

**Synthesis and Preliminary Pharmacological Evaluation of Aryl
Dithiolethiones with Cyclooxygenase-2 Selective Inhibitory
Activity and Hydrogen-Sulfide-Releasing Properties**

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Representative procedure for the MOM protection of phenols

Acetyl chloride (5.00 mmol) was added dropwise to a solution of dimethoxymethane (5 mmol), and ZnCl₂ (0.02 mmol) in toluene (6 mL). The reaction was stirred at rt for 4 h, and then the phenol (1.00 mmol) was added followed by *N*-ethyl-*N,N*-diisopropylamine (1.50 mmol). The reaction was then stirred at rt overnight. Water was added and the mixture was stirred for 15 min. The aqueous layer was extracted with EtOAc (× 2) and the combined organic extracts washed with 1 M NaOH (× 3), sat. NaHCO₃ (× 1), water (× 2), brine (× 1), dried (Na₂SO₄) and concentrated.

1-[4-(Methoxymethoxy)-3,5-dimethylphenyl]ethanone 5b

The title compound was prepared by the representative procedure starting from 1-(4-hydroxy-3,5-dimethylphenyl)ethanone^[1] (**4b**). Flash chromatography (10% EtOAc/petrol) afforded **5b** as a yellow oil (427 mg, 68%). δ_H (500 MHz, CDCl₃) 2.25 (s, 6H, ArCH₃ × 2), 2.46 (s, 3H, COCH₃), 3.52 (s, 3H, CH₃), 4.92 (s, 2H, CH₂), 7.56 ppm (s, 2H, Ar); δ_C (100 MHz, CDCl₃) 16.7 (ArCH₃), 26.1 (COCH₃), 57.1 (OCH₃), 98.8 (CH₂), 129.1, 131.1, 133.0, 158.9 (6C, Ar), 197.0 ppm (CO); IR ν 2925, 1677, 1596, 1155, 959, 769 cm⁻¹; HRMS-ESI⁺ *m/z* [M+Na]⁺ Calc. for C₁₂H₁₇O₃: 209.1172, found: 209.1170.

1-[3,5-Diethyl-4-(methoxymethoxy)phenyl]ethanone 5c

The title compound was prepared the representative procedure starting from 1-(3,5-diethyl-4-hydroxyphenyl)ethanone^[2] (**4c**). Flash chromatography (5% EtOAc/petrol) afforded **5c** as a yellow oil (691 mg, 46%). δ_H (400 MHz, CDCl₃) 1.25 (t, *J* = 7.5 Hz, 6H, CH₂CH₃ × 2), 2.56 (s, 3H, COCH₃), 2.71 (q, *J* = 7.5 Hz, 4H, CH₂CH₃ × 2), 3.60 (s, 3H, OCH₃), 4.97 (s, 2H, OCH₂O), 7.68 ppm (s, 2H, Ar); δ_C (100 MHz, CDCl₃) 14.5 (CH₂CH₃), 23.3 (CH₂CH₃), 26.5 (COCH₃), 57.3 (OCH₃), 99.7 (OCH₂O), 127.5, 133.5, 137.4, 158.3 (6C, Ar), 197.6 ppm (CO); IR ν 2968, 1679, 1357, 1288, 1157, 1072, 882 cm⁻¹; HRMS-ESI⁺ *m/z* [M+H]⁺ Calc. for C₁₄H₂₁O₃: 237.1485, found 237.1485.

1-[3,5-Diisopropyl-4-(methoxymethoxy)phenyl]ethanone 5d

The title compound was prepared by the representative procedure starting from 1-[4-hydroxy-3,5-diisopropylphenyl]ethanone^[3] (**4d**). Flash chromatography (5% EtOAc/petrol) afforded **5d** as a yellow oil (206 mg, 37%). δ_H (500 MHz, CDCl₃) 1.26 (d, *J* = 7 Hz, 12H, CH(CH₃)₂ × 2), 2.59 (s, 3H, COCH₃), 3.36 (septet, *J* = 7.0 Hz, 2H, (CH₃)₂CH × 2) 3.62 (s, 3H, OCH₃),

4.96 (s, 2H, CH₂), 7.73 ppm (s, 2H, Ar); δ_{C} (100 MHz, CDCl₃) 23.8 (CH(CH₃)₂) 26.5 (COCH₃), 26.6 (CH(CH₃)₂), 62.1 (OCH₃), 99.1 (CH₂), 124.7, 133.6, 142.0, 158.9 (6C, Ar), 197.5 ppm (CO); IR ν 2963, 1680, 1300, 1192, 1006, 798 cm⁻¹; HRMS-ESI⁺ m/z [M+H]⁺ Calc. for C₁₆H₂₅O₃: 256.1798, found 265.1798.

1-[3,5-di-(tert-Butyl)-4-(methoxymethoxy)phenyl]ethanone 5e

The title compound was prepared by the representative procedure starting from 1-[3,5-di-(*tert*-butyl)-4-hydroxyphenyl]ethanone^[4] (**4e**). Flash chromatography (10% EtOAc/petrol) and recrystallisation from EtOH/water afforded **5e** as a colourless solid (1.67 g, 71%). mp 60-61 °C; δ_{H} (500 MHz, CDCl₃) 0.88 (s, 18H, (C(CH₃)₃)₂), 1.98 (s, 3H, COCH₃), 3.06 (s, 3H, OCH₃), 4.33 (s, 2H, CH₂), 7.32 ppm (s, 2H, Ar); δ_{C} (100 MHz, CDCl₃) 26.4 (COCH₃), 31.8 (C(CH₃)₃), 35.8 (C(CH₃)₃), 57.4 (CH₃), 100.7 (CH₂), 127.0, 132.1, 144.7, 159.0 (6C, Ar), 197.8 ppm (CO); IR ν 2956, 2873, 1762, 1676, 1589, 1227, 881 cm⁻¹; HRMS-ESI⁺ m/z [M+Na]⁺ Calc. for C₁₈H₂₈NaO₃: 315.1931, found 315.1931; Anal. Calc. for C₁₈H₂₈O₃: C 73.93, H 9.65. Found: C 73.92, H 9.70%.

Representative procedure for the etherification of phenols

Iodoalkane (2.50 mmol) was added to a mixture of anhydrous potassium carbonate (1.70 mmol) and the phenol (1.00 mmol). The mixture was heated at reflux for 18 h. Diethyl ether was then added to the cooled solution and the organic phase washed with water (\times 2), brine (\times 1), dried (Na₂SO₄) and concentrated.

1-(4-Methoxy-3,5-dimethylphenyl)ethanone 9b2^[5]

The title compound was prepared by the representative procedure starting from 1-(4-hydroxy-3,5-dimethylphenyl)ethanone^[1] (**4b**) and iodomethane. After flash chromatography (5% EtOAc/petrol), **9b2** was obtained as a yellow oil (1.19 g, 70%). δ_{H} (400 MHz, CDCl₃) 2.21 (s, 6H, ArCH₃ \times 2), 2.44 (s, 3H, COCH₃), 3.65 (s, 3H, OCH₃), 7.53 ppm (s, 2H, Ar); δ_{C} (100 MHz, CDCl₃) 15.9 (ArCH₃), 26.1 (COCH₃), 59.2 (OCH₃), 129.0, 130.7, 132.5, 160.9 (6C, Ar), 197.1 ppm (CO); IR ν 2940, 1674, 1591, 1482, 1092, 874 cm⁻¹; HRMS-ESI⁺ m/z [M+H]⁺ Calc. for C₁₁H₁₅O₂: 179.1067, found 179.1066.

1-(4-Ethoxy-3,5-dimethylphenyl)ethanone 9b3^[6]

The title compound was prepared by the representative procedure starting from 1-(4-hydroxy-3,5-dimethylphenyl)ethanone^[1] (**4b**) and iodoethane. After flash chromatography (5% EtOAc/petrol), **9b3** was obtained as a yellow oil (94% 1.08 g). δ_{H} (400 MHz, CDCl₃) 1.30 (t, $J = 6.4$ Hz, 3H, CH₂CH₃), 2.27 (s, 6H, ArCH₃ × 2), 2.50 (s, 3H, COCH₃), 3.84 (q, $J = 6.4$ Hz, 2H, CH₂), 7.59 ppm (s, 2H, Ar); δ_{C} (100 MHz, CDCl₃) 15.6, 16.3 (ArCH₃, CH₂CH₃), 26.3 (COCH₃), 67.8 (CH₂), 129.1, 131.0, 132.5, 160.3 (6C, Ar), 197.4 ppm (CO); IR ν 2980, 2929, 1677, 1306, 1030, 900, 777 cm⁻¹; HRMS-ESI⁺ m/z [M+H]⁺ Calc. for C₁₂H₁₇O₂: 193.1223, found 193.1223.

1-(3,5-Diethyl-4-methoxyphenyl)ethanone 9c2

The title compound was prepared by the representative procedure starting from 1-(3,5-diethyl-4-hydroxyphenyl)ethanone^[2] (**4c**) and iodomethane. After flash chromatography (5% EtOAc/petrol), **9c2** was obtained as a yellow oil (59%, 505 mg). δ_{H} (500 MHz, CDCl₃) 1.25 (t, $J = 7.5$ Hz, 6H, CH₂CH₃), 2.56 (s, 3H, COCH₃), 2.70 (q, $J = 7.5$ Hz, 4H, CH₂), 3.76 (s, 3H, OCH₃), 7.62 ppm (s, 2H, Ar); δ_{C} (125 MHz, CDCl₃) 14.7 (CH₂CH₃), 22.8 (CH₂), 26.4 (COCH₃), 61.0 (OCH₃), 127.6, 133.3, 137.2, 160.5 (6C, Ar), 197.6 ppm (CO); IR ν 2968, 1679, 1595, 1356, 1191, 1164 cm⁻¹; HRMS-ESI⁺ m/z [M+Na]⁺ Calc. for C₁₃H₁₉NaO₂: 229.1199, found 229.1199.

1-[3,5-Diisopropyl-4-methoxyphenyl]ethanone 9d2

The title compound was prepared by the representative procedure starting from 1-(4-hydroxy-3,5-diisopropylphenyl)ethanone^[3] (**4d**) and iodomethane. After flash chromatography (5% EtOAc/petrol), **9d2** was obtained as a yellow oil (46%, 836 mg). δ_{H} (500 MHz, CDCl₃) 1.30 (d, $J = 6.5$ Hz, 12H, (CH₃)₂CH × 2), 2.57 (s, 3H, COCH₃), 3.33 (septet, $J = 6.5$ Hz, 2H, (CH₃)₂CH × 2), 3.75 (s, 3H, OCH₃), 7.72 ppm (s, 2H, Ar); δ_{C} (125 MHz, CDCl₃) 23.8 (CH(CH₃)₂), 26.4 (COCH₃), 26.5 (CH(CH₃)₂), 62.1 (OCH₃), 124.7, 133.6, 142.0, 158.9 (6C, Ar), 197.5 ppm (CO); IR ν 2963, 1680, 1300, 1192, 1006, 798 cm⁻¹; HRMS-ESI⁺ m/z [M+H]⁺ Calc. for C₁₅H₂₃O₂: 235.1693, found 235.1693.

1-[4-Ethoxy-3,5-diisopropylphenyl]ethanone 9d3

The title compound was prepared by the representative procedure starting from 1-(4-hydroxy-3,5-diisopropylphenyl)ethanone (**4d**) and iodoethane. After flash chromatography (5% EtOAc/petrol) and recrystallisation from EtOH/water, **9d3** was obtained as a yellow oil (72%,

772 mg). mp 81-82 °C; δ_{H} (500 MHz, CDCl_3) 1.26 (d, $J = 7$ Hz, 12H, $\text{CH}(\text{CH}_3)_2 \times 2$), 1.47 (t, $J = 7$ Hz, CH_2CH_3), 2.59 (s, 3H, COCH_3), 3.34 (septet, $J = 7$ Hz, $\text{CH}(\text{CH}_3)_2 \times 2$), 3.84 (q, $J = 7$ Hz, 2H, CH_2), 7.73 ppm (s, 2H, Ar); δ_{C} (125 MHz, CDCl_3) 15.8 (CH_2CH_3), 24.0 ($\text{CH}(\text{CH}_3)_2$), 26.5 (COCH_3), 26.7 ($\text{CH}(\text{CH}_3)_2$), 70.6 (CH_2), 133.6, 142.3, 144.7, 158.0 (6C, Ar), 197.8 ppm (CO); IR ν 2963, 1680, 1462, 1192, 1007, 973, 816, 730 cm^{-1} ; HRMS-ESI⁺ m/z $[\text{M}+\text{H}]^+$ Calc. for $\text{C}_{16}\text{H}_{25}\text{O}_2$: 249.1849, found 249.1850.

1-[3,5-di-(tert-Butyl)-4-methoxyphenyl]ethanone 9e2

The title compound was prepared by the representative procedure starting from 1-[3,5-di-(*tert*-butyl)-4-hydroxyphenyl]ethanone^[4] (**4e**) and iodomethane. After flash chromatography (10% EtOAc/petrol) and recrystallisation from EtOH/water, **9e3** was obtained as a colourless solid (2.68 g, 82%). mp 52-53 °C (lit.^[7] mp 49-50 °C). δ_{H} (400 MHz, CDCl_3) 1.45 (s, 18H, $\text{C}(\text{CH}_3)_3 \times 2$), 2.57 (s, 3H, COCH_3), 3.71 (s, 1H, OCH_3), 7.88 ppm (s, 2H, Ar).

1-[3,5-di-(tert-Butyl)-4-ethoxyphenyl]ethanone 9e3

The title compound was prepared by the representative procedure starting from 1-[3,5-di-(*tert*-butyl)-4-hydroxyphenyl]ethanone (**4e**) and iodoethane. After flash chromatography (5% EtOAc/petrol), **9e3** was obtained as a yellow oil (171 mg, 65%). δ_{H} (400 MHz, CDCl_3) 1.43 (t, 3H, $J = 7$ Hz, CH_2CH_3), 1.44 (s, 18H, $\text{C}(\text{CH}_3)_3 \times 2$), 2.57 (s, 3H, COCH_3), 3.77 (t, 2H, $J = 7$ Hz, CH_2), 7.78 ppm (s, 2H, Ar); δ_{C} (100 MHz, CDCl_3) 14.8 (CH_2CH_3), 26.4 (COCH_3), 31.8 ($\text{C}(\text{CH}_3)_3$), 35.9 ($\text{C}(\text{CH}_3)_3$), 72.0 (CH_2), 127.1, 131.7, 144.0, 162.6 (6C, Ar), 197.8 ppm (CO); IR ν 2963, 1682, 1590, 1298, 1105, 971, 887 cm^{-1} ; HRMS-ESI⁺ m/z $[\text{M}+\text{H}]^+$ Calc. for $\text{C}_{18}\text{H}_{29}\text{O}_2$: 277.2162, found 277.2162; Anal. Calc. for $\text{C}_{18}\text{H}_{28}\text{O}_2$: C 78.21, H 10.21. Found C 78.24, H 10.20%.

References

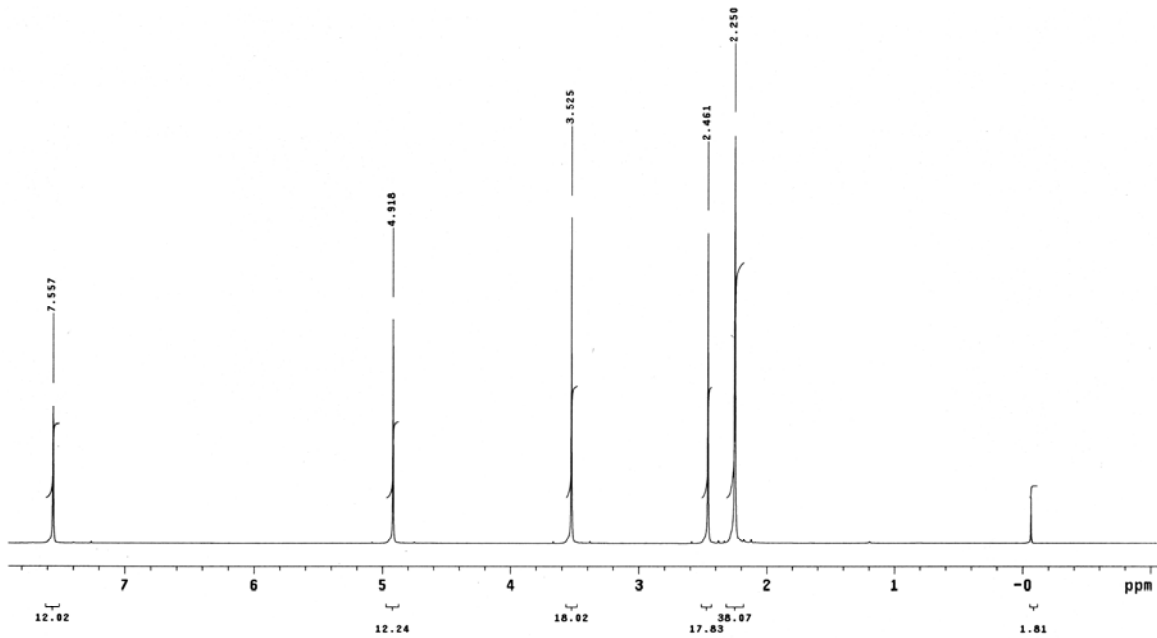
- [1] S. L. Goldstein, E. McNelis, *J. Org. Chem.* **1984**, *49*, 1613.
- [2] R. Breslow, K. Groves, M. U. Mayer, *J. Am. Chem. Soc.* **2002**, *124*, 3622.
- [3] P.-e. Chabrier De Lassauniere, J. Harnett, D. Bigg, A.-M. Liberatore, J. Pommier, J. Lannoy, C. Thurieau, Z. X. Dong, Patent US 2005/0038087. 2005.
- [4] A. Nishinaga, T. Shimizu, Y. Toyoda, T. Matsuura, K. Hirotsu, *J. Org. Chem.* **1982**, *47*, 2278.
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- [7] D. Braun, B. Maier, *Makromol. Chem.* **1973**, *167*, 119.

¹H NMR spectrum of compound (5b)

STANDARD PROTON PARAMETERS

Solvent: cdcl3
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Operator: sjw
INOVA-500 "chem500"

Pulse 45.0 degrees
Acq. time 3.995 sec
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16 repetitions
OBSERVE H1, 499.6853746 MHz
DATA PROCESSING
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FT size 65536
Total time 1 min, 12 sec

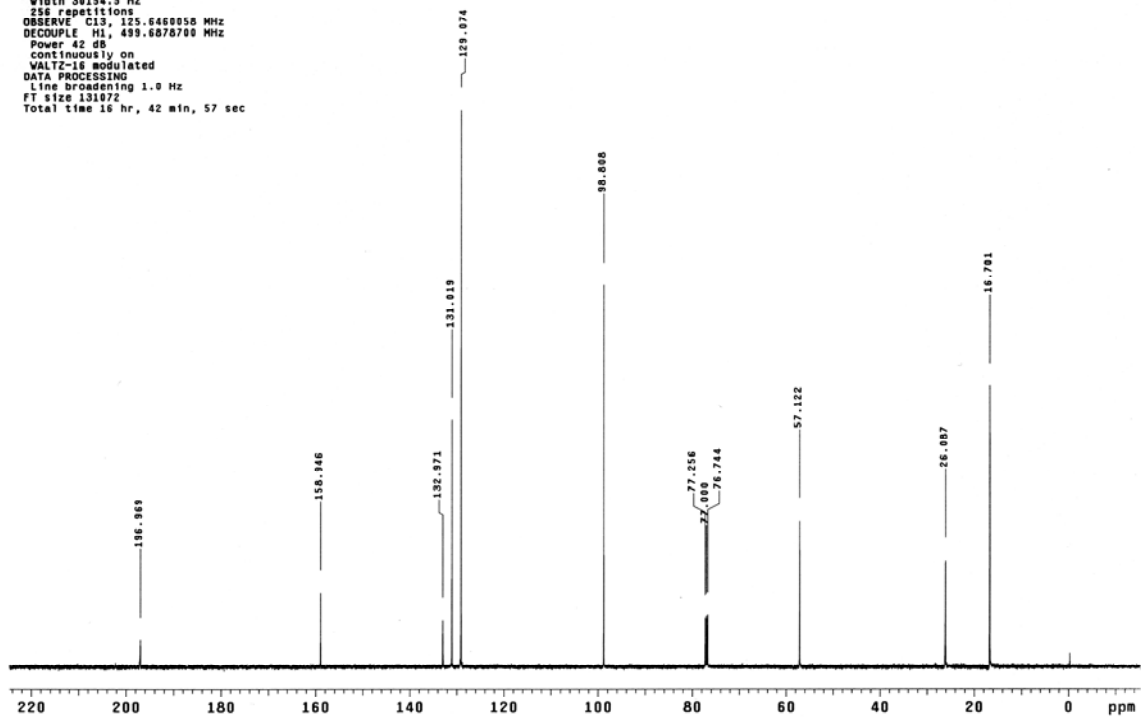


¹³C NMR spectrum

Std proton

Solvent: cdcl3
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Operator: sjw
INOVA-500 "chem500"

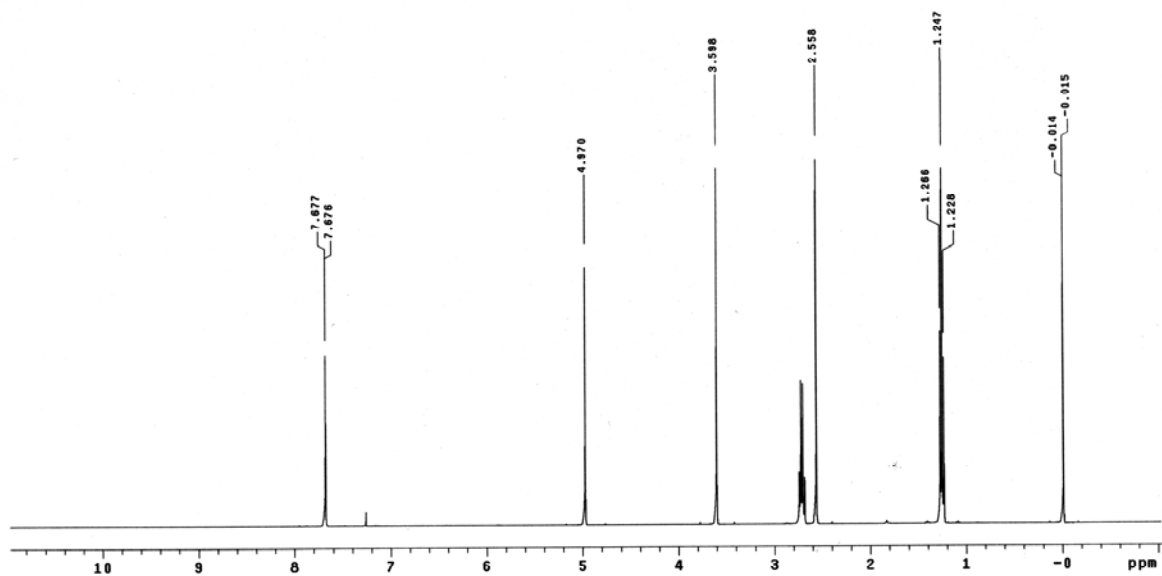
Relax. delay 1.500 sec
Pulse 45.0 degrees
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Width 30154.5 Hz
256 repetitions
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DECOUPLE H1, 499.6870700 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 16 hr, 42 min, 57 sec



¹H NMR spectrum of compound (5c)

HF1c2-1-141
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Operator: sjw
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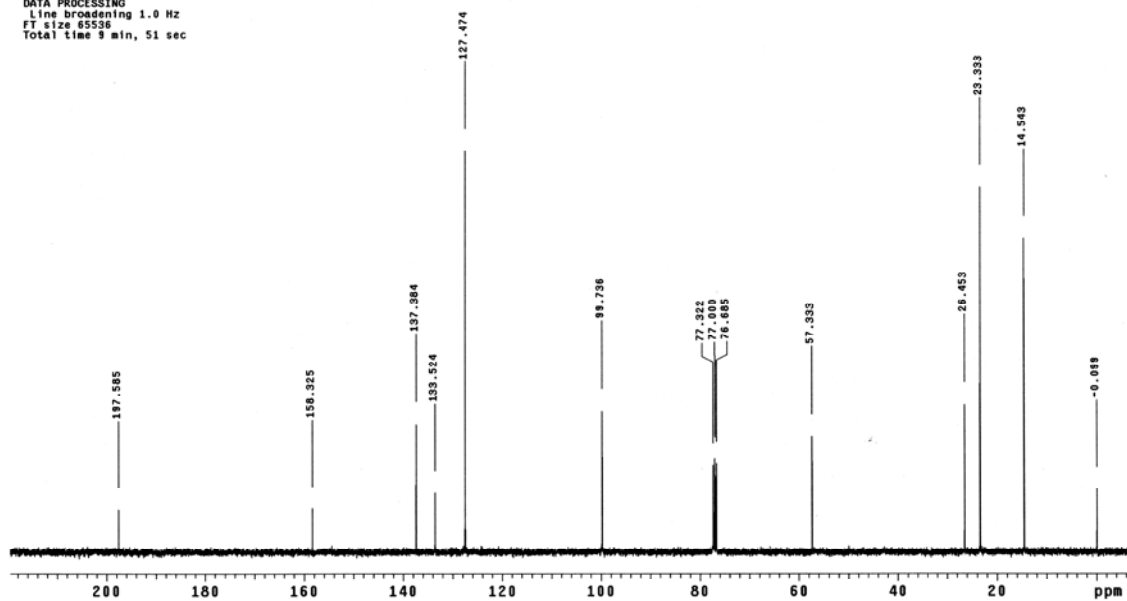
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 6395.9 Hz
32 repetitions
OBSERVE H1, 399.7506305 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 8 sec



¹³C NMR spectrum

Std proton
File: Carbon
Pulse Sequence: s2pul
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24125.5 Hz
64 repetitions
OBSERVE C13, 100.5173813 MHz
DECUPLE H1, 399.7526414 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 9 min, 51 sec

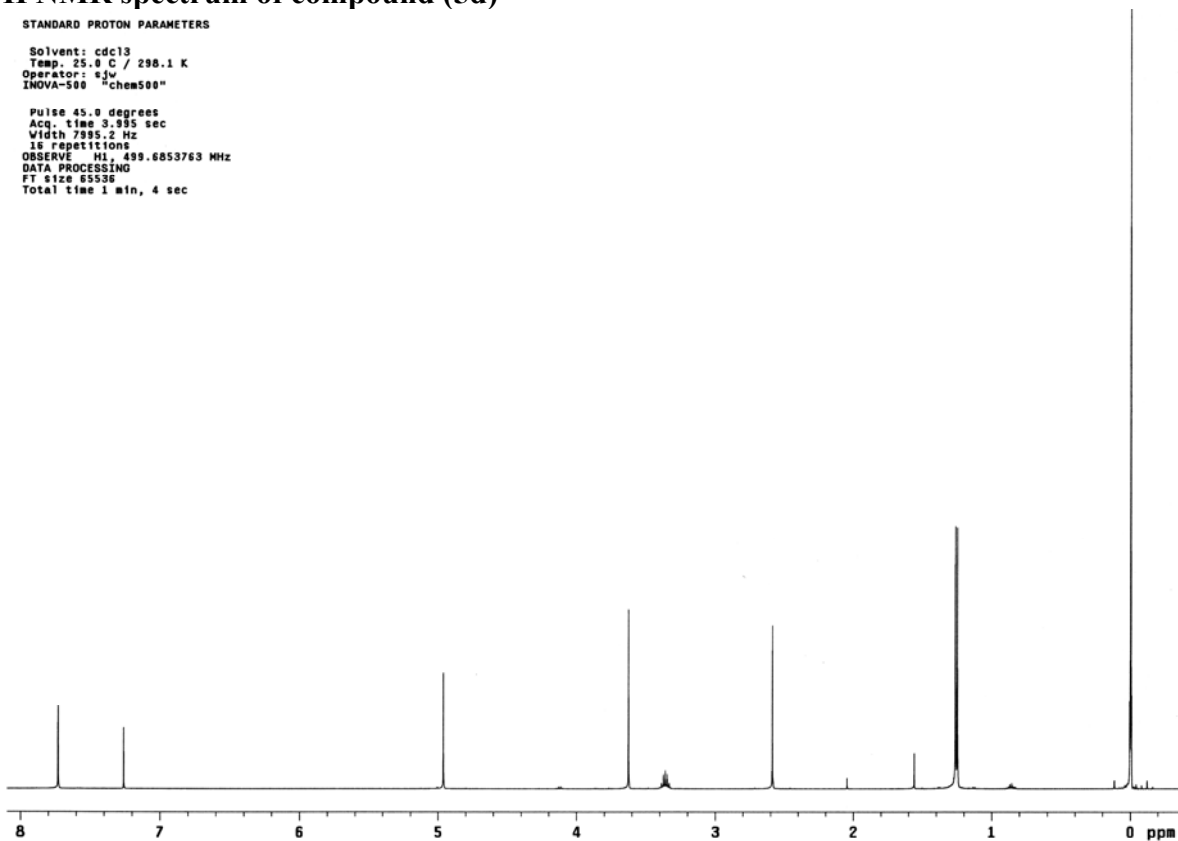


¹H NMR spectrum of compound (5d)

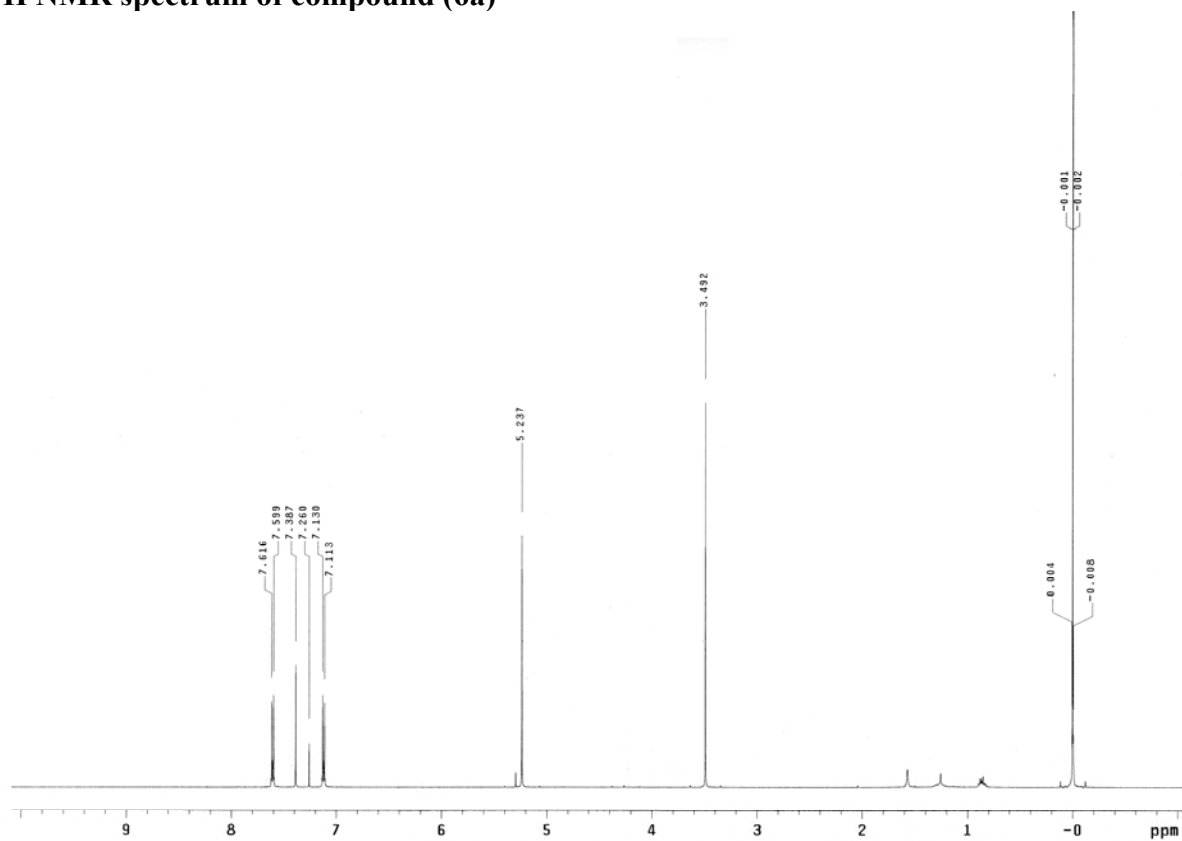
STANDARD PROTON PARAMETERS

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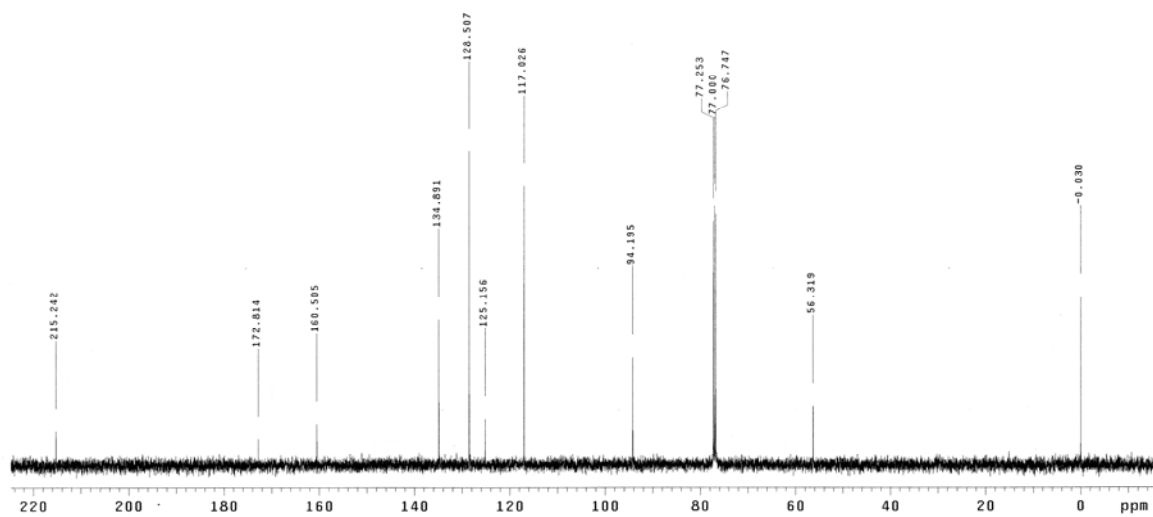
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DATA PROCESSING
FT size 65536
Total time 1 min, 4 sec



¹H NMR spectrum of compound (6a)



¹³C NMR spectrum

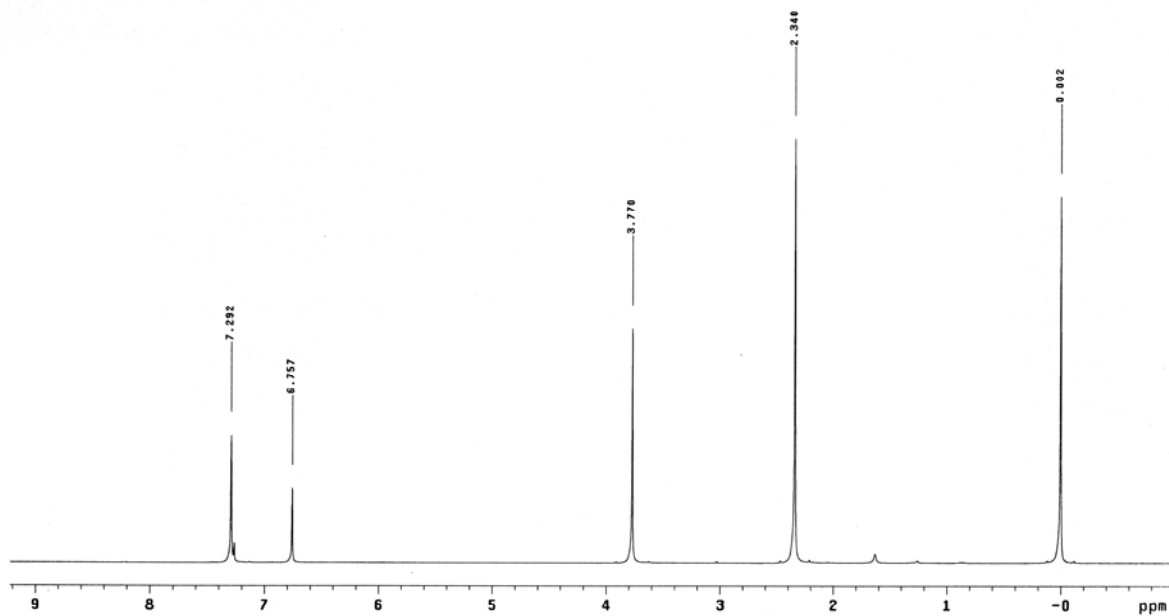


¹H NMR spectrum of compound (6b)

STANDARD PROTON PARAMETERS

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Temp. 25.0 C / 298.1 K
Operator: sjw
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Pulse 45.0 degrees
Acq. time 3.995 sec
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16 repetitions
OBSERVE H1, 499.6853715 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 6536
Total time 1 min, 12 sec

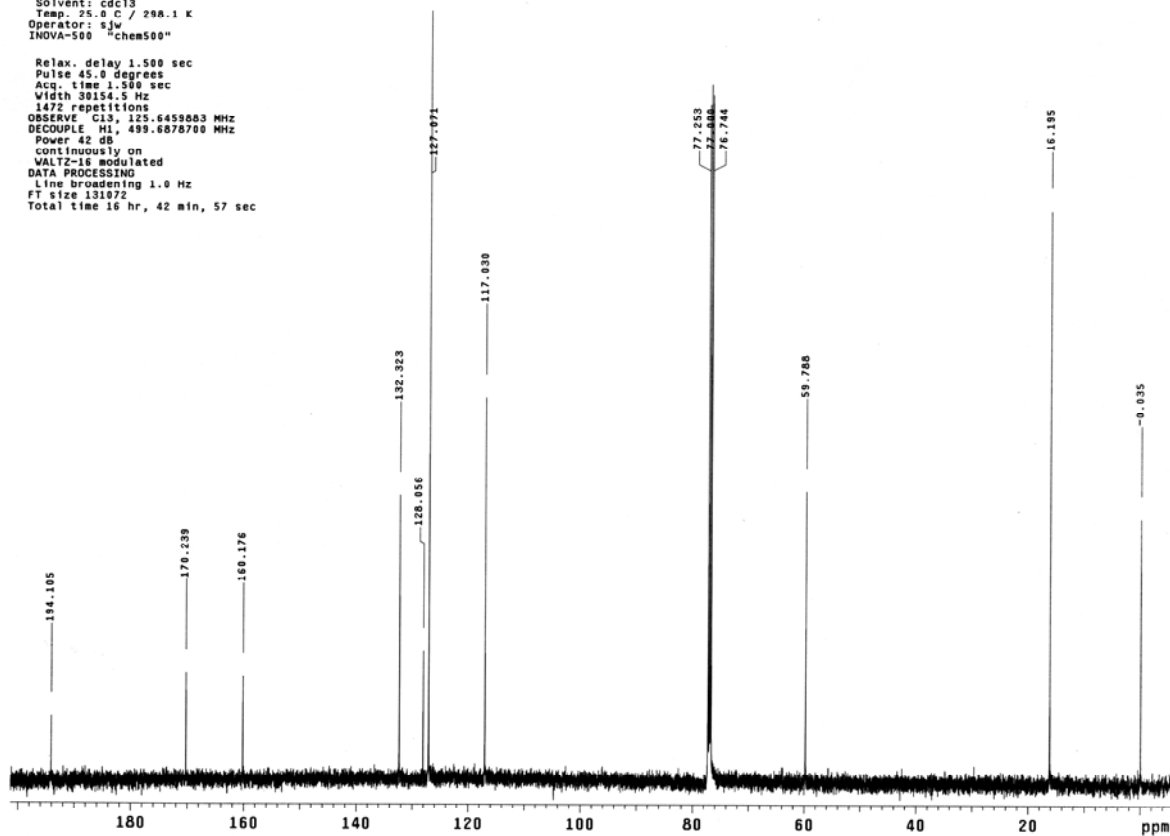


¹³C NMR spectrum

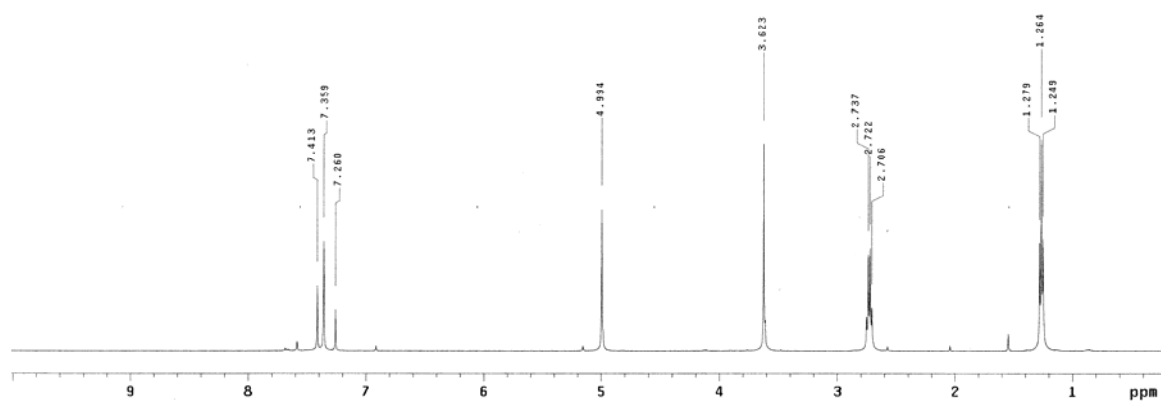
Std proton

Solvent: cdc13
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Operator: sjw
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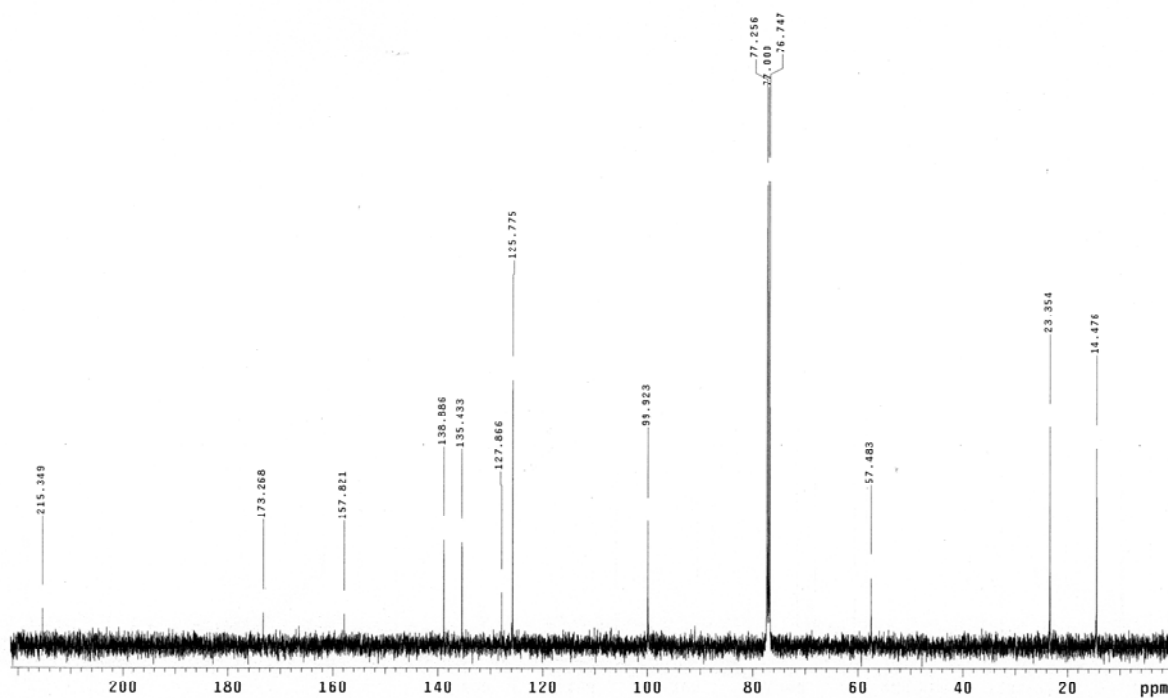
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1472 repetitions
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DECOUPLE H1, 499.6878700 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131972
Total time 16 hr, 42 min, 57 sec



¹H NMR spectrum of compound (6c)



¹³C NMR spectrum

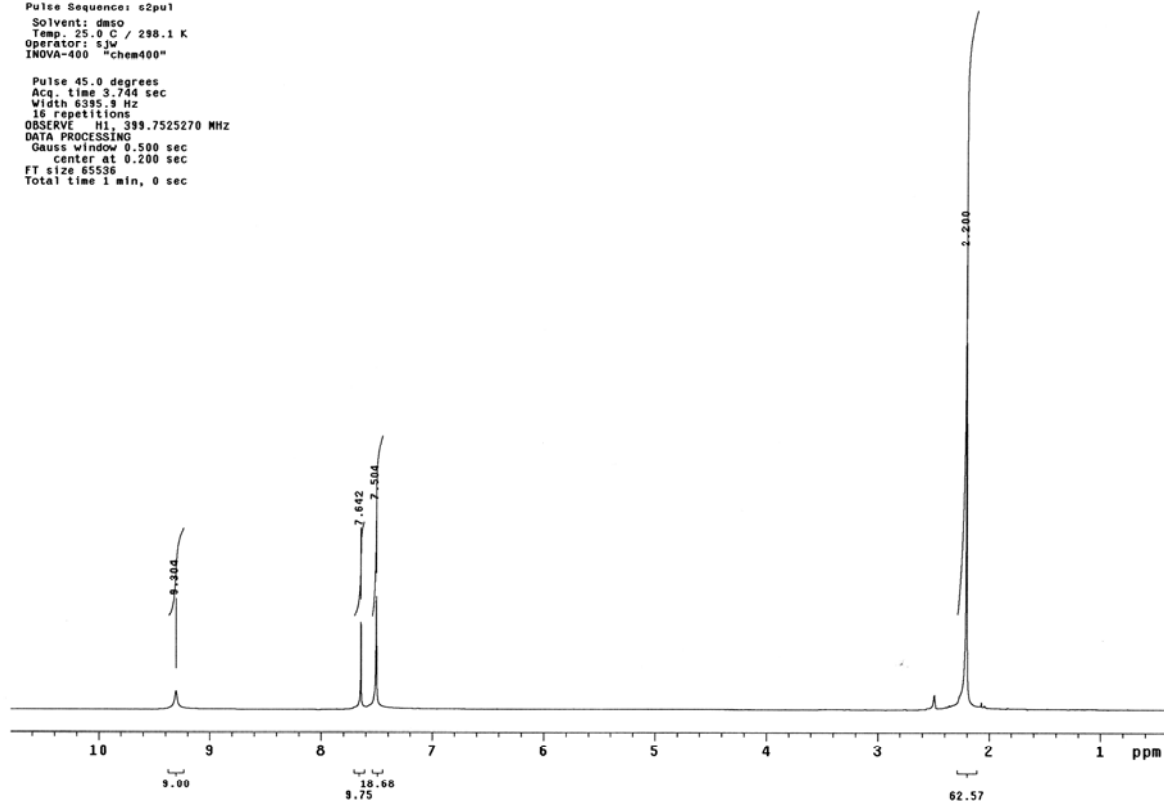


¹H NMR spectrum of compound (7b1)

Std proton

Sample: sy3-140
Pulse Sequence: s2pu1
Solvent: dms0
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"

Pulse 45.0 degrees
Acq. time 3.744 sec
Width 6395.9 Hz
16 repetitions
OBSERVE H1, 399.7525270 MHz
DATA PROCESSING
Gauss window 0.500 sec
Center at 0.200 sec
FT size 65536
Total time 1 min, 0 sec

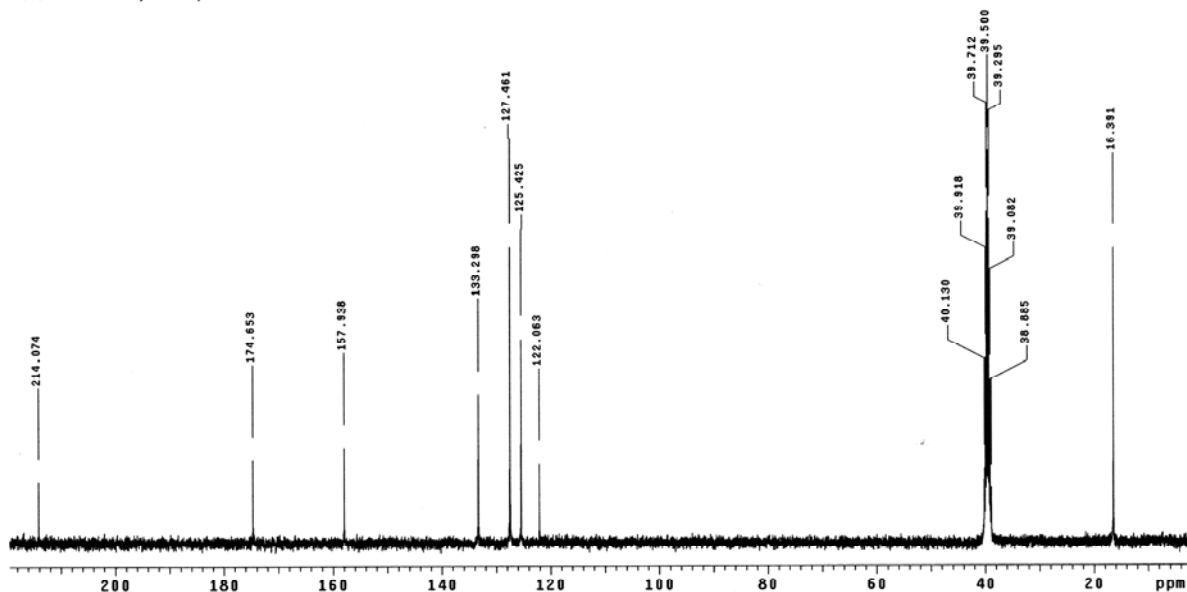


¹³C NMR spectrum

Std proton

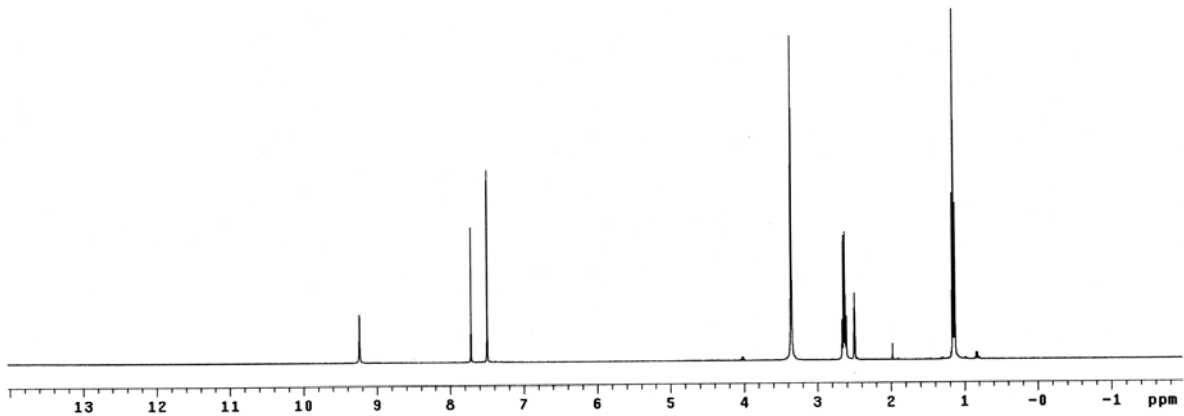
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Solvent: dms0
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Relax. delay 1.700 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24125.5 Hz
56 repetitions
OBSERVE C13, 100.5179027 MHz
DECOUPLE H1, 399.7545402 MHz
Power 44 db
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 16 hr, 42 min, 58 sec



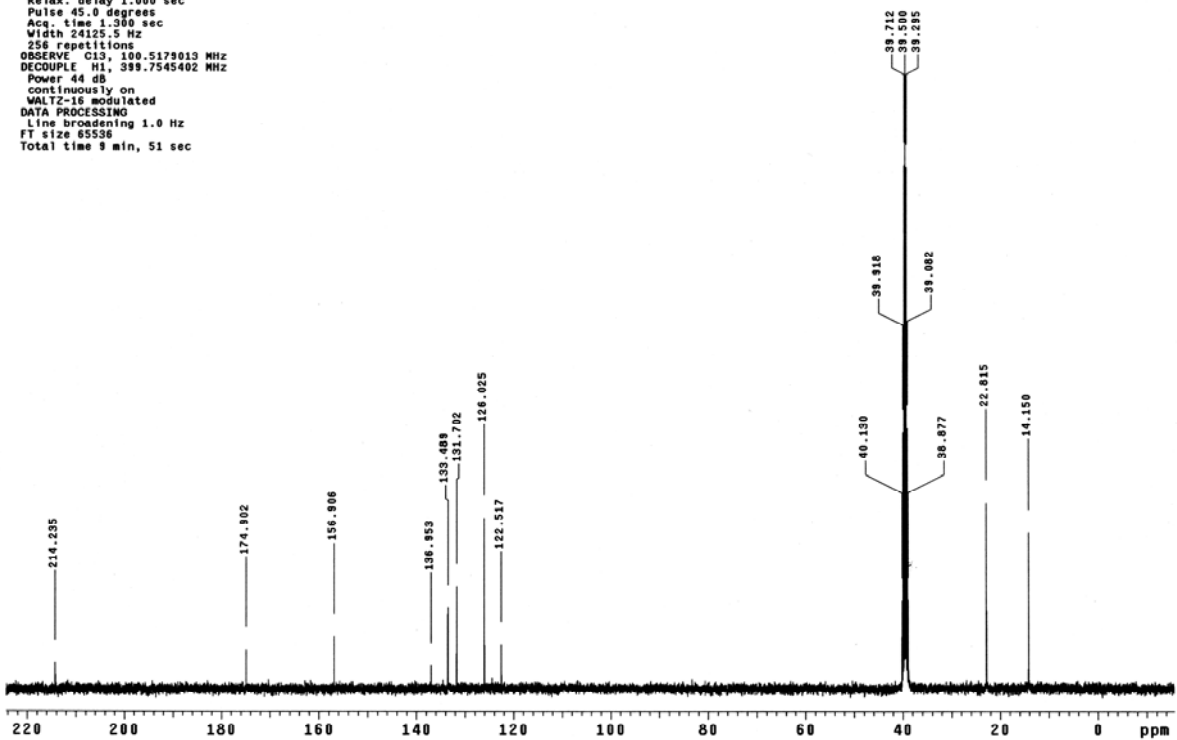
¹H NMR spectrum of compound (7c1)

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Pulse Sequence: s2pu1
Solvent: DMSO
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 6395.1 Hz
16 repetitions
OBSERVE H1, 399.7525272 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 8 sec



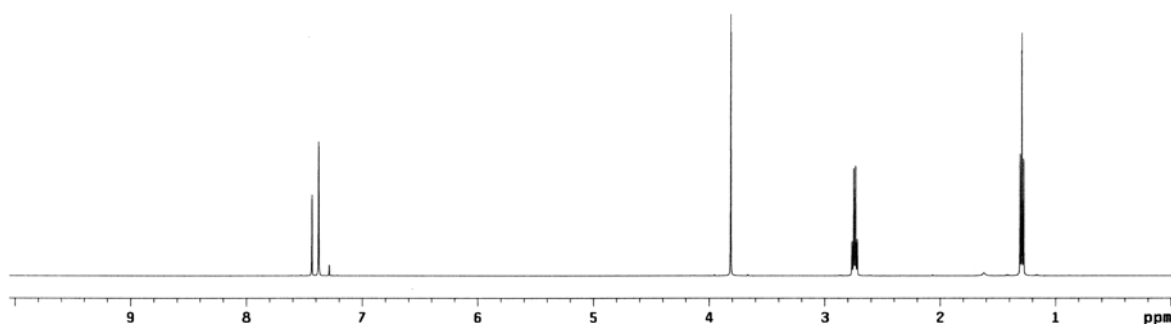
¹³C NMR spectrum

Std proton
File: Carbon
Pulse Sequence: s2pu1
Solvent: DMSO
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24125.5 Hz
256 repetitions
OBSERVE C13, 100.5179013 MHz
DECOUPLE H1, 399.7545402 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 9 min, 51 sec



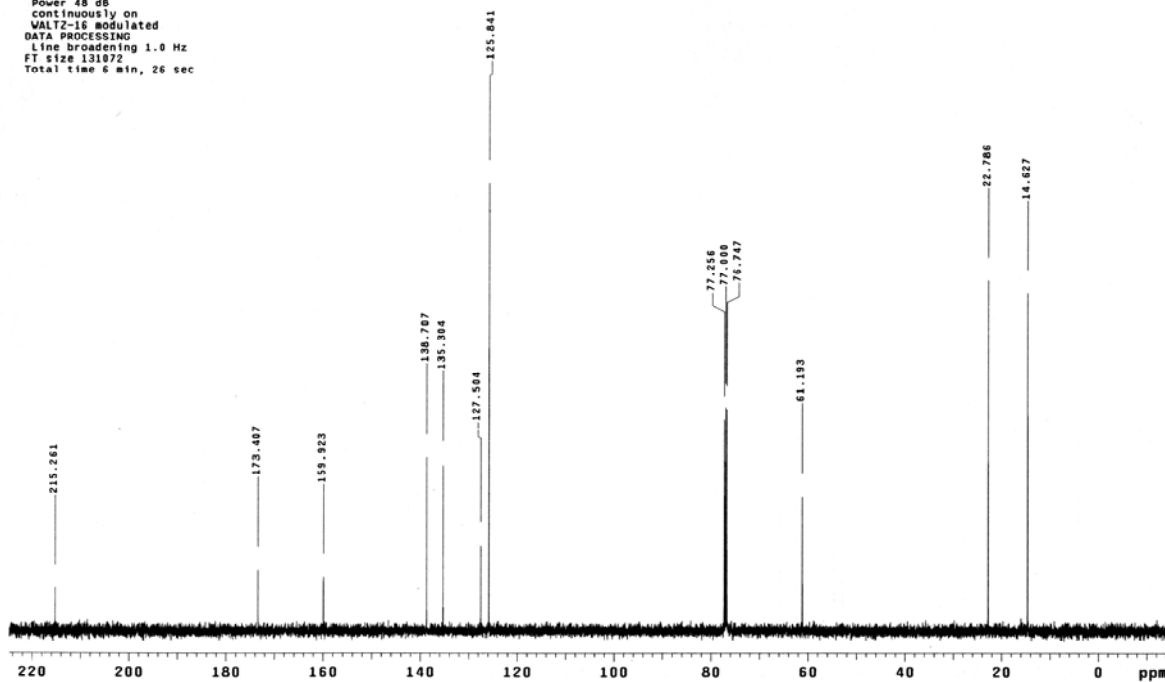
¹H NMR spectrum of compound (7c2)

Proton Standard Parameters
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Pulse Sequence: s2pu1
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
File: HFISZ-1-138H1
INOVA-500 "bios00"
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 8985.2 Hz
32 repetitions
OBSERVE H1, 500.2110797 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 8 sec



¹³C NMR spectrum

Carbon Standard Parameters
File: Carbon
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bios00"
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30188.7 Hz
64 repetitions
OBSERVE C13, 125.7781839 MHz
DECOUPLE H1, 500.2140810 MHz
Power 48 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 6 min, 26 sec

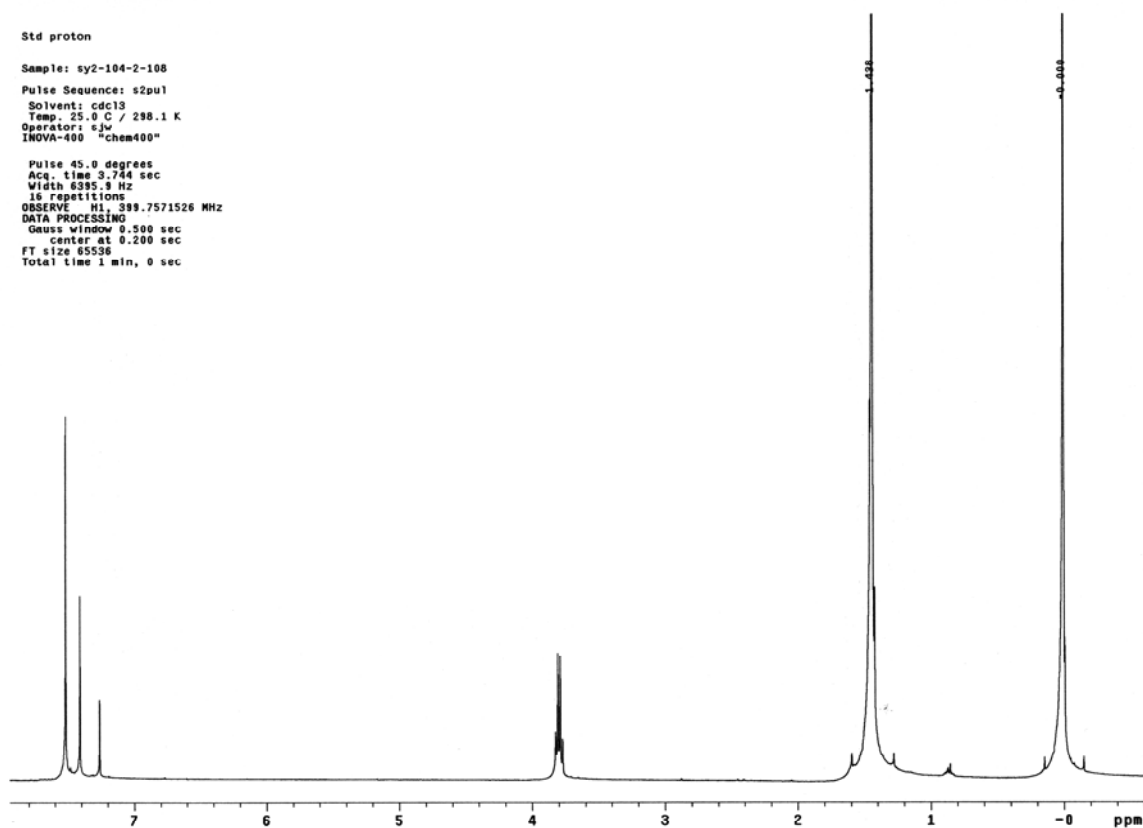


¹H NMR spectrum of compound (7e3)

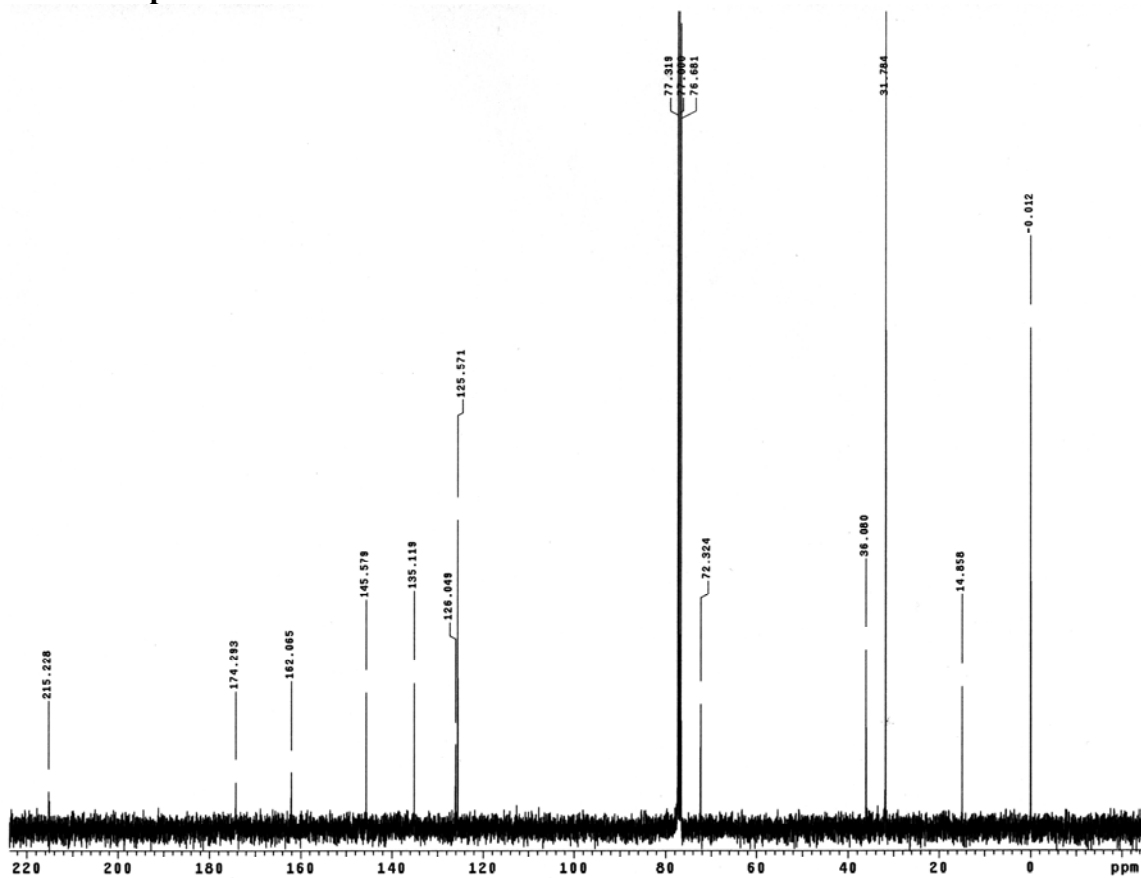
Std proton

Sample: sy2-104-2-108
Pulse Sequence: s2pu1
Solvent: cdc13
Temp: 25.0 C / 298.1 K
Operator: ejw
INOVA-400 "chem400"

Pulse 45.0 degrees
Acq. time 3.744 sec
Width 6385.9 Hz
16 repetitions
OBSERVE H1, 399.7571526 MHz
DATA PROCESSING
Gauss window 0.500 sec
center at 0.200 sec
FT size 65536
Total time 1 min, 0 sec



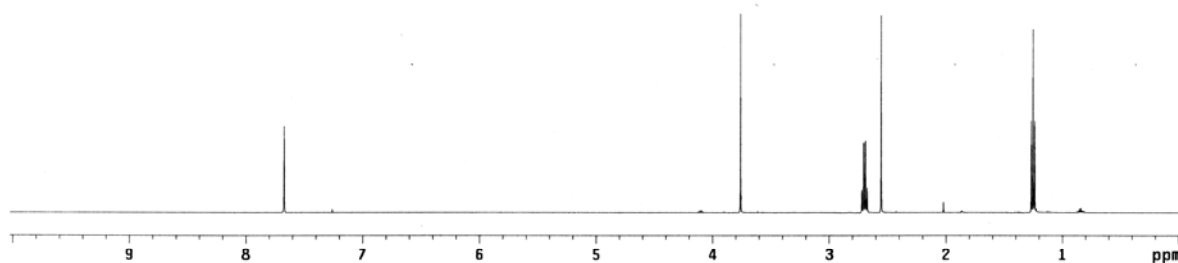
¹³C NMR spectrum



¹H NMR spectrum of compound (9c2)

Proton Standard Parameters
File: Proton
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Operator: eju
INOVA-500 "bio500"

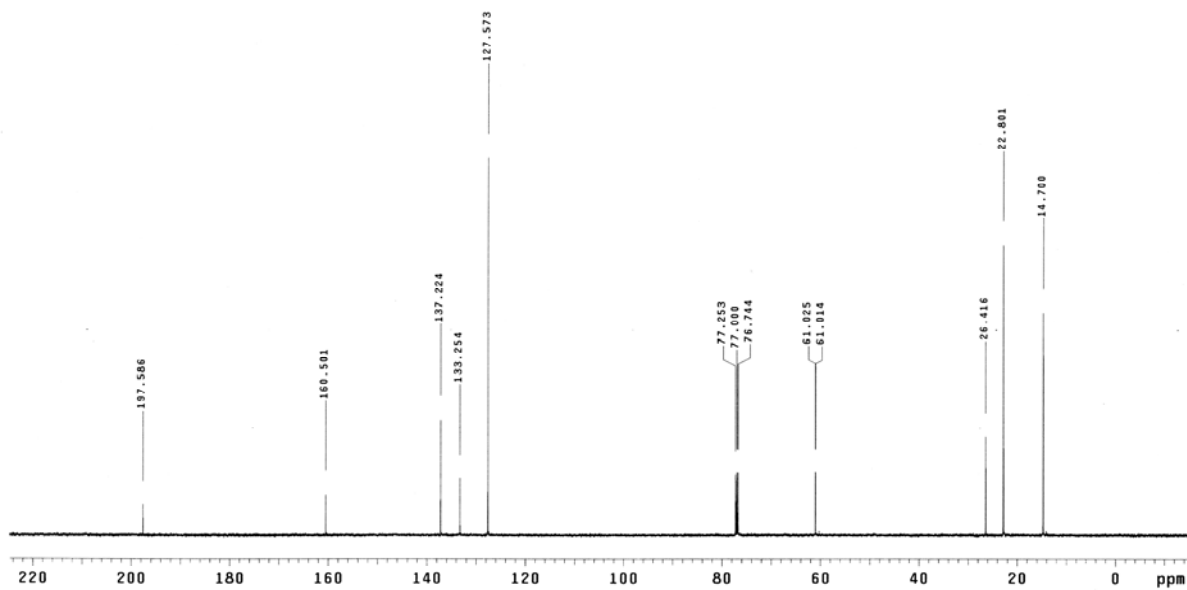
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 8003.2 Hz
32 repetitions
OBSERVE H1, 500.2110845 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 8 sec



¹³C NMR spectrum

Carbon Standard Parameters
File: Carbon
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Operator: eju
INOVA-500 "bio500"

Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30188.7 Hz
128 repetitions
OBSERVE C13, 125.7781844 MHz
DECOUPLE H1, 500.2140810 MHz
Power 48 dB
CONTINUOUSLY on
WALTZ-16 Modulated
DATA PROCESSING
Line Broadening 1.0 Hz
FT size 131072
Total time 6 min, 26 sec

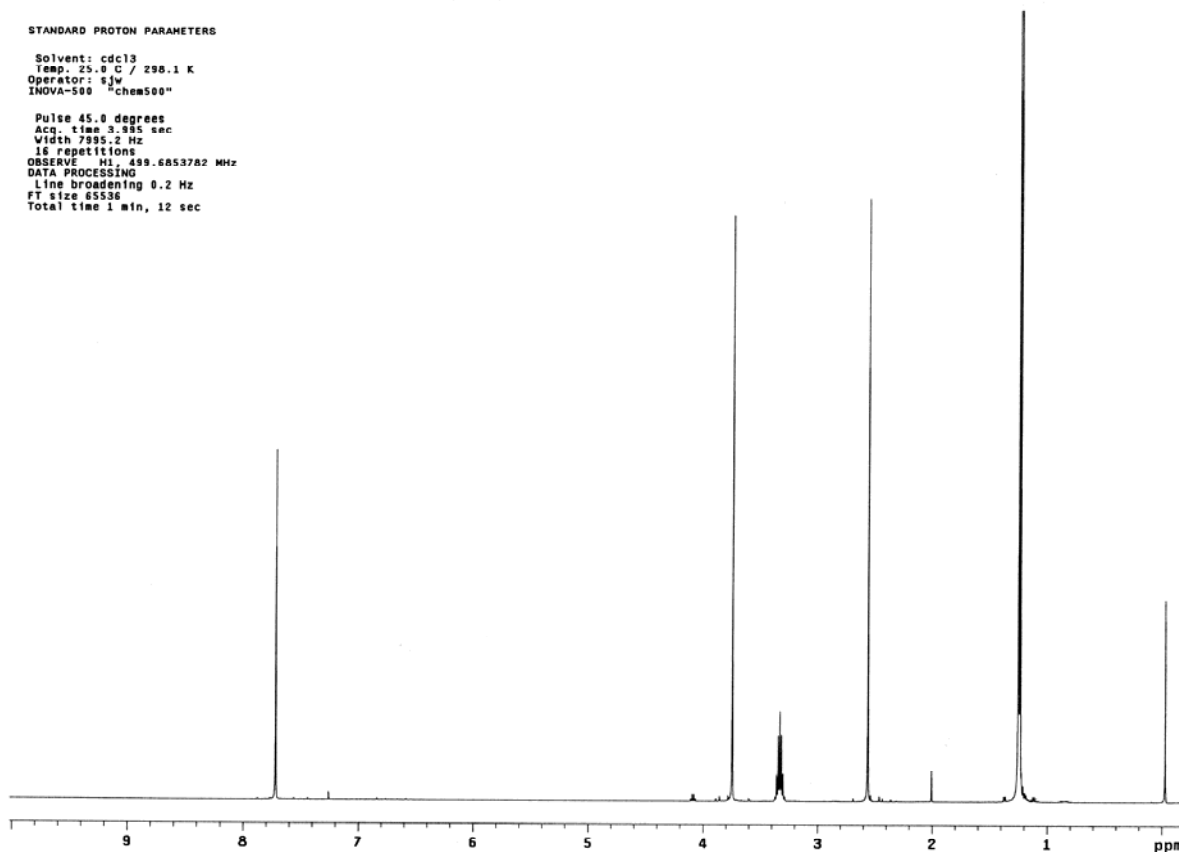


¹H NMR spectrum of compound (9d2)

STANDARD PROTON PARAMETERS

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "chem500"

Pulse 45.0 degrees
Acq. time 3.995 sec
Width 7995.2 Hz
16 repetitions
OBSERVE H1, 499.6853782 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min, 12 sec

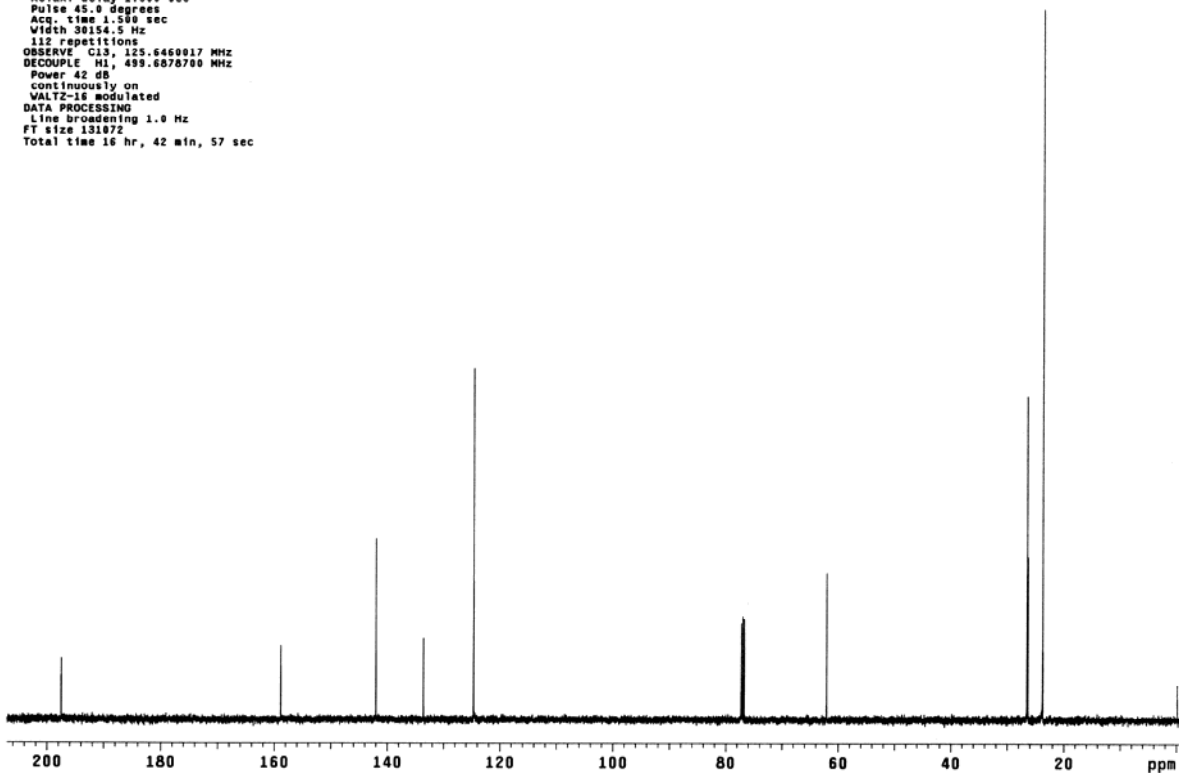


¹³C NMR spectrum

Std proton

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "chem500"

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 38154.5 Hz
112 repetitions
OBSERVE C13, 125.6460017 MHz
DECOUPLE H1, 499.6878700 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 16 hr, 42 min, 57 sec

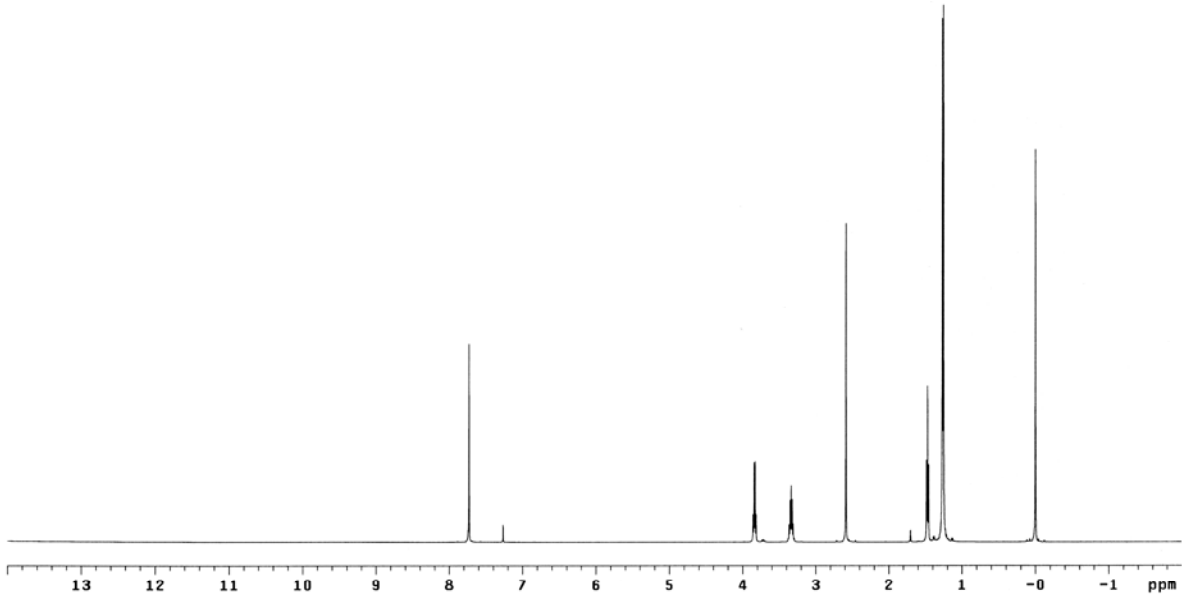


¹H NMR spectrum of compound (9d3)

STANDARD PROTON PARAMETERS

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "chem500"

Pulse 45.0 degrees
Acq. time 3.995 sec
Width 7995.2 Hz
0 repetitions
OBSERVE H1, 499.6053715 MH
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min, 12 sec

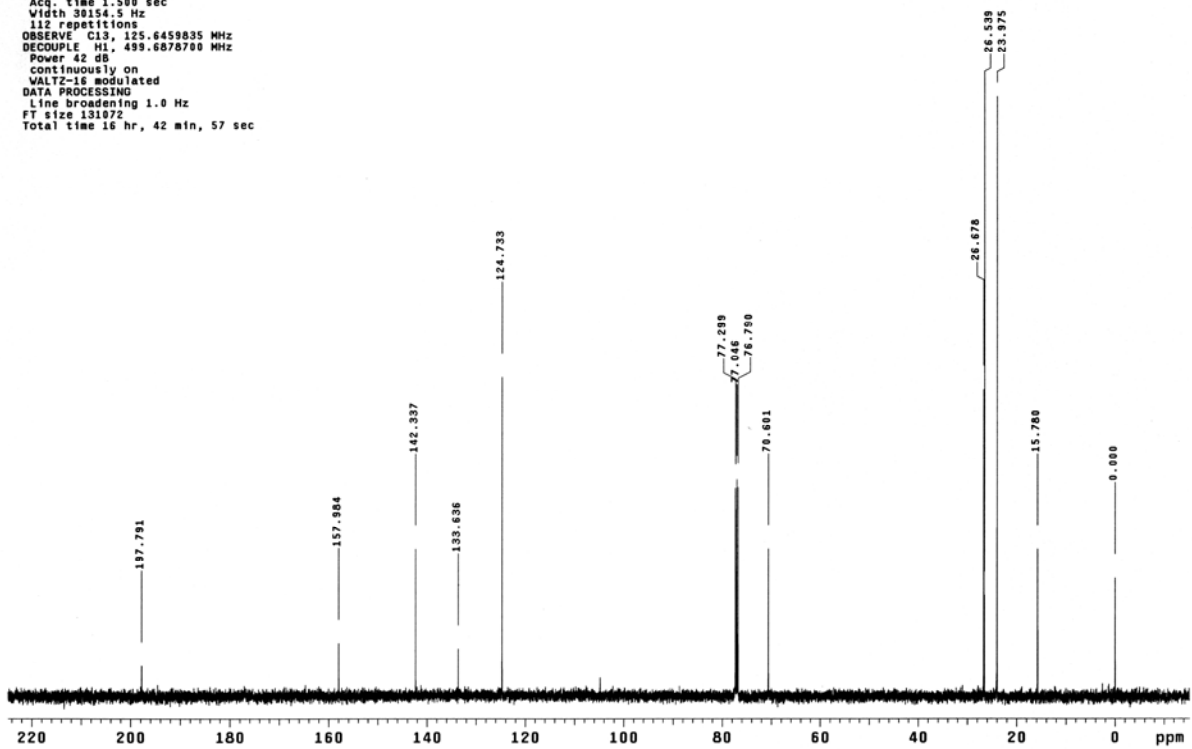


¹³C NMR spectrum

Std proton

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
File: HFISZ-1-75C13
INOVA-500 "chem500"

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30154.5 Hz
112 repetitions
OBSERVE C13, 125.6459835 MHz
DECUPLE H1, 499.6070700 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 16 hr, 42 min, 57 sec

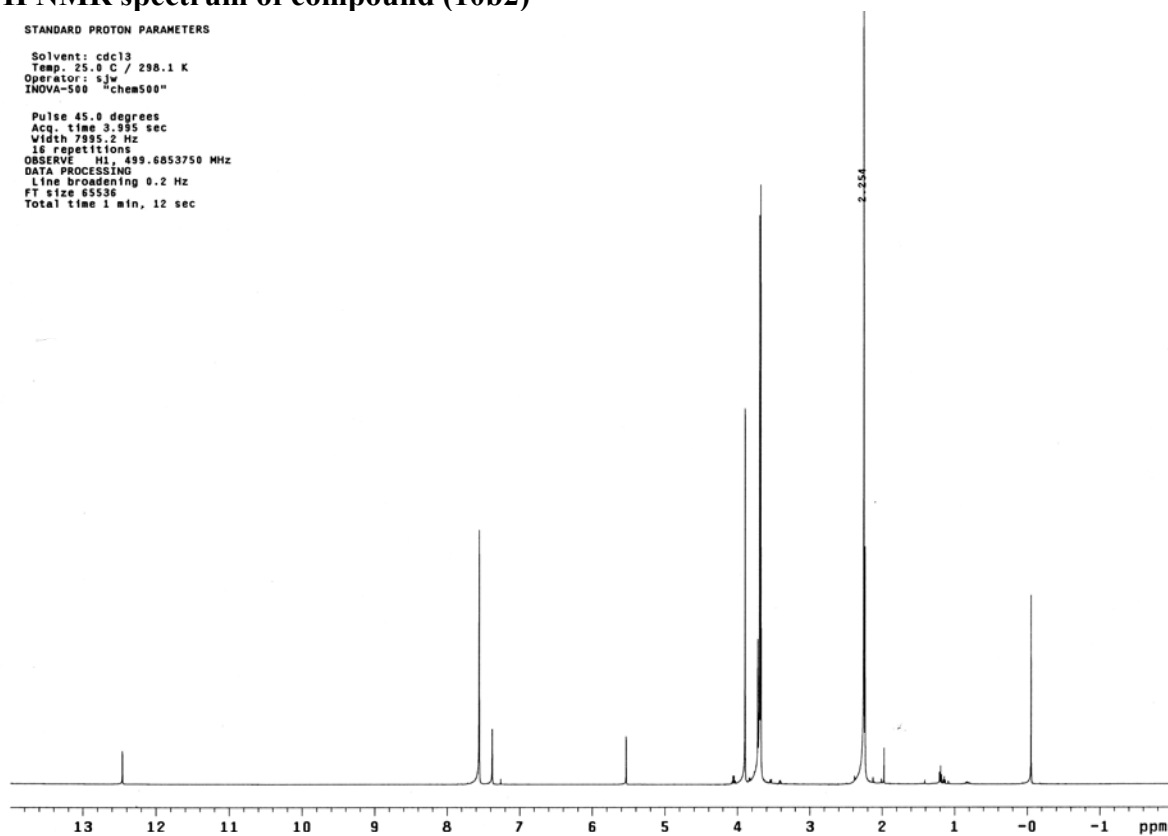


¹H NMR spectrum of compound (10b2)

STANDARD PROTON PARAMETERS

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "chem500"

Pulse 45.0 degrees
Acq. time 3.995 sec
Width 7995.2 Hz
15 repetitions
OBSERVE H1, 499.6853750 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min, 12 sec

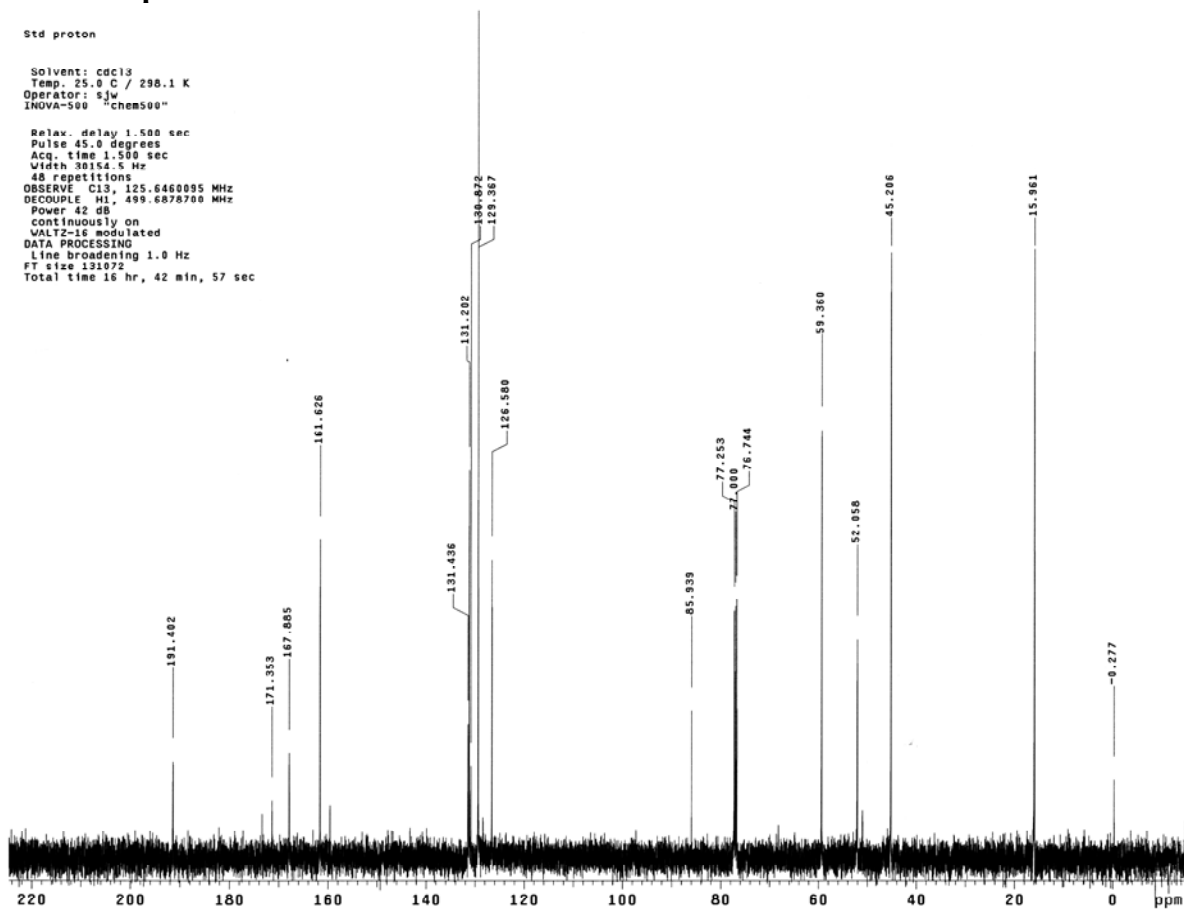


¹³C NMR spectrum

Std proton

Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "chem500"

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30154.5 Hz
48 repetitions
OBSERVE C13, 125.6460895 MHz
DECOUPLE H1, 499.6878709 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 121072
Total time 16 hr, 42 min, 57 sec

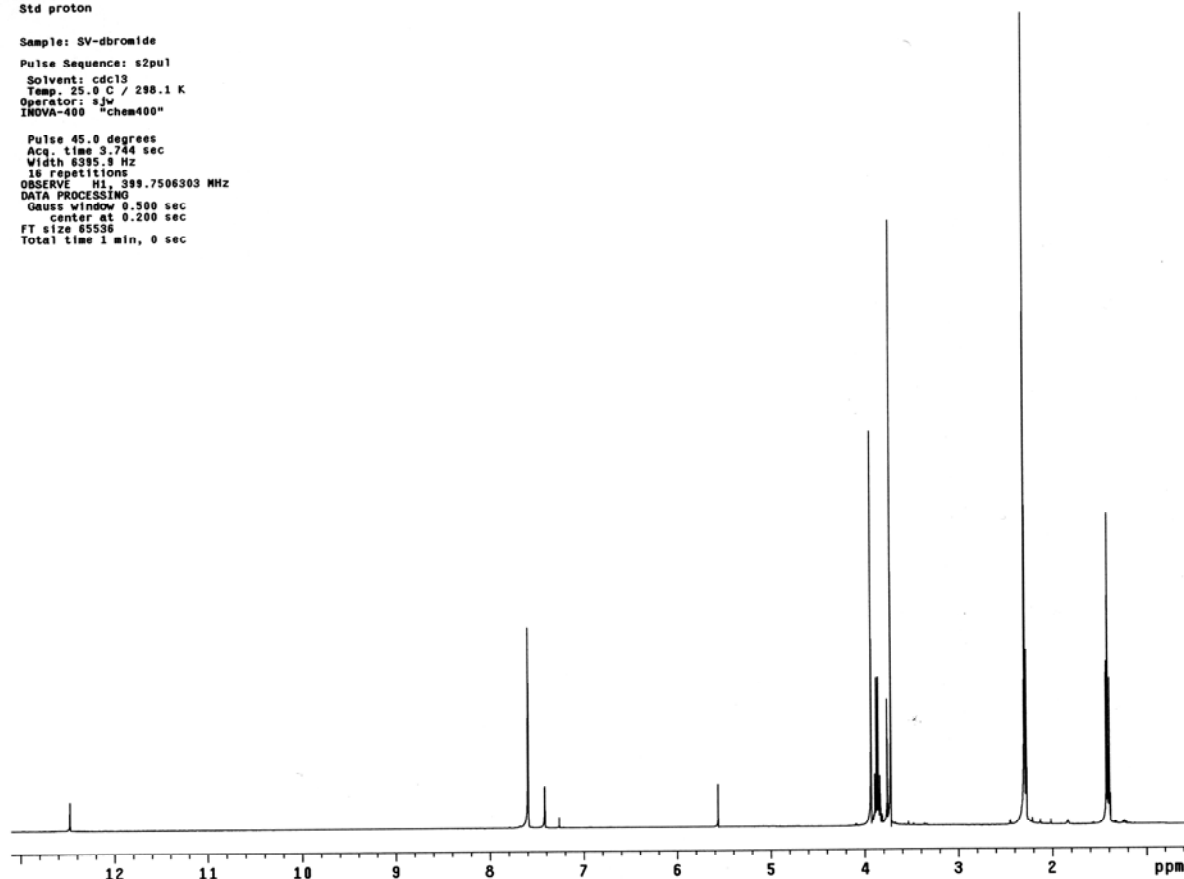


¹H NMR spectrum of compound (10b3)

Std proton

Sample: SV-dibromide
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"

Pulse 45.0 degrees
Acq. time 3.744 sec
Width 6395.9 Hz
18 repetitions
OBSERVE H1, 399.7506303 MHz
DATA PROCESSING
Gauss window 0.500 sec
center at 0.200 sec
FT size 65536
Total time 1 min, 0 sec

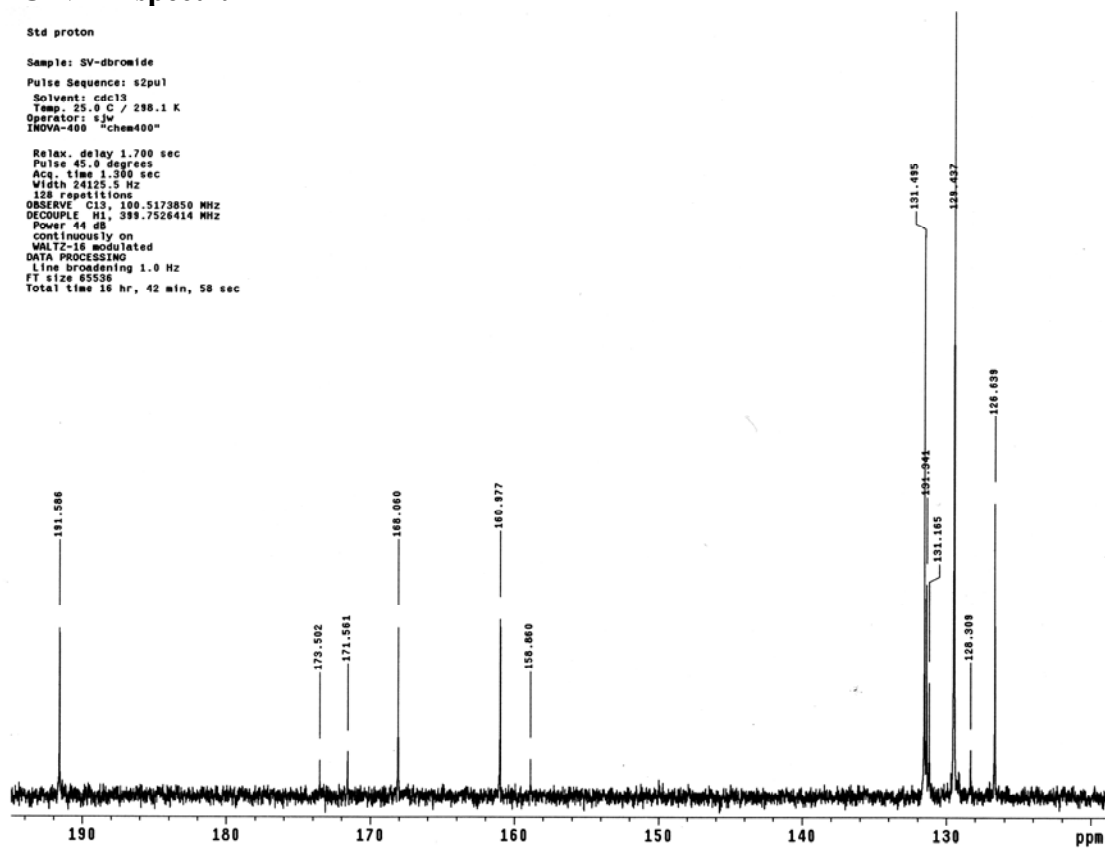


¹³C NMR spectrum

Std proton

Sample: SV-dibromide
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"

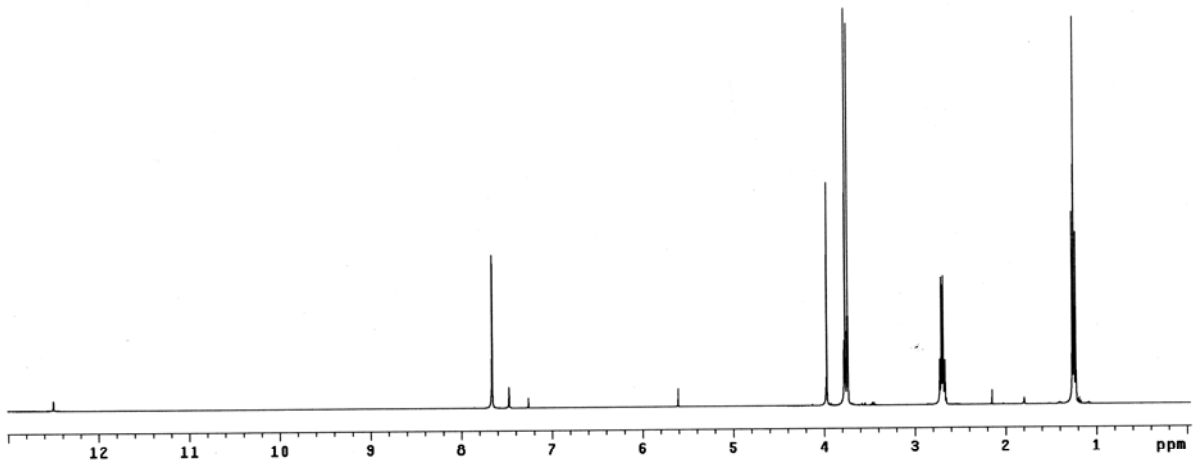
Relax. delay 1.700 sec
Pulse 45.0 degrees
Acq. time 1.360 sec
Width 24125.5 Hz
128 repetitions
OBSERVE C13, 100.5173850 MHz
DECOUPLE H1, 399.7526414 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 16 hr, 42 min, 58 sec



¹H NMR spectrum of compound (10c3)

Std proton

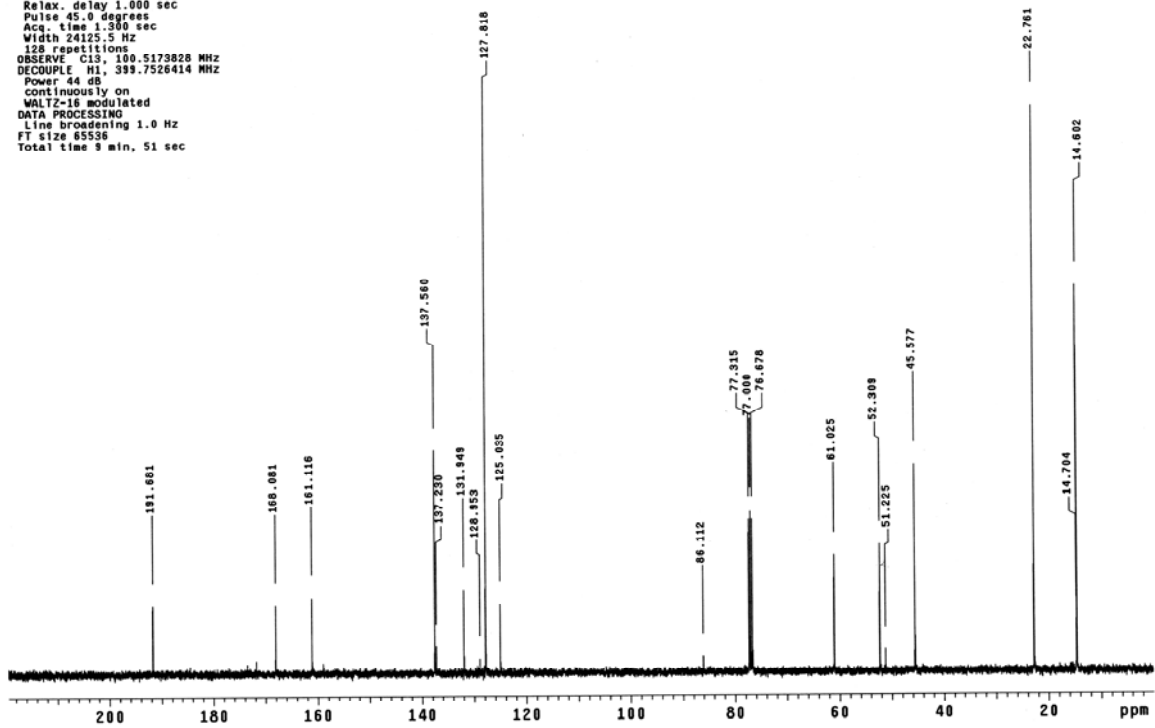
File: Proton
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 6295.5 Hz
24 repetitions
OBSERVE H1, 399.7506305 MHz
DATA PROCESSING
FT size 65536
Total time 2 min, 8 sec



¹³C NMR spectrum

Std proton

File: Carbon
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24125.5 Hz
128 repetitions
OBSERVE C13, 100.5173828 MHz
DECOUPLE H1, 399.7526414 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 5 min, 51 sec

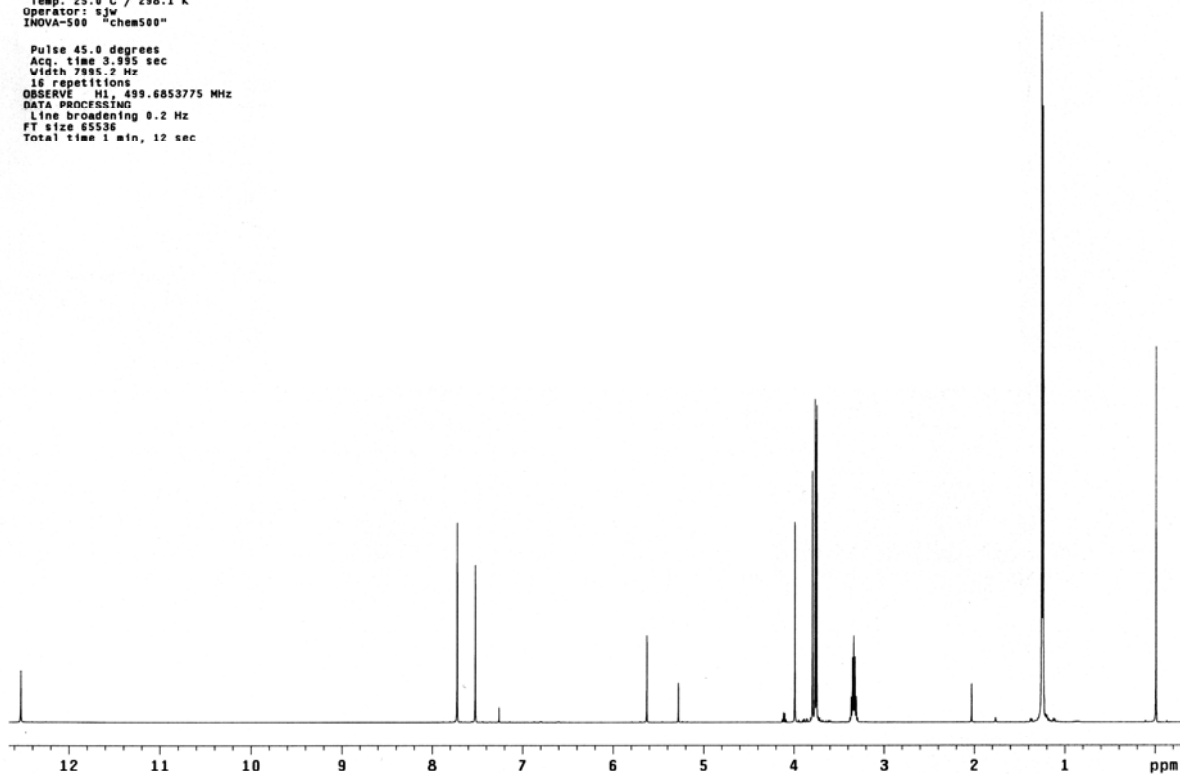


¹H NMR spectrum of compound (10d2)

STANDARD PROTON PARAMETERS

Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INNOVA-500 "chem500"

Pulse 45.0 degrees
Acq. time 3.995 sec
Width 7995.2 Hz
16 repetitions
OBSERVE H1, 499.6853775 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 1 min, 12 sec

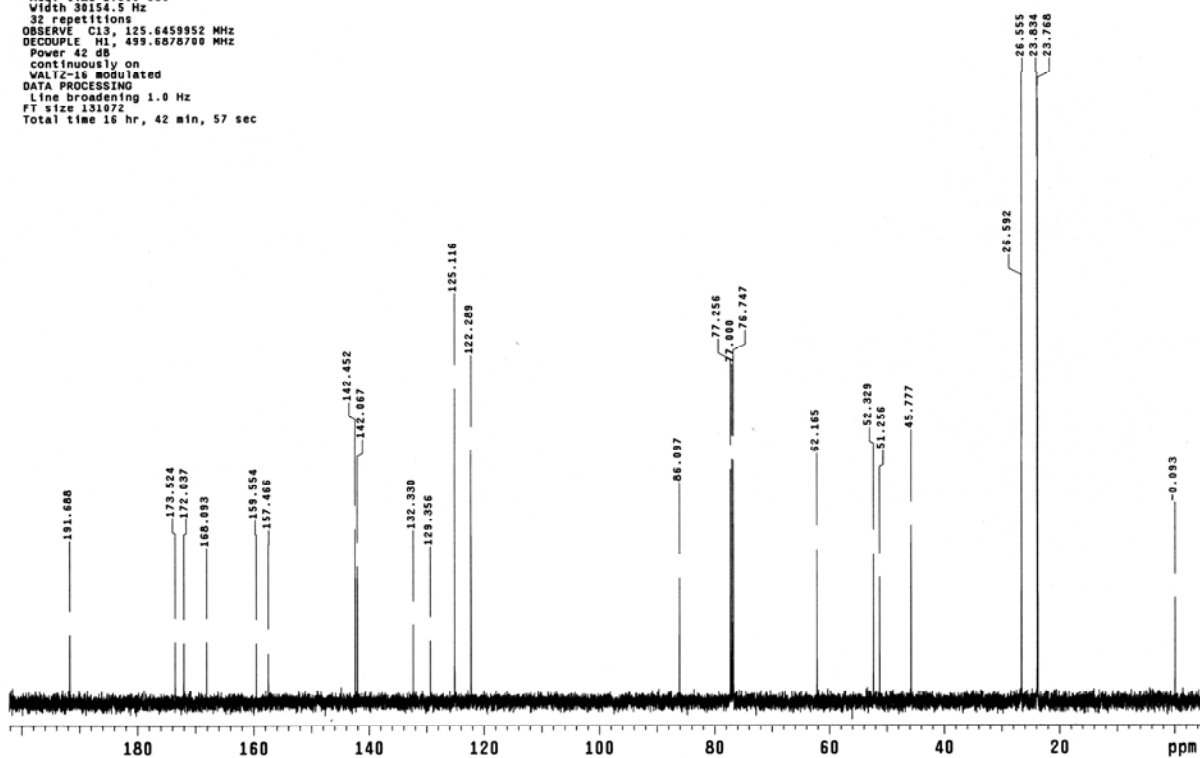


¹³C NMR spectrum

Std proton

Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INNOVA-500 "chem500"

Relax. delay 1.500 sec
Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30154.5 Hz
32 repetitions
OBSERVE C13, 125.6459952 MHz
DECOUPLE H1, 499.6878700 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 16 hr, 42 min, 57 sec

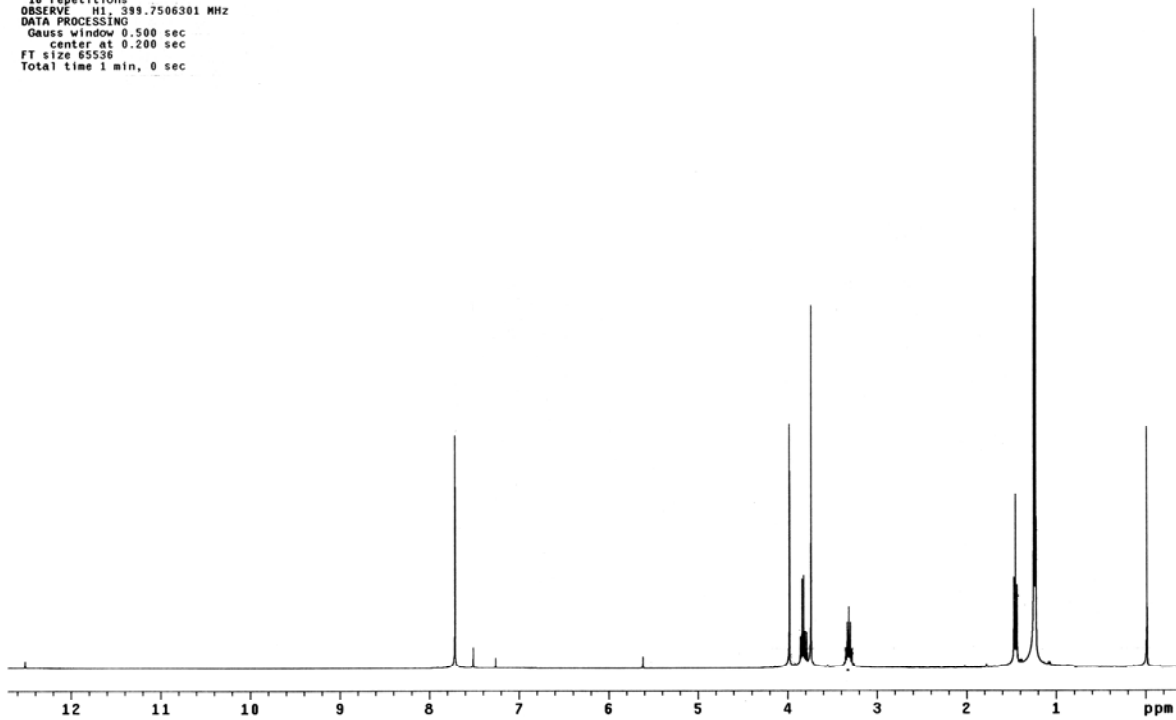


¹H NMR spectrum of compound (10d3)

Std proton

Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INNOVA-400 "chem400"

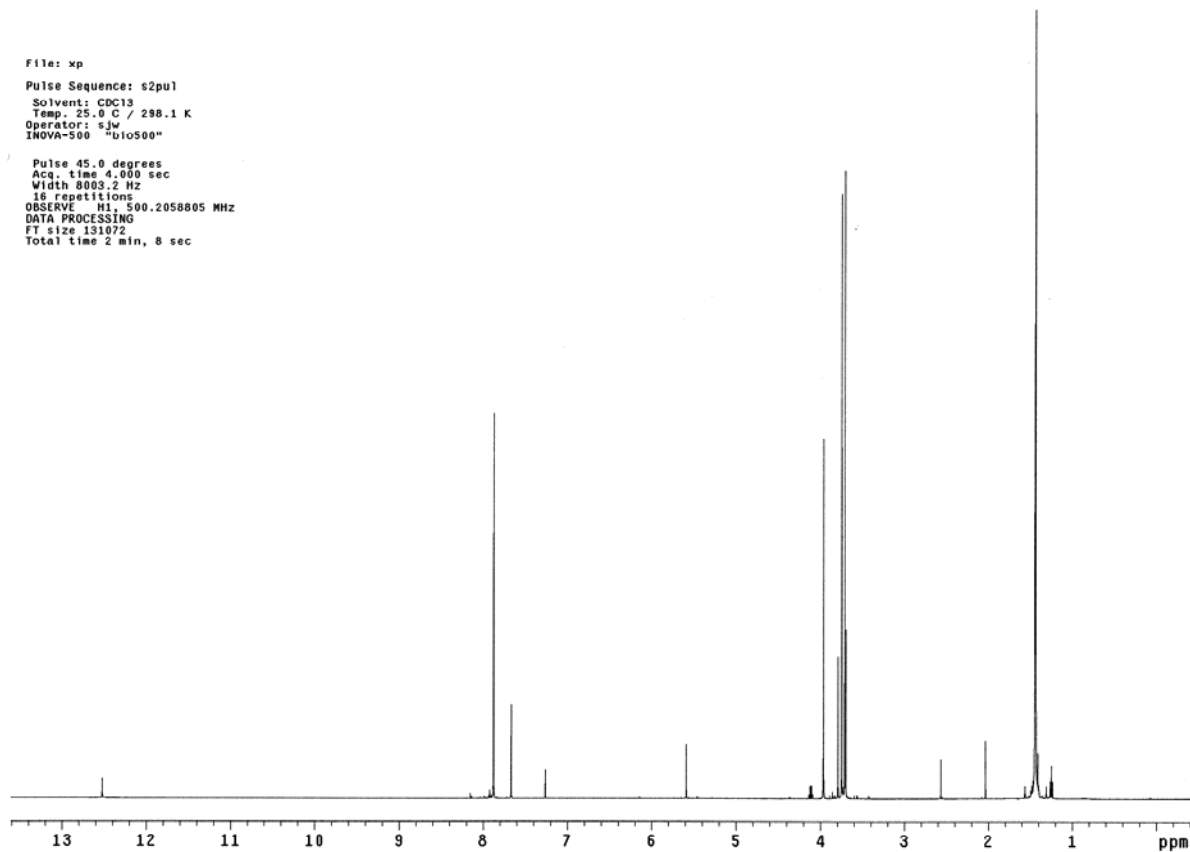
Pulse 45.0 degrees
Acq. time 3.744 sec
Width 6395.9 Hz
16 repetitions
OBSERVE H1, 399.7506301 MHz
DATA PROCESSING
Gauss window 0.500 sec
center at 0.200 sec
FT size 65536
Total time 1 min, 0 sec



¹H NMR spectrum of compound (10e2)

File: xp
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"

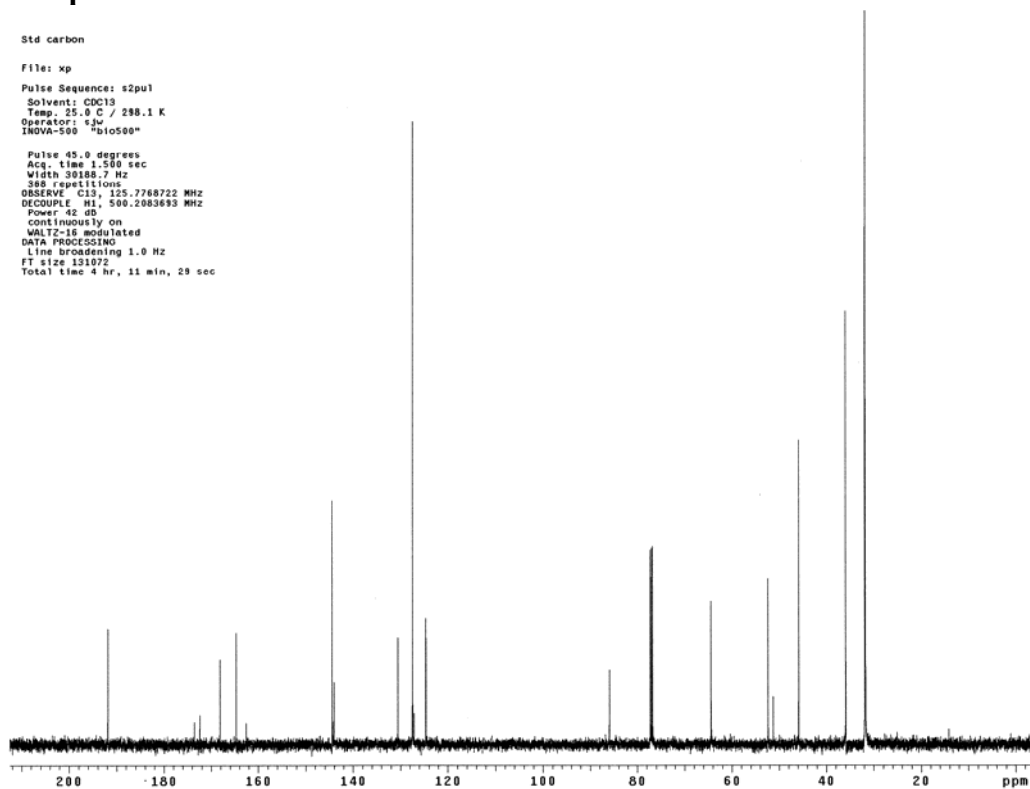
Pulse 45.0 degrees
Acq. time 4.000 sec
Width 8003.2 Hz
16 repetitions
OBSERVE H1, 500.2058805 MHz
DATA PROCESSING
FT size 131072
Total time 2 min, 8 sec



¹³C NMR spectrum

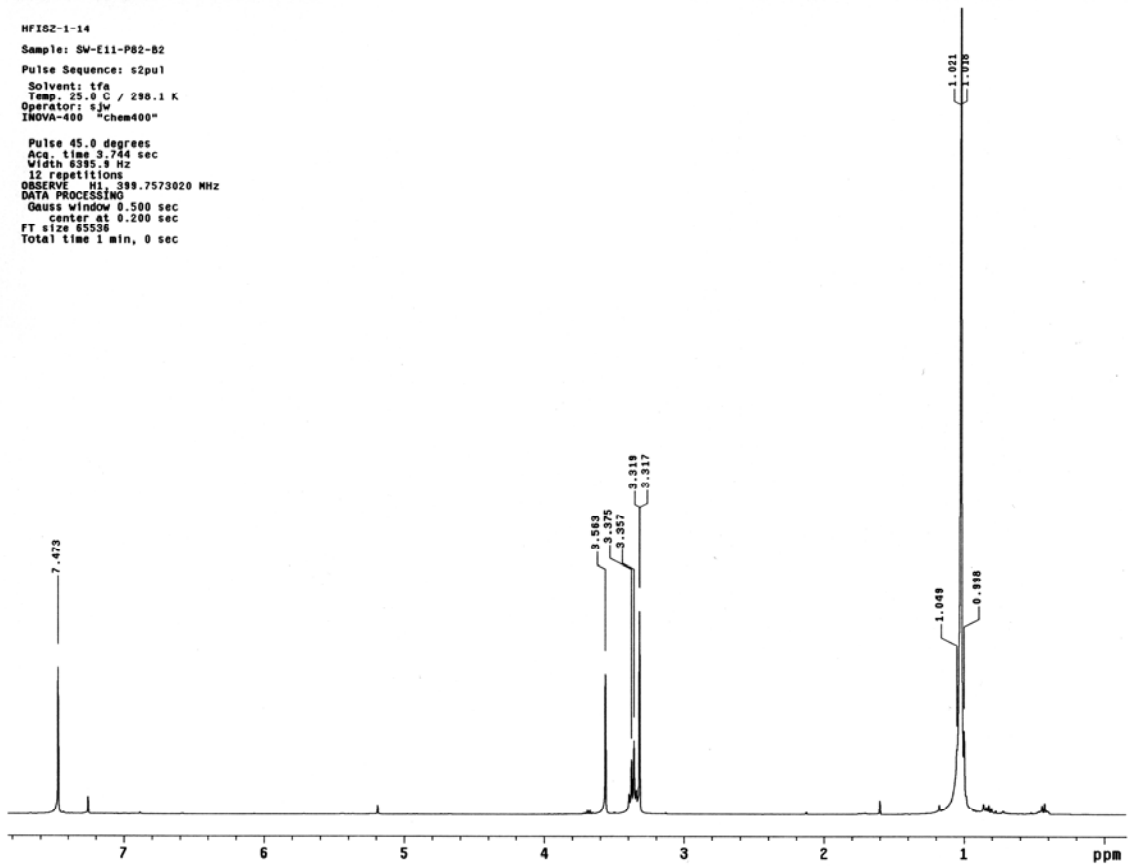
Std carbon
File: xp
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"

Pulse 45.0 degrees
Acq. time 1.500 sec
Width 30188.7 Hz
388 repetitions
OBSERVE C13, 125.7768722 MHz
DECUPLE H1, 500.2083693 MHz
Power 42 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 131072
Total time 4 hr, 11 min, 29 sec



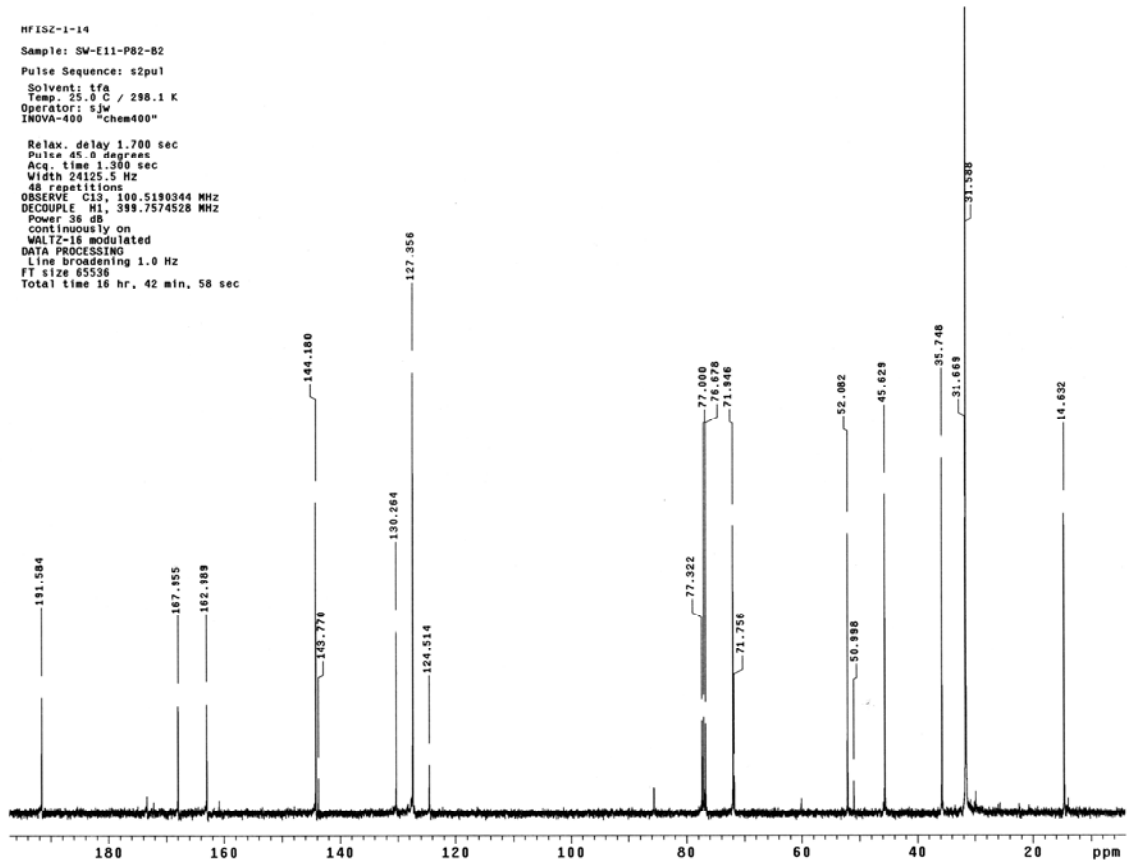
¹H NMR spectrum of compound (10e3)

HF162-1-14
Sample: SW-E11-P82-B2
Pulse Sequence: s2pu1
Solvent: tfa
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"
Pulse 45.0 degrees
Acq. time 3.744 sec
Width 8585.9 Hz
12 repetitions
OBSERVE M1, 399.7573020 MHz
DATA PROCESSING
Gauss window 0.500 sec
center at 0.200 sec
FT size 65536
Total time 1 min, 0 sec



¹³C NMR spectrum

HF162-1-14
Sample: SW-E11-P82-B2
Pulse Sequence: s2pu1
Solvent: tfa
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-400 "chem400"
Relax. delay 1.700 sec
Pulse 45.0 degrees
Acq. time 1.300 sec
Width 24125.5 Hz
48 repetitions
OBSERVE C13, 100.5190344 MHz
DECOUPLE M1, 399.7574528 MHz
Power 36 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 65536
Total time 16 hr, 42 min, 58 sec



¹H NMR spectrum of compound (11)

Std proton

Sample: nm-1-94-fraci4

Pulse Sequence: s2pu1

Solvent: cdcl3

Temp: 24.0 C / 297.1 K

Operator: sjw

INOVA-500 "chem500"

Pulse 45.0 degrees

Acq. time 4.000 sec

Width 7995.2 Hz

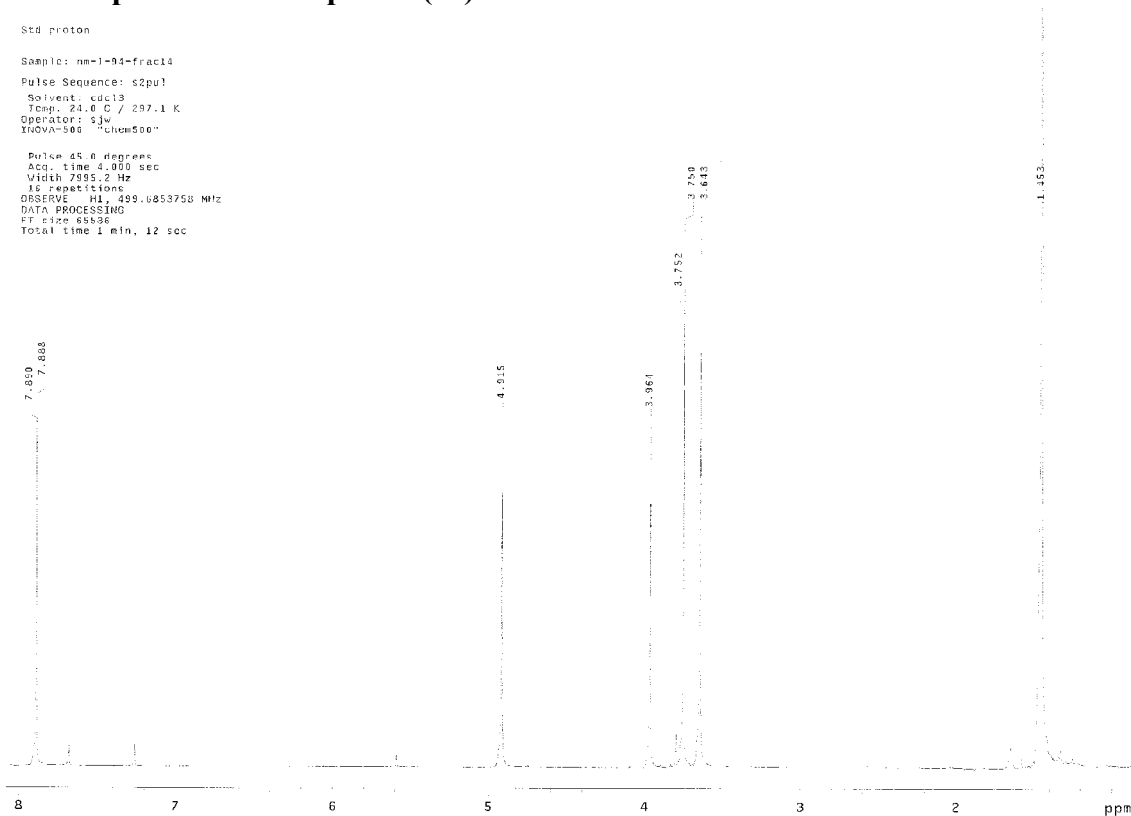
16 repetitions

OBSERVE H1, 499.0853750 MHz

DATA PROCESSING

FT size 65536

Total time 1 min, 12 sec



¹³C NMR spectrum

Std proton

Sample: nm-1-94-fraci4

Pulse Sequence: s2pu1

Solvent: cdcl3

Temp: 24.0 C / 297.1 K

Operator: sjw

INOVA-500 "chem500"

Relax. delay 1.000 sec

Pulse 45.0 degrees

Acq. time 1.500 sec

Width 30154.5 Hz

960 repetitions

OBSERVE C13, 125.6459566 MHz

DECOUPLE H1, 499.6878700 MHz

Power 33 dB

continuously on

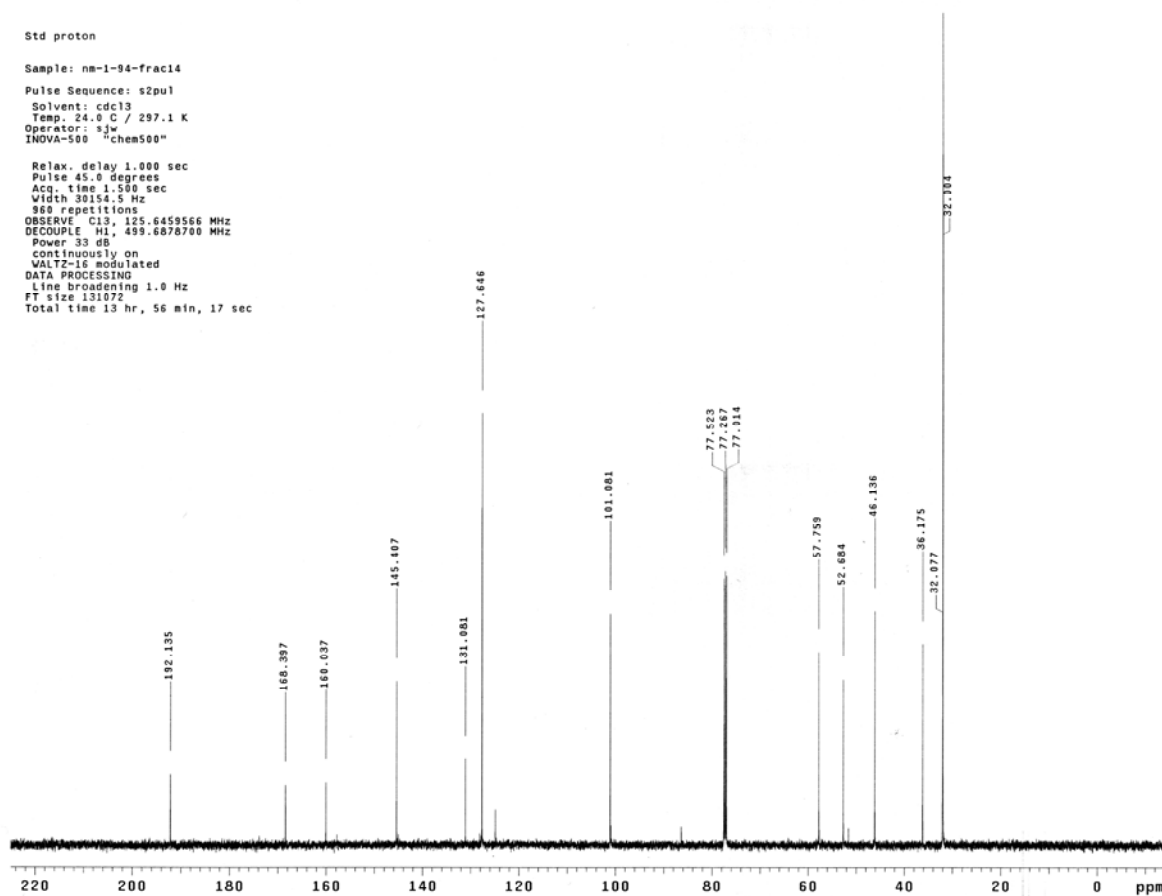
WALTZ-16 modulated

DATA PROCESSING

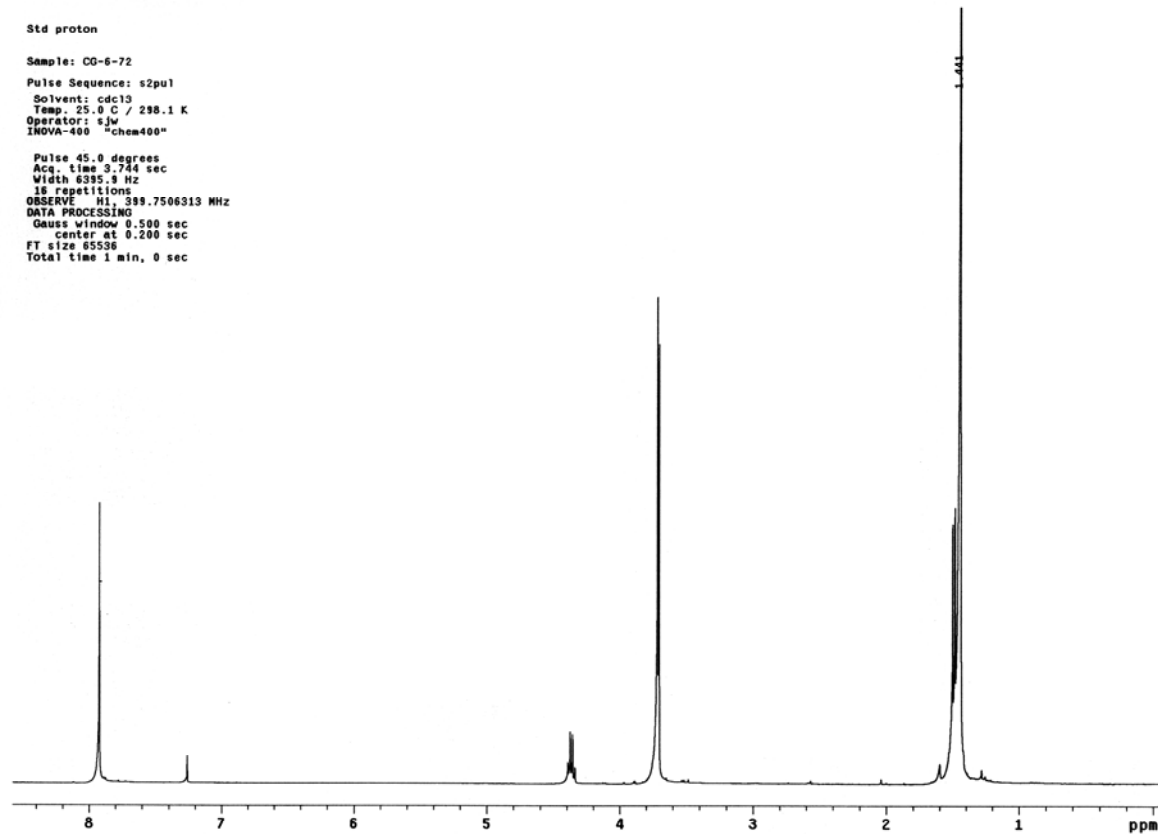
Line broadening 1.0 Hz

FT size 131072

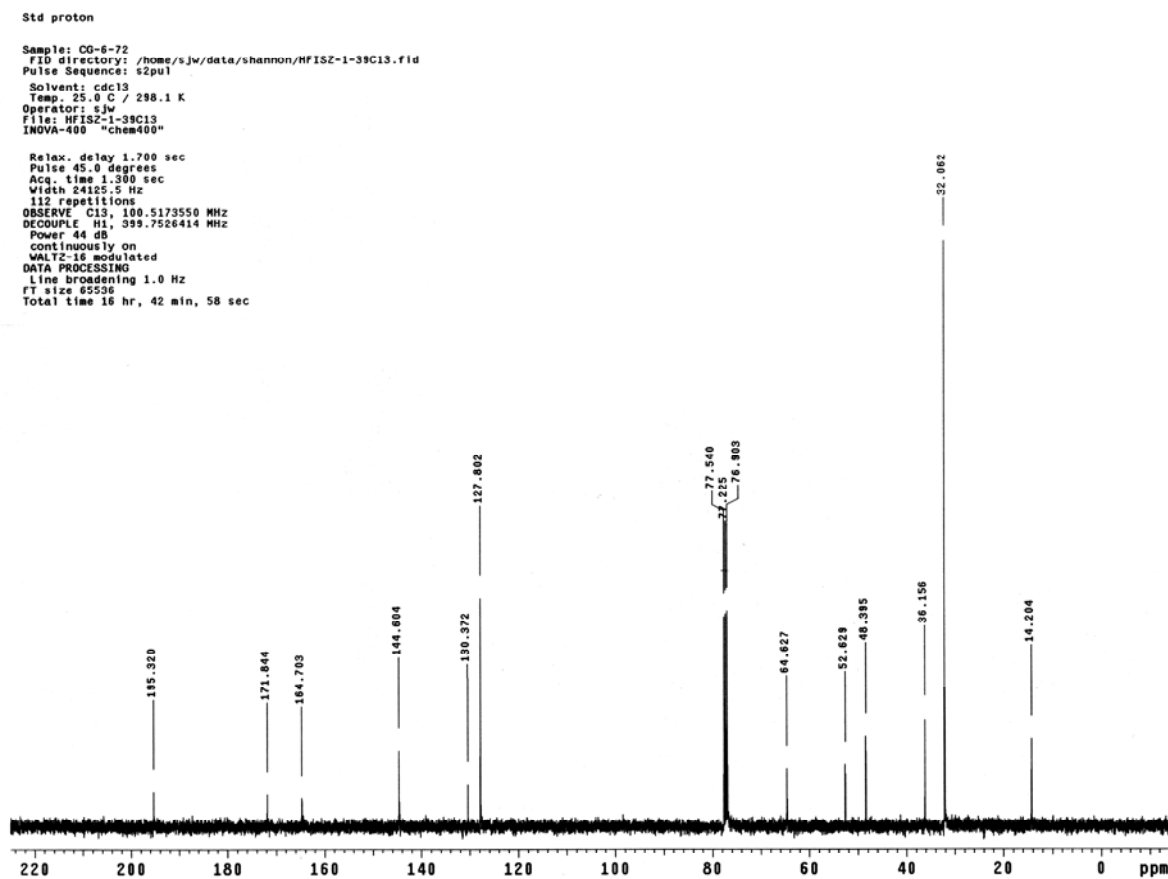
Total time 13 hr, 56 min, 17 sec



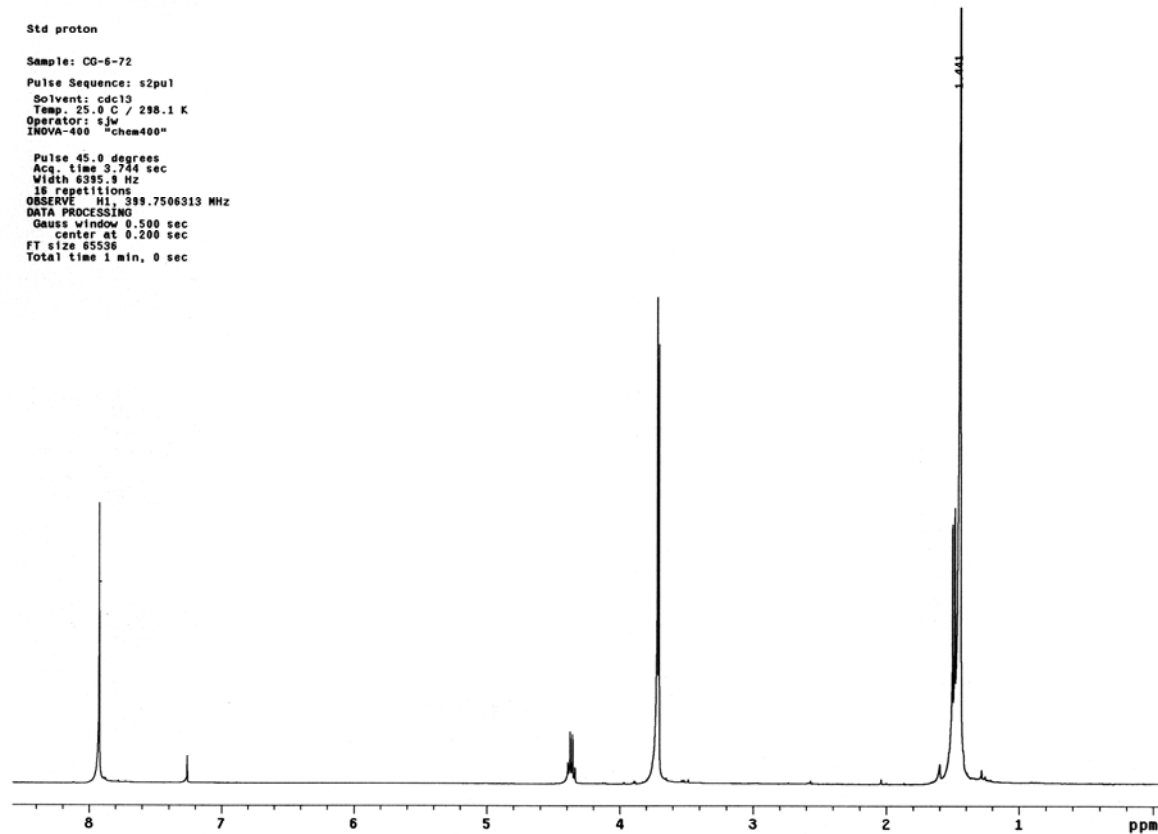
¹H NMR spectrum of compound (12e2)



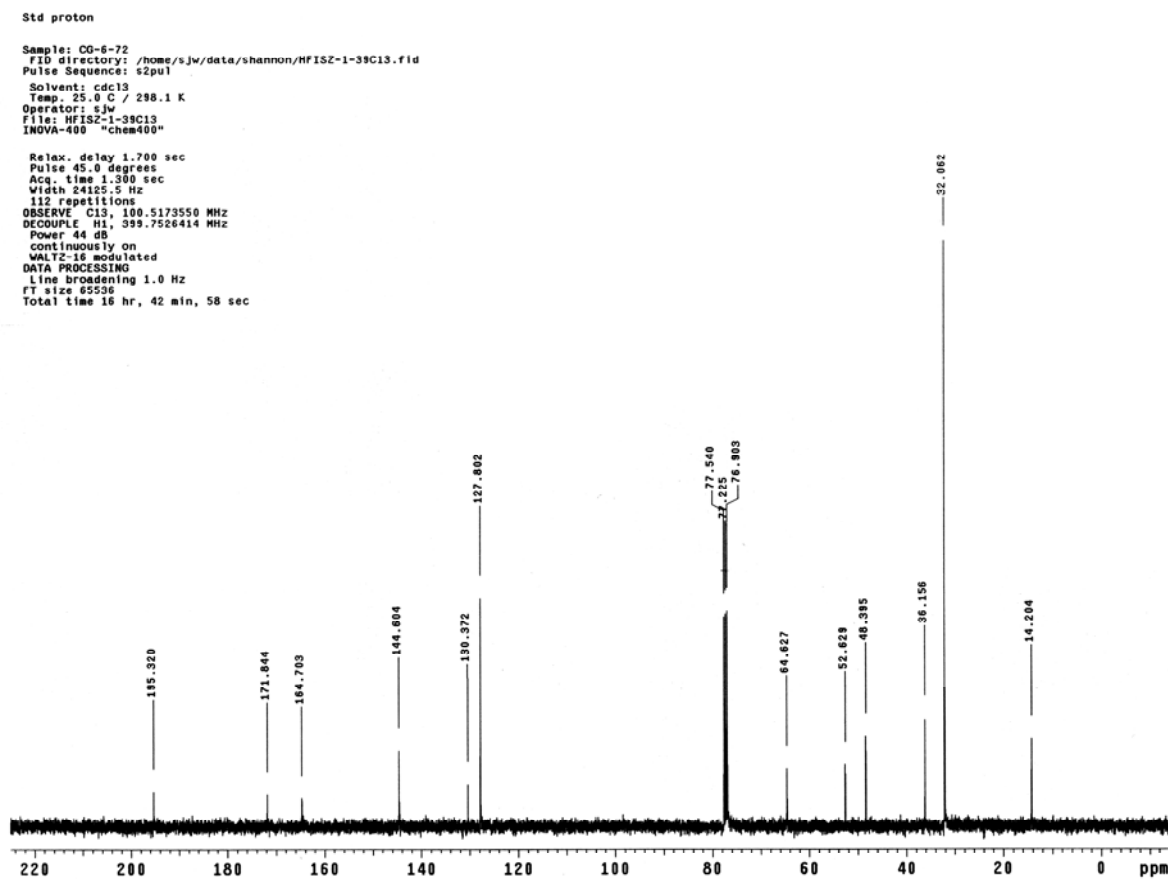
¹³C NMR spectrum



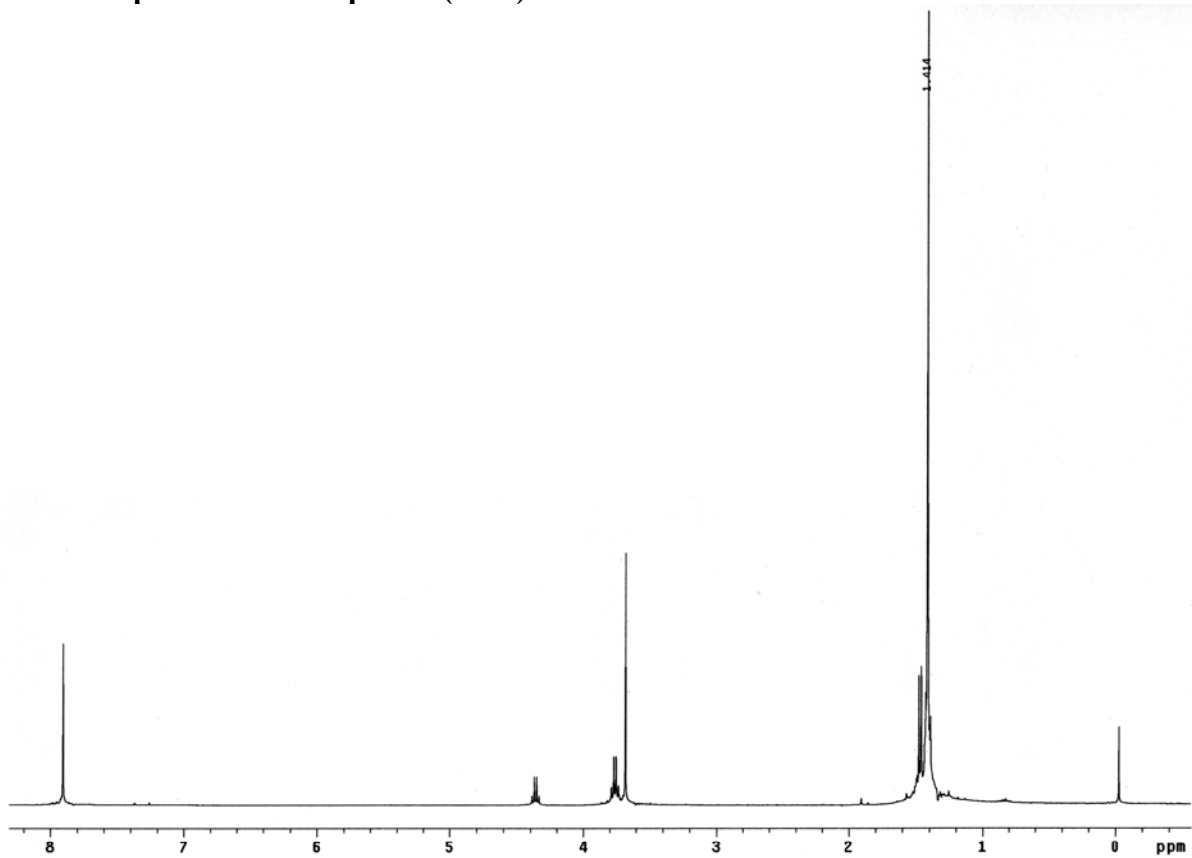
¹H NMR spectrum of compound (12e2)



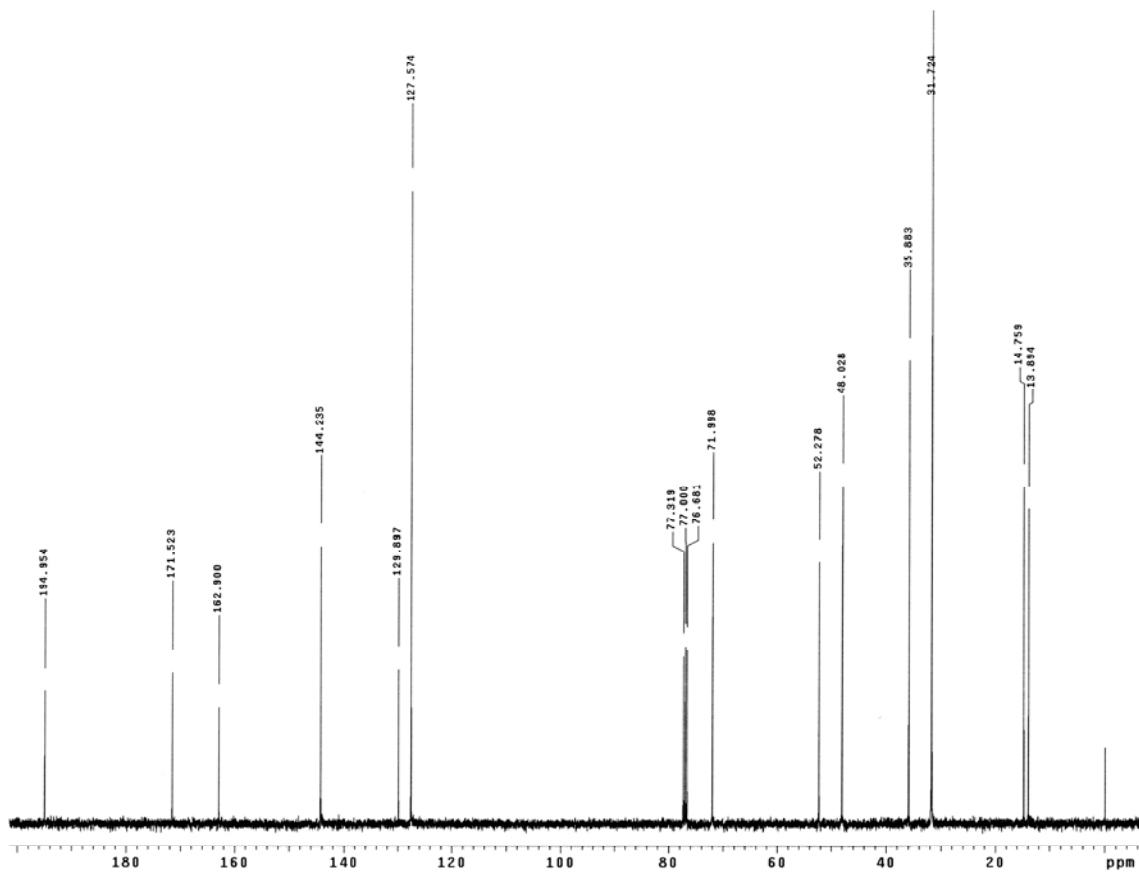
¹³C NMR spectrum



^1H NMR spectrum of compound (12e3)



^{13}C NMR spectrum

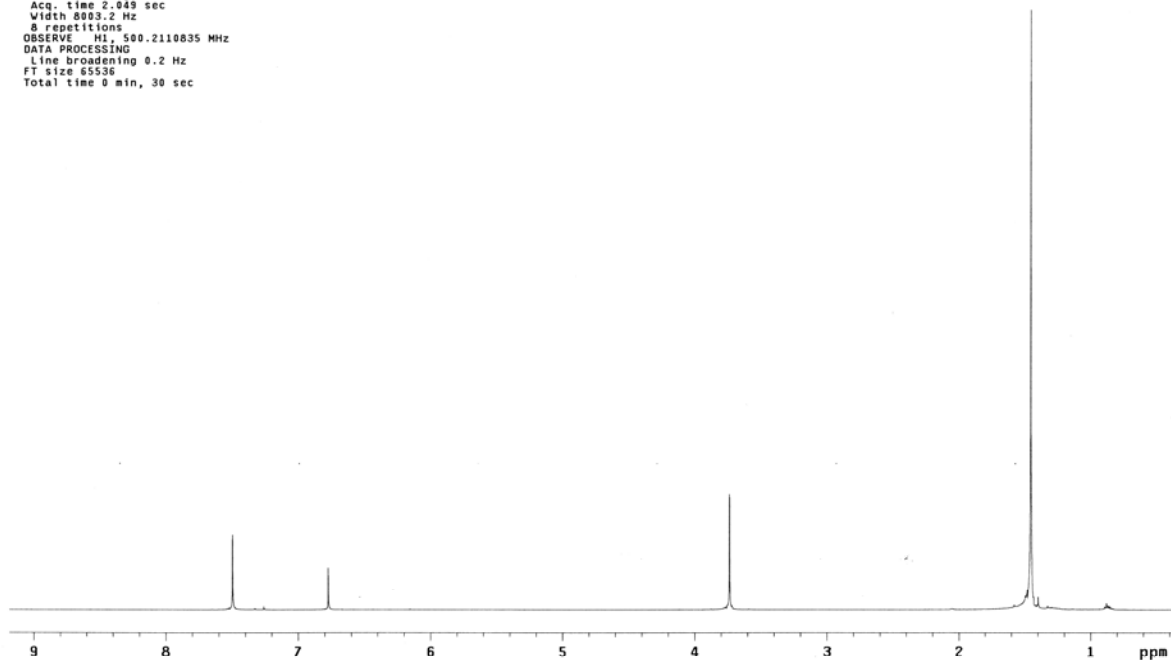


¹H NMR spectrum of compound (14e2)

Std proton

File: Proton
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.949 sec
Width 8003.2 Hz
8 repetitions
OBSERVE H1, 500.2110835 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min, 30 sec

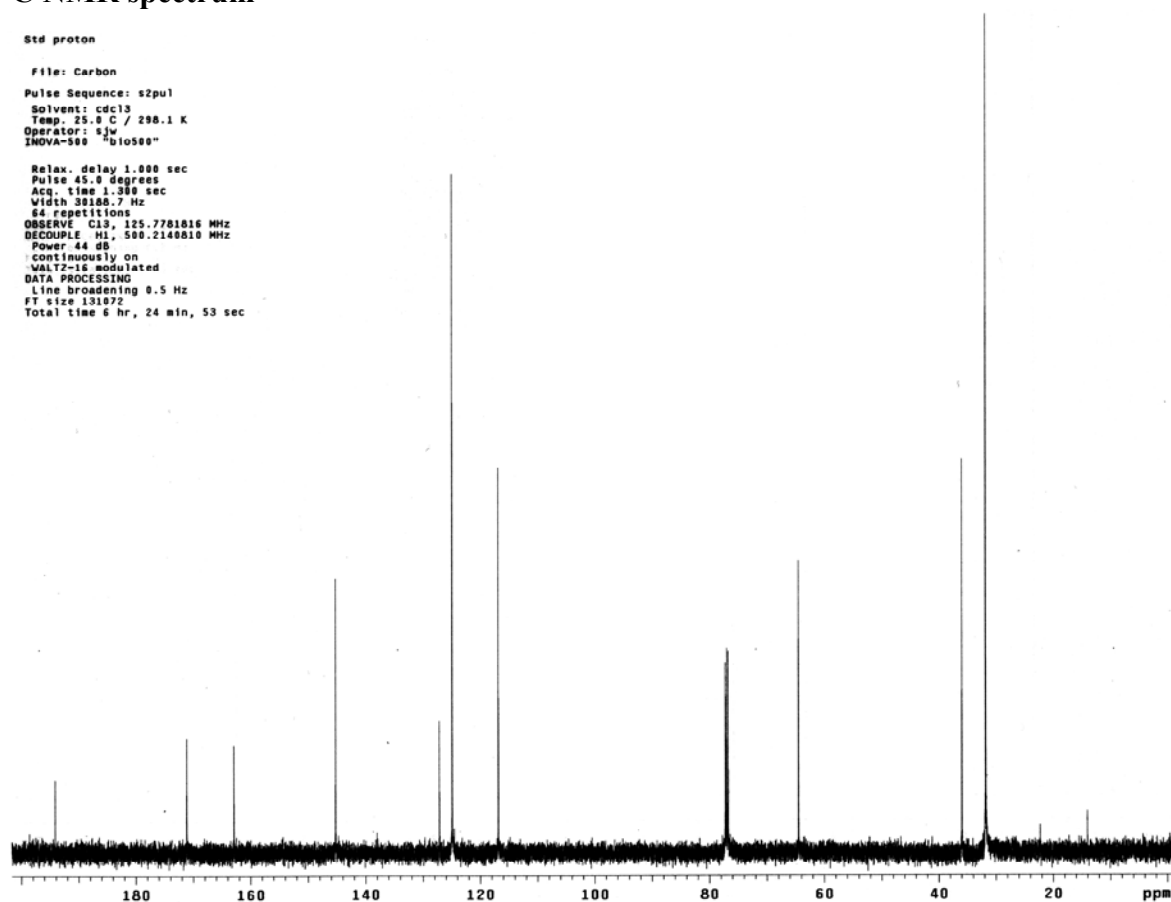


¹³C NMR spectrum

Std proton

File: Carbon
Pulse Sequence: s2pul
Solvent: cdcl3
Temp. 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"

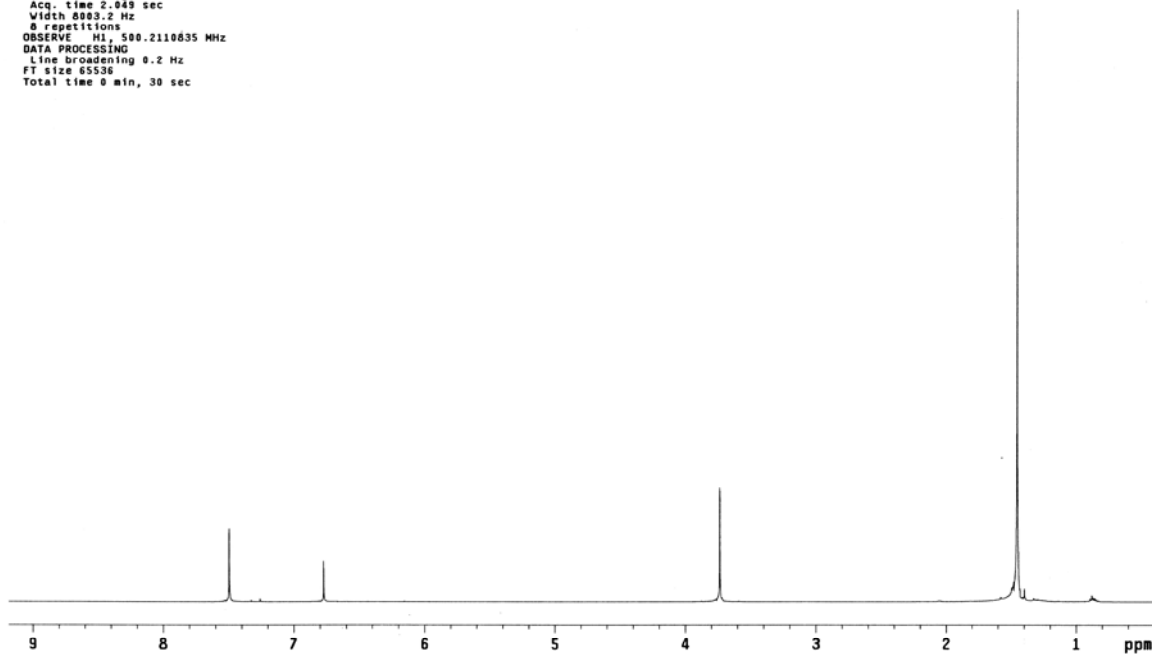
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.389 sec
Width 30160.7 Hz
64 repetitions
OBSERVE C13, 125.7781816 MHz
DECOUPLE H1, 500.2140810 MHz
Power 44 dB
Continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131972
Total time 6 hr, 24 min, 53 sec



¹H NMR spectrum of compound (15e2)

Std proton

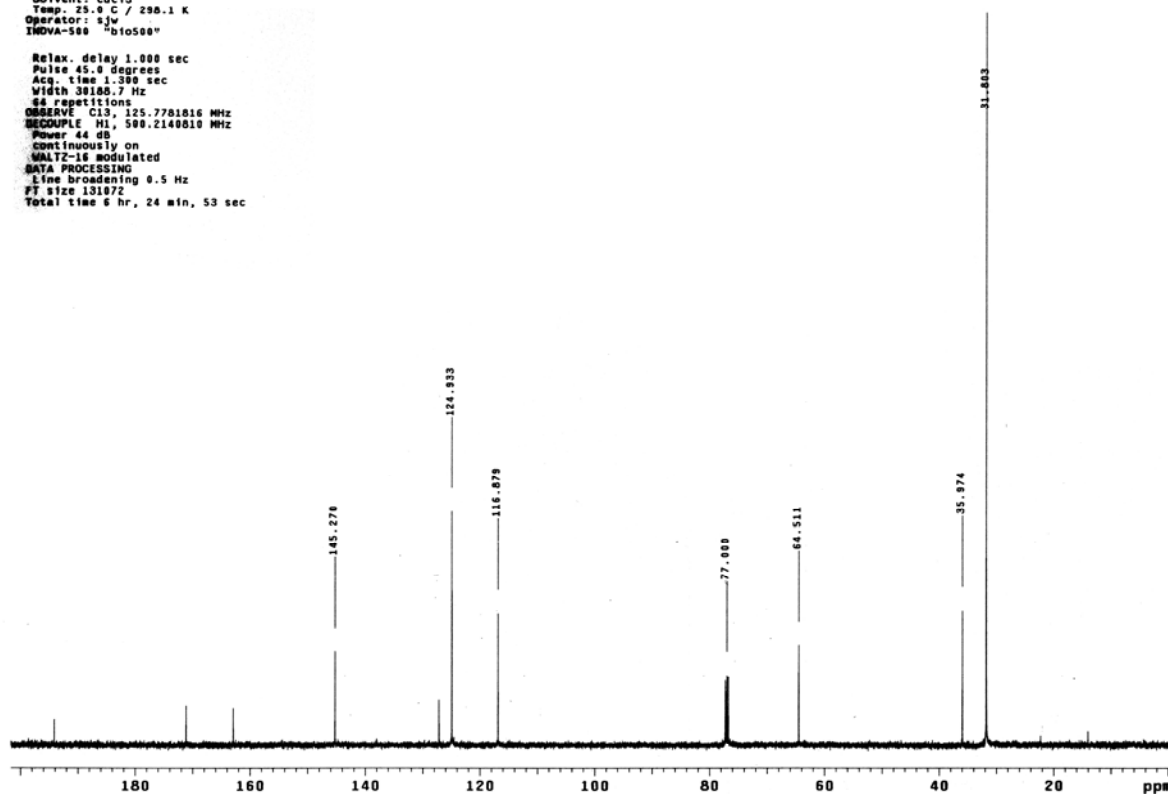
File: Proton
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8983.2 Hz
8 repetitions
OBSERVE H1, 500.2110635 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min, 30 sec



¹³C NMR spectrum

Std proton

File: Carbon
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"
Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 1.390 sec
Width 30180.7 Hz
64 repetitions
OBSERVE C13, 125.7701016 MHz
DECOUPLE H1, 500.2140610 MHz
Power 44 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 0.5 Hz
FT size 131072
Total time 6 hr, 24 min, 53 sec

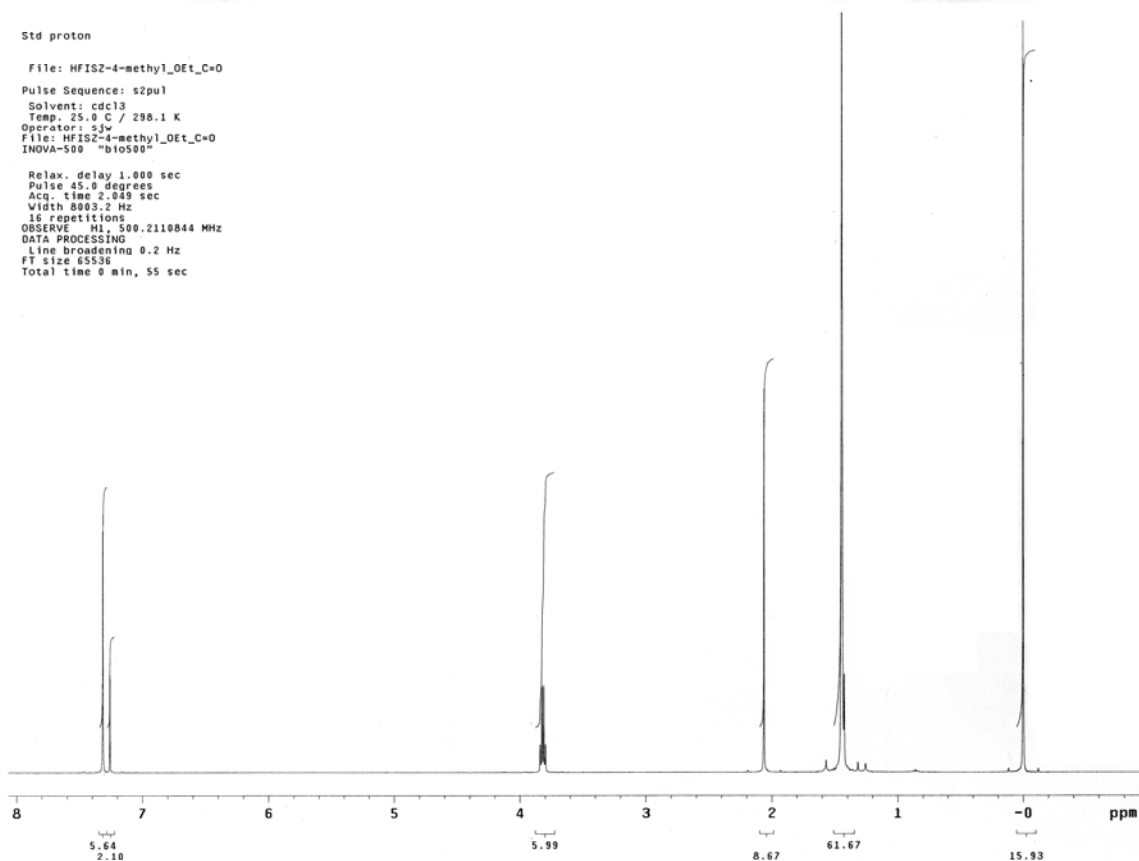


¹H NMR spectrum of compound (15e3)

Std proton

File: HFISZ-4-methyl_OEt_C=O
Pulse Sequence: s2pu1
Solvent: cdcl3
Temp: 25.0 C / 298.1 K
Operator: sjw
File: HFISZ-4-methyl_OEt_C=O
INOVA-500 "bio500"

Relax. delay 1.000 sec
Pulse 45.0 degrees
Acq. time 2.049 sec
Width 8003.2 Hz
16 repetitions
OBSERVE H1, 500.2110844 MHz
DATA PROCESSING
Line broadening 0.2 Hz
FT size 65536
Total time 0 min, 55 sec



¹³C NMR spectrum

Std carbon

File: xp
Pulse Sequence: s2pu1
Solvent: CDCl3
Temp: 25.0 C / 298.1 K
Operator: sjw
INOVA-500 "bio500"

Pulse 45.0 degrees
Acq. time 1.500 sec
Width 50188.7 Hz
240 repetitions
OBSERVE C13, 125.7788690 MHz
DECOUPLE H1, 500.2083693 MHz
Power: 02 dB
continuously on
WALTZ-16 modulated
DATA PROCESSING
Line broadening 1.0 Hz
FT size 191072
Total time 4 hr, 11 min, 29 sec

