Abstract

First Total Synthesis of the Novel Brominated Polyacetylenic Diol (+)–Diplyne A and (+)–Diplyne C

By Craig R Gibeau

This thesis describes the methodology and experimental work in the total synthesis of two novel brominated polyacetylenic diols, diplynes A and C (Figure 1.2) which were isolated from the Philippines sponge *Diplastrella sp*. The work contained herein represents the first total synthesis of diplynes A and C. All the compounds isolated from *Diplastrella sp*. have shown activity in the HIV-1 integrase inhibition assay. The pathway envisioned for the synthesis of diplyne A (**1**) involved a Sonogashira cross coupling reaction to couple a terminal acetylene **9** with 1,2-dibromoethylene **10**, forming the left hand portion of the molecule. The right hand portion was produced through a Cadiot-Chodkiewicz coupling of a terminal acetylene **12** with the bromo-alkyne **11**. The synthesis of diplyne C **3** followed a similar strategy, with a Cadiot-Chodkiewicz coupling on the right hand fragment. The left hand fragment of the molecule was assembled through a hydroboration-mercuration-bromination procedure, producing stereoselectively the trans isomer.

First Total Synthesis of the Novel Brominated Polyacetylenic Diols (+)–Diplyne A and (+)–Diplyne C

A Thesis

Submitted to the

Faculty of Miami University

in partial fulfillment of

the Requirements in the degree of

Masters of Science

Department of Chemistry and Biochemistry

By

Craig Gibeau

Miami University

Oxford, Ohio

2005

Advisor: _____

Professor Benjamin Gung

Reader: _____

Professor Richard Taylor

Reader: _____

Professor James Hershberger

Reader: _____

Professor Hongcai Zhou

Table of Contents

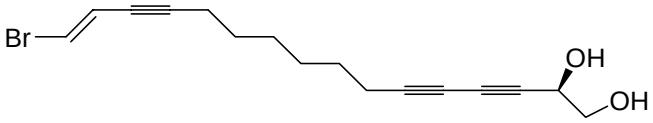
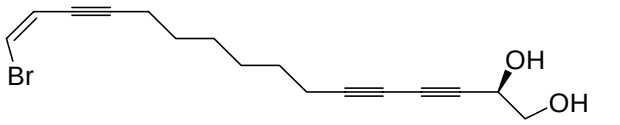
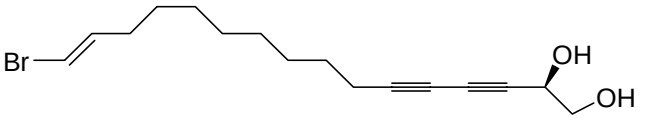
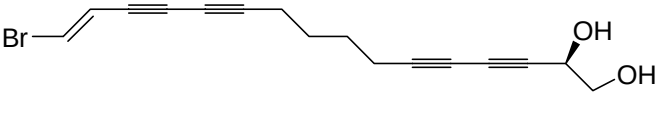
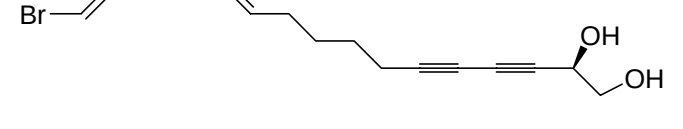
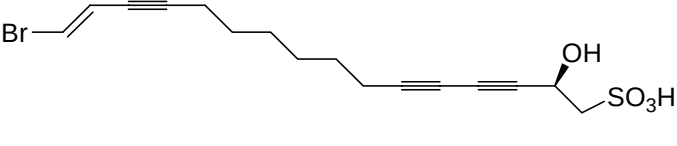
List of Abbreviations

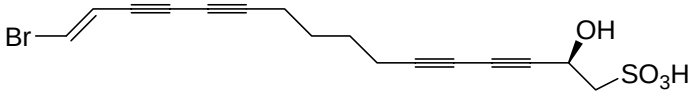
Et	Ethyl
DMF	Dimethylformamide
Me	Methyl
PCC	Pyridinium Chloro Chromate
PPTS	Pyridinium *p*-Toluenesulfonate
PTSA	*p*-Toluenesulfonic acid
TEA	Triethylamine
THF	Tetrahydrofuran
THP	Tetrahydropyran
HRMS	High Resolution Mass Spectroscopy
IR	Infrared Spectroscopy
UV	Ultraviolet Spectroscopy

List of Figures

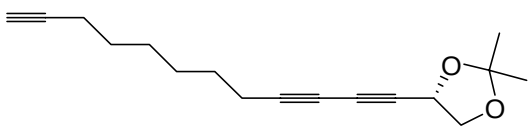
List of Schemes

List of Structures

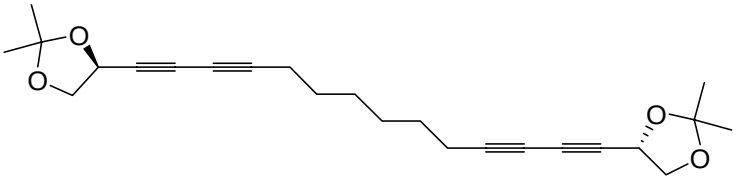
No.	Structure
1	
2	
3	
4	
5	
6	
7	



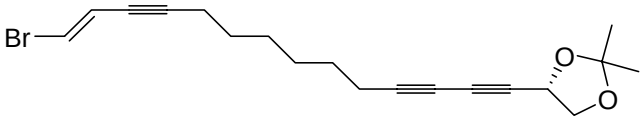
8



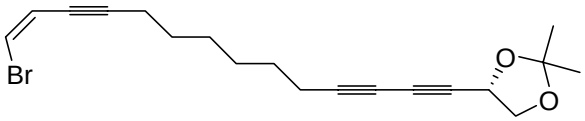
12



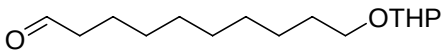
13



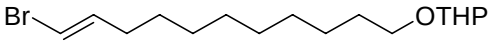
14



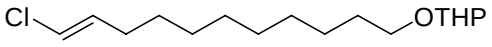
15



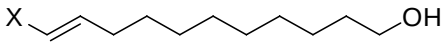
19



20

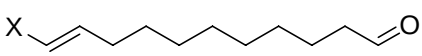


21



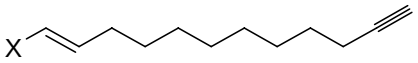
X = Br, Cl

22



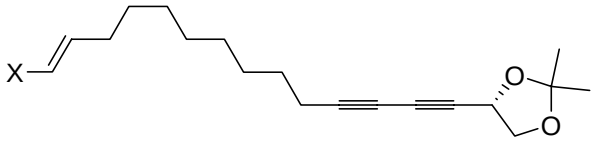
X = Br, Cl

23



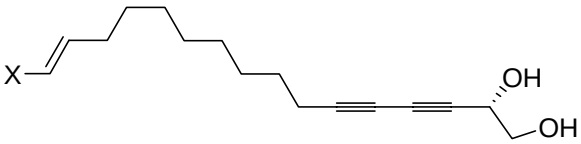
X = Br, Cl

24



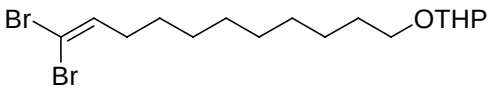
X = Br, Cl

25

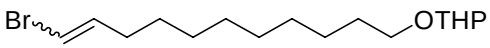


X = Br, Cl

26

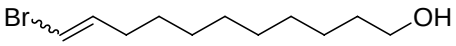


28



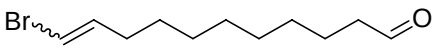
Trans = **29a**, *Cis* = **29b**

29



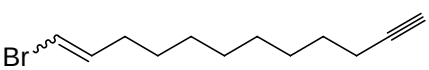
Trans = **30a**, *Cis* = **30b**

30



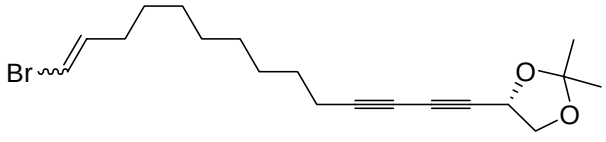
Trans = **31a**, *Cis* = **31b**

31



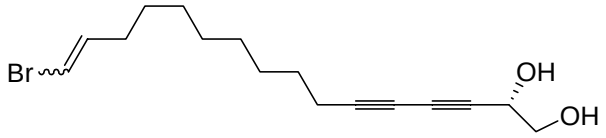
Trans = **32a**, *Cis* = **32b**

32



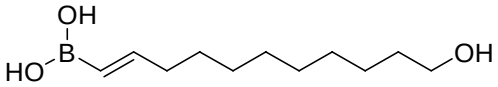
Trans = **33a**, *Cis* = **33b**

33

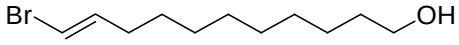


Trans = **34a**, *Cis* = **34b**

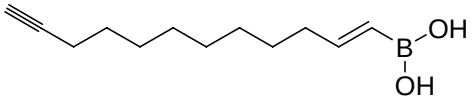
34



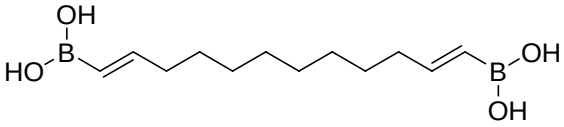
42



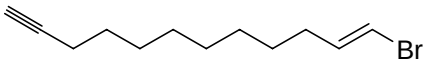
43



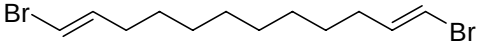
45



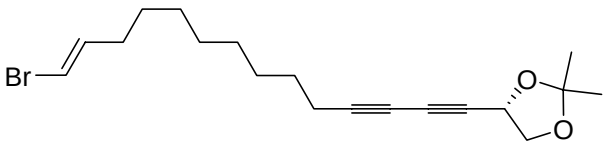
46



47



48

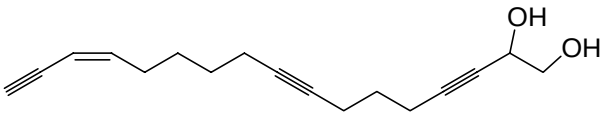


49

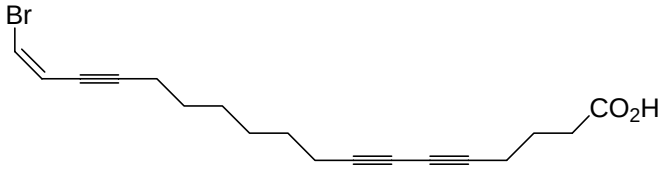
Chapter 1: Introduction to Polyacetylenes

Polyacetylenic natural products have become increasingly important to synthetic groups throughout the scientific community. The interest in these compounds from a synthetic standpoint stems from their high degree of unstaturation. Attaining this degree is often a daunting task in organic synthesis. Aside from the intriguing structures found in nature, polyacetylenic compounds can possess biological activity. The ability to produce and carry out a synthetic scheme of a natural product is often a very challenging and often rewarding task. Presented within this work are some of the successes and failures in the total synthesis of brominated polyacetylenic compounds.

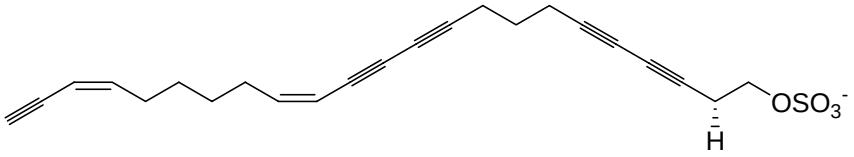
There are thousands of reported organobromo compounds, many of which are isolated from marine sources.[1] In particular, marine sponges produce many brominated polyacetylenic compounds, polyacetylenic sulfates, and polyacetylene diols. Some examples of these sponges and their natural products include the following (Figure 1): the marine sponge Petrosia volcano, which shows antifungal activity with the compound xestospongic acid;[2] the marine sponge Siphonochalina truncata, from which was obtained an antibacterial polyacetylene diol named siphonodiol;[3] and the sponge Callyspongia truncata, which shows antifouling activity due to callyspongin A.[4]



Siphonodiol



Xestosponic acid



Callyspongin A

Figure 1.1: Polyacetylenic natural products.

In selecting an area for the research to be presented herein, there was an interest in finding a natural product containing a brominated polyacetylenic unit. These products are of increasing interest to synthetic organic groups due to their potentially potent biological activities. We chose the brominated polyacetylenes from the Philippine sponge *Diplastrella sp.*; these include diplynes A-E (Figure 1.2).[5]

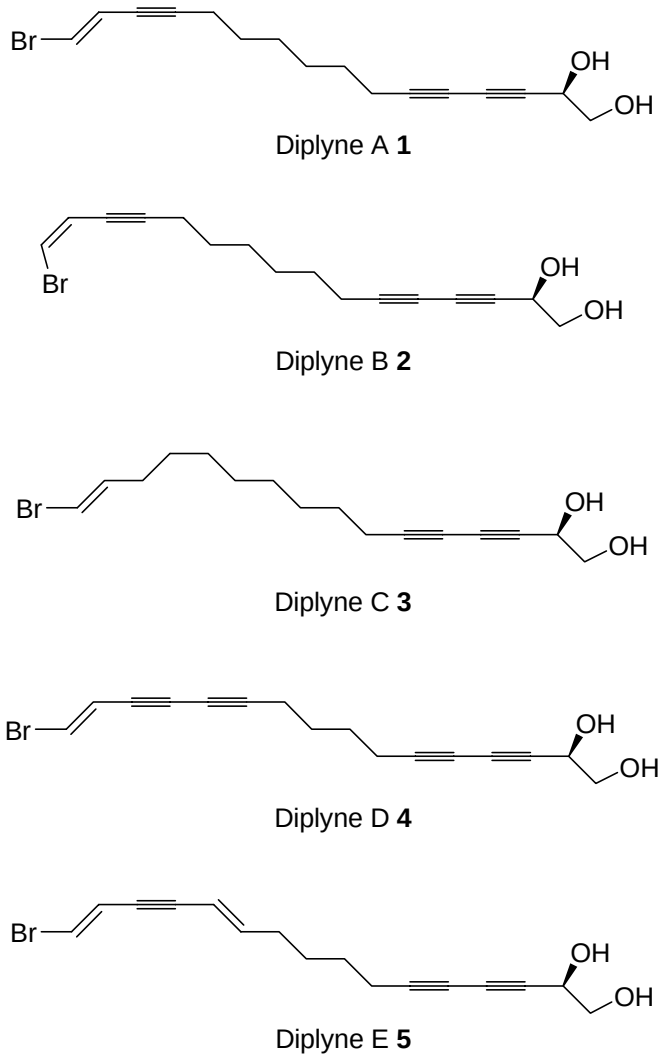
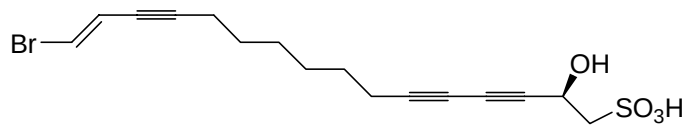
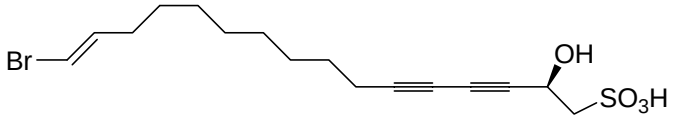


Figure 1.2: Diplyne A-E isolated from *Diplastrella sp.*

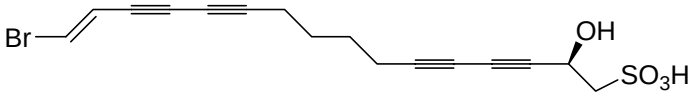
Three unstable sulfated derivatives, diplyne A 1-sulfate, diplyne C sulfate, and 2-deoxydiplyne D sulfate, shown below, (Figure 1.3) also come from this species of marine sponge.



Diplyne A 1-sulfate **6**



Diplyne C sulfate **7**



2-Deoxydiplyne D sulfate **8**

Figure 1.3: Sulfate derivatives of diplyne A, C, and E.

Diplastrella sp. is a type of marine sponge found off the Boracay Island in the Philippines. These are the first reported metabolites from the genus *Diplastrella*.[5] This orange colored sieve encrusting sponge, which is part of Spirastrellidae family of the order Hadromerida, is identified by the shape and size of the circular sieve areas on the sponge. The sponge is found around the sheltered side of ledges, crevices and caves. Canals on the surface of the sponge and throughout its body let the current flow through it. This is how it captures its food supply.

While analyzing such compounds and their interactions with biological systems, a great deal of information can be obtained, which can be used in other fields and may lead to further scientific developments. Furthermore, deducing the exact structure and a synthesis for a naturally occurring product, along with understanding how it will interact with biological systems, can provide valuable tools in the synthesis of different analogs. In addition, this increases the probability that enantiomerically pure drugs will be produced in a more efficient manner and therefore contain the ability to target specific ailments.

This thesis describes the synthetic work towards the synthesis of brominated polyacetylenic compounds isolated from nature. This synthesis represents the first total synthesis of diplynes A and C isolated from the marine sponge *Diplastrella sp*.

Chapter 2: Synthesis of Diplyne A.

2.1 Introduction

Five novel brominated polyacetylenic diols (Figure 1.2) and three sulfated derivatives (Figure 1.3) have been isolated. These crude extracts from the Philippine sponge *Diplastrella sp*. have recently been shown to inhibit the activity of the HIV-1 intregrase.[5] The isolation of the brominated polyacetylenic diols, diplyne A-E and the three sulfated analogues, was done through the inhibitory activity guided screen.[5] These are the first reported natural brominated polyacetylenic diols as well as the first reported metabolites from *Diplastrella sp*. Diplynes A-E are biologically active natural products with diplyne A being isolated as an optically active white powder. Because of the small amount of diplyne A extracted from *Diplastrella sp*., the exact configuration was not determined from the isolated quantity. We now wish to report the first total synthesis of the enantiomer of diplyne A, thus establishing that the naturally occurring diplyne A has an (R) configuration.[6]

The synthetic pathway envisioned for the synthesis of diplyne A was based on previous syntheses of polyacetylenes in our group.[7,8] A retrosynthetic analysis reveals that this particular molecule may be derived from three main components (Figure 2.1), with the center of the molecule being 1,9-decadiyne **9** and the left side being a Sonogashira coupling reaction between 1,2-dibromoethylene **10** and the terminal acetylene **12**.[9] The right hand side could be a Cadiot-Chodkiewicz coupling[10] between the terminal acetylene **9** and the bromoalkyne **11** derived from the D-mannitol derivative.[7] This would be followed by the deprotection of the diol.

2.2 Results and Discussion

Through the retrosynthetic analysis given above for diplyne A (Figure 2.1), we now devised a synthetic pathway (Scheme 2.1) and set out to synthesize diplyne A.

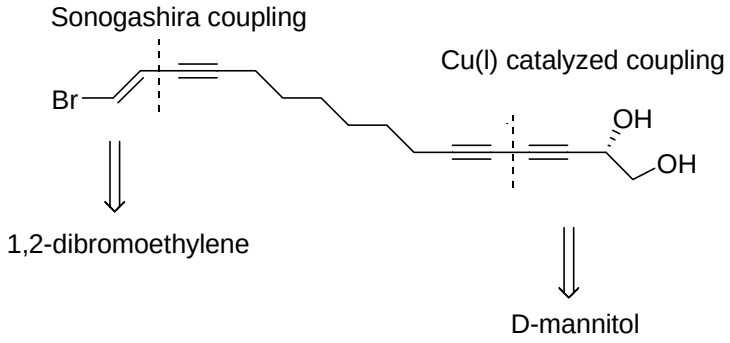
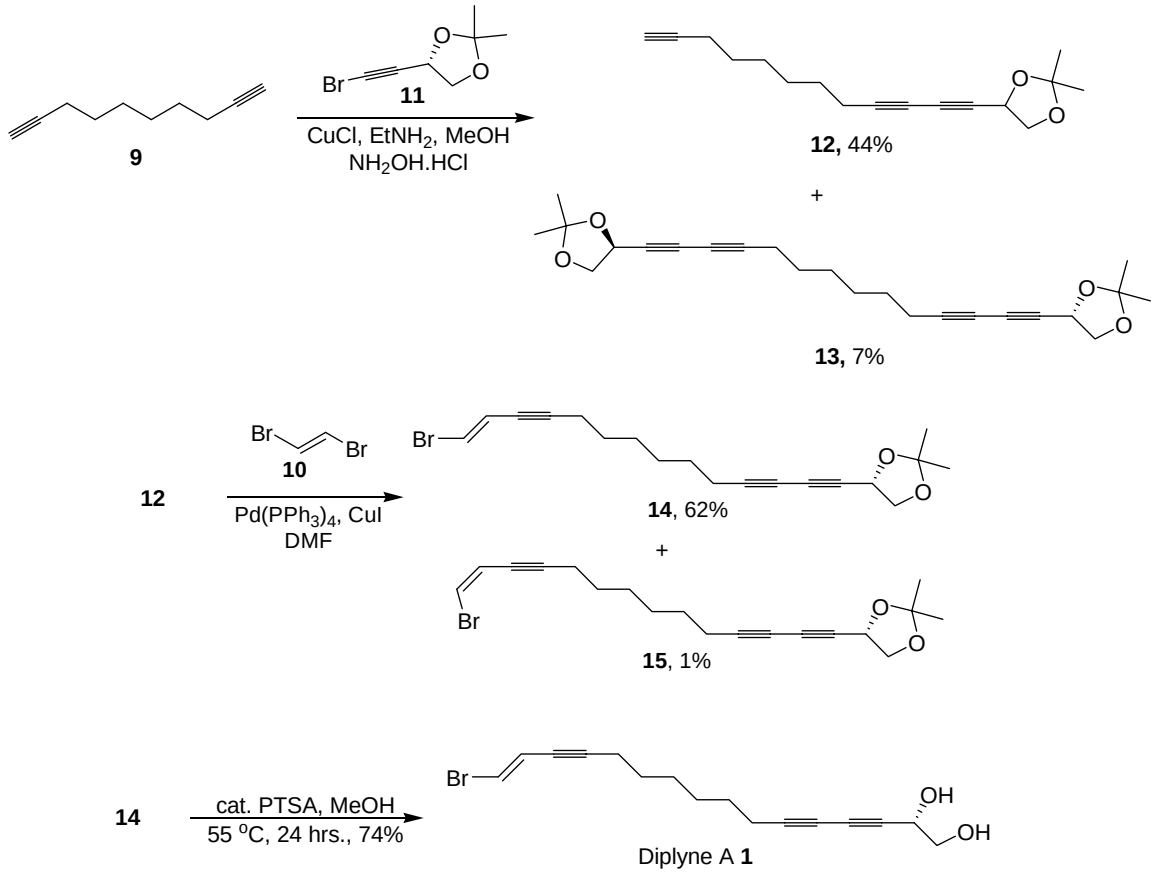


Figure 2.1: Retrosynthetic analysis of diplyne A

Scheme 2.1



This task began with 1,9–decadiyne, which is commercially available, and the bromo-alkyne **11**, which was prepared as previously reported from our laboratory.[7] This Cadiot-Chodkiewicz coupling reaction was done using CuCl. Since the starting material is a diyne the brominated alkyne needed to be added dropwise in order to reduce the risk of reaction with both sides of the diyne. Another reason for the slow addition is that in higher concentrations **11** has a tendency couple with itself.[10] This reaction ran smoothly with the product **12** being obtained in a 44% yield, as well as trace amounts of **13** (7%).

With the right hand side of the molecule now being set, we turned our attention to the left hand side. This was to be accomplished through a Sonogashira coupling using the terminal alkyne **12** and 1,2 – dibromoethylene **10**. This was done using $Pd(PPh_3)_4$ in combination with CuI and TEA.[11] The enyne **14** was obtained in a 63% yield along with isomer **15** in a 1% yield as light yellow oils. The ratio of *trans/cis* isomer was 98:2. This mixture was separated using flash chromatography. Using an equivalence ratio of 4:1 between the *cis*/*trans* mixture of **10** a 50:50 ratio and the terminal alkyne **12**, respectively, **12** preferentially reacted with the *trans* isomer of 1,2 – dibromoethylene.[12]

With **15** firmly in hand, we now set our sites on the final step in order to complete diplyne A **1**. The final step involved the removal of the acetonide protecting group to give the diol.[13] This was accomplished through the use of a catalytic amount of PTSA in methanol, which gave the desired product **1** in a 74% yield. The spectroscopic data for both the natural diplyne A and our synthetic product were nearly identical with the major exception being the optical rotation. The natural diplyne A had a reported rotation of $[\alpha]_D$ = -8.7 in methanol.[5] Our synthetic diplyne A, on the other hand, had an optical rotational value of $[\alpha]_D$ = +9.6 using the same solvent reported in the literature. The rotation of the synthetic product represents an (S)–configuration owing to the fact that it was obtained from D–mannitol. Though the D–mannitol has an (R)–configuration, the synthetic Diplyne A has an absolute configuration of (S). This is due to a change in the priority of the substituents when D–mannitol was transformed into the acetylenic diol derivative **11**. Thus, the natural diplyne A obtained from the marine sponge is believed to possess an (R)–configuration.

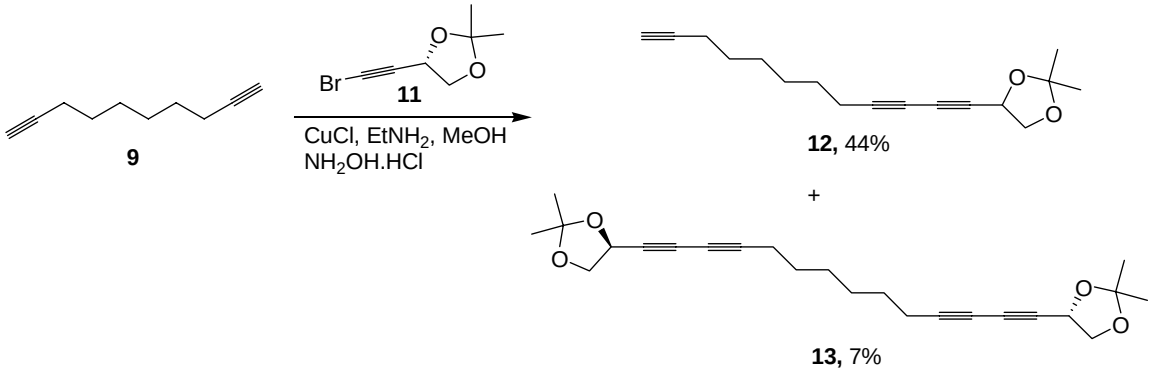
2.3 Conclusions

The first total synthesis of the enantiomer of the brominated polyacetylenic natural product (+)–diplyne A has been completed. The configuration of the natural product (-)–diplyne A has been established as (R) since our synthetic product shows a (+) sign in specific rotation, which corresponds to an (S)–configuration.

2.4 Experimental

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware. Reagents were purchased from commercial sources and used without further purification. Flash column chromatographic separations were performed using silica gel 40-63 μm, unless otherwise noted. Reactions were monitored with TLC and UV light. NMR spectra (^{1}H, ^{13}C) were recorded on Bruker 200, 300, and 500 MHz spectrometers with $CDCl_3$ or CD_3OD as the solvents. Melting points are not corrected.

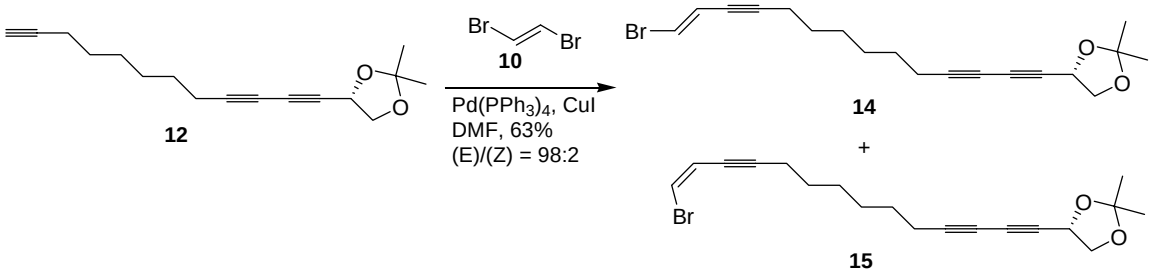
1,2-Isopropylidenetetradeca-3,5,13-triyne (12)



To a 50 ml round-bottom flask was added 5 ml of MeOH, 0.22 ml of an aqueous solution of $NH_2OH.HCl$ (18 mg, 0.25 mmol), 5 ml 70% aqueous solution of $EtNH_2$, and CuI (25 mg, 0.25 mmol) under an atmosphere of N_2, followed by the addition of diyne **3** (682 mg, 5.0 mmol) in that order. The bromoalkyne **11** (1.02g, 5.0 mmol) was added over a period of one and a half hours via a syringe pump, keeping the temperature between 30-35° C.[11] After an additional 30 minutes a solution of 1.2g of KCN and 5g of NH_4Cl in 16 ml of H_2O was added with vigorous stirring. The product was isolated by extraction with Et_2O (3x 20 ml) and the combined organic layers were washed with saturated NH_4Cl solution, then dried over $MgSO_4$. The solvents were removed under reduced pressure and the residue was purified over silica gel (5% EtOAc/Hex) to afford 569 mg (44%) of a light yellow oil, as well as a 7% yield of **11** coupling to both ends of **9.** $[\alpha]_D$ = +38.37 ($CHCl_3$, c = 1.63). **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 1.36 (3H, s), 1.41 (4H, m), 1.48 (3H, s), 1.52 (4H, m), 1.94 (1H, t, J = 2.6 Hz), 2.17 (2H, t, J = 13.7Hz), 2.28 (2H, dt, J = 6.8, 2.5Hz), 3.93 (1H, dd, J = 8.1, 6.1 Hz), 4.14 (1H, dd, J = 8.0, 6.5 Hz), 4.76 (1H, dd, J = 6.5, 5.2). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 18.2, 19.1, 25.8, 26.0, 27.8, 28.0, 28.1 (2), 64.4, 65.7, 68.2,

69.6, 70.6, 72.7, 81.8, 84.3, 110.4. **IR**: ν cm^{-1} 3300 (sharp), 2256, 2217, 1458, 1235, 1065, 839. **HRMS**: calcd for $C_{17}H_{22}O_2$ + Na, 281.1518, found M + Na, 281.1517.

(15E)-1,2-Isopropylidene-16-bromohexadeca-15-en-3,5,13-triyne (14)

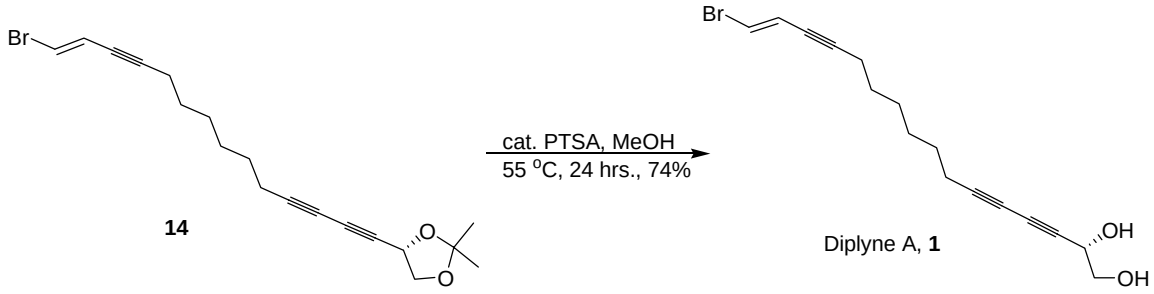


To a 50 ml round-bottom flask under an atmosphere of N_2 was added 19 ml of Et_3N, triyne **12** (100 mg, 0.387 mmol), 1,2-dibromoethylene (0.127 ml, 1.54 mmol), $Pd(PPh_3)_4$ (27 mg, 0.023 mmol), and CuI (9 mg, 0.046 mmol) in that order.[12] The resulting mixture was stirred overnight at room temperature. After 12 hours the mixture was filtered through a plug of Florisil with excess hexanes. The filtrate was concentrated and the residue was purified over silica gel (5% EtOAc/Hex) to afford a mixture of **14** (87.1 mg 62%) and **15** (1.6 mg 1%) as light yellow oils.

Compound **14** $[\alpha]_D$ = +27.28 ($CHCl_3$, c = 0.68). UV (MeOH) 238 nm. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 1.35 (3H, s), 1.37 (4H, m), 1.46 (3H, s), 1.51 (4H,m), 2.25 (4H, m), 3.91 (1H, dd, J = 7.8, 6.3 Hz), 4.12 (1H, dd, J = 7.8, 6.7 Hz), 4.73 (1H, dd, J = 6.2, 5.3 Hz), 6.15 (1H, dt, J = 14.0, 2.0 Hz), 6.54 (1H, d, J = 14.0). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.2, 19.4, 25.9, 26.1, 28.0, 28.1 (2), 28.2, 64.5, 65.9, 69.7, 70.6, 70.8, 72.9, 76.8, 81.9, 93.0, 117.0, 118.0. **IR** ν cm^{-1} 2256, 2216, 1458, 1235, 1064. **HRMS**: calcd for $C_{19}H_{23}BrO_2$ + Na, 385.0779, found M + Na, 385.0751.

Compound **15** **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 1.35 (3H, s), 1.37 (4H, m), 1.46 (3H, s), 1.51 (4H,m), 2.25 (4H, m), 3.91 (1H, dd, J = 7.8, 6.3 Hz), 4.12 (1H, dd, J = 7.8, 6.7 Hz), 4.73 (1H, dd, J = 6.2, 5.3 Hz), 6.26 (1H, dt, J = 6.6, 2.1 Hz), 6.45 (1H, d, J = 7.4 Hz)

(15E)-16-Bromohexadeca-15-en-3,5,13-triyne-1,2-diol (1)



A solution of **14** (51 mg, 0.14 mmol) and PTSA (2.6 mg, 0.014 mmol) in MeOH (2.8 ml) was stirred for 24 h at room temperature.[13] To the reaction mixture, solid $NaHCO_3$ (29 mg, 0.28 mmol) was added and allowed to stir for 15 min. The resulting solution was filtered and MeOH was evaporated. The remaining residue was purified over silica gel (50% EtOAc/Hex) to afford 32.6 mg (74%) of **1** as a white solid.

$[\alpha]_D$ = +9.59 (MeOH, c = 0.29) (literature value $[\alpha]_D$ = -8.7). **UV** (MeOH) 238 nm. m.p. 95-96 C. **^{1}H-NMR** (500 MHz, MeOH): δ 1.45 (4H, m), 1.55 (4H, m), 2.31 (4H, m), 3.56 (1H, dd, J = 11.2, 6.8 Hz), 3.61 (1H, dd, J = 11.2, 5.0 Hz), 4.36 (1H, dd, J = 6.0, 5.6 Hz), 6.25 (1H, dt, J = 14.0, 2.3Hz), 6.71 (1H, d, J = 14.0 Hz). **^{13}C-NMR** (125 MHz, MeOH): δ 19.6, 19.9, 29.2, 29.3 (2), 29.4, 64.5, 65.6,67.1, 70.7, 75.8, 78.2, 81.7, 93.7, 117.9, 119.1. **IR**: ν cm^{-1} 3298 (broad), 2254, 2216, 1693, 1461, 1085, 922, 728. **HRMS**: calcd for $C_{16}H_{19}BrO_2$ + Na, 345.0466, found M + Na, 345.0487.

Chapter 3: Synthesis of Diplyne C.

3.1: Introduction

The preparation of diplyne C **3** proved to be a much more difficult task than that of diplyne A **1**. This was particularly because of the alkenyl halide functionality. The right hand side of the molecule was prepared using the Cadiot – Chodkiewicz coupling reaction[10] as in diplyne A **1**. The problem arose when we tried to control the stereoselectivity of the alkenyl halide, favoring an (E)-configuration over the (Z).

3.2 Results and Discussion

Through retrosynthetic analysis (Figure 3.1), diplyne C can be made from the coupling of the D-mannitol derivative for the right side of the molecule. The left side of the molecule was synthesized by means of hydroboration-mercuration-bromination[14] giving the (E)-configuration. However, a few other attempts at the (E)-configuration were made before a suitable method was found.

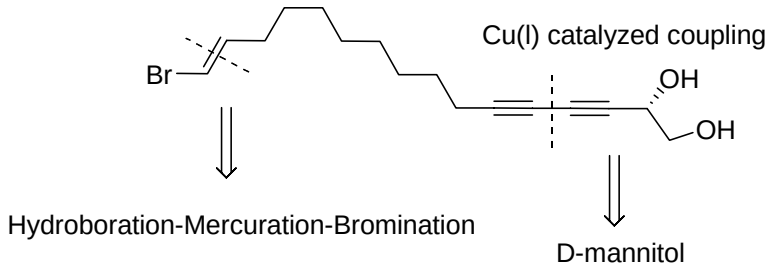
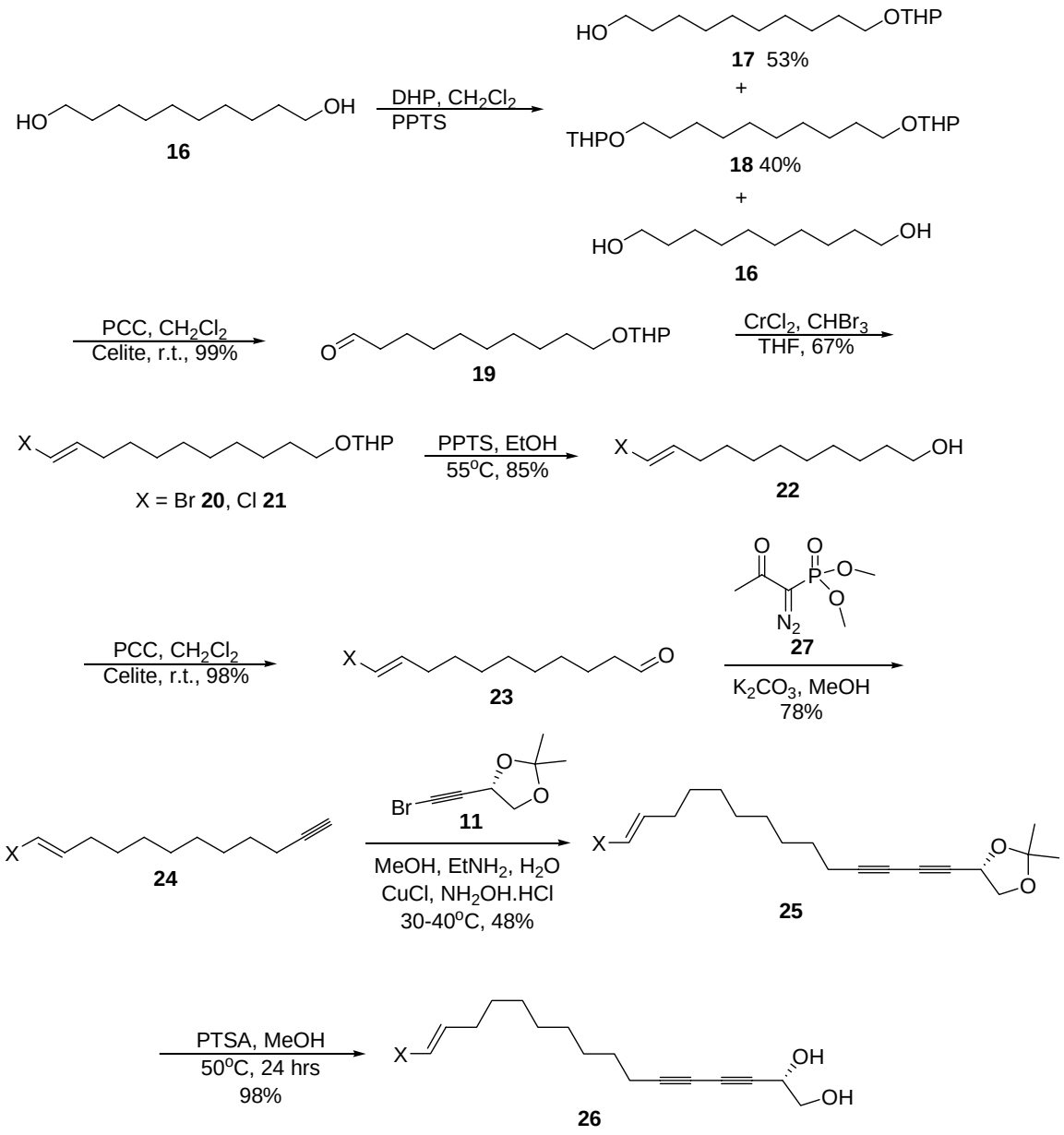


Figure 3.1: Retrosynthetic analysis of diplyne C

3.2.1 Synthesis of Diplyne C via Takai Reaction

Scheme 3.1

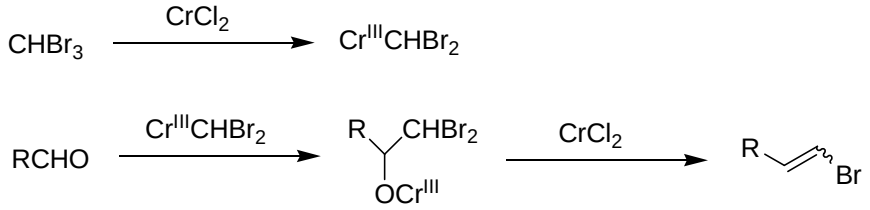


The first attempt to synthesize diplyne C involved the Takai reaction (Scheme 3.1).[15] Starting from the commercially available 1,10-decandiol **16**, we wanted to protect one of the alcohols in order to oxidize the other. This was accomplished through the use of 2,3-Dihydro-4H-pyran (DHP), added slowly over a period of 45 minutes to a solution of the diol **16** and PPTS in CH_2Cl_2.[16] The monoprotected alcohol **17** was obtained in a 53% yield along with the diprotected alcohol **18** in a 40% yield. A small amount of

starting material was also recovered. All of these products were easily separated through the use of flash chromatography.

The next step consisted of taking the free alcohol of the monoprotected species and oxidizing it to the aldehyde[17] using PCC and celite. The product **19** was obtained in a 99% overall yield. The following step involved the formation of the stereocontrolled alkenyl halide. This reaction is referred to as the Takai reaction (Scheme 3.2), in reference to Kazuhiko Takai who in 1986 found a simple method for the stereoselective formation of certain (E)–alkenyl halides from aldehydes through the use of organochromium reagents.[15]

Scheme 3.2



For this reaction, the aldehyde **19** and bromoform in solution was added dropwise to a solution of the $CrCl_2$ in THF over a period of 30 minutes at 0 ^oC. However, when bromoform is used with the aldehyde in combination with $CrCl_2$, a mixture of the vinyl bromide **20** and the undesired vinyl chloride **21** were obtained. This mixture of the two alkenyl halides **20** and **21** were obtained in 67% yield as a 1:1 ratio according to NMR analysis. Furthermore, these two products showed up as a single spot on TLC plates under varying solvents, and were not separated using flash chromatography. The decision was made to carry out the synthesis as planned in hopes that a separation between the brominated and chlorinated species could be made in a later step.

The next step in this series was to remove the THP protecting group to expose the terminal alcohol for oxidation.[16] This was accomplished in an 85% yield of **22** and done with the aid of PPTS in ethanol at 55 ^oC. Once again, no separation of the chlorinated and brominated species were obtained. This led us to believe that the final step in this synthesis may be the best opportunity to get a separation due to the influence of varying polarities. With **22** as a mixture in hand, the free alcohol was oxidized to the

corresponding aldehyde **23**[17] with the aid of PCC and celite to yield 98% of an inseparable mixture.

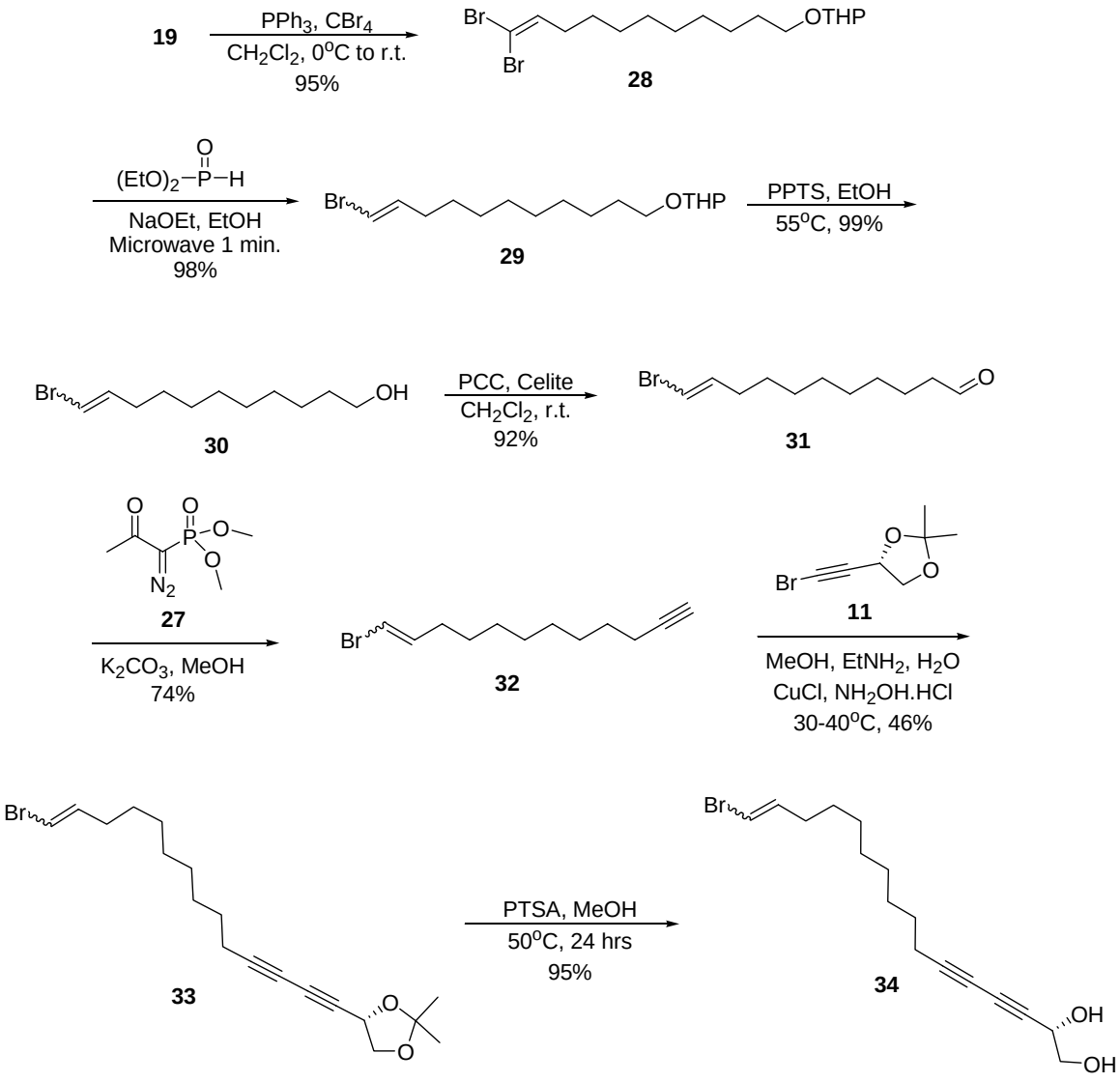
Through a one carbon addition via the Ohira–Bestman reagent,[18] the aldehyde **23** was transformed into the terminal acetylene **24** in a one pot procedure,[19] under fairly mild conditions, with an overall yield of 78%. The next step involved the Cadiot–Chodkiewicz coupling of the terminal acetylene **24** with the bromoalkyne **11**.[10] This was accomplished through the use of CuCl as the catalyst and gave 48% of **25** along with some homocoupling of the bromoalkyne **11** to itself (13%).

The final step involved the deprotection of the diol.[13] To remove the acetonide group, **25** was placed into a round bottom flask along with PTSA in methanol and refluxed for 24 hours at 50 ^{o}C, giving a 99% yield of **26**. However, once again we obtained a mixture of the bromo- and chloro-alkenes. Due to the failure to separate the chloro- and bromo-products, another method was needed to obtain the vinyl bromide in a stereospecific manner, or at least in a manner which would allow for separation.

3.2.2 Synthesis of Diplyne C via Olefination with Terminal Dibromide-Debromination.

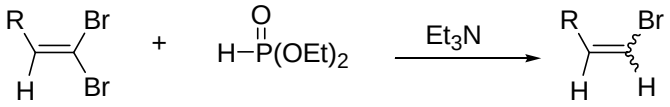
The inability to separate the chloro- and bromo- species resulting from the Takai reaction led us to attempt a different route (Scheme 3.3). The first two steps of the procedure were the same as previously mentioned, namely the monoprotection of diol **16** using DHP,[16] followed by oxidation[17] with PCC to afford the aldehyde **19** in a 99% yield. The next step required making a *gem*–dibromoalkene **28** from the aldehyde **19**.[20] This procedure had been done before in our lab when making bromoalkyne **11**.[7] This was accomplished using PPh_3 and CBr_4 and resulted in the *gem*–dibromoalkene **28** in 95% yield.

Scheme 3.3



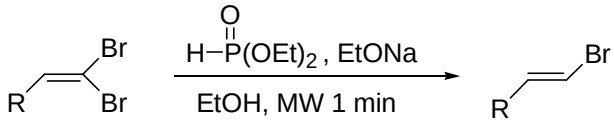
Next, we envisioned doing a reduction of the *gem*–dibromoalkene to the monobromide (Scheme 3.4) using diethyl phosphite. Toshikazu Hirao first reported this reaction in 1981. In his procedure, he had used diethyl phosphite and triethylamine with several different dibromoalkenes to form the monobromides.[21] However, his reaction with a *gem*–dibromoalkene attached to a long aliphatic chain appeared to produce a mixture of *cis*/*trans* isomers.

Scheme 3.4



Over two decades later, Masao Tokuda picked up Hirao's idea and modified it by irradiating the compound with microwaves and diethyl phosphite/ EtONa/EtOH (Scheme 3.5).[22]

Scheme 3.5

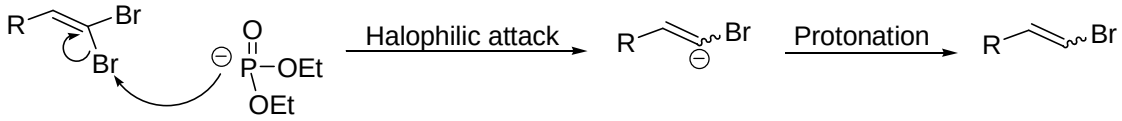


This current method showed it could be used with both aromatic and aliphatic systems. However, microwave irradiation of alkyl–substituted 1,1–dibromoethenes gave very low stereoselectivities. Our hope was that even if there was a substantial mixture of both *cis* and *trans* isomers, they might be able to be separated through flash chromatography, as was the case with diplyne A **1**.

Following Tokuda's procedure,[22] **28** was put in a microwave safe vessel with diethyl phosphate/EtONa/EtOH and irradiated for 1 minute. This gave a 98% yield of **29** as a inseparable mixture of *cis*/*trans* isomers in a ratio of 1:1.

One possible reason for the lack of selectivity may lie in the mechanism proposed by Hirao.[21] He believed that halophilic attack by the diethyl phosphite anion was occurring on the dibromoalkene, which would probably result in lower selectivity of the vinyl bromide (Scheme 3.7).

Scheme 3.6



This was the case with diplyne C **3**, when we obtained a mixture of both *cis* and *trans* isomers and were not able to separate them through the use of chromatography. We believed that by carrying through the synthesis, that there would be a separation between the two isomers.

We next proceeded to remove the THP protecting group[16] from **29.** This was done using PPTS and gave a 99% yield of the alcohol **30**. However, only a single spot

appeared on TLC plates. This was followed by the oxidation[17] of **30**, with PCC giving aldehyde **31** in a 92% yield. Next came the use of the Ohira–Bestman reagent **27** which led to the formation of **32**[19] in 74% yield with no separation of the two enantiomers. The use of bromoalkyne **11** and terminal acetylene **32** with CuCl as the catalyst yielded **33**[10] in 46% yield. Lastly, the acetonide group was removed using PTSA in methanol to afford the final product **34** as a mixture of *cis*/*trans* isomers in a 95% yield.[13]

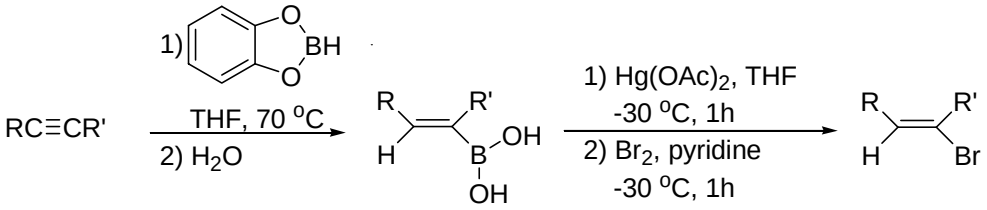
While this reaction may be favorable with aromatic systems as shown by Tokuda,[22] diethyl phosphite was not a good choice for our particular synthesis. The *gem*-dibromoalkene attached to a long aliphatic chain may give an outstanding yield at 98%, but the selectivity of forming the (E)–vinyl bromide over the (Z)–vinyl bromide was poor, giving a fairly even mixture of the two. Without separation, a new method will need to be explored in order to obtain better control over selectivity.

3.2.3 Synthesis of Diplyne C via Hydroboration-Mercuration-Bromination

It has been found that catecholborane (1,3,2–benzodioxaborale) **36** is a convenient method for the synthesis of alkenylboronic esters and acids from alkynes through hydroboration.[23] Much of this work has been done by Brown at Purdue. In fact, he has published several manuscripts concerning how one can convert (E)–1–alkenylboronic acids into (E)–1– halo–1–alkenes.[14,24,25] This method is fairly stereospecific and is essentially a one pot procedure.

As was mentioned above, catecholborane **36** is a very good hydroborating agent. It easily hydroborates alkenes and alkynes, both terminal and internal. To create the alkenylboronic ester from the alkyne and catecholborane, all one needs to do is stir a combination of the two under an atmosphere of nitrogen at 70 ^{o}C for one hour. For internal alkynes, which tend to be less reactive, more time may be required for completion.[26] To obtain the boronic acid, water is added forming catechol and the boronic acid (Scheme 3.7).

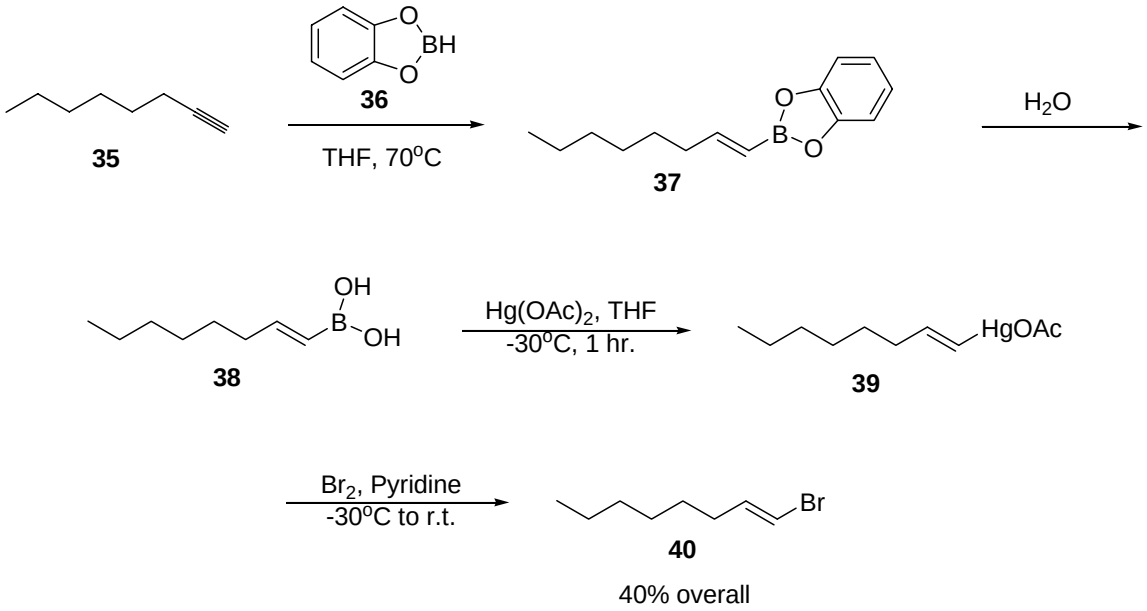
Scheme 3.7



Hydroboration with catecholborane proceeds in a stereospecific *cis* manner; the regioselectivity is good in that boron will attach to the less hindered atom of the alkyne. Several methods have been developed for the halogenation of the alkenylboronic acids or esters directly, but in the case of bromine, this leads to an inversion of configuration.[27,28] Naturally this would serve us no purpose, however, a hydroboration–mercuration sequence would serve to retain the configuration. The mercury (II) salt, $Hg(OAc)_2$, has been used for just such cases. The mercuration can then be followed with halogenation. All this can be accomplished with retention configuration.[14]

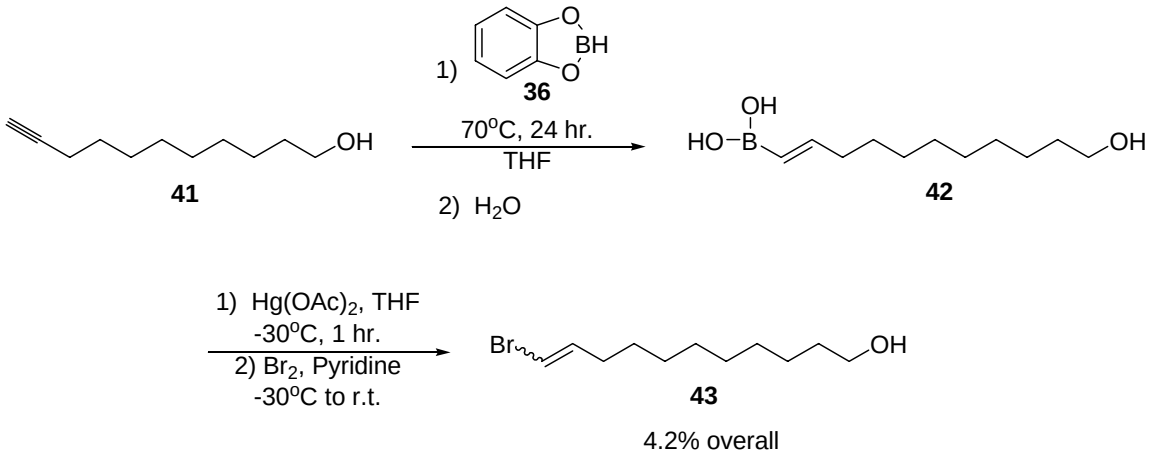
We decided to attempt this method to obtain the desired (E)–1–halo–1–alkene. It was first decided to run a test compound which Brown had previously worked with. We chose 1–octyne (Scheme 3.10). The reaction went very smoothly with an overall yield of 40% for the synthesis of 1–octyne to (E)–1–bromo–1– octene.

Scheme 3.8



Feeling fairly confident that this procedure may finally lead to our targeted goal of diplyne C **3** with the correct (E) configuration, we proceeded in a similar manner to that of our trial attempt on 1–octyne **35**. Believing that the boron may indeed go after the oxygen as well as the acetylene, we decided to run the reaction with 10–undecyn–1–ol **41** (Scheme 3.11) and 2 equivalents of the catecholborane **36** in THF. This was allowed to stir for 24 hours at 70 ^{o}C.[29] After 24 hours, the solution was cooled down, the solvent removed, and water added. The mixture was then stirred for an additional hour at room temperature. The white solid that formed was added directly into THF at -30 ^{o}C, mercuric acetate was added, and stirring was continued. After one hour a 1M solution of Br_2 and pyridine was added at -30 ^{o}C under constant stirring for one hour.[14] After the work up and a column, **43** was produced in 4% yield as a 1:1 mixture of *cis/trans* isomers.

Scheme 3.9

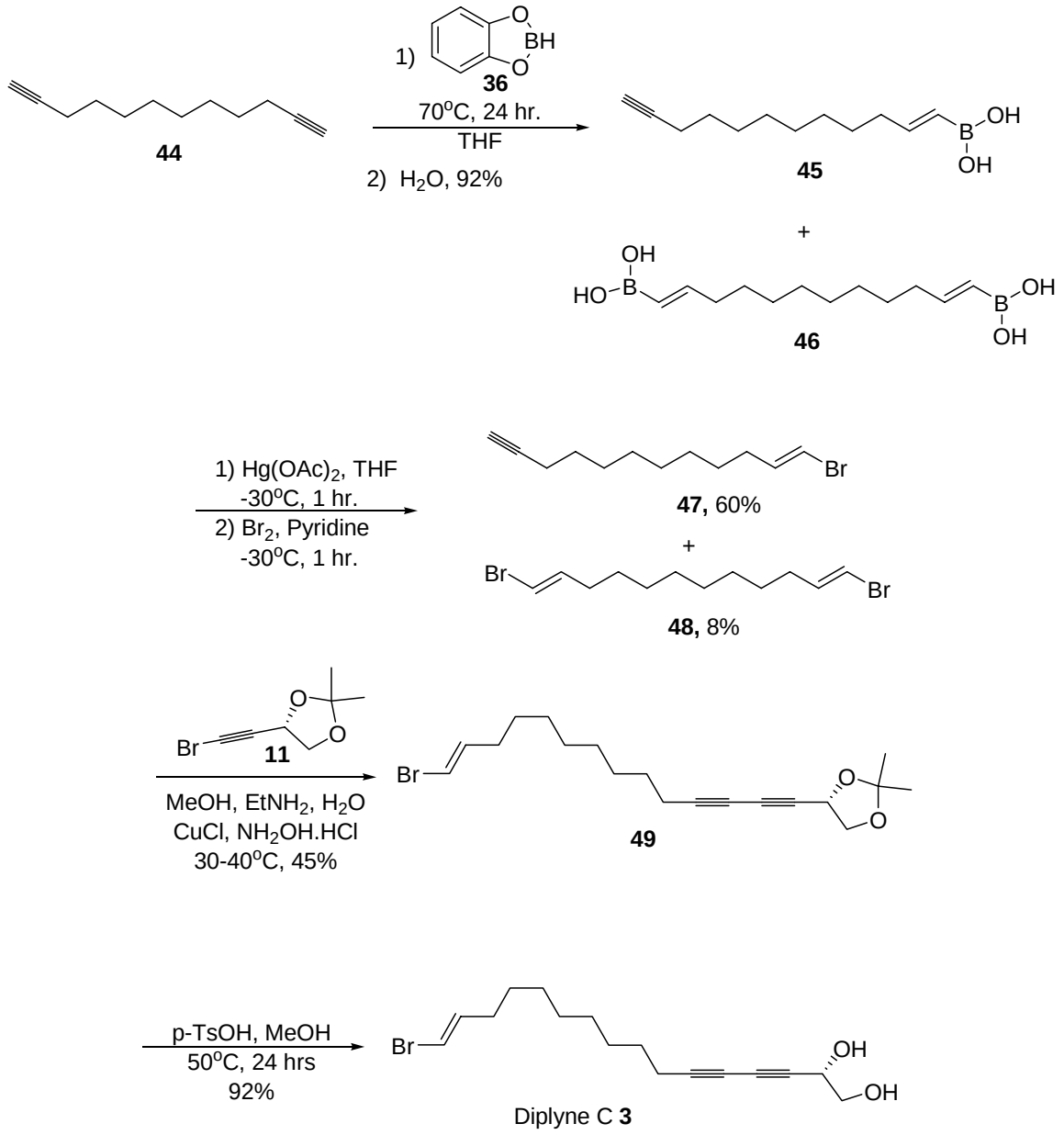


4.2% overall

Not giving up on this method, we decided to revert back to a procedure that had worked for us in the synthesis of diplyne A **1**. This called for using 1,11–dodecadiyne **44** (Scheme 3.10), which is commercially available. To this was added 0.25 equivalents of catecholborane **36** in THF at 70 ^{o}C over a period of 12 hours. After 24 hours at 70 ^{o}C the solution was removed from the heat and allowed to cool. The solvent was again removed and water added, then stirring was continued for an additional hour.[29] Slowing the addition of the borane **36** in THF into the diyne **44** greatly helped in controlling the products that were obtained. This was monitored through the use of NMR. It is believed that a mixture of **45** and **46** was obtained along with some of the starting material **44**.

After converting the boronic ester into the acid, we were not able to obtain an accurate ratio because several protons overlapped in the region where the terminal proton on the acetylene would show up.

Scheme 3.10



With what we believed to be both **45** and **46** in hand we proceeded to the mercuration of the alkenylborane.[14] The mercuric (II) acetate was added to a stirred solution of **45** and **46** in THF at -30 °C. After one hour, a 1M solution of Br_2 in pyridine was added in order to complete the bromination–demercuration. This resulted in

compounds **47** and **48** as two very distinct spots on the TLC plate, which could easily be separated in 60% and 8% yield, respectively. Through the use of NMR, the ratio of (E)/(Z) was approximately 96:4.

With finally being able to control the selectivity, and the major product being the (E) isomer, we felt confident in proceeding with the synthesis of diplyne C **3**. Next was the Cadiot–Chodkiewicz coupling[10] of the terminal acetylene **47** with the bromoalkyne **11**, which gave **49** in a 45% yield, along with homocoupling of **11** in a 13% yield. Lastly was the removal of the acetonide group[13] with PTSA to afford the final product diplyne C **3** in a 92% yield.

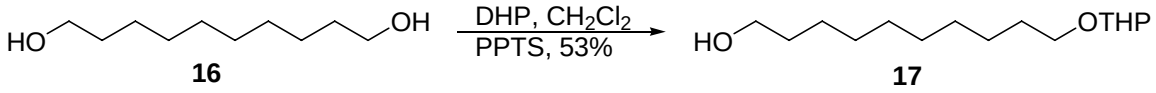
3.3: Conclusions

While undertaking the first total synthesis of the novel polyacetylenic brominated compound (+)-diplyne C, the challenging part proved to be the stereoselective formation of the (E)-isomer. After trying several unsuccessful methods, we were finally able to obtain (E)/(Z) ratio of 96:4, respectively. The optical rotation of the synthetic diplyne C was +13.33. However, the optical rotation for the naturally occurring diplyne C was not reported.[5]

3.4: Experimental

All reactions were carried out under an atmosphere of nitrogen in oven-dried glassware. Reagents were purchased from commercial sources and used without further purification. Flash column chromatographic separations were performed using silica gel 40-63 μm, unless otherwise noted. Reactions were monitored with TLC and UV light. NMR spectra (^{1}H, ^{13}C) were recorded on Bruker 200, 300, and 500 MHz spectrometers with $CDCl_3$ or CD_3OD as the solvents. Melting points are not corrected.

10-(Tetrahydro-Pyran-2-yloxy)-decan-1-ol (18)

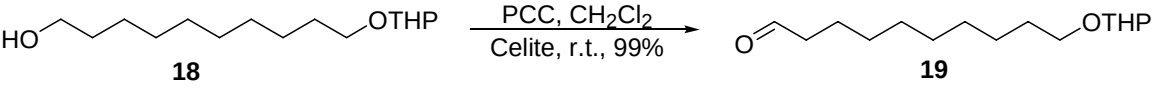


16 **17**

To a solution of the 1,10-diol **16** (2 g, 11.5 mmol) and PPTS (0.29 g, 1.15 mmol) in 82 ml of dry CH_2Cl_2 was added DHP (1.0 ml, 11.5 mmol) dropwise over 45 minutes at room temperature under an atmosphere of nitrogen.[16] The reaction was allowed to run for an additional 4 h and then it was then diluted with ether, washed once with brine to remove the catalyst, then dried with Na_2SO_4. The resulting solution was filtered, concentrated and purified over silica gel (40% EtOAc/Hex) to give 1.58 g (53%) of the product **17** as a colorless oil. Also obtained was 1.19 g (40%) of the diprotected alcohol **18**.

^{1}H-NMR (200 MHz, $CDCl_3$): δ 1.21 (14H, m), 1.45 (8H, m), 1.67 (2H, m), 2.23 (1H, bs), 3.29 (1H, m), 3.41 (1H, m), 3.64 (1H, m), 3.78 (1H, m), 4.49 (1H, t, J = 3.0 Hz).

10-(Tetrahydro-pyran-2-yloxy)-decanal (19)



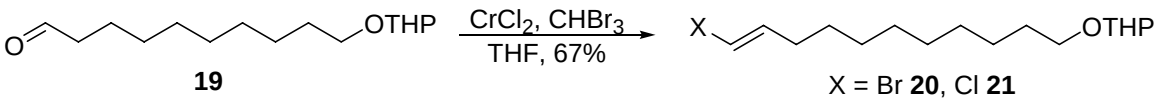
18 **19**

The alcohol **18** (1.5 g, 5.88 mmol) was dissolved in 15 ml of dry CH_2Cl_2 and added to a stirred solution of PCC (1.9 g, 8.82 mmol) and Celite (1.9 g) in 35 ml of dry CH_2Cl_2.[17] This was done under an atmosphere of nitrogen at room temperature. The reaction was allowed to run for 2 h until all the starting material had disappeared. This mixture was diluted with 200 ml of ether and filtered through a pad of florisil with excess ether as the rinse. The solvent was removed affording the aldehyde **19**, 1.49 g (99%) as a pale yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.24 (10H, m), 1.49 (8H, m), 1.58 (2H, m), 2.36 (2H, dt, J = 7.3, 1.8 Hz), 3.49 (2H, dt, 9.5, 6.9 Hz), 3.62 (2H, m), 4.51 (1H, t, J = 2.6 Hz), 9.70

(1H, t, J = 1.8 Hz). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.6, 22.0, 25.4, 26.1, 29.0, 29.2 (2), 29.3, 29.6, 30.2, 30.7, 43.8, 62.2, 67.5, 98.7.

2-(11-Halo-undec-10-enyloxy_tetrahydro-pyran (20, 21)

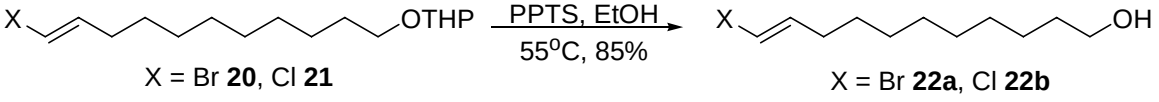


19 X = Br **20**, Cl **21**

A solution of $CrCl_2$ (11.3 g, 91.7 mmol) in 38 ml of dry THF was allowed to stir at room temperature under an atmosphere of nitrogen. To this was added drop wise a solution of the aldehyde **19** (3.9 g, 15.3 mmol) and $CHBr_3$ (2.67 ml, 30.6 mmol) in 76 ml of dry THF at 0 ^oC for a period of 30 minutes.[15] The reaction was allowed to run an additional 2 h, until no starting material was observed. Upon completion, the mixture was diluted with water and extracted with Et_20 (3x), then dried over Na_2SO_4. The resulting solution was filtered, concentrated and purified over silica gel (10% EtOAc/Hex), to give 3.4 g (67%) of a mixture of the bromo- and chloro-vinyl products **20** and **21** in a ratio of approximately 1:1.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.22 (8H, m), 1.29 (4H, m), 1.51 (6H, m), 1.65 (1H, m), 1.76 (1H, m), 1.97 (2H, q, J = 7.4 Hz), 3.32 (1H, dt, J = 9.5, 6.6 Hz), 3.44 (1H, m), 3.67 (1H, dt, J = 9.5, 6.8 Hz), 3.80 (1H, m), 4.52 (1H, t, J = 2.7 Hz), 5.97 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.5, 25.4, 26.1, 28.4, 28.7, 28.8, 29.1, 29.3, 29.4, 30.6, 32.8, 62.1, 67.5, 98.6, 103.9 (**20**), 116.5 (**21**), 133.9 (**21**), 138.1 (**20**).

11-Halo-undec-10-en-1-ol (22a,b)



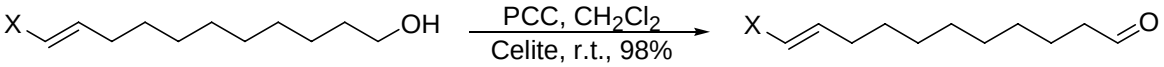
X = Br **20**, Cl **21** X = Br **22a**, Cl **22b**

A solution of the vinyl halides **20** and **21**(3.4 g, 10.2 mmol) and PPTS (0.26 g, 1.02 mmol) in 81 ml of dry ethanol was stirred at 55 ^oC under an atmosphere of nitrogen, for 5 h until there were no signs of starting material.[16] The solvent was then removed

under vacuum and the residue was purified over silica gel (10% EtOAc/Hex), giving 2.15 g (85%) of the desired alcohol **22a,b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.24 (12H, m), 1.52 (2H, m), 1.97 (2H, q, J = 7.5 Hz), 2.09 (1H, bs), 3.55 (2H, t, J = 6.6 Hz), 5.96 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 25.6, 28.4, 28.7, 28.8, 29.3, 29.5, 30.7, 32.6, 62.7, 103.9 (**22a**), 116.5 (**22b),** 133.9 (**22b),** 138.1 (**22a**)

11-Halo-undec-10-enal (23a,b)

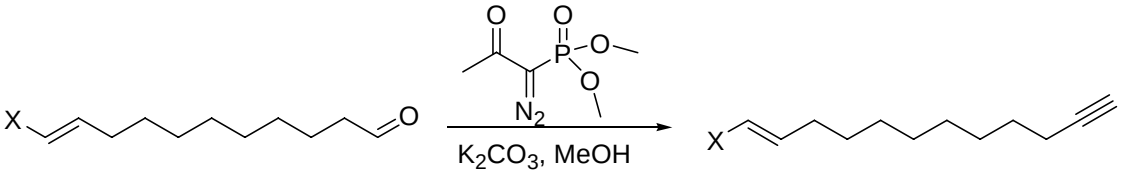


X = Br **22a**, Cl **22b** X = Br **23a**, Cl **23b**

The alcohols **22a,b** (2.14 g, 8.59 mmol) were dissolved in 22 ml of dry CH_2Cl_2. This mixture was added to a stirred solution of PCC (2.78 g, 12.9 mmol) and celite (2.78 g) in 51 ml of dry CH_2Cl_2 under an atmosphere of nitrogen.[17] Once the starting material had disappeared, the mixture was diluted with Et_2O and filtered through a pad of florisil using excess Et_2O for the rinse. The solvent was removed affording 2.0 g (98%) of the aldehydes **23a,b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.23 (10H, m), 1.56 (2H, m), 1.98 (2H, q, J = 6.0 Hz), 2.36 (2H, t, J = 6.7), 5.95 (2H, m), 9.70 (1H, s). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 21.8, 28.7, 28.9, 29.0, 29.1, 30.7, 32.7, 43.7, 103.9 (**23a**), 116.5 (**23b**), 133.8 (**23b**), 138.0 (**23a**), 202.6.

1-Halo-dodec-1-en-11-yne (24a,b)

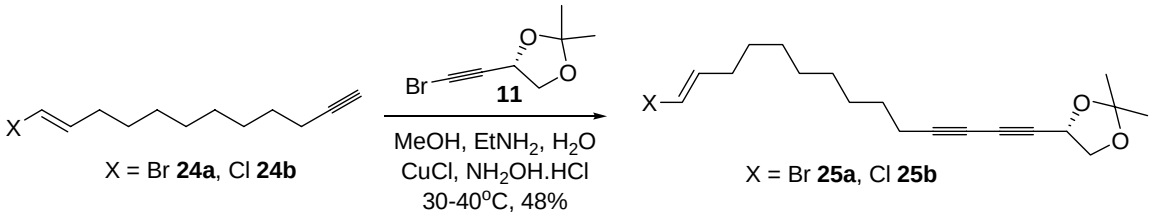


X = Br **23a**, Cl **23b** X = Br **24a**, Cl **24b**

The aldehydes **23a,b**(146 mg, 0.59 mmol) and K_2CO_3 (163 mg, 1.18 mmol) were dissolved in 6.0 ml of MeOH. The azo-phosphonate (140 mg, 0.71 mmol) in 0.3 ml of MeOH was added in one portion under an atmosphere of nitrogen.[19] The reaction was allowed to proceed until no starting material remained. Upon completion, the mixture was diluted with Et_2O and quenched with saturated aqueous $NaCO_3$ solution. The aqueous layer was extracted with Et_2O (2x) and the combined organic layer was washed with brine and was dried over $MgSO_4$. The resulting solution was filtered, concentrated and purified over silica gel (10% EtOAc/Hex), giving 0.112 g (78%) of the terminal alkyne **24a,**b as a yellowish oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.25 (6H, m), 1.34 (4H, m), 1.47 (2H, m), 1.89 (1H, t, J = 2.6 Hz), 1.99 (2H, q, J = 7.4 Hz), 2.13 (2H, dt, J = 7.1, 2.6 Hz), 5.99 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 18.2, 28.3, 28.6, 28.7, 28.9, 30.7, 32.8, 68.0, 84.5, 103.9 (**24a**), 116.6 (**24b**), 133.9 (**24b**), 138.0 (**24a**).

4-(14-Halo-tetradec-13-ene-1,3-diynyl)-2,2-dimethyl-[1,3]dioxolane (25a,b)

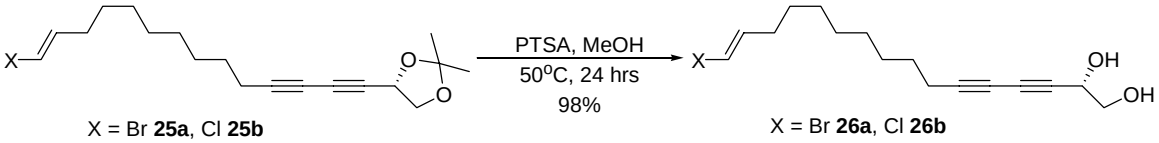


In 0.5 ml of MeOH, a solution of $NH_2OH.HCl$ (2 mg, 0.022 mmol) in 90 μl of water, 0.5 ml of 70% of $EtNH_2$, and CuCl (2 mg, 0.022 mmol) were placed in a round bottom flask, the air was removed and replaced with nitrogen. The acetylene **24a,b** (110 mg, 0.45 mmol) was added in one portion and a yellow solution formed. The bromoalkyne **11** (92 mg, 0.45 mmol) was added over a period of 30 minutes.[10] The reaction was allowed to stir for an additional 40 minutes. This was followed by the addition of a mixture of KCN (0.6 g) and NH_4Cl (2.5 g) in 8 ml of water with vigorous stirring. The extraction was done with Et_2O (3x) and the combined organic layers were washed with NH_4Cl and dried over $MgSO_4$. The solution was filtered, concentrated and

purified over silica gel. (5% EtOAc/Hex), affording 79 mg (48%) of the products **25a,b** and 16 mg (10%) of the bromo-alkyne homo coupled to itself.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.24 (8H, m), 1.33 (3H, s), 1.37 (2H, m), 1.45 (3H, s), 1.48 (2H, m), 2.00 (2H, q, J = 7.4 Hz), 2.24 (2H, t, J = 6.8 Hz), 3.90 (1H, dd, J = 8.0, 1.9 Hz), 4.11 (1H, dd, J = 8.0, 1.7 Hz), 4.72 (1H, m), 5.99 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.1, 25.8, 26.0, 27.9, 28.4, 28.6, 28.8, 29.1, 30.7, 32.8, 64.3, 65.8, 69.6, 70.7, 72.7, 82.0, 104.0 (**25a**), 110.5, 116.6 (**25b**), 133.9 (**25b**), 138.1 (**25a**).

16-Halo-hexadec-15-ene-3,5-diyne-1,2-diol (26a,b)

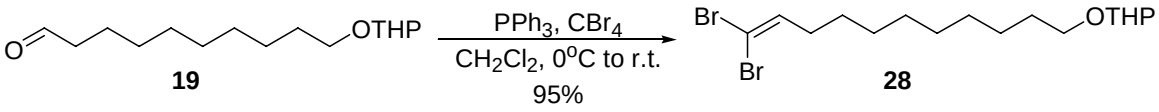


X = Br **25a**, Cl **25b** X = Br **26a**, Cl **26b**

To a solution of the vinyl halides **25a,b**(50 mg, 0.136 mmol) in 2.7 ml of MeOH was added PTSA (3 mg, 0.014 mmol). The reaction was allowed to run for 24 h at 50 ^{o}C.[13] $NaHCO_3$ (29 mg, 0.27 mmol) was then added to the mixture and stirring was continued an additional 15 minutes. The solids were removed by filtration and the solution was concentrated and purified over silica gel (50% EtOAc/Hex), yielding 43 mg (98%) of the product **26a,b** as a white powder.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.25 (6H, m), 1.35 (4H, m), 1.49 (2H, m), 2.01 (2H, q, J = 7.5 Hz), 2.25 (2H, t, J = 6.8 Hz), 2.55 (2H, bs), 3.68 (1H, dd, J = 11.4, 6.4 Hz), 3.70 (1H, dd, J = 11.4, 8.8 Hz), 4.47 (1H, m), 6.00 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.1, 28.5, 28.7, 28.8, 28.9, 29.1, 30.8, 32.8, 63.6, 64.1, 66.2, 71.2, 72.9, 82.2, 104.0 (**26a**), 116.6 (**26b**), 134.0 (**26b**), 138.1 (**26a**).

2-(11,11-Dibromo-undec-10-enyloxy)-tetrahydro-pyran (28)

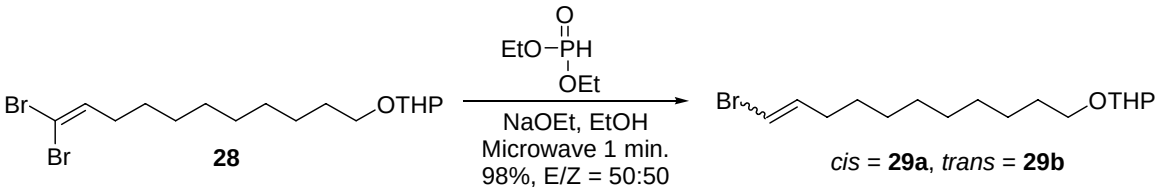


19 **28**

To a solution of PPh_3 (11.4 g, 43.6 mmol) in 36 ml of dry CH_2Cl_2 was added CBr_4 (7.2 g, 21.8 mmol) over 20 minutes at 0 ^oC under an atmosphere of nitrogen. The reaction was then allowed to warm to room temperature and stir for 30 minutes, followed by cooling back down to 0 ^oC for the addition of the aldehyde **19** (2.8 g, 10.9 mmol) in 2.0 ml of dry CH_2Cl_2 over a period of 10 minutes.[20] The reaction was run at room temperature for 45 minutes until no signs of starting material remained, where upon hexanes were added and stirring was continued for an additional hour. The solution was then filtered through a cake of celite, rinsed with excess hexanes, and dried with $MgSO_4$. The resulting solution was filtered, concentrated, and purified over silica gel (10% EtOAc/Hex) to give 4.5 g (95%) of the desired product **28** as a yellow oil.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.24 (10H, m), 1.35 (2H, m), 1.51 (6H, m), 1.77 (1H, m), 2.03 (2H, q, J = 7.2 Hz), 3.32 (1H, dt, J = 9.6, 6.6 Hz), 3.44 (1H, M), 3.67 (1H, dt, J = 9.6, 6.8 Hz), 3.81 (1H, m), 4.52 (1H, t, J = 2.7 Hz), 6.33 (1H, t, J = 7.2 Hz). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 14.0, 19.6, 25.4, 26.1, 27.6, 28.9, 29.1, 29.3, 29.6, 30.6, 32.9, 62.2, 67.5, 88.3, 98.7, 138.7.

2-(11-Bromo-undec-10-enyloxy)-tetrahydro-pyran (29a,b)

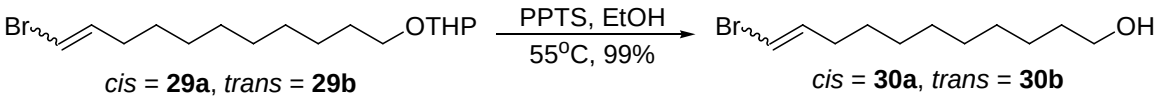


A mixture of EtONa (330 mg, 4.85 mmol), 0.62 ml of diethyl phosphite, and the dibromo-alkene **28** (1.0 g, 2.4 mmol) in 12 ml of ethanol were placed in an Erlenmeyer flask in a microwave oven, operated at 60% of 1500 watts, and irradiated for 1 minute.[22] The reaction mixture was then cooled to room temperature, the solvent was removed, and the product was purified over silica gel (5% EtOAc/Hex), giving 780 mg (98%) of a 1:1 mixture of (E) and (Z) isomers **29a,b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.22 (10H, m), 1.30 (2H, m), 1.48 (6H, m), 1.62 (1H, m), 1.74 (1H, m), 1.94 (1H, q, J = 6.8 Hz), 2.10 (1H, q, J = 6.8 Hz), 3.29 (1H, dt, J = 9.5, 6.6

Hz), 3.41 (1H, m), 3.65 (1H, dt, J = 9.5, 6.8 Hz), 3.78 (1H, m), 4.50 (1H, t, J = 4.1 Hz), 6.01 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.5, 25.3, 26.0, 27.9, 28.4, 28.7, 28.9, 29.1, 29.2, 29.6, 30.6, 32.7, 62.0, 67.4, 98.6 (**29b**), 107.4 (**29a**), 103.9, 134.8 (**29a**), 138.0 (**29b**).

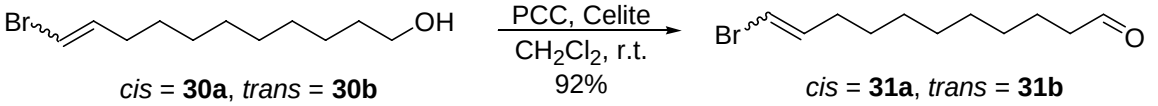
11-Bromo-undec-10-en-1-ol (30a,b)



cis = **29a**, *trans* = **29b** *cis* = **30a**, *trans* = **30b**

A solution of the vinyl bromides **29a,b** (220 mg, 0.66 mmol) and PPTS (16 mg, 0.066 mmol) in 5.3 ml of ethanol was stirred at 55 °C, under an atmosphere of nitrogen, for 5 h.[16] Upon completion, the solvent was removed under vacuum and the product was purified over silica gel (10% EtOAc/Hex), yielding 160 mg (99%) of the alcohol **30a,b**. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 1.28 (12H, m), 1.35 (2H, m), 1.54 (2H, m), 2.01 (1H, q, J = 7.1 Hz), 2.16 (1H, q, J = 6.9 Hz), 3.62 (2H, t, J = 6.6), 6.07 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 25.6, 28.0, 28.5, 29.0, 29.3, 29.4, 29.6, 32.7, 63.0, 103.9 (**30b**), 107.5 (**30a**), 135.0 (**30a**), 138.2 (**30b**).

11-Bromo-undec-10-enal (31a,b)

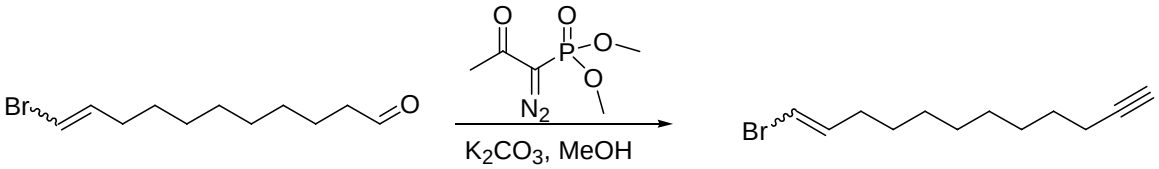


cis = **30a**, *trans* = **30b** *cis* = **31a**, *trans* = **31b**

The alcohols **30a,b** (450 mg, 1.8 mmol) was dissolved in 4.5 ml of dry CH_2Cl_2. This mixture was added to a stirred solution of PCC (580 mg, 2.7 mmol) and celite (580 mg) in 10.6 ml of dry CH_2Cl_2, under an atmosphere of nitrogen.[17] The reaction was allowed to run for 2 h. before being diluted with ether and filtered through a pad of florisil with excess ether as the rinse. The solvent was removed under reduced pressure giving 410 mg (92%) of the aldehydes **31a,b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.23 (10H, m), 1.56 (2H, m), 1.98 (2H, q, J = 6.0 Hz), 2.36 (2H, t, J = 6.7 Hz), 5.97 (2H, m), 9.70 (1H, s). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 21.8, 28.4, 28.7, 28.9, 29.1, 30.7, 32.7, 43.7, 103.9 (**31b**), 107.5 (**31a**), 133.8 (**31a**), 138.0 (**31b**), 202.6.

1-Bromo-dodec-1-en-11-yne (32a,b)

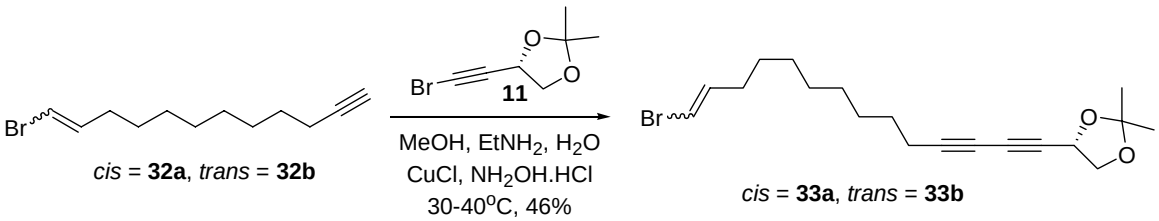


cis = **31a**, *trans* = **31b**

cis = **32a**, *trans* = **32b**

The aldehydes **31a,b**(400 mg, 1.65 mmol) and K_2CO_3 (460 mg, 3.3 mmol) were dissolved in 16.5 ml of dry MeOH. To this was added a mixture of the azo-phosphonate (380 mg, 1.99 mmol) in 0.8 ml of dry MeOH at room temperature, under an atmosphere of nitrogen.[19] After 16 h the reaction was diluted with ether and quenched with saturated aqueous Na_2CO_3. The aqueous layer was extracted with ether and the combined organic layers were washed with brine and dried over $MgSO_4$. The product was purified over silica gel (10% EtOAc/Hex) to give 290 mg (74%) of the terminal acetylenes **32a,b**. **^{1}H-NMR** (300 MHz, $CDCl_3$): δ 1.27 (8H, m), 1.38 (4H, m), 1.49 (2H, m), 1.90 (1H, t, J = 2.6 Hz), 2.00 (2H, q, J = 6.3 Hz), 2.14 (2H, dt, J = 6.8, 2.5 Hz), 6.06 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 18.3, 28.0, 28.6, 28.8, 28.9, 29.1, 29.6, 32.8, 68.0, 84.6, 104.0 (**32b**), 107.5 (**32a**), 134.9 (**32a**), 138.1 (**32b**).

4-(14-Bromo-tetradec-13-ene-1,3-diynyl)-2,2-dimethyl-[1,3]dioxolane (33a,b)



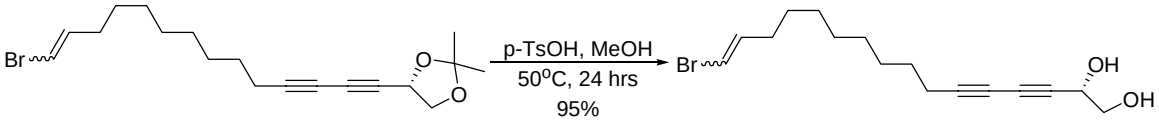
cis = **32a**, *trans* = **32b**

cis = **33a**, *trans* = **33b**

In 1.2 ml of MeOH, a solution of $NH_2OH.HCl$ (4 mg, 0.06 mmol) in 0.017 ml of water, 1.2 ml of 70% $EtNH_2$, and CuCl (6 mg, 0.06 mmol) were placed in a round bottom flask under an atmosphere of nitrogen. To this was added the acetylenes **32a,b**(295 mg, 1.2 mmol) in one portion. Next, bromoalkyne **11** was added over a period of 0.5 h, then the reaction was allowed to run an additional 40 minutes.[10] Next, was added a mixture of KCN (1.2 g), NH_4Cl (5 g), in 16 ml of water with constant stirring followed by extraction with Et_2O (2x). The combined organic layers were washed once with saturated aqueous NH_4Cl and dried over $MgSO_4$. The solution was filtered, concentrated and purified over silica gel (5% EtOAc/Hex), affording 200 mg (46%) of the product **33a,b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.26 (8H, m), 1.34 (3H, s), 1.37 (2H, m), 1.46 (3H, s), 1.49 (2H, m), 2.00 (2H, q, J = 6.8 Hz), 2.25 (2H, t, J = 6.8), 3.91 (1H, dd, J = 6.2, 1.9 Hz), 4.12 (1H, dd, J = 6.45, 1.6 Hz), 4.73 (1H, m), 6.06 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.2, 25.8, 26.0, 28.0, 28.1, 28.5, 28.7, 28.8, 28.9, 29.1, 29.6, 32.8, 65.8, 69.7, 70.8, 72.7, 104.0 (**33b**), 107.5 (**33a**), 110.5, 134.9 (**33a**), 138.2 (**33b**).

16-Bromo-hexadec-15-ene-3,5-diyne-1,2-diol (34a,b)



cis = **33a**, *trans* = **33b**

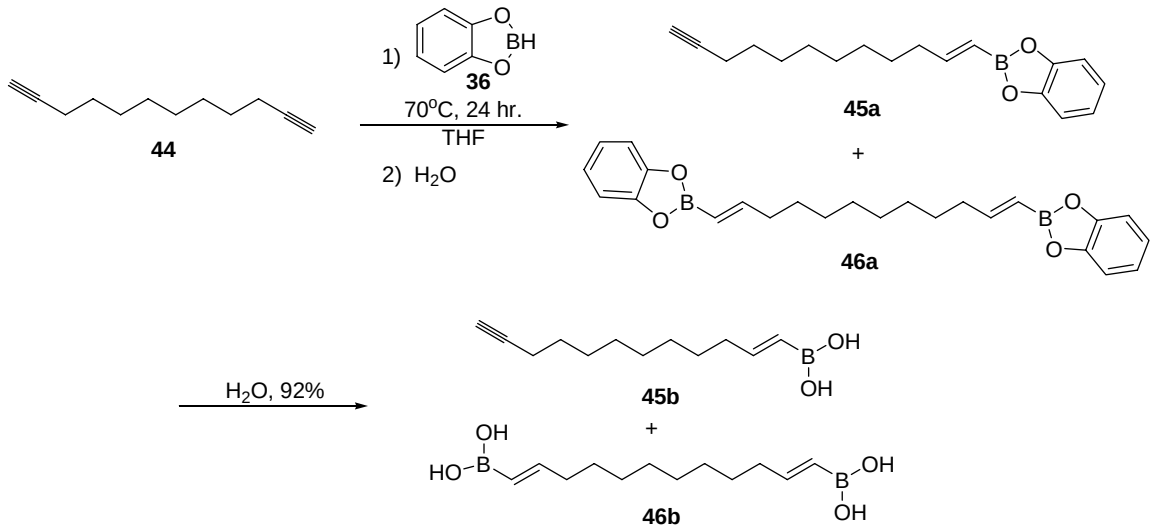
cis = **34a**, *trans* = **34b**

To a solution of the protected diols **33a,b** (200 mg, 0.55 mmol) in 11 ml of MeOH was added PTSA (10 mg, 0.055 mmol) at 50 °C under an atmosphere of nitrogen. The reaction was allowed to run for 24 h.[13] $NaHCO_3$ (120 mg, 1.1 mmol) was added and stirred for 15 minutes. The solids were removed via filtration and the product purified over silica gel (50% EtOAc/Hex), giving 170 mg (95%) of a mixture of cis and trans diplyne C **34a,b**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.26 (6H, m), 1.35 (4H,m), 1.49 (2H, m), 2.00 (1H, q, J = 6.6 Hz), 2.16 (1H, q, J = 7.0 Hz), 2.24 (2H, t, J = 6.8 Hz), 2.68 (1H, bs), 3.00 (1H, bs), 3.65 (1H, dd, J = 11, 6.6 Hz), 3.72 (1H, dd, J = 11, 5.2 Hz), 4.46 (1H, m), 6.06 (2H, m).

^{13}C-NMR (75 MHz, $CDCl_3$): δ 19.1, 27.9, 28.5, 28.7, 28.8, 29.1, 29.6, 32.8, 63.5, 64.1, 66.2, 71.1, 72.9, 82.2, 104.0 (**34b**), 107.5 (**34a**), 134.9 (**34a**), 138.1 (**34b**).

Dodec-1-en-11-ynyl-boranediol (45b)



To the diyne **44** (402 mg, 2.46 mmol) was added a 1M solution of catecholborane (65 µl, 0.61 mmol) in 0.6 ml of THF. This was added through the aid of a syringe pump over a period of 15 h, under an atmosphere of nitrogen in an oil bath at 70 °C. The reaction was allowed to run for a total of 24 h, yielding the boronic ester. The solvent was then removed and 0.6 ml of water was added and allowed to stir for 3 h.[29] The solids were filtered, resulting in the boronic acids **45b** and **46b** (117 mg, 92%) as a mixture of yellow and white solids.

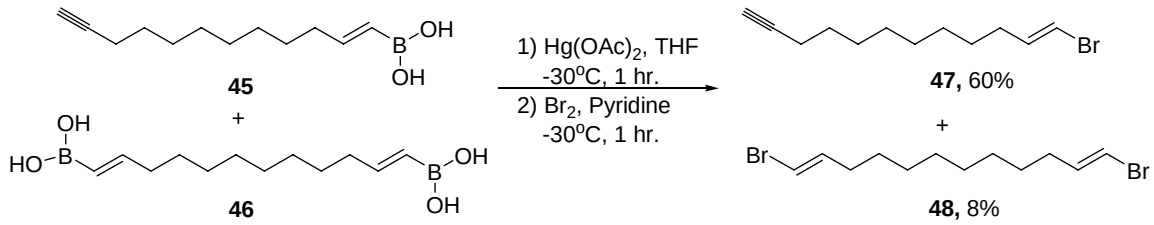
Compound **45a**

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.30 (6H, m), 1.38 (2H, m), 1.48 (4H, m), 1.92 (1H, t, J = 2.6 Hz), 2.15 (2H, dt, J = 6.9, 2.6 Hz), 2.25 (2H, q, J = 6.8 Hz), 5.76 (1H, d, J = 18.0 Hz), 7.02 (3H, m), 7.17 (2H, m). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 18.2, 25.4, 28.0, 28.3, 28.5, 28.6, 28.9, 29.0, 29.2, 35.9, 68.0, 84.5, 112.1 (2), 122.4 (2), 148.2, 157.8.

Compound **45b**

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.30 (8H, m), 1.40 (4H, m), 1.48 (2H, m) 2.14 (5H, m), 5.55 (1H, d, J = 17.6), 6.52 (1H, dt, J = 17.7, 6.5 Hz). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 19.0, 29.6, 30.1, 30.2, 30.2, 30.4, 36.9, 69.3, 85.0, 116.3, 120.9, 153.9.

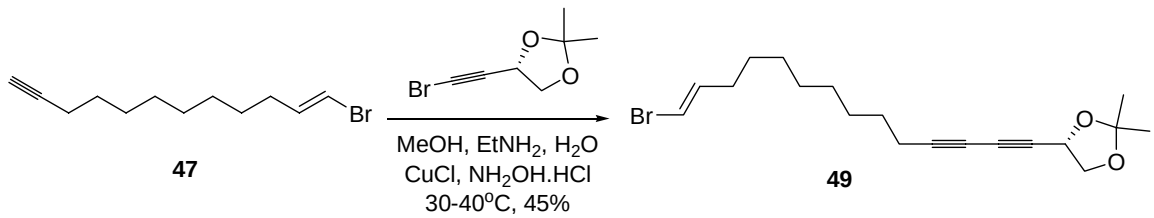
(E)-1-Bromo-dodec-1-en-11-yne (47)



To a solution of the boronic acids **45** and **46** (99 mg, 0.50 mmol) in 0.50 ml of THF at –30 °C was added $Hg(OAc)_2$ (152 mg, 0.50 mmol). This was allowed to stir for 1 h at –30 °C. Next, a solution of Br_2 (30 µl, 0.50 mmol) in 0.50 ml of pyridine was added at –30 °C. This was allowed to stir for 1h.[14] The solution was warmed to room temperature and slowly poured into an ice cold mixture of n-pentane and 6N HCl. The layers were separated and the aqueous layer was extracted with n-pentane (2x). The combined organic layers were then washed with 6N HCl and saturated aqueous $Na_2S_2O_3$ then dried over $MgSO_4$. The resulting solution was filtered, concentrated and purified over silica gel (10% EtOAc/Hex) to give 80 mg (60%) of the product **47** as a yellow oil as well as 9 mg (8%) of the dibromiated species **48**.

^{1}H-NMR (300 MHz, $CDCl_3$): δ 1.26 (4H, m), 1.35 (4H, m), 1.48 (4H, m), 1.91 (1H, t, J = 2.6 Hz), 2.01 (2H, q, J = 6.5 Hz), 2.15 (2H, dt, J = 6.9, 2.8 Hz), 5.97 (1H, d, J = 13.5 Hz), 6.12 (1H, dt, J = 14.0, 7.0 Hz). **^{13}C-NMR** (75 MHz, $CDCl_3$): δ 18.3, 28.3, 28.5, 28.6, 28.8, 28.9, 29.1, 32.8, 68.0, 84.6, 104.0, 138.1. **IR:** υ cm^{-1} 3307, 3064, 2929, 2856, 2117, 1620, 1463, 1434, 1231, 940.

(13E)-4-(14-Bromo-tetradec-13-ene-1,3-diynyl)-2,2-dimethyl-[1,3]dioxolane (49)



In 0.16 ml of methanol, a solution of $NH_2OH.HCl$ (16 mg, 0.23 mmol) in 58 µl of water, 0.13 ml of a 70% aqueous solution of ethylamine, and CuCl (2 mg, 0.025 mmol) were placed in a round bottom flask. The air was removed and replaced by nitrogen, then the acetylene **47** (80 mg, 0.32 mmol) was added in one portion. The bromoalkyne **11** (67 mg, 0.32 mmol) was added over a period of 1 h keeping the temperature between 30-35 ^oC.[10] The reaction was allowed to run for an additional 1.5 h at about 40 ^oC, then a solution of 0.6g of KCN and 2.5 g of NH_4Cl in 8 ml of water was added with vigorous stirring. The product was then extracted with diethyl ether (2x), and the combined organic layers were washed with saturated aqueous NH_4Cl, then dried over $MgSO_4$. The resulting solution was filtered, concentrated, and purified over silica gel (5% EtOAc/Hex), yielding 54 mg (45%) of the product **49** as a light yellow oil, along with the homo-coupled bromoalkyne **11** 21 mg (17%).

$[\alpha]_D$ = +28.63 (MeOH). **^{1}H-NMR** (500 MHz, $CDCl_3$): δ 1.25 (8H, m), 1.34 (3H, s), 1.34 (2H, m), 1.46 (3H, s), 1.48 (2H, m), 2.00 (2H, q, J = 6.7 Hz), 2.24 (2H, t, J = 7.0 Hz), 3.91 (1H, dd, J = 6.1, 1.9 Hz), 4.12 (1H, dd, J = 6.4, 1.6 Hz), 4.73 (1H, m), 5.98 (1H, d, J = 13.4), 6.14 (1H, dt, J = 13.4, 7.2 Hz). **^{13}C-NMR** (125 MHz, $CDCl_3$): δ 19.2, 25.8, 26.0, 28.0, 28.5, 28.7, 28.8, 28.9, 29.1, 32.8, 64.0, 65.8, 69.7, 70.8, 72.7, 82.0, 104.0, 110.5, 138.1. **IR**: υ cm^{-1} 3064, 2927, 2855, 2256, 1620, 1458, 1323, 1235, 1065, 939. **HRMS**: calcd for $C_{19}H_{28}BrO_2$ + Na, 389.1092, found M + Na, 389.1109.

(15E)-16-Bromo-hexadec-15-ene-3,5-diyne-1,2-diol (3)

To a solution of the protected diol **47** (30 mg, 0.08 mmol) in 1.6 ml of MeOH was added PTSA (2 mg, 0.008 mmol) at 50 ^oC, under an atmosphere of nitrogen. The

reaction was allowed to run for 24 h.[13] $NaHCO_3$ (17 mg, 0.16 mmol) was added and stirred for 15 minutes. The solids were removed via filtration and the product purified over silica gel (50% EtOAc/Hex), affording 24 mg (92%) of diplyne C **3** as a white solid. $[\alpha]_D$ = +13.33 (MeOH). mp 61-63 ^oC. **^{1}H-NMR** (500 MHz, MeOD): δ 1.24 (6H,m), 1.32 (4H, m), 1.44 (2H, m), 1.98 (2H, q, J = 7 Hz), 2.20 (2H, m), 3.46 (1H, dd, J = 11, 5.6 Hz), 3.51 (1H, dd, J = 11, 6.0 Hz), 4.27 (1H, dd, J = 6.0, 5.7 Hz), 6.05 (1H, d, J = 14 Hz), 6.10 (1H, dt, J = 14, 7.0 Hz). **^{13}C-NMR** (125 MHz, MeOD): δ 19.6, 29.2, 29.7, 29.8, 29.9, 30.0, 30.2, 33.7, 64.5, 65.5, 67.0, 70.7, 75.7, 81.7, 105.0, 139.4. **IR**: υ cm^{-1} 3377 (broad), 3054, 2931, 2856, 2254, 1620, 1422, 941, 739. **HRMS**: calcd for $C_{16}H_{24}BrO_2$ + Na, 349.0779, found M + Na, 349.0779.

References

(1) Gribble, G. W. *Chemical Society Reviews* **1999**, *28*, 335-346. "The diversity of naturally occurring organobromine compounds"

(2) Fusetani, N.; Li, H. Y.; Tamura, K.; Matsunaga, S. *Tetrahedron* **1993**, *49*, 1203-10. "Bioactive marine metabolites. 46. Antifungal brominated C18 acetylenic acids from the marine sponge Petrosia volcano Hoshino"

(3) Tada, H.; Yasuda, F. *Chemistry Letters* **1984**, 779-80. "Siphonodiol, a new polyacetylenic metabolite from the sponge Siphonochalina truncata"

(4) Tsukamoto, S.; Kato, H.; Hirota, H.; Fusetani, N. *Journal of Natural Products* **1997**, *60*, 126-130. "Seven new polyacetylene derivatives, showing both potent metamorphosis-inducing activity in ascidian larvae and antifouling activity against barnacle larvae, from the marine sponge Callyspongia truncata"

(5) Lerch, M. L.; Harper, M. K.; Faulkner, D. J. *Journal of Natural Products* **2003**, *66*, 667-670. "Brominated polyacetylenes from the Philippines sponge Diplastrella sp"

(6) Gung, B. W.; Gibeau, C.; Jones, A. *Tetrahedron: Asymmetry* **2004**, *15*, 3973-3977. "First total synthesis of the brominated polyacetylenes (+)-diplyne A and D: proof of absolute configuration"

(7) Gung Benjamin, W.; Kumi, G. *Journal of organic chemistry* **2003**, *68*, 5956-60. "Remarkable reactivity difference in oxygen-substituted versus non-oxygen-substituted bromoalkynes in Cu(I)-catalyzed cross-coupling reactions: total synthesis of (-)-S-18-hydroxyminquartynoic acid"

(8) Gung Benjamin, W.; Dickson, H. *Organic letters* **2002**, *4*, 2517-9. "Total synthesis of (-)-minquartynoic acid: an anti-cancer, anti-HIV natural product"

(9) Sonogashira, K. *Journal of Organometallic Chemistry* **2002**, *653*, 46-49. "Development of Pd-Cu catalyzed cross-coupling of terminal acetylenes with sp2-carbon halides"

(10) Brandsma, L. *Preparative Acetylenic Chemistry*; 2nd ed.; Elsevier: New York, 1988.

(11) Alami, M.; Linstrumelle, G. *Tetrahedron Letters* **1991**, *32*, 6109-12. "An efficient palladium-catalyzed reaction of vinyl chlorides with terminal acetylenes"

(12) Andreini, B. P.; Benetti, M.; Carpita, A.; Rossi, R. *Gazzetta Chimica Italiana* **1988**, *118*, 469-74. "Palladium-mediated reactions between 1-alkynylzinc chlorides and (E)/(Z)-1,2-dibromoethylene or (E)-1,2-dibromo-1,2-diphenylethylene"

(13) Mukai, C.; Kim, J. S.; Sonobe, H.; Hanaoka, M. *Journal of Organic Chemistry* **1999**, *64*, 6822-6832. "Stereocomplementary Construction of Optically Active Bicyclo[4.3.0]nonenone Derivatives"

(14) Brown, H. C.; Larock, R. C.; Gupta, S. K.; Rajagopalan, S.; Bhat, N. G. *Journal of Organic Chemistry* **1989**, *54*, 6079-84. "Vinylic organoboranes. 15. Mercuration of 2-alkenyl-1,3,2-benzodioxaboroles and boronic acids. A convenient stereospecific procedure for the conversion of alkynes into (E)-1-halo-1-alkenes via mercuric salts"

(15) Takai, K.; Nitta, K.; Utimoto, K. *Journal of the American Chemical Society* **1986**, *108*, 7408-10. "Simple and selective method for aldehydes (RCHO) -> (E)-haloalkenes (RCH:CHX) conversion by means of a haloform-chromous chloride system"

(16) Miyashita, M.; Yoshikoshi, A.; Grieco, P. A. *Journal of Organic Chemistry* **1977**, *42*, 3772-4. "Pyridinium p-toluenesulfonate. A mild and efficient catalyst for the tetrahydropyranylation of alcohols"

(17) Gung, B. W.; Dickson, H. D.; Seggerson, S.; Bluhm, K. *Synthetic Communications* **2002**, *32*, 2733-2740. "A short synthesis of an acetylenic alcohol from the sponge cribrochalina vasculum"

(18) Callant, P.; D'Haenens, L.; Vandewalle, M. *Synthetic Communications* **1984**, *14*, 155-61. "An efficient preparation and the intramolecular cyclopropanation of a-diazo-b-ketophosphonates and a-diazophosphonoacetates"

(19) Mueller, S.; Liepold, B.; Roth, G. J.; Bestmann, H. J. *Synlett* **1996**, 521-522. "An improved one-pot procedure for the synthesis of alkynes from aldehydes"

(20) Marshall, J. A.; Xie, S. *Journal of Organic Chemistry* **1995**, *60*, 7230-7. "Synthesis of a C22-34 Subunit of the Immunosuppressant FK-506"

(21) Hirao, T.; Masunaga, T.; Ohshiro, Y.; Agawa, T. *Journal of Organic Chemistry* **1981**, *46*, 3745-7. "Reduction of gem-dibromides with diethyl phosphite"

(22) Kuang, C.; Senboku, H.; Tokuda, M. *Tetrahedron* **2002**, *58*, 1491-1496. "Facile and stereoselective synthesis of (E)-vinyl bromides by microwave-induced reaction of 1,1-dibromoalkenes using a diethyl phosphonate/EtONa/EtOH system"

(23) Brown, H. C.; Gupta, S. K. *Journal of the American Chemical Society* **1972**, *94*, 4370-1. "Catecholborane (1,3,2-benzodioxaorole) as a new, general monohydroboration reagent for alkynes. Convenient synthesis of alkeneboronic esters and acids from alkynes via hydroboration"

(24) Brown, H. C.; Subrahmanyam, C.; Hamaoka, T.; Ravindran, N.; Bowman, D. H.; Misumi, S.; Unni, M. K.; Somayaji, V.; Bhat, N. G. *Journal of Organic Chemistry* **1989**, *54*, 6068-75. "Vinylic organoboranes. 13. A convenient stereospecific synthesis of (Z)-1-halo-1-alkenes from 1-alkynes via (E)-1-alkenylborane derivatives with halogens"

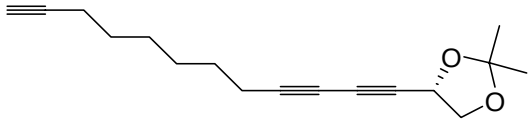
(25) Brown, H. C.; Hamaoka, T.; Ravindran, N.; Subrahmanyam, C.; Somayaji, V.; Bhat, N. G. *Journal of Organic Chemistry* **1989**, *54*, 6075-9. "Vinylic organoboranes. 14. A stereospecific synthesis of (E)-1-halo-1-alkenes from 1-alkynes"

(26) Brown, H. C. *Organic Syntheses via Boranes*, 1975.

(27) Kunda, S. A.; Smith, T. L.; Hylarides, M. D.; Kabalka, G. W. *Tetrahedron Letters* **1985**, *26*, 279-80. "Chlorination of organoboranes: synthesis of (Z)-vinyl chlorides"

(28) Kabalka, G. W.; Sastry, K. A. R.; Knapp, F. F.; Srivastava, P. C. *Synthetic Communications* **1983**, *13*, 1027-32. "Synthesis of vinyl bromides via reaction of vinyl boronic acids with sodium bromide"

(29) White, J. D.; Choi, Y. *Organic Letters* **2000**, *2*, 2373-2376. "Catalyzed Asymmetric Diels-Alder Reaction of Benzoquinone. Total Synthesis of (-)-Ibogamine"



12

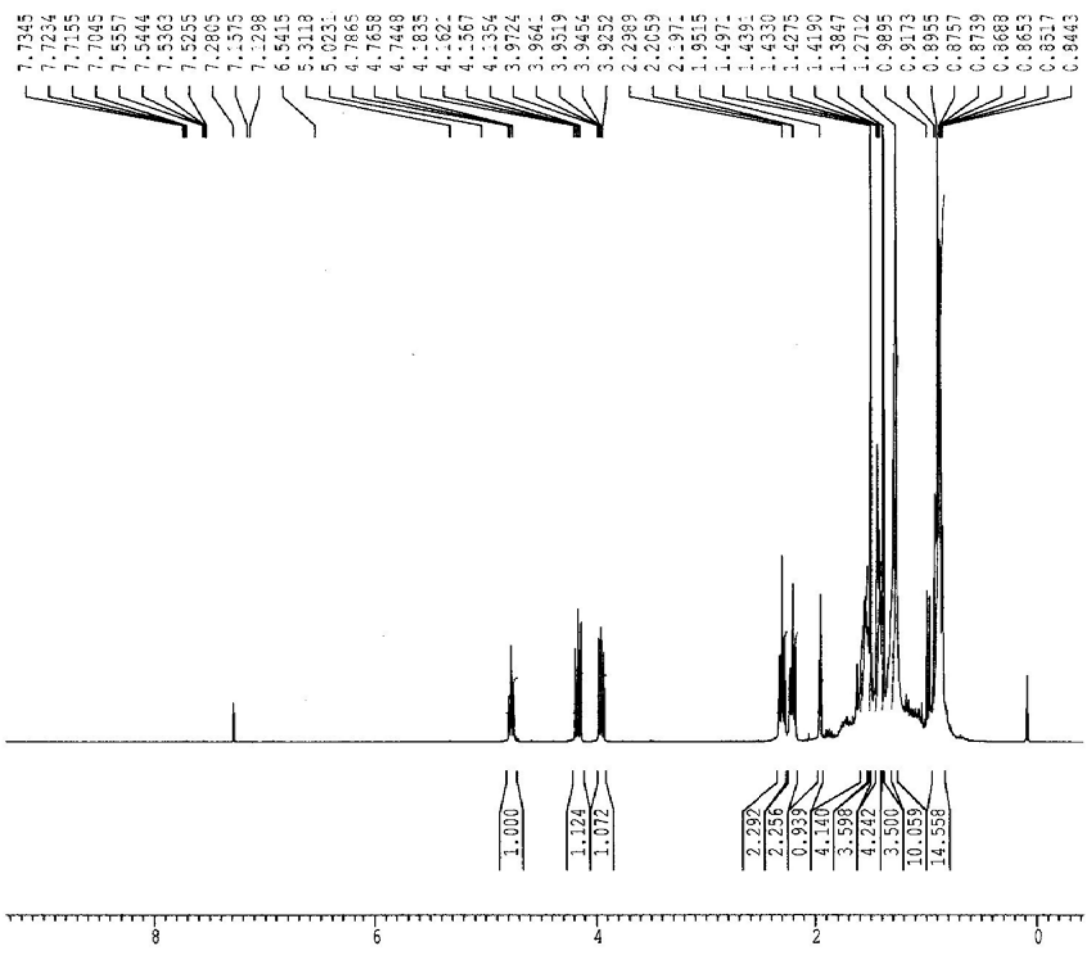
1,2-Isopropylidenetetradeca-3,5,13-triyne

<1> ^{1}H NMR

<2> IR

<3> HRMS

p73 T 1-10



Current Data Parameters

NAME	DCCMalicDcid
EXPNO	6
PROCNO	1

F2 - Acquisition Parameters

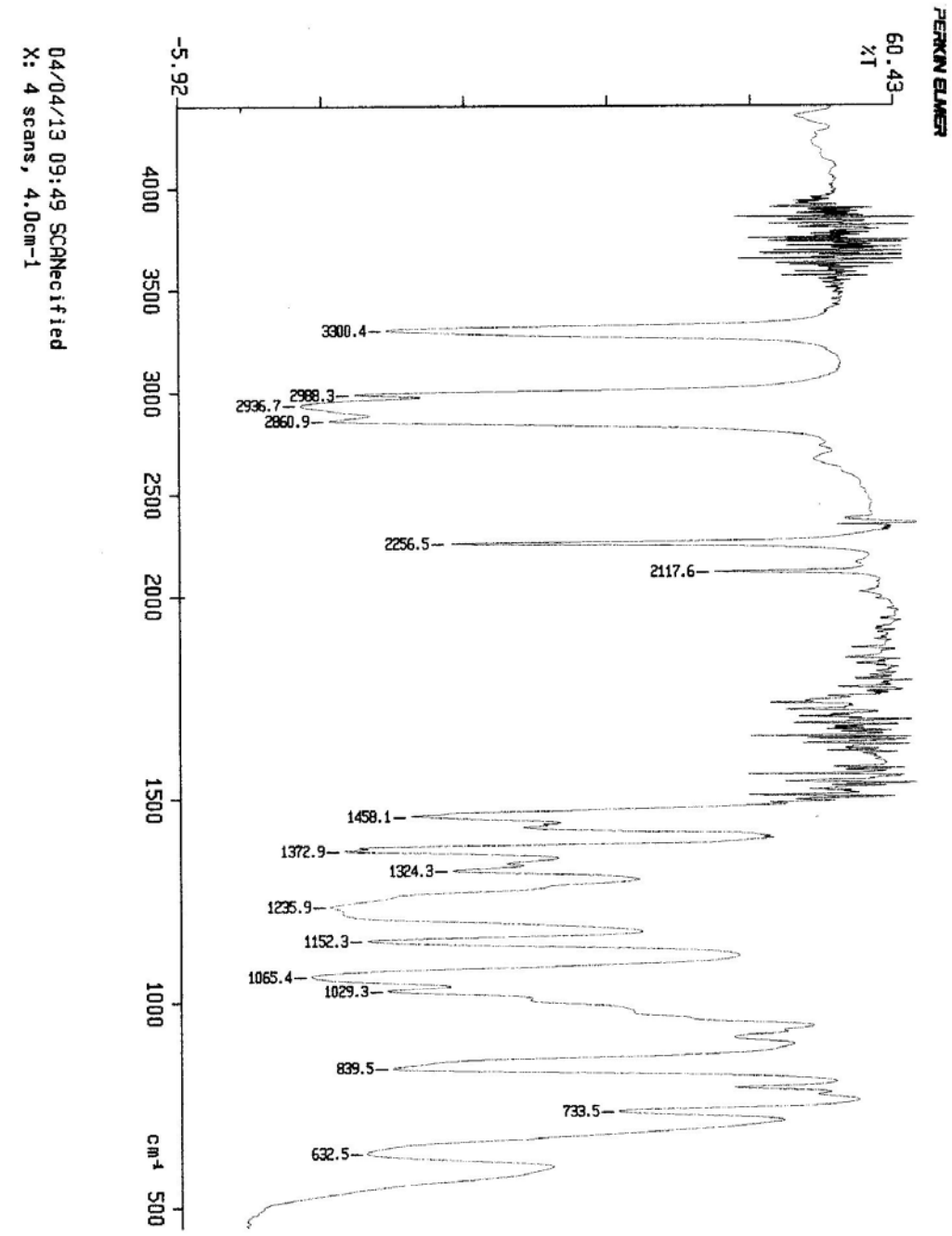
Date_	20040221
Time	1.04
INSTRUM	spect
PROBHD	5 mm Multinu
PULPROG	zg30
TD	32768
SOLVENT	CDCl3
NS	16
DS	2
SWH	6188.119 Hz
FIDRES	0.188846 Hz
AQ	2.6477044 sec
RG	71.8
DW	80.800 usec
DE	6.00 usec
TE	300.0 K
D1	1.00000000 sec
P1	14.10 usec
SFO1	300.1318534 MHz
NUC1	1H
PL1	3.00 dB

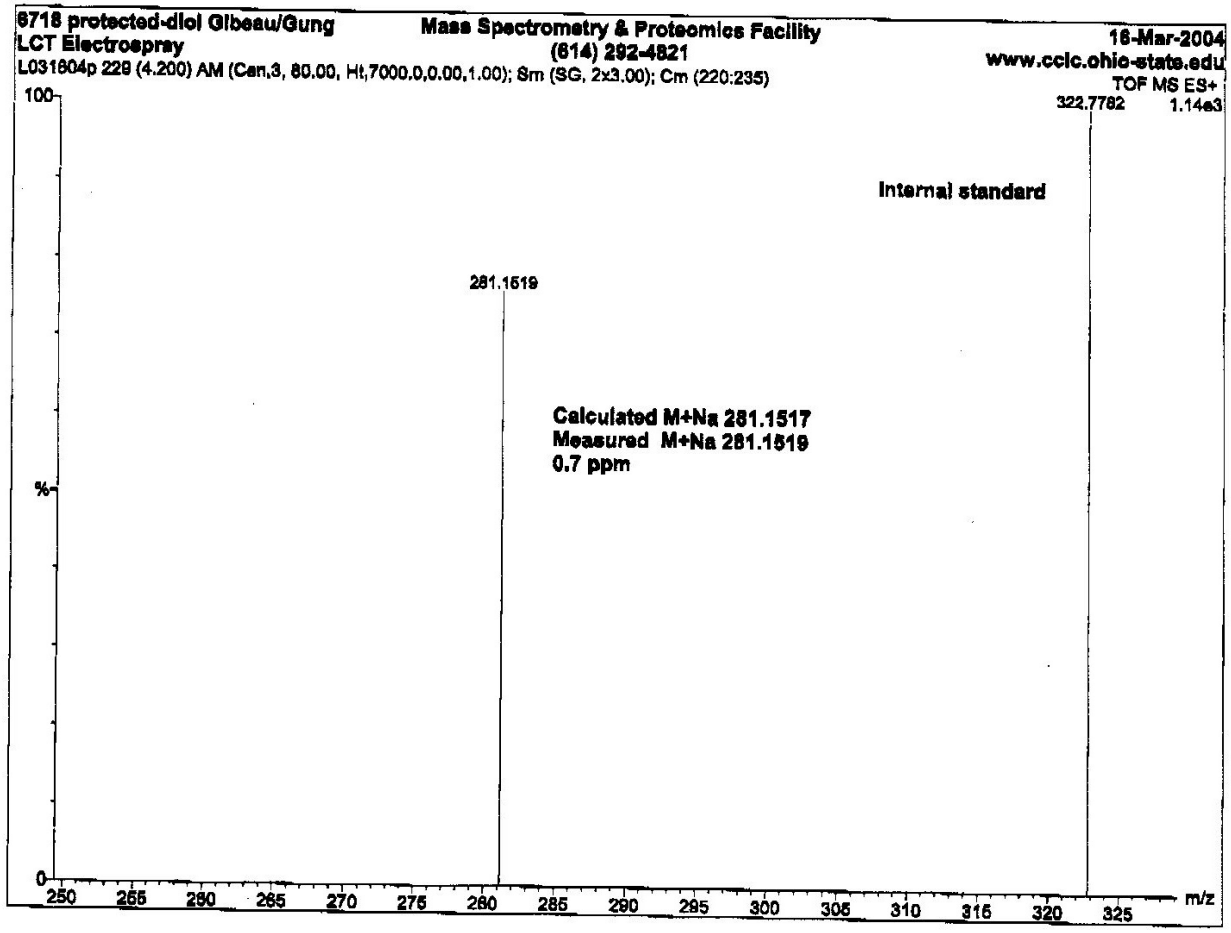
F2 - Processing parameters

SI	16384
SF	300.1300000 MHz
WDW	EM
SSB	0
LB	0.30 Hz
GB	0
PC	1.00

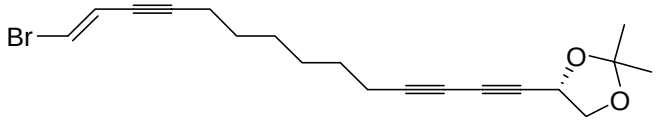
1D NMR plot parameters

CX	20.00 cm
F1P	10.008 ppm
F1	3003.65 Hz
F2P	-0.429 ppm
F2	-128.87 Hz
PPMCM	0.52186 ppm/cm
HZCM	156.62584 Hz/cm


PERKIN ELMER
60.43
%T
-5.92
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3300.4
2988.3
2936.7
2860.9
2256.5
2117.6
1458.1
1372.9
1324.3
1235.9
1152.3
1065.4
1029.3
839.5
733.5
632.5
04/04/13 09:49 SCANecified
X: 4 scans, 4.0cm-1



Mar.22. 2004 9:46AM CCIC No.1412 P. 9



13

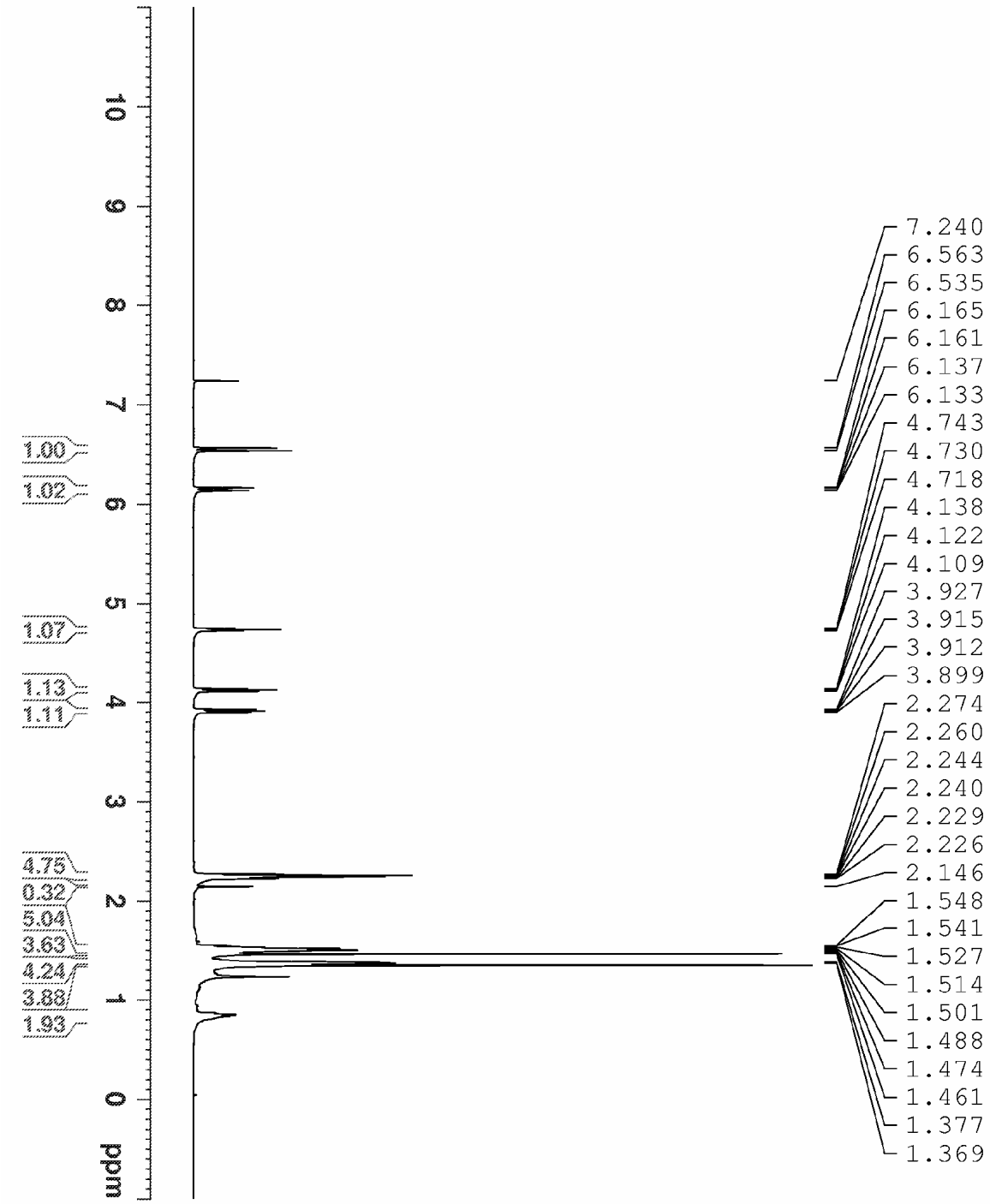
(15E)-1,2-Isopropylidene-16-bromohexadeca-15-en-3,5,13-triyne

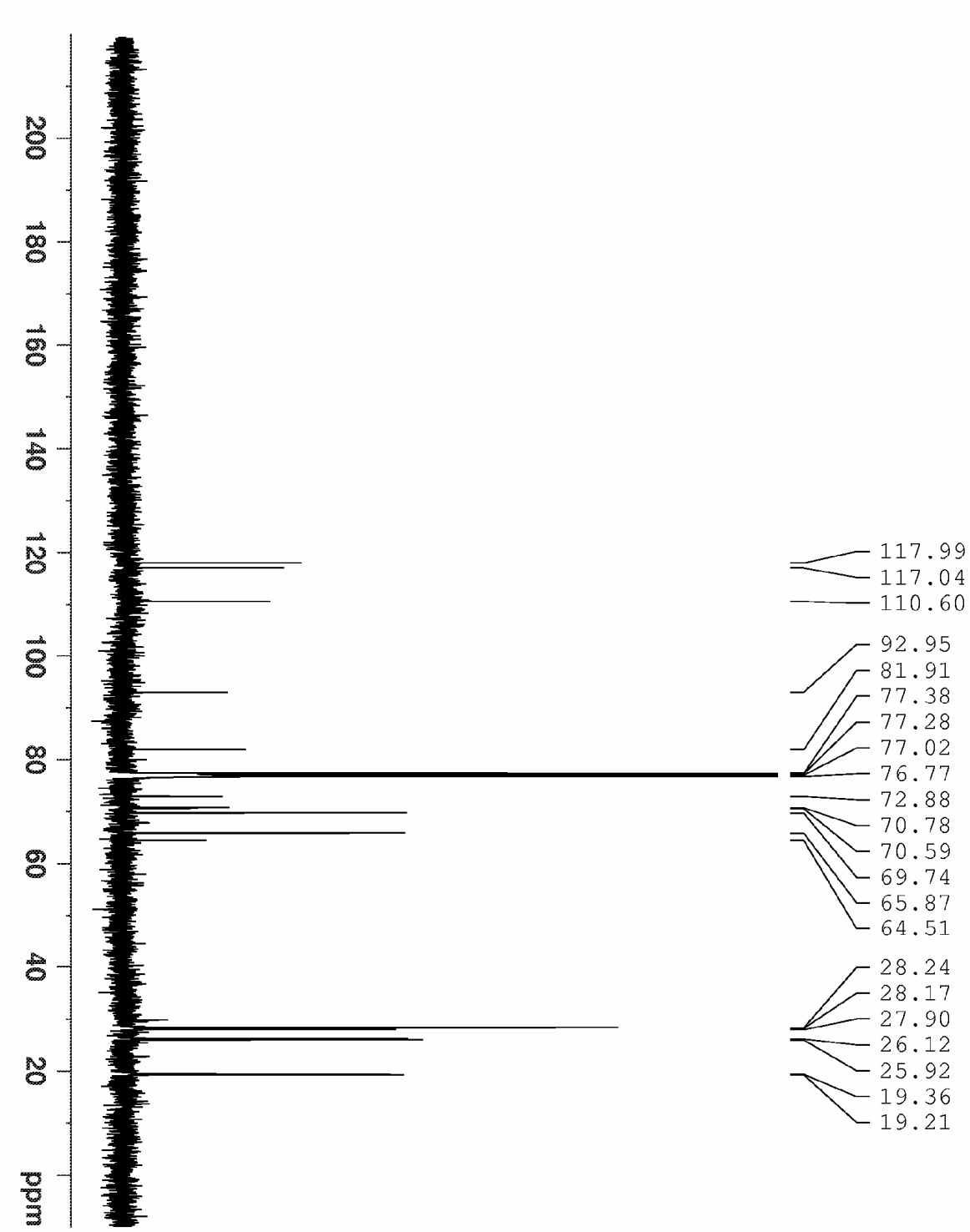
<1> ^{1}H NMR

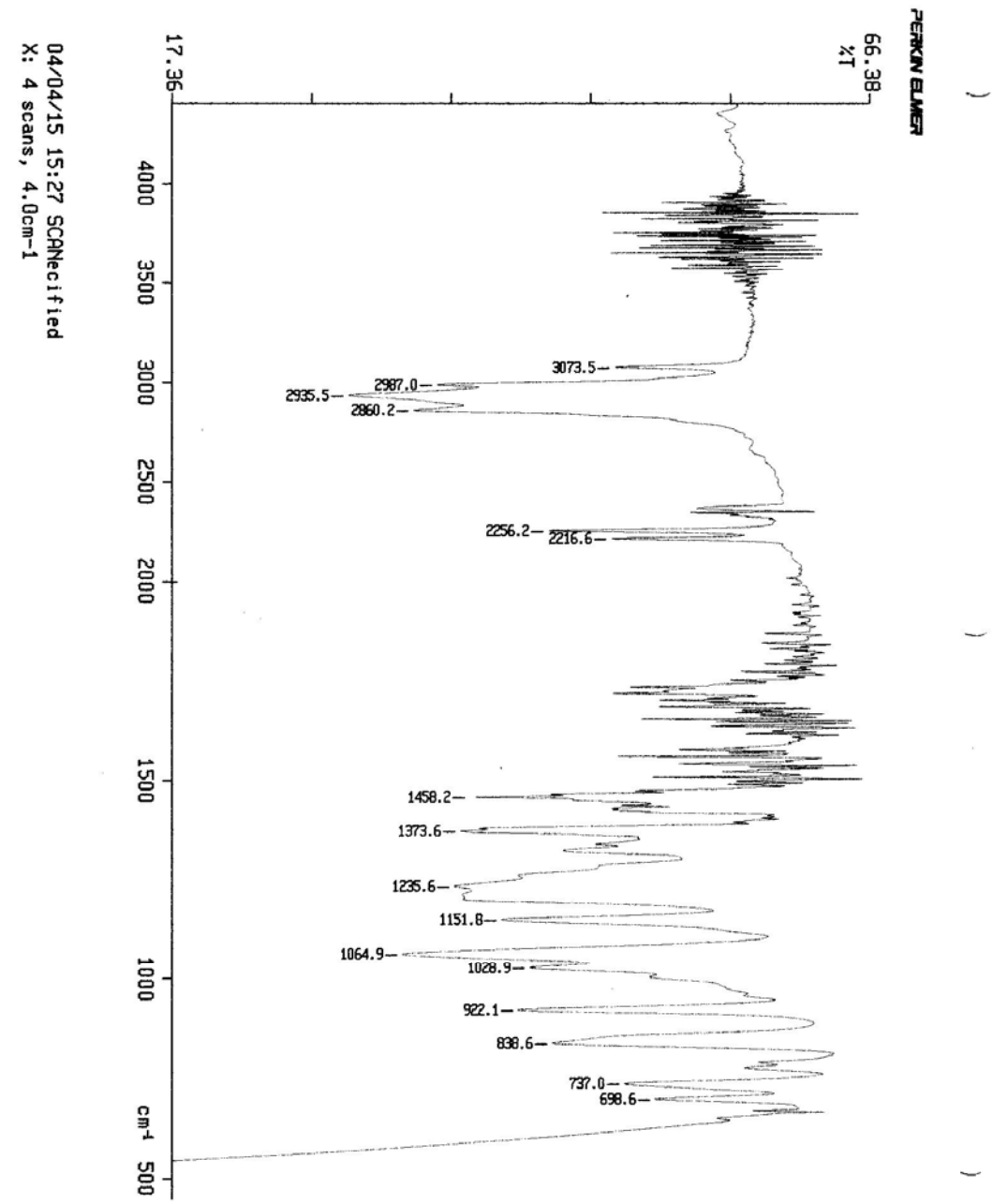
<2> ^{13}C NMR

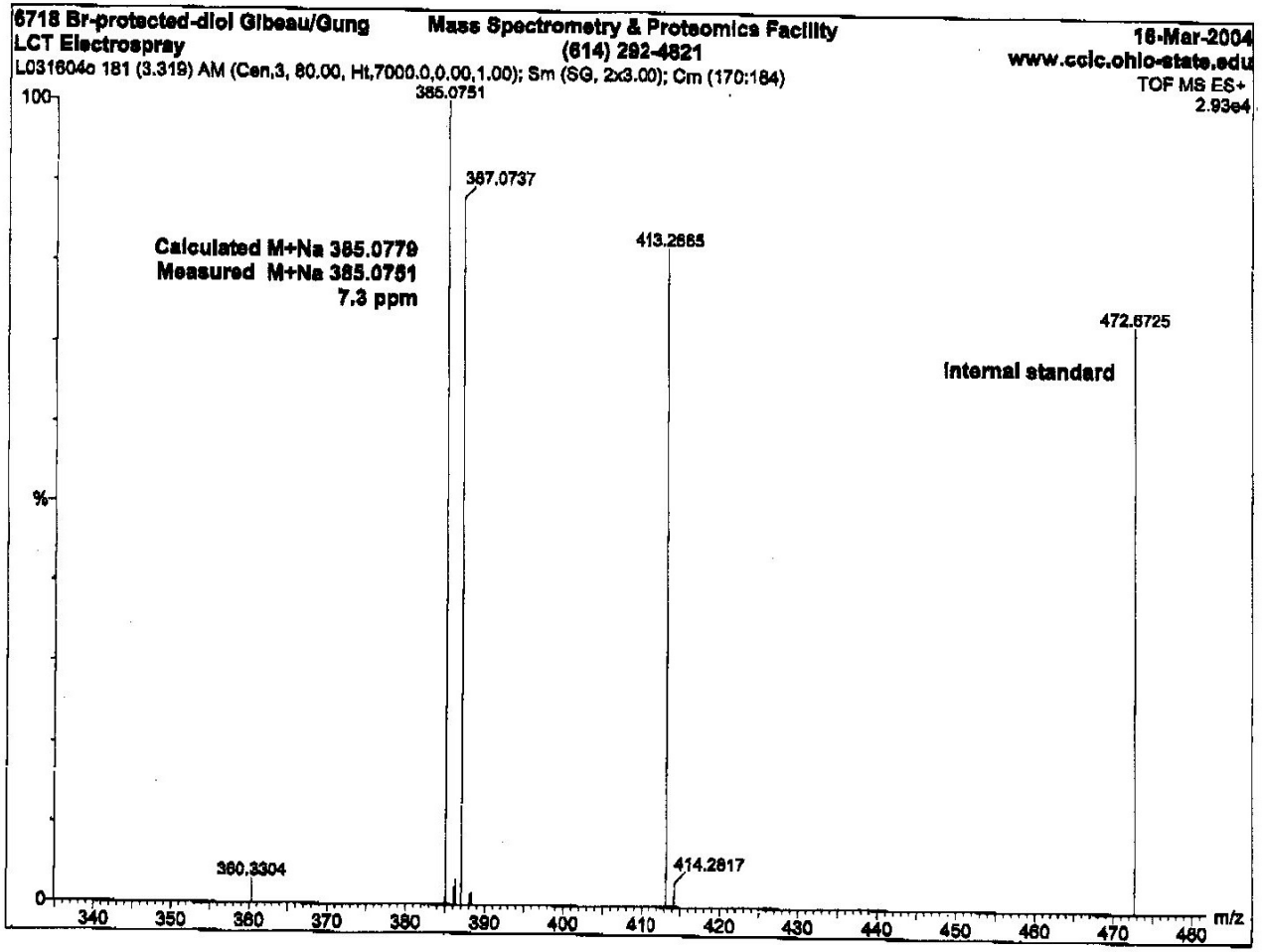
<3> IR

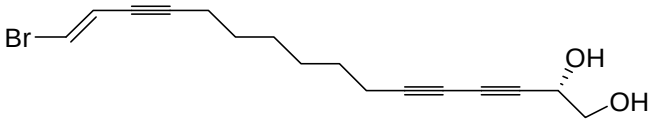
<4> HRMS


7.240
6.563
6.535
6.165
6.161
6.137
6.133
4.743
4.730
4.718
4.138
4.122
4.109
3.927
3.915
3.912
3.899
2.274
2.260
2.244
2.240
2.229
2.226
2.146
1.548
1.541
1.527
1.514
1.501
1.488
1.474
1.461
1.377
1.369
1.00
1.02
1.07
1.13
1.11
4.75
0.32
5.04
3.63
4.24
3.88
1.93
ppm


200
180
160
140
120
100
80
60
40
20
ppm
117.99
117.04
110.60
92.95
81.91
77.38
77.28
77.02
76.77
72.88
70.78
70.59
69.74
65.87
64.51
28.24
28.17
27.90
26.12
25.92
19.36
19.21


PERKIN ELMER
66.38
%T
17.36
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3073.5
2987.0
2935.5
2860.2
2256.2
2216.6
1458.2
1373.6
1235.6
1151.8
1064.9
1028.9
922.1
838.6
737.0
698.6
04/04/15 15:27 SCANecified
X: 4 scans, 4.0cm-1





1

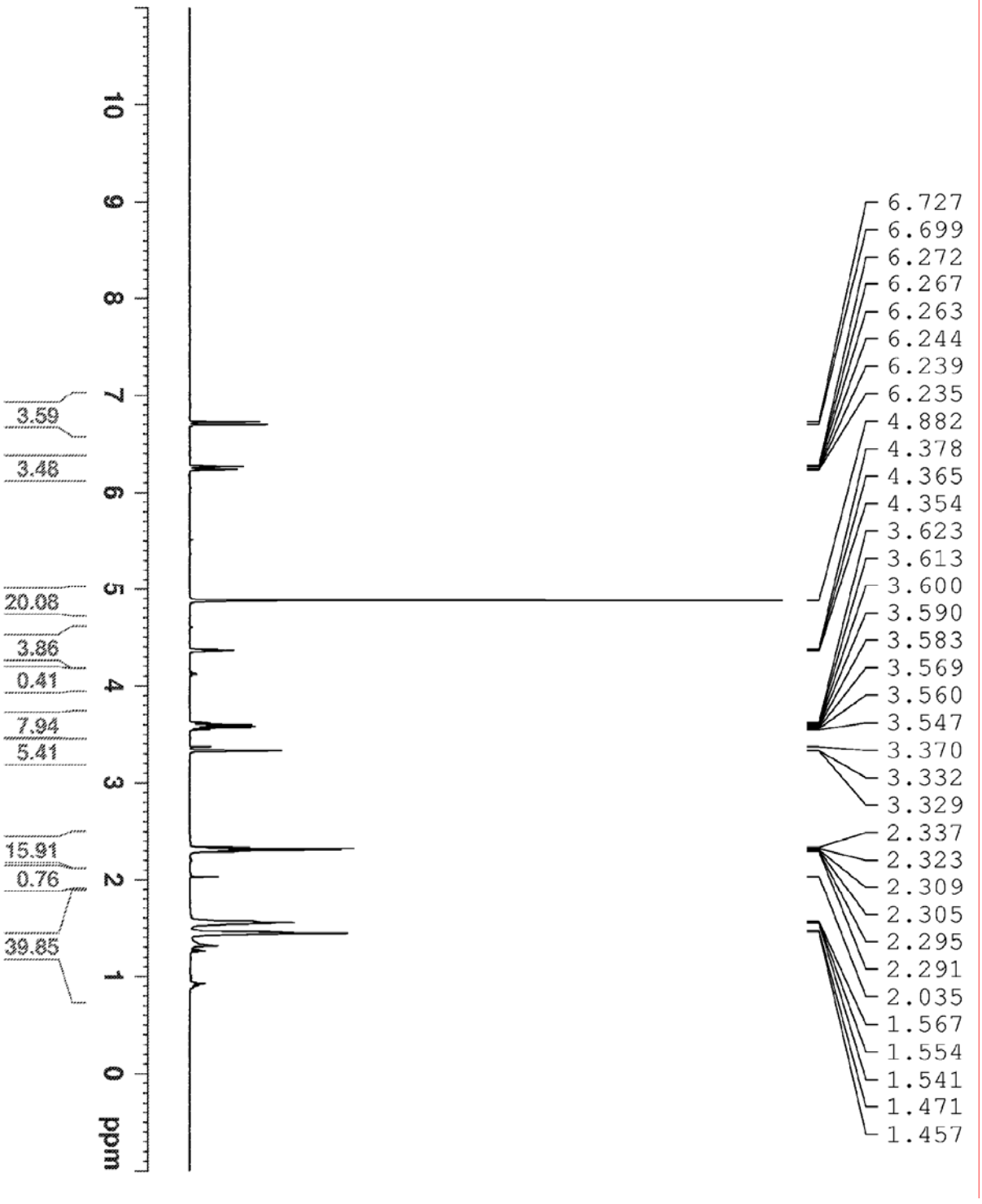
(+)-Diplyne A

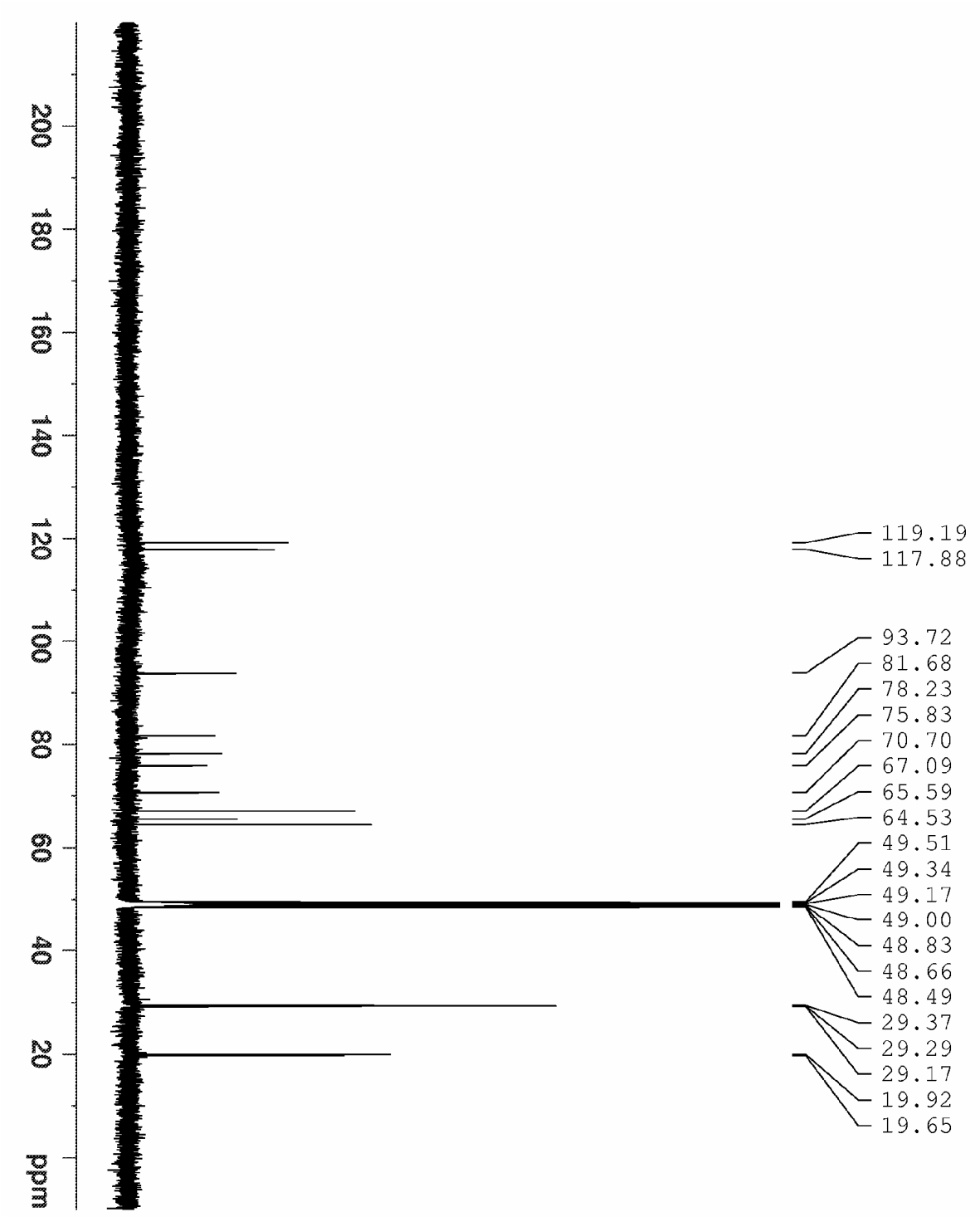
<1> ^{1}H NMR

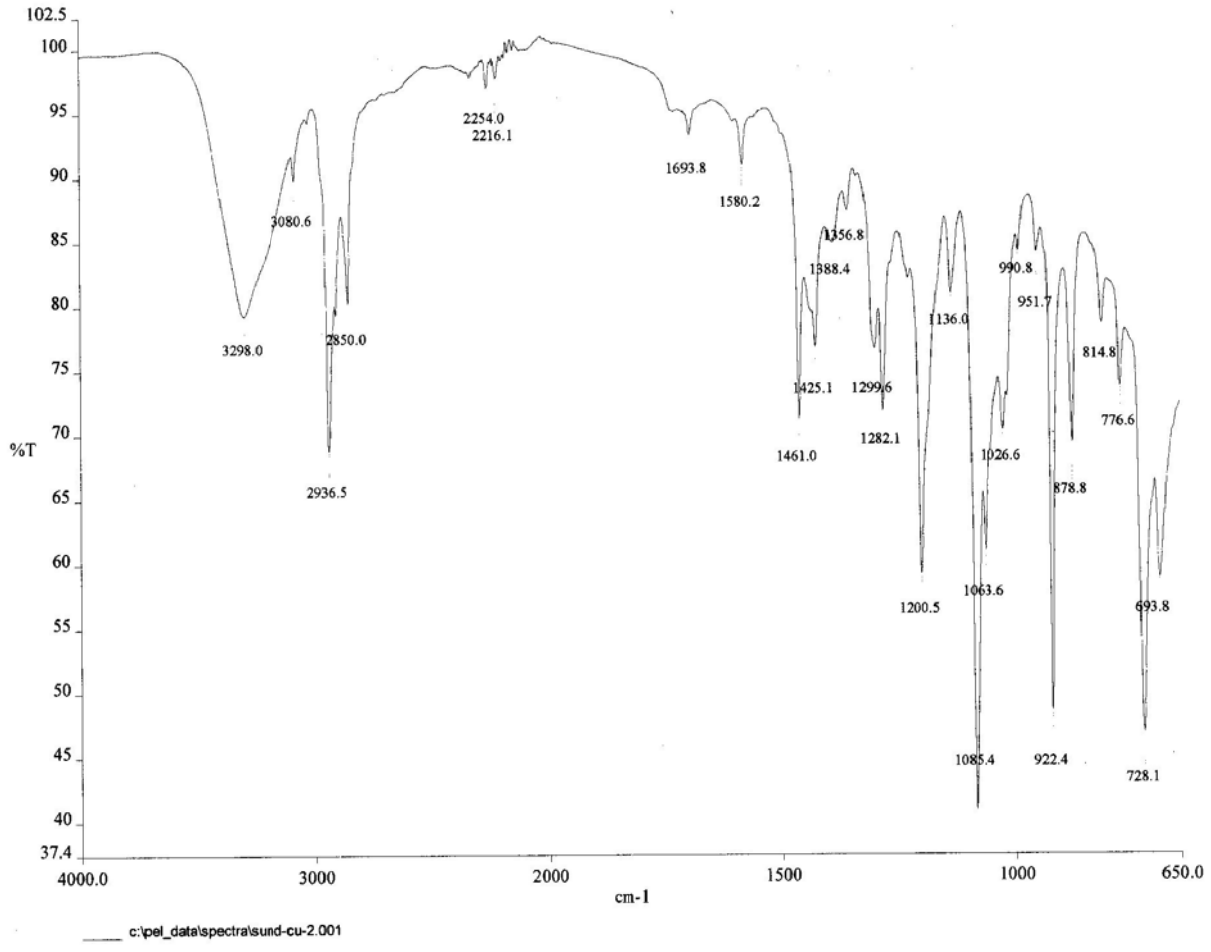
<2> ^{13}C NMR

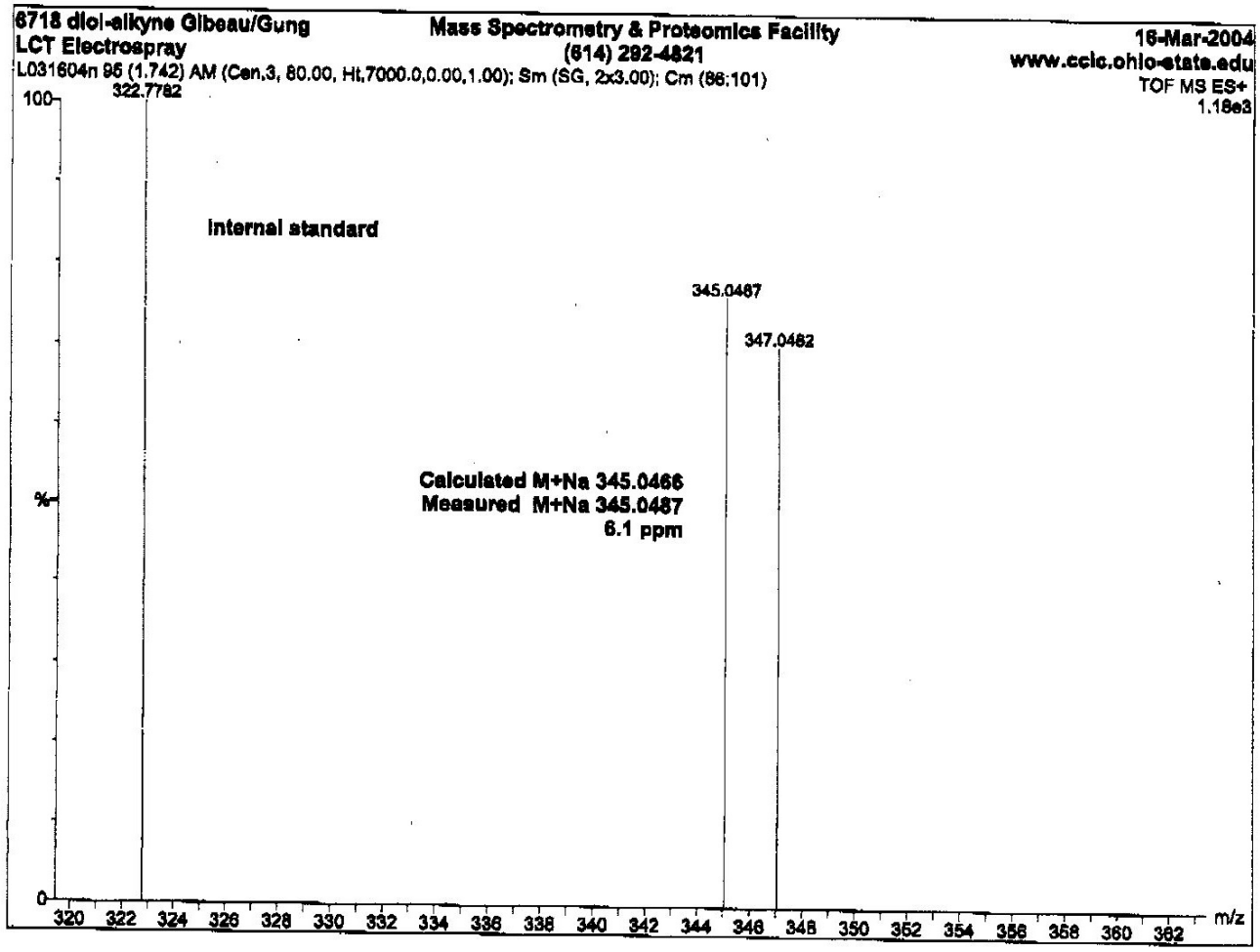
<3> IR

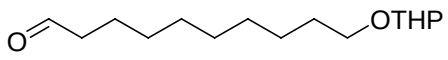
<4> HRMS


6.727
6.699
6.272
6.267
6.263
6.244
6.239
6.235
4.882
4.378
4.365
4.354
3.623
3.613
3.600
3.590
3.583
3.569
3.560
3.547
3.370
3.332
3.329
2.337
2.323
2.309
2.305
2.295
2.291
2.035
1.567
1.554
1.541
1.471
1.457
3.59
3.48
20.08
3.86
0.41
7.94
5.41
15.91
0.76
39.85
ppm


200
180
160
140
120
100
80
60
40
20
ppm
119.19
117.88
93.72
81.68
78.23
75.83
70.70
67.09
65.59
64.53
49.51
49.34
49.17
49.00
48.83
48.66
48.49
29.37
29.29
29.17
19.92
19.65


102.5
100
95
90
85
80
75
70
65
60
55
50
45
40
37.4
%T
4000.0
3000
2000
1500
1000
650.0
cm-1
3298.0
3080.6
2936.5
2850.0
2254.0
2216.1
1693.8
1580.2
1461.0
1425.1
1388.4
1356.8
1299.6
1282.1
1200.5
1136.0
1085.4
1063.6
1026.6
990.8
951.7
922.4
878.8
814.8
776.6
728.1
693.8
c:\pel_data\spectra\sund-cu-2.001



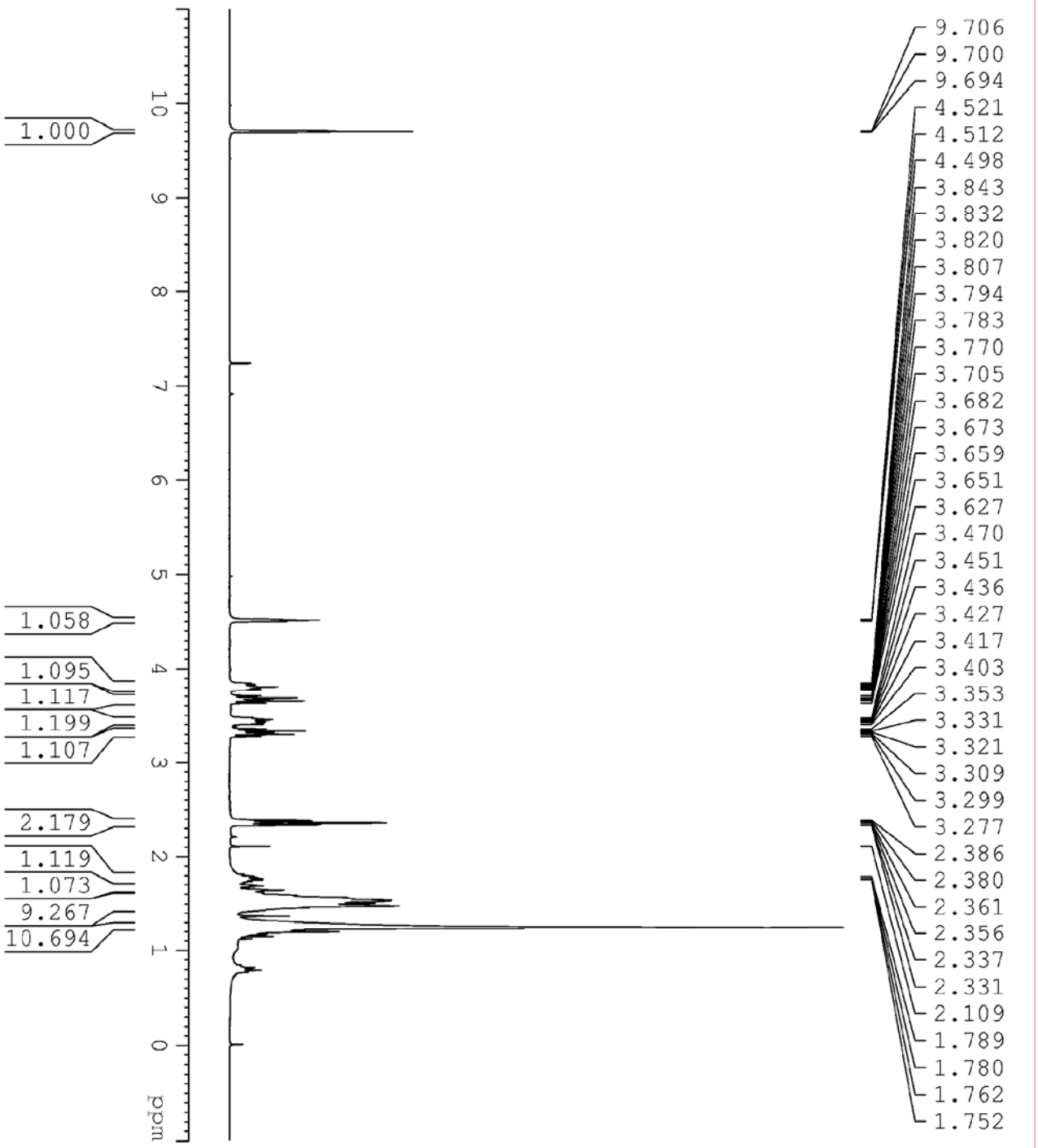


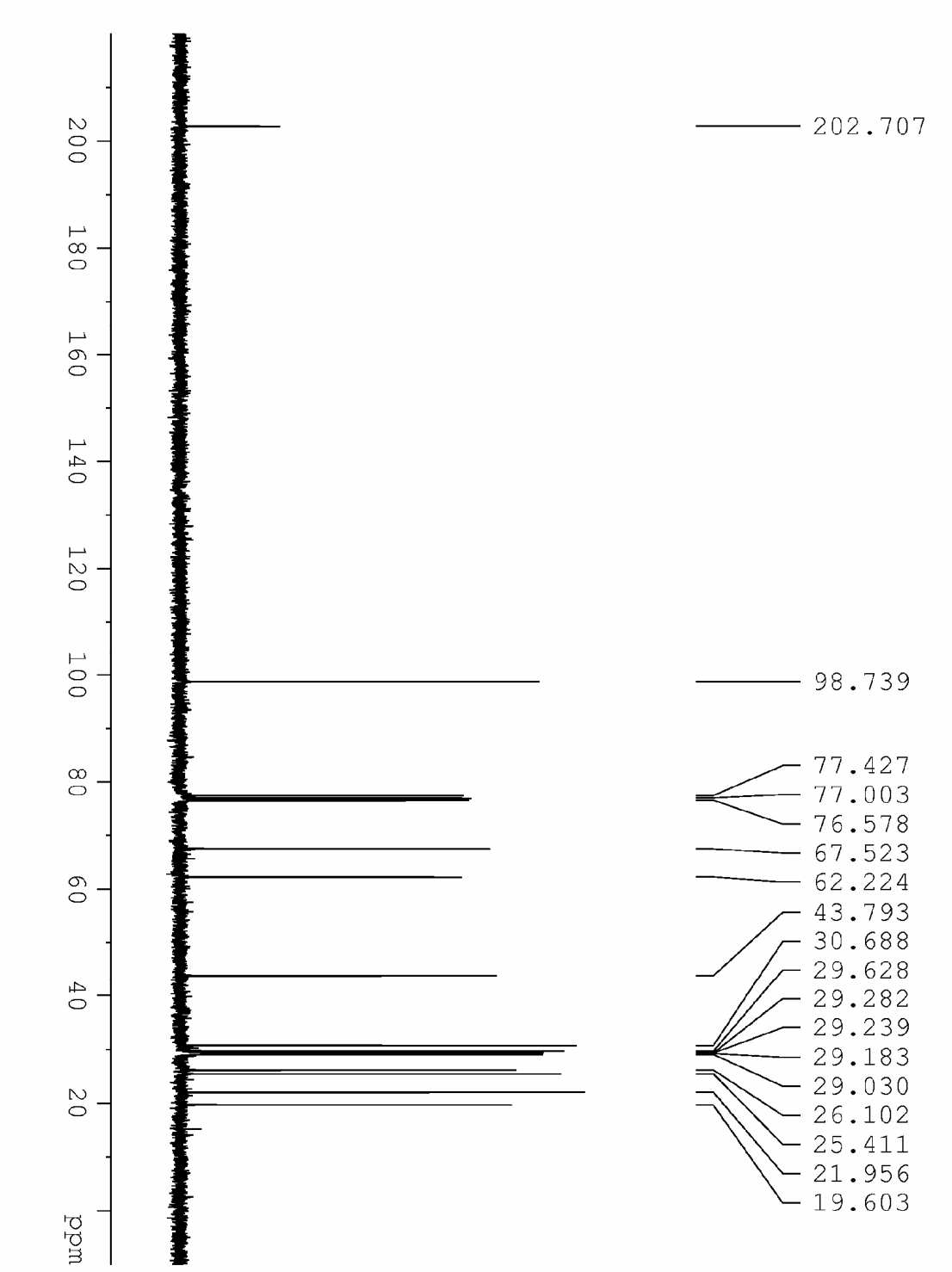
19

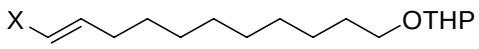
10-(Tetrahydro-pyran-2-yloxy)-decanal

<1> ^{1}H NMR

<2> ^{13}C NMR


1.000
1.058
1.095
1.117
1.199
1.107
2.179
1.119
1.073
9.267
10.694
10
9
8
7
6
5
4
3
2
1
0
ppm
9.706
9.700
9.694
4.521
4.512
4.498
3.843
3.832
3.820
3.807
3.794
3.783
3.770
3.705
3.682
3.673
3.659
3.651
3.627
3.470
3.451
3.436
3.427
3.417
3.403
3.353
3.331
3.321
3.309
3.299
3.277
2.386
2.380
2.361
2.356
2.337
2.331
2.109
1.789
1.780
1.762
1.752


202.707
98.739
77.427
77.003
76.578
67.523
62.224
43.793
30.688
29.628
29.282
29.239
29.183
29.030
26.102
25.411
21.956
19.603
200
180
160
140
120
100
80
60
40
20
ppm

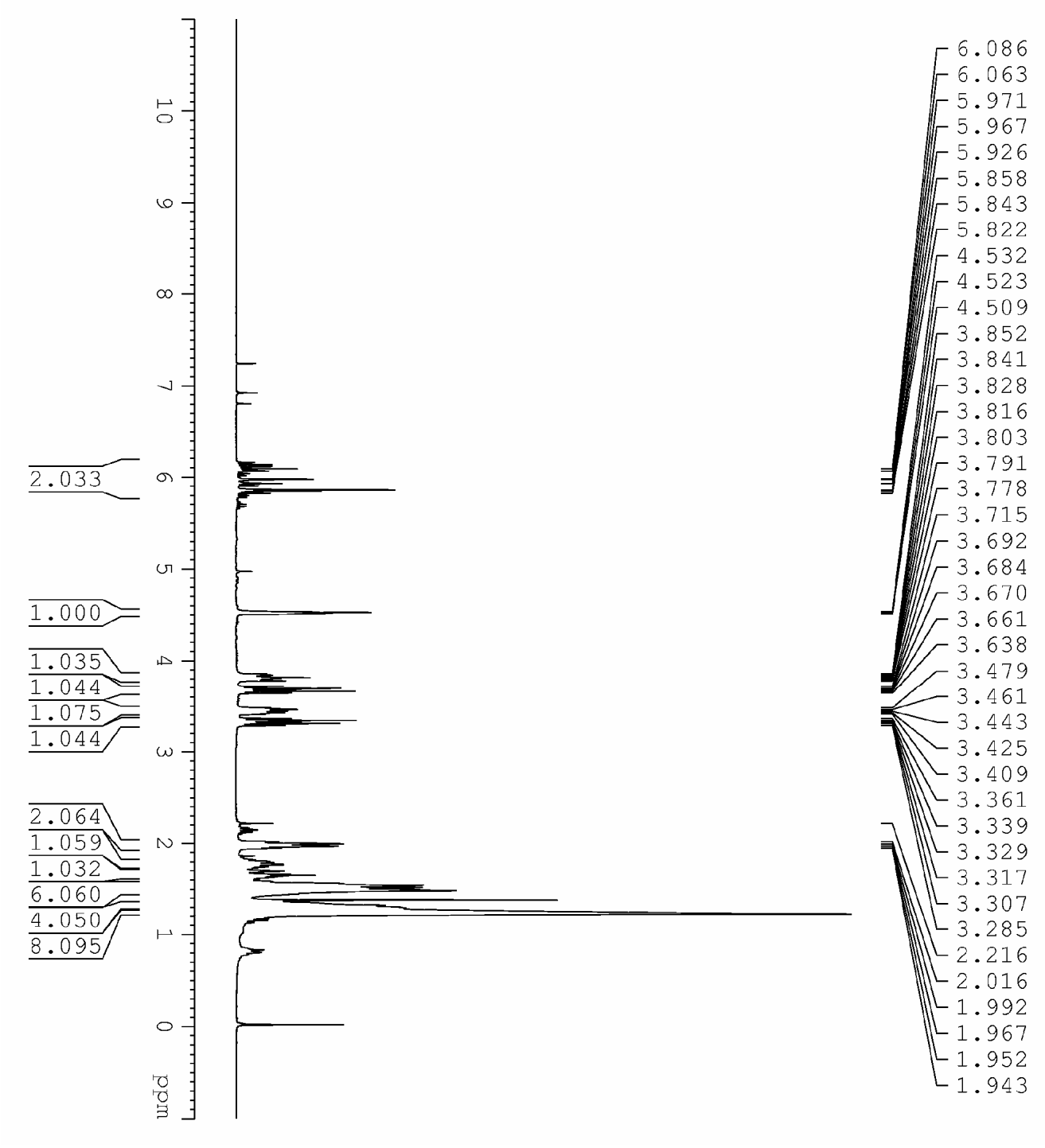


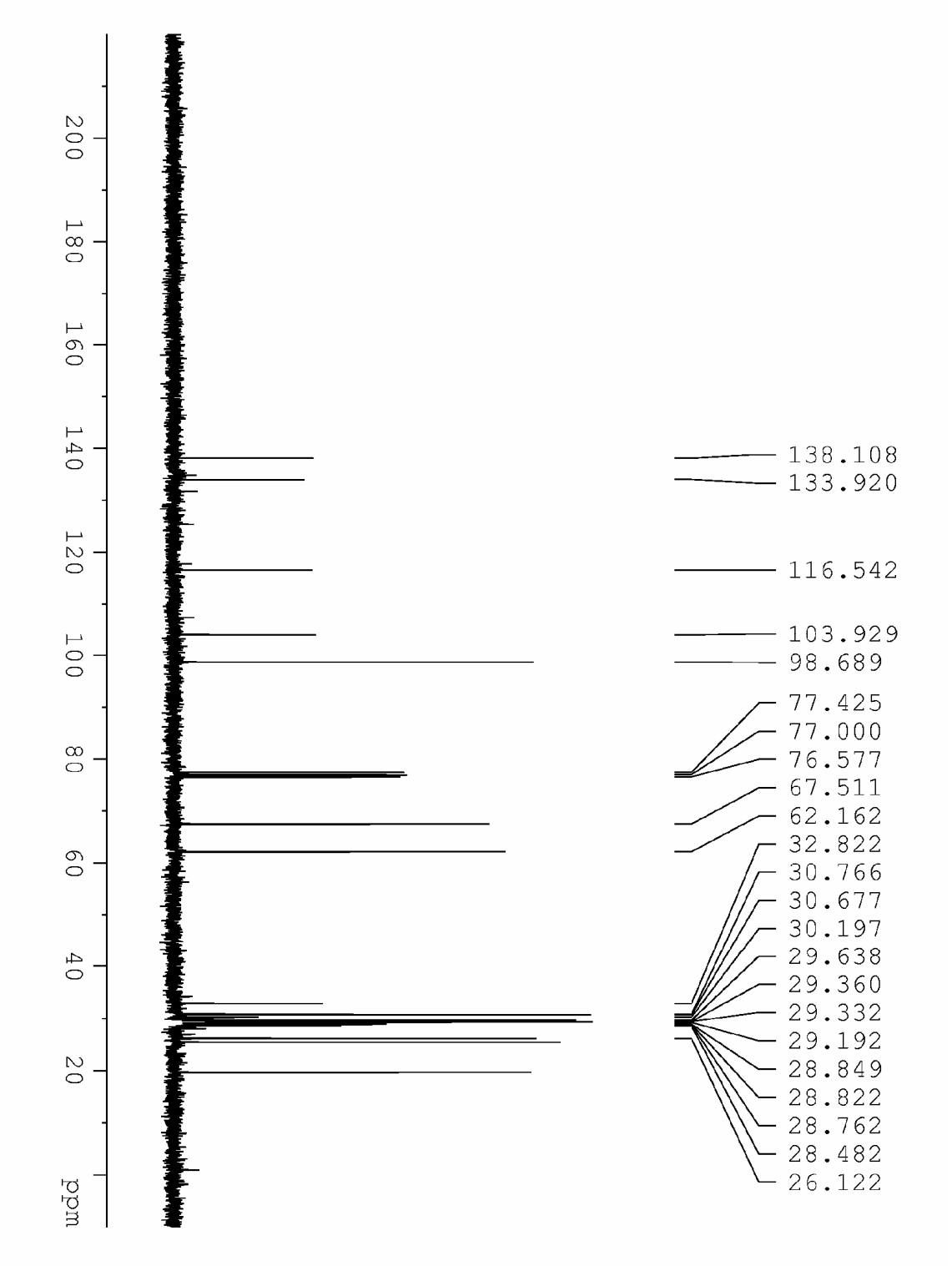
20, 21

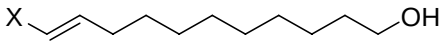
2-(11-Halo-undec-10-enyloxy_tetrahydro-pyran

<1> ^{1}H NMR

<2> ^{13}C NMR


6.086
6.063
5.971
5.967
5.926
5.858
5.843
5.822
4.532
4.523
4.509
3.852
3.841
3.828
3.816
3.803
3.791
3.778
3.715
3.692
3.684
3.670
3.661
3.638
3.479
3.461
3.443
3.425
3.409
3.361
3.339
3.329
3.317
3.307
3.285
2.216
2.016
1.992
1.967
1.952
1.943
2.033
1.000
1.035
1.044
1.075
1.044
2.064
1.059
1.032
6.060
4.050
8.095
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.108
133.920
116.542
103.929
98.689
77.425
77.000
76.577
67.511
62.162
32.822
30.766
30.677
30.197
29.638
29.360
29.332
29.192
28.849
28.822
28.762
28.482
26.122

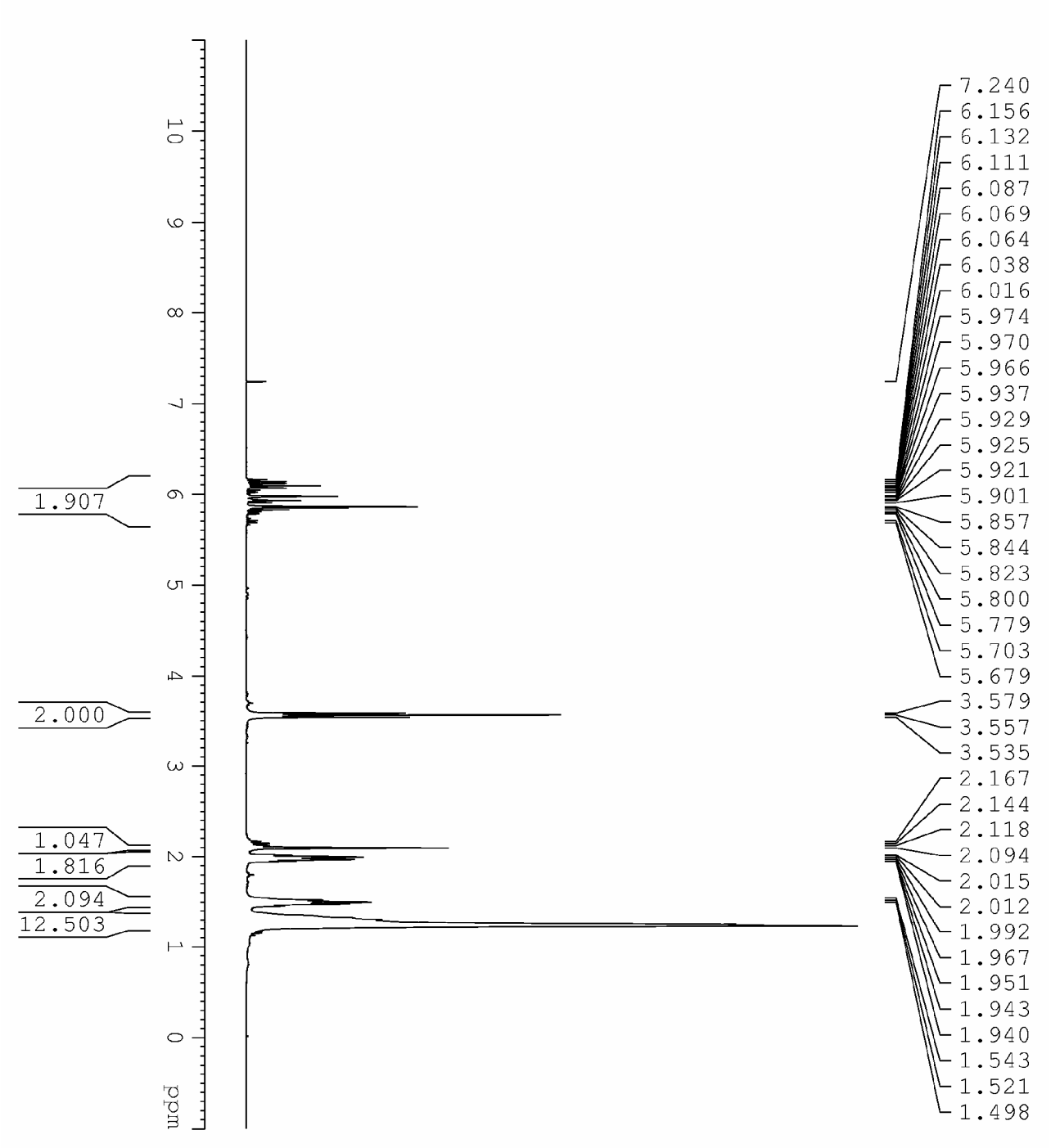


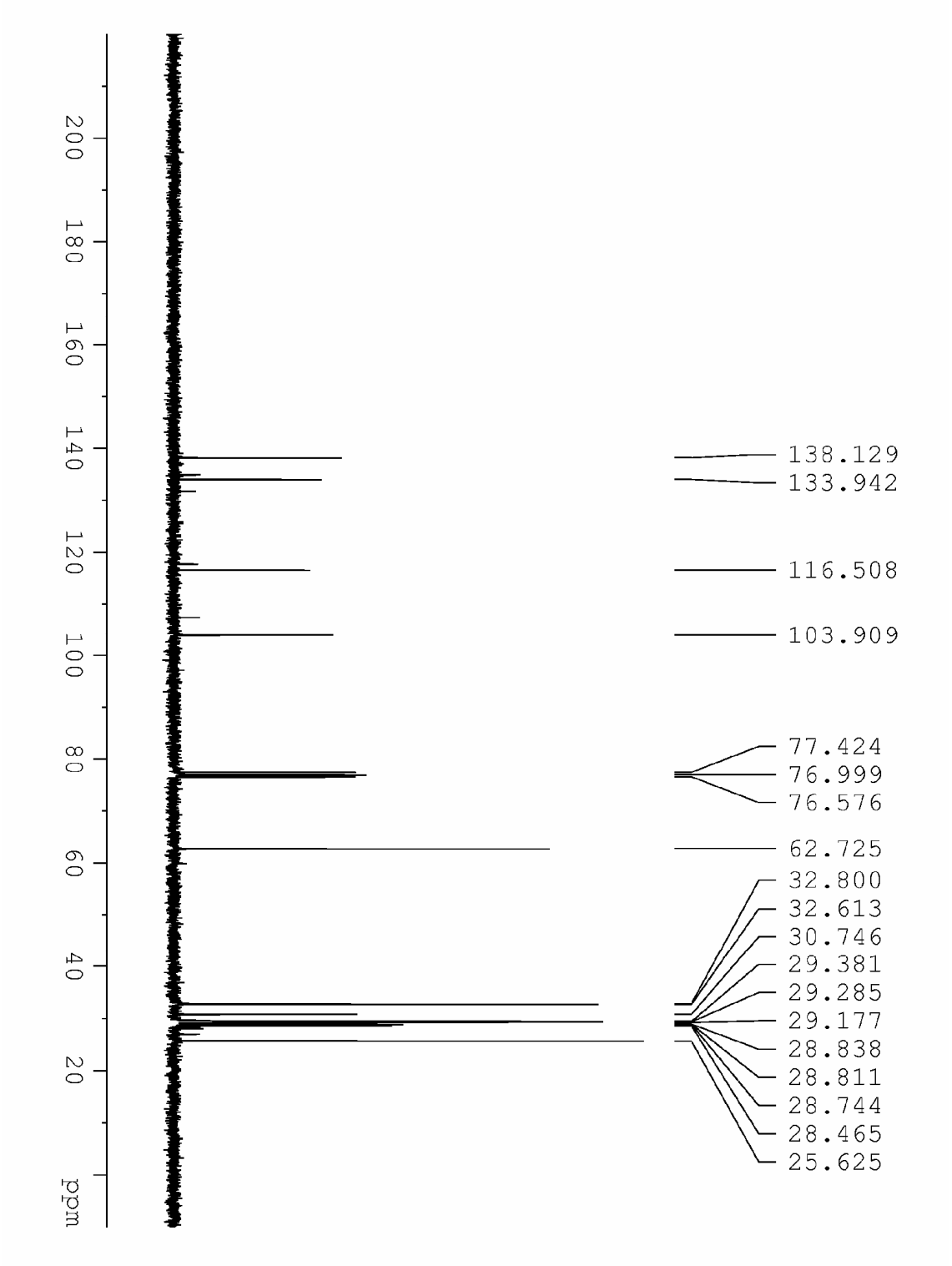
22a,b

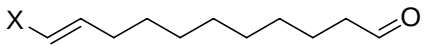
11-Halo-undec-10-en-1-ol

<1> ^{1}H NMR

<2> ^{13}C NMR


7.240
6.156
6.132
6.111
6.087
6.069
6.064
6.038
6.016
5.974
5.970
5.966
5.937
5.929
5.925
5.921
5.901
5.857
5.844
5.823
5.800
5.779
5.703
5.679
3.579
3.557
3.535
2.167
2.144
2.118
2.094
2.015
2.012
1.992
1.967
1.951
1.943
1.940
1.543
1.521
1.498
1.907
2.000
1.047
1.816
2.094
12.503
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.129
133.942
116.508
103.909
77.424
76.999
76.576
62.725
32.800
32.613
30.746
29.381
29.285
29.177
28.838
28.811
28.744
28.465
25.625

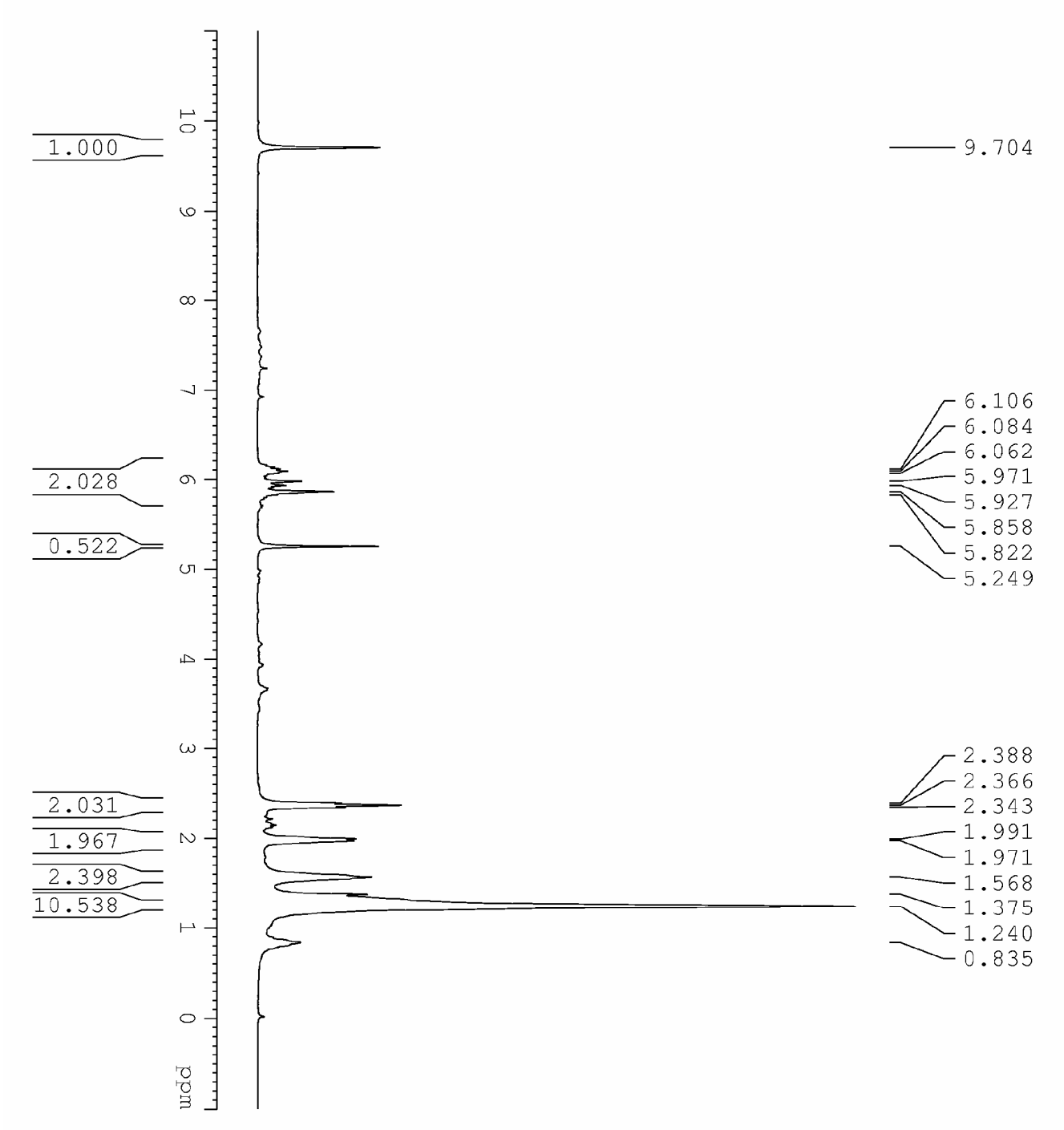


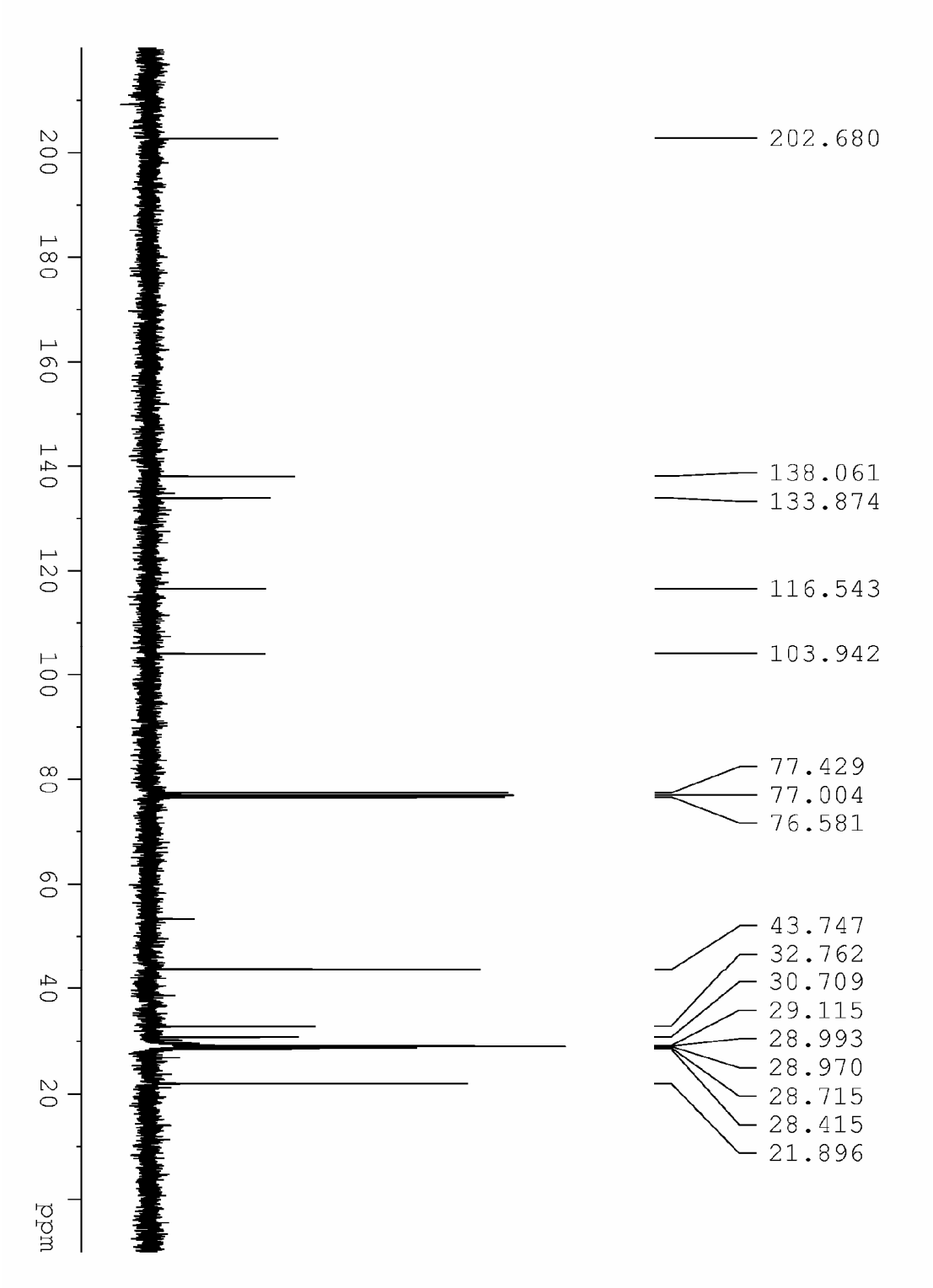
23a,b

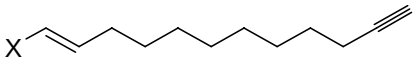
11-Halo-undec-10-enal

<1> ^{1}H NMR

<2> ^{13}C NMR


1.000
2.028
0.522
2.031
1.967
2.398
10.538
9.704
6.106
6.084
6.062
5.971
5.927
5.858
5.822
5.249
2.388
2.366
2.343
1.991
1.971
1.568
1.375
1.240
0.835
10
9
8
7
6
5
4
3
2
1
0
ppm


202.680
138.061
133.874
116.543
103.942
77.429
77.004
76.581
43.747
32.762
30.709
29.115
28.993
28.970
28.715
28.415
21.896
200
180
160
140
120
100
80
60
40
20
ppm

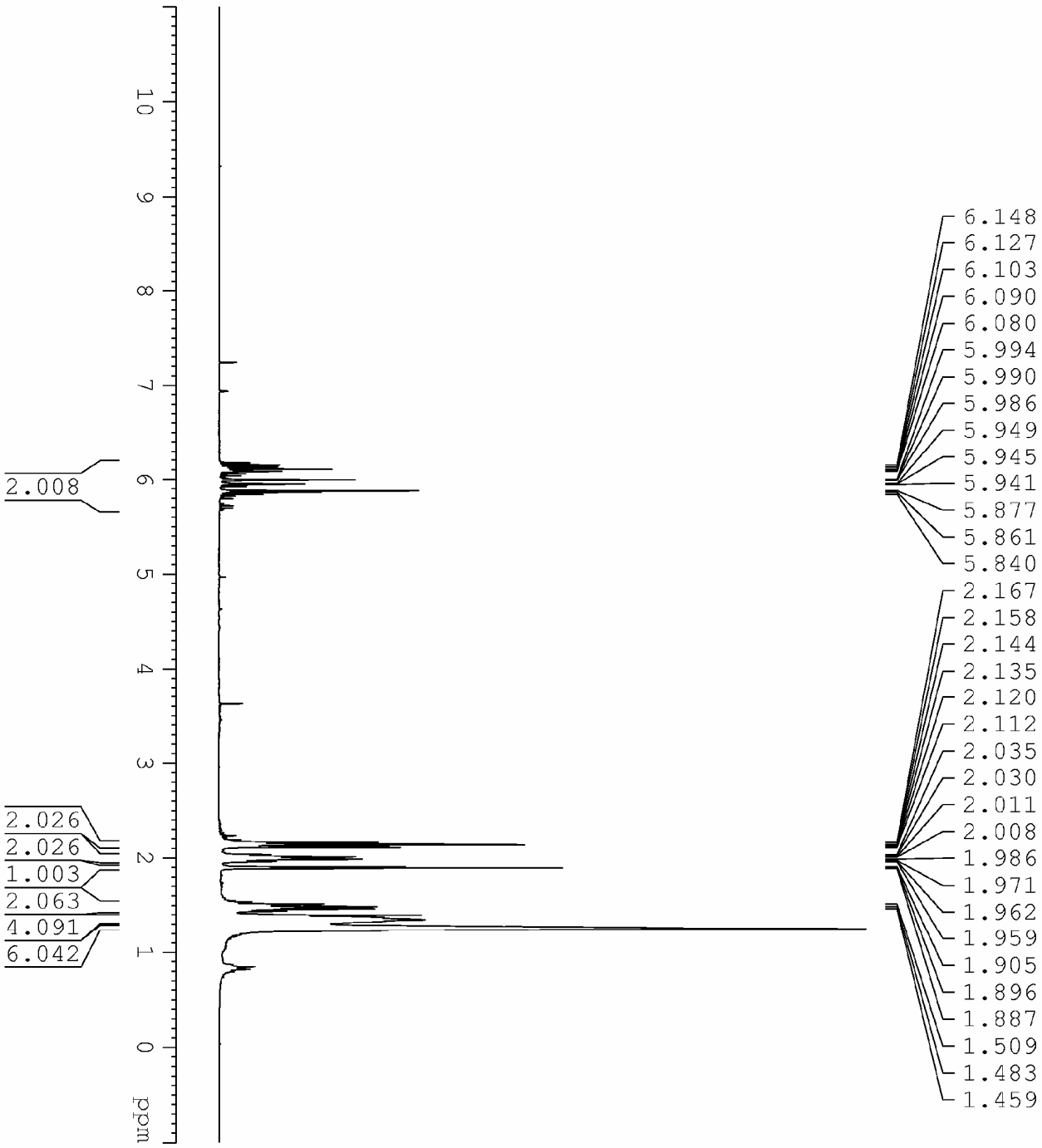


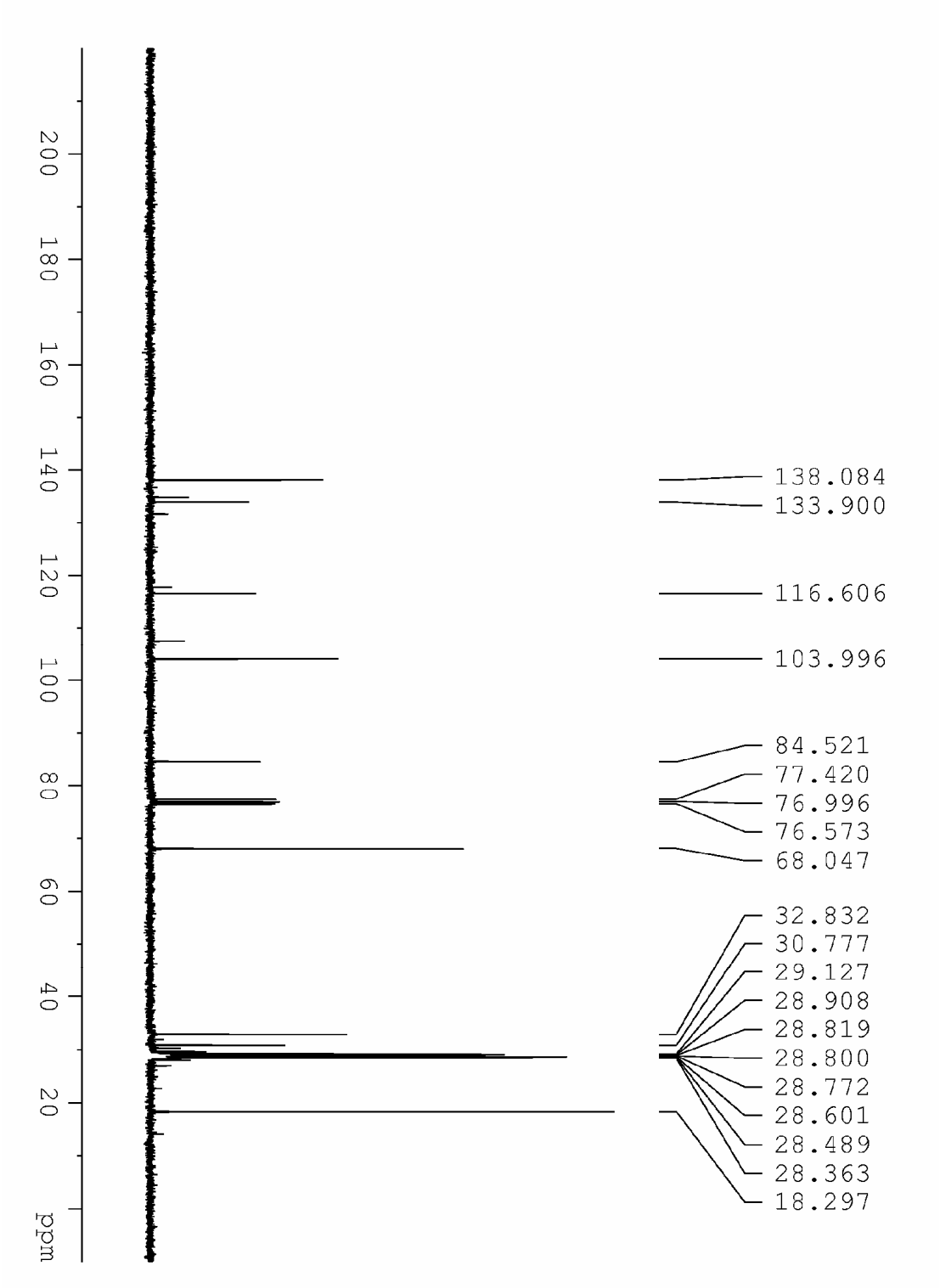
24a,b

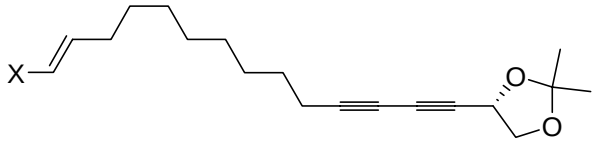
1-Halo-dodec-1-en-11-yne

<1> ^{1}H NMR

<2> ^{13}C NMR


6.148
6.127
6.103
6.090
6.080
5.994
5.990
5.986
5.949
5.945
5.941
5.877
5.861
5.840
2.167
2.158
2.144
2.135
2.120
2.112
2.035
2.030
2.011
2.008
1.986
1.971
1.962
1.959
1.905
1.896
1.887
1.509
1.483
1.459
2.008
2.026
2.026
1.003
2.063
4.091
6.042
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.084
133.900
116.606
103.996
84.521
77.420
76.996
76.573
68.047
32.832
30.777
29.127
28.908
28.819
28.800
28.772
28.601
28.489
28.363
18.297

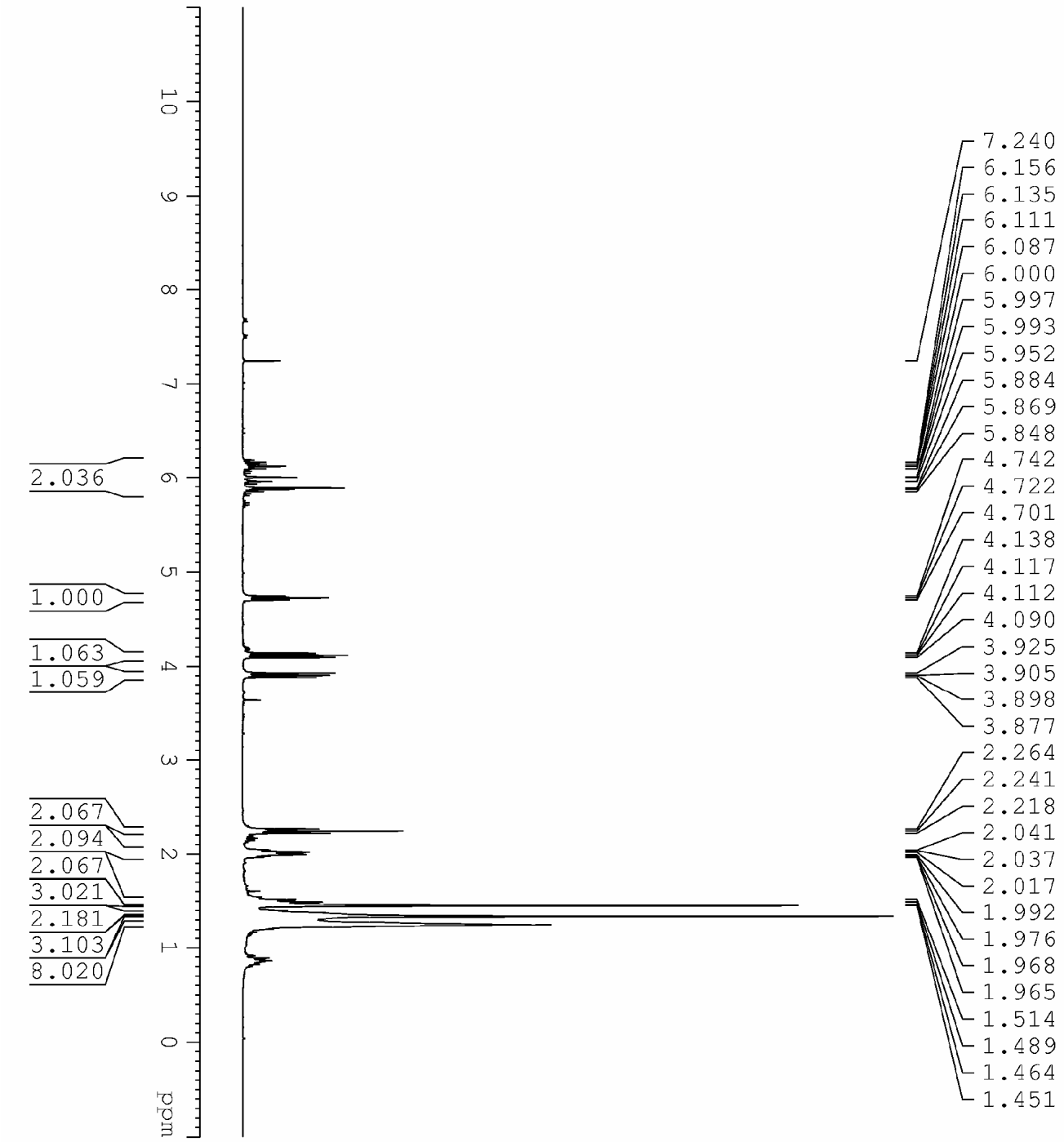


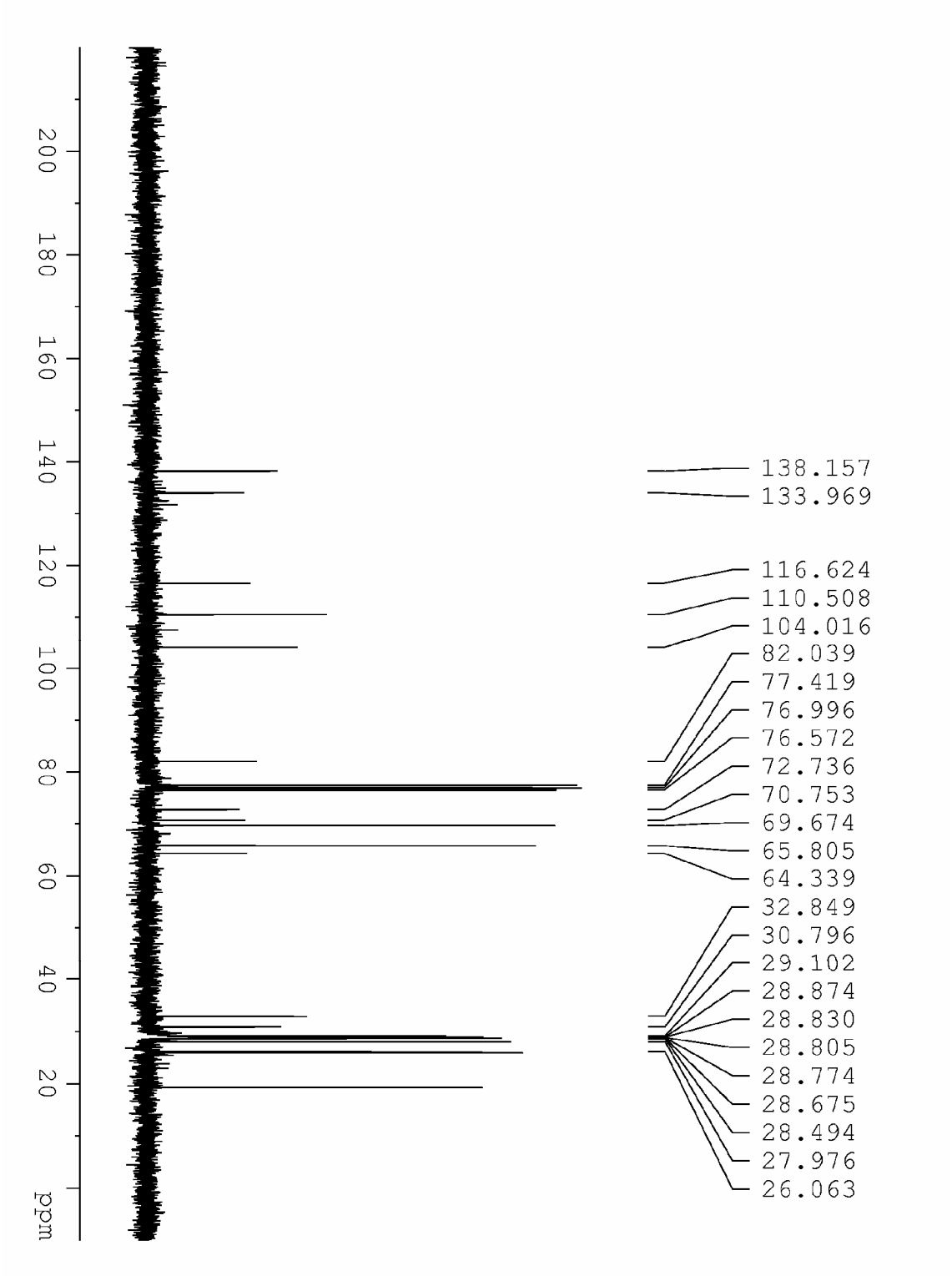
25a,b

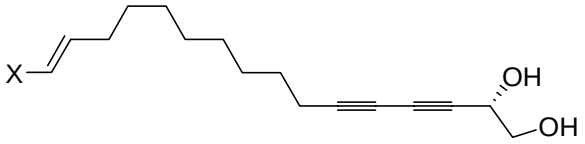
4-(14-Halo-tetradec-13-ene-1,3-diynyl)-2,2-dimethyl-[1,3]dioxolane

<1> ^{1}H NMR

<2> ^{13}C NMR


7.240
6.156
6.135
6.111
6.087
6.000
5.997
5.993
5.952
5.884
5.869
5.848
4.742
4.722
4.701
4.138
4.117
4.112
4.090
3.925
3.905
3.898
3.877
2.264
2.241
2.218
2.041
2.037
2.017
1.992
1.976
1.968
1.965
1.514
1.489
1.464
1.451
2.036
1.000
1.063
1.059
2.067
2.094
2.067
3.021
2.181
3.103
8.020
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.157
133.969
116.624
110.508
104.016
82.039
77.419
76.996
76.572
72.736
70.753
69.674
65.805
64.339
32.849
30.796
29.102
28.874
28.830
28.805
28.774
28.675
28.494
27.976
26.063

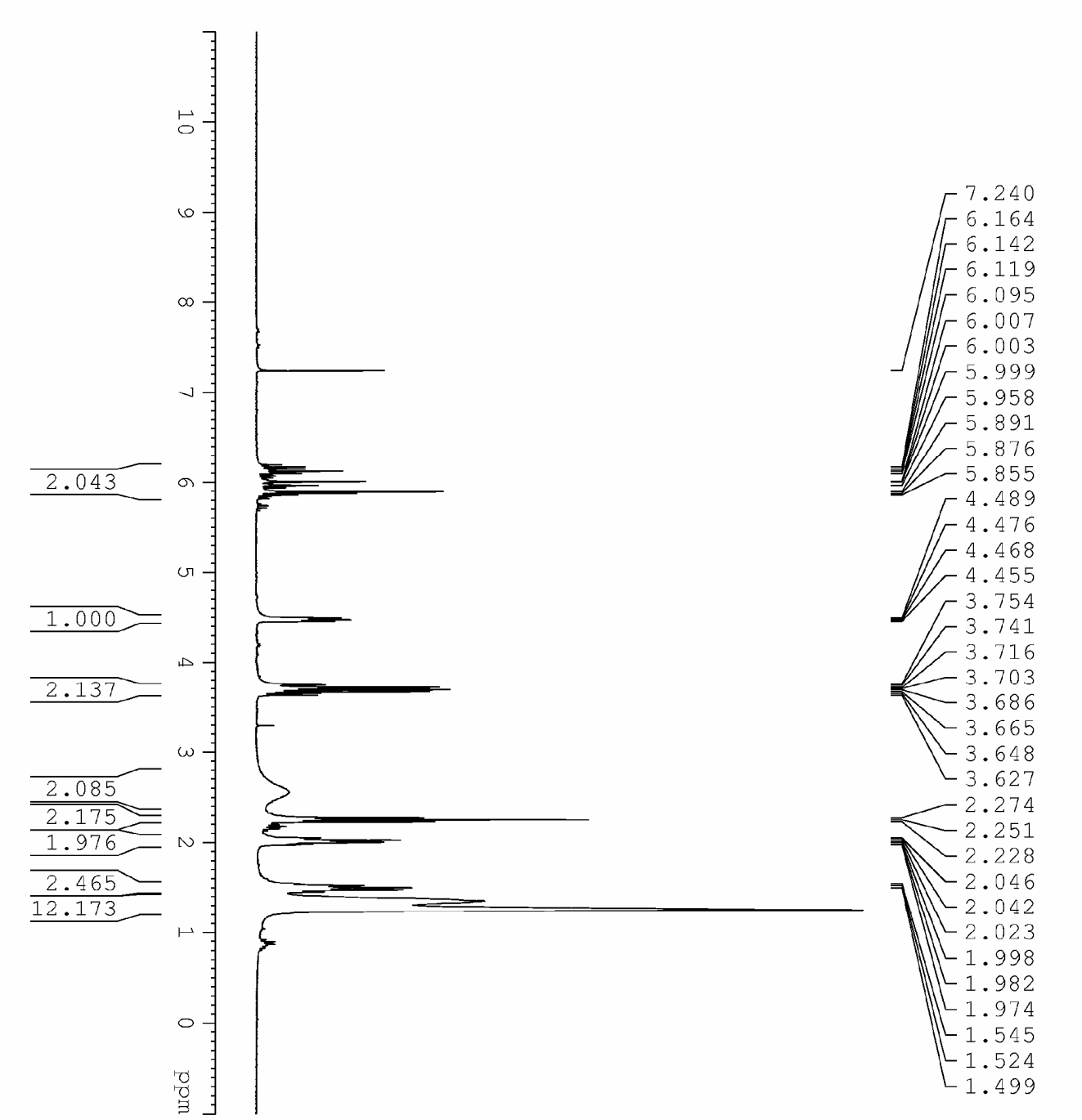


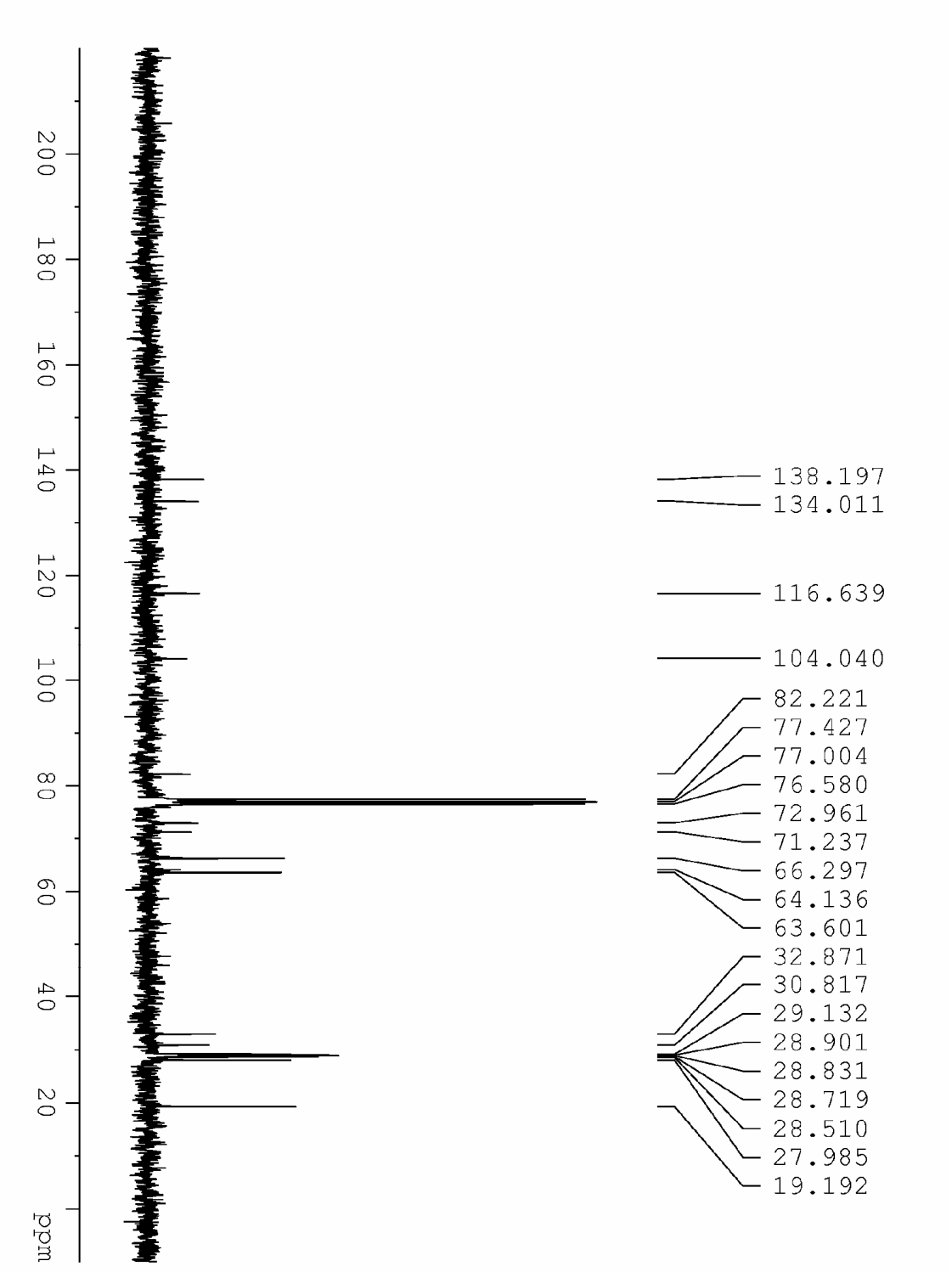
26a,b

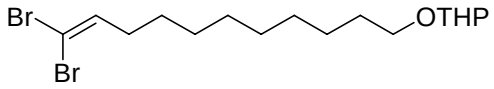
16-Halo-hexadec-15-ene-3,5-diyne-1,2-diol

<1> ^{1}H NMR

<2> ^{13}C NMR


2.043
1.000
2.137
2.085
2.175
1.976
2.465
12.173
10
9
8
7
6
5
4
3
2
1
0
ppm
7.240
6.164
6.142
6.119
6.095
6.007
6.003
5.999
5.958
5.891
5.876
5.855
4.489
4.476
4.468
4.455
3.754
3.741
3.716
3.703
3.686
3.665
3.648
3.627
2.274
2.251
2.228
2.046
2.042
2.023
1.998
1.982
1.974
1.545
1.524
1.499


200
180
160
140
120
100
80
60
40
20
ppm
138.197
134.011
116.639
104.040
82.221
77.427
77.004
76.580
72.961
71.237
66.297
64.136
63.601
32.871
30.817
29.132
28.901
28.831
28.719
28.510
27.985
19.192

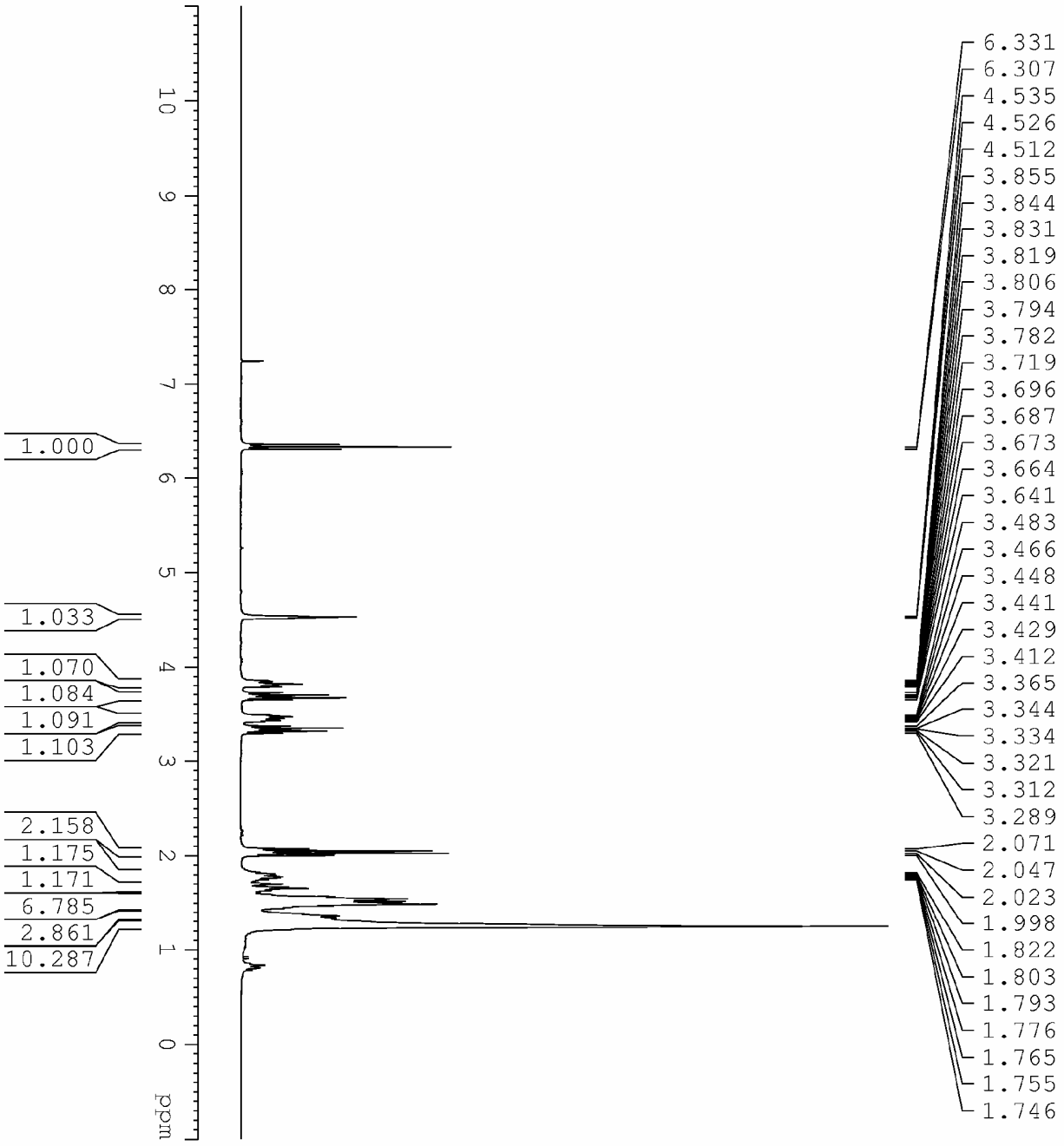


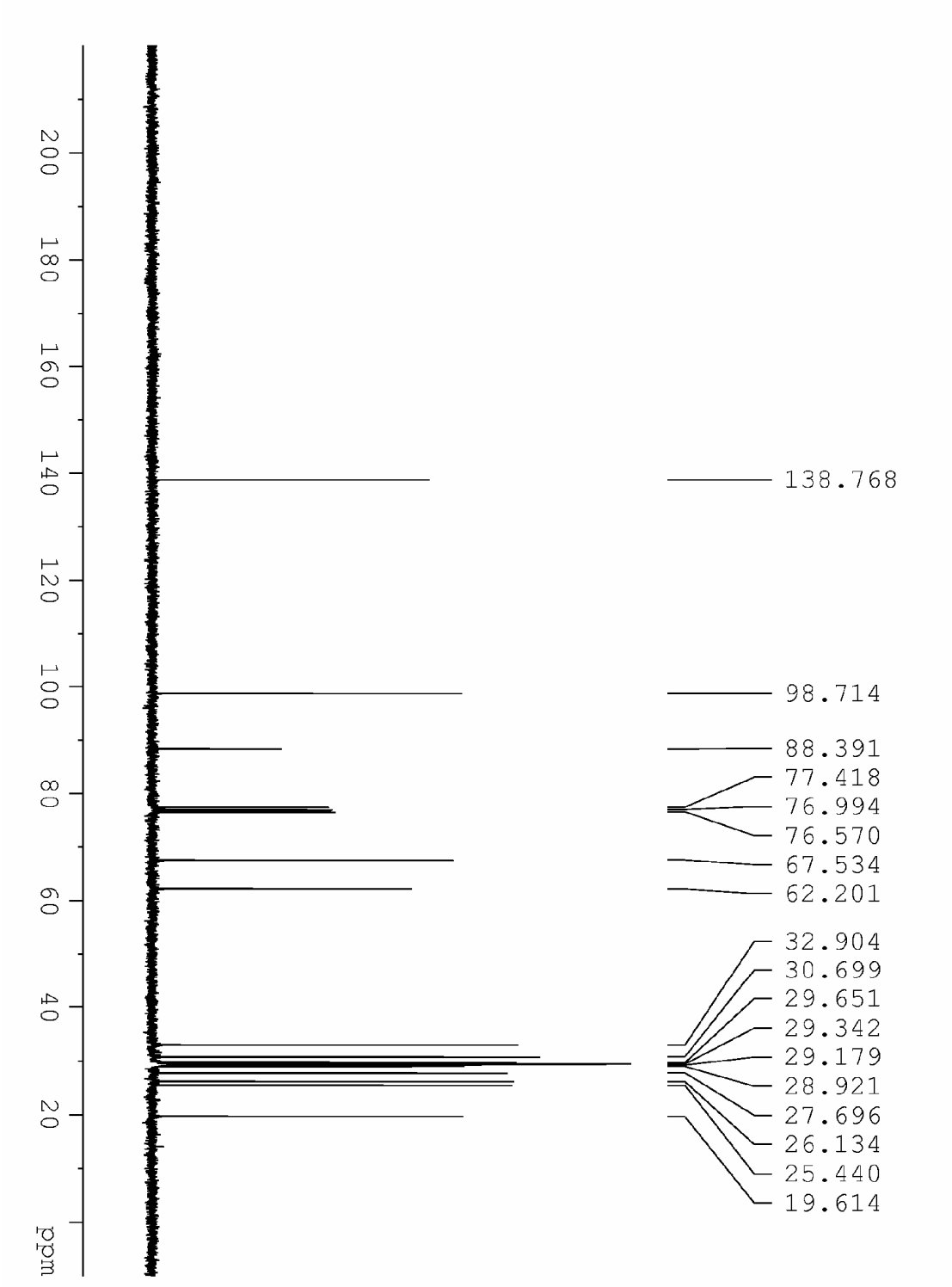
28

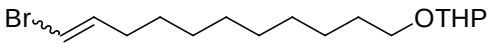
2-(11,11-Dibromo-undec-10-enyloxy)-tetrahydro-pyran

<1> ^{1}H NMR

<2> ^{13}C NMR


6.331
6.307
4.535
4.526
4.512
3.855
3.844
3.831
3.819
3.806
3.794
3.782
3.719
3.696
3.687
3.673
3.664
3.641
3.483
3.466
3.448
3.441
3.429
3.412
3.365
3.344
3.334
3.321
3.312
3.289
2.071
2.047
2.023
1.998
1.822
1.803
1.793
1.776
1.765
1.755
1.746
1.000
1.033
1.070
1.084
1.091
1.103
2.158
1.175
1.171
6.785
2.861
10.287
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.768
98.714
88.391
77.418
76.994
76.570
67.534
62.201
32.904
30.699
29.651
29.342
29.179
28.921
27.696
26.134
25.440
19.614

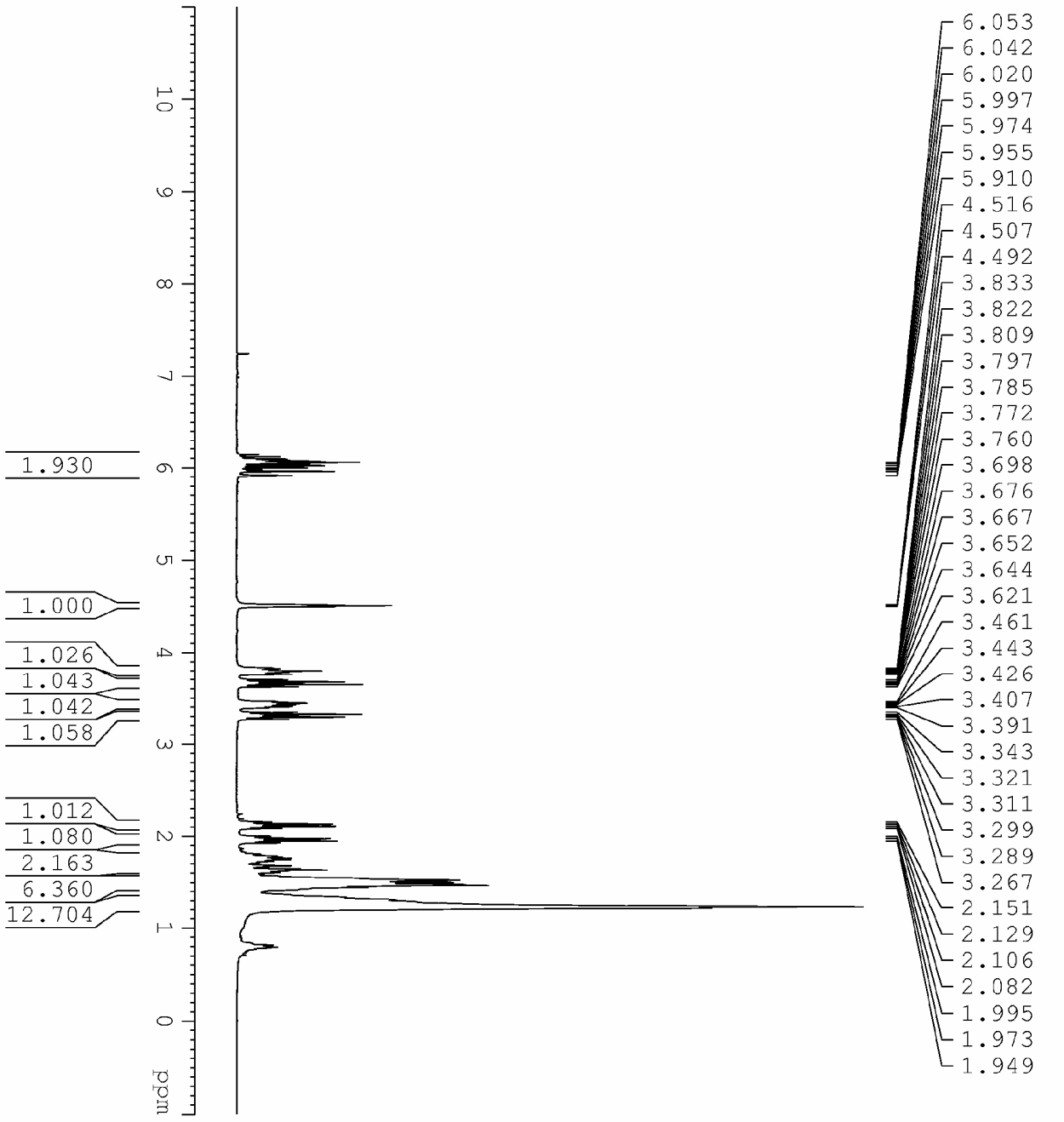


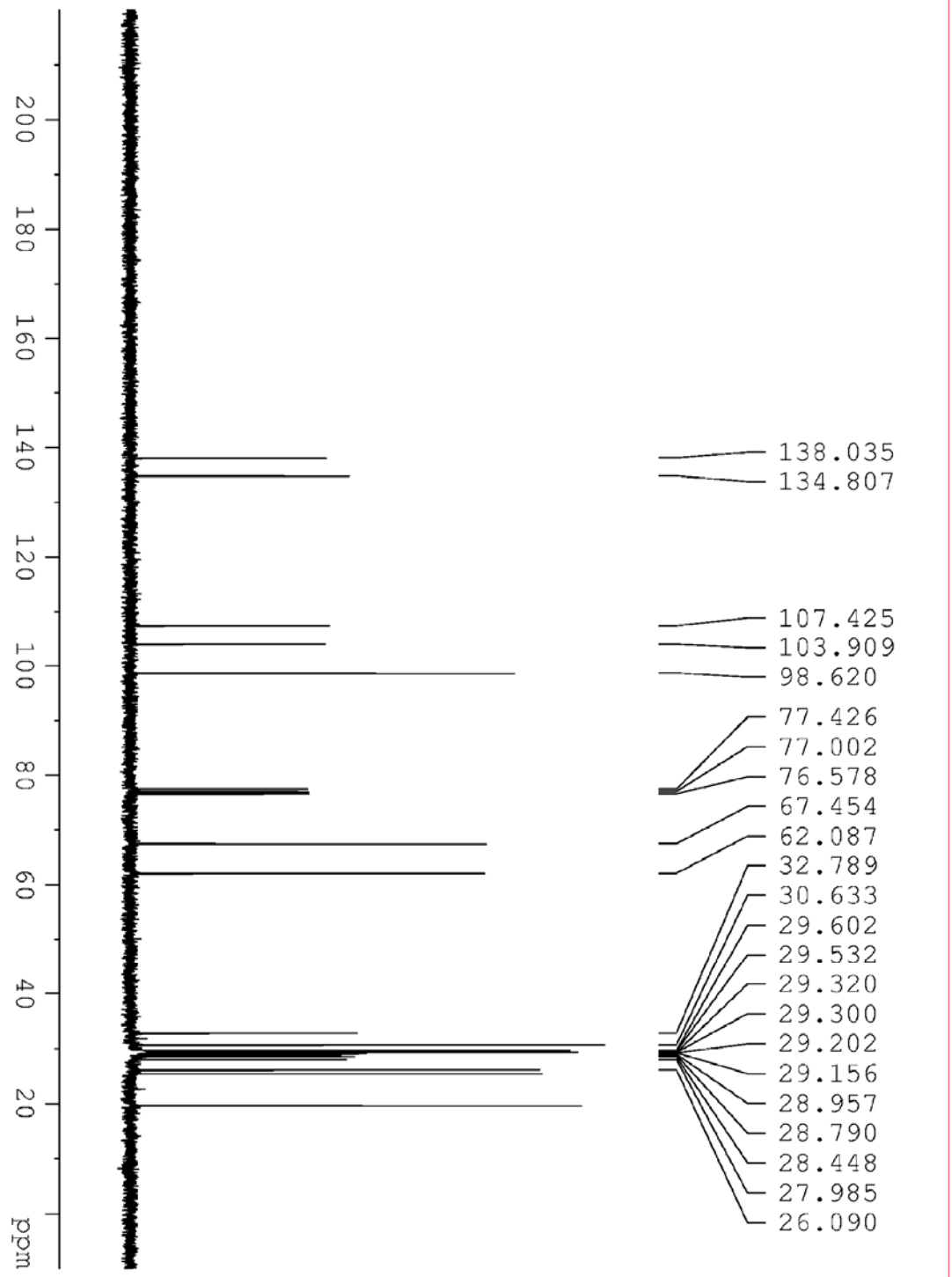
29a,b

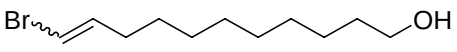
2-(11-Bromo-undec-10-enyloxy)-tetrahydro-pyran

<1> ^{1}H NMR

<2> ^{13}C NMR


6.053
6.042
6.020
5.997
5.974
5.955
5.910
4.516
4.507
4.492
3.833
3.822
3.809
3.797
3.785
3.772
3.760
3.698
3.676
3.667
3.652
3.644
3.621
3.461
3.443
3.426
3.407
3.391
3.343
3.321
3.311
3.299
3.289
3.267
2.151
2.129
2.106
2.082
1.995
1.973
1.949
1.930
1.000
1.026
1.043
1.042
1.058
1.012
1.080
2.163
6.360
12.704
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.035
134.807
107.425
103.909
98.620
77.426
77.002
76.578
67.454
62.087
32.789
30.633
29.602
29.532
29.320
29.300
29.202
29.156
28.957
28.790
28.448
27.985
26.090

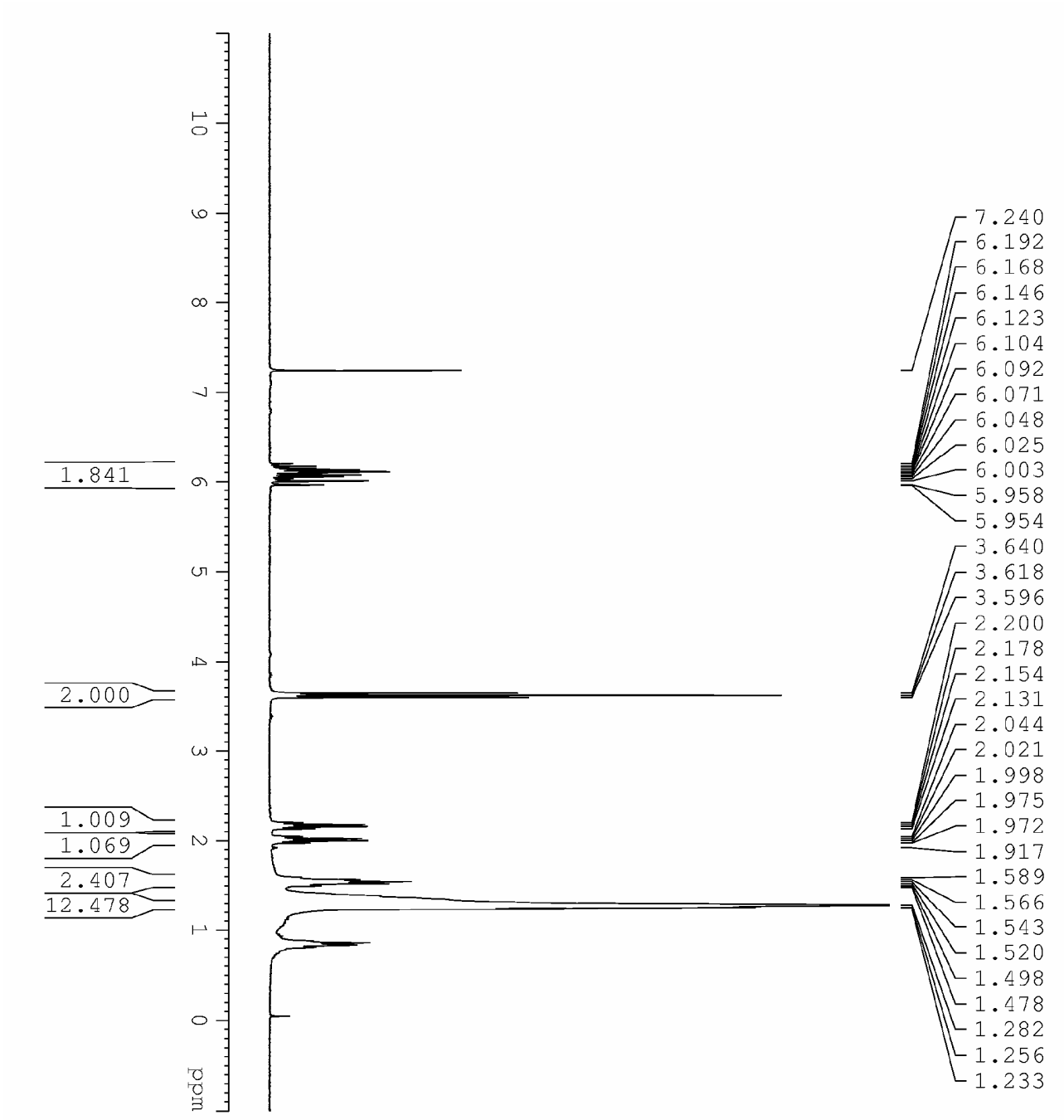


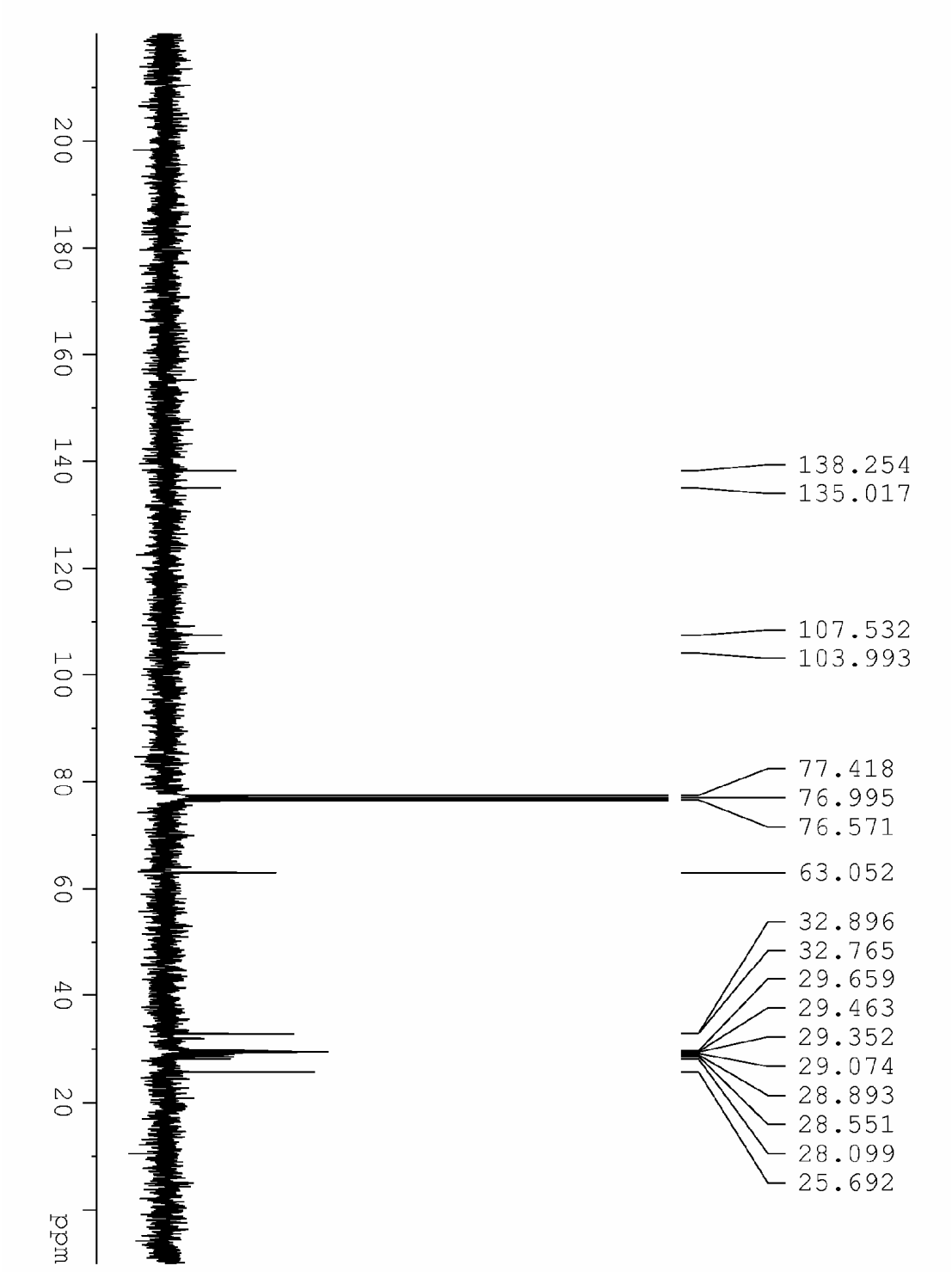
30a,b

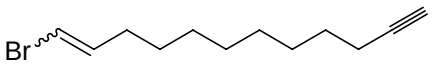
11-Bromo-undec-10-en-1-ol

<1> ^{1}H NMR

<2> ^{13}C NMR


7.240
6.192
6.168
6.146
6.123
6.104
6.092
6.071
6.048
6.025
6.003
5.958
5.954
3.640
3.618
3.596
2.200
2.178
2.154
2.131
2.044
2.021
1.998
1.975
1.972
1.917
1.589
1.566
1.543
1.520
1.498
1.478
1.282
1.256
1.233
1.841
2.000
1.009
1.069
2.407
12.478
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.254
135.017
107.532
103.993
77.418
76.995
76.571
63.052
32.896
32.765
29.659
29.463
29.352
29.074
28.893
28.551
28.099
25.692

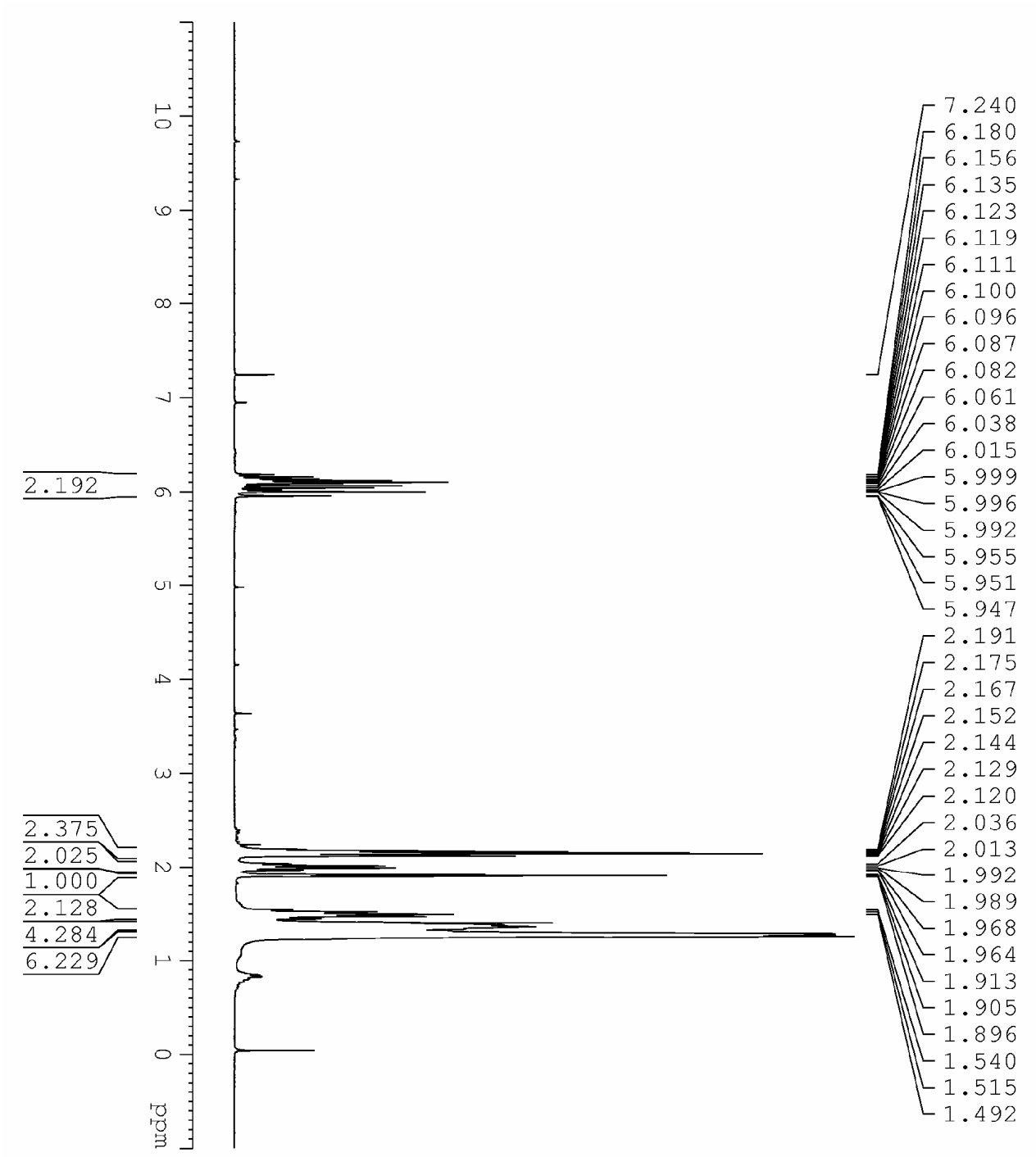


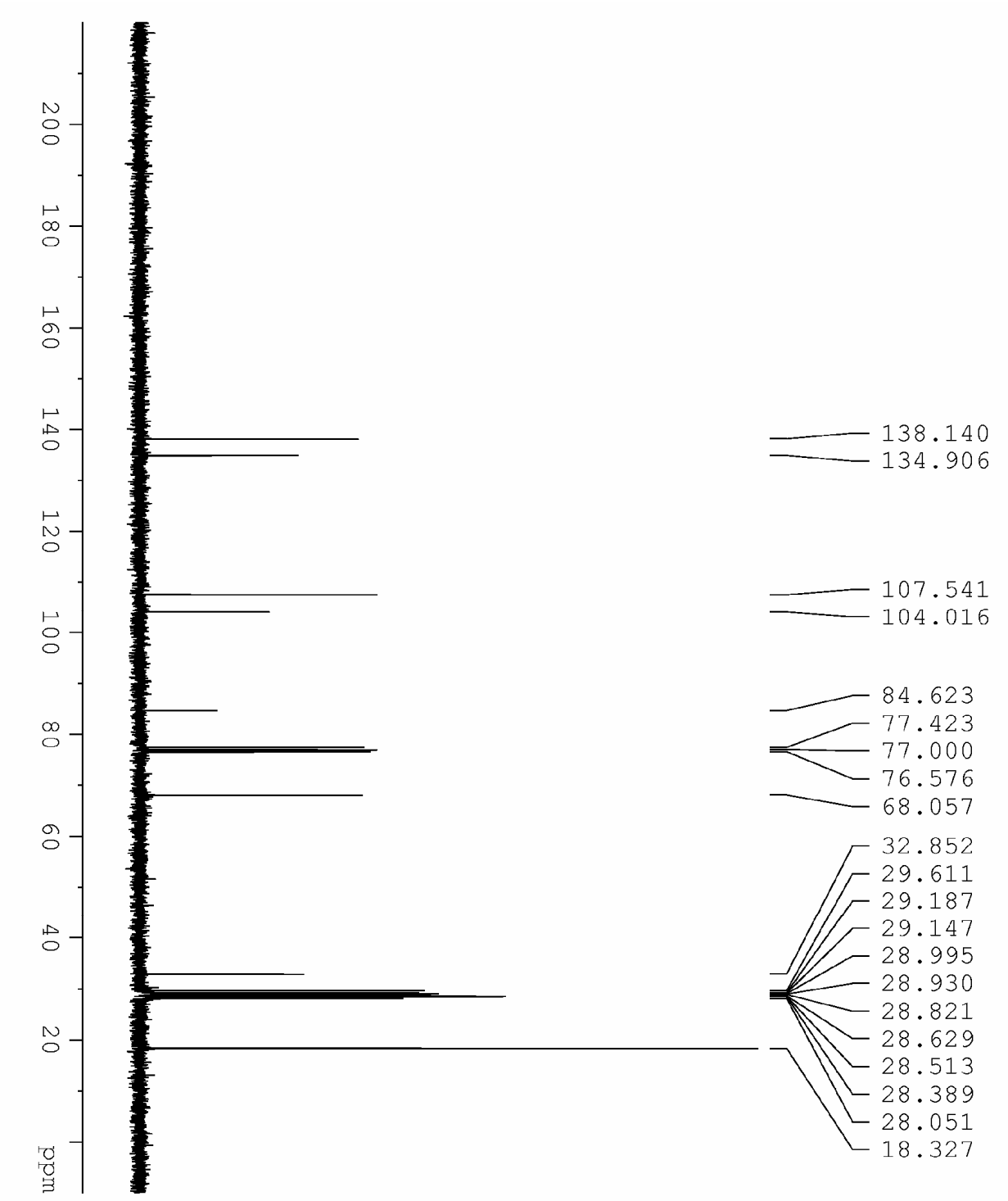
32a,b

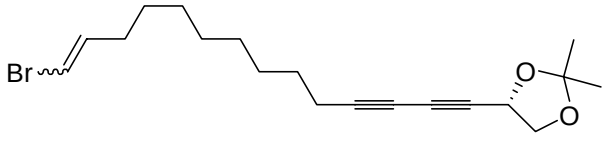
1-Bromo-dodec-1-en-11-yne

<1> ^{1}H NMR

<2> ^{13}C NMR


7.240
6.180
6.156
6.135
6.123
6.119
6.111
6.100
6.096
6.087
6.082
6.061
6.038
6.015
5.999
5.996
5.992
5.955
5.951
5.947
2.191
2.175
2.167
2.152
2.144
2.129
2.120
2.036
2.013
1.992
1.989
1.968
1.964
1.913
1.905
1.896
1.540
1.515
1.492
2.192
2.375
2.025
1.000
2.128
4.284
6.229
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.140
134.906
107.541
104.016
84.623
77.423
77.000
76.576
68.057
32.852
29.611
29.187
29.147
28.995
28.930
28.821
28.629
28.513
28.389
28.051
18.327

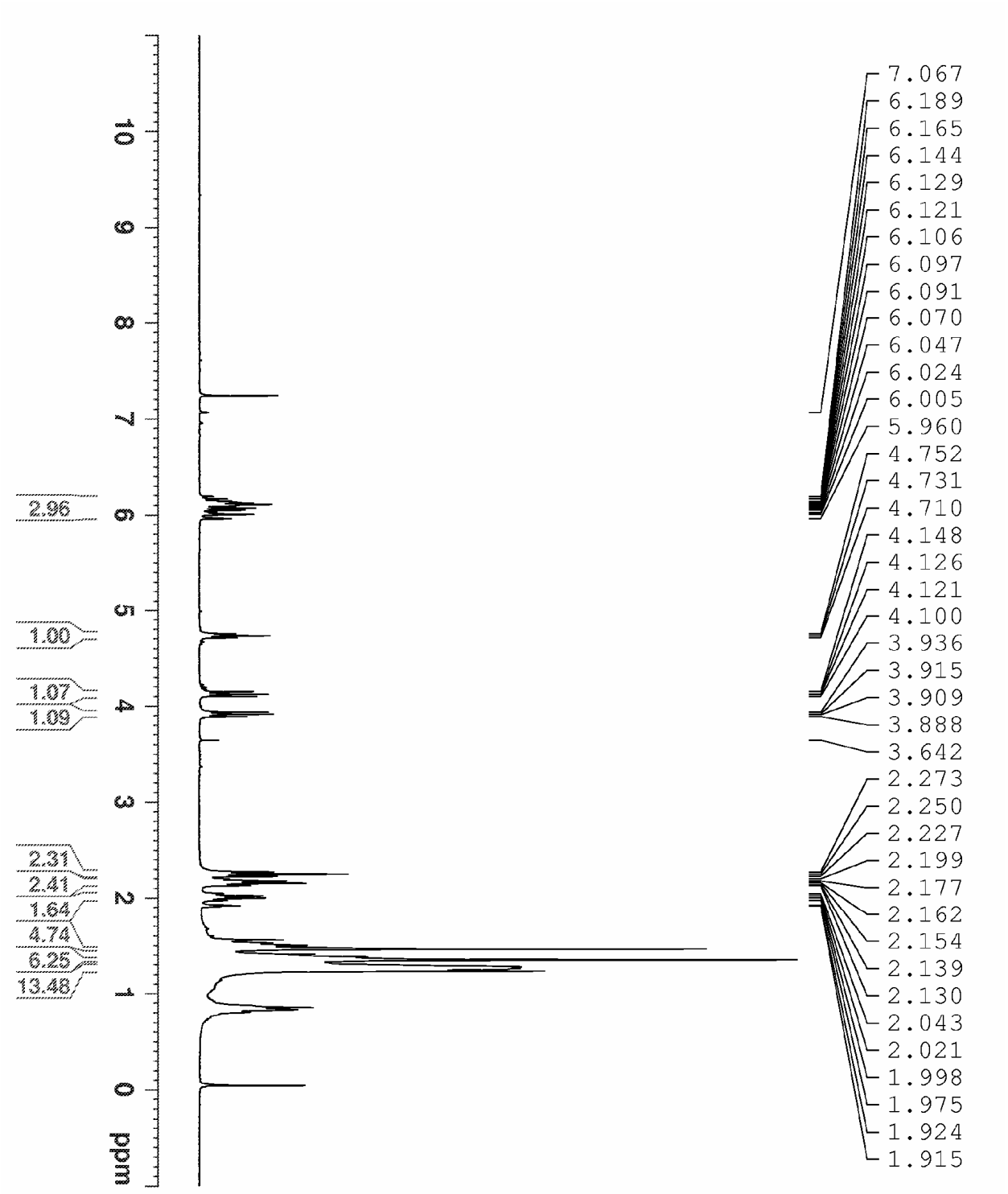


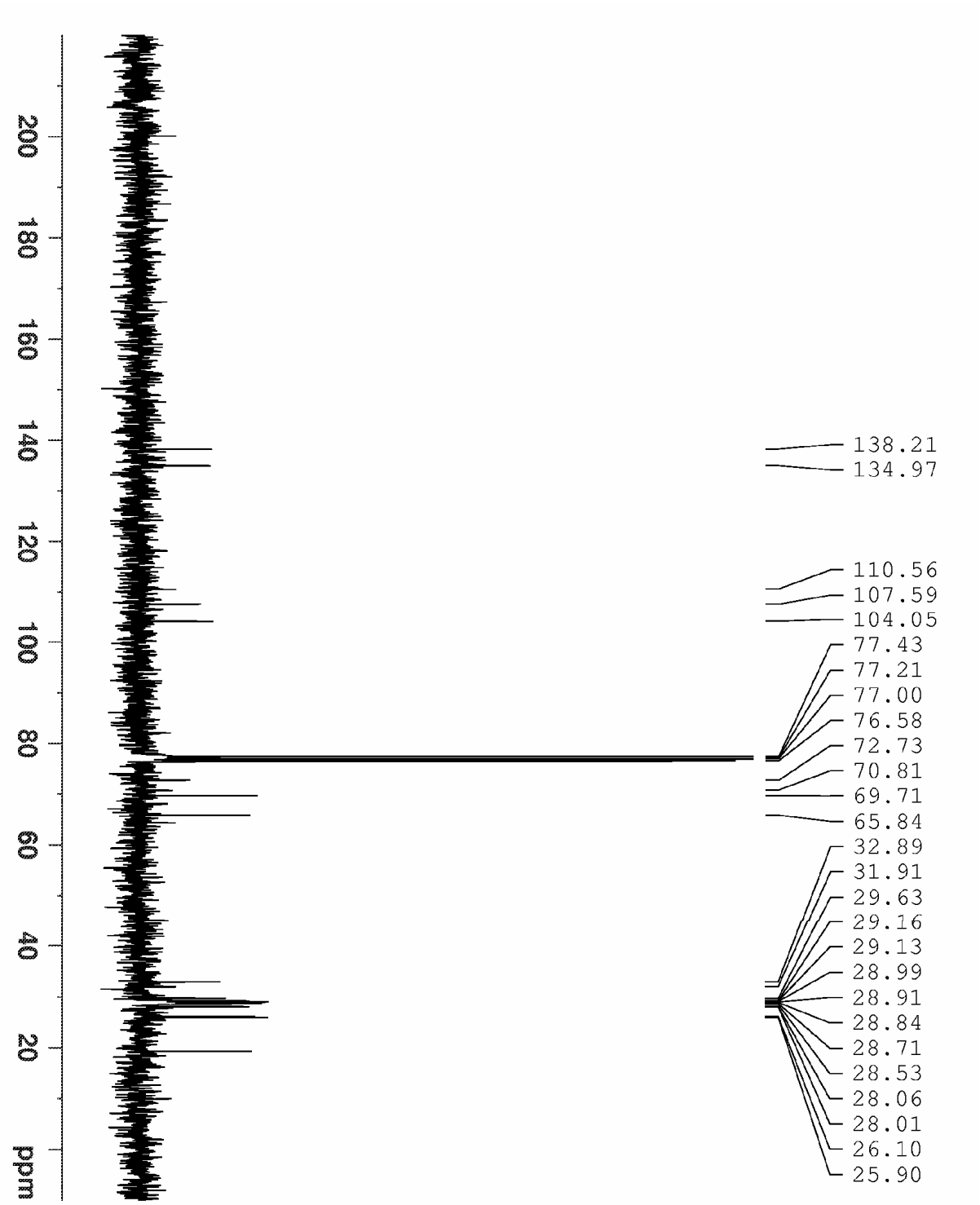
33a,b

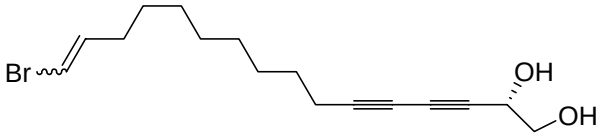
4-(14-Bromo-tetradec-13-ene-1,3-diynyl)-2,2-dimethyl-[1,3]dioxolane

<1> ^{1}H NMR

<2> ^{13}C NMR


7.067
6.189
6.165
6.144
6.129
6.121
6.106
6.097
6.091
6.070
6.047
6.024
6.005
5.960
4.752
4.731
4.710
4.148
4.126
4.121
4.100
3.936
3.915
3.909
3.888
3.642
2.273
2.250
2.227
2.199
2.177
2.162
2.154
2.139
2.130
2.043
2.021
1.998
1.975
1.924
1.915
2.96
1.00
1.07
1.09
2.31
2.41
1.64
4.74
6.25
13.48
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.21
134.97
110.56
107.59
104.05
77.43
77.21
77.00
76.58
72.73
70.81
69.71
65.84
32.89
31.91
29.63
29.16
29.13
28.99
28.91
28.84
28.71
28.53
28.06
28.01
26.10
25.90

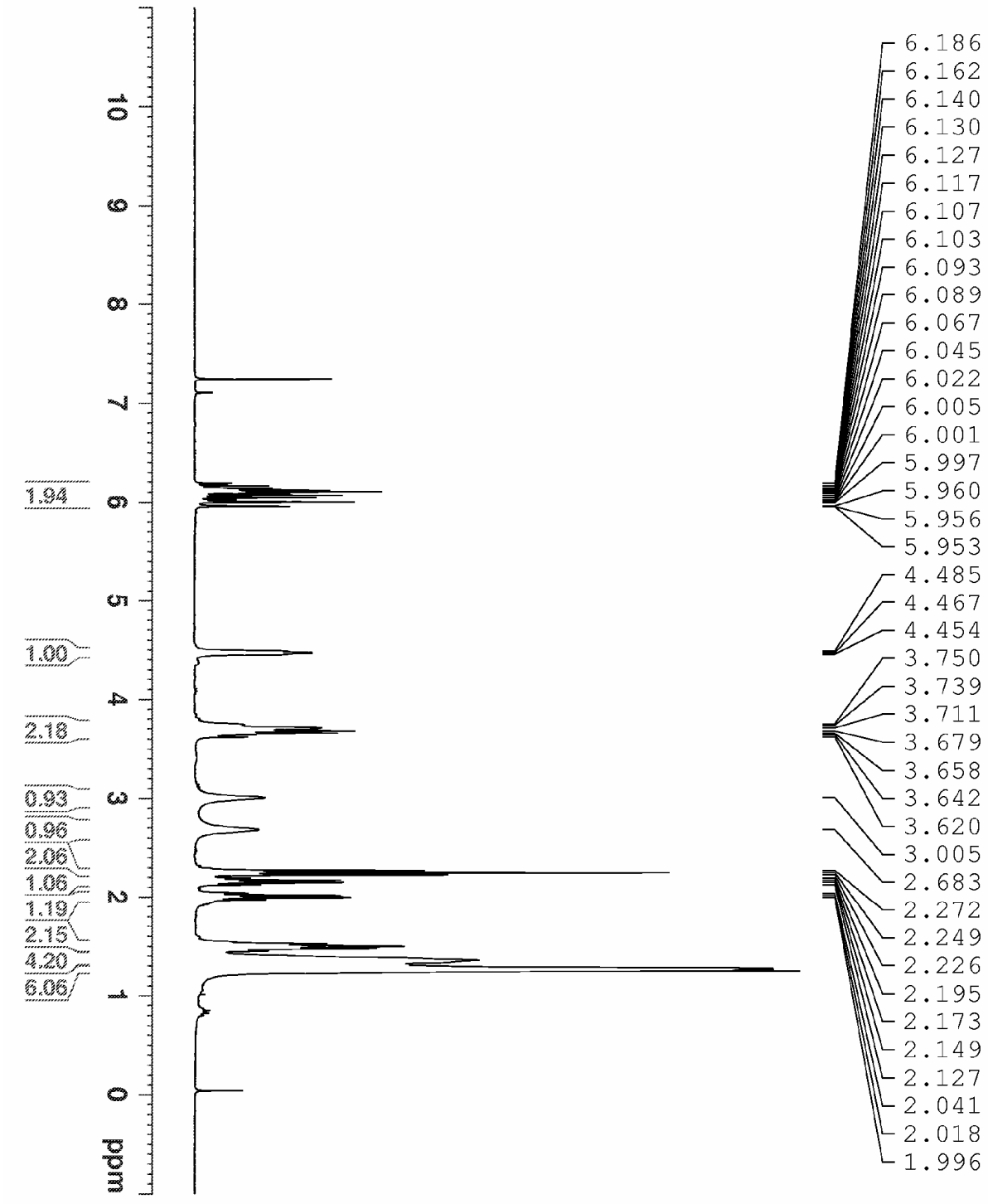


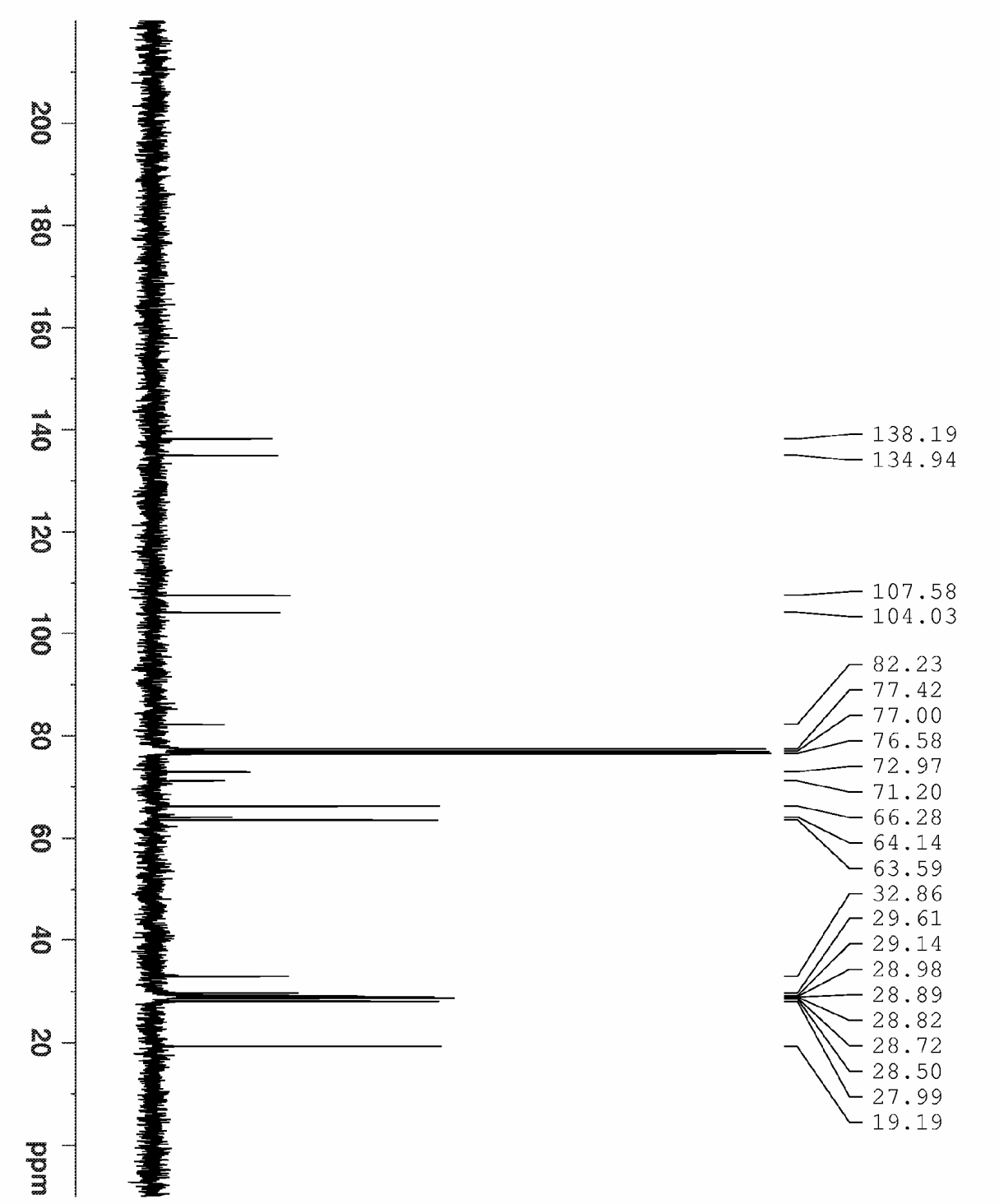
34a,b

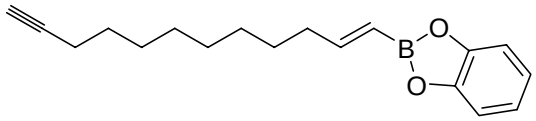
16-Bromo-hexadec-15-ene-3,5-diyne-1,2-diol

<1> ^{1}H NMR

<2> ^{13}C NMR


6.186
6.162
6.140
6.130
6.127
6.117
6.107
6.103
6.093
6.089
6.067
6.045
6.022
6.005
6.001
5.997
5.960
5.956
5.953
4.485
4.467
4.454
3.750
3.739
3.711
3.679
3.658
3.642
3.620
3.005
2.683
2.272
2.249
2.226
2.195
2.173
2.149
2.127
2.041
2.018
1.996
1.94
1.00
2.18
0.93
0.96
2.06
1.06
1.19
2.15
4.20
6.06
ppm

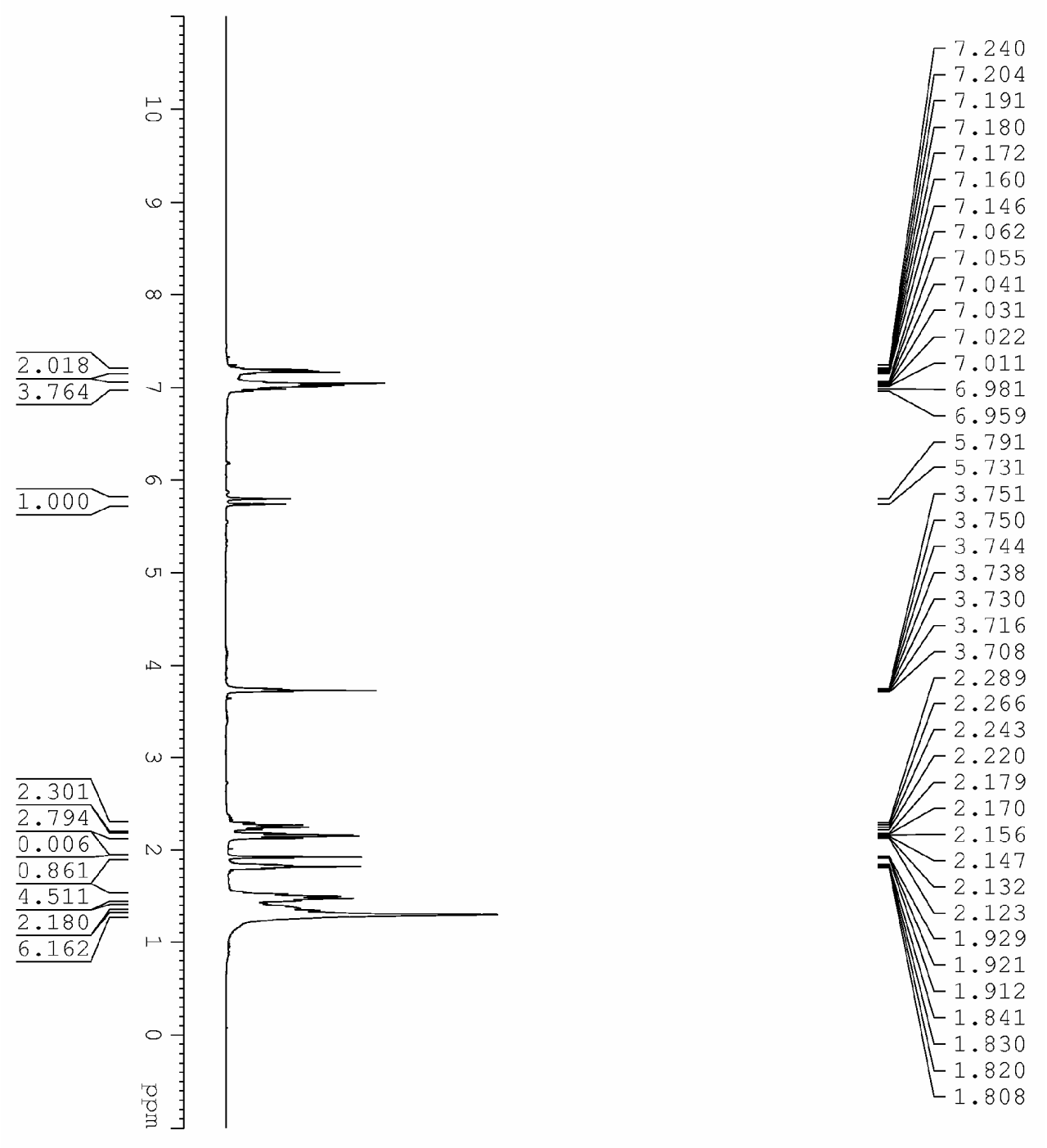

200
180
160
140
120
100
80
60
40
20
ppm
138.19
134.94
107.58
104.03
82.23
77.42
77.00
76.58
72.97
71.20
66.28
64.14
63.59
32.86
29.61
29.14
28.98
28.89
28.82
28.72
28.50
27.99
19.19

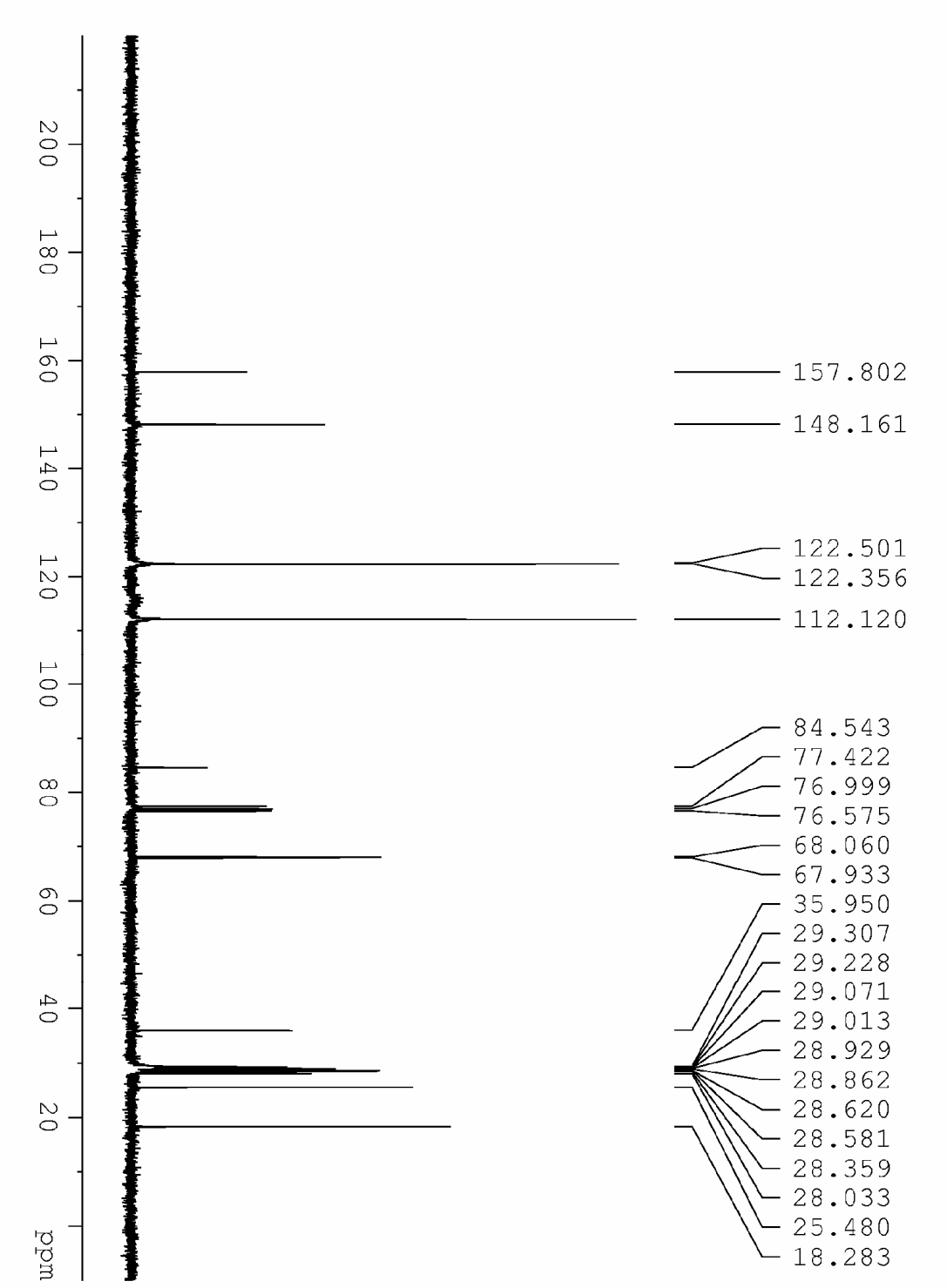


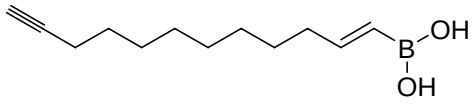
45a

<1> ^{1}H NMR

<2> ^{13}C NMR


7.240
7.204
7.191
7.180
7.172
7.160
7.146
7.062
7.055
7.041
7.031
7.022
7.011
6.981
6.959
5.791
5.731
3.751
3.750
3.744
3.738
3.730
3.716
3.708
2.289
2.266
2.243
2.220
2.179
2.170
2.156
2.147
2.132
2.123
1.929
1.921
1.912
1.841
1.830
1.820
1.808
2.018
3.764
1.000
2.301
2.794
0.006
0.861
4.511
2.180
6.162
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
157.802
148.161
122.501
122.356
112.120
84.543
77.422
76.999
76.575
68.060
67.933
35.950
29.307
29.228
29.071
29.013
28.929
28.862
28.620
28.581
28.359
28.033
25.480
18.283

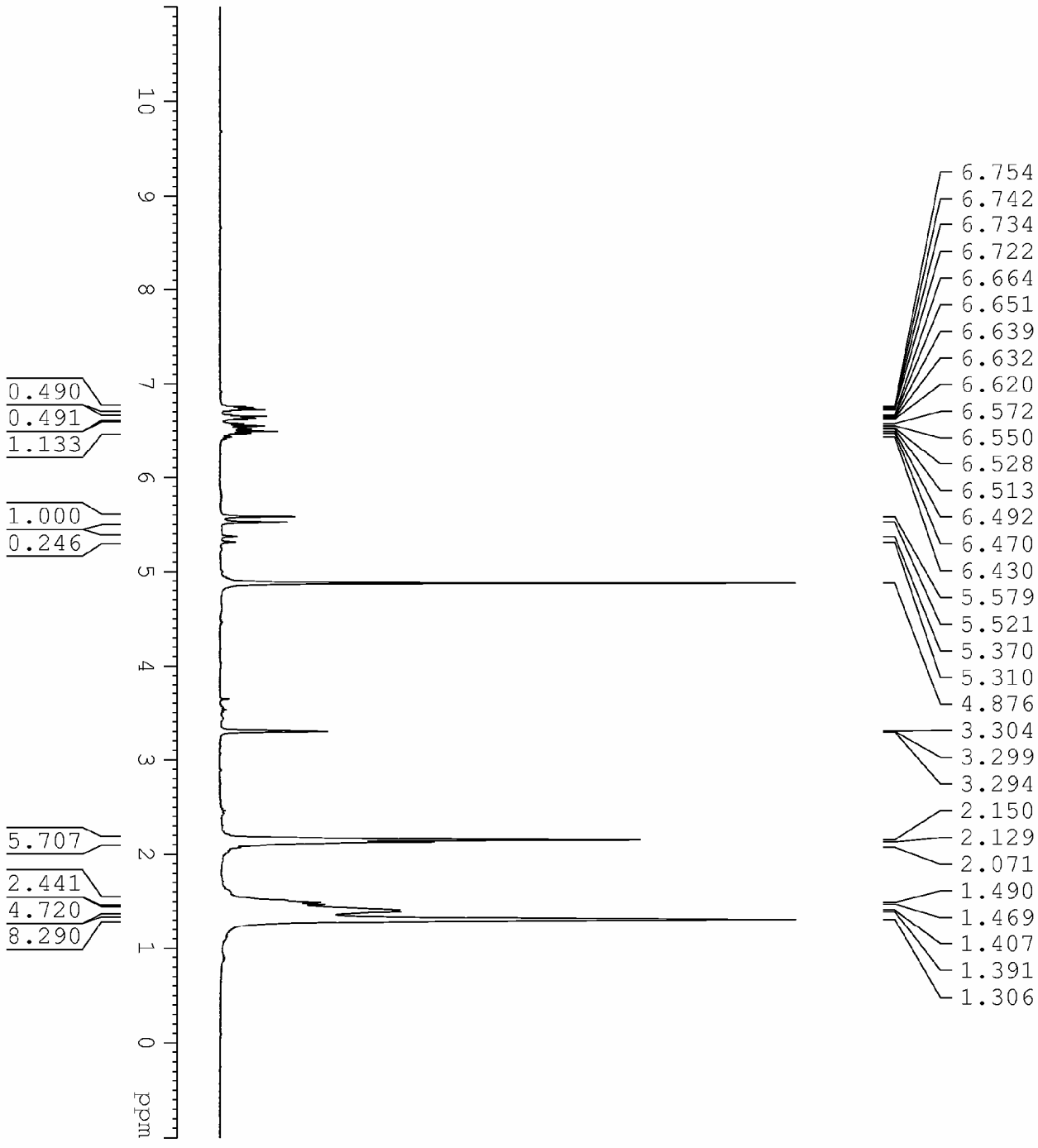


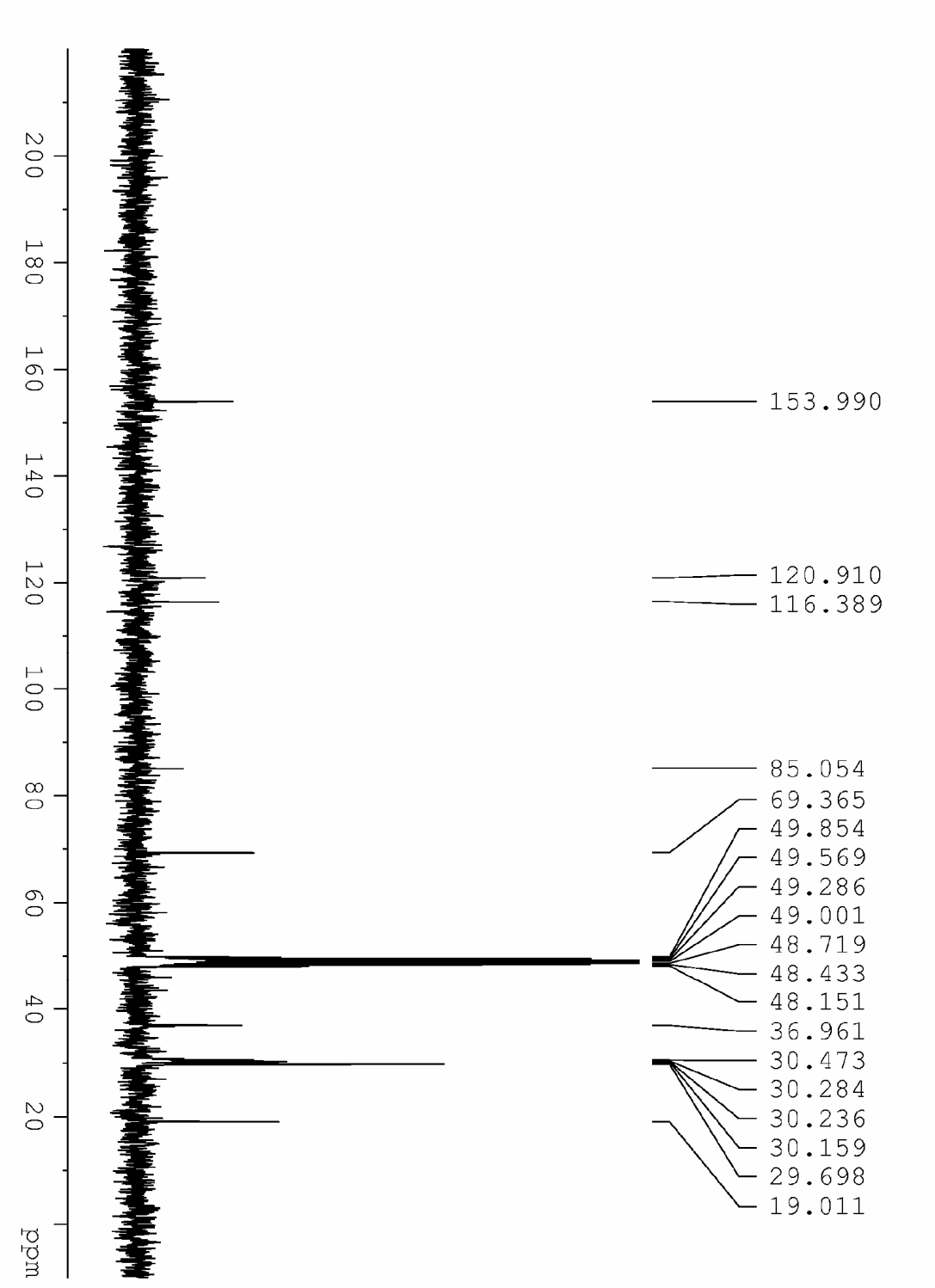
45b

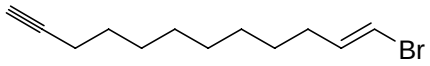
Dodec-1-en-11-ynyl-boranediol

<1> ^{1}H NMR

<2> ^{13}C NMR


0.490
0.491
1.133
1.000
0.246
5.707
2.441
4.720
8.290
10
9
8
7
6
5
4
3
2
1
0
ppm
6.754
6.742
6.734
6.722
6.664
6.651
6.639
6.632
6.620
6.572
6.550
6.528
6.513
6.492
6.470
6.430
5.579
5.521
5.370
5.310
4.876
3.304
3.299
3.294
2.150
2.129
2.071
1.490
1.469
1.407
1.391
1.306


200
180
160
140
120
100
80
60
40
20
ppm
153.990
120.910
116.389
85.054
69.365
49.854
49.569
49.286
49.001
48.719
48.433
48.151
36.961
30.473
30.284
30.236
30.159
29.698
19.011

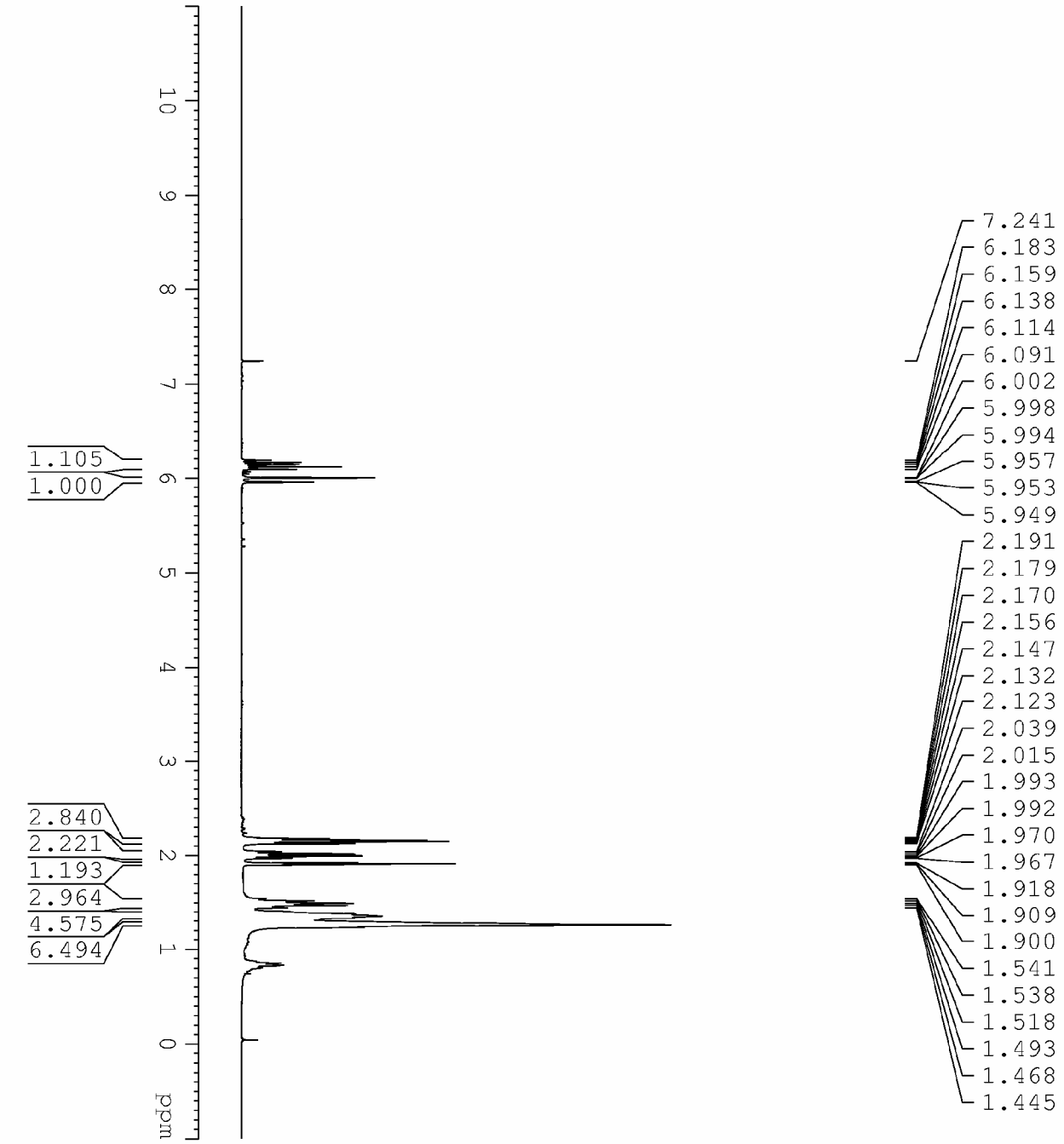


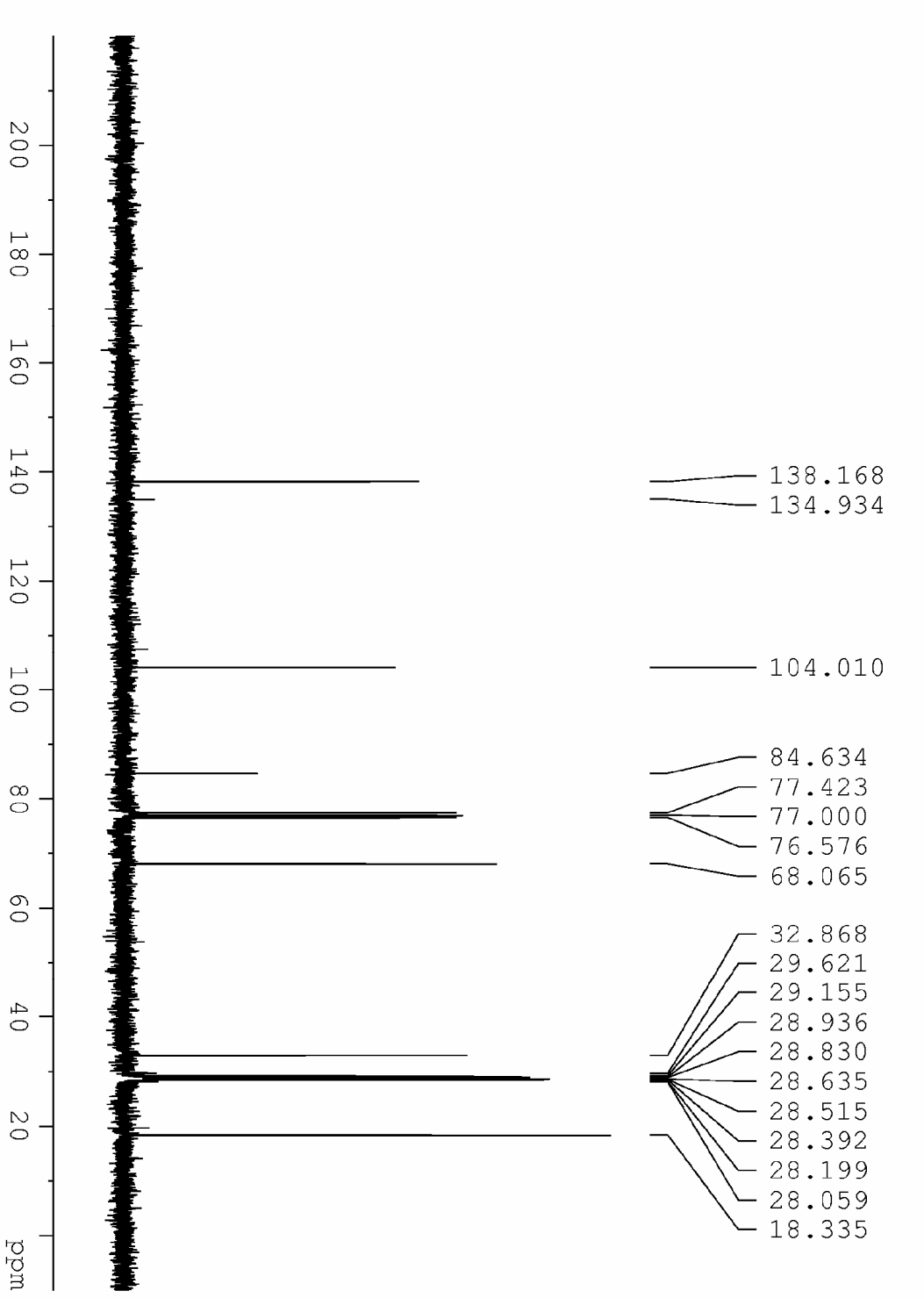
47

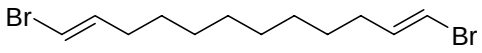
(E)-1-Bromo-dodec-1-en-11-yne

<1> ^{1}H NMR

<2> ^{13}C NMR


7.241
6.183
6.159
6.138
6.114
6.091
6.002
5.998
5.994
5.957
5.953
5.949
2.191
2.179
2.170
2.156
2.147
2.132
2.123
2.039
2.015
1.993
1.992
1.970
1.967
1.918
1.909
1.900
1.541
1.538
1.518
1.493
1.468
1.445
1.105
1.000
2.840
2.221
1.193
2.964
4.575
6.494
10
9
8
7
6
5
4
3
2
1
0
ppm

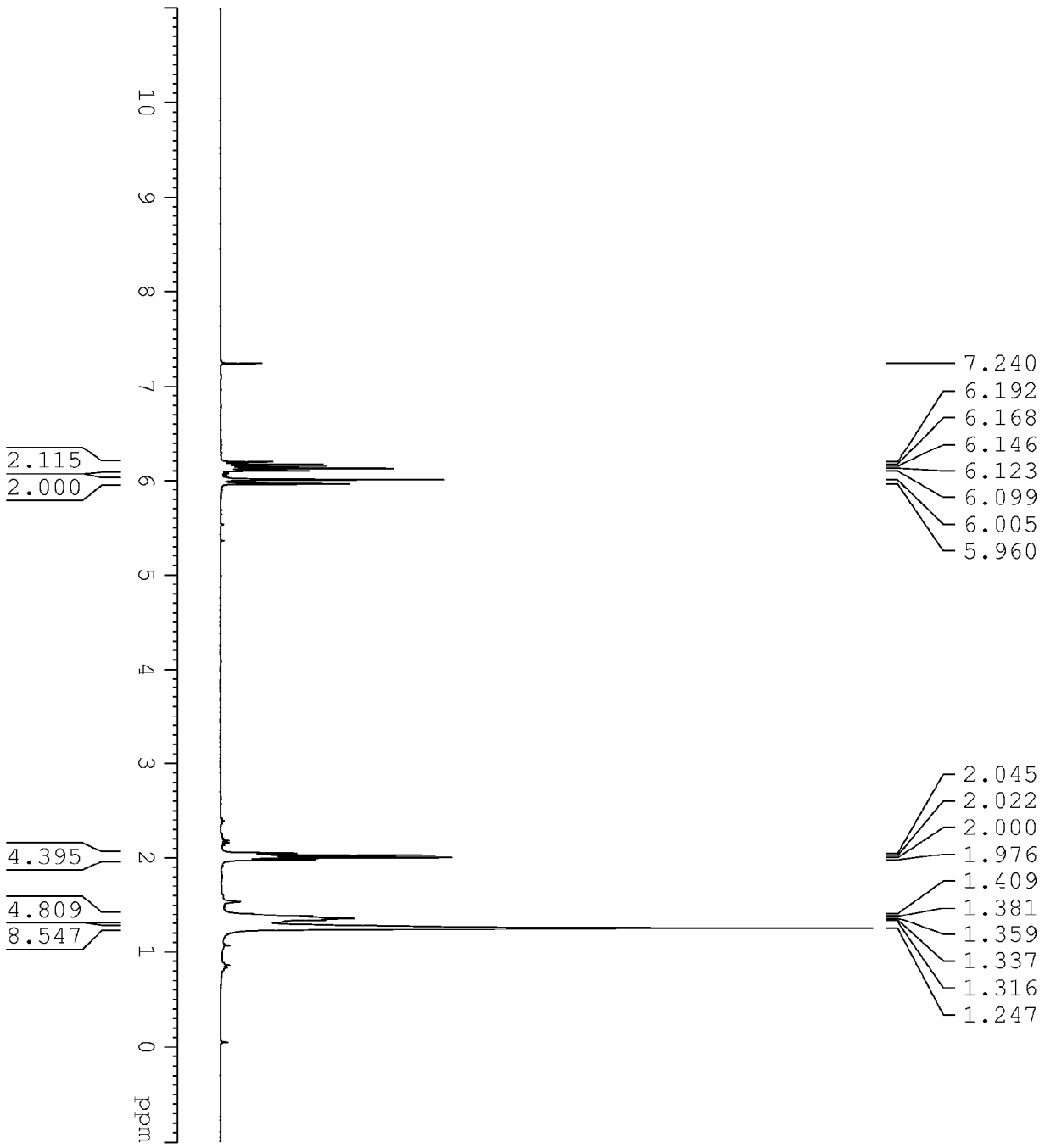

200
180
160
140
120
100
80
60
40
20
ppm
138.168
134.934
104.010
84.634
77.423
77.000
76.576
68.065
32.868
29.621
29.155
28.936
28.830
28.635
28.515
28.392
28.199
28.059
18.335

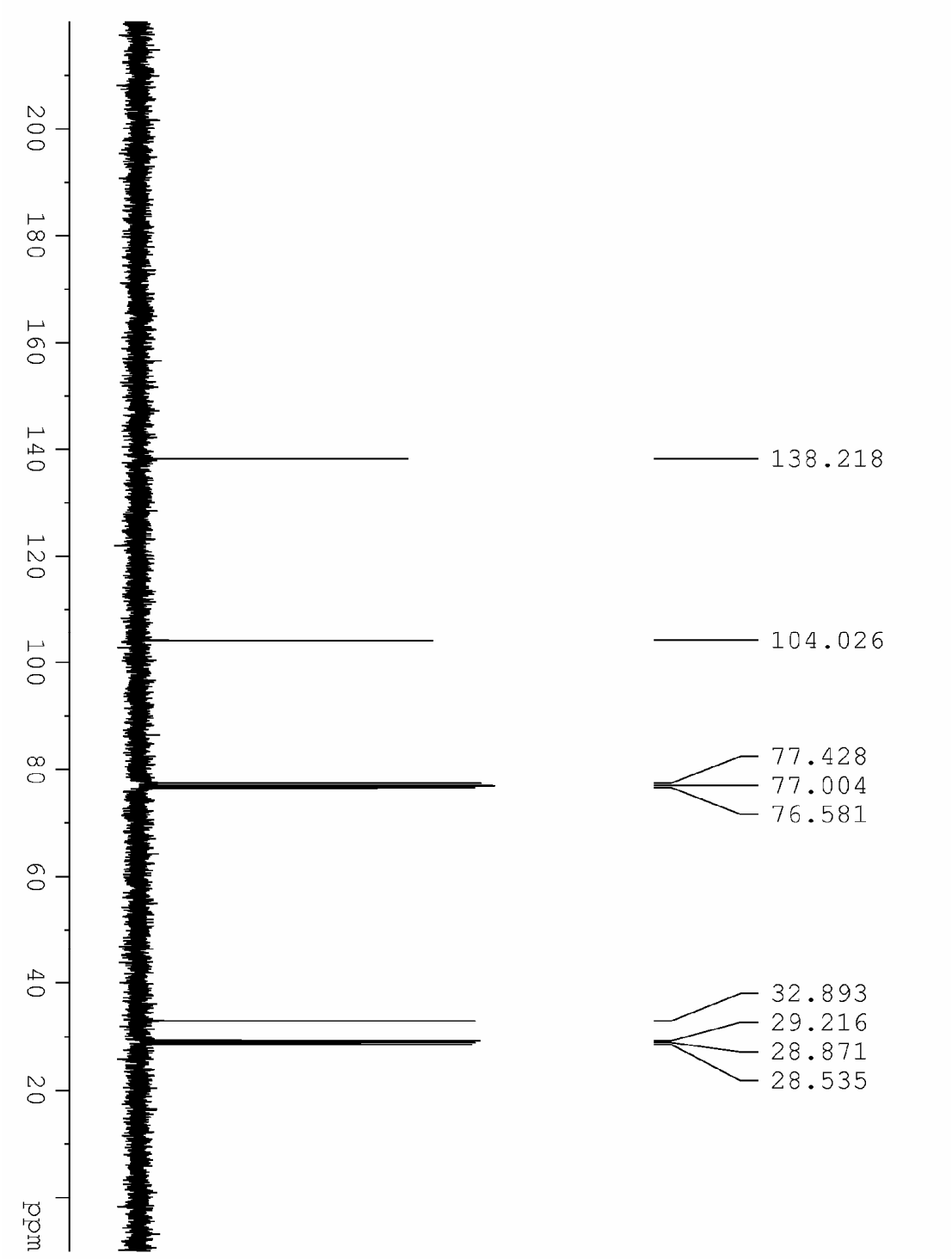


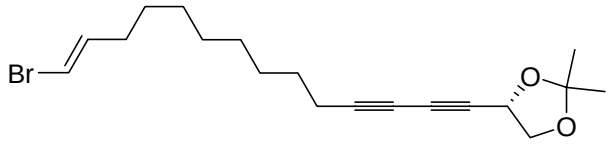
48

<1> ^{1}H NMR

<2> ^{13}C NMR


7.240
6.192
6.168
6.146
6.123
6.099
6.005
5.960
2.115
2.000
2.045
2.022
2.000
1.976
1.409
1.381
1.359
1.337
1.316
1.247
4.395
4.809
8.547
10
9
8
7
6
5
4
3
2
1
0
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.218
104.026
77.428
77.004
76.581
32.893
29.216
28.871
28.535



49

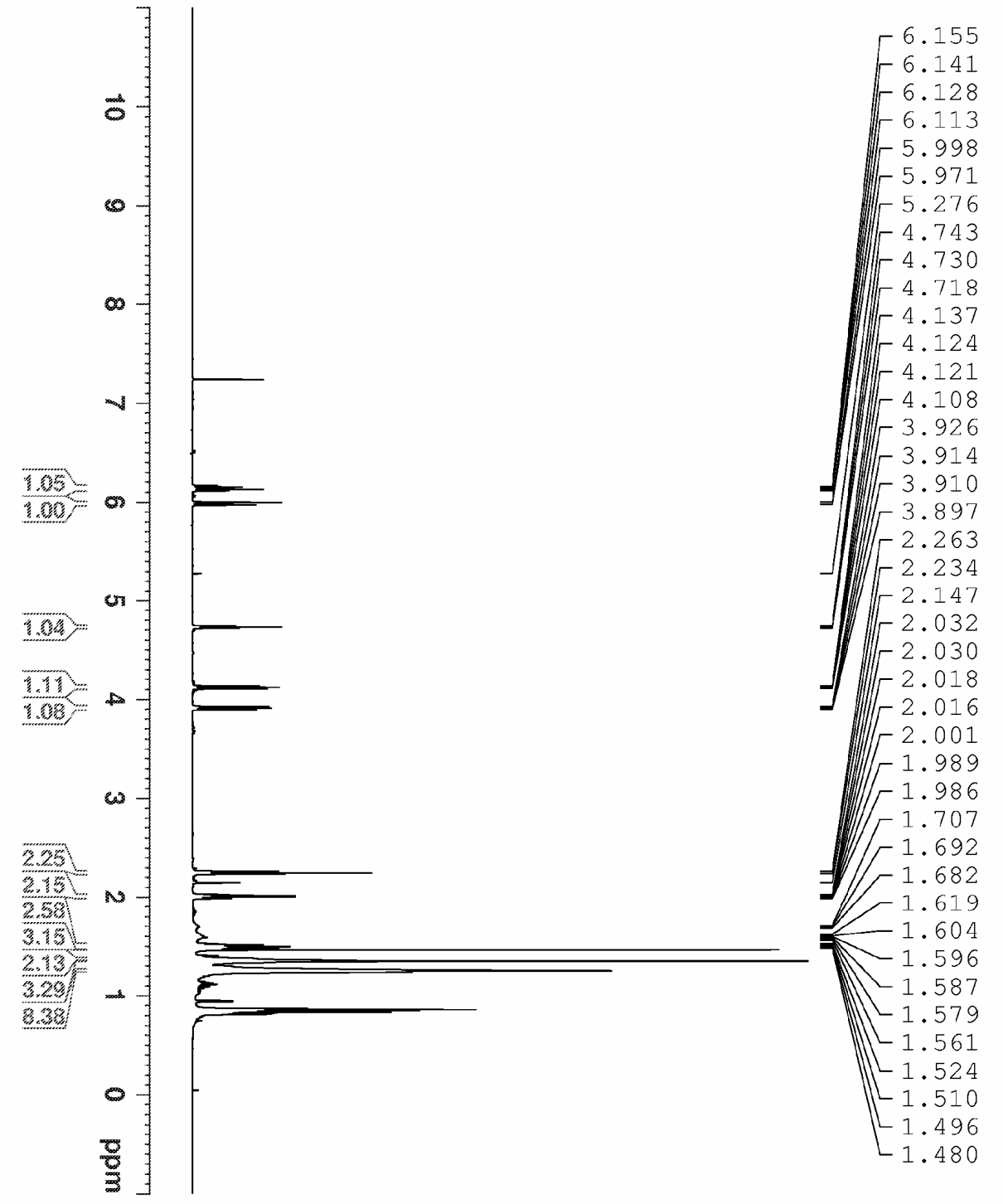
(13E)-4-(14-Bromo-tetradec-13-ene-1,3-diynyl)-2,2-dimethyl-[1,3]dioxolane

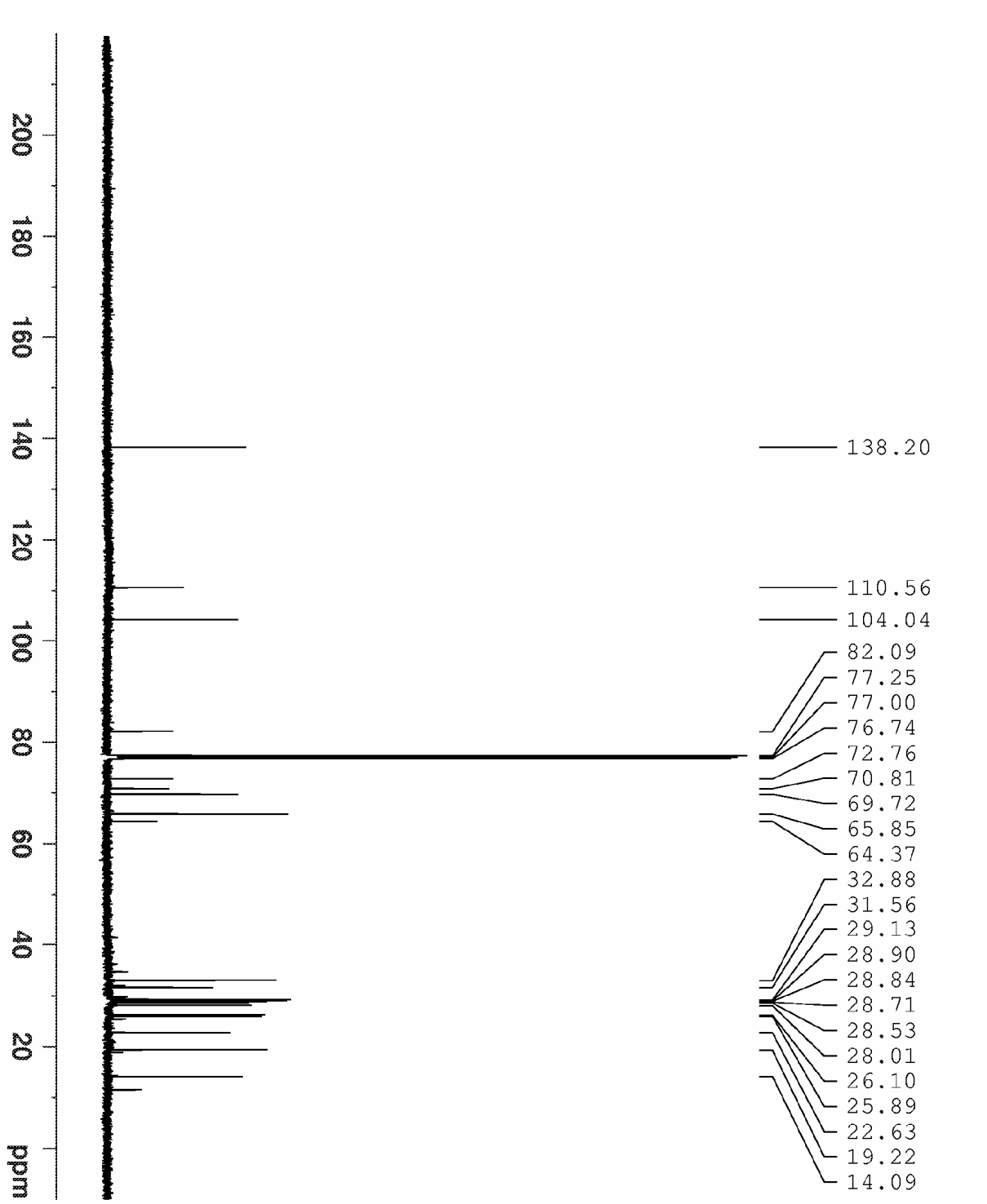
<1> ^{1}H NMR

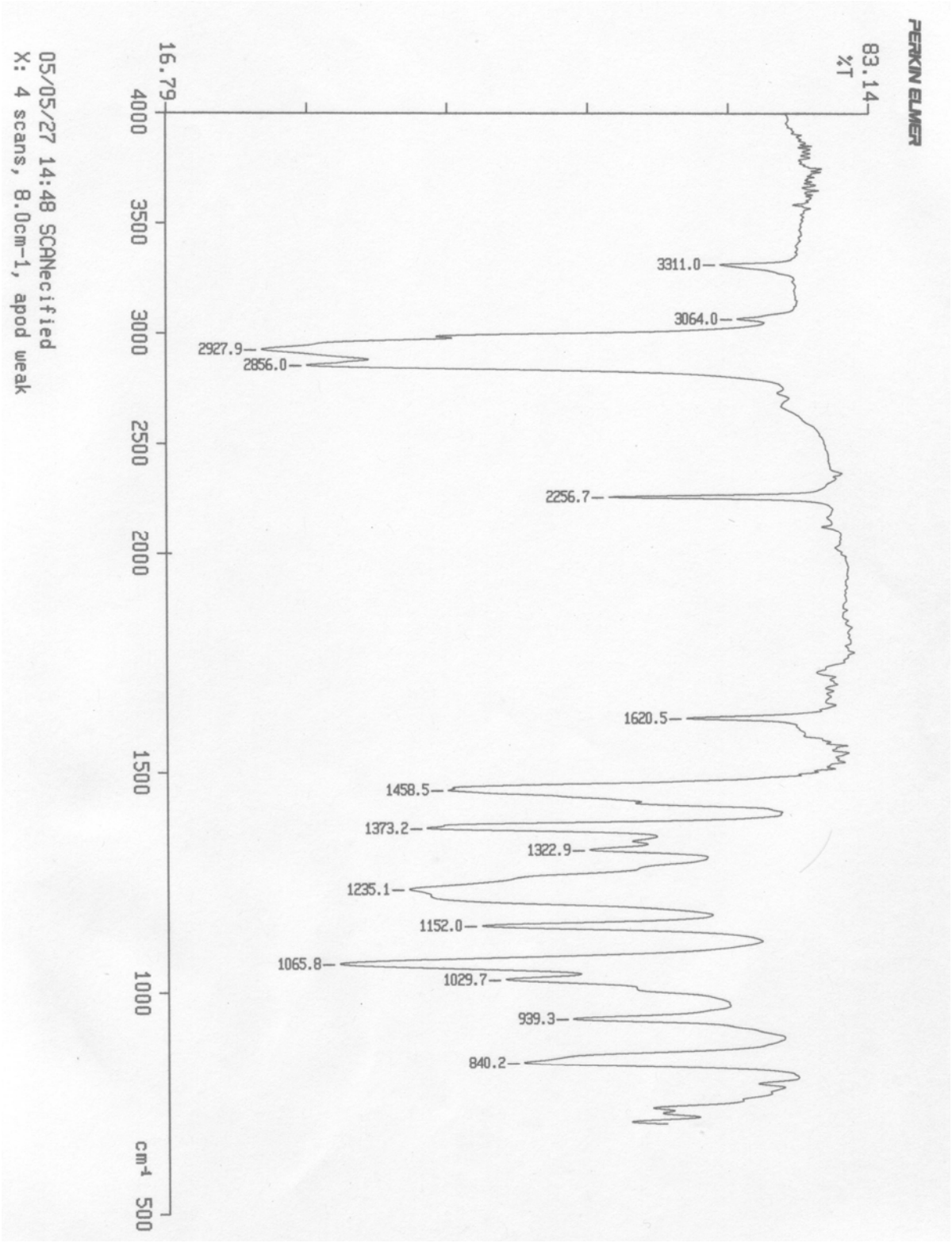
<2> ^{13}C NMR

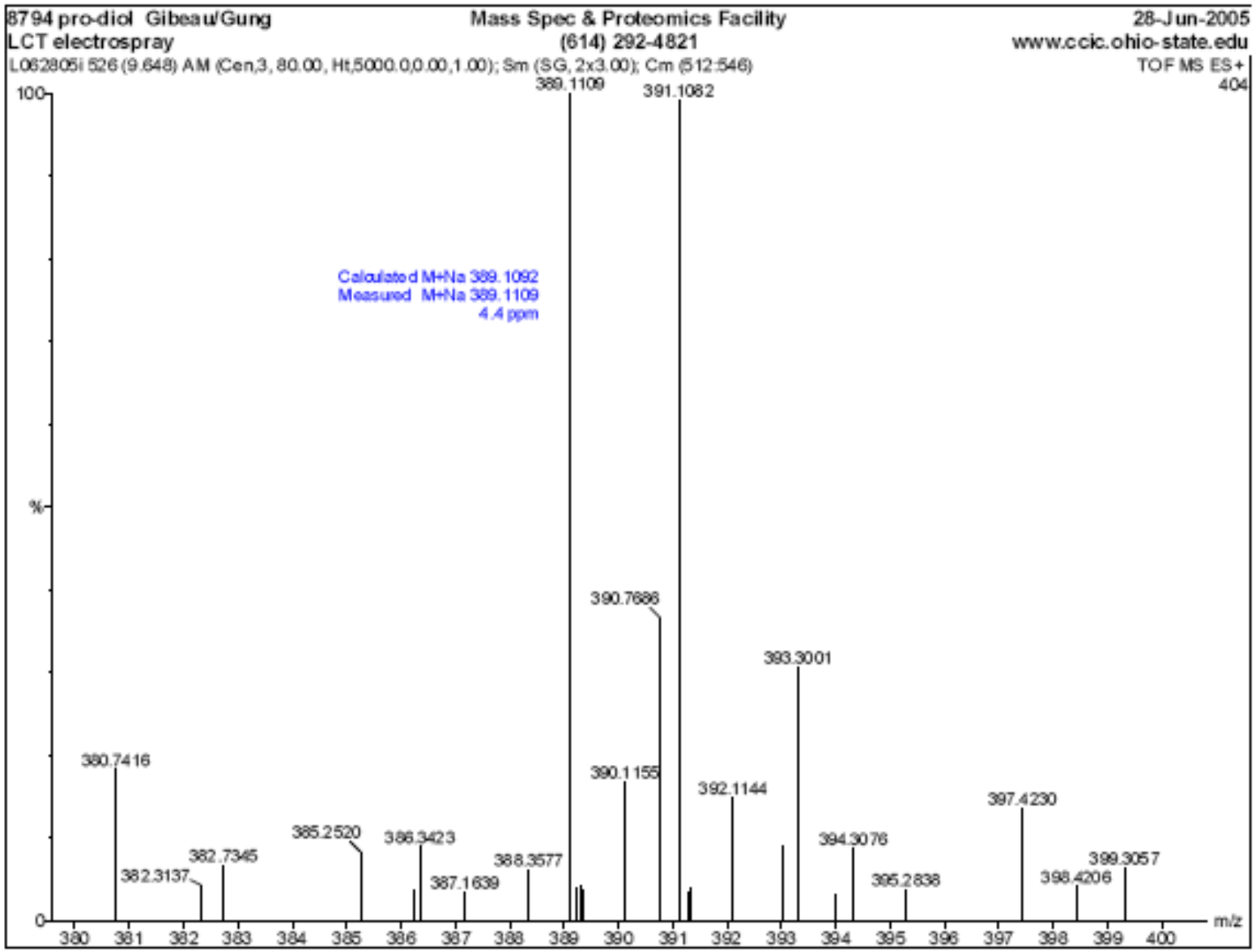
<3> IR

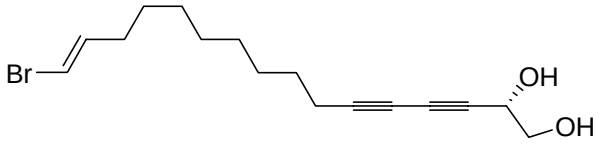
<4> HRMS


6.155
6.141
6.128
6.113
5.998
5.971
5.276
4.743
4.730
4.718
4.137
4.124
4.121
4.108
3.926
3.914
3.910
3.897
2.263
2.234
2.147
2.032
2.030
2.018
2.016
2.001
1.989
1.986
1.707
1.692
1.682
1.619
1.604
1.596
1.587
1.579
1.561
1.524
1.510
1.496
1.480
1.05
1.00
1.04
1.11
1.08
2.25
2.15
2.58
3.15
2.13
3.29
8.38
ppm


200
180
160
140
120
100
80
60
40
20
ppm
138.20
110.56
104.04
82.09
77.25
77.00
76.74
72.76
70.81
69.72
65.85
64.37
32.88
31.56
29.13
28.90
28.84
28.71
28.53
28.01
26.10
25.89
22.63
19.22
14.09


PERKIN ELMER
83.14
%T
16.79
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3311.0
3064.0
2927.9
2856.0
2256.7
1620.5
1458.5
1373.2
1322.9
1235.1
1152.0
1065.8
1029.7
939.3
840.2
05/05/27 14:48 SCANecified
X: 4 scans, 8.0cm-1, apod weak


8794 pro-diol Gibeau/Gung
LCT electrospray
L062805i 526 (9.648) AM (Cen,3, 80.00, Ht,5000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (512:546)
Mass Spec & Proteomics Facility
(614) 292-4821
28-Jun-2005
www.ccic.ohio-state.edu
TOF MS ES+
404
Calculated M+Na 389.1092
Measured M+Na 389.1109
4.4 ppm
389.1109
391.1082
390.7686
393.3001
380.7416
390.1155
392.1144
397.4230
385.2520
386.3423
394.3076
382.7345
388.3577
399.3057
382.3137
387.1639
395.2838
398.4206
%
m/z
0
100
380
381
382
383
384
385
386
387
388
389
390
391
392
393
394
395
396
397
398
399
400



3

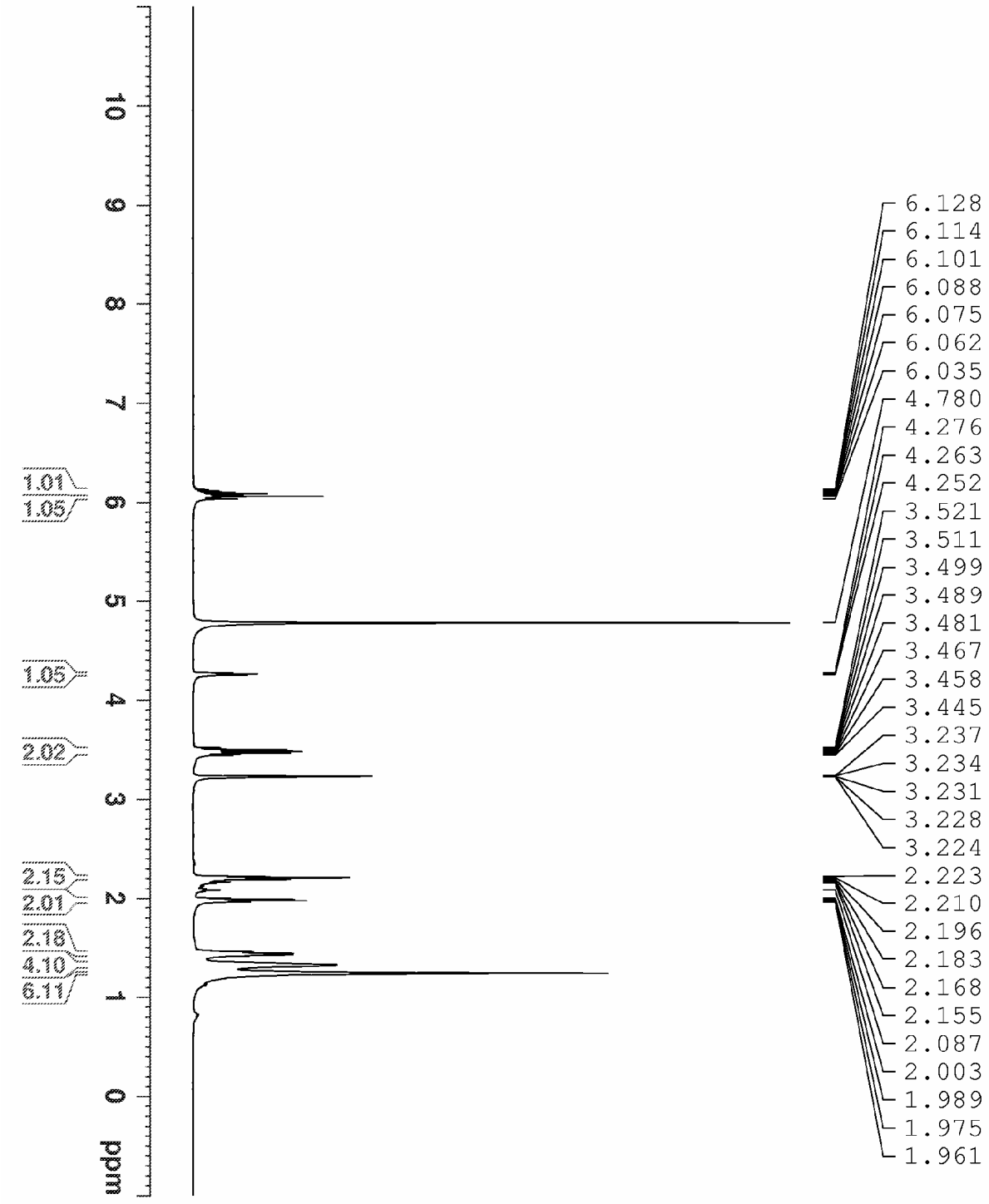
(+)-Diplyne C

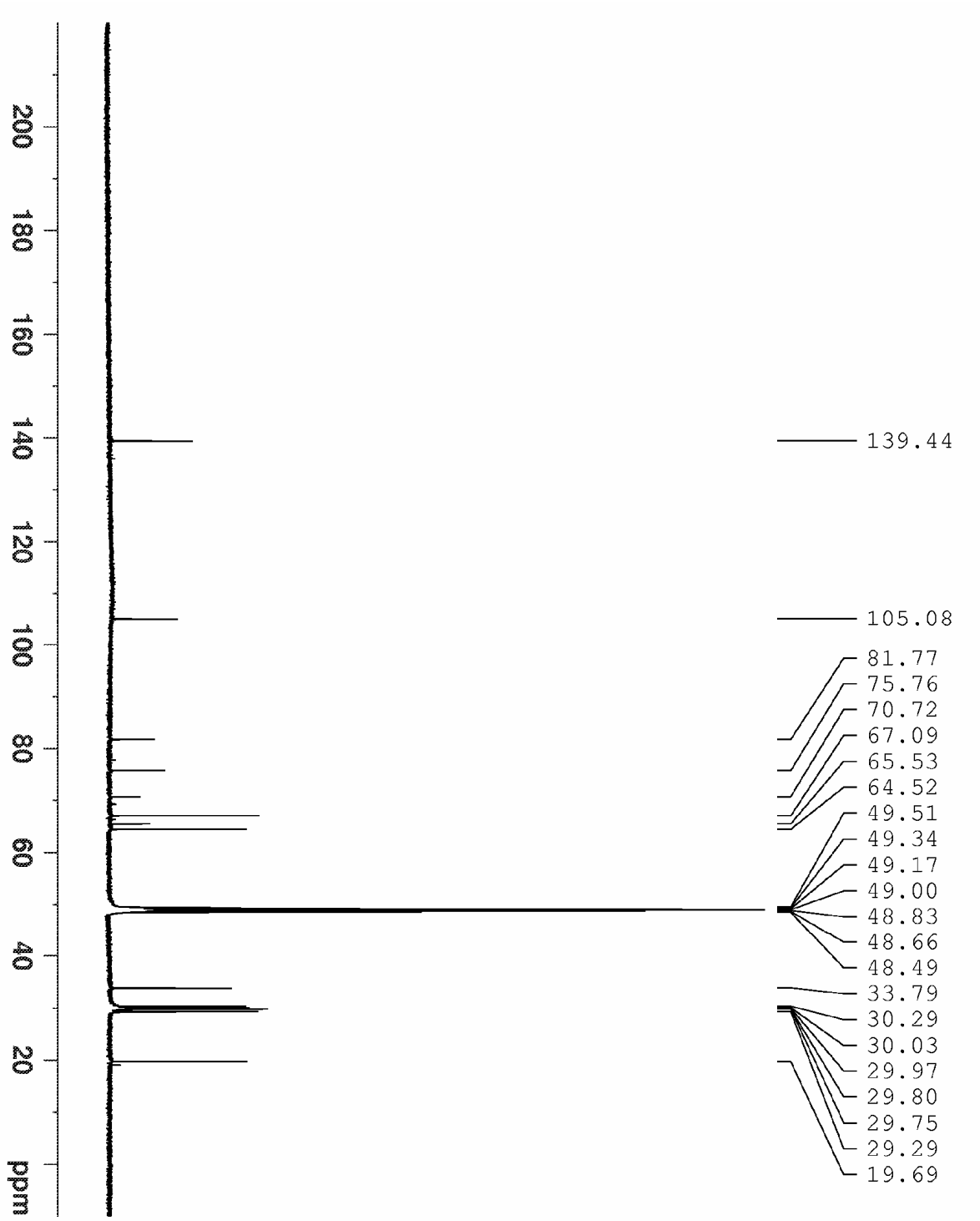
<1> ^{1}H NMR

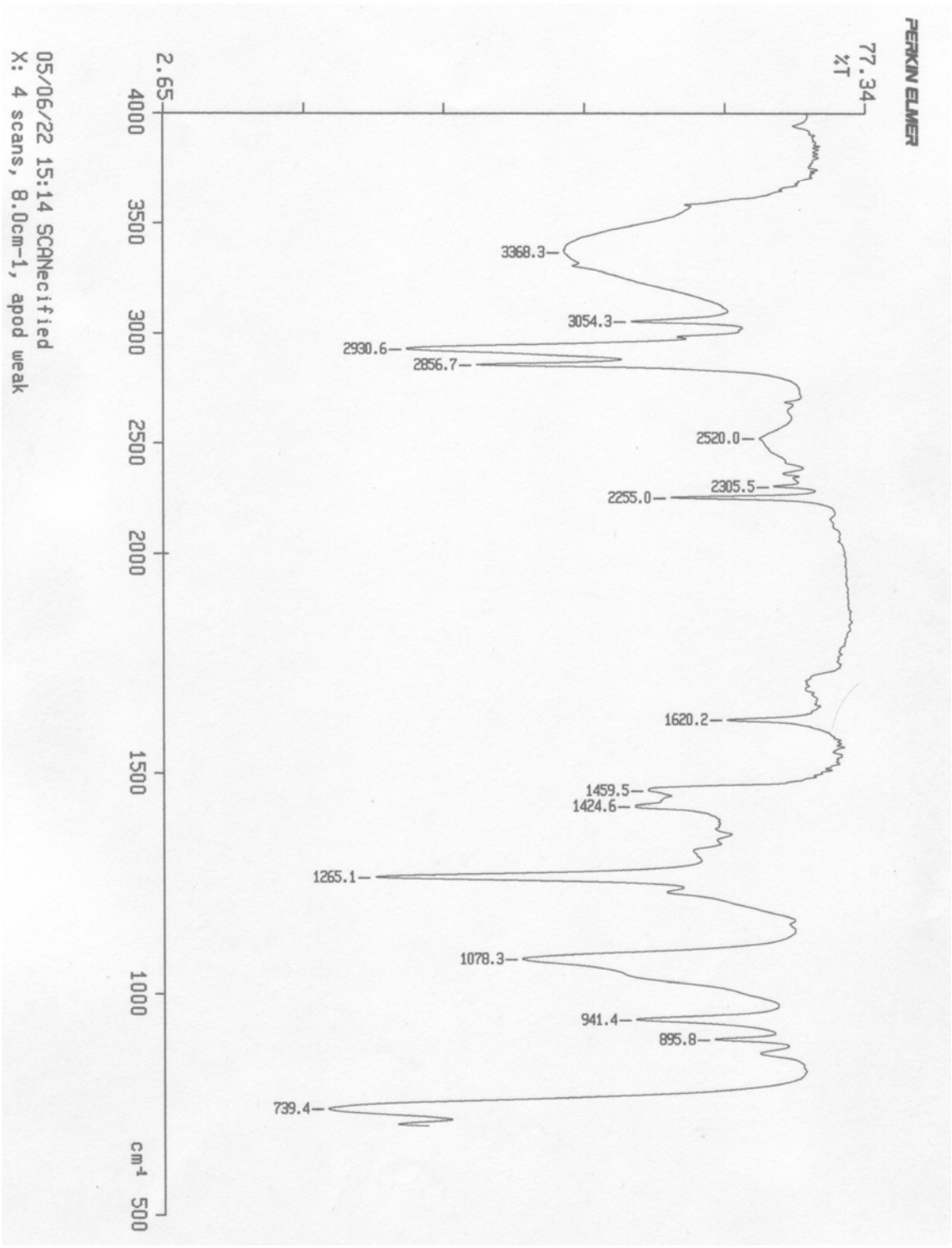
<2> ^{13}C NMR

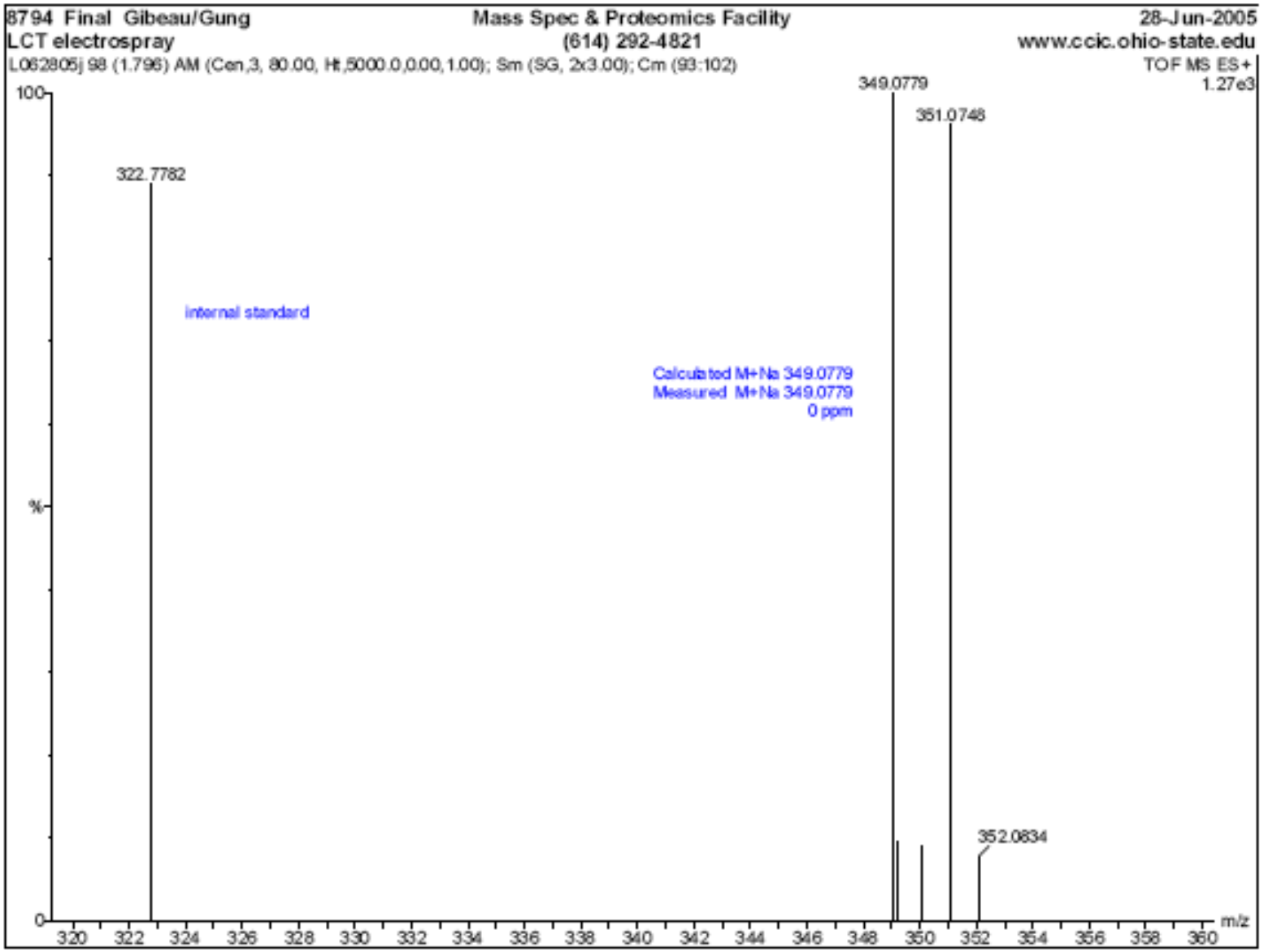
<3> IR

<4> HRMS


6.128
6.114
6.101
6.088
6.075
6.062
6.035
4.780
4.276
4.263
4.252
3.521
3.511
3.499
3.489
3.481
3.467
3.458
3.445
3.237
3.234
3.231
3.228
3.224
2.223
2.210
2.196
2.183
2.168
2.155
2.087
2.003
1.989
1.975
1.961
1.01
1.05
1.05
2.02
2.15
2.01
2.18
4.10
6.11
ppm


200
180
160
140
120
100
80
60
40
20
ppm
139.44
105.08
81.77
75.76
70.72
67.09
65.53
64.52
49.51
49.34
49.17
49.00
48.83
48.66
48.49
33.79
30.29
30.03
29.97
29.80
29.75
29.29
19.69


PERKIN ELMER
77.34
%T
2.65
4000
3500
3000
2500
2000
1500
1000
500
cm-1
3368.3
3054.3
2930.6
2856.7
2520.0
2305.5
2255.0
1620.2
1459.5
1424.6
1265.1
1078.3
941.4
895.8
739.4
05/06/22 15:14 SCANecified
X: 4 scans, 8.0cm-1, apod weak


8794 Final Gibeau/Gung
LCT electrospray
Mass Spec & Proteomics Facility
(614) 292-4821
28-Jun-2005
www.ccic.ohio-state.edu
L062805j 98 (1.796) AM (Cen,3, 80.00, Ht,5000.0,0.00,1.00); Sm (SG, 2x3.00); Cm (93:102)
TOF MS ES+
1.27e3
349.0779
351.0748
322.7782
internal standard
Calculated M+Na 349.0779
Measured M+Na 349.0779
0 ppm
352.0834
100
%
0
m/z
320
322
324
326
328
330
332
334
336
338
340
342
344
346
348
350
352
354
356
358
360