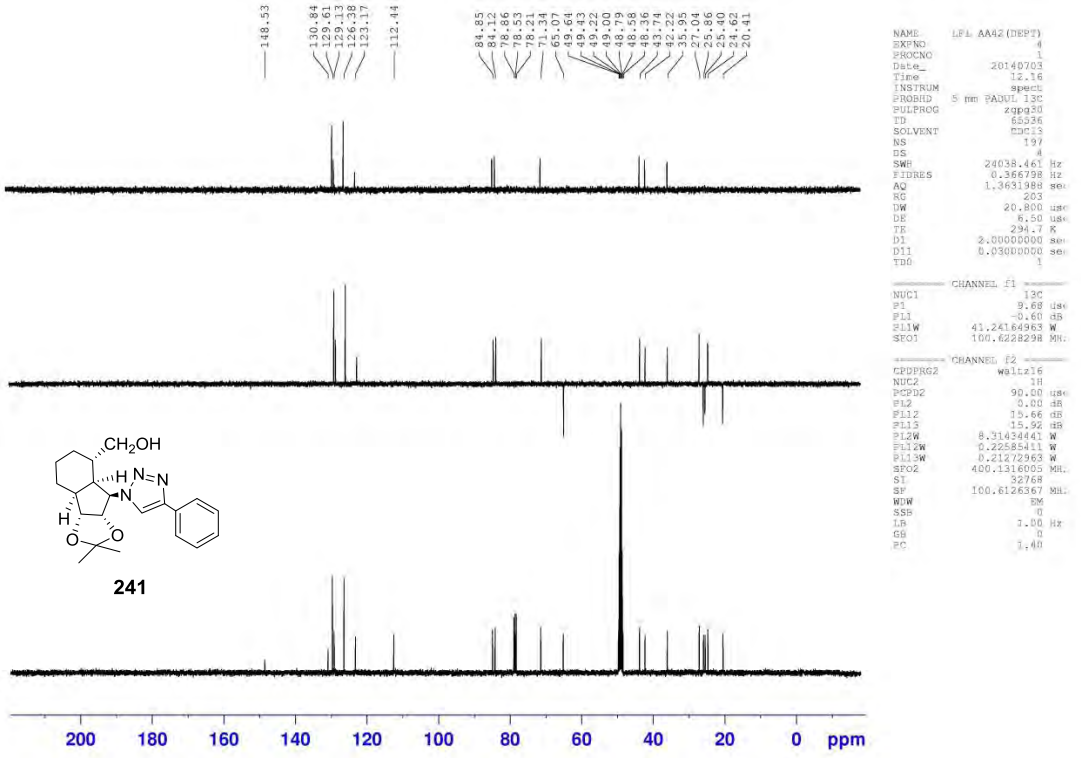
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



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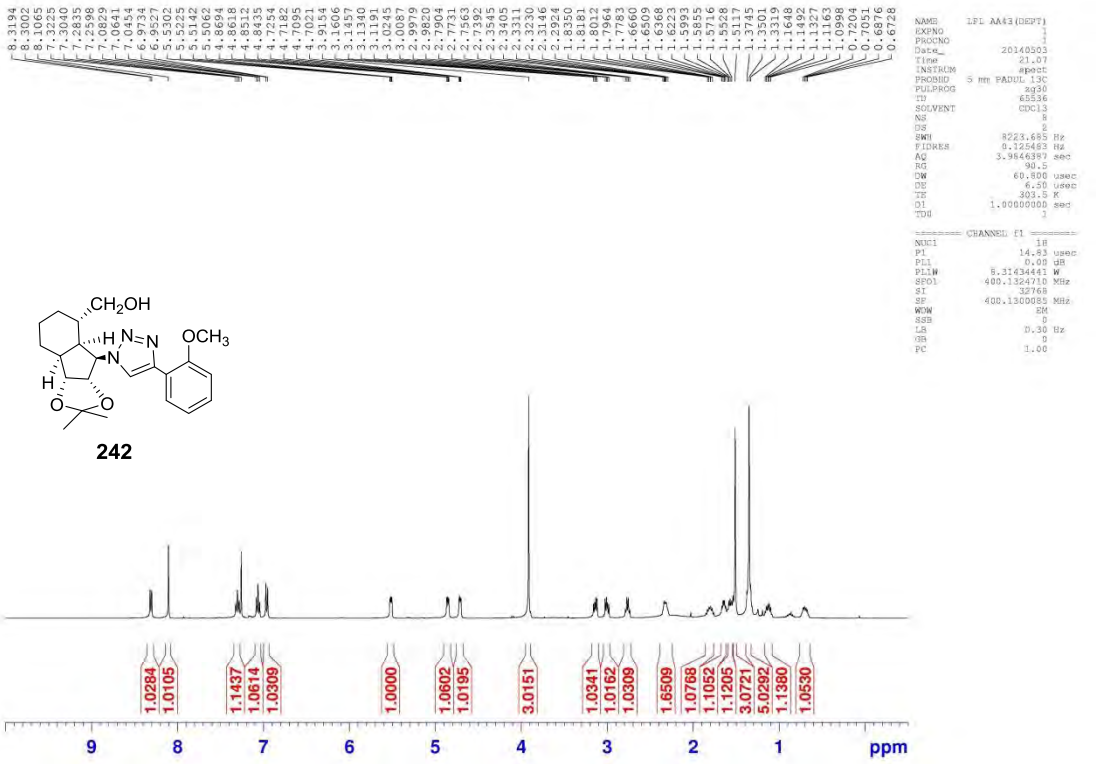

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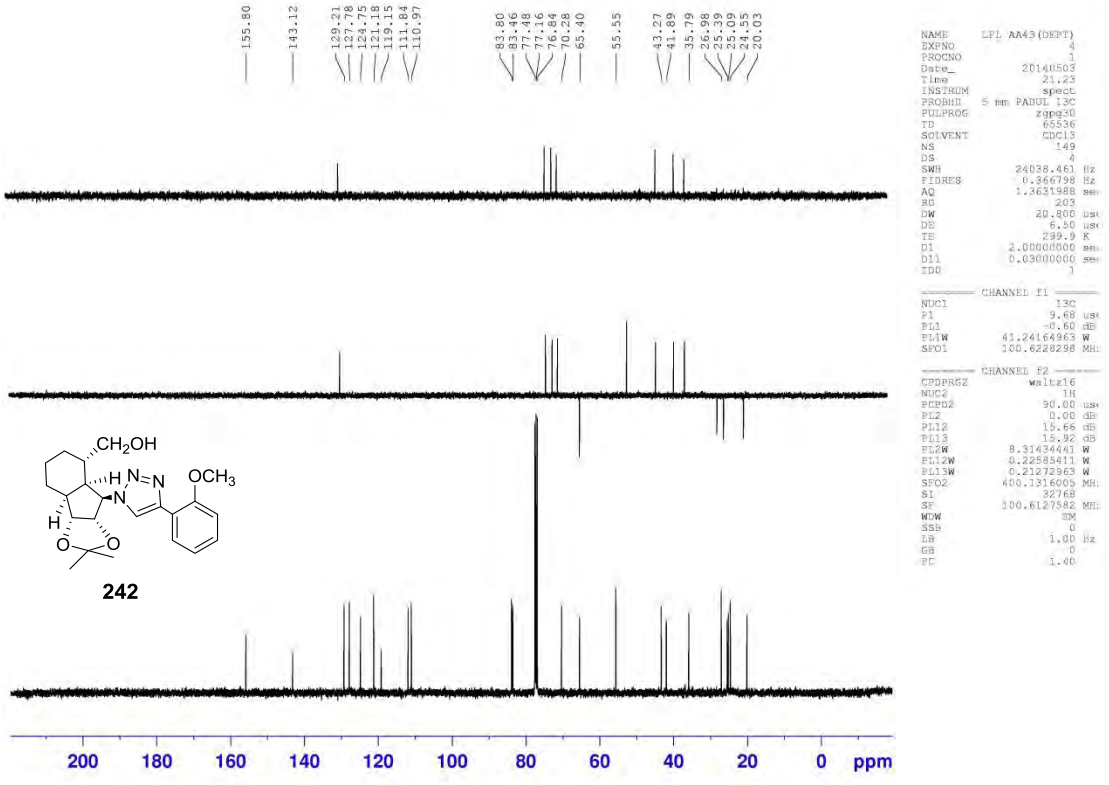

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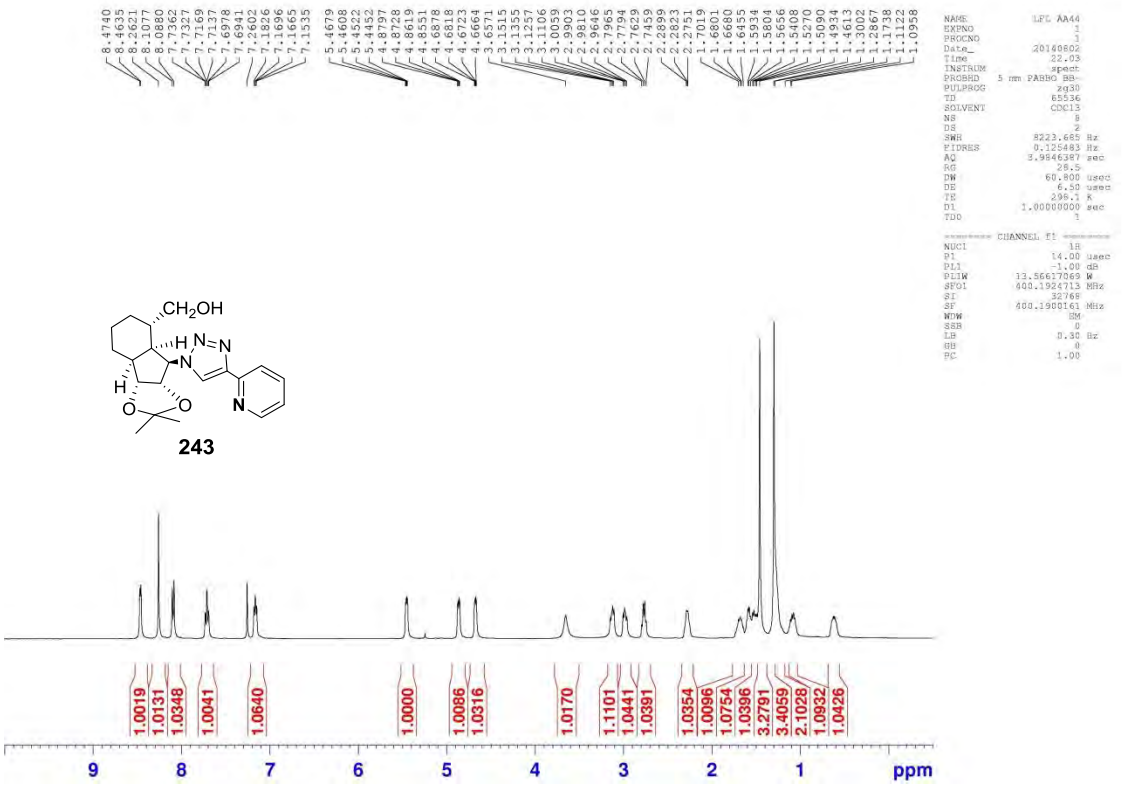

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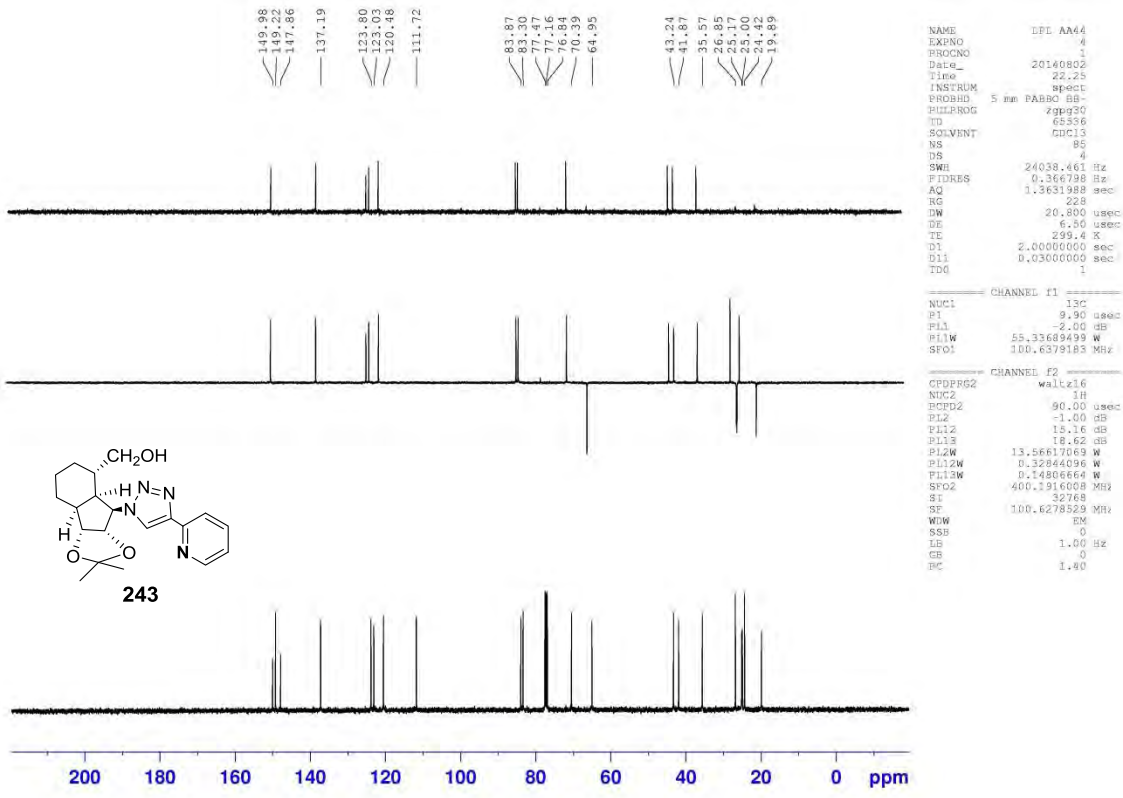

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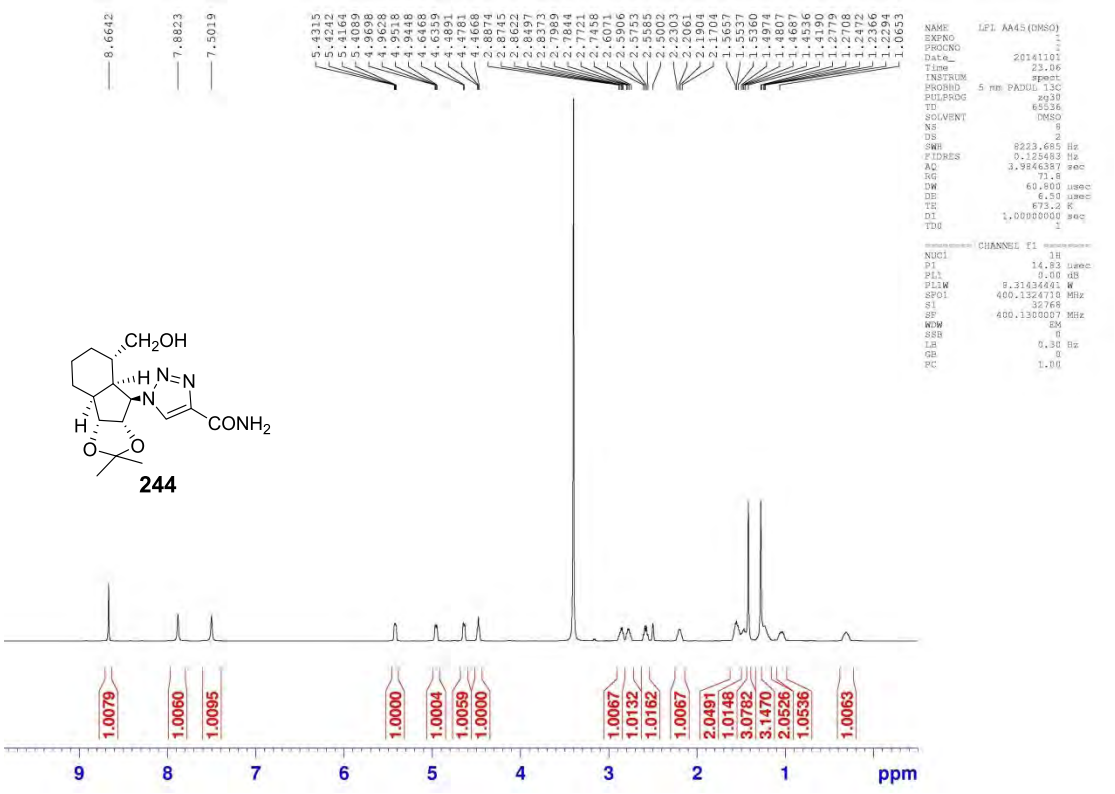

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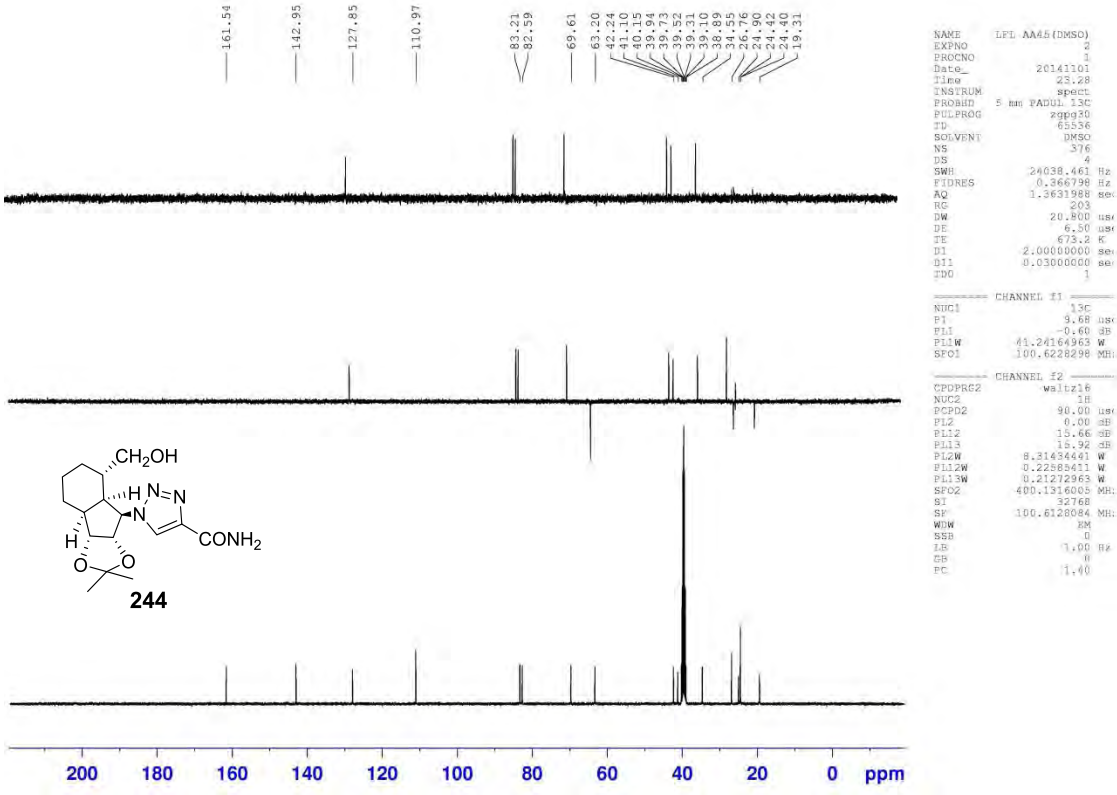

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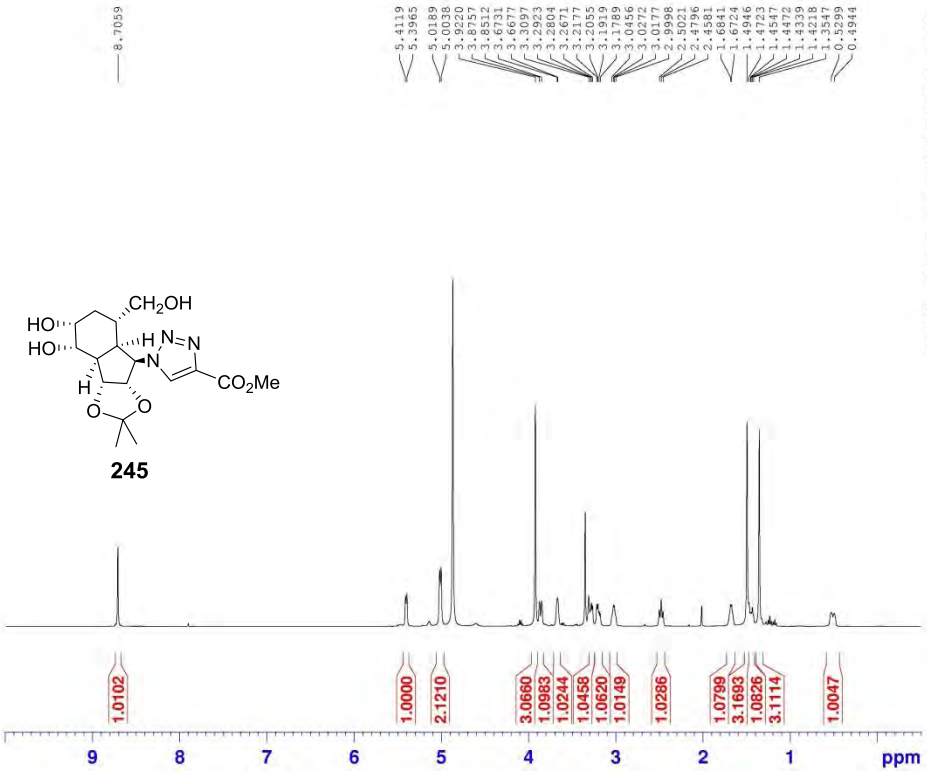

245

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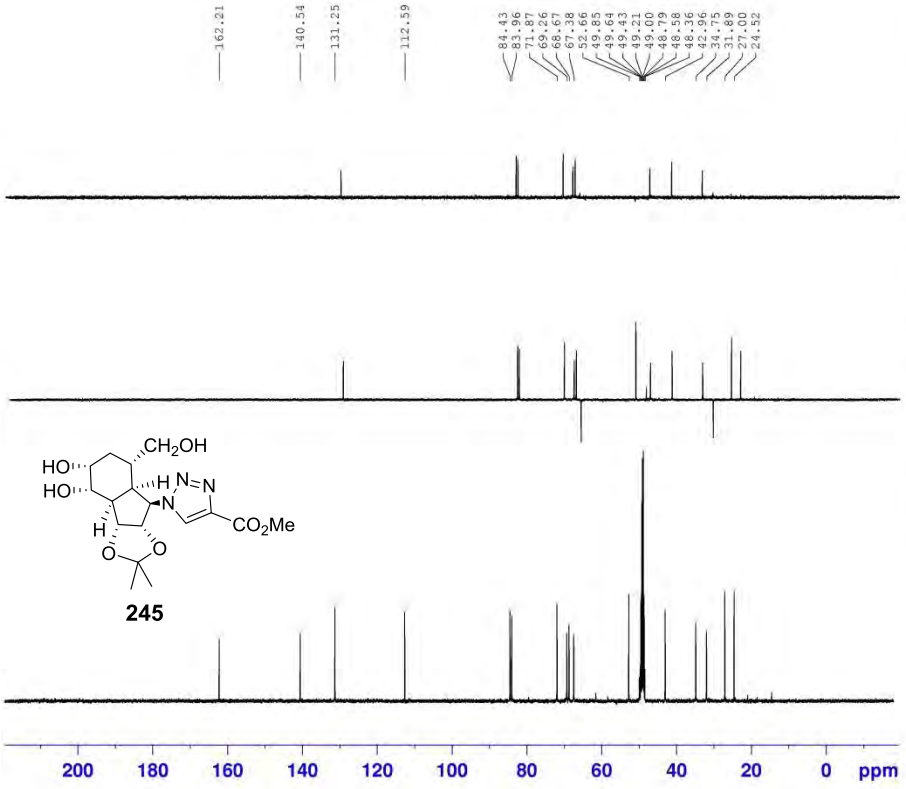
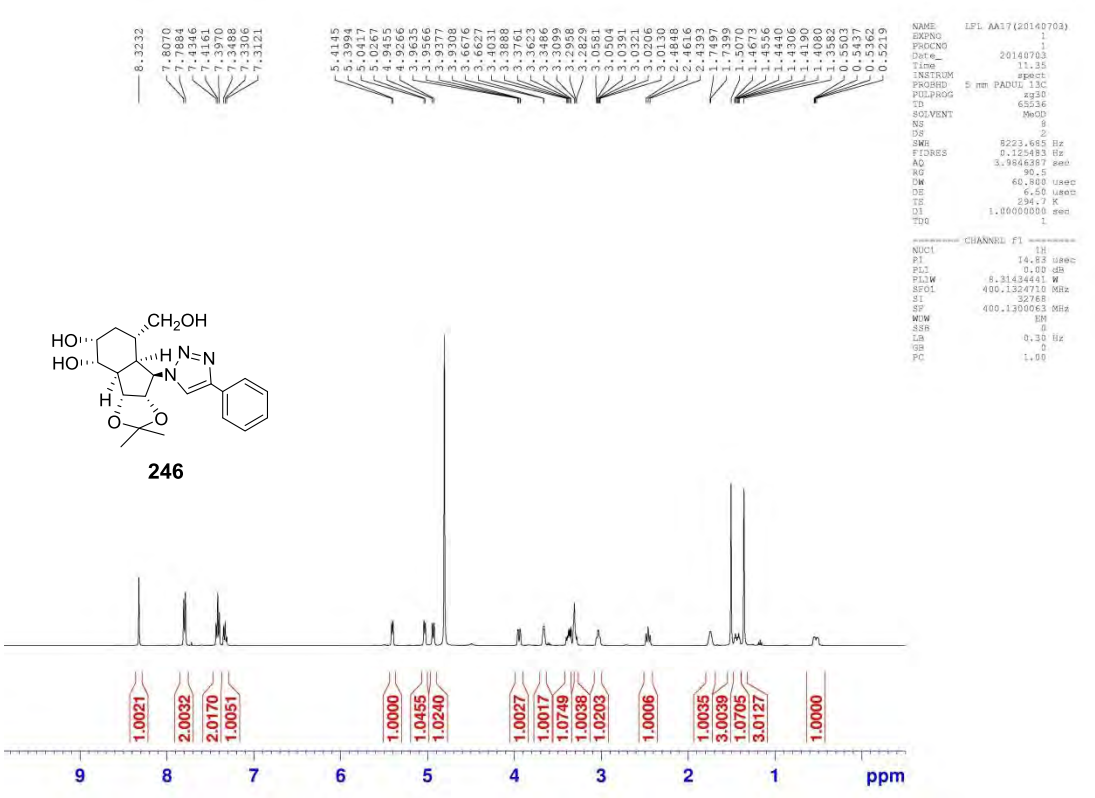


245

^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



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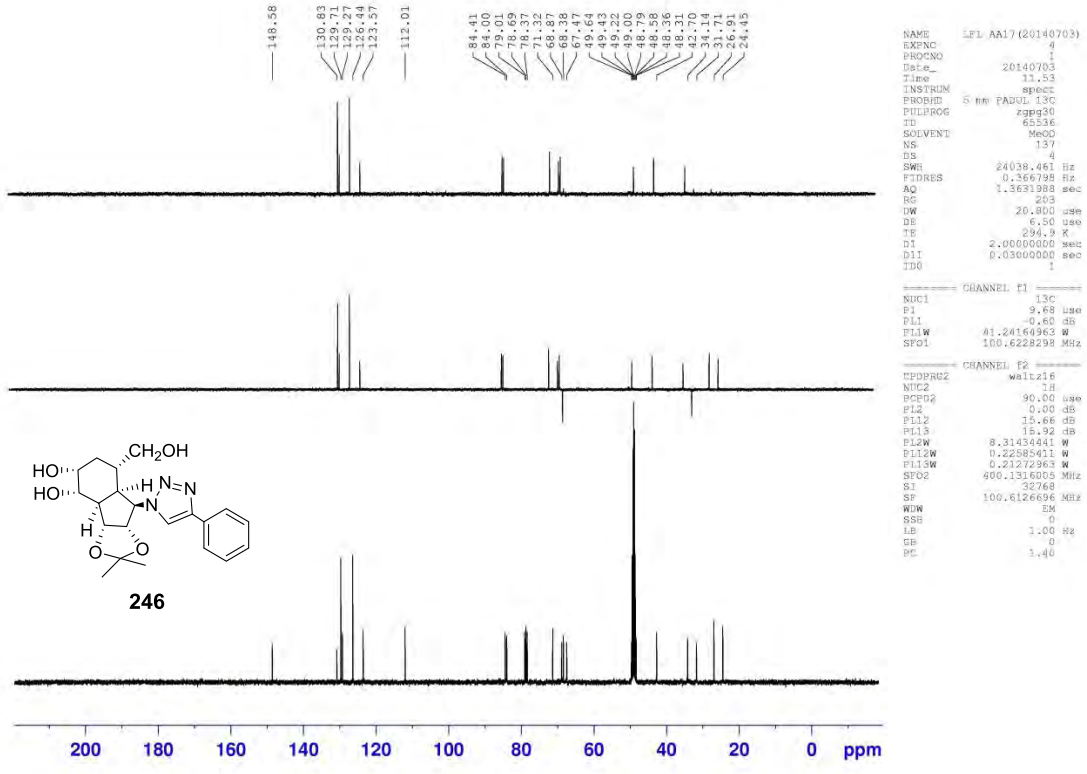

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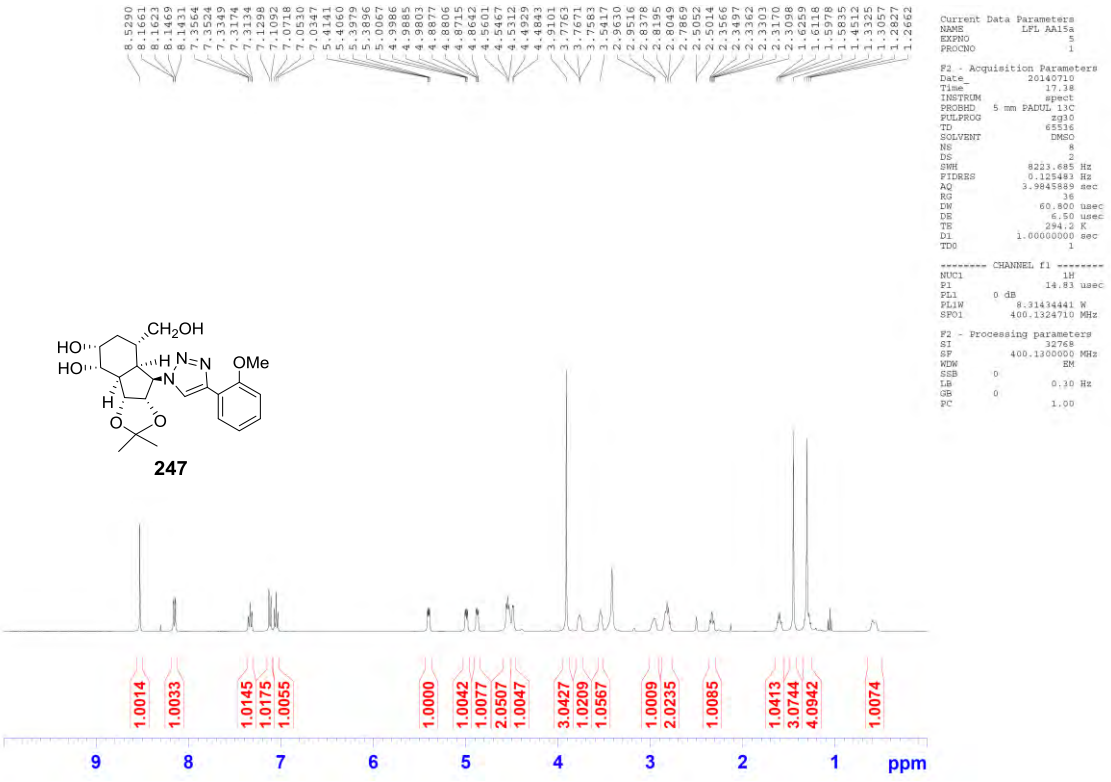

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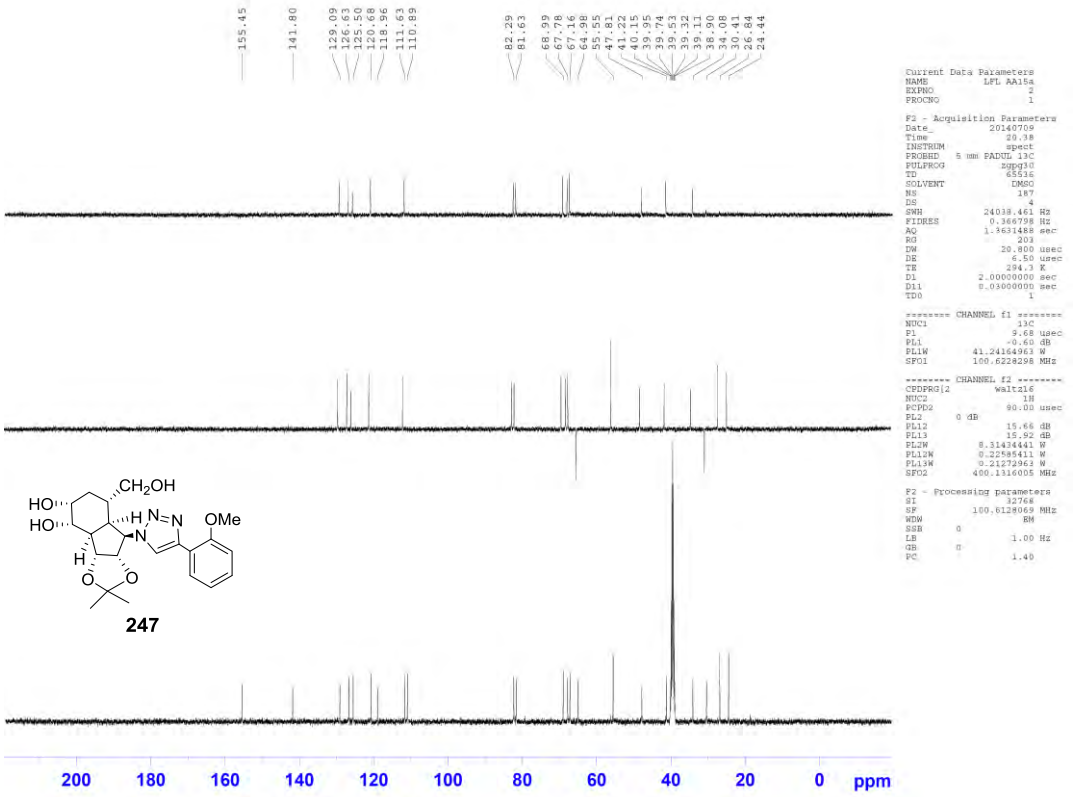
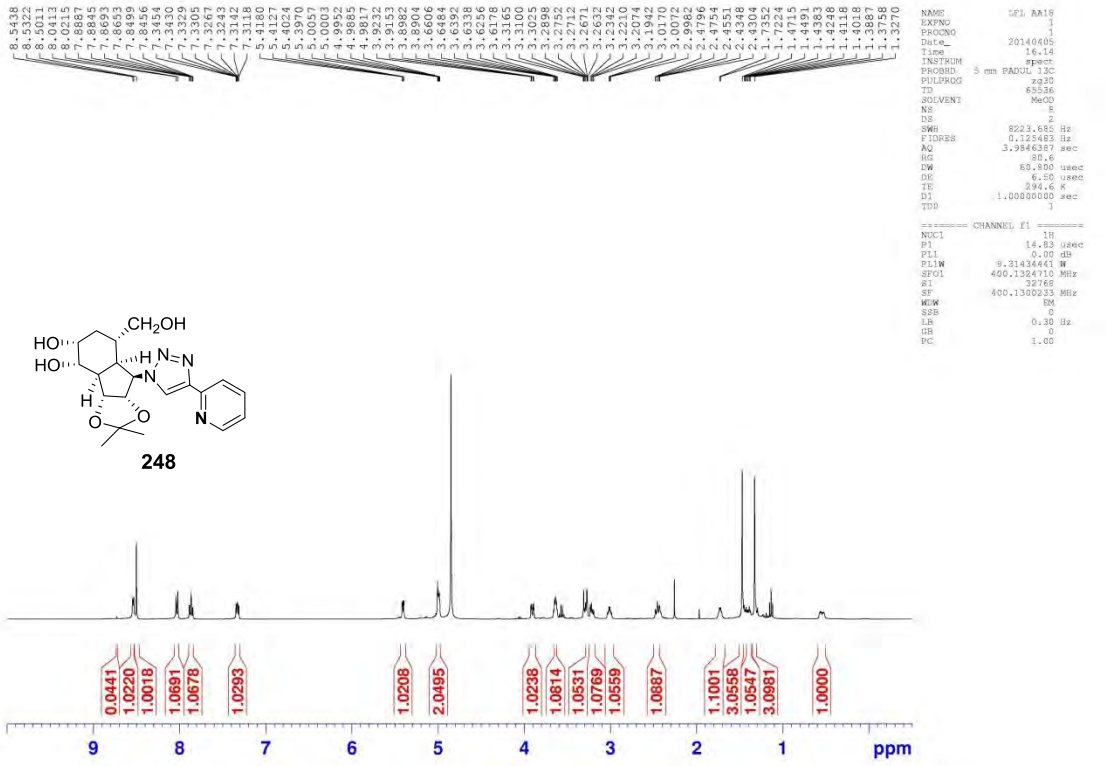
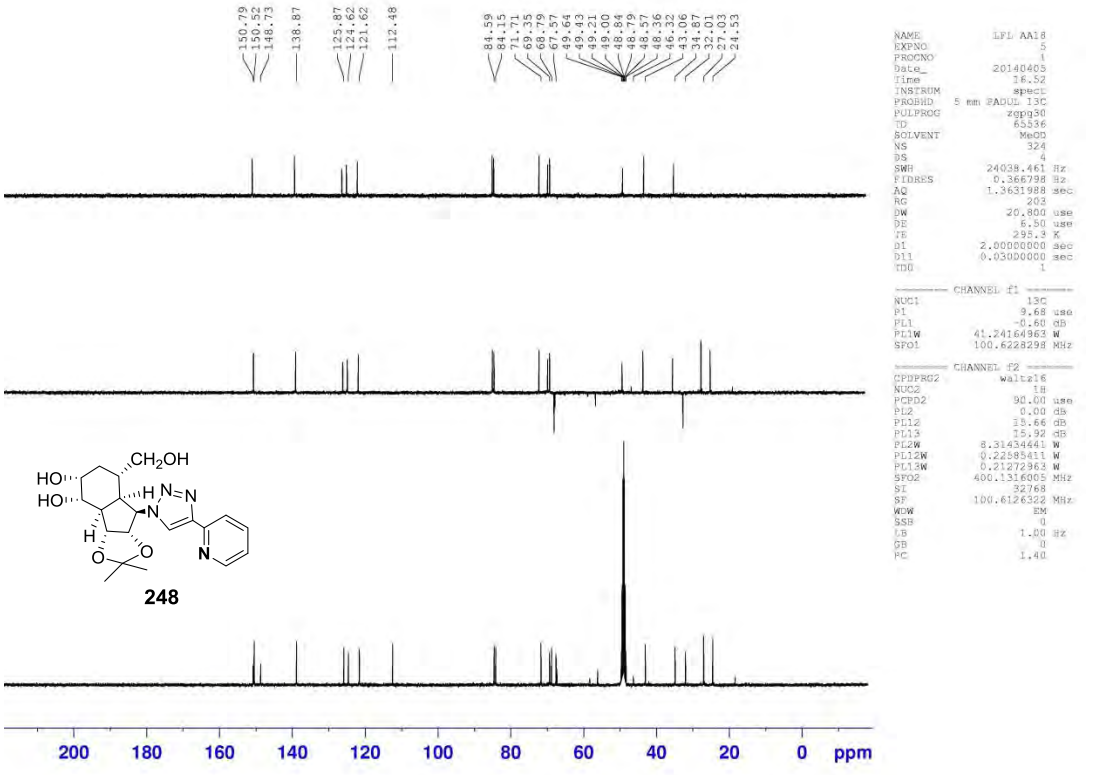


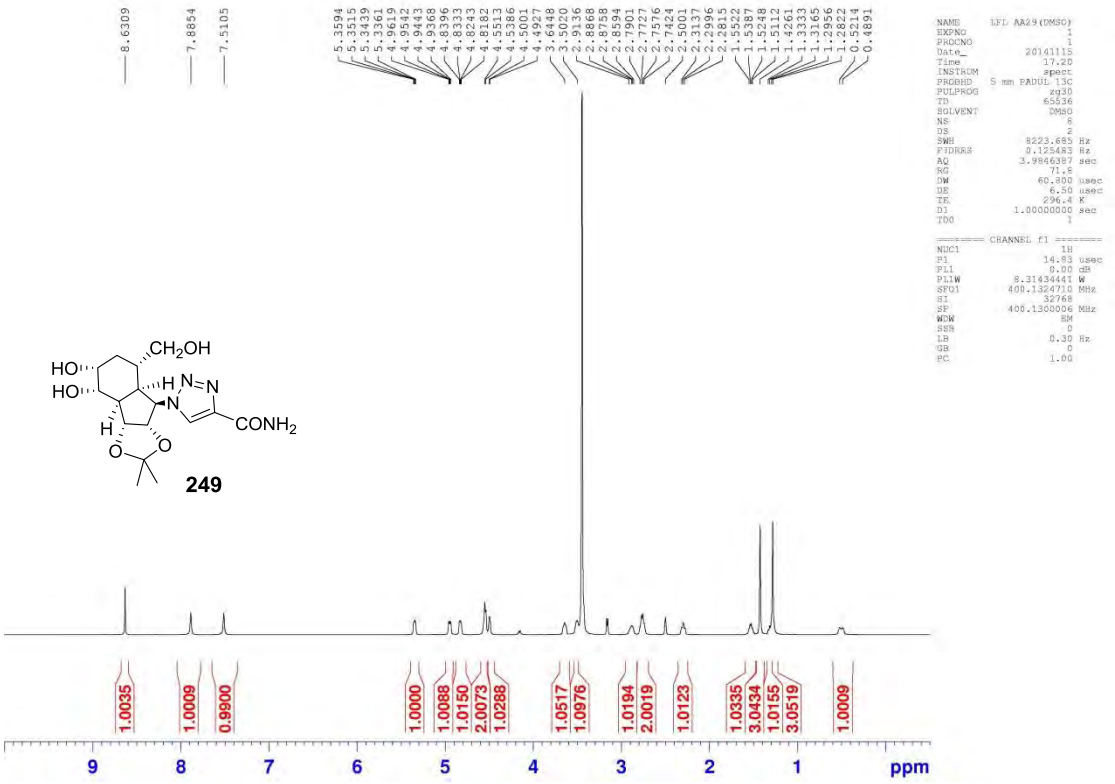
^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)



^{1}H NMR (Solvent: DMSO-d_6)



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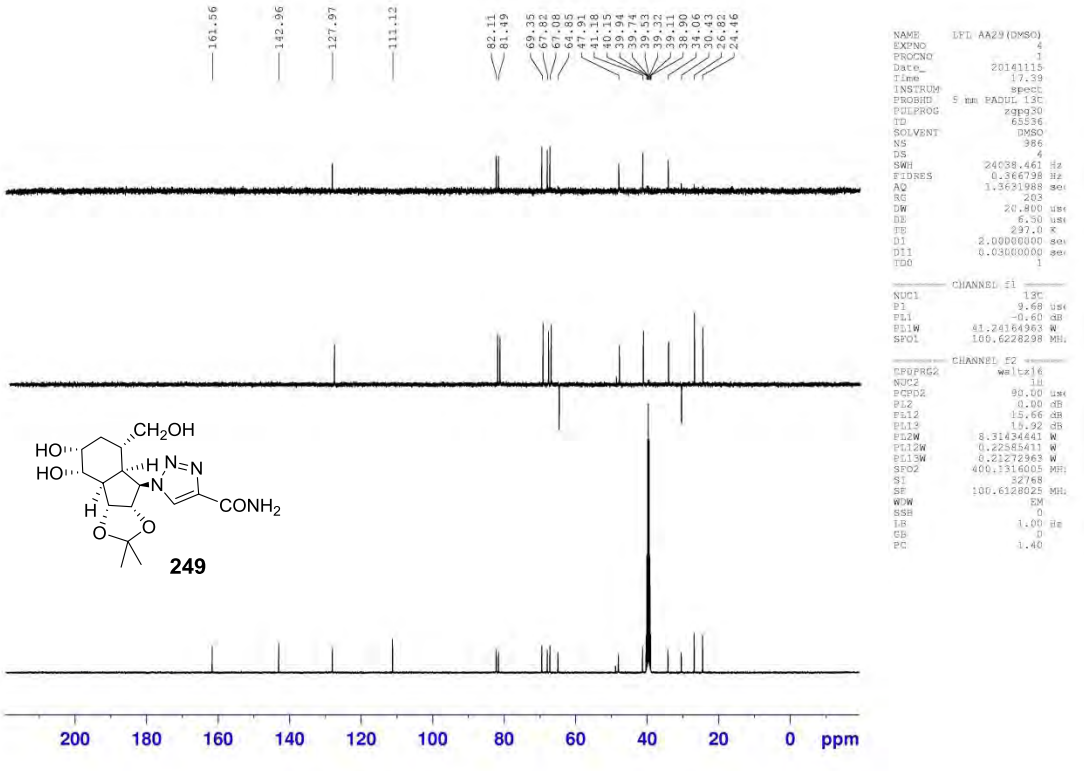

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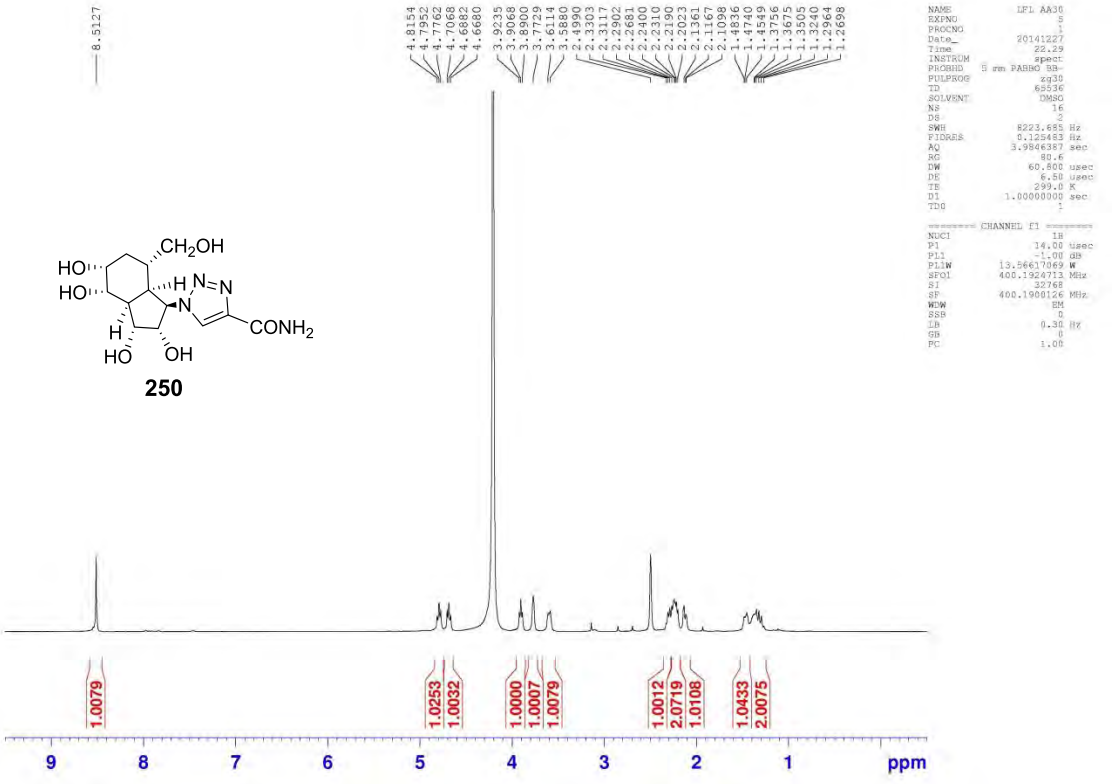

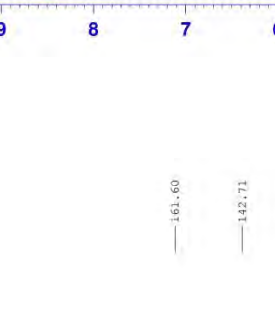

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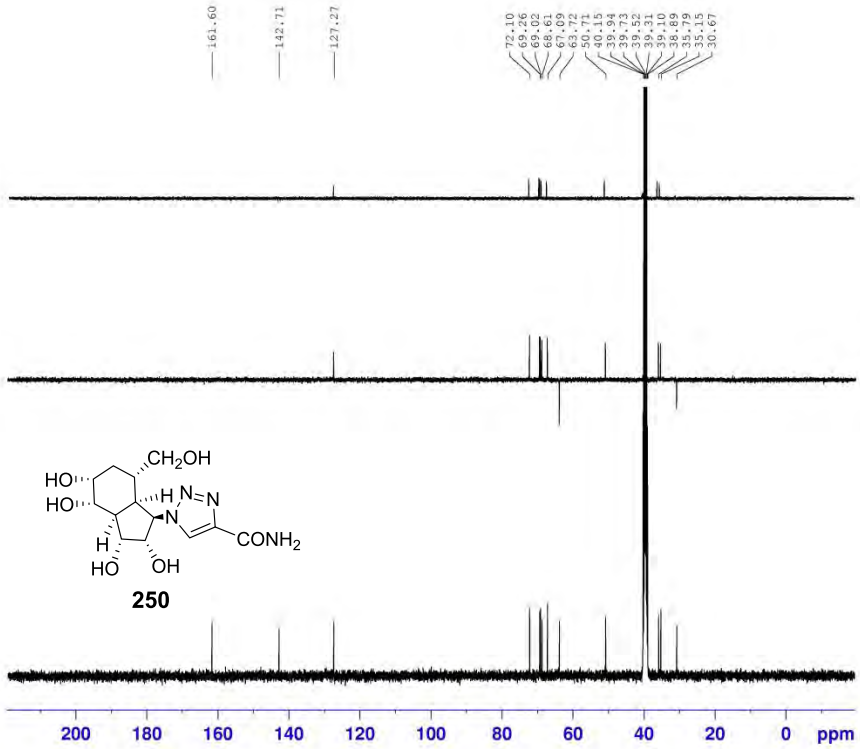

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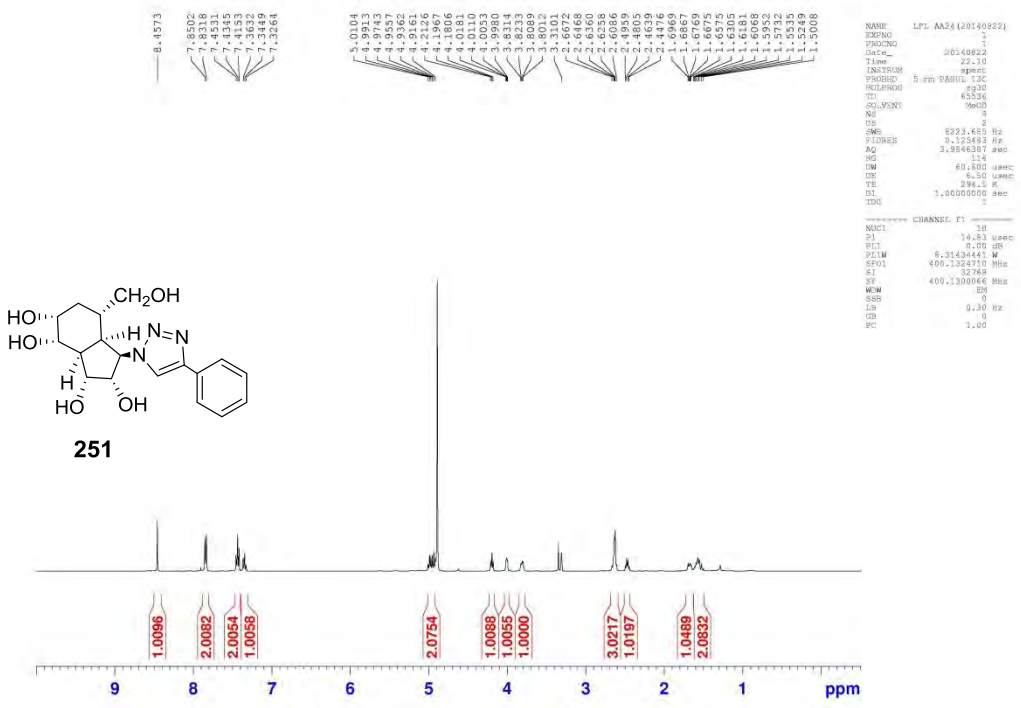

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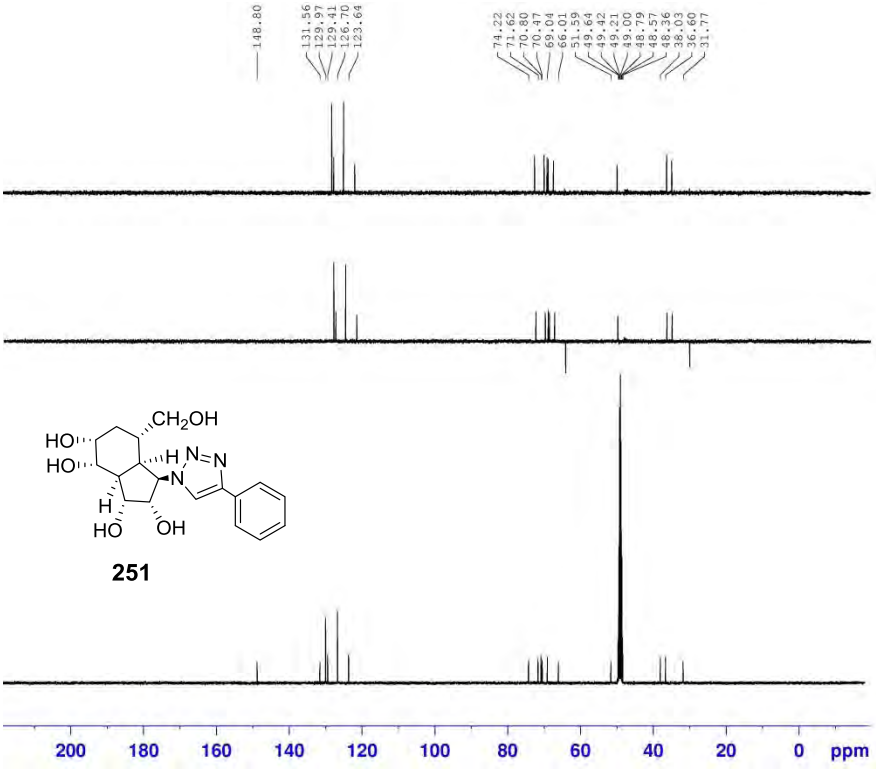

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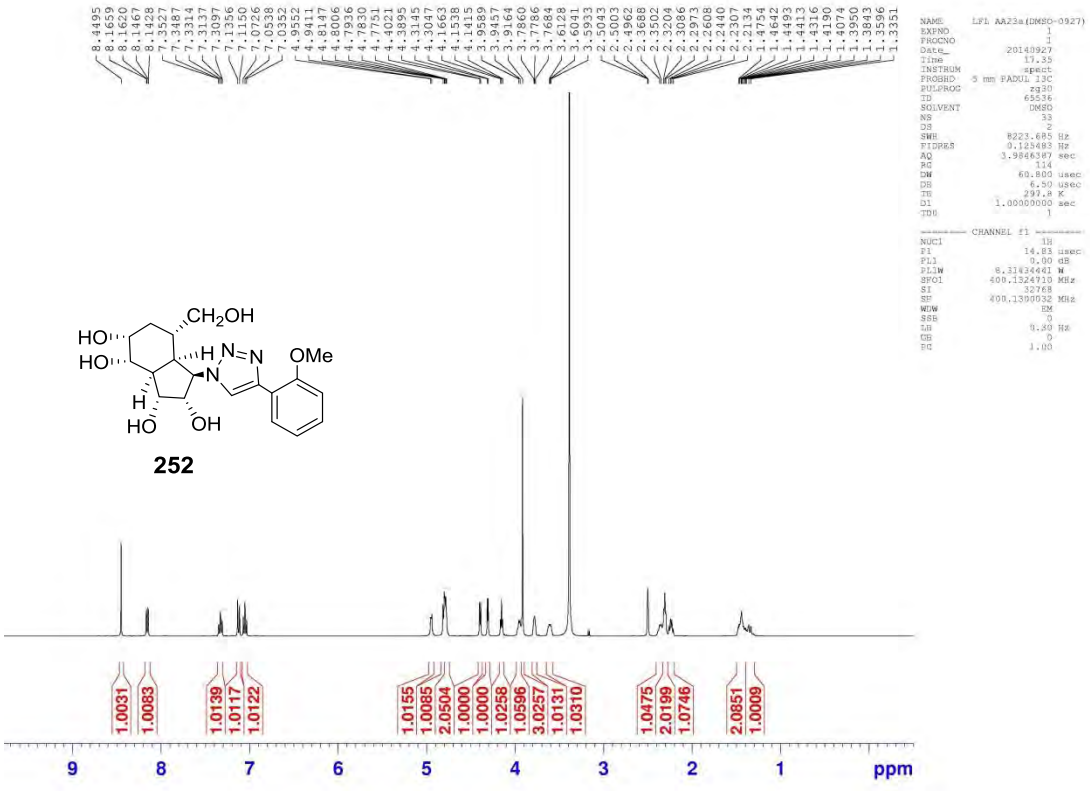

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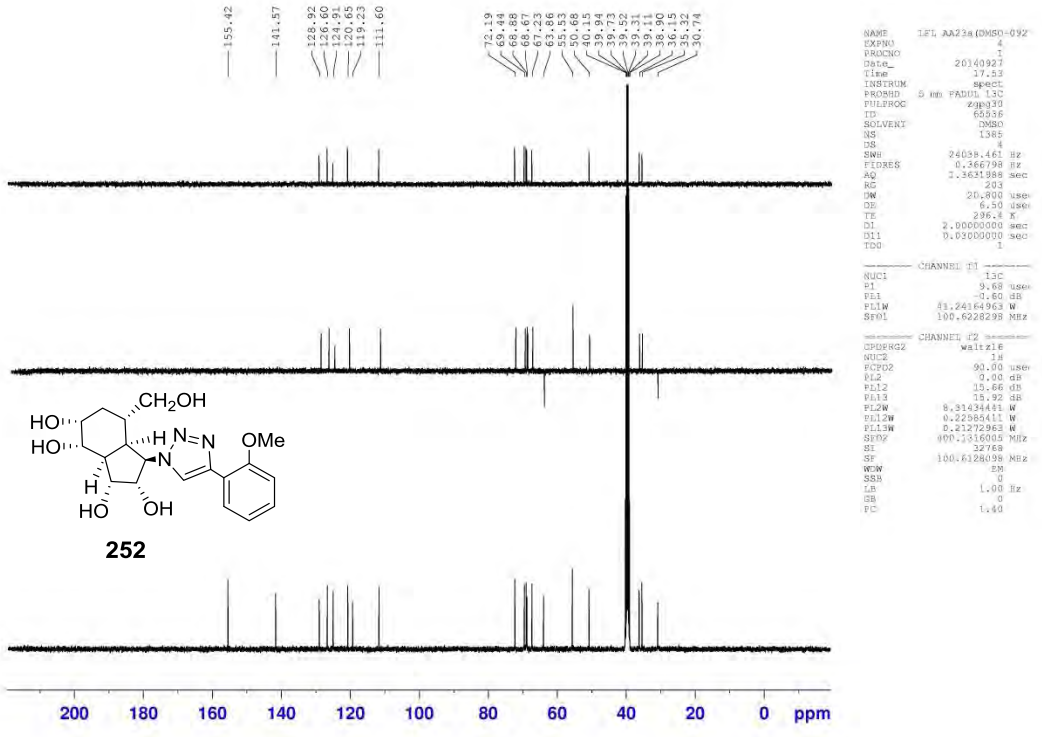

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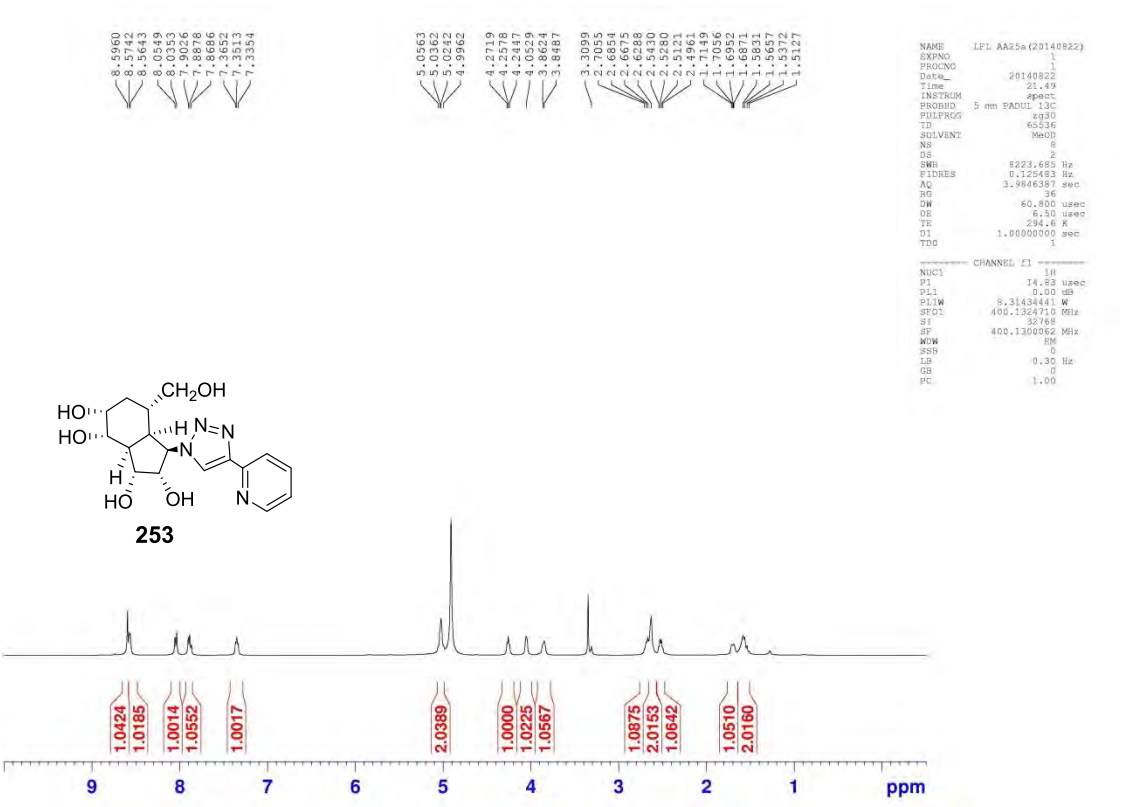

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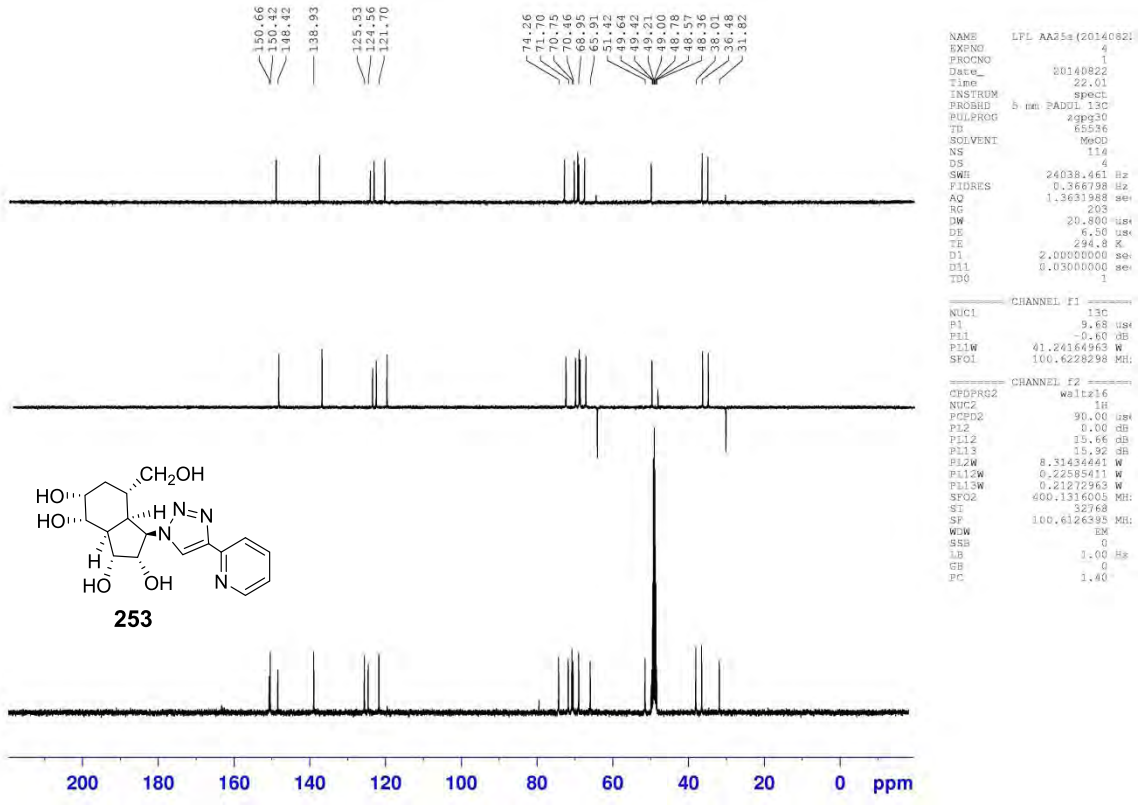
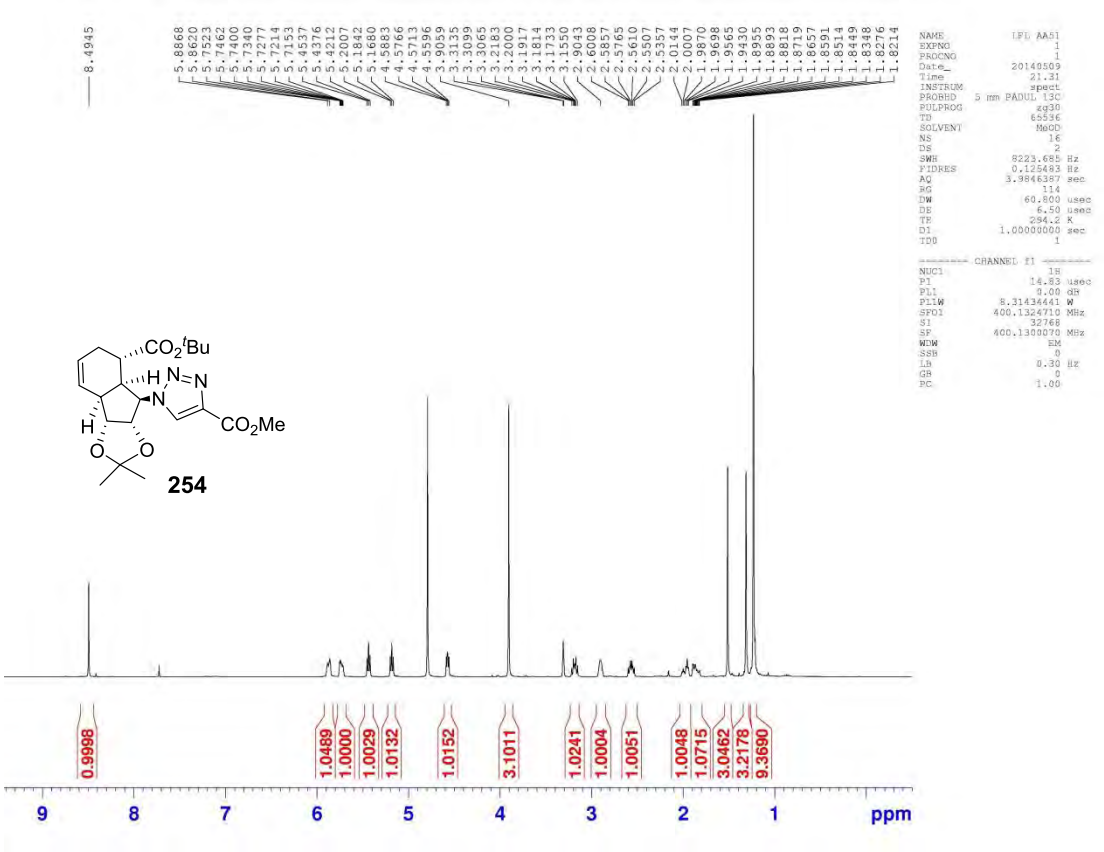


^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



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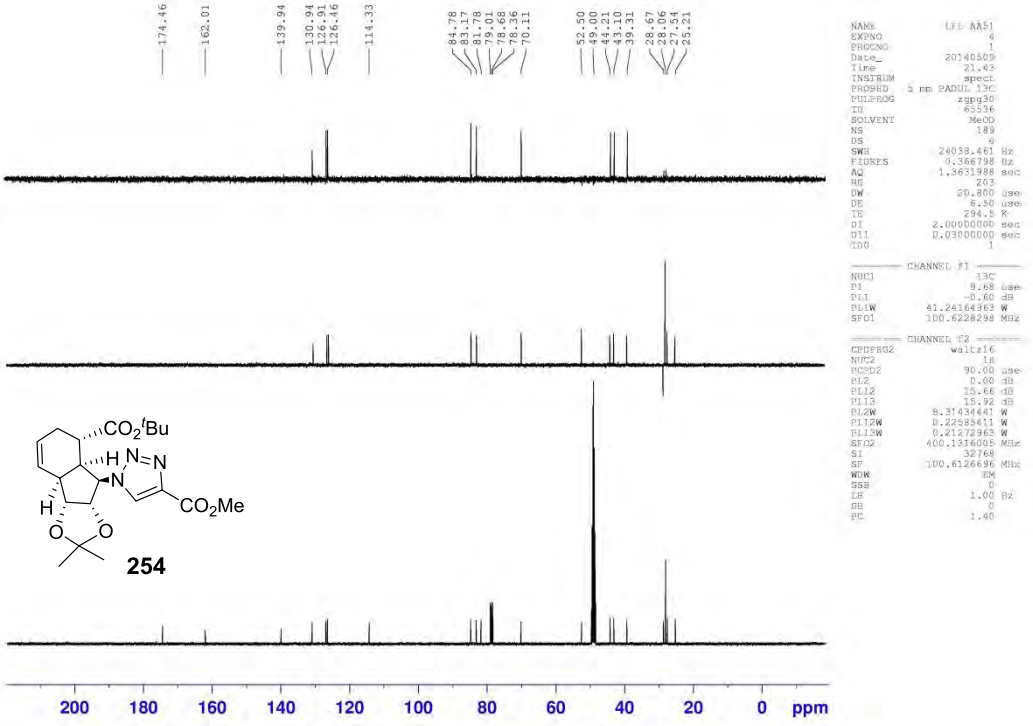

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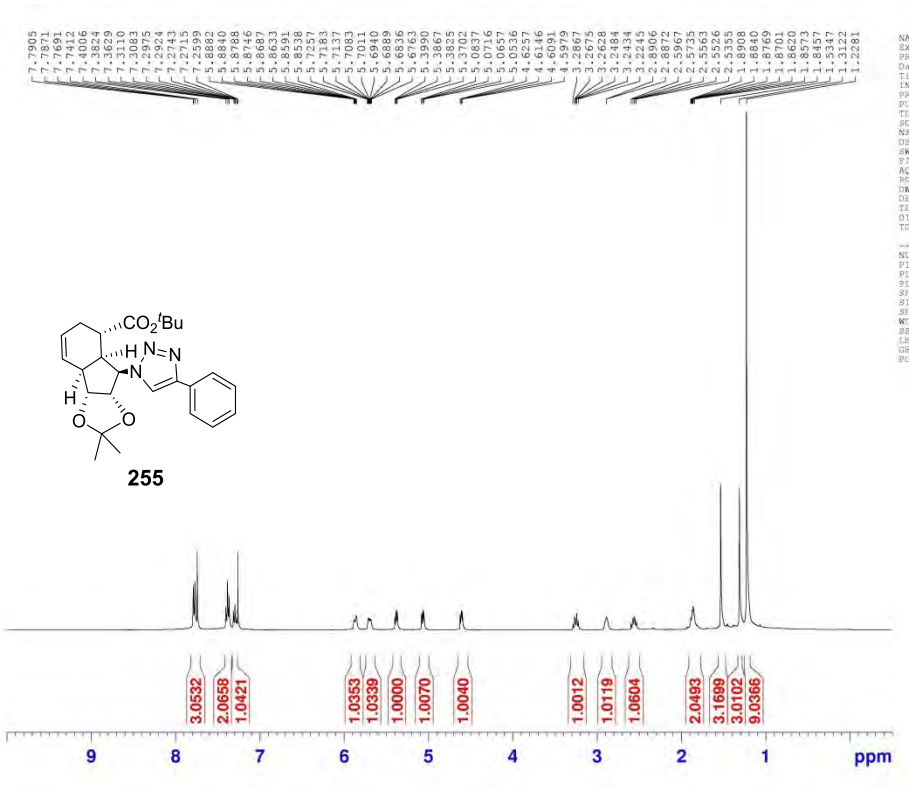
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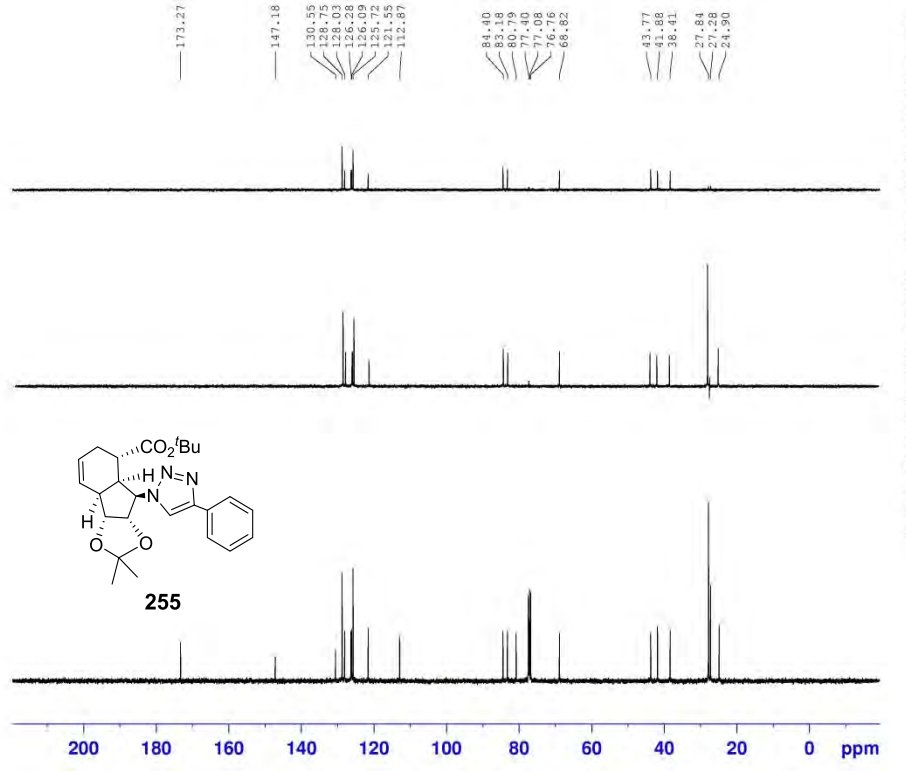
^{13}C NMR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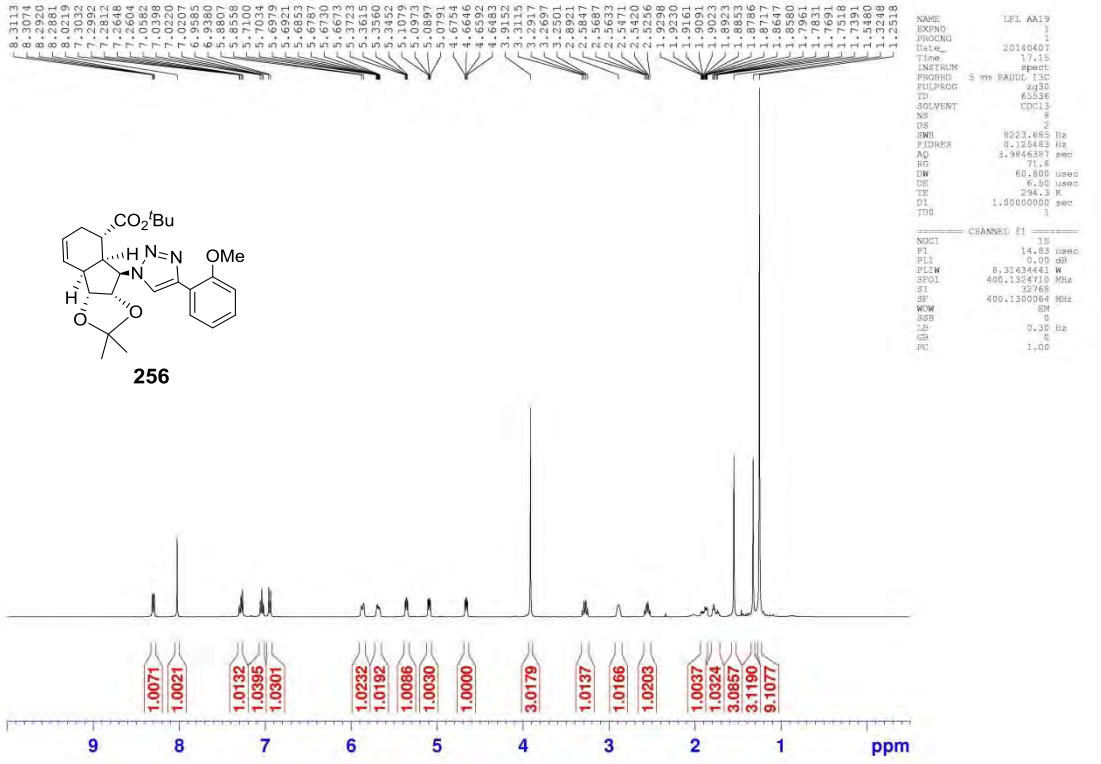
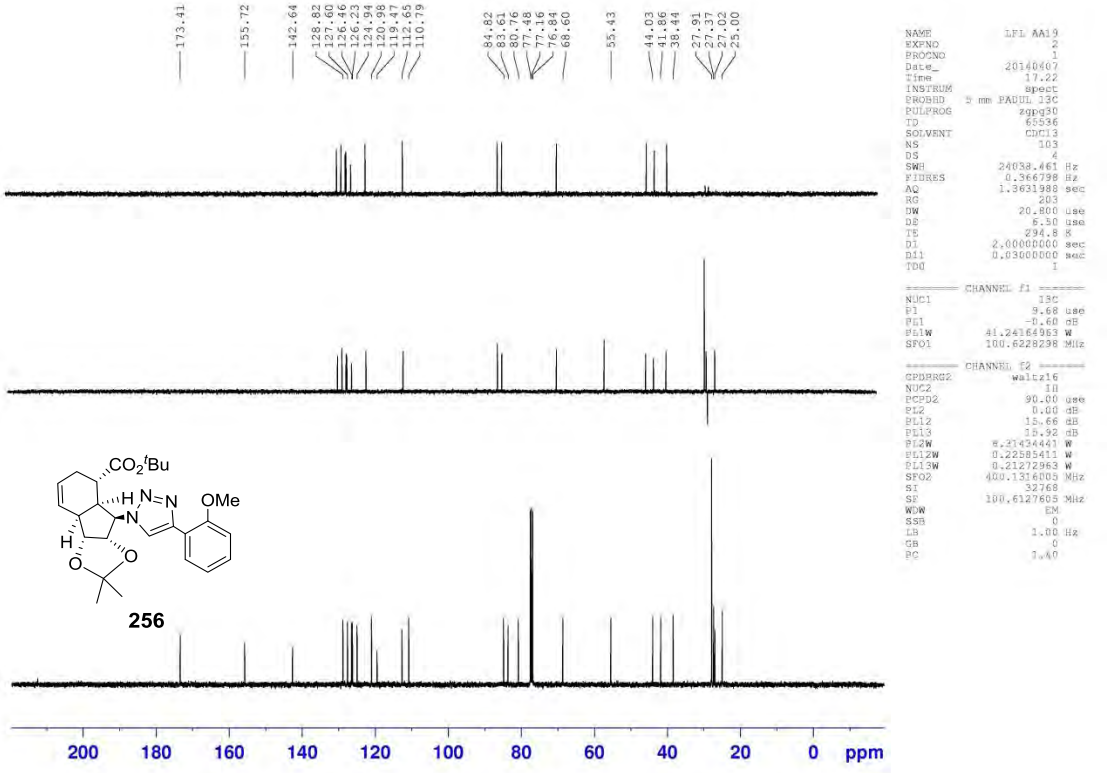
ppm

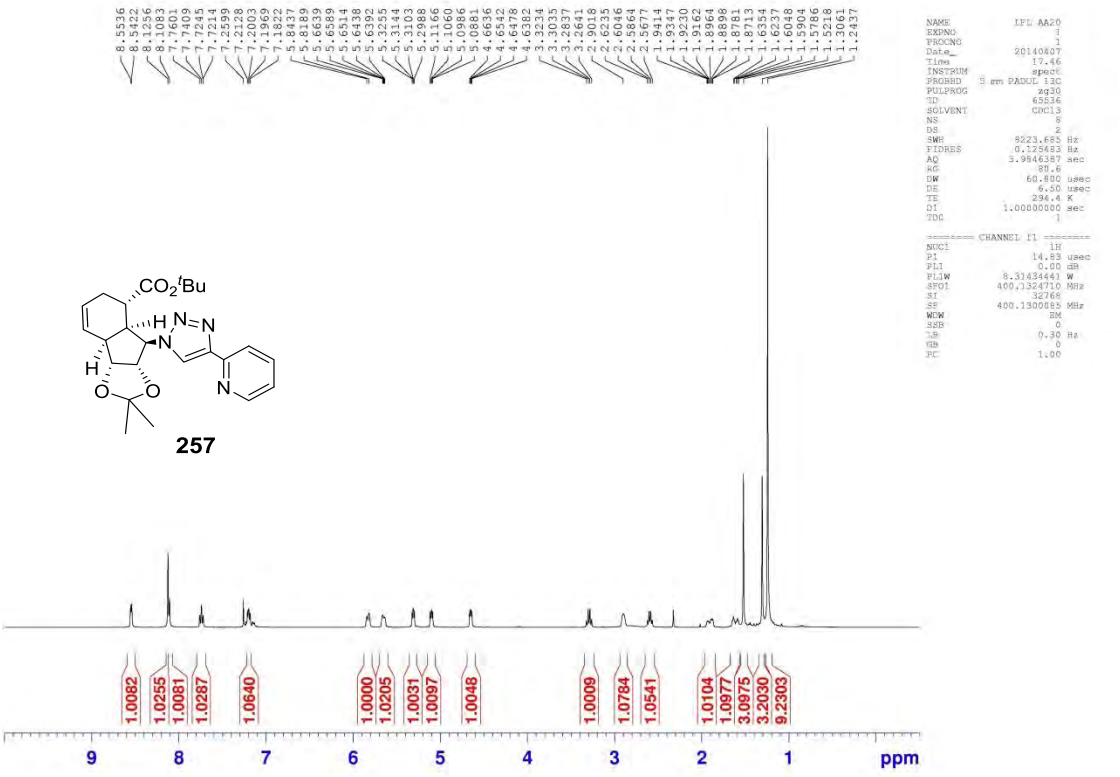
^{1}H NMR



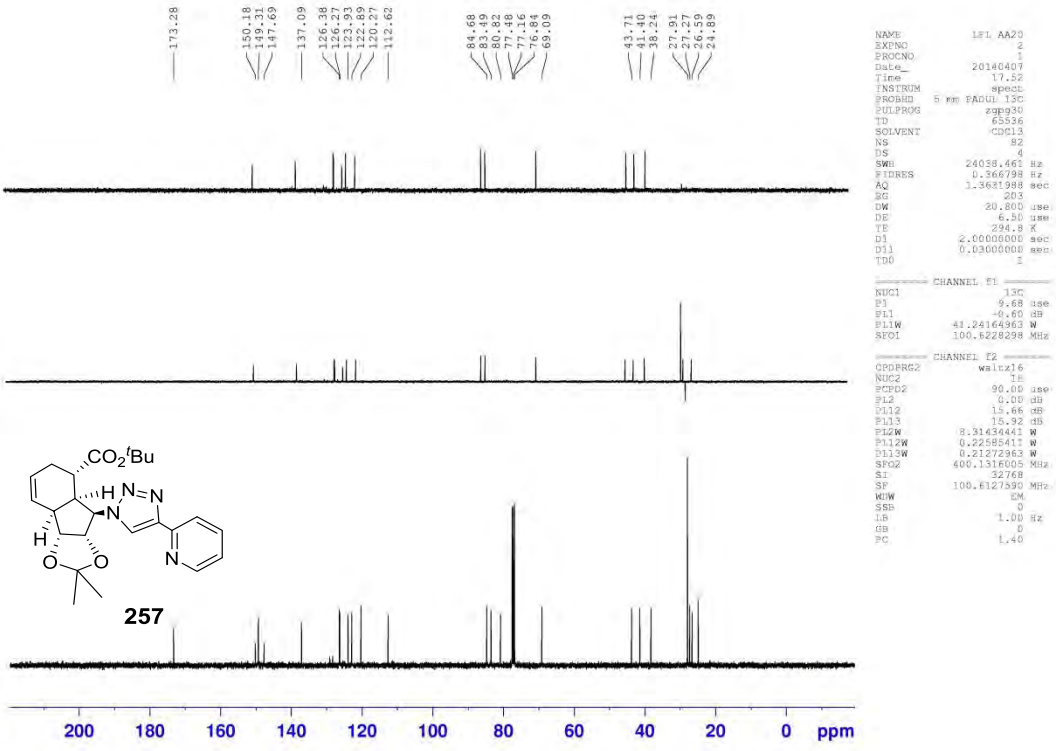
^{13}C NMR



^{1}H NMR



^{13}C NMR



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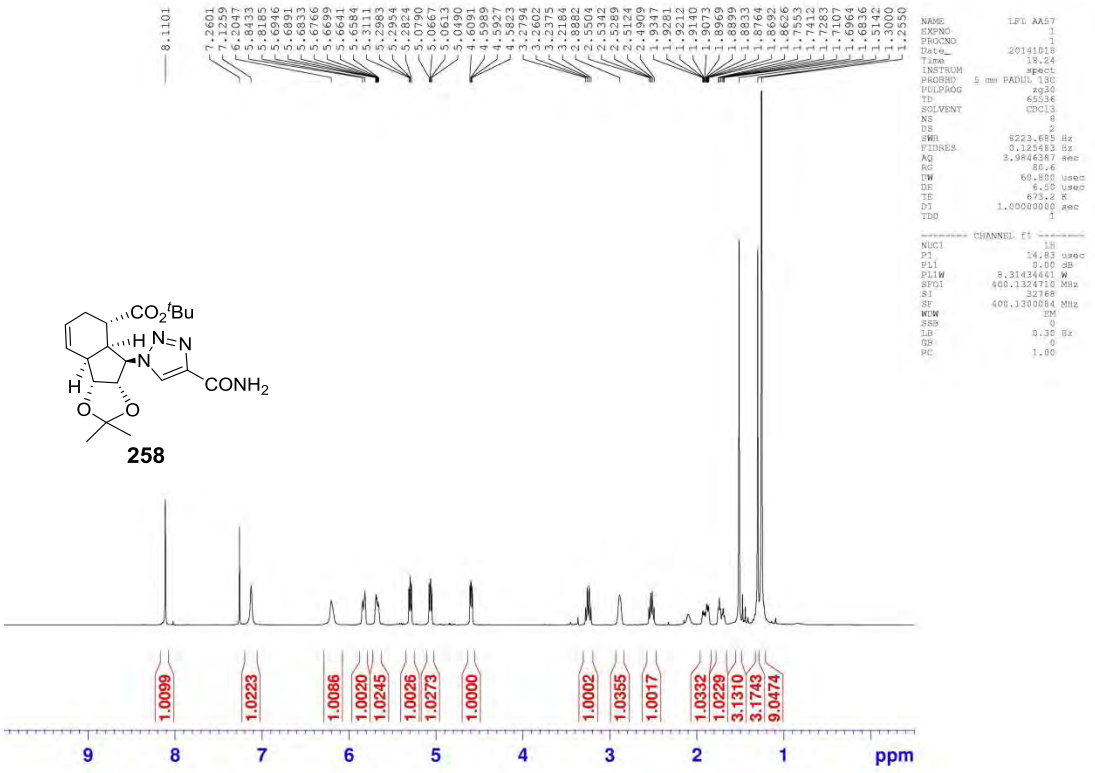

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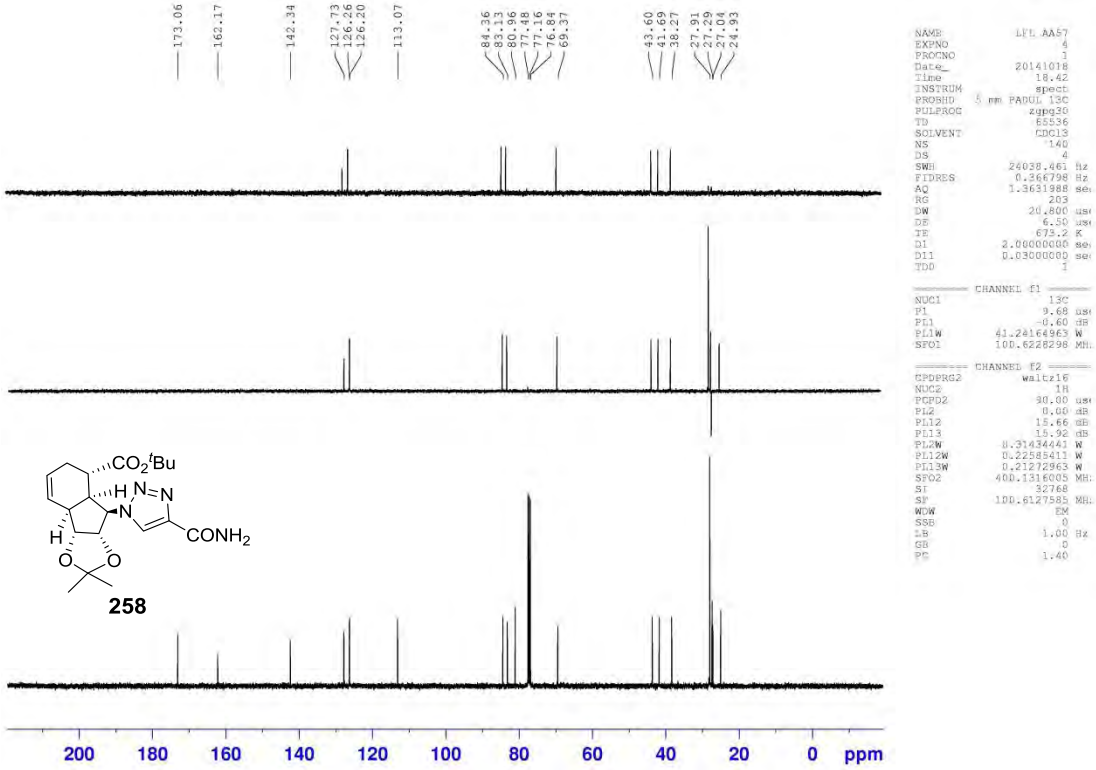
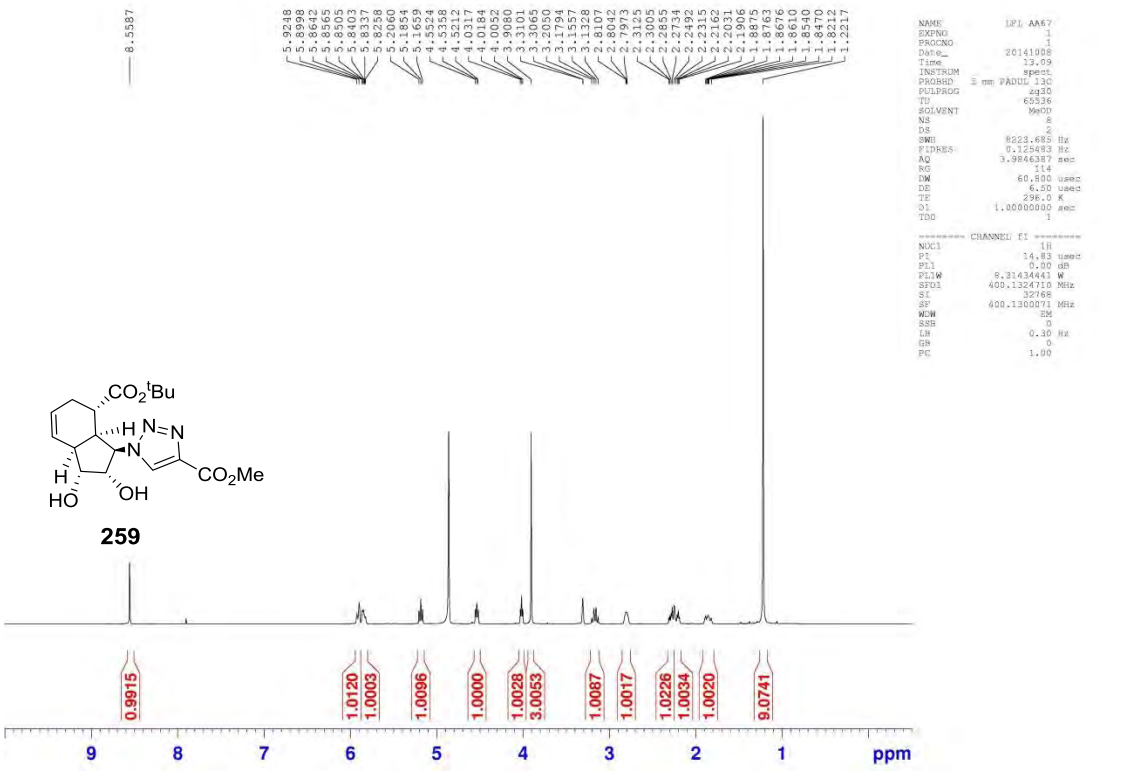
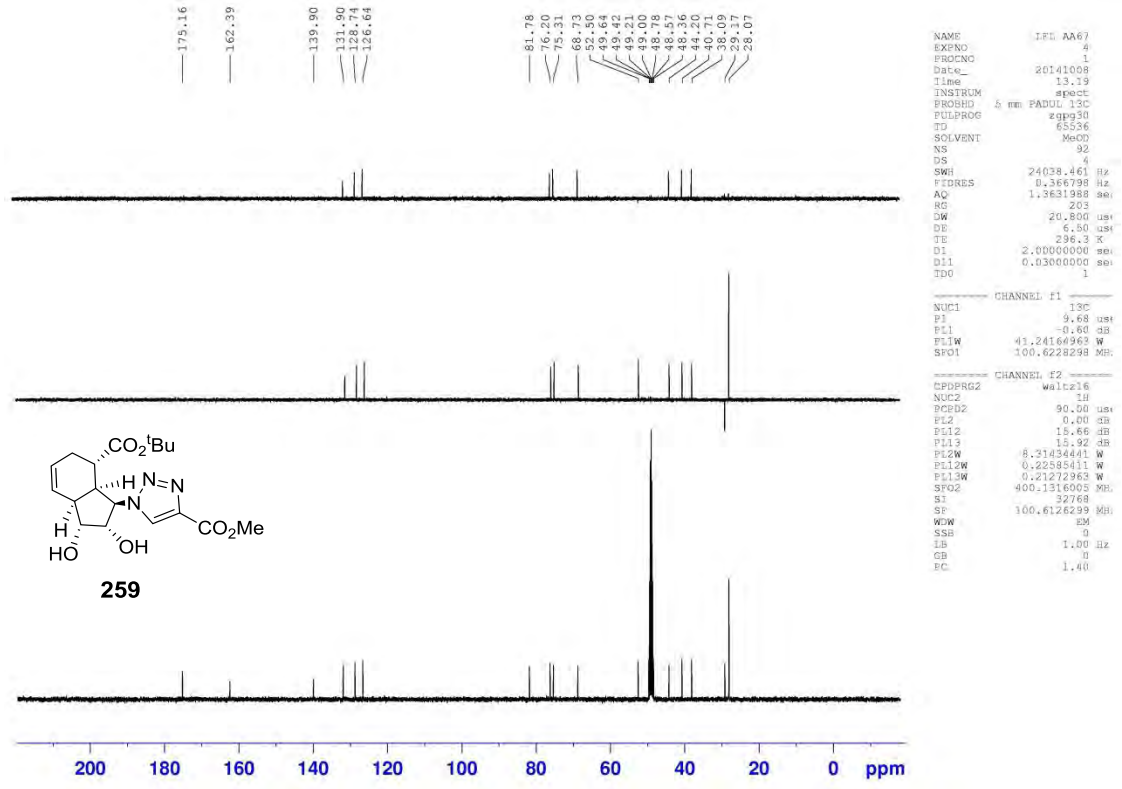


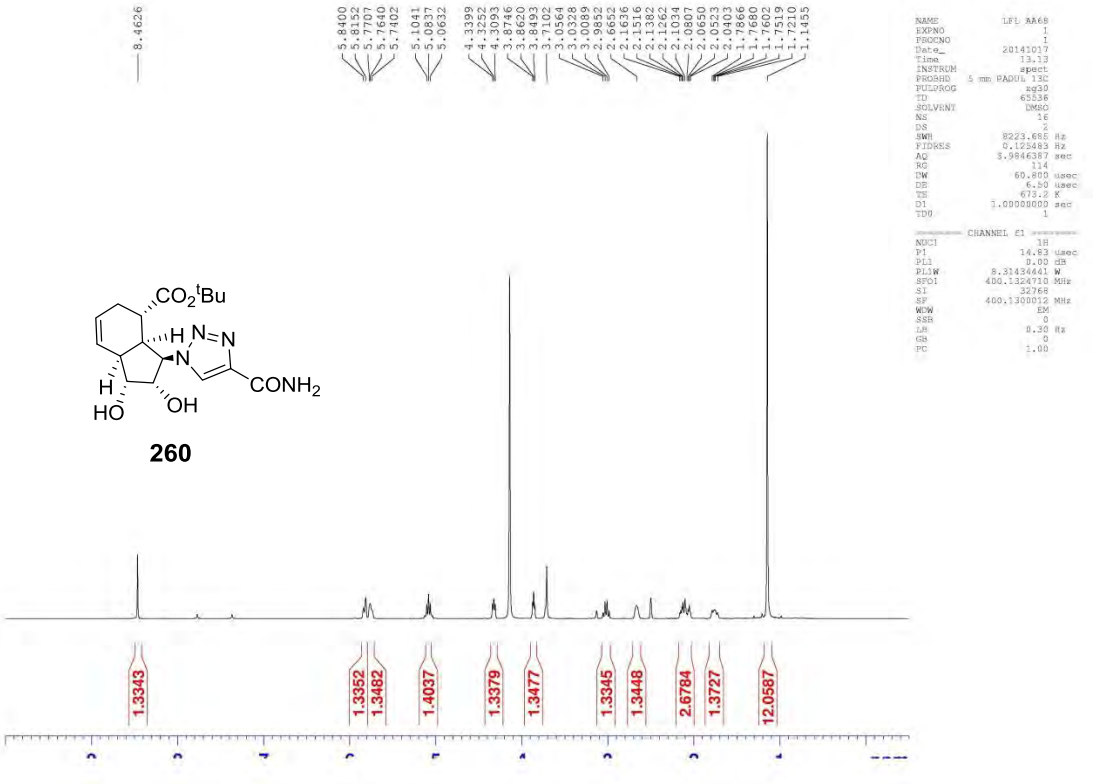
^{1}H NMR (Solvent: CD_3OD)



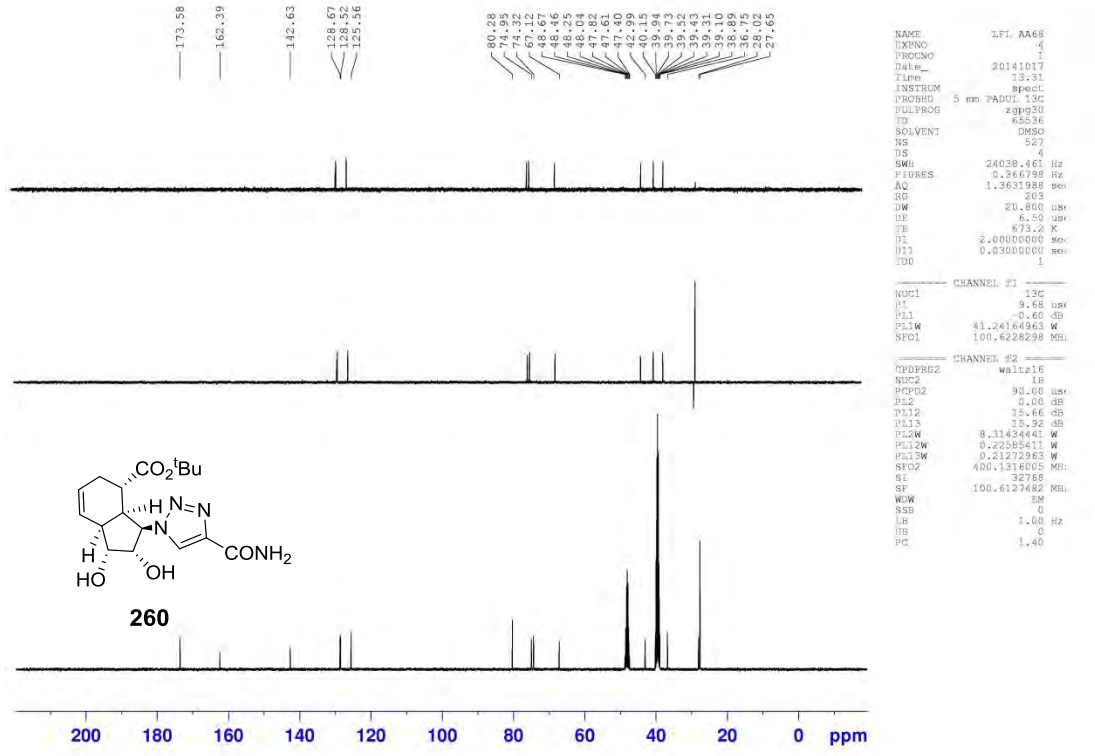
^{13}C NMR (Solvent: CD_3OD)



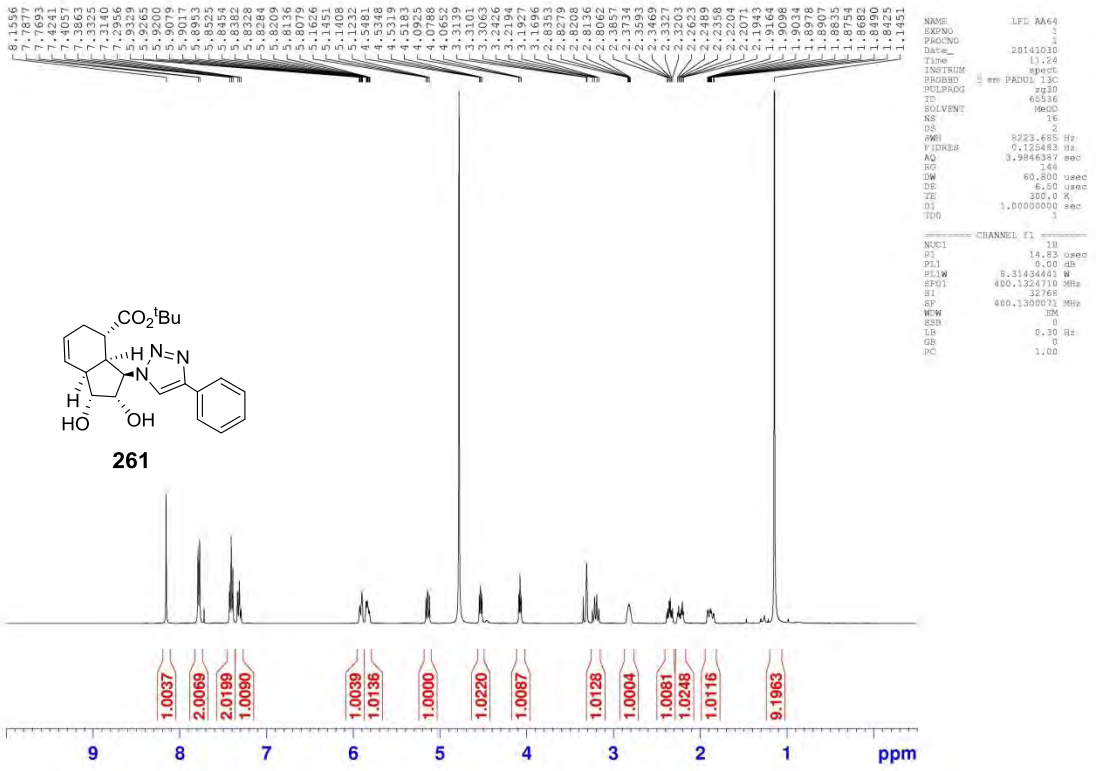
^{1}H NMR (Solvent: DMSO-d_6)



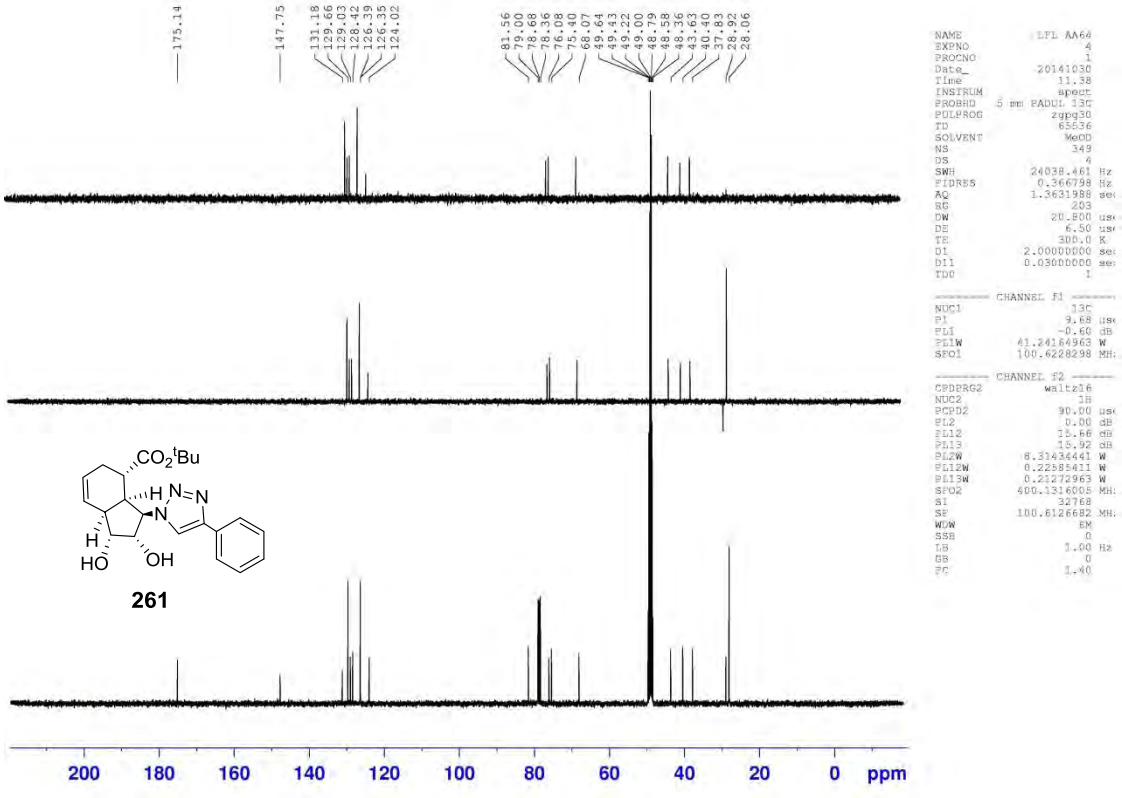
^{13}C NMR (Solvent: DMSO-d_6)



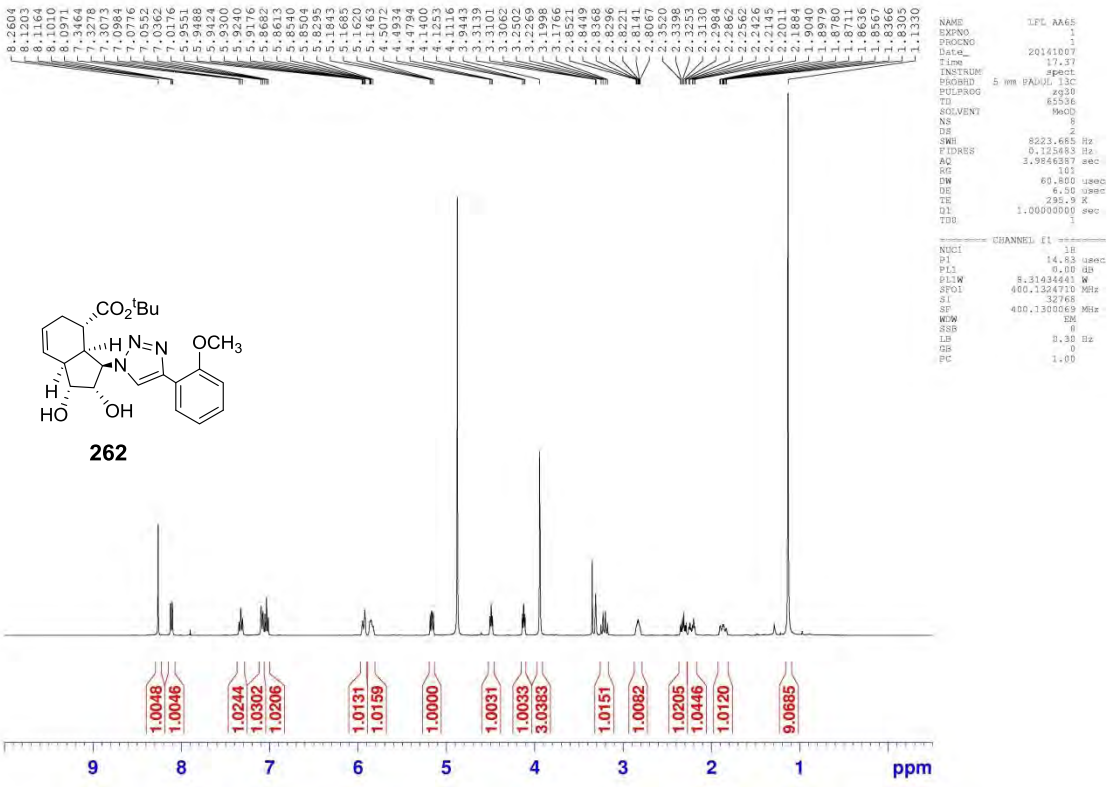
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 3:1)



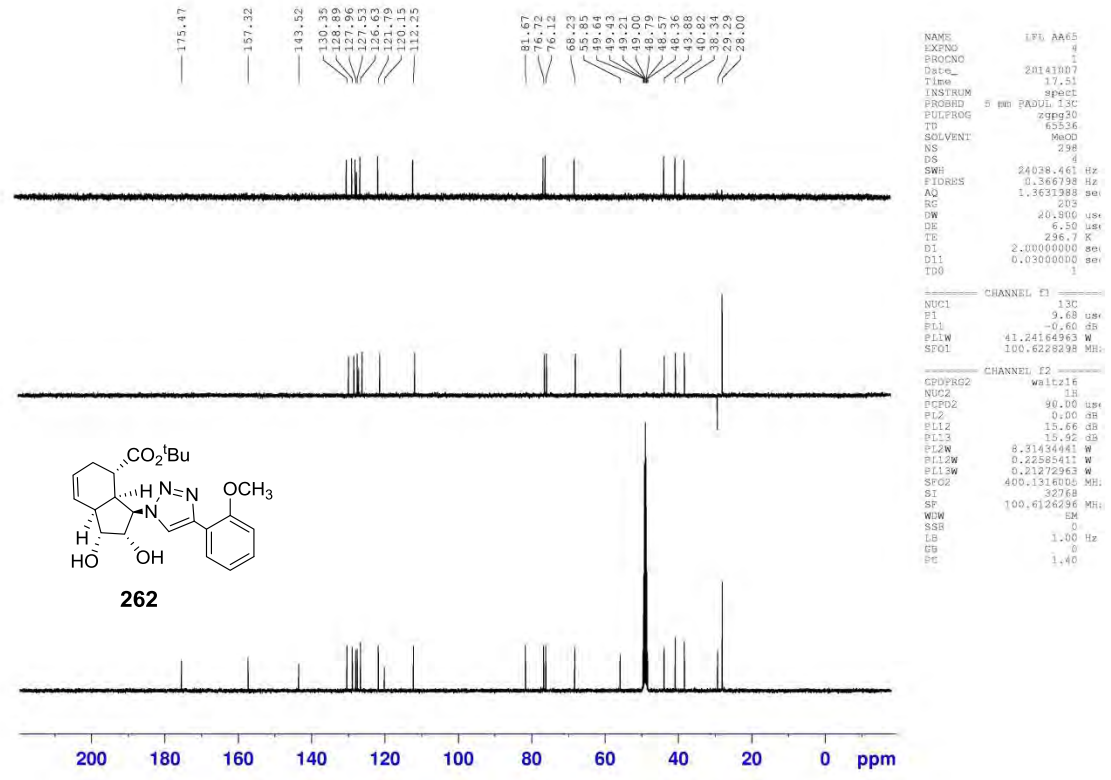
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 3:1)



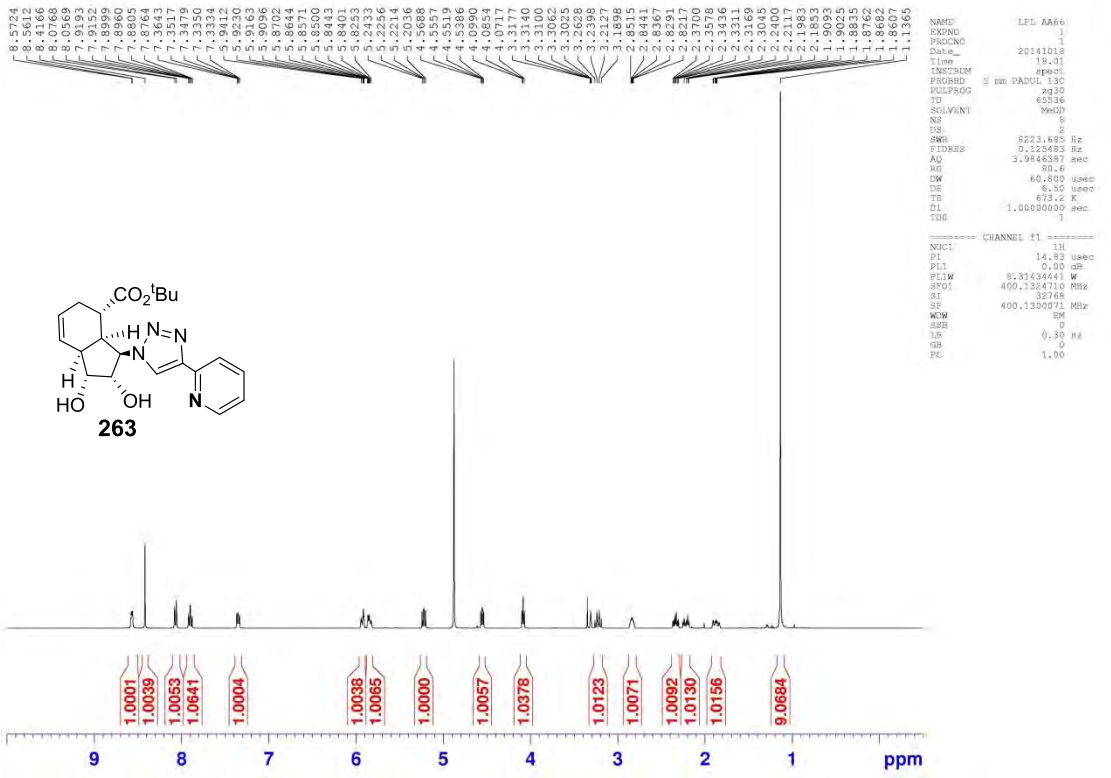
^{1}H NMR (Solvent: CD_3OD)



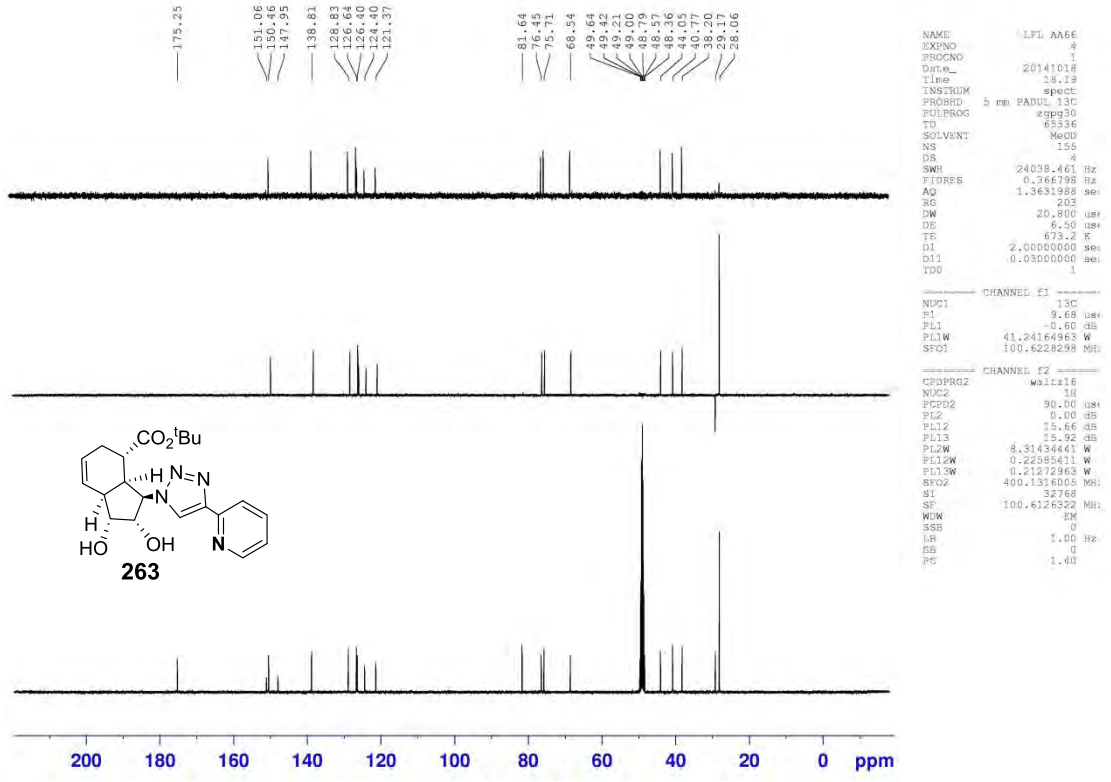
^{13}C NMR (Solvent: CD_3OD)



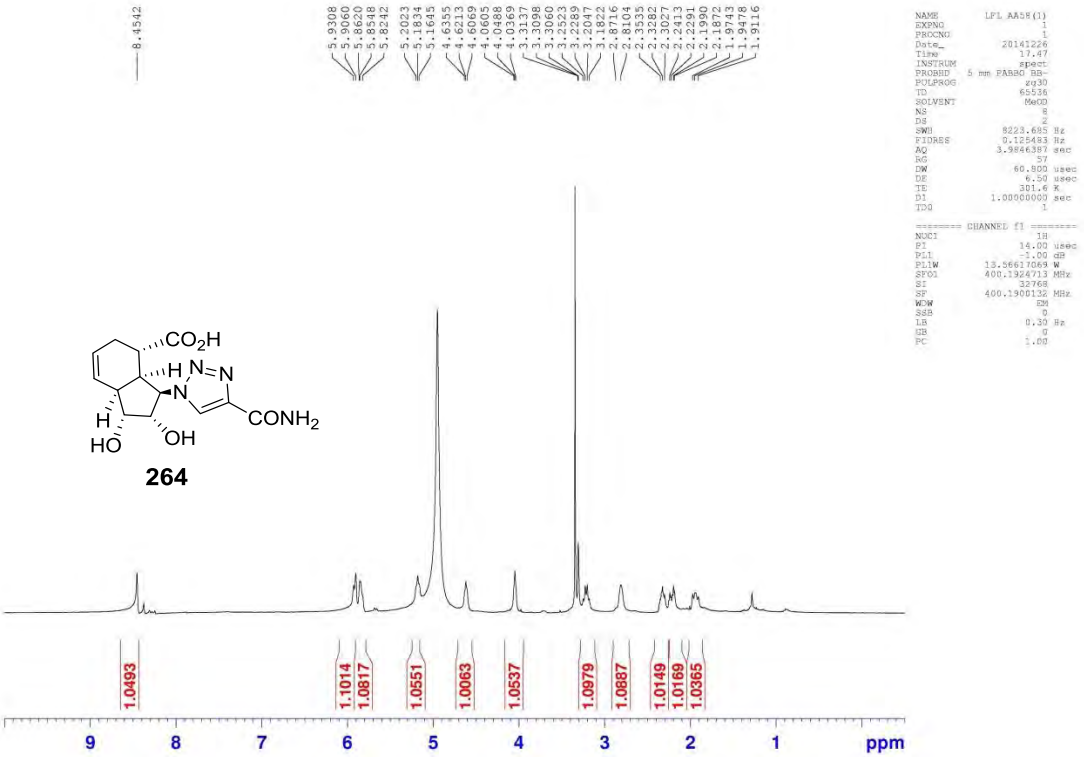
^{1}H NMR (Solvent: CD_3OD)



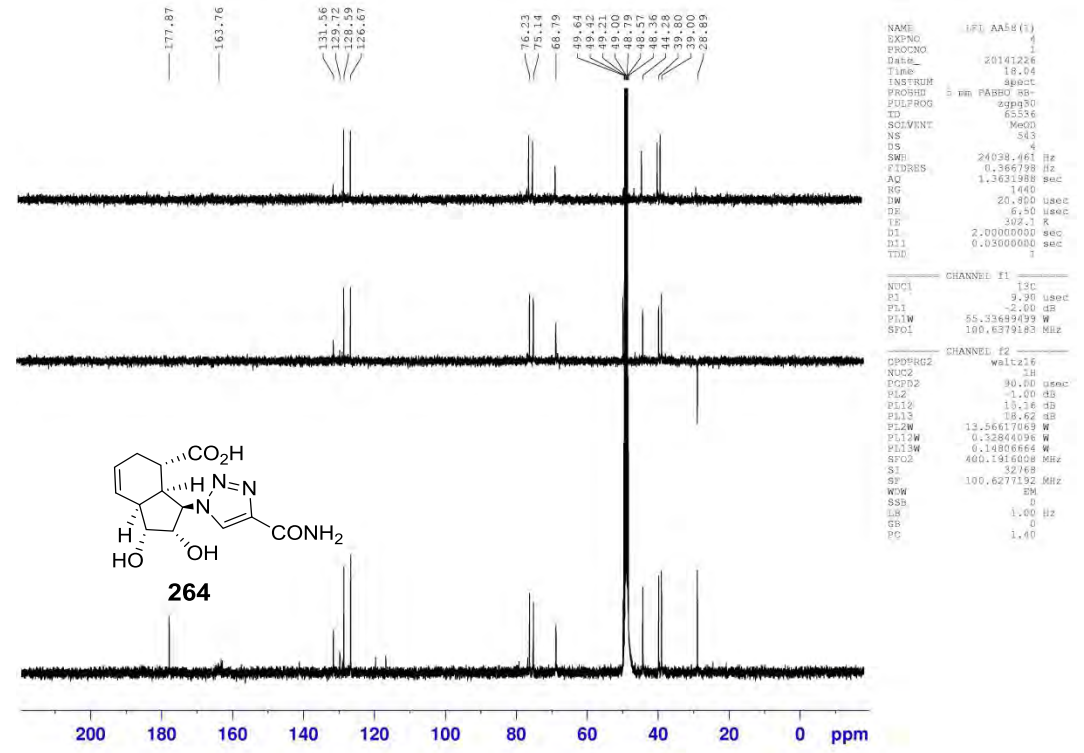
^{13}C NMR (Solvent: CD_3OD)



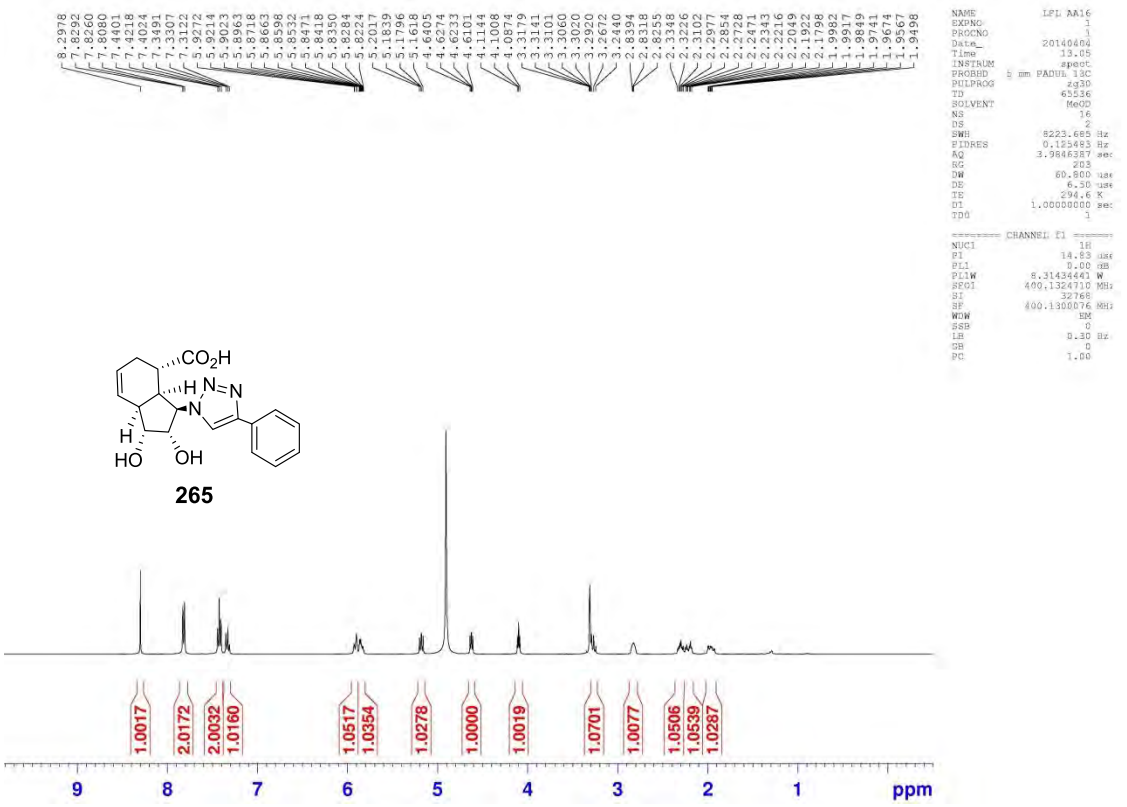
^{1}H NMR (Solvent: CD_3OD)



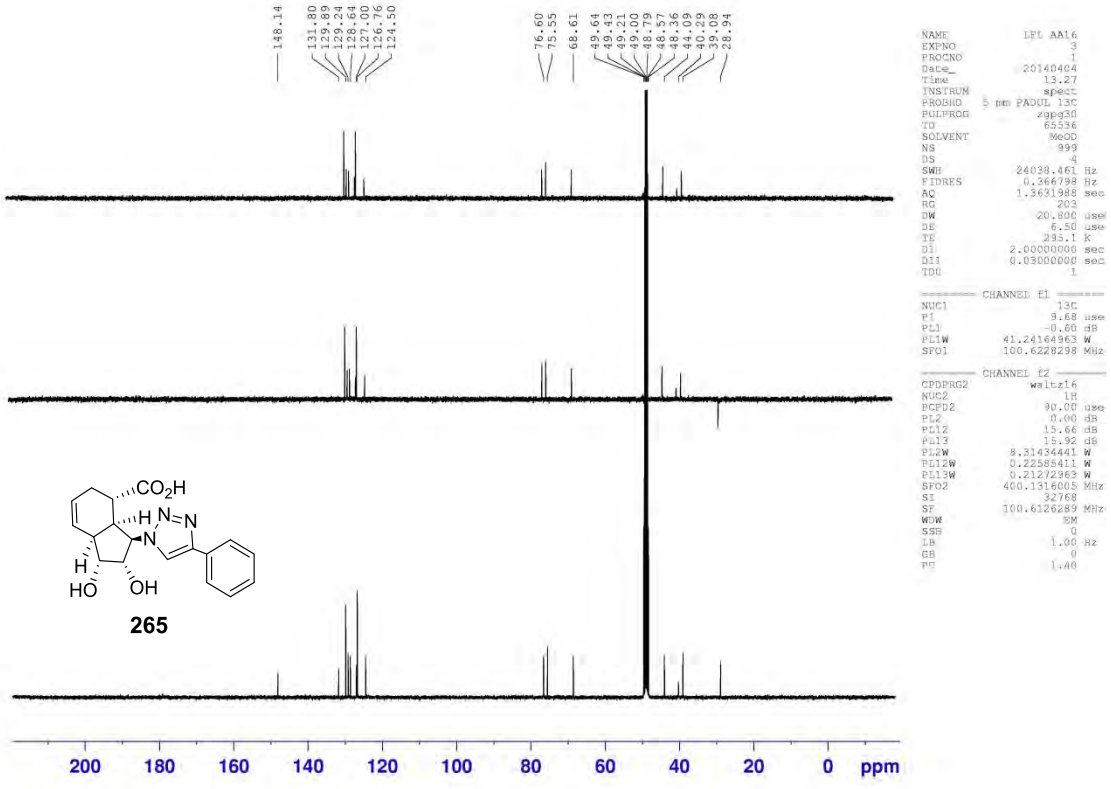
^{13}C NMR (Solvent: CD_3OD)



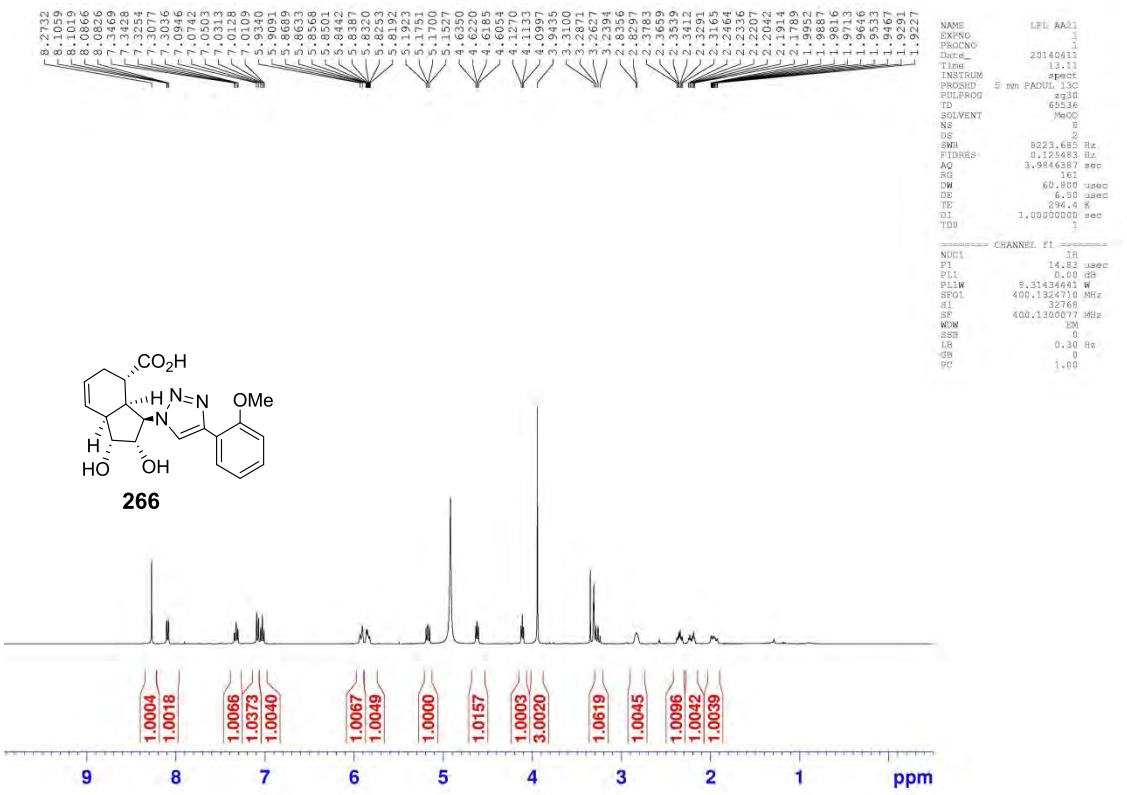
^{1}H NMR (Solvent: CD_3OD)



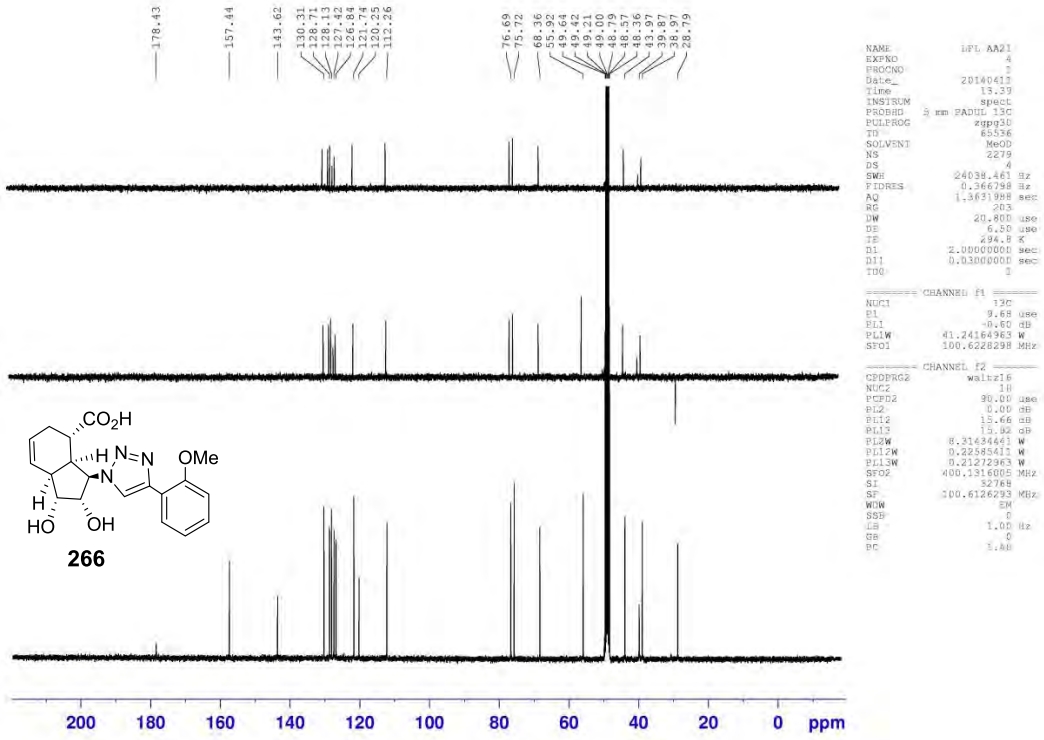
^{13}C NMR (Solvent: CD_3OD)



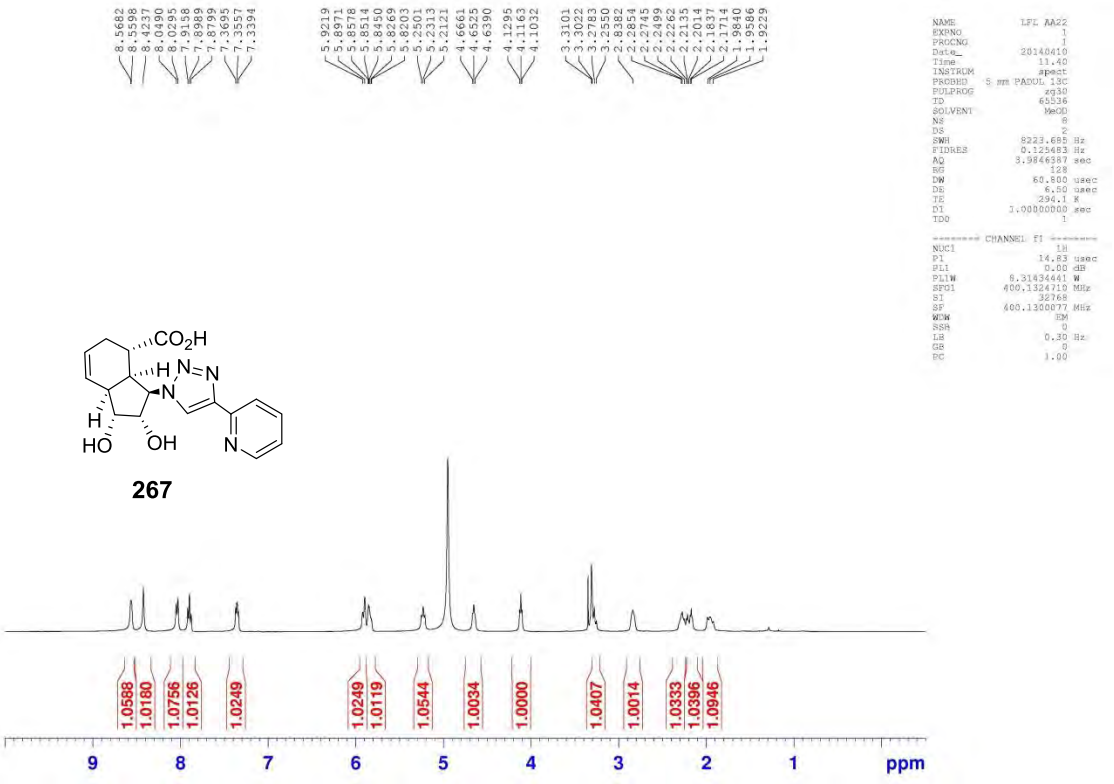
^{1}H NMR (Solvent: CD_3OD)



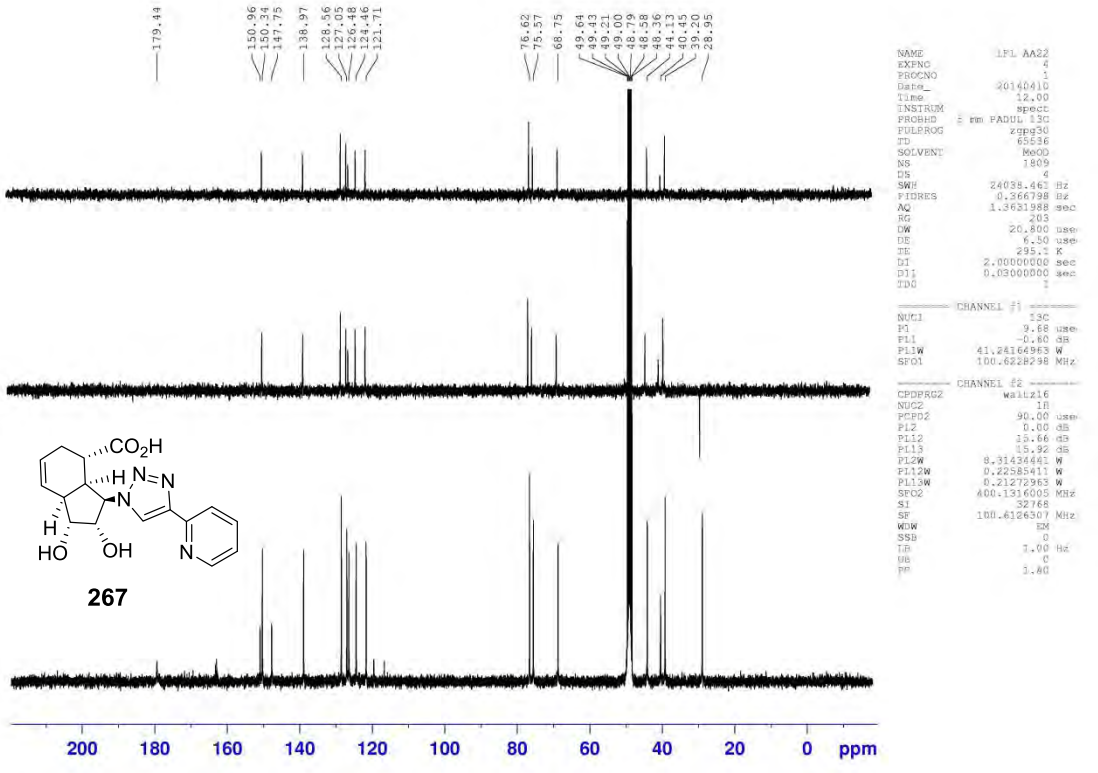
^{13}C NMR (Solvent: CD_3OD)



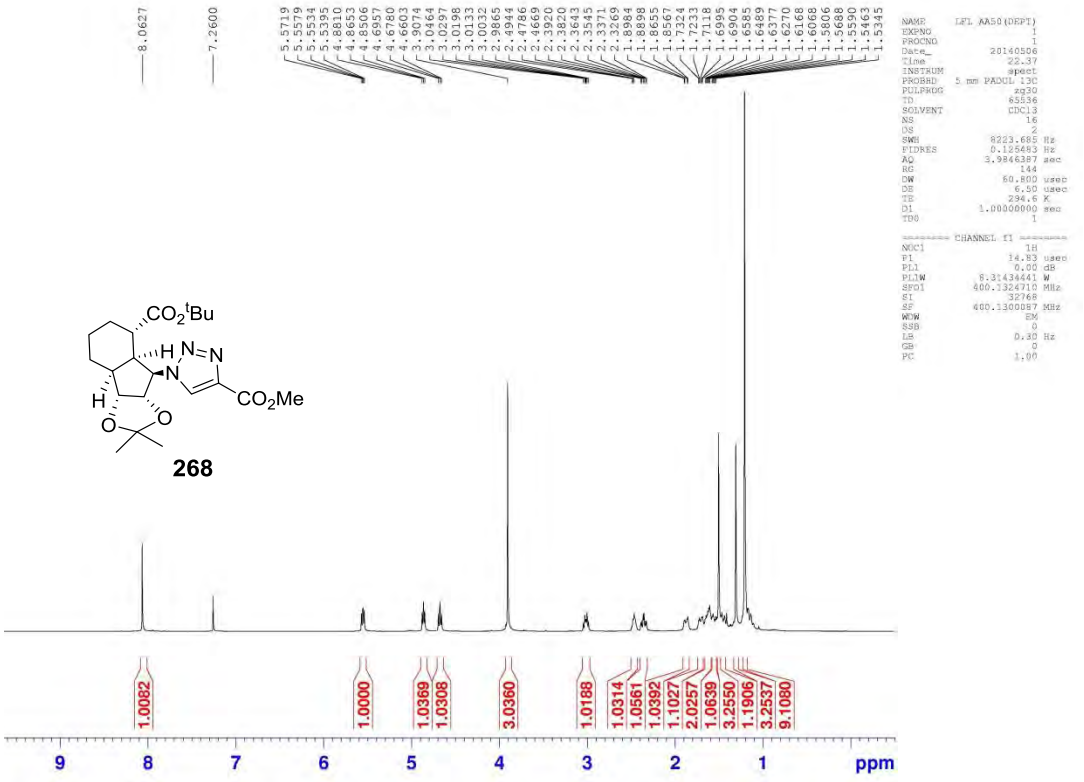
^{1}H NMR (Solvent: CD_3OD)



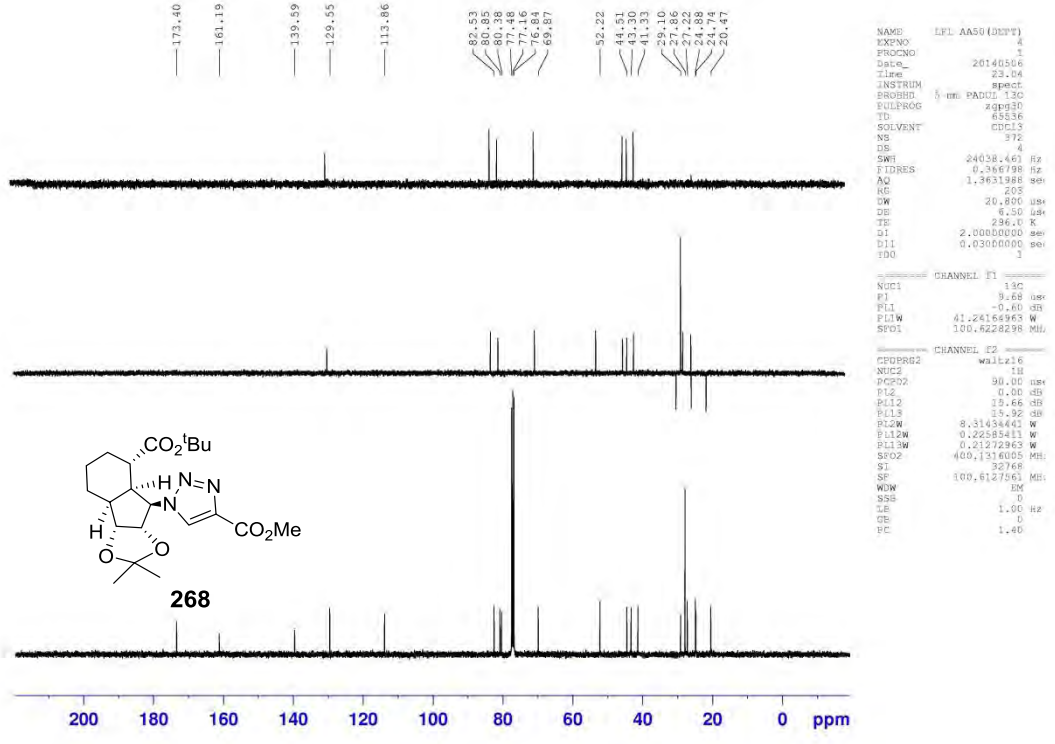
^{13}C NMR (Solvent: CD_3OD)



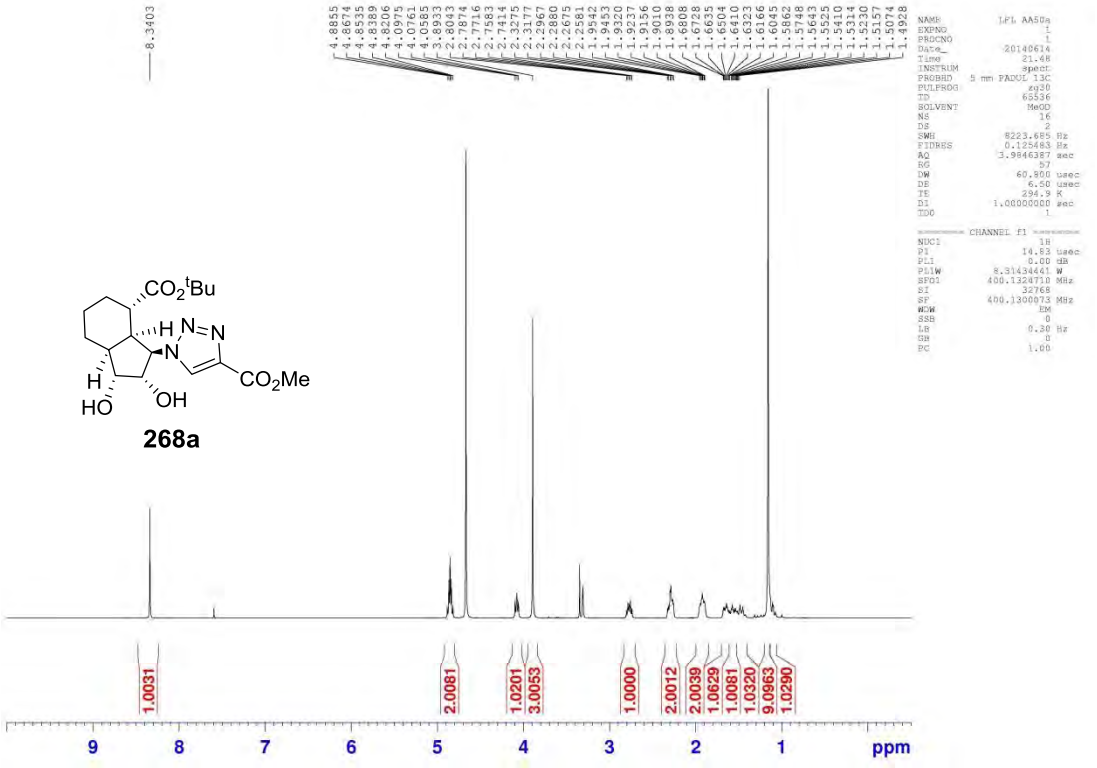
^{1}H NMR



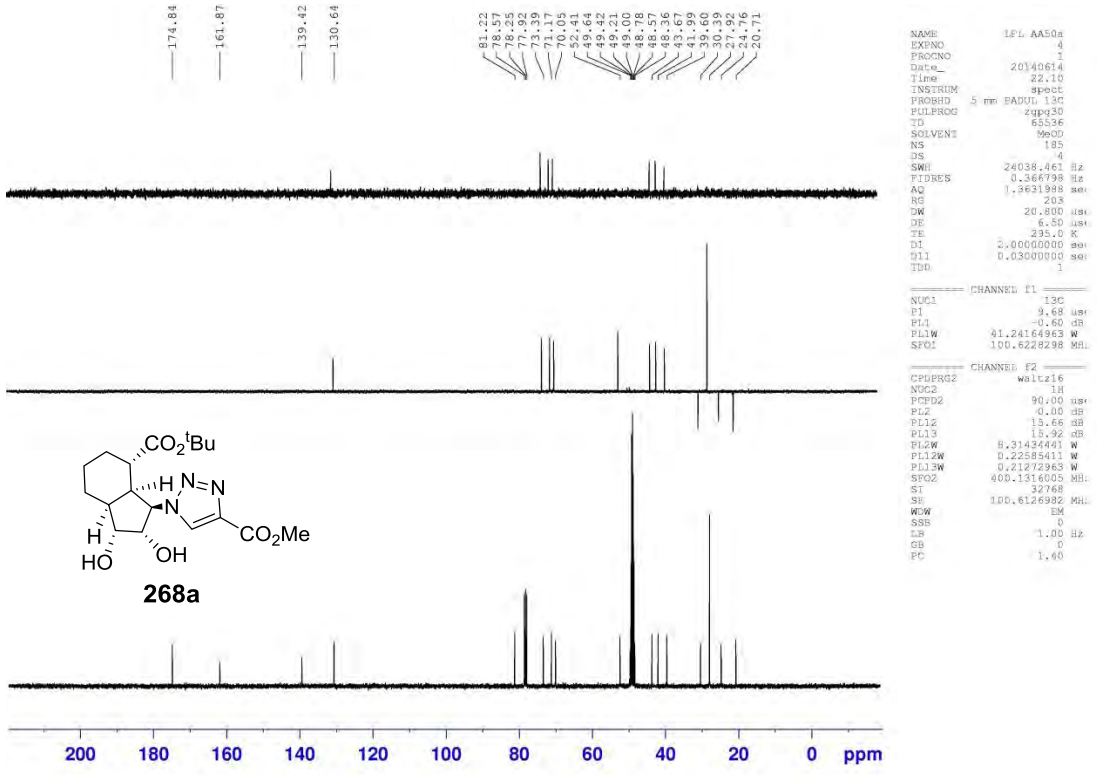
^{13}C NMR



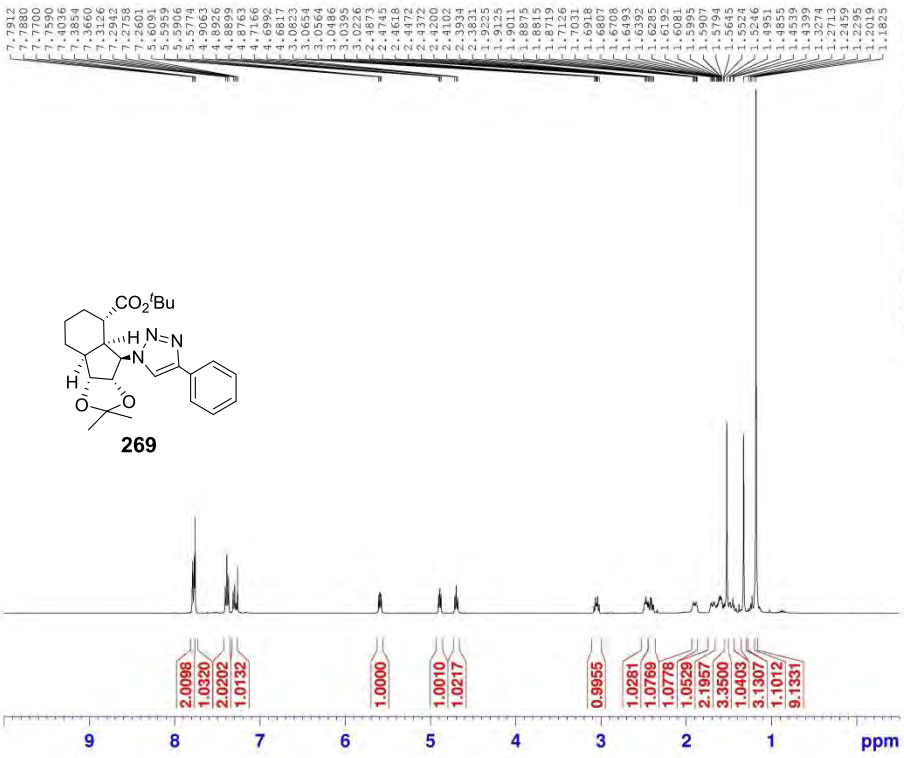
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



^{1}H NMR



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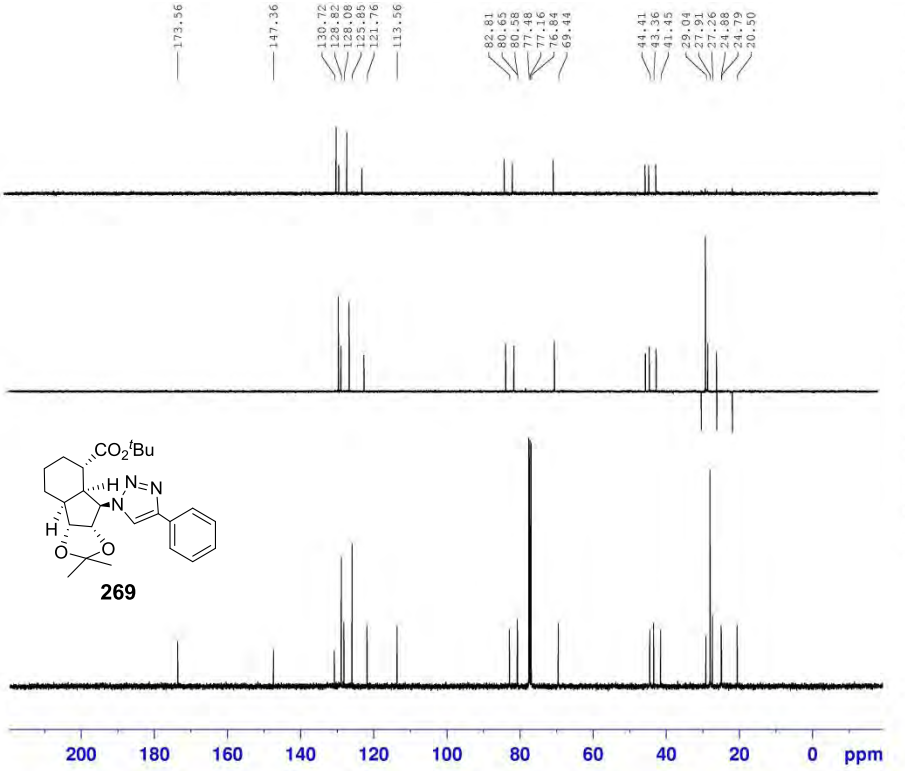
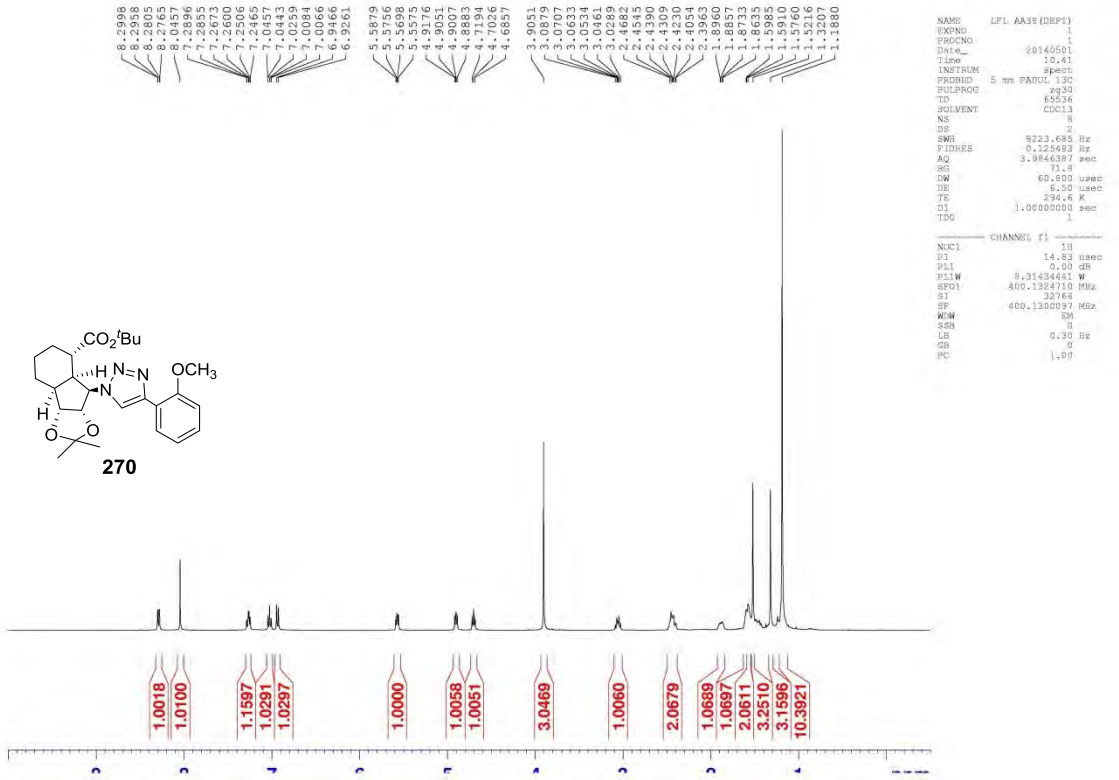


^{1}H NMR



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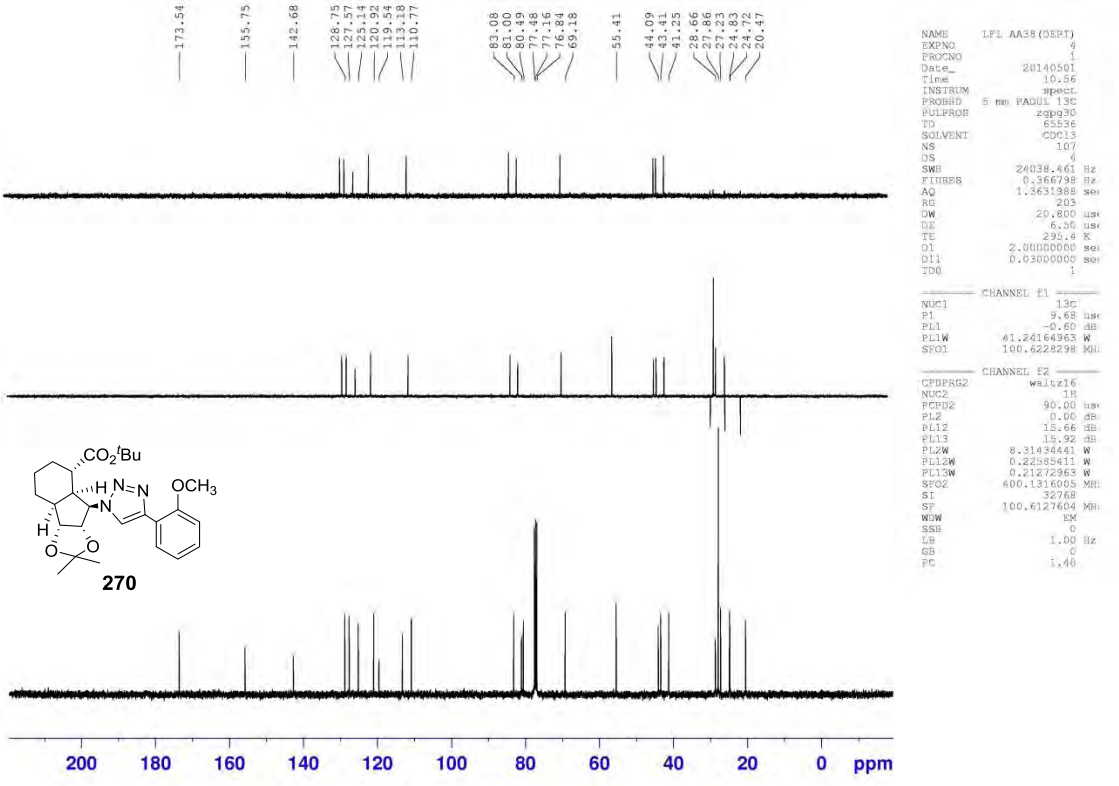
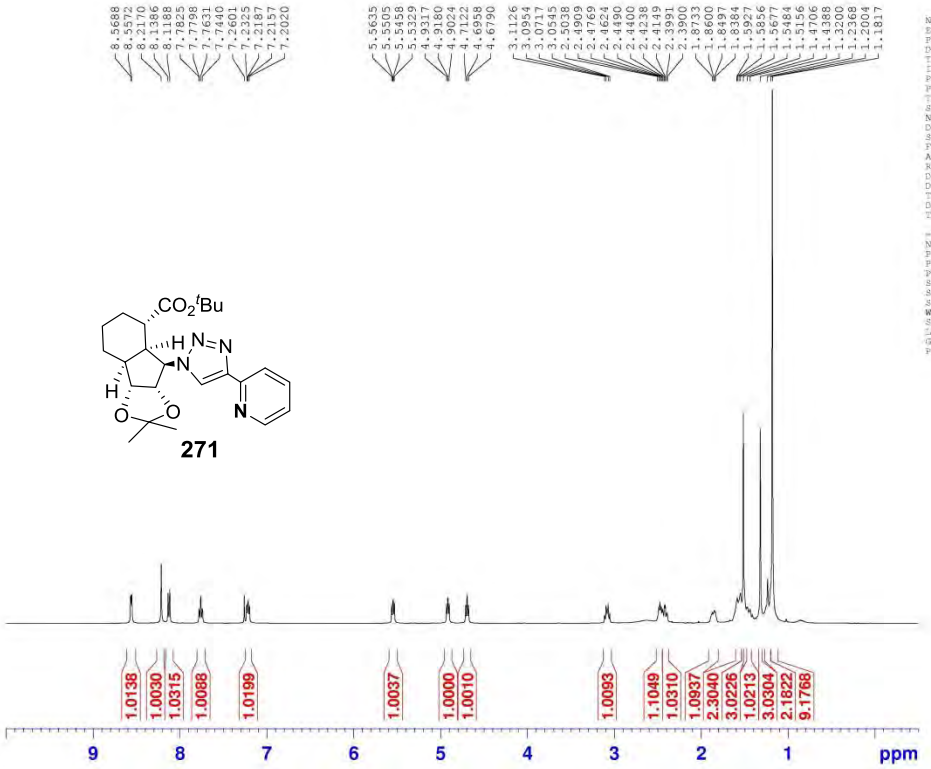


^{1}H NMR



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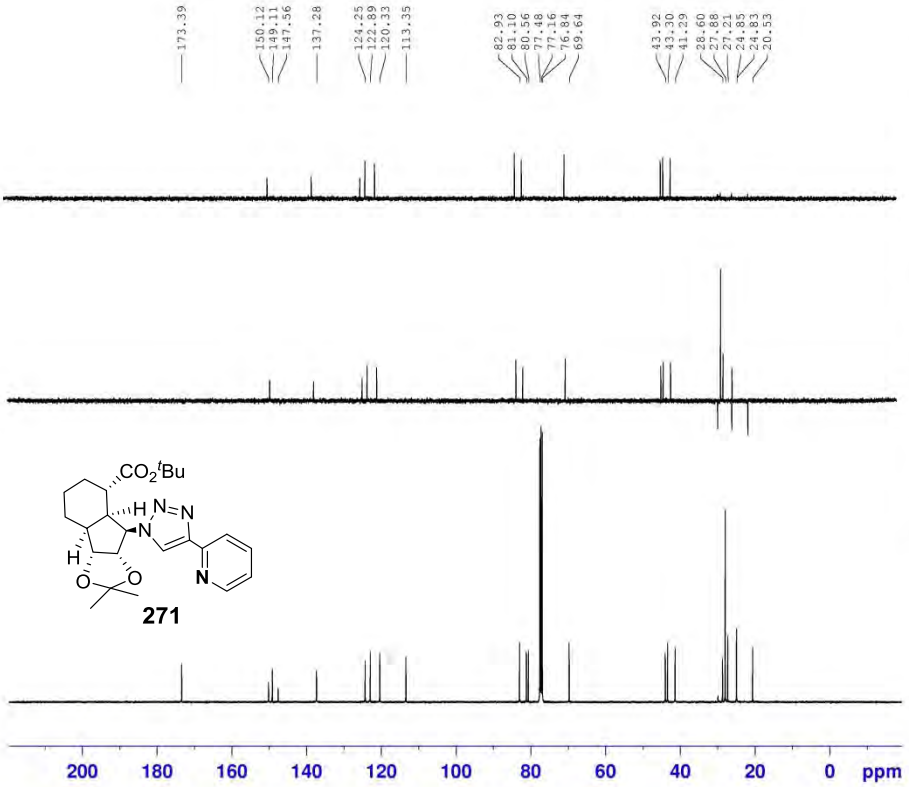
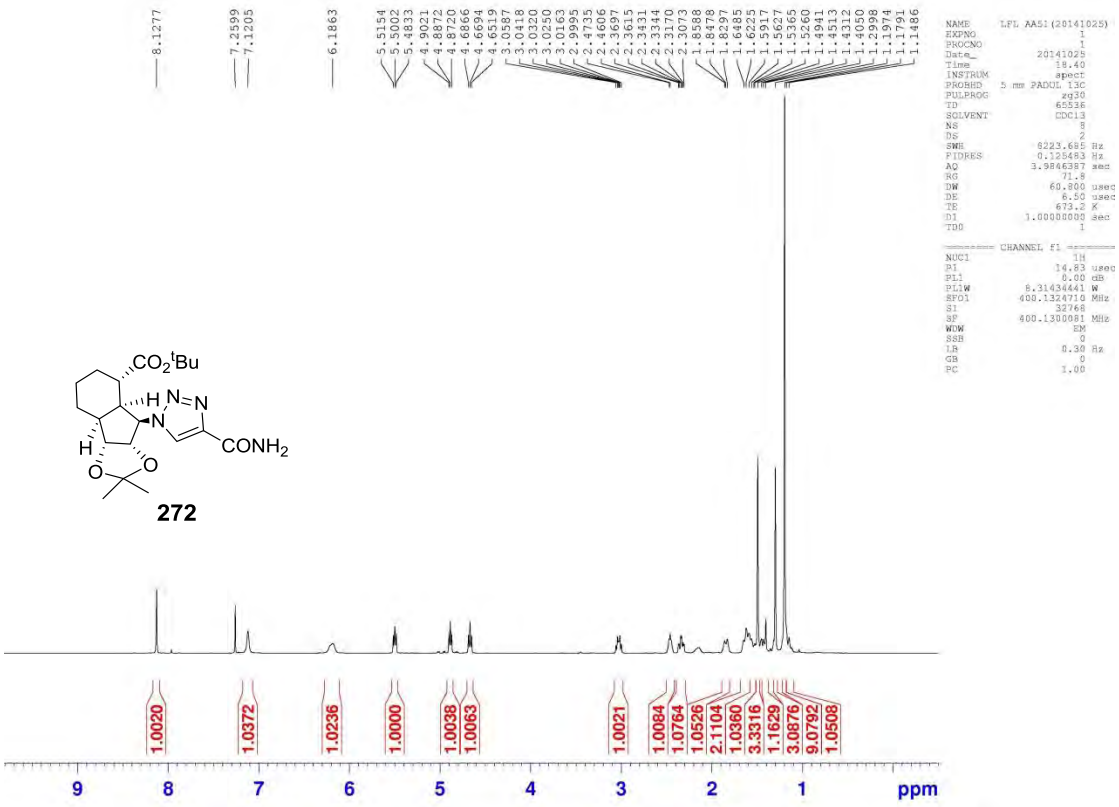
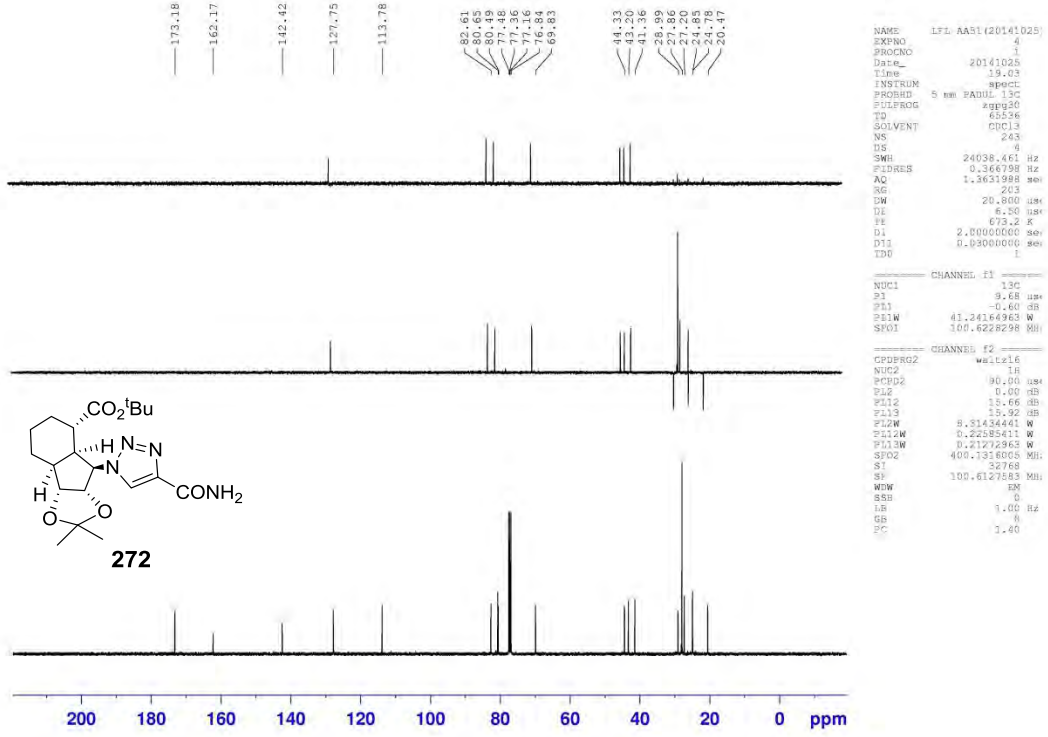


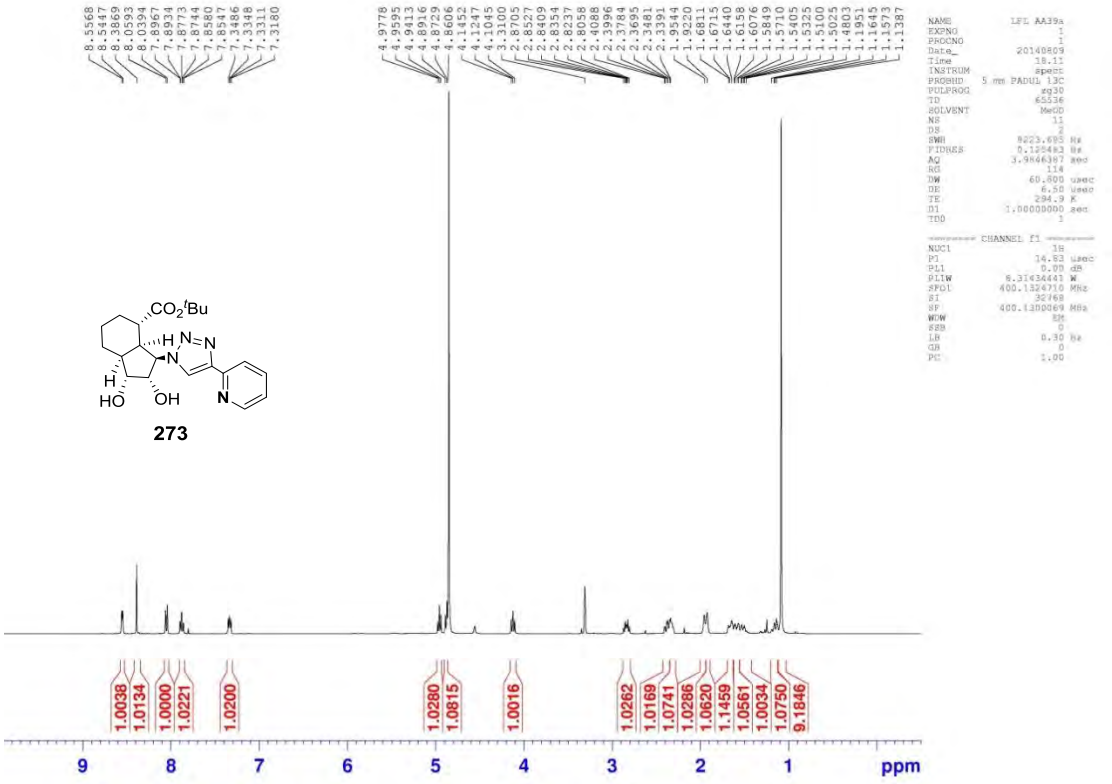
^{1}H NMR



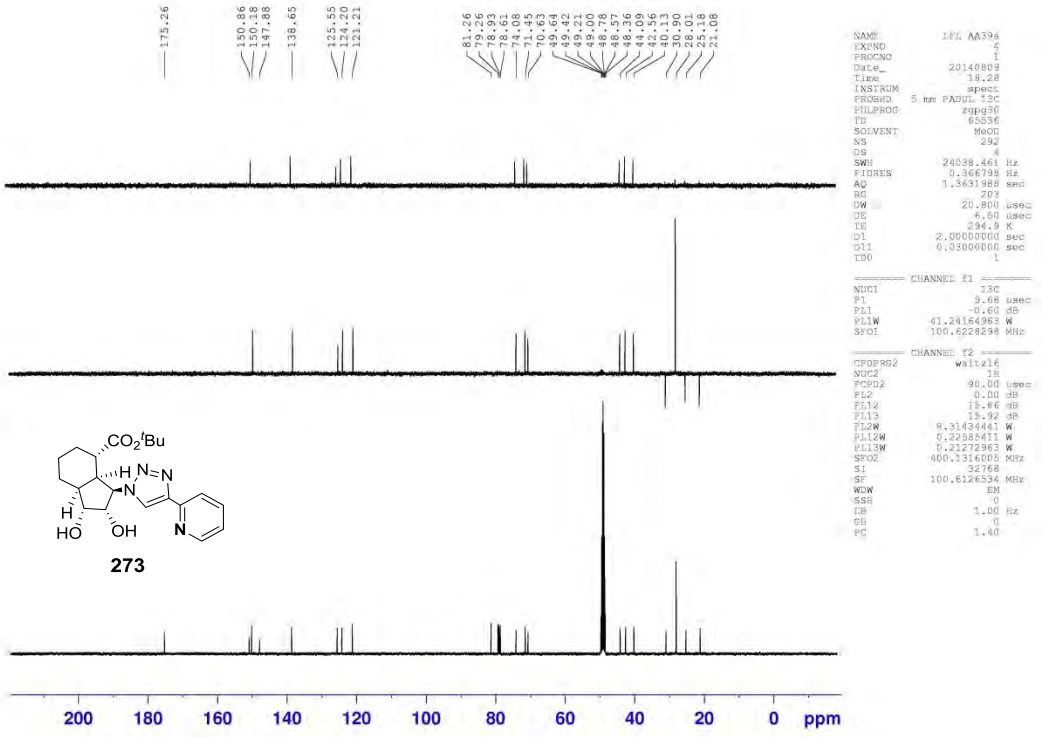
^{13}C NMR



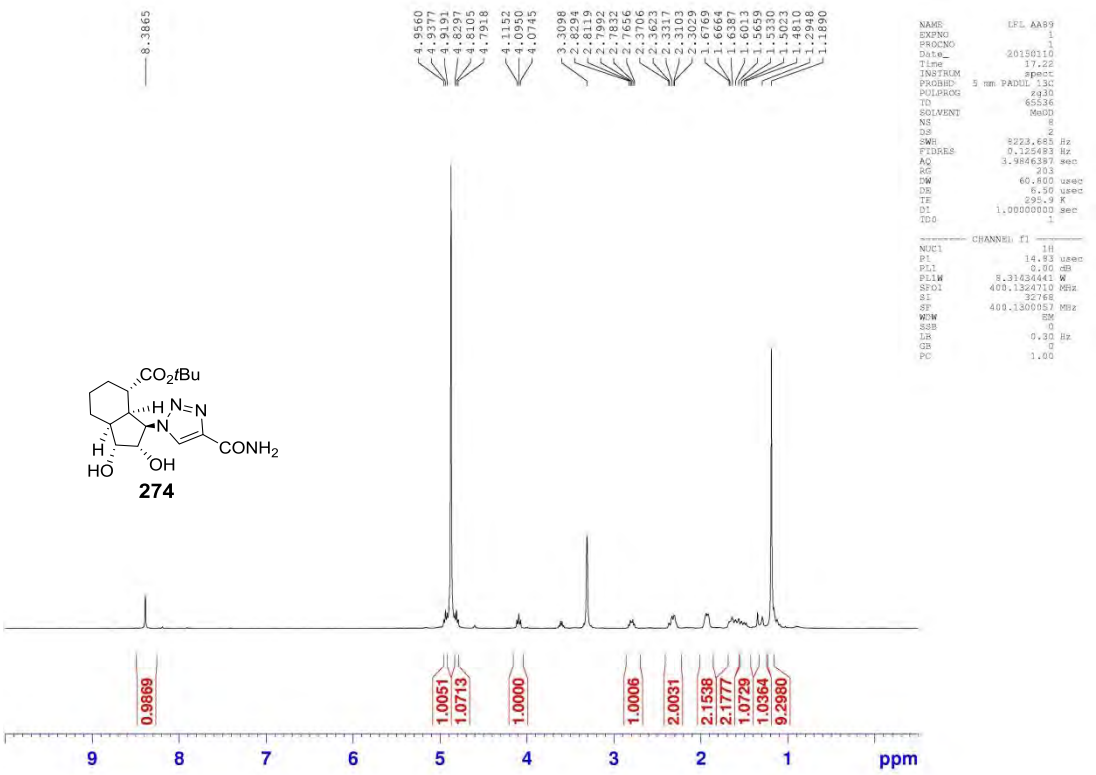
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



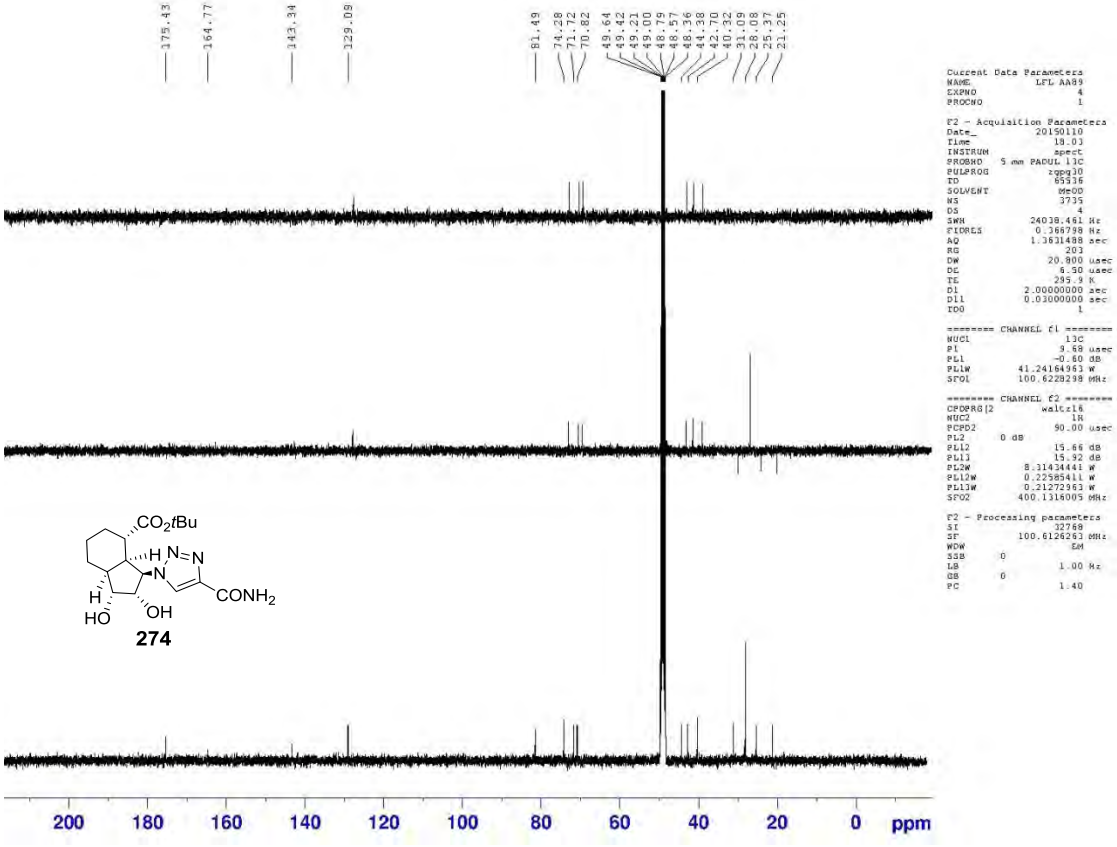
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



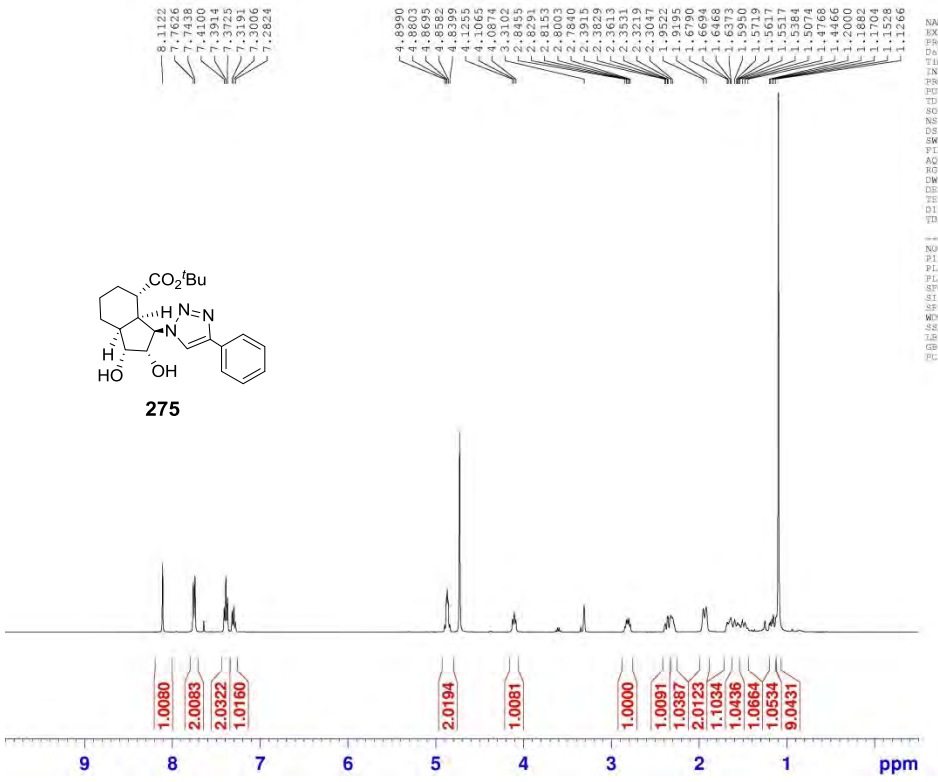
^{1}H NMR (Solvent: CD_3OD)



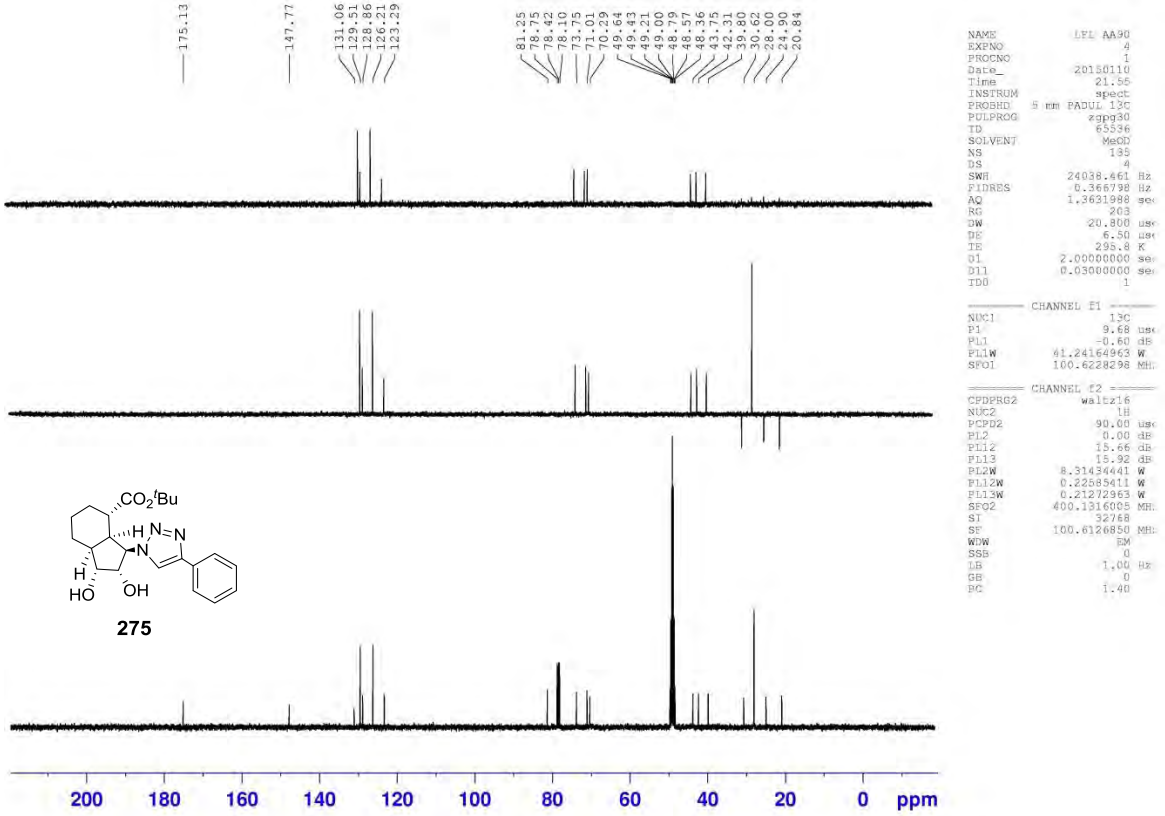
^{13}C NMR (Solvent: CD_3OD)



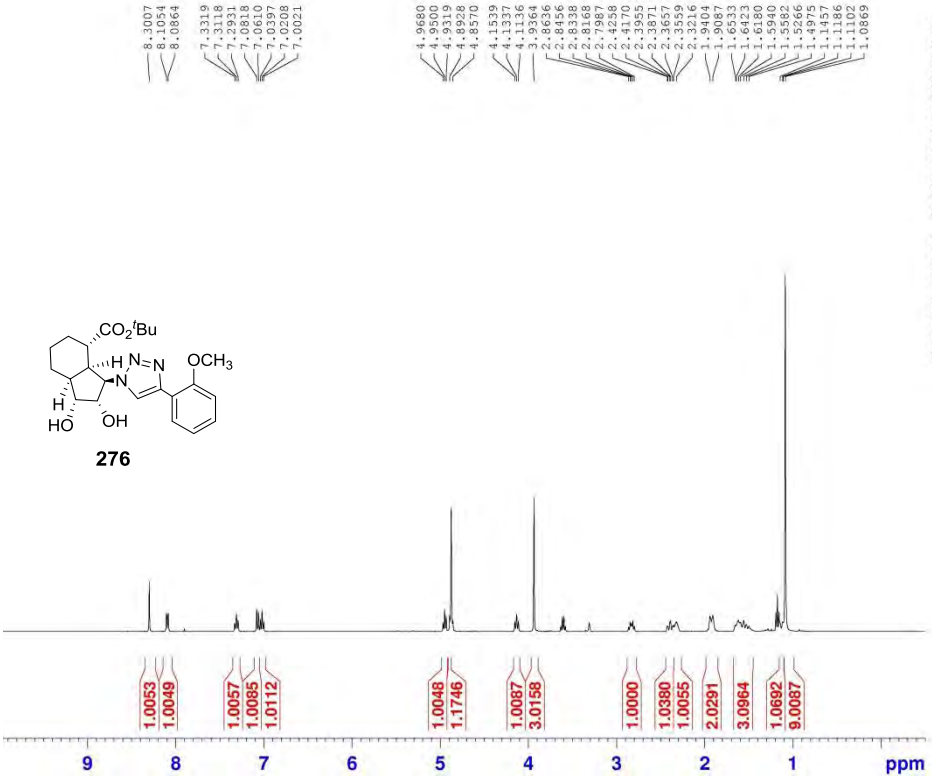
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 2:3)



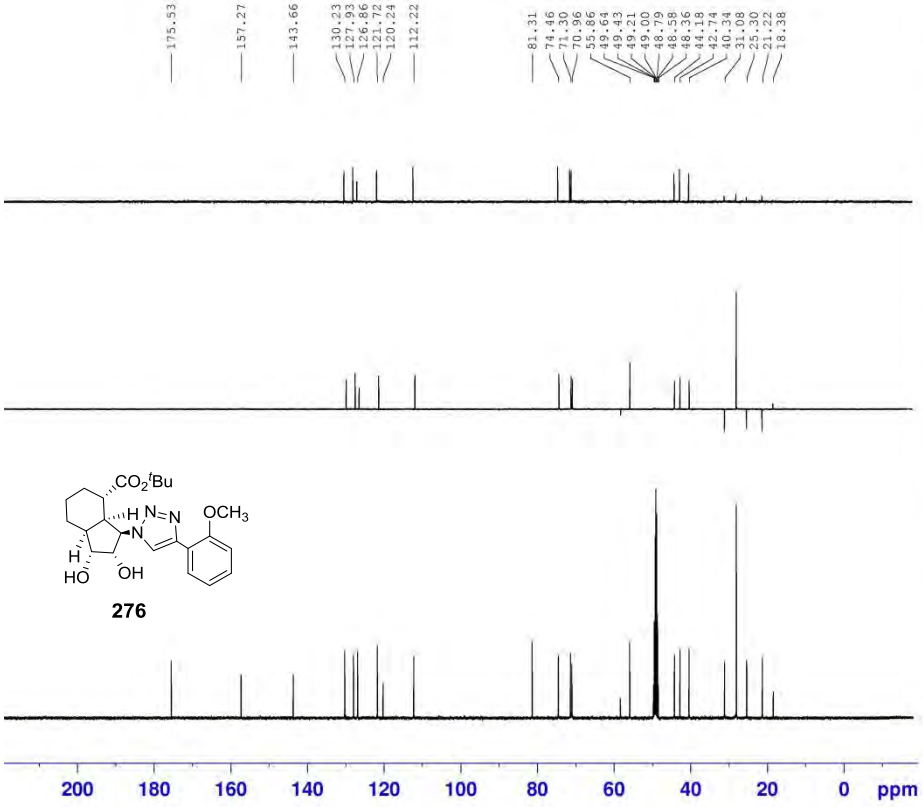
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 2:3)



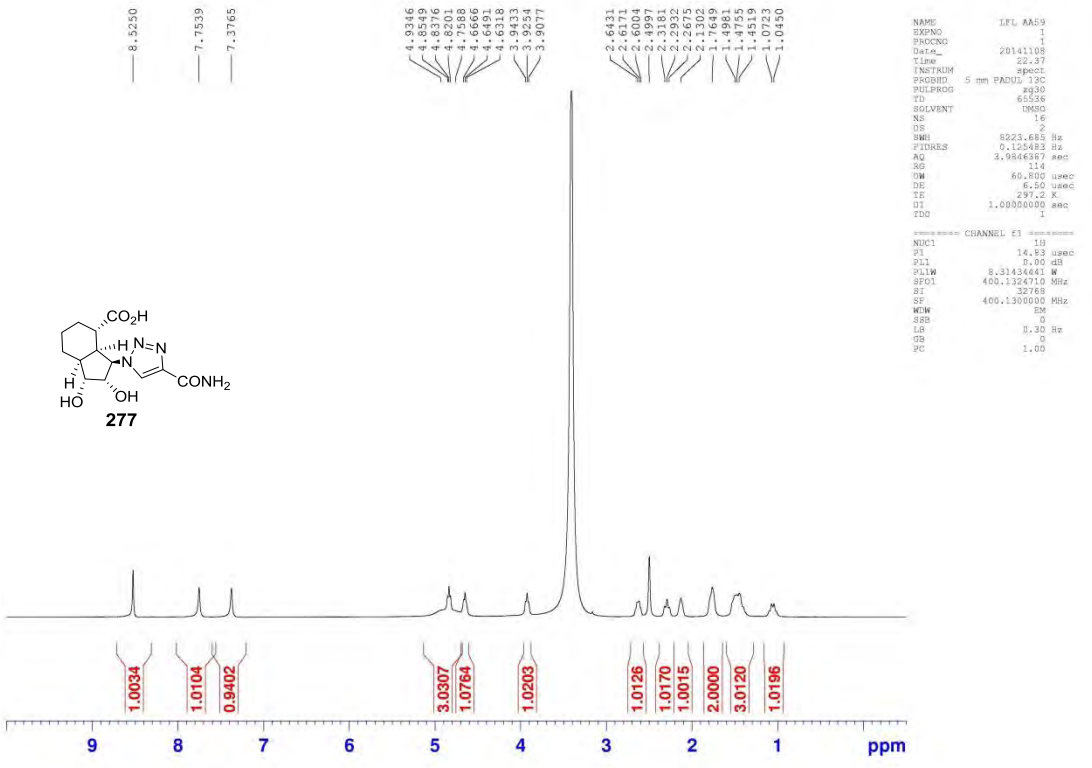
^{1}H NMR (Solvent: CD_3OD)



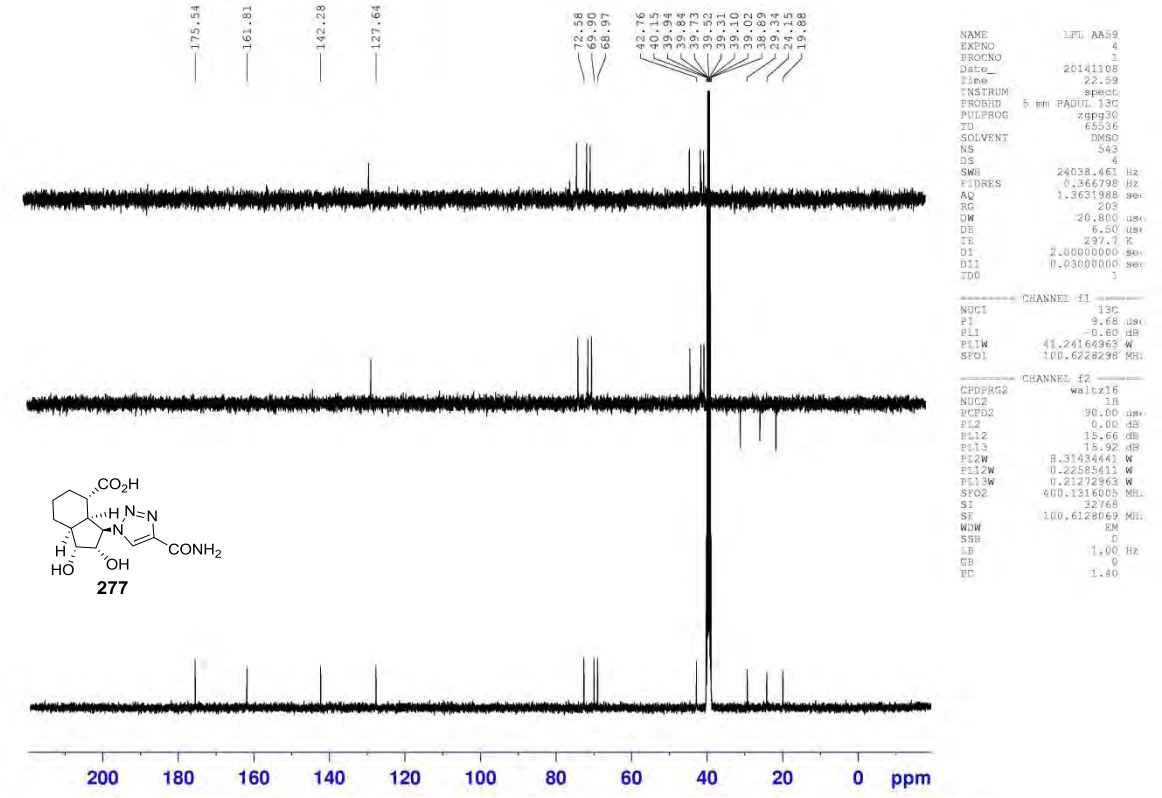
^{13}C NMR (Solvent: CD_3OD)



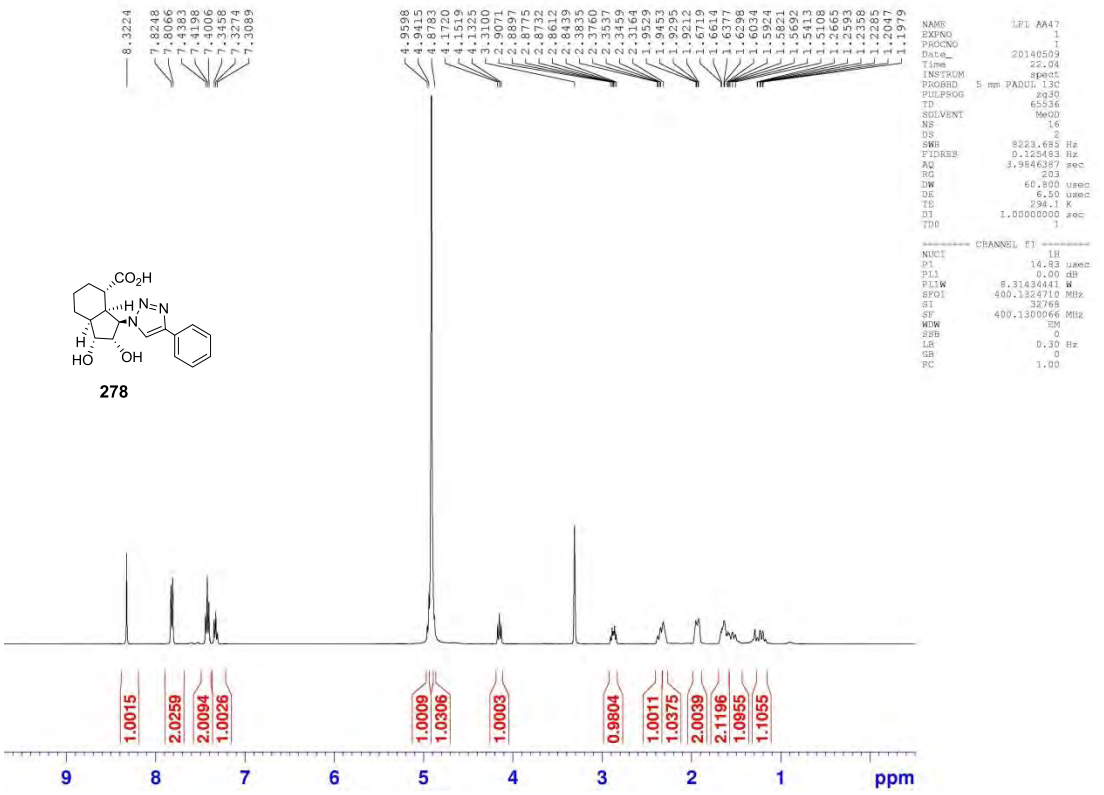
^{1}H NMR (Solvent: DMSO-d_6)



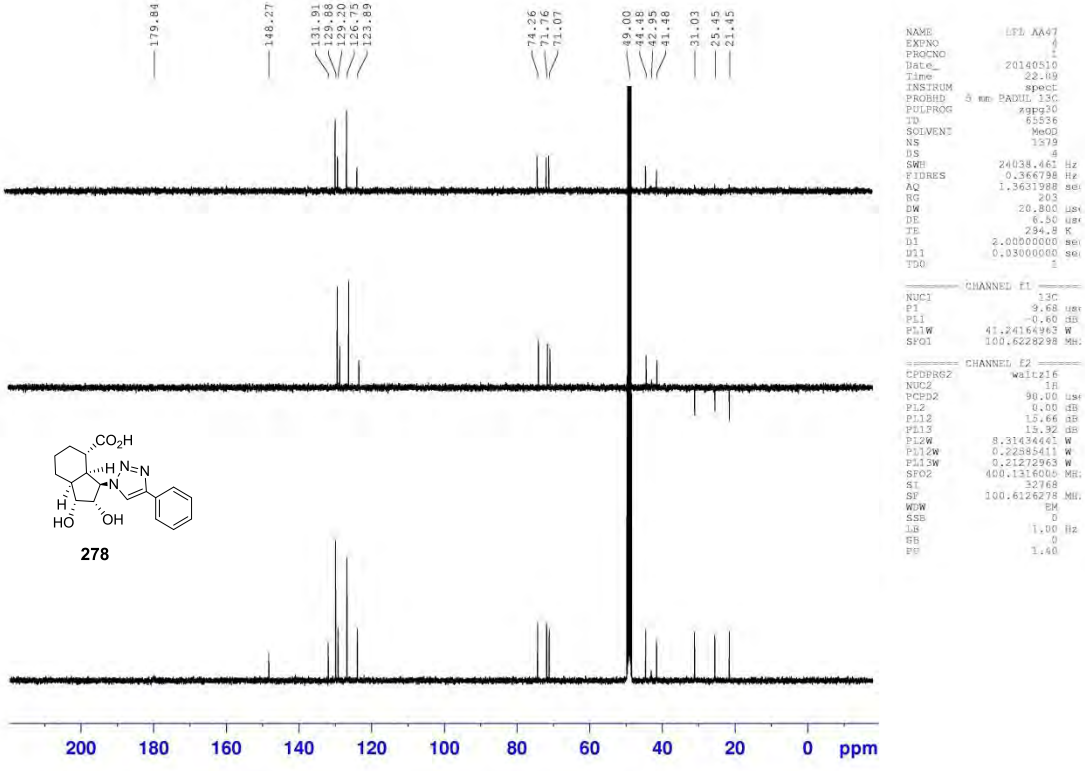
^{13}C NMR (Solvent: DMSO-d_6)



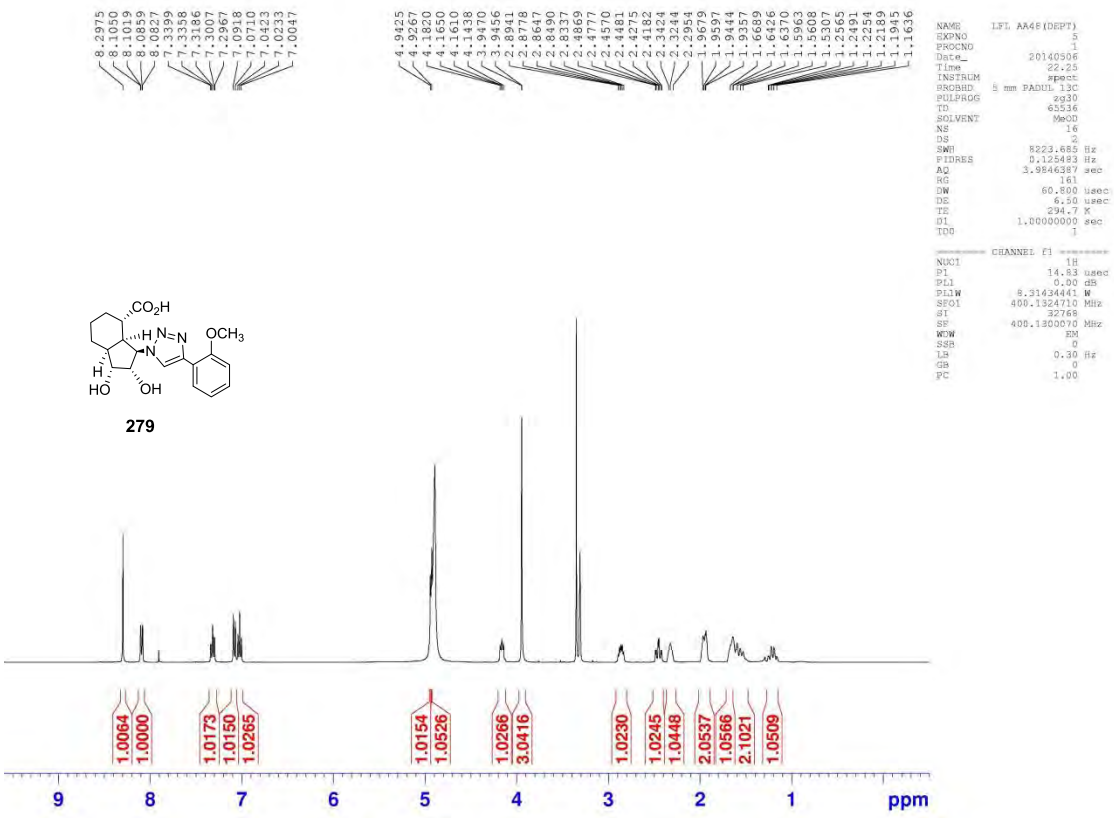
^{1}H NMR (Solvent: CD_3OD)



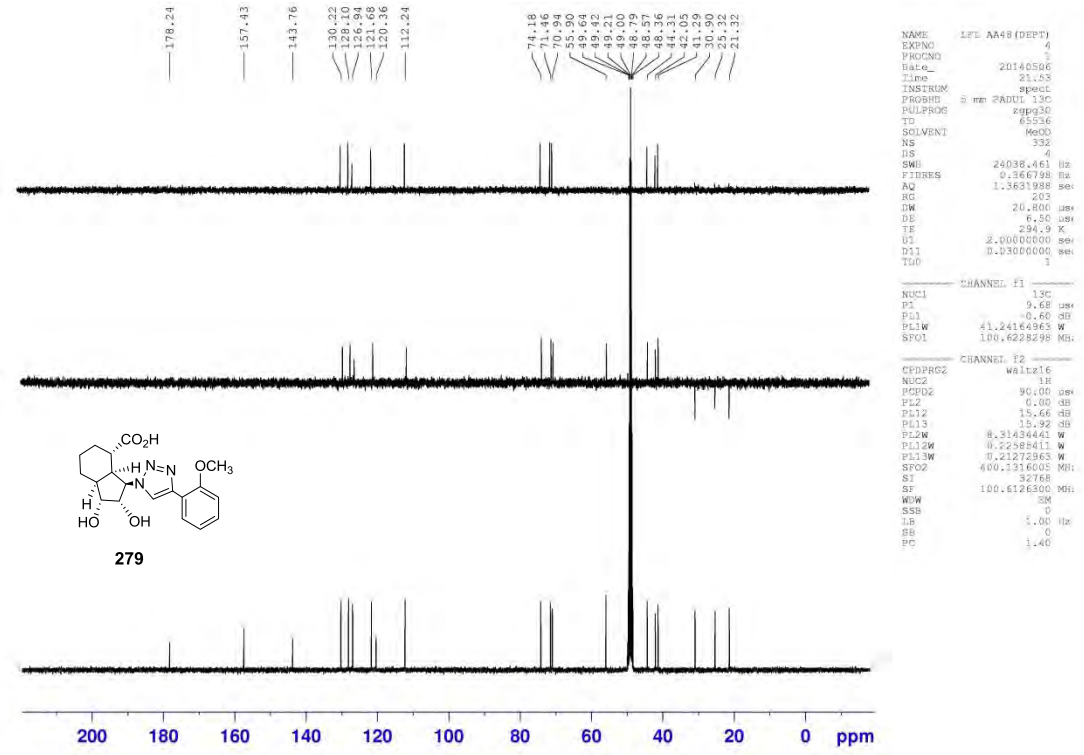
^{13}C NMR (Solvent: CD_3OD)



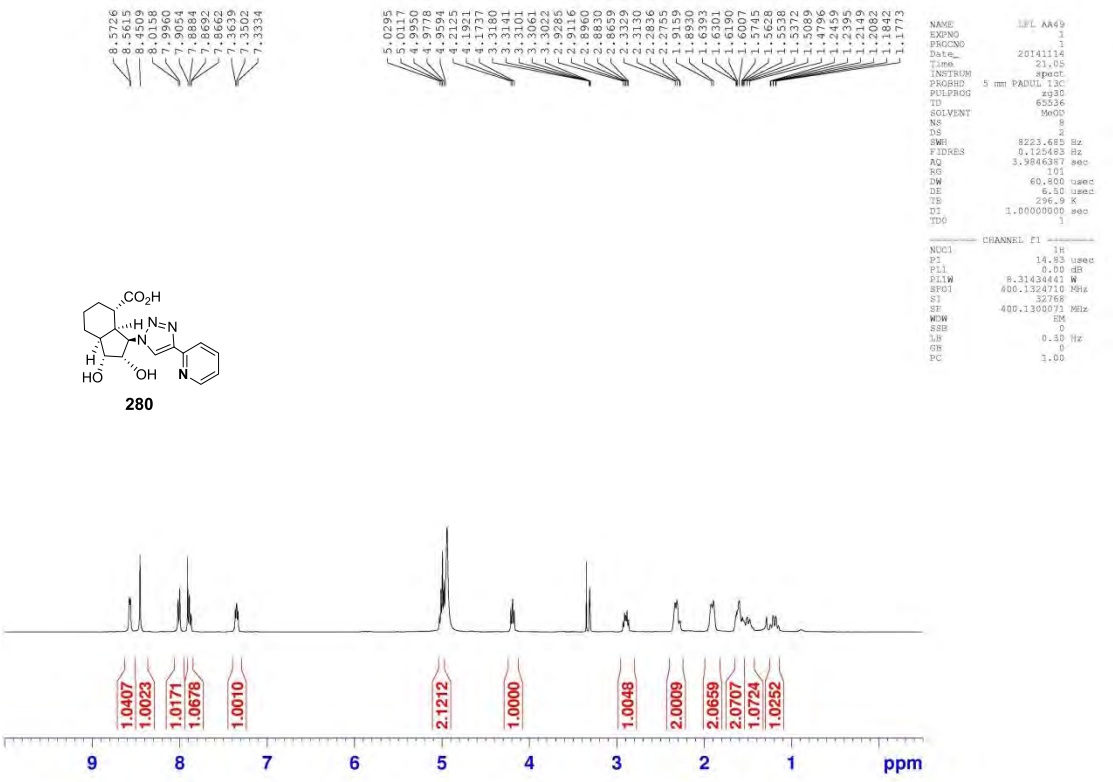
^{1}H NMR (Solvent: CD_3OD)



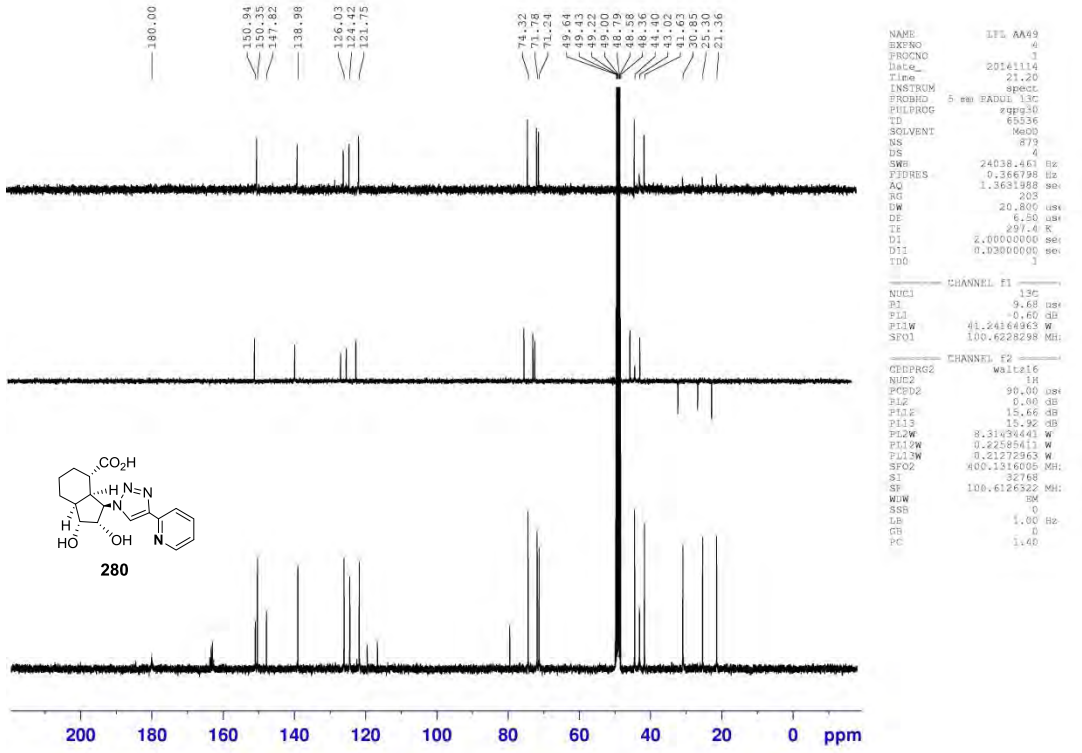
^{13}C NMR (Solvent: CD_3OD)



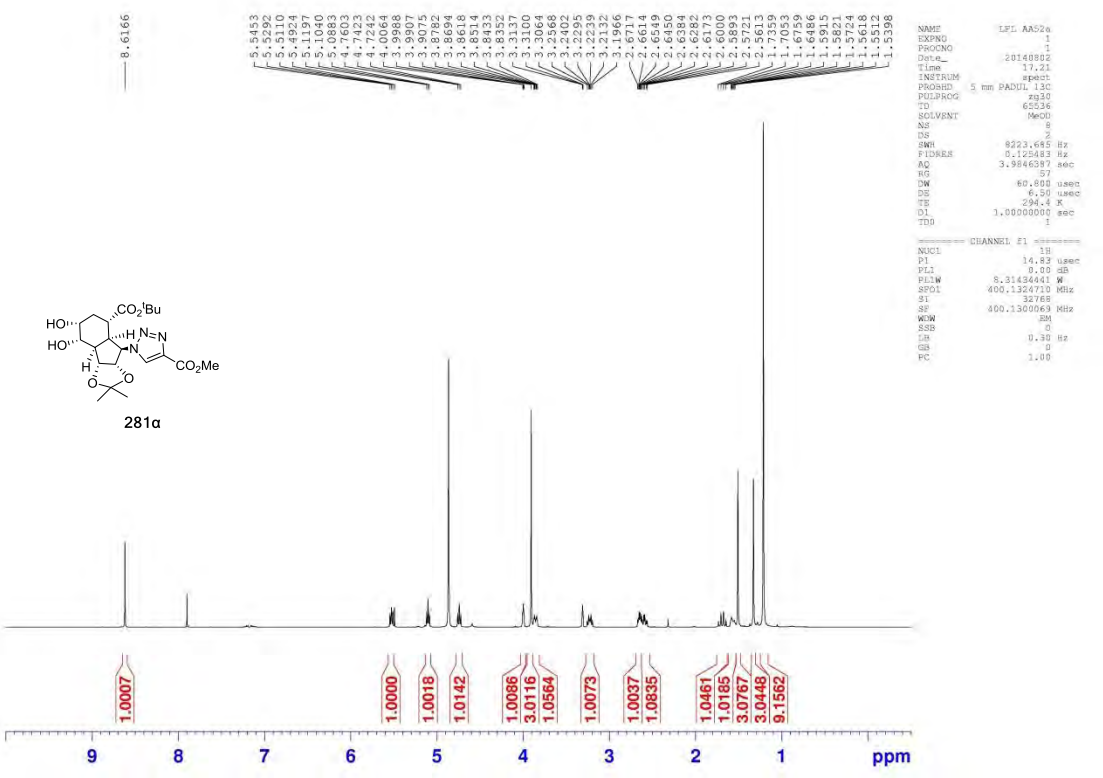
^{1}H NMR (Solvent: CD_3OD)



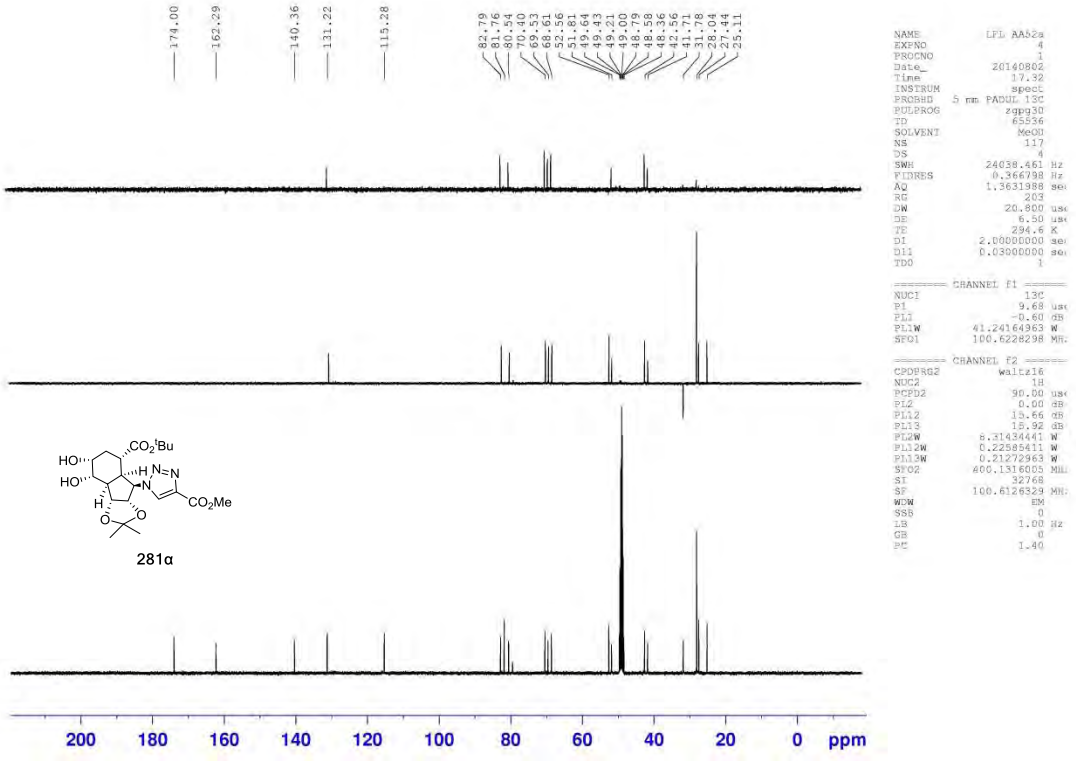
^{13}C NMR (Solvent: CD_3OD)



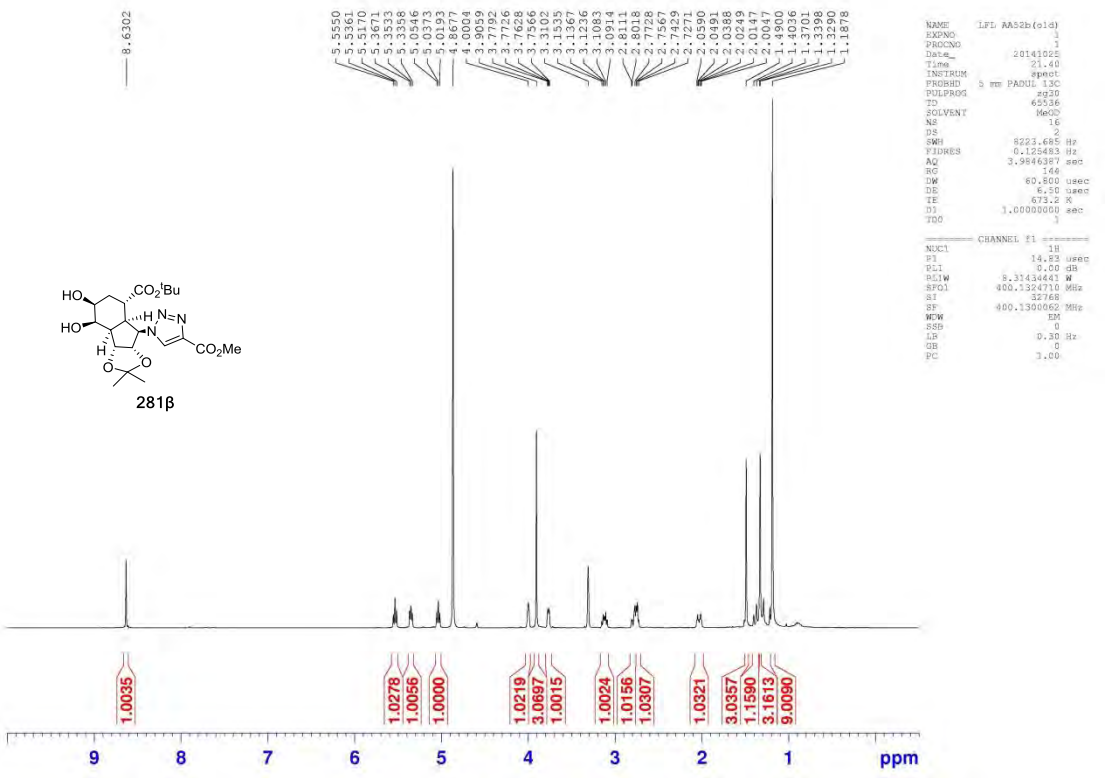
^{1}H NMR (Solvent: CD_3OD)



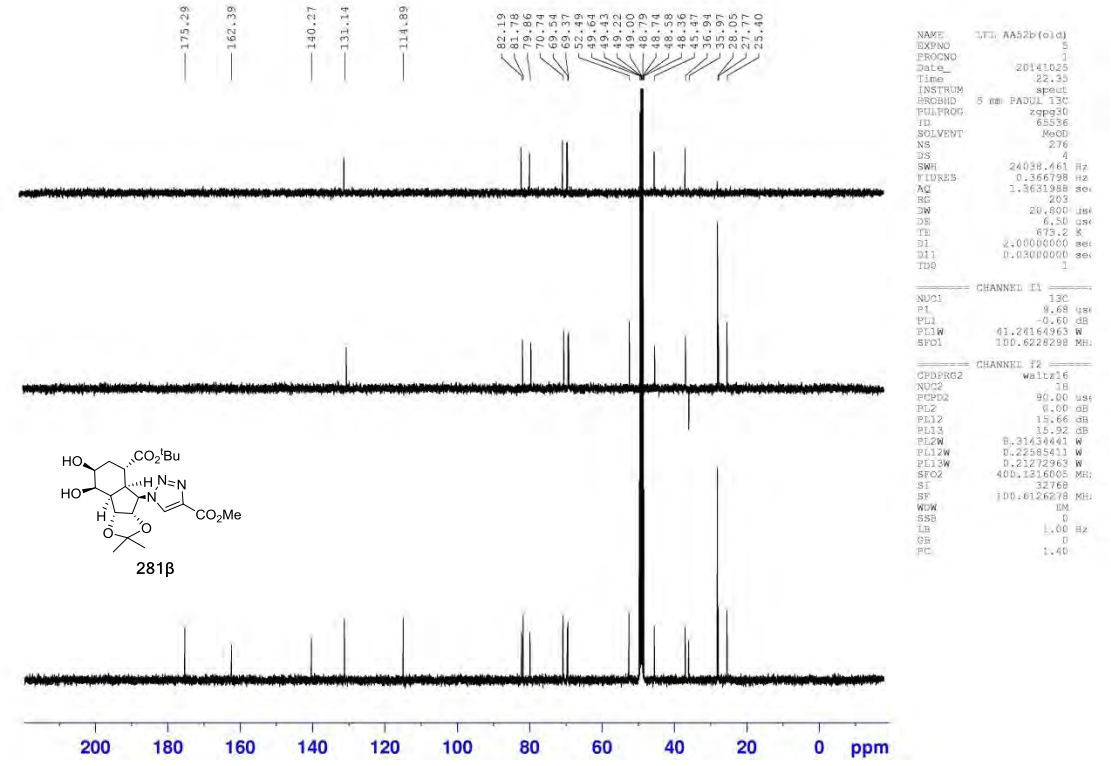
^{13}C NMR (Solvent: CD_3OD)



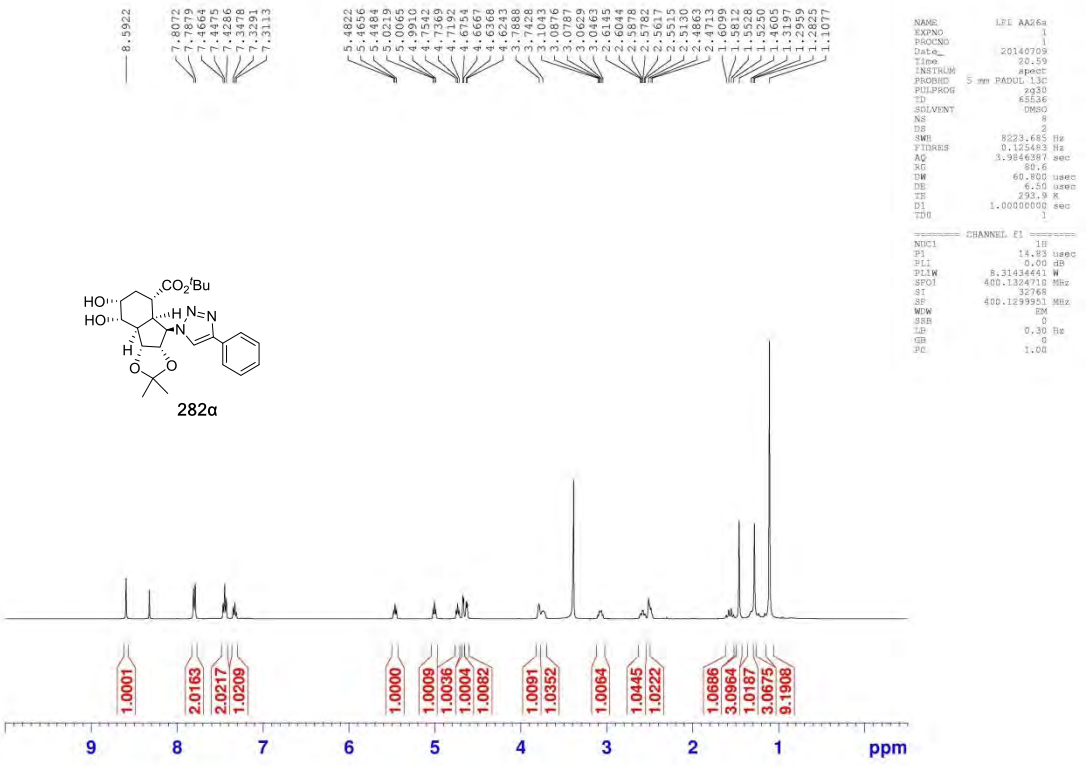
^{1}H NMR (Solvent: CD_3OD)



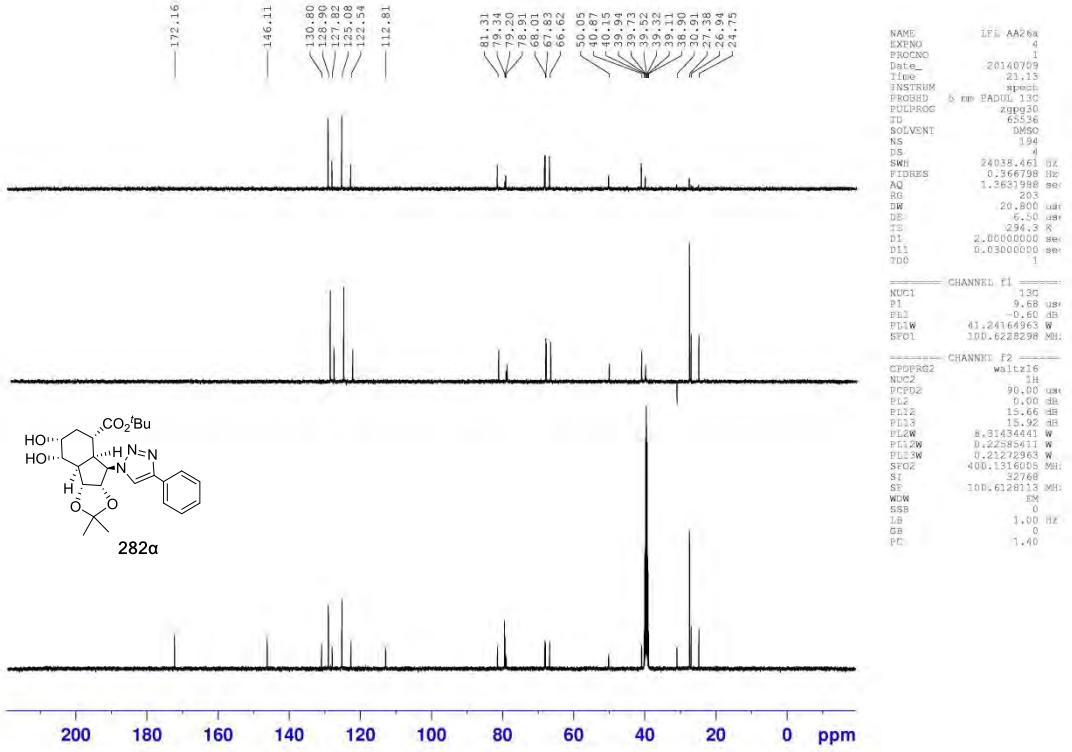
^{13}C NMR (Solvent: CD_3OD)



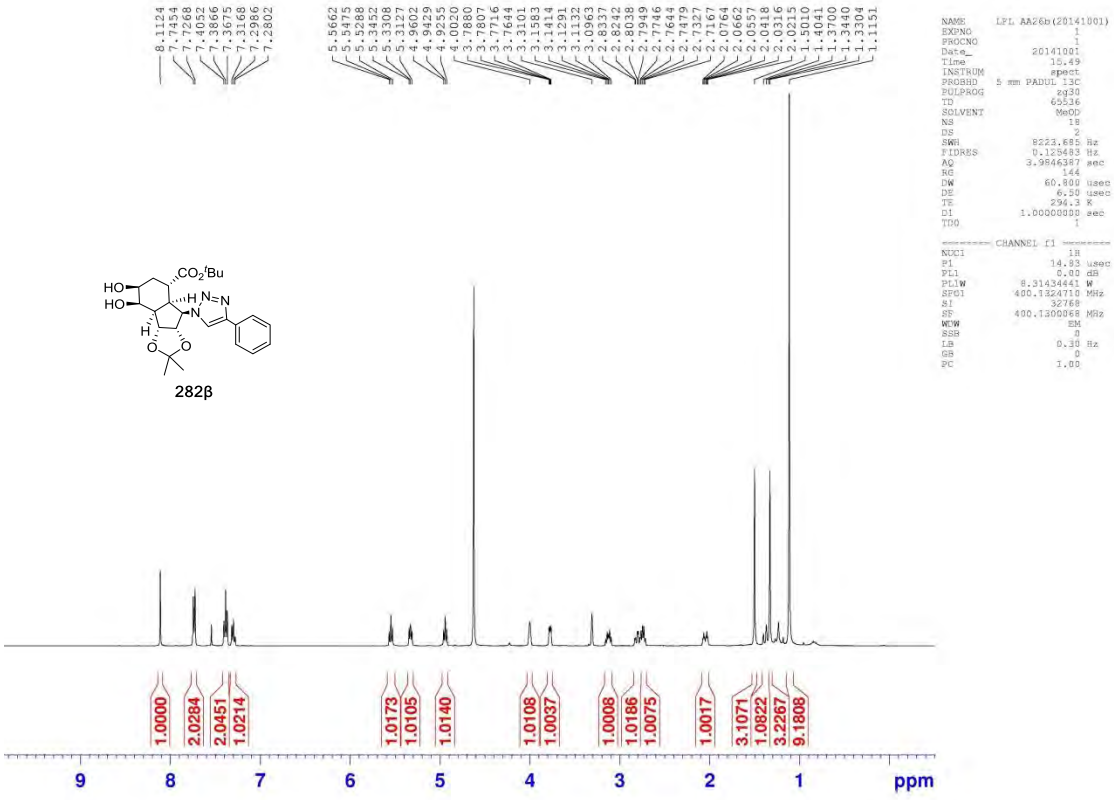
^{1}H NMR (Solvent: DMSO-d_6)



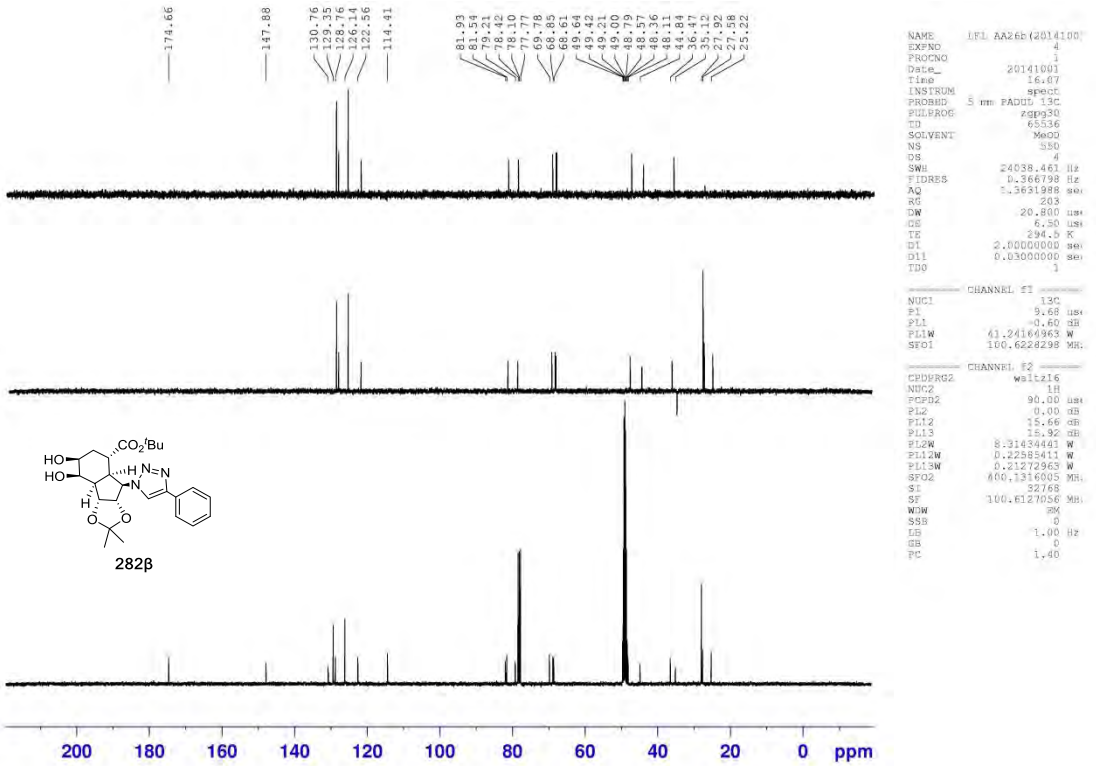
^{13}C NMR (Solvent: DMSO-d_6)



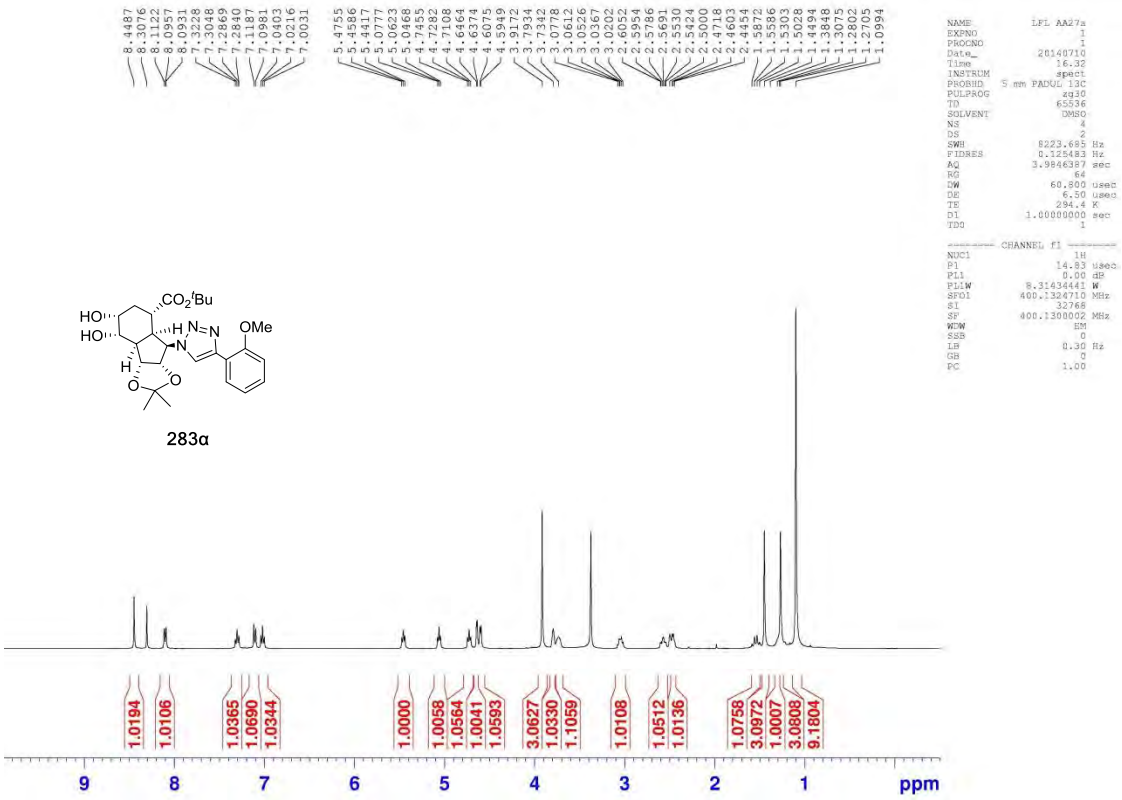
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:1)



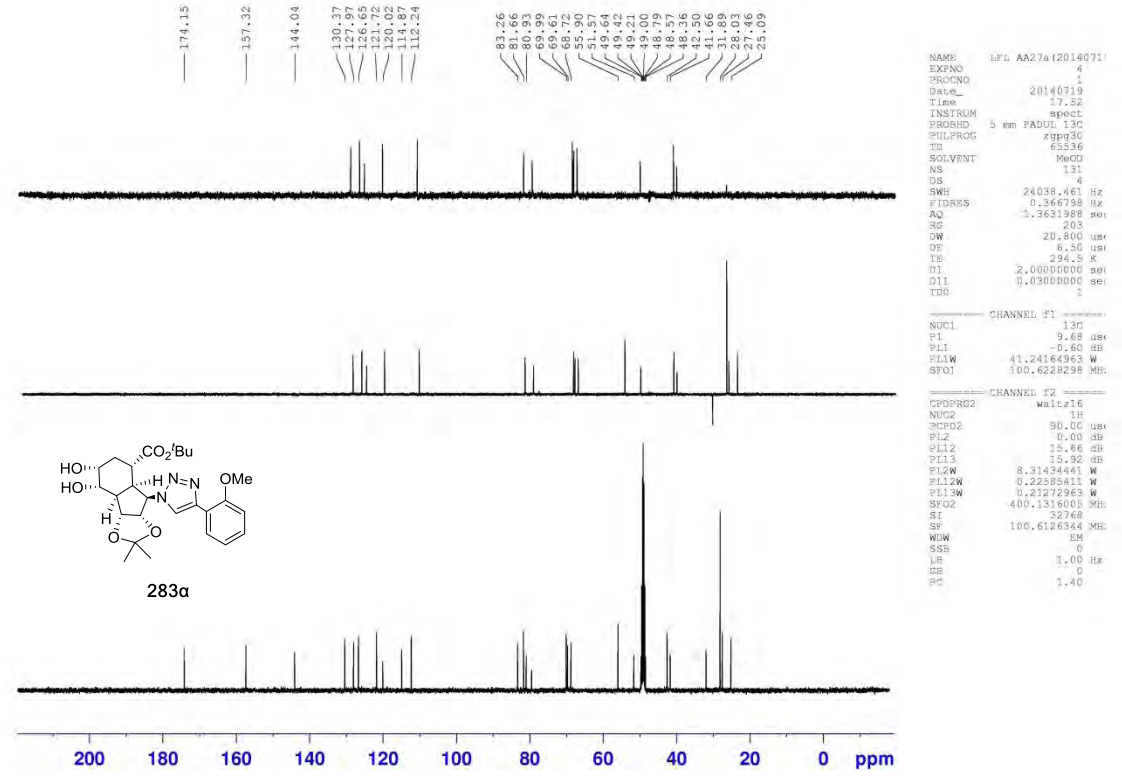
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:1)



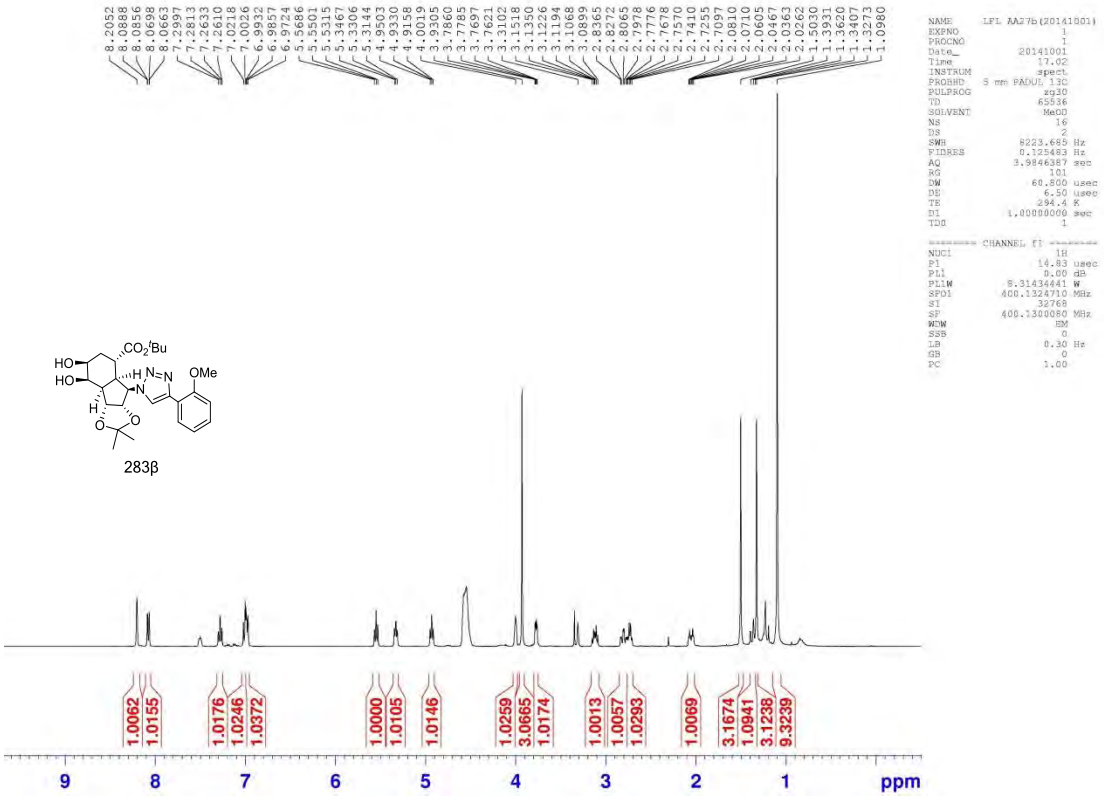
^{1}H NMR (Solvent: DMSO-d_6)



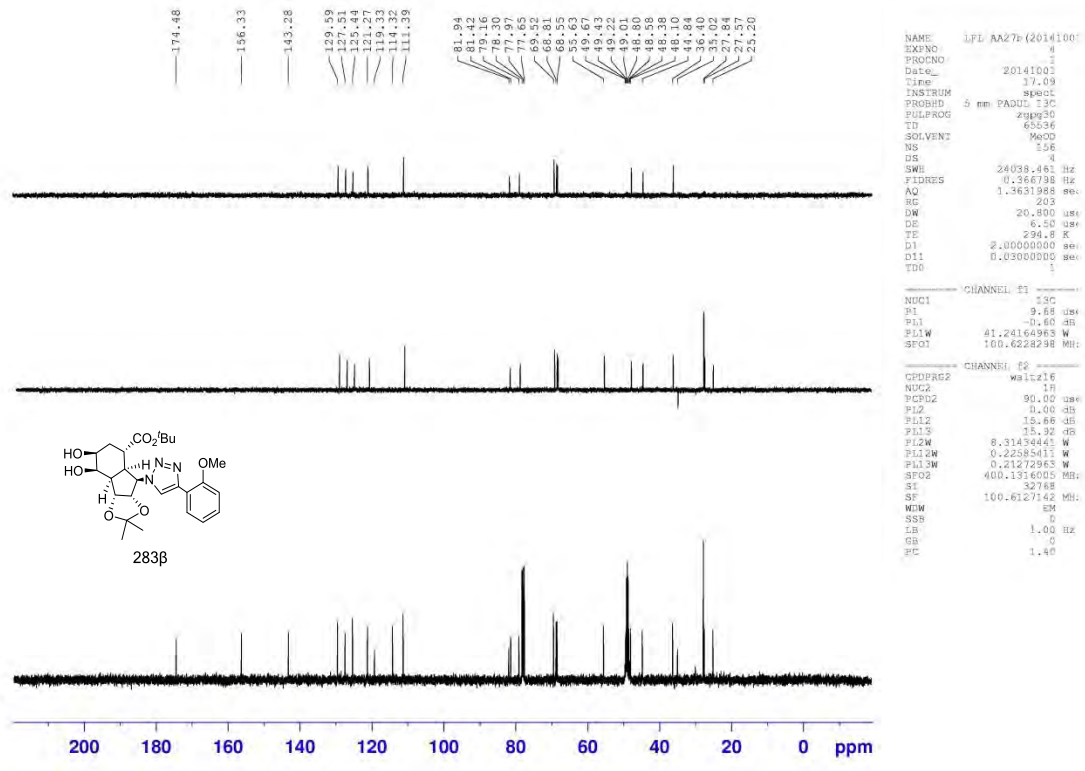
^{13}C NMR (Solvent: CD_3OD)



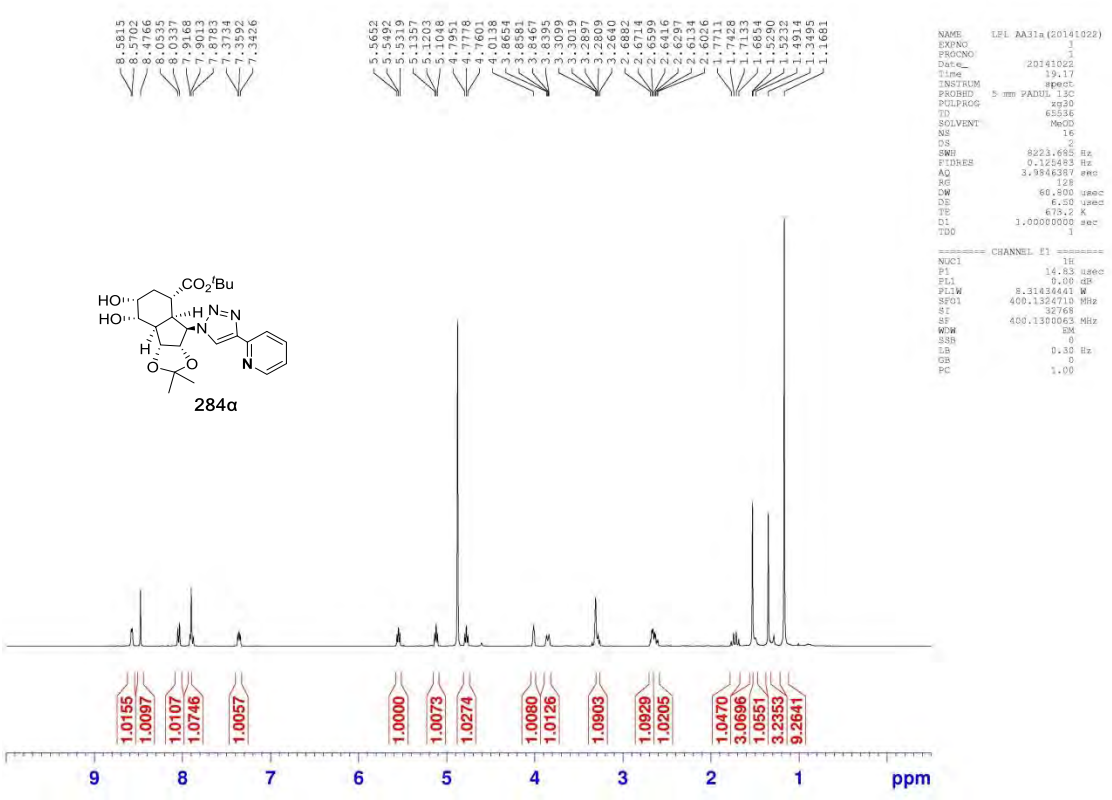
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 2:1)



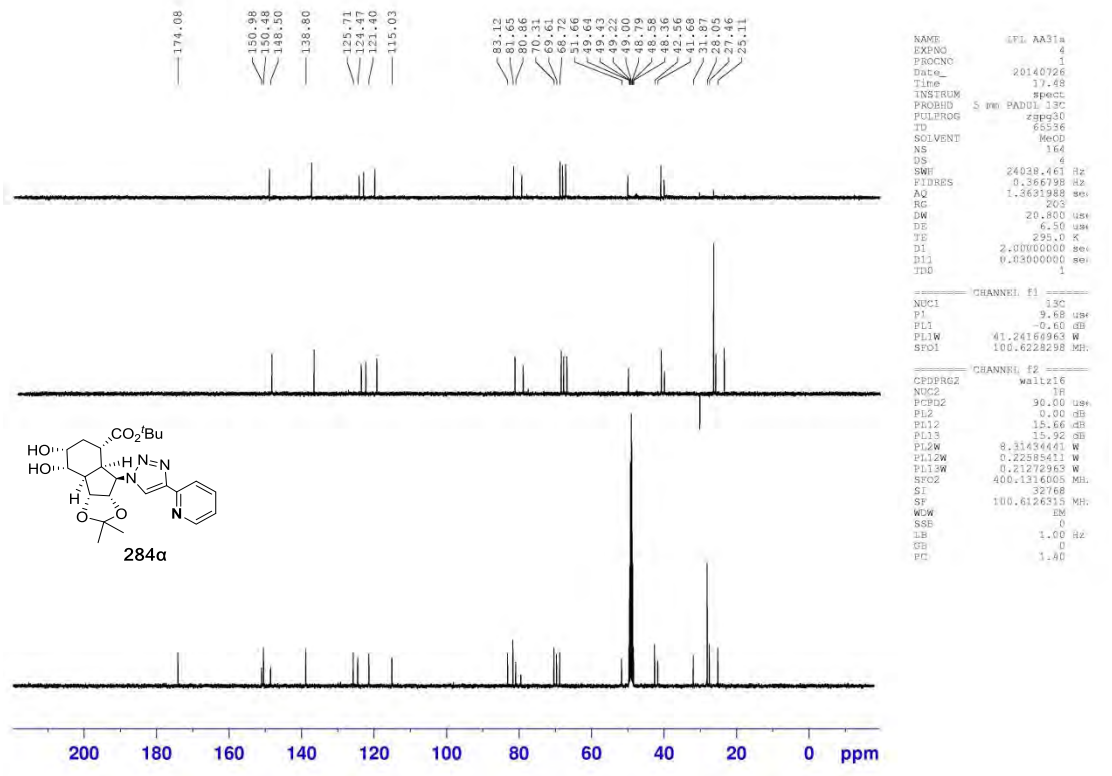
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 2:1)



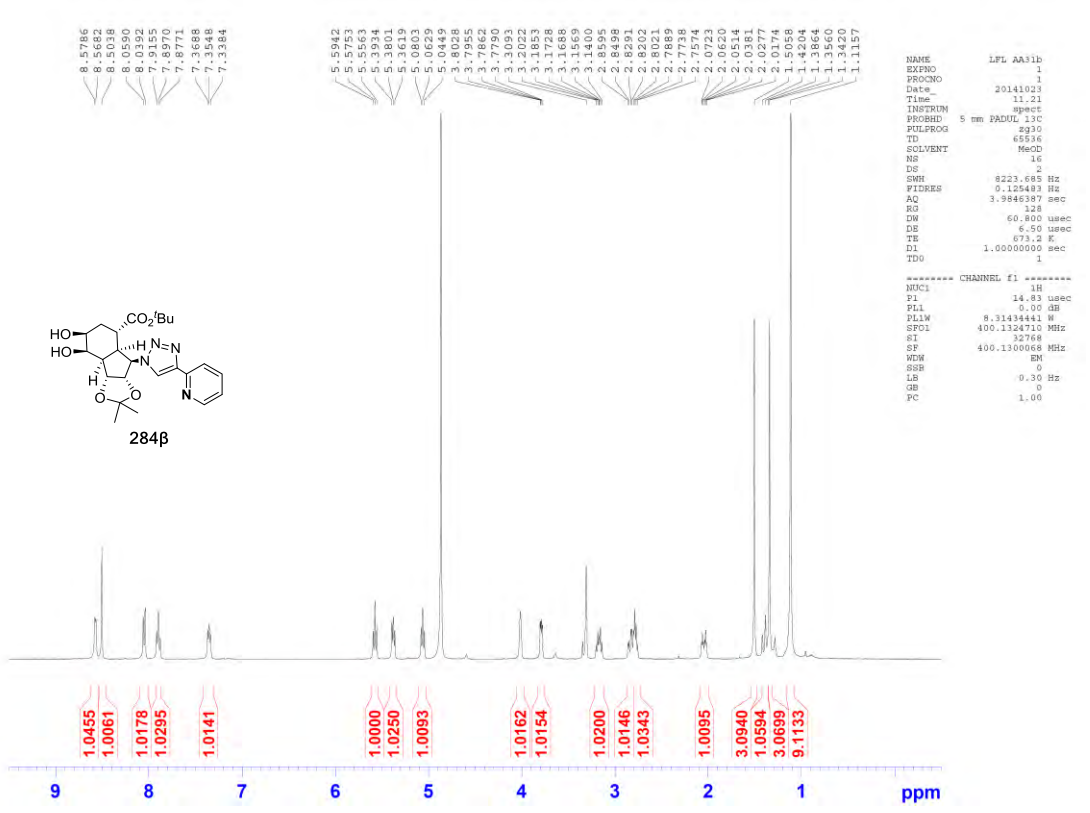
^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)



^{1}H NMR (Solvent: CD_3OD)

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PROCNO                  1
Date_            20141023
Time_               11.21
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PROBHD   5 mm PADUL 13C
PULPROG             zg30
TD                 65536
SOLVENT             MeOD
NS                    16
DS                     2
SWH             8223.685 Hz
FIDRES          0.125483 Hz
AQ              3.9846387 sec
RG                   128
DW                60.800 usec
DE                 6.50 usec
TE                673.2 K
D1             1.00000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                  1H
P1                 14.83 usec
PL1                0.00 dB
PL1W          8.31434441 W
SFO1          400.1324710 MHz
SI                 32768
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WDW                   EM
SSB                    0
LB                 0.30 Hz
GB                     0
PC                  1.00
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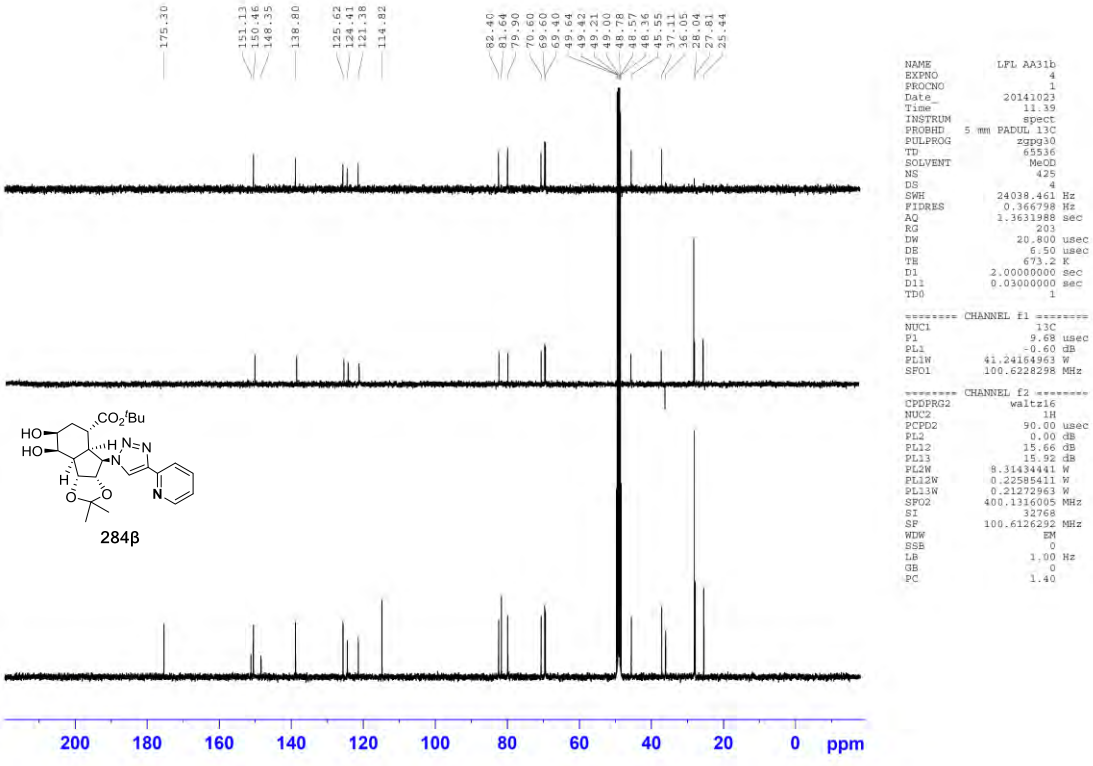
^{13}C NMR (Solvent: CD_3OD)

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PROCNO                  1
Date_            20141023
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TD                 65536
SOLVENT             MeOD
NS                   425
DS                     4
SWH            24038.461 Hz
FIDRES          0.366798 Hz
AQ              1.3631988 sec
RG                   203
DW                20.800 usec
DE                 6.50 usec
TE                673.2 K
D1             2.00000000 sec
D11            0.03000000 sec
TD0                    1

======== CHANNEL f1 ========
NUC1                 13C
P1                 9.68 usec
PL1               -0.60 dB
PL1W          41.24164963 W
SFO1          100.6228298 MHz

======== CHANNEL f2 ========
CPDPRG2          waltz16
NUC2                  1H
PCPD2              90.00 usec
PL2                0.00 dB
PL12              15.66 dB
PL13              15.92 dB
PL2W          8.31434441 W
PL12W         0.22585411 W
PL13W         0.21272963 W
SFO2          400.1316005 MHz
SI                 32768
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WDW                   EM
SSB                    0
LB                 1.00 Hz
GB                     0
PC                  1.40
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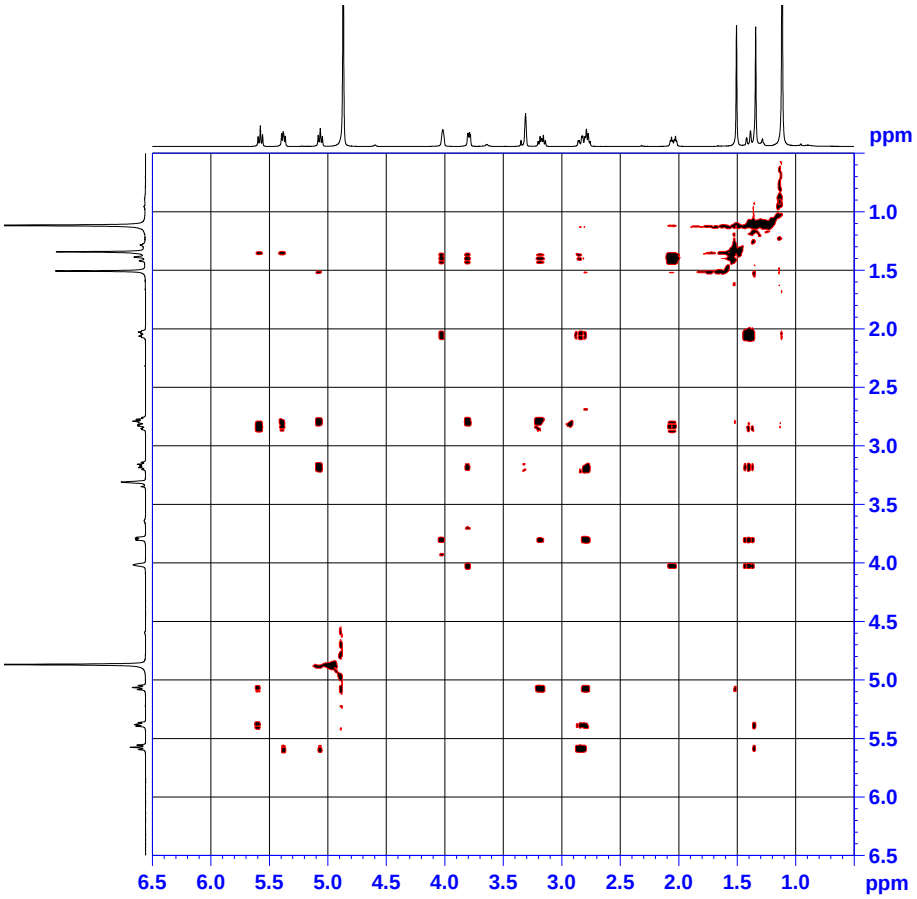
NOESY (Solvent: CD_3OD)

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Current Data Parameters
NAME      LFL AA31b(COPY)
EXPNO                  6
PROCNO                 1

F2 - Acquisition Parameters
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Time              23.54
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PULPROG         noesyph
TD                2048
SOLVENT           MeOD
NS                  32
DS                   4
SWH           4084.967 Hz
FIDRES        1.994613 Hz
AQ            0.2506752 sec
RG                  64
DW              122.400 usec
DE                6.50 usec
TE               673.2 K
D0          0.00010352 sec
D1          2.00000000 sec
D8          0.30000001 sec
IN0         0.00024480 sec

======== CHANNEL f1 ========
NUC1                1H
P1              14.83 usec
PL1       0 dB
PL1W       8.31434441 W
SFO1     400.1318419 MHz

F1 - Acquisition parameters
TD                 256
SFO1        400.1318 MHz
FIDRES     15.956903 Hz
SW            10.209 ppm
FnMODE     States-TPPI

F2 - Processing parameters
SI                1024
SF          400.1300002 MHz
WDW               QSINE
SSB                   2
LB        0 Hz
GB        0
PC                1.00

F1 - Processing parameters
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MC2        States-TPPI
SF          400.1300001 MHz
WDW               QSINE
SSB                   2
LB        0 Hz
GB        0
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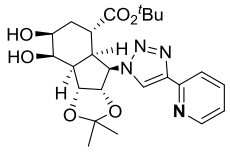
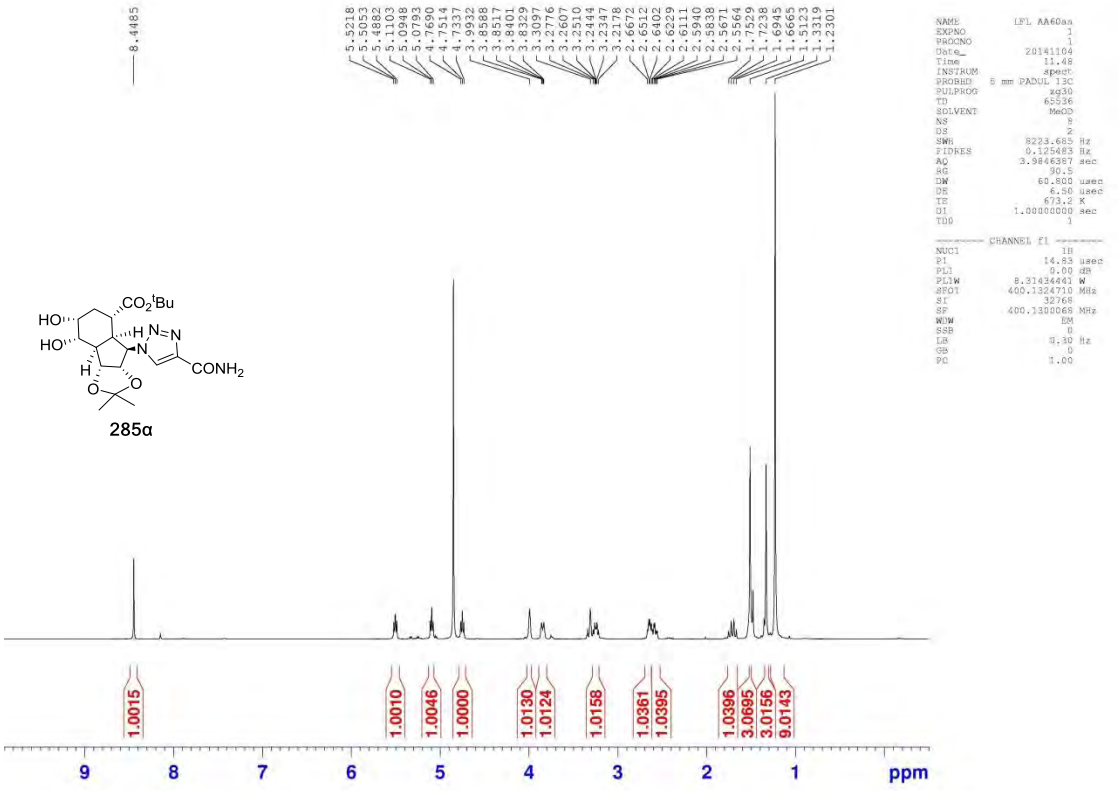
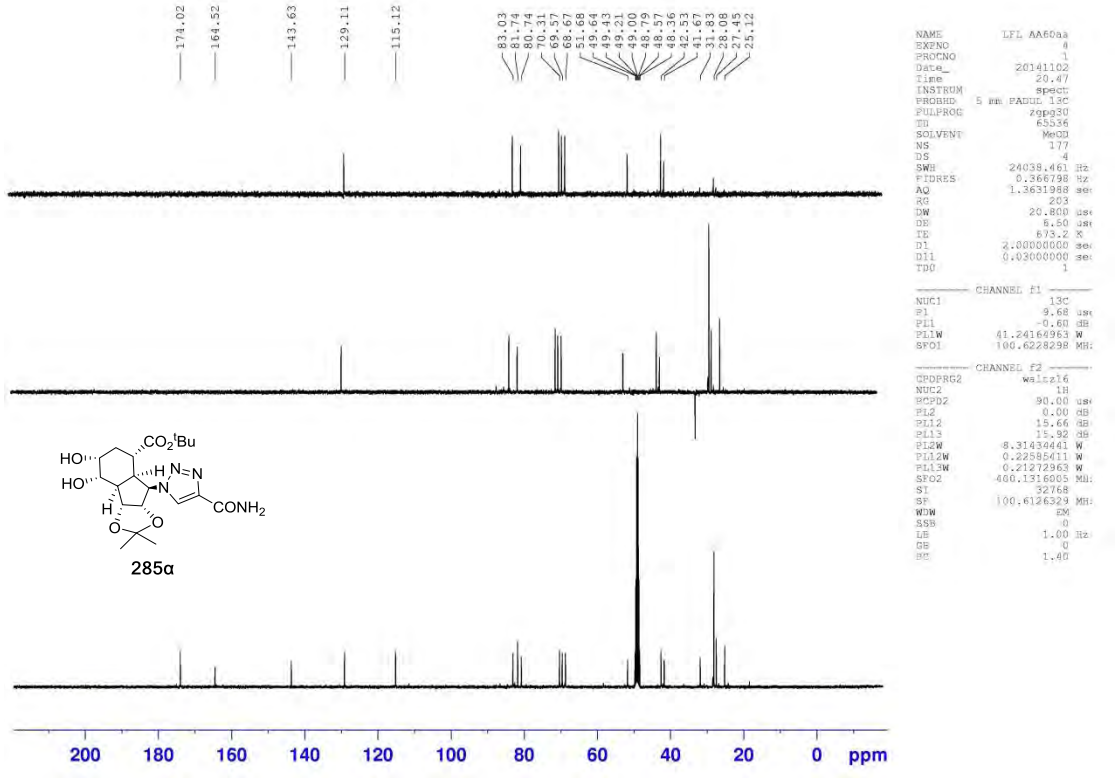


284β

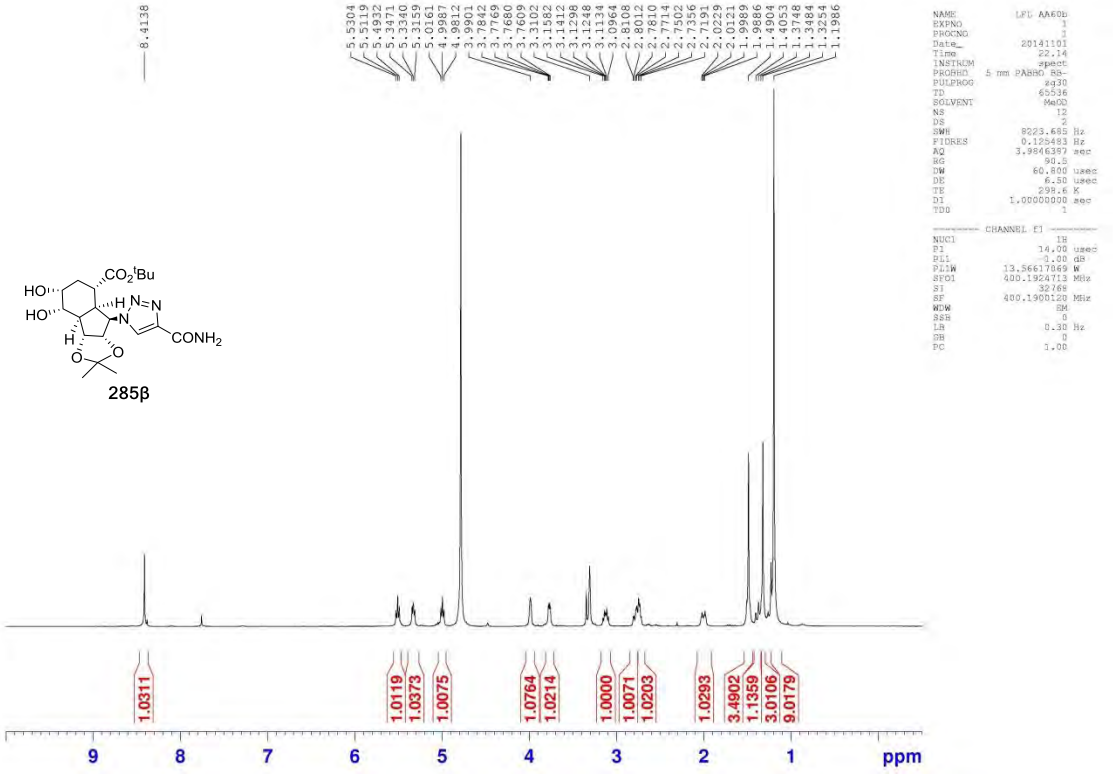
^{1}H NMR (Solvent: CD_3OD)



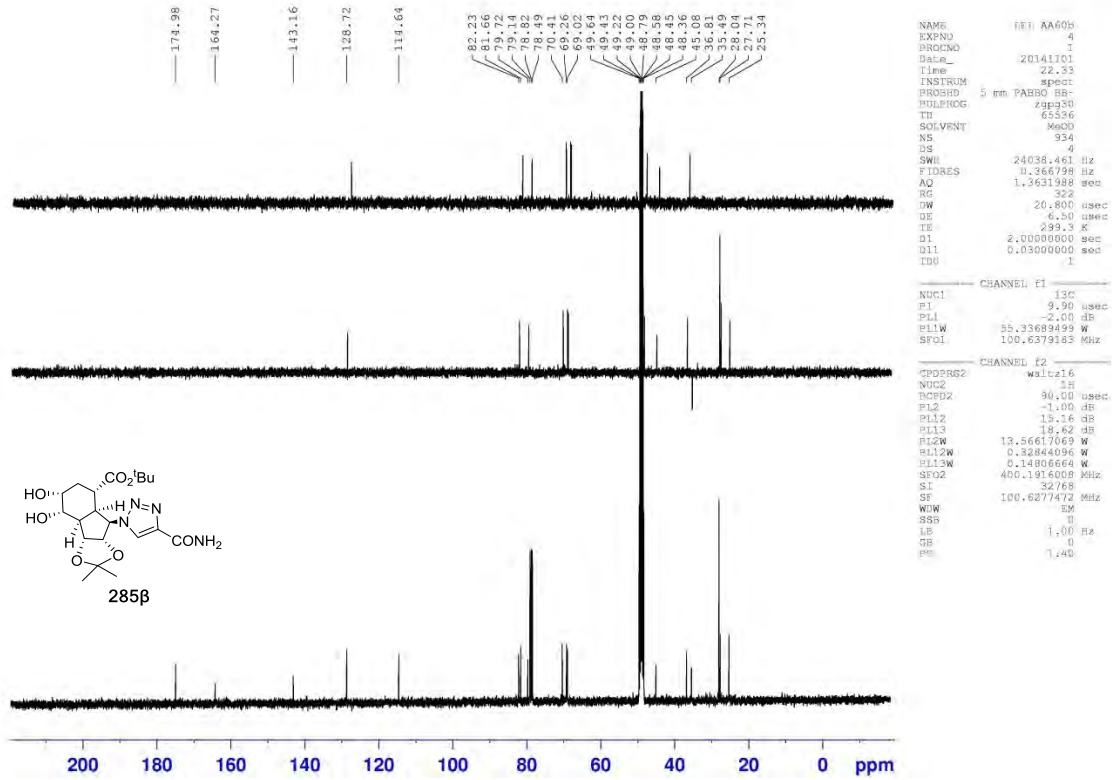
^{13}C NMR (Solvent: CD_3OD)



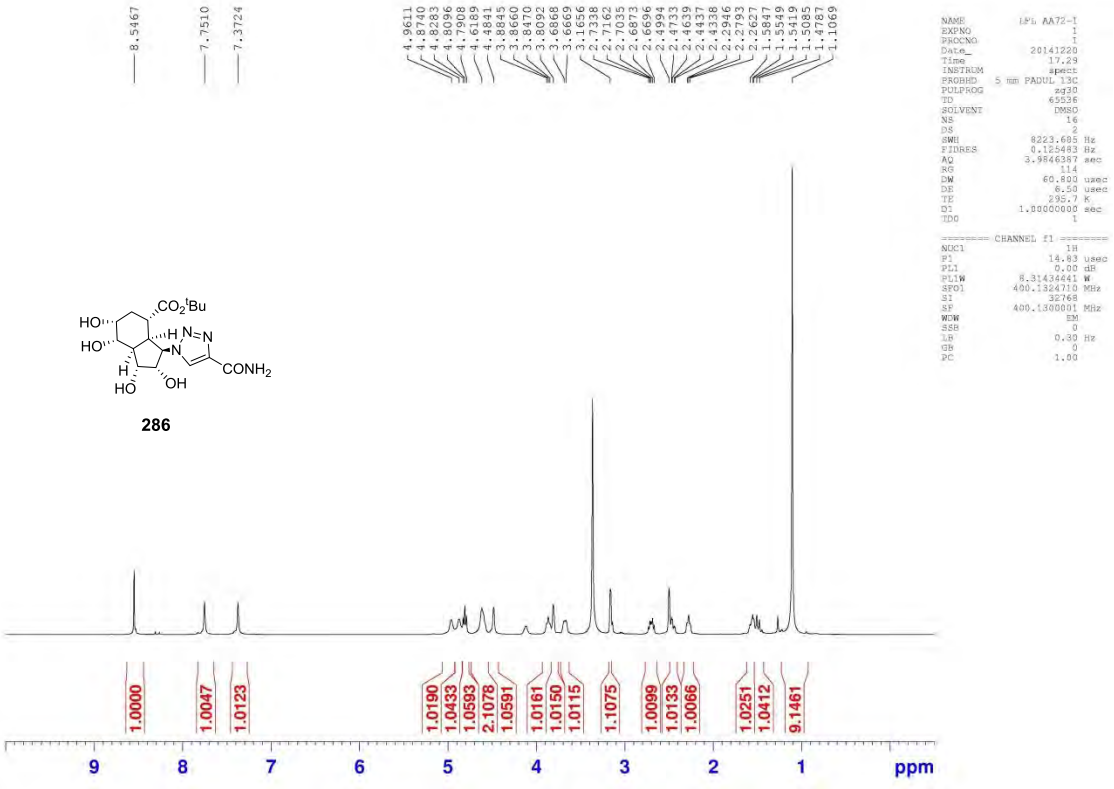
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:2)



^{1}H NMR (Solvent: DMSO-d_6)



286

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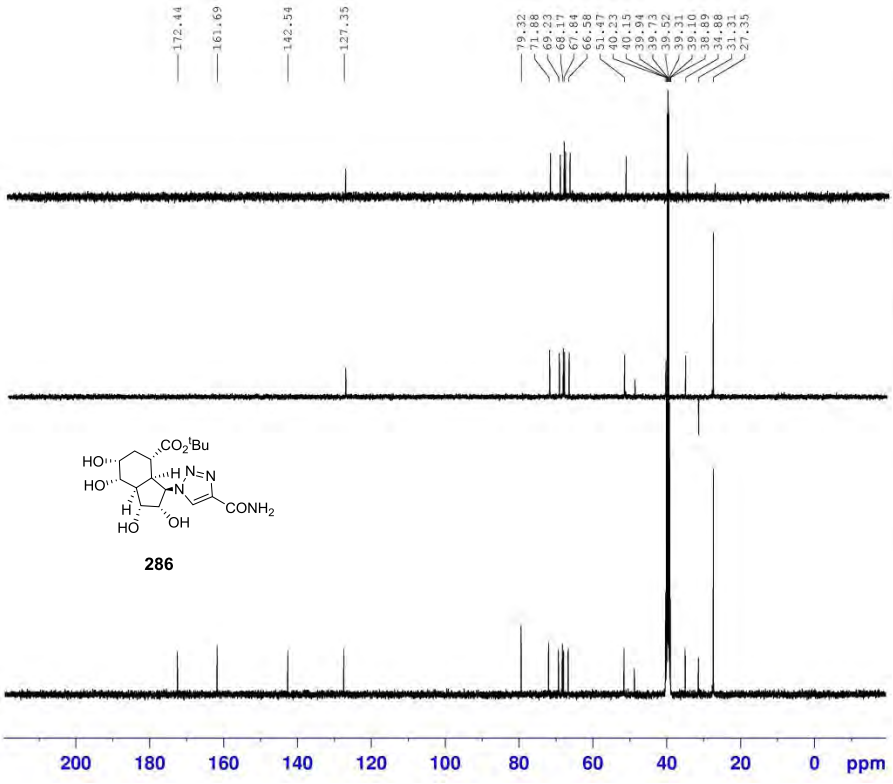
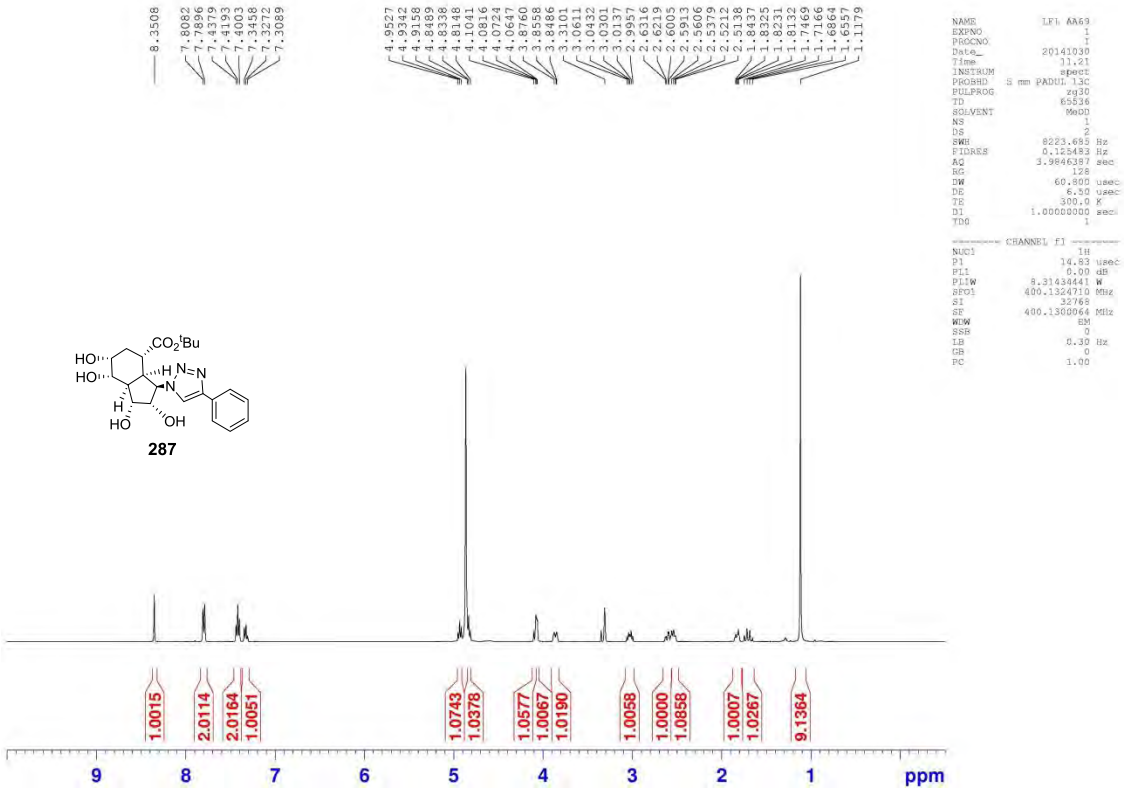
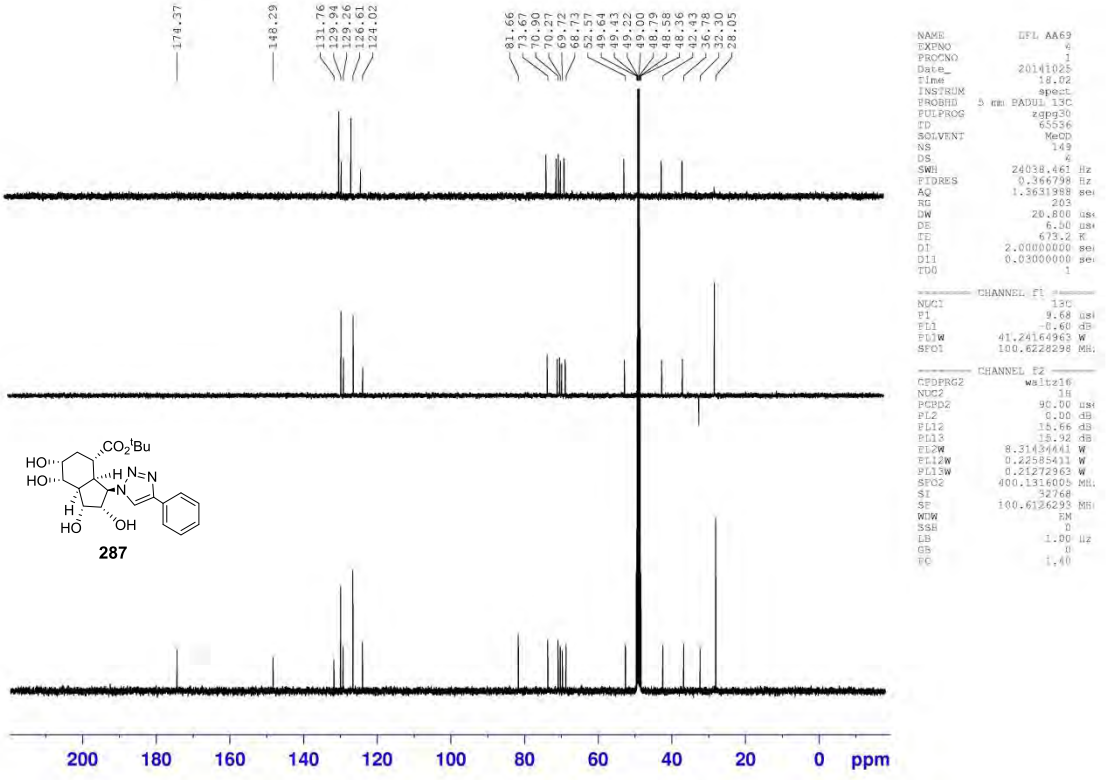


286

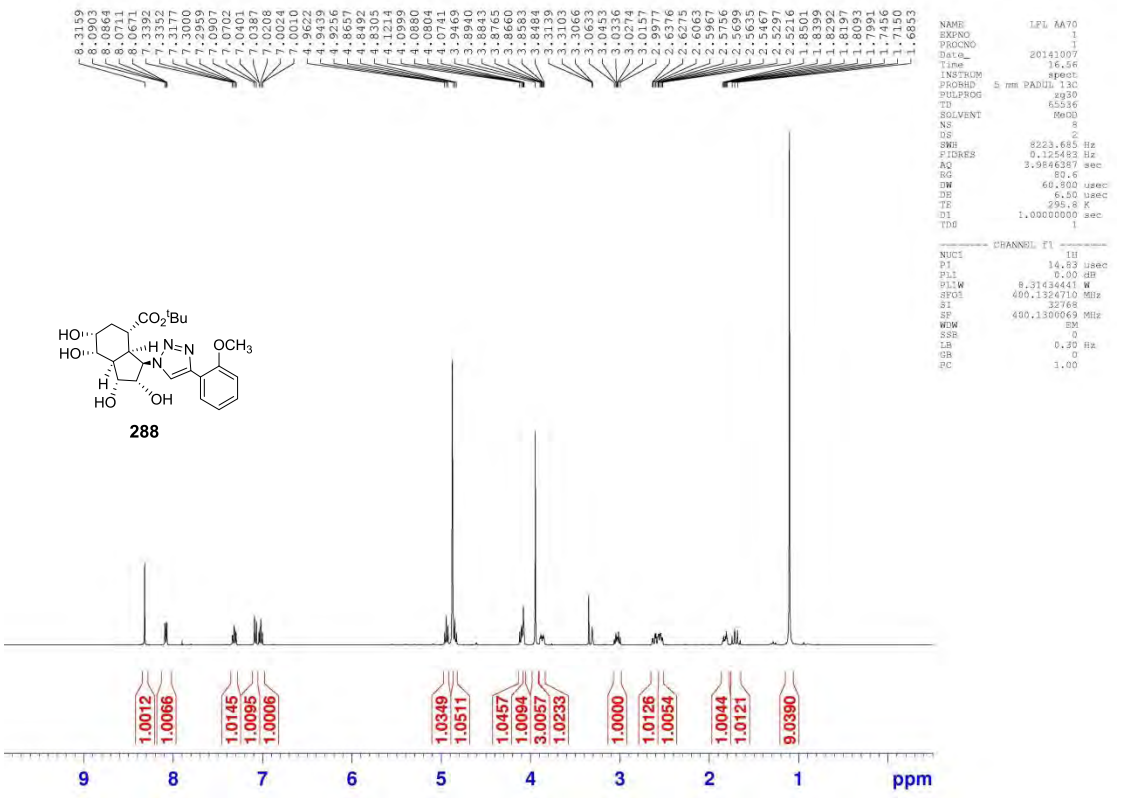
^{1}H NMR (Solvent: CD_3OD)



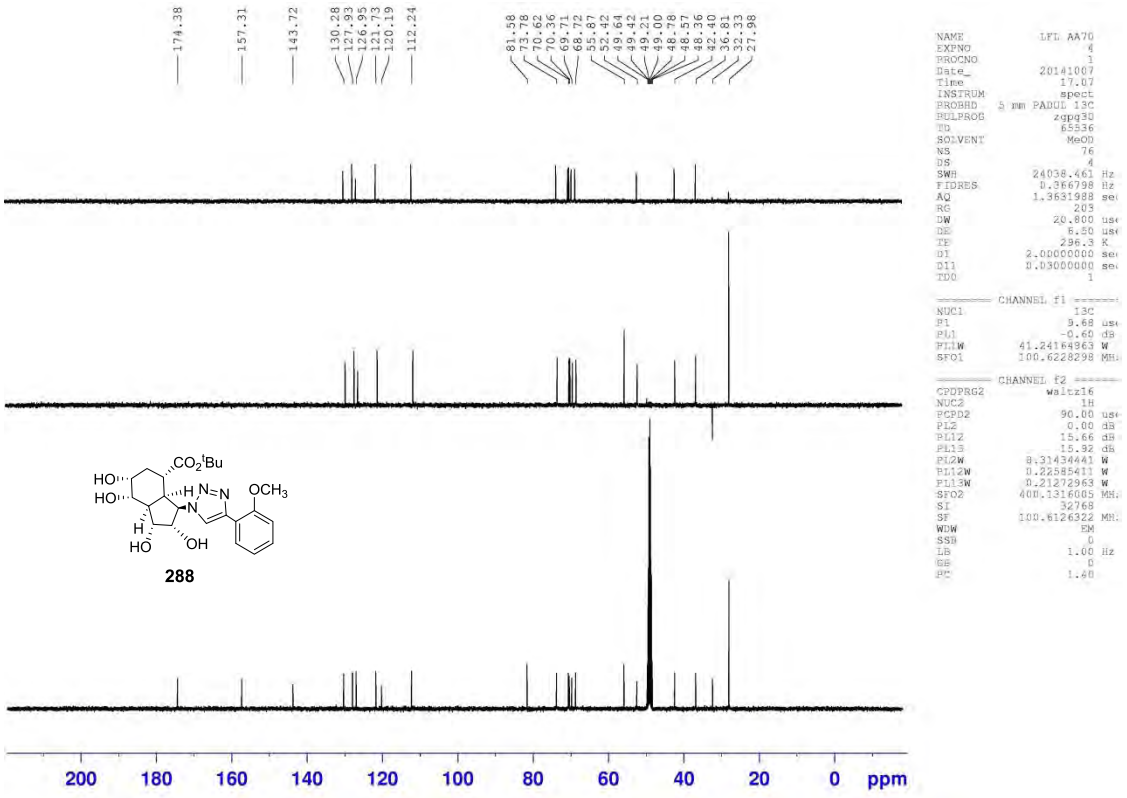
^{13}C NMR (Solvent: CD_3OD)



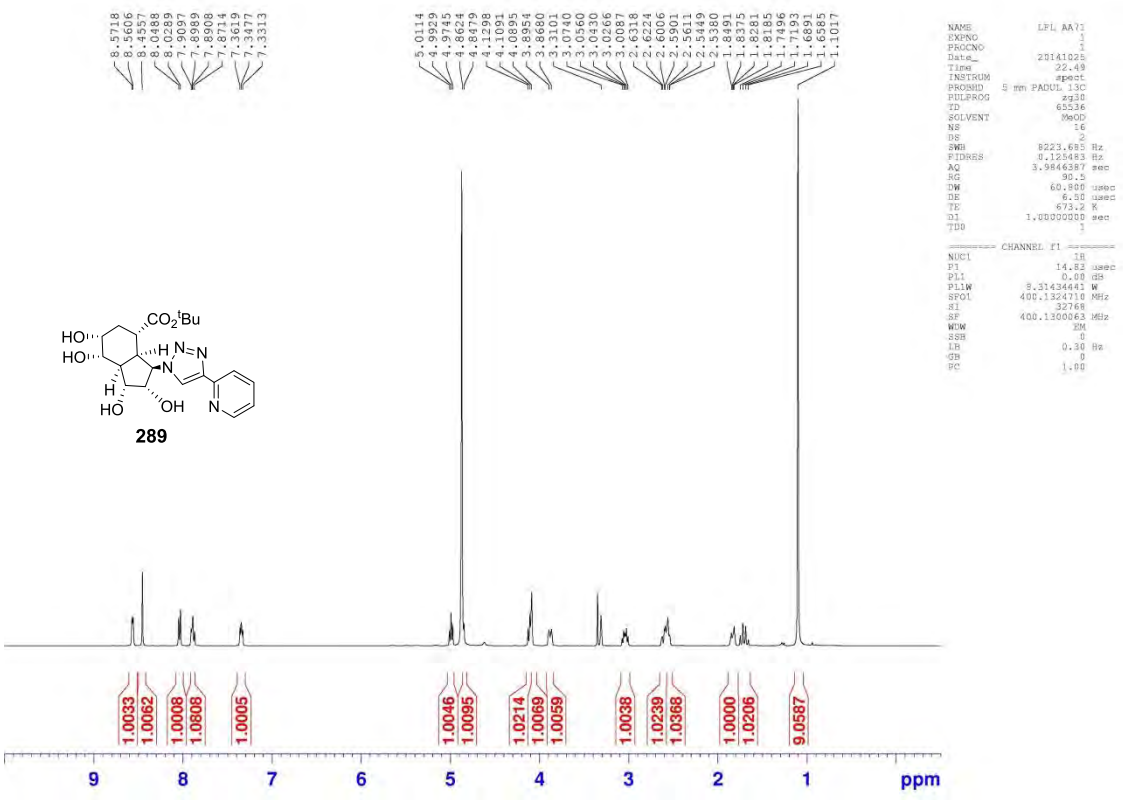
^{1}H NMR (Solvent: CD_3OD)



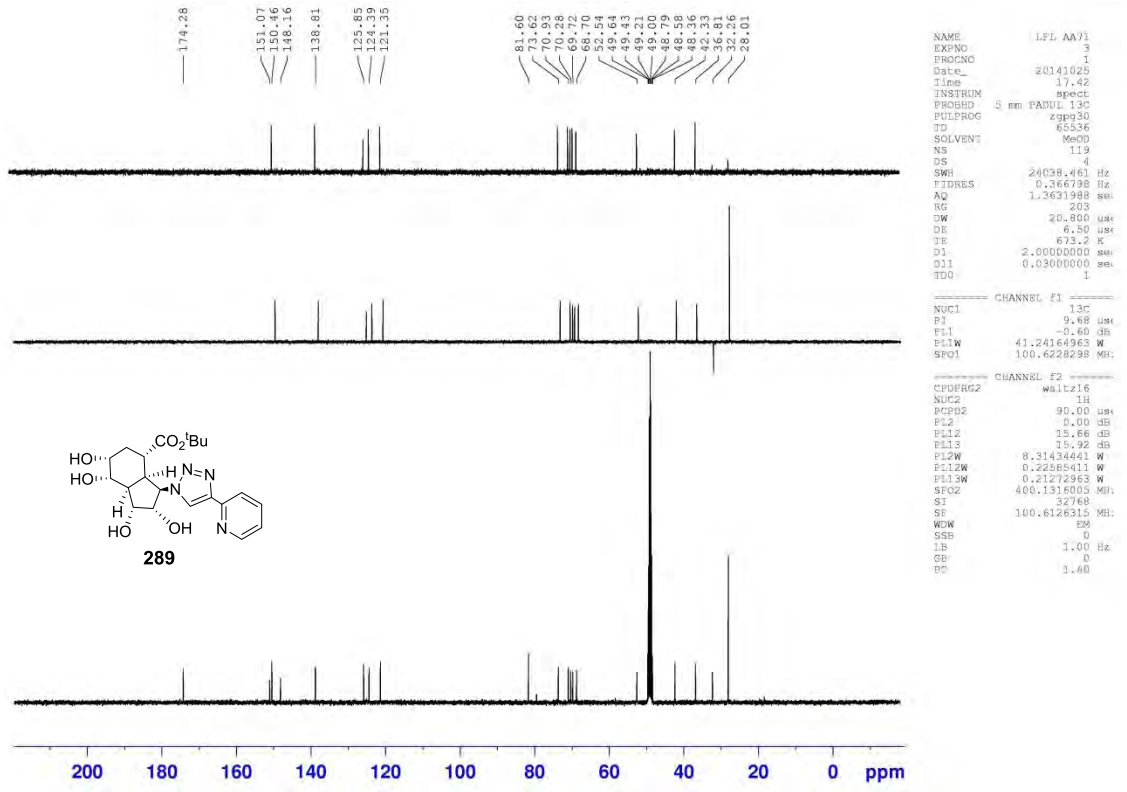
^{13}C NMR (Solvent: CD_3OD)



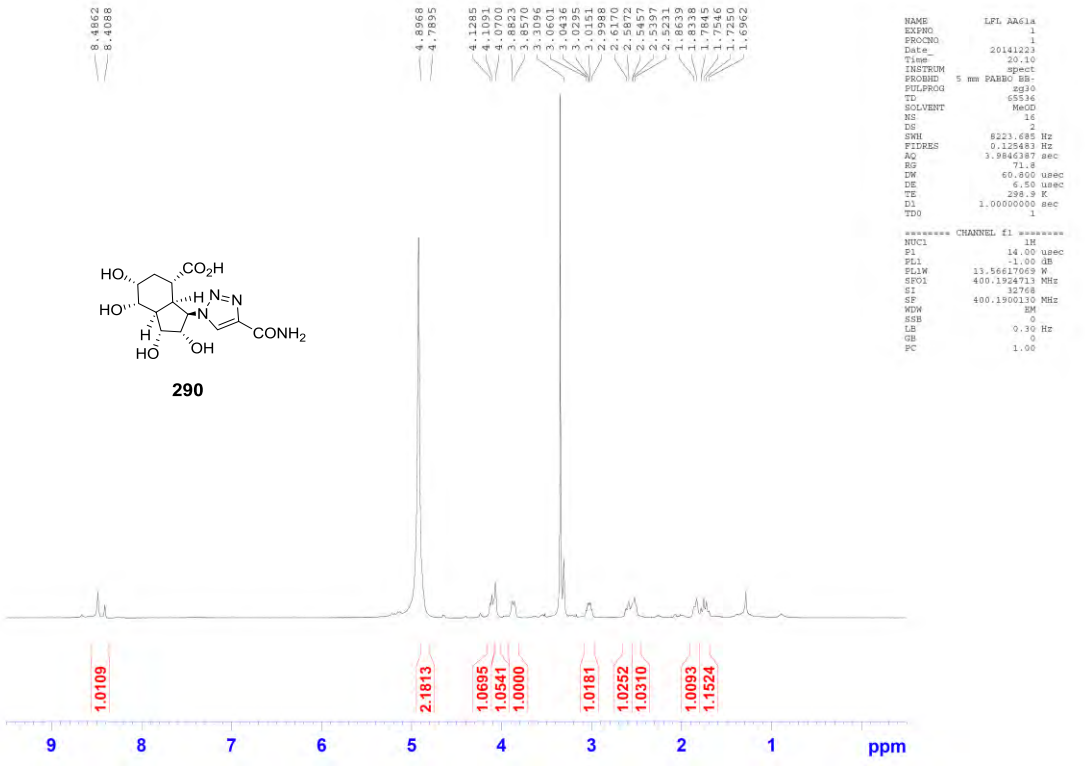
^{1}H NMR (Solvent: CD_3OD)



^{13}C NMR (Solvent: CD_3OD)

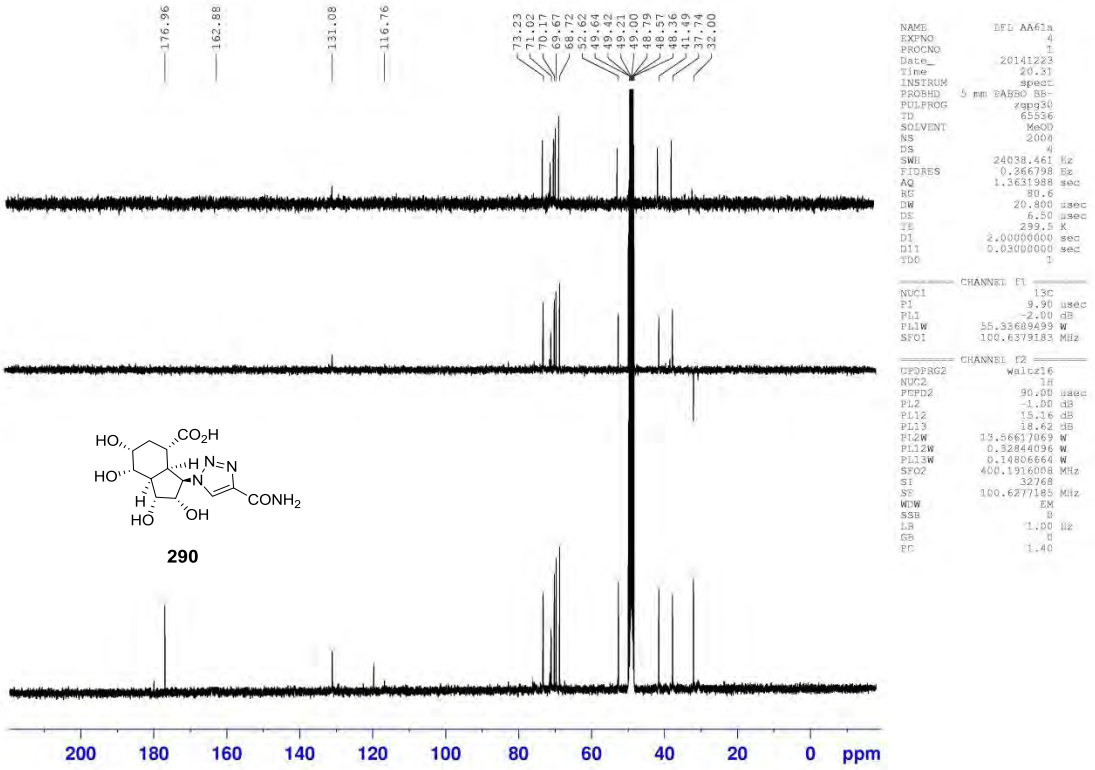


^{1}H NMR (Solvent: CD_3OD)



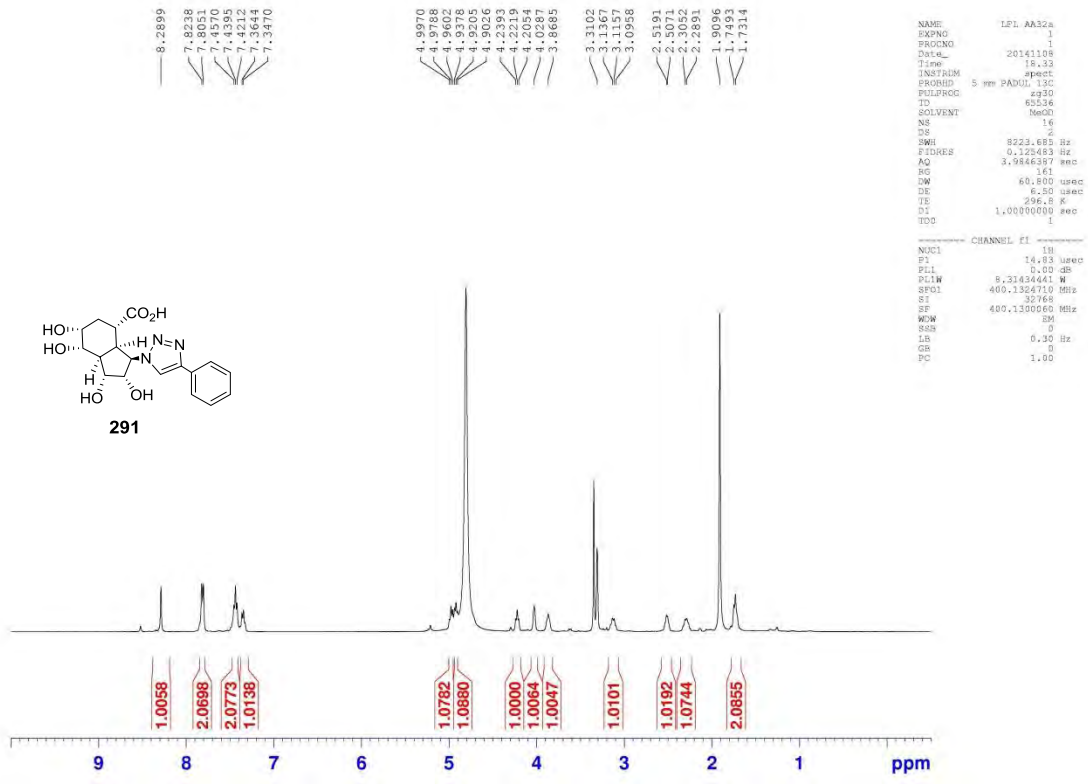
290

^{13}C NMR (Solvent: CD_3OD)

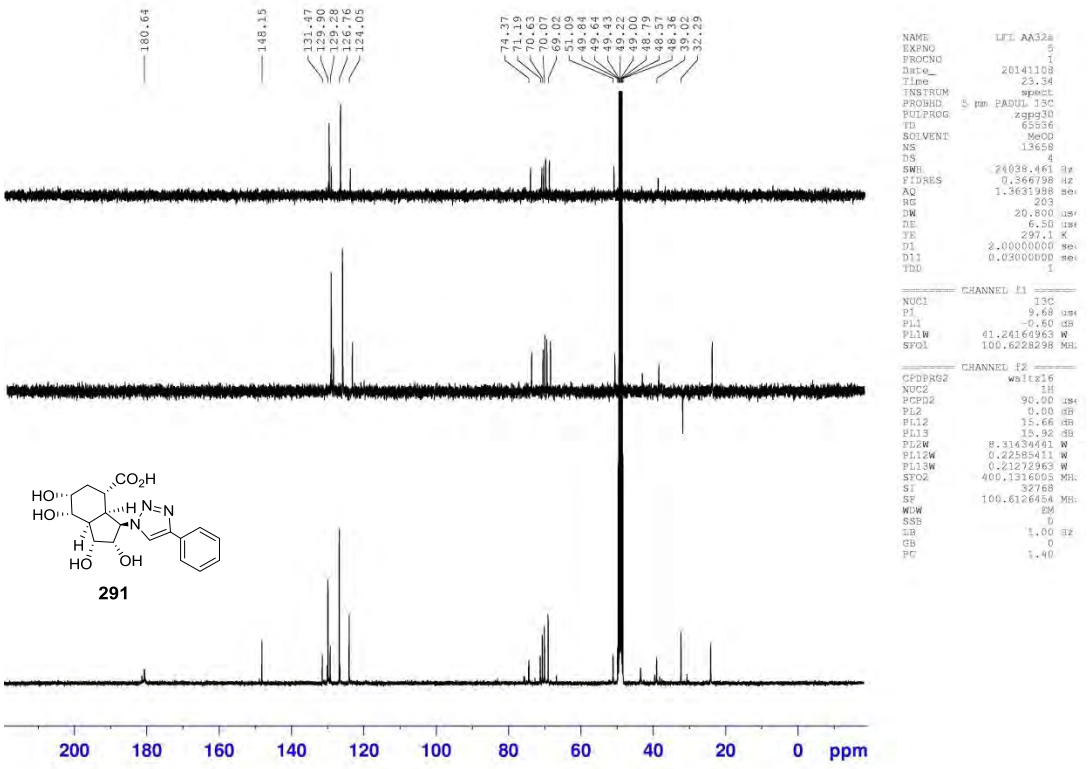


290

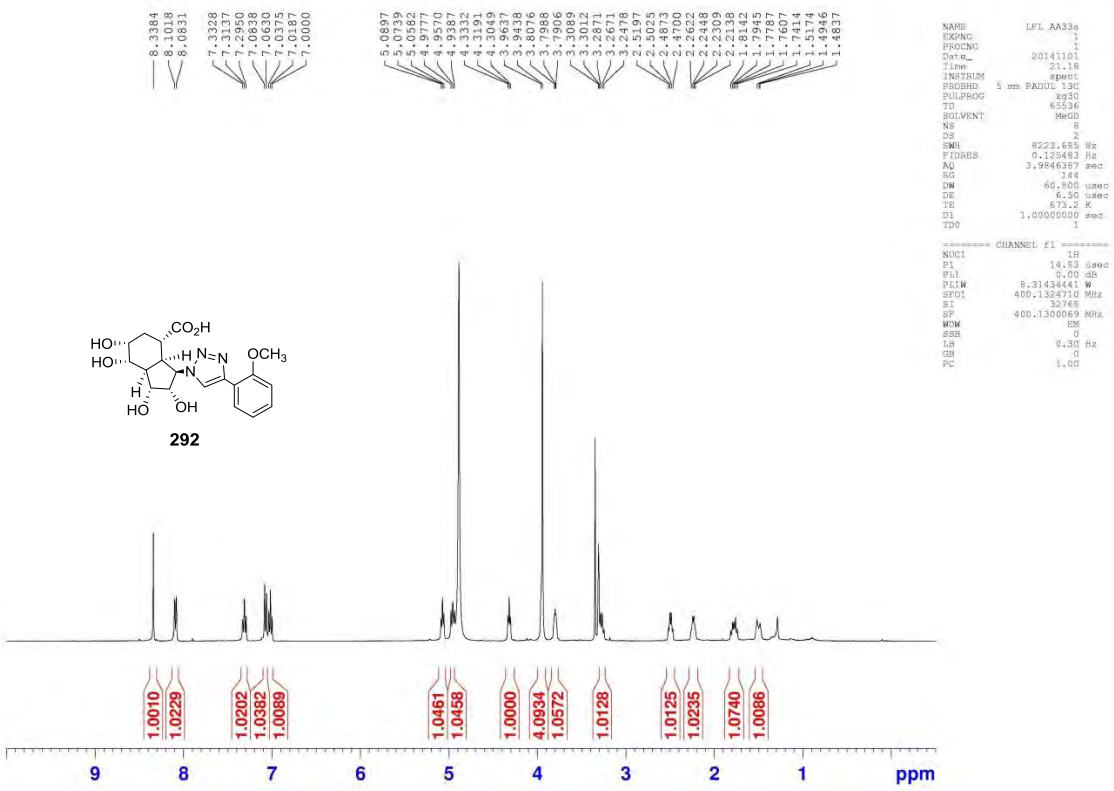
^{1}H NMR (Solvent: $CD_3OD:D_2O$:AcOH 2:1:0.1)



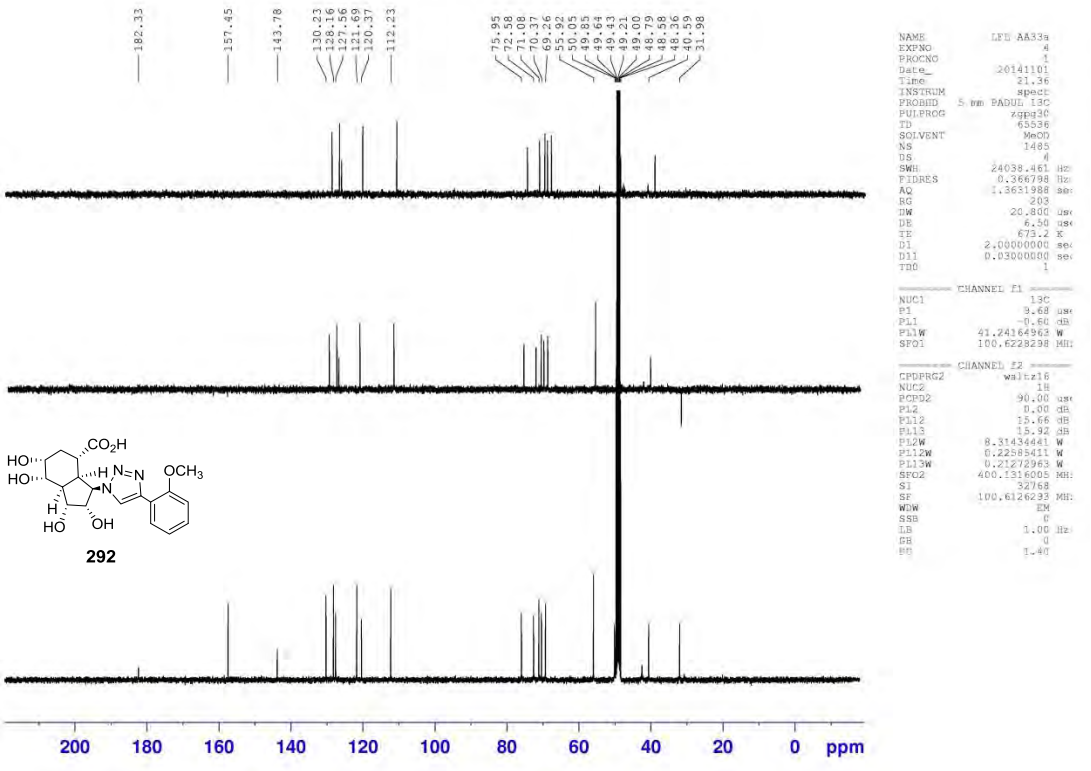
^{13}C NMR (Solvent: $CD_3OD:D_2O$:AcOH 2:1:0.1)



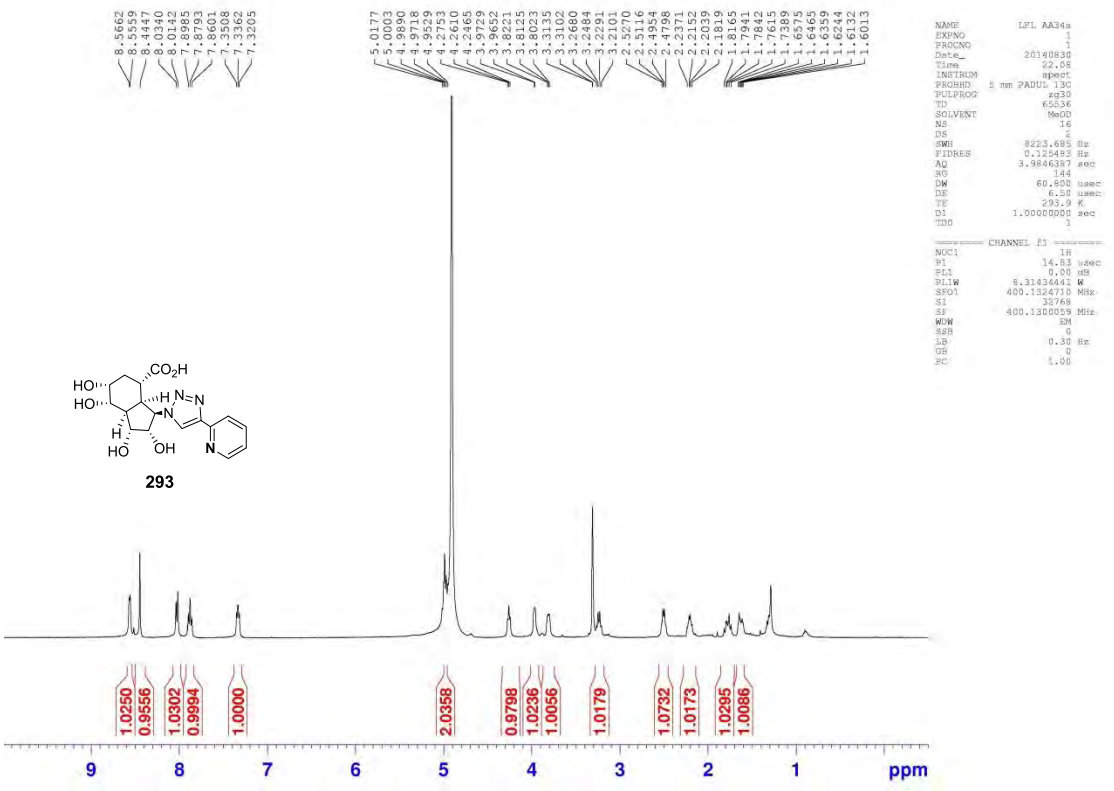
^{1}H NMR (Solvent: CD_3OD)



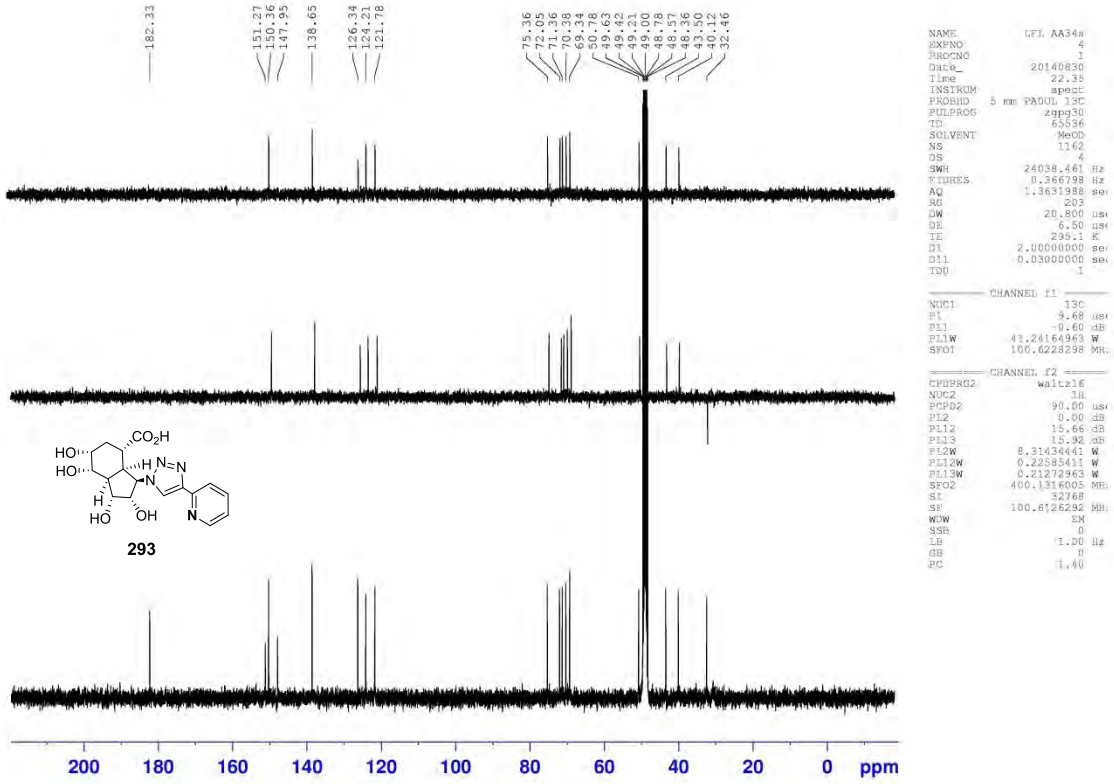
^{13}C NMR (Solvent: CD_3OD)



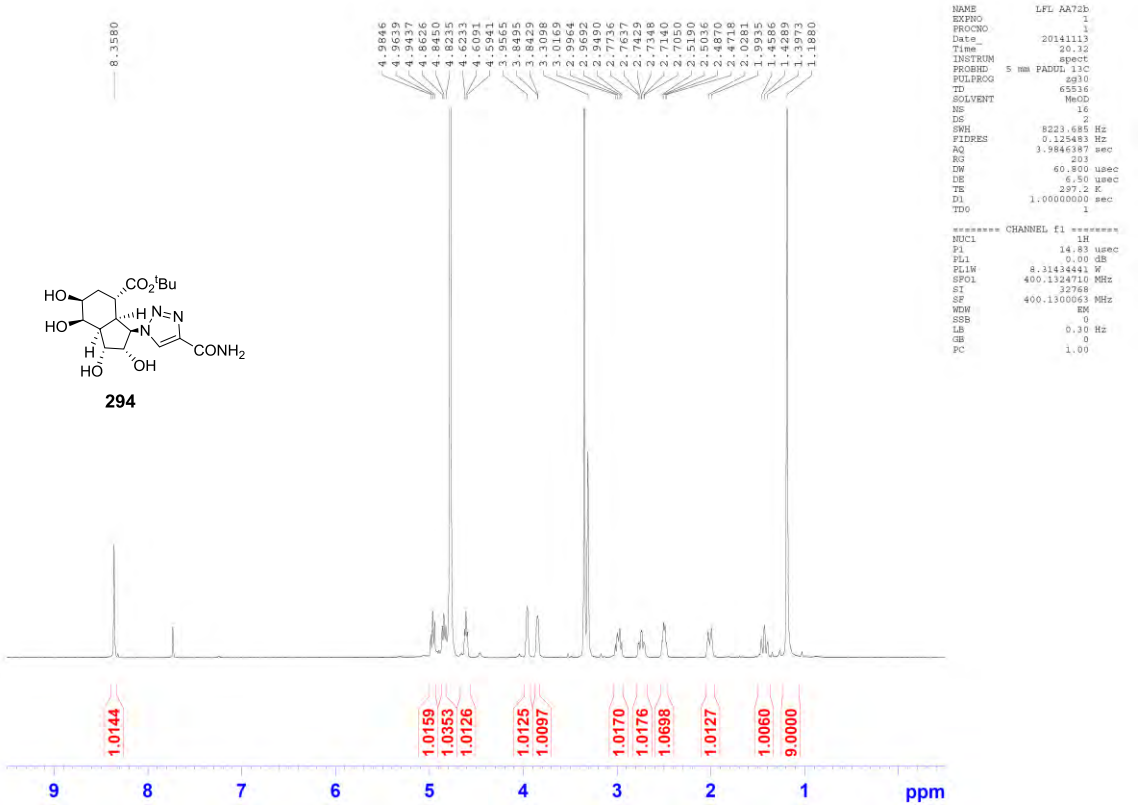
^{1}H NMR (Solvent: CD_3OD)



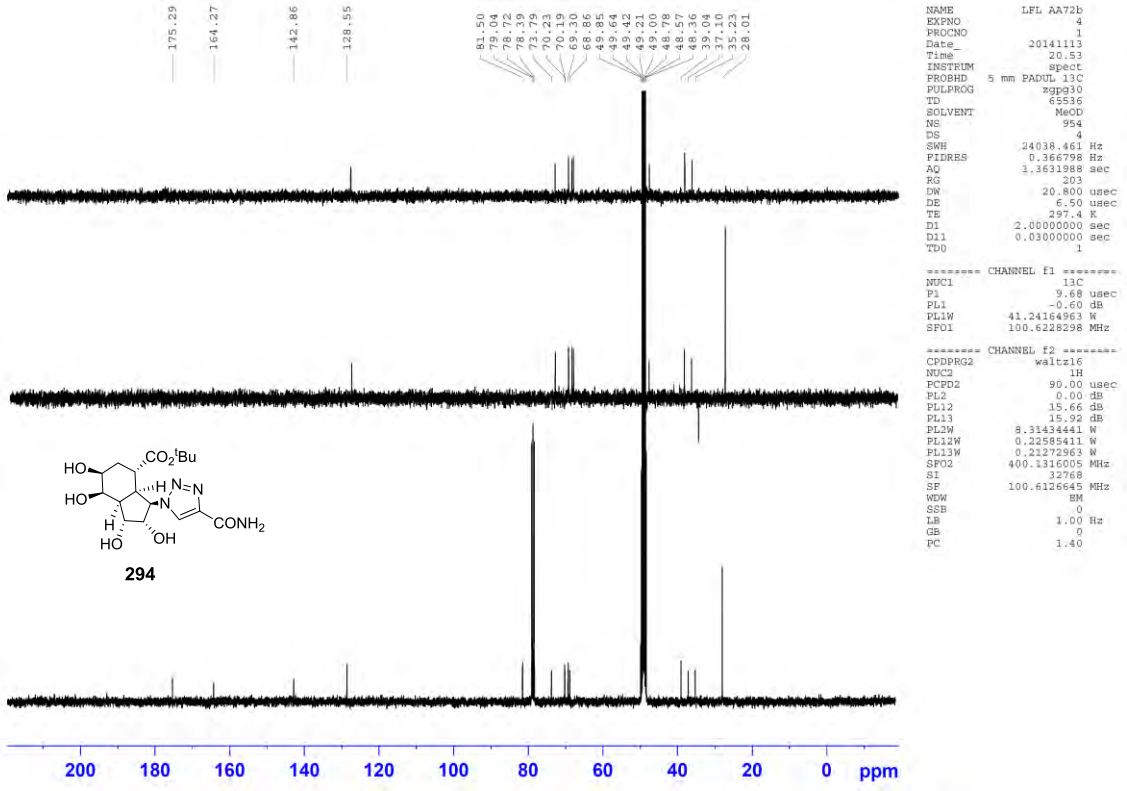
^{13}C NMR (Solvent: CD_3OD)



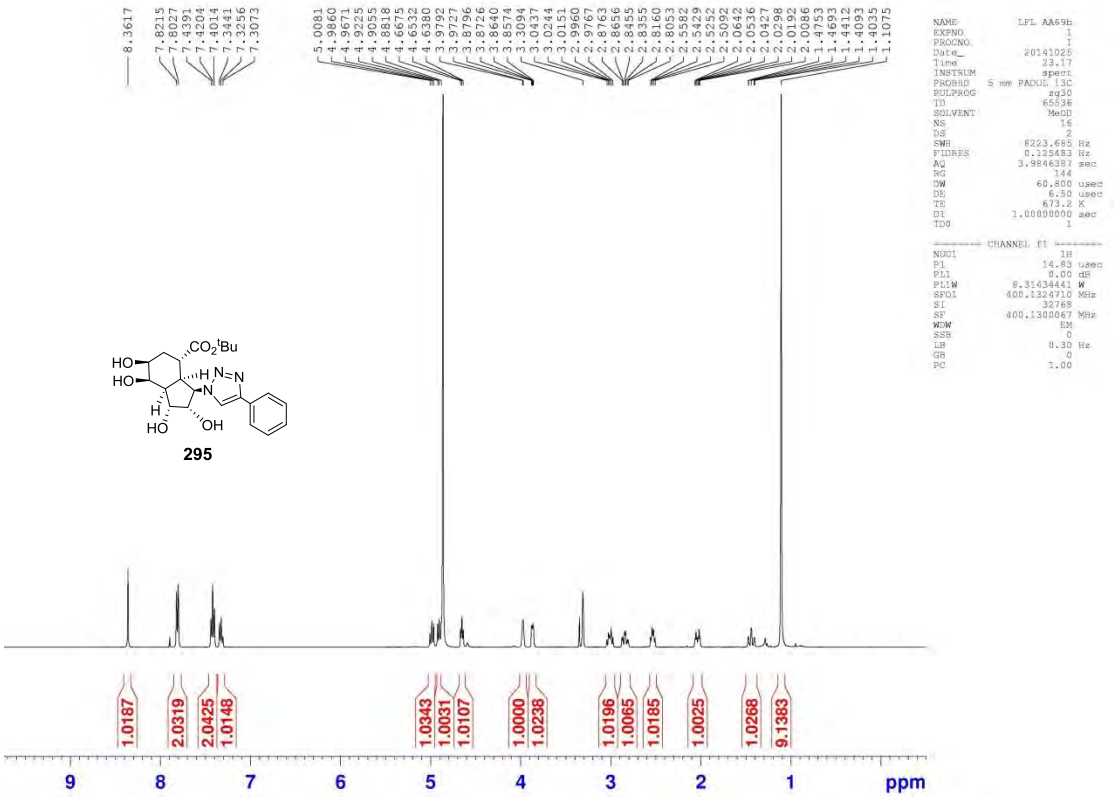
^{1}H NMR (Solvent: $CDCl_3$:CD_3OD 1:3)



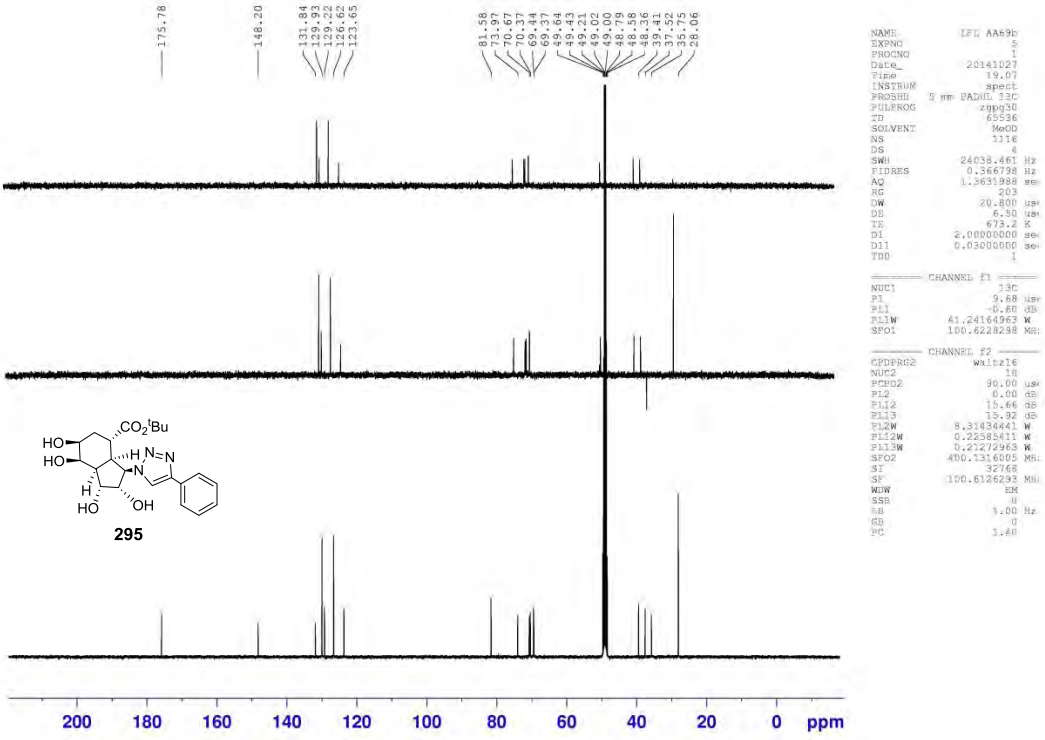
^{13}C NMR (Solvent: $CDCl_3$:CD_3OD 1:3)



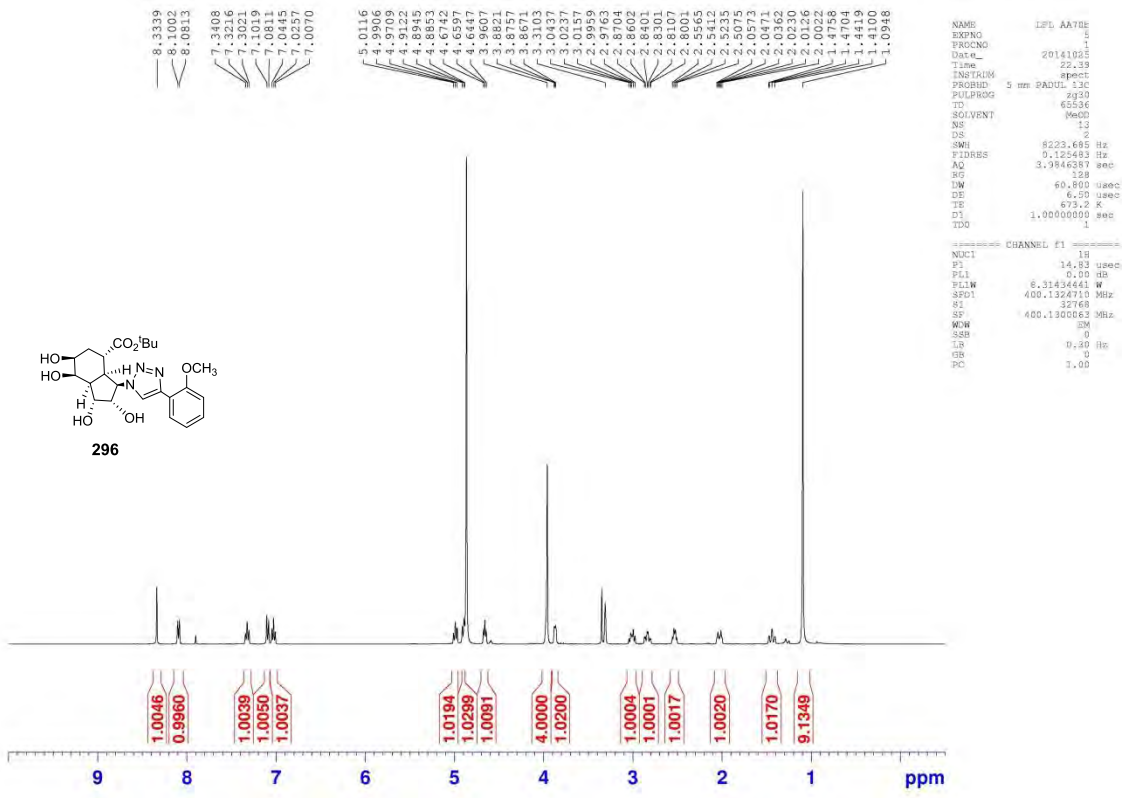
^{1}H NMR (Solvent: CD_3OD)



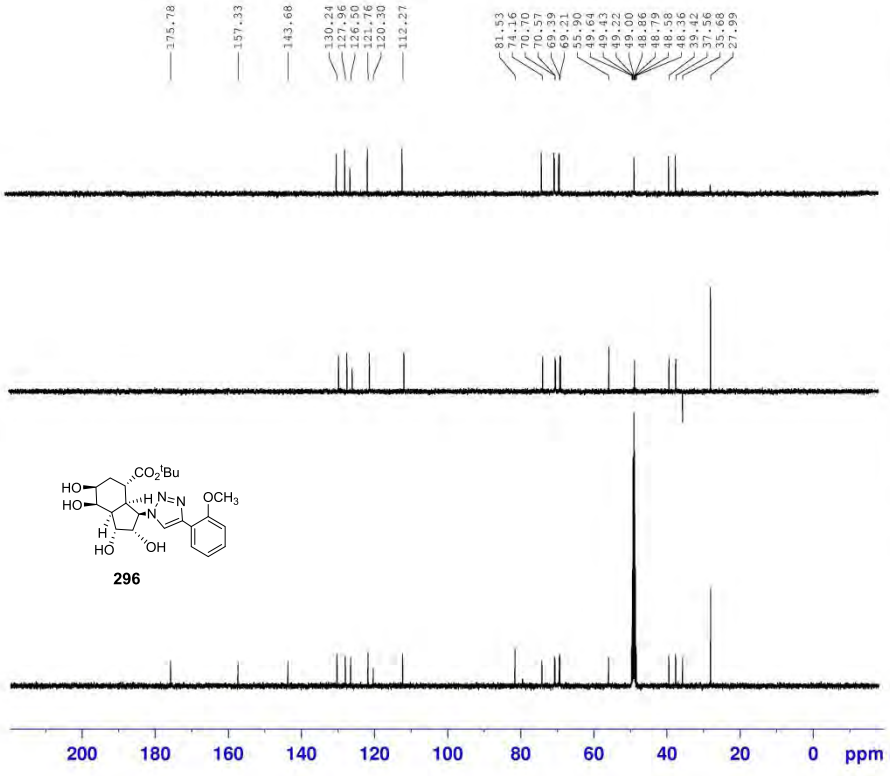
^{13}C NMR (Solvent: CD_3OD)



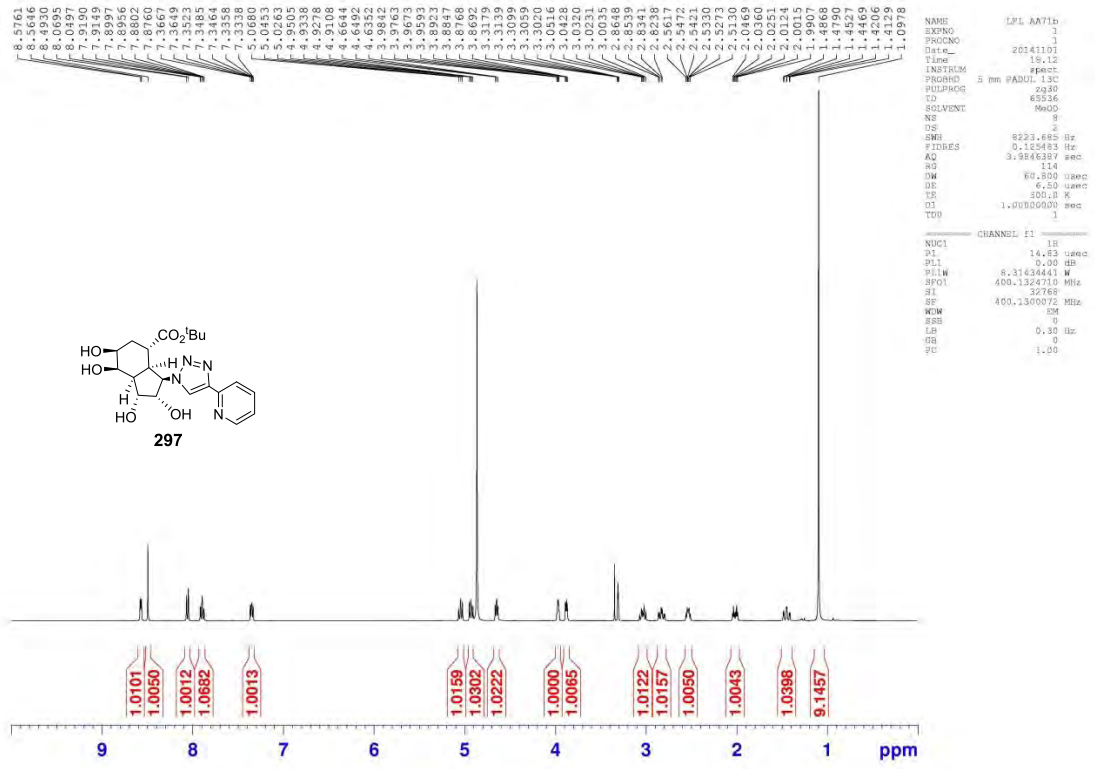
^{1}H NMR (Solvent: CD_3OD)



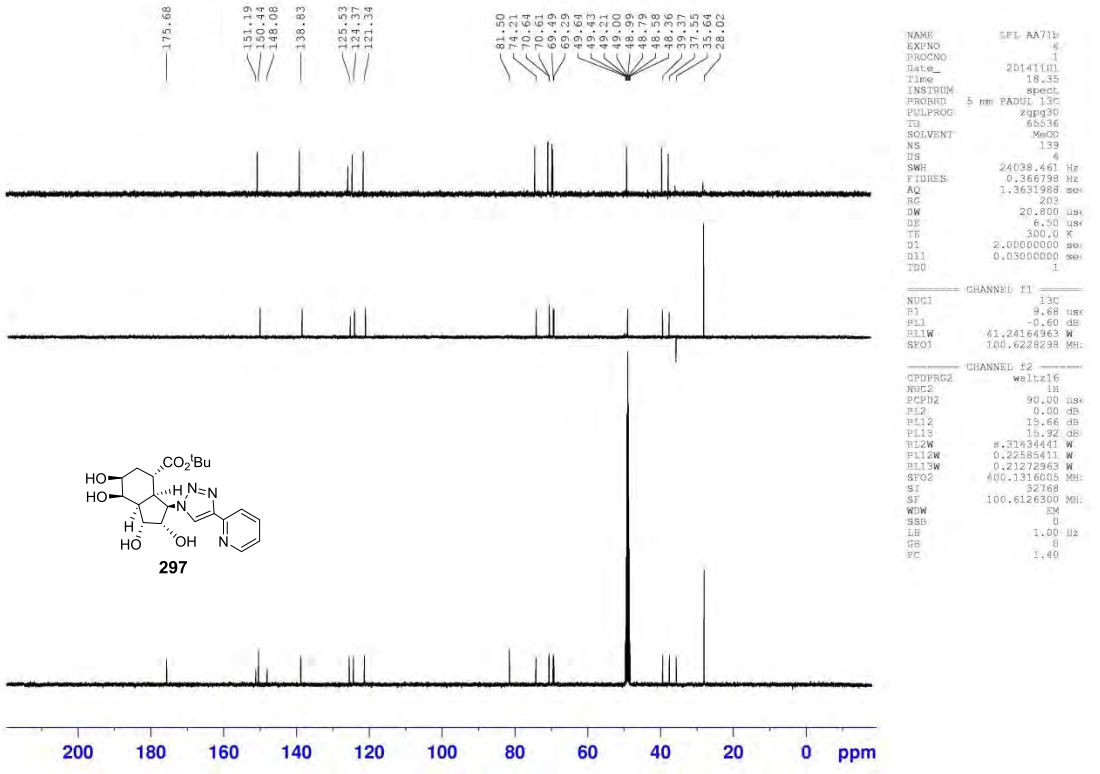
^{13}C NMR (Solvent: CD_3OD)



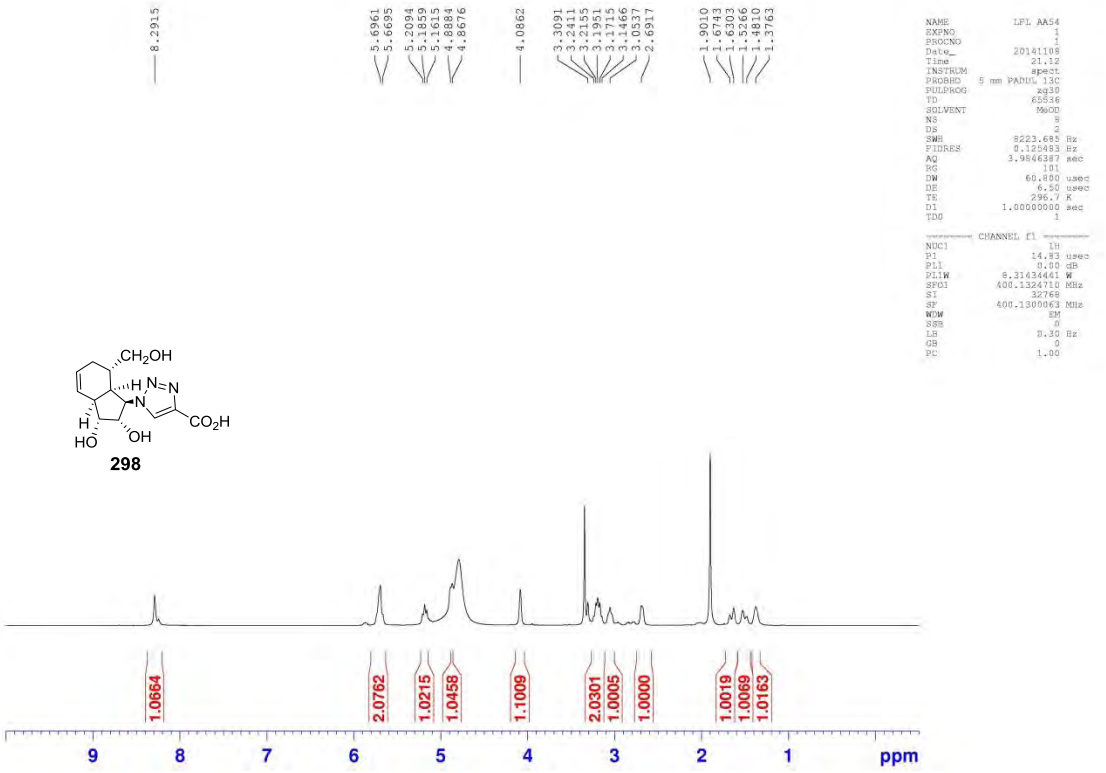
^{1}H NMR (Solvent: CD_3OD)



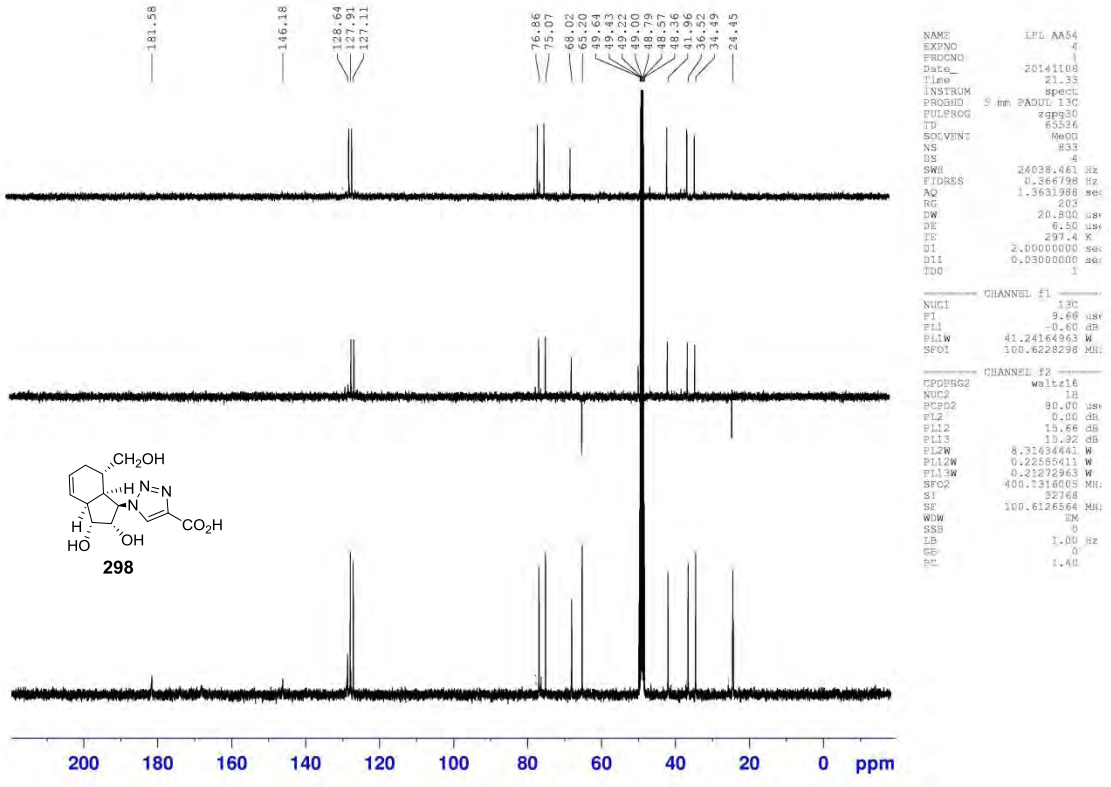
^{13}C NMR (Solvent: CD_3OD)



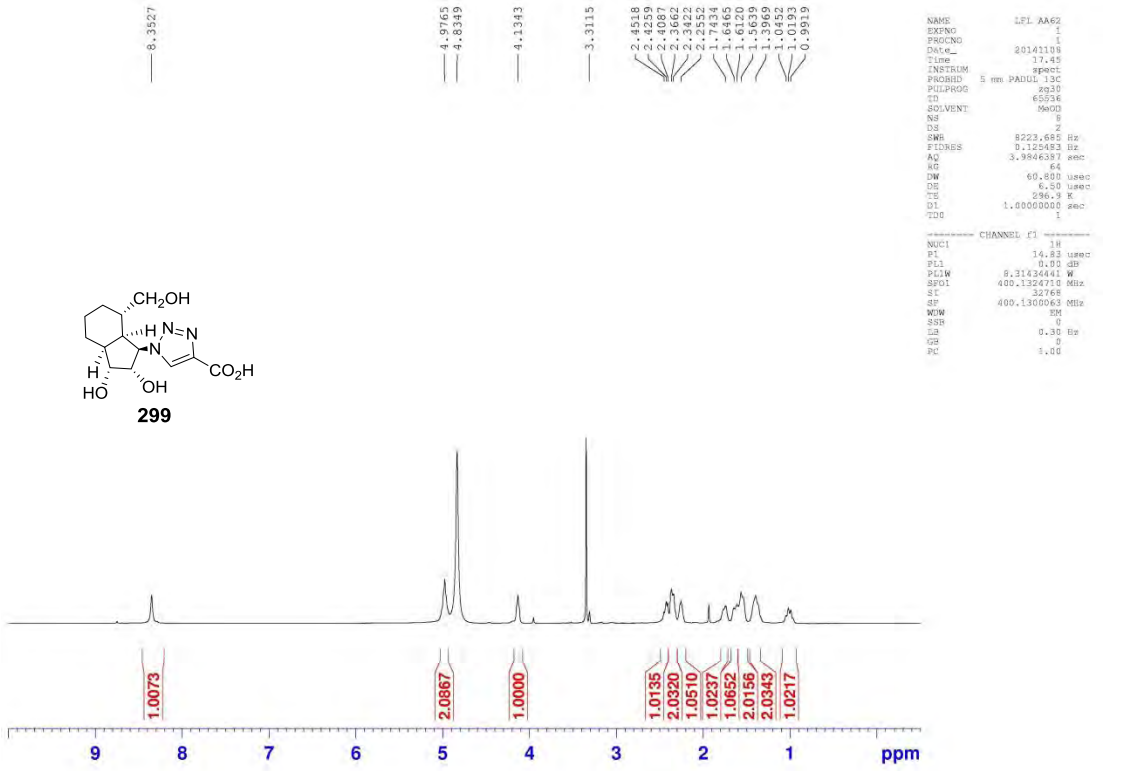
^{1}H NMR (Solvent: CD_3OD:D_2O:AcOH 1:1:0.1)



^{13}C NMR (Solvent: CD_3OD:D_2O:AcOH 1:1:0.1)



^{1}H NMR (Solvent: CD_3OD:D_2O 1:1)



^{13}C NMR (Solvent: CD_3OD:D_2O 1:1)