Copper-catalysed enantioselective intramolecular etherification of propargylic esters: Synthetic approach to chiral isochromans

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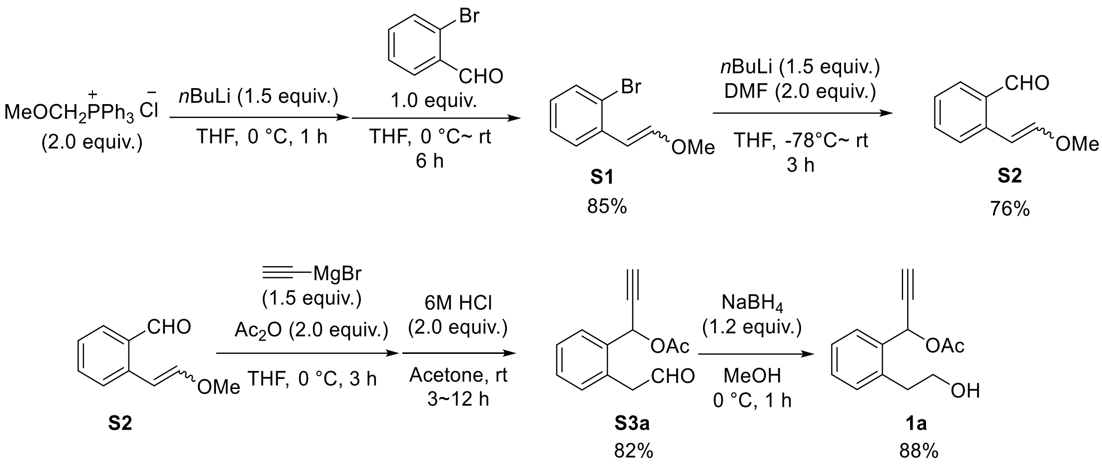
List of Contents of Supporting Information

General Methods.

^{1}H NMR (400 MHz) and ^{13}C NMR (100 MHz) spectra were measured on a JEOL ECS400 400 MHz spectrometer using $CDCl_3$ as solvent. The data are reported as (s = singlet, d = doublet, dd = double doublet, dt = double triplet, t = triplet, q = quartet, br = broad, m = multiplet or unresolved, coupling constant(s) in Hz, integration). HPLC analyses were performed on Hitachi L-7100 and GL-7480 apparatuses equipped with a UV detector using 25 cm x 4.6 mm DAICEL Chiralpak OJ, OZ columns. Mass spectra were measured on a JEOL JMS-700 mass spectrometer. Specific rotations were measured on a JASCO DIP-1000 polarimeter. All reactions were carried out under dry nitrogen atmosphere. The synthesis of racemic products were carried out by using racemic Ph-pybox ligand at 60 °C. Commercially obtained reagents were used without further purification. All reactions were monitored by TLC with silica gel-coated plates. Solvents were dried by the usual methods, then distilled under N_2 and degassed before use. Optically pure pybox ligands **L2**, **L5** are commercially available reagents. Optically pure pybox ligands **L1**[S1], **L3**[s2], **L4**[s3] were prepared according to literature procedures. The absolute configuration of chiral derivative product **S16** were determined by unequivocally according to the X-ray diffraction analysis, and the absolute configuration chiral alkynyl isochromans **2** were deduced on the basis of this result.

General Procedure for the Preparation of Propargylic Acetates.

Scheme S1 Preparation of propargylic acetate **1a**



A typical experimental procedure for the preparation of 1-(2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate **1a** is described below. In a 50 mL Schlenk flask were placed (methoxymethyl)triphenylphosphoniumcChloride (3.43 g, 10.0 mmol) and anhydrous THF (20 mL) under N_2 atmosphere and cooled down the solution to 0 °C. To the solution, *n*BuLi (1.57 M in hexane, 4.8 mL, 7.5 mmol) was added dropwise and the mixture was stirred at 0 °C for 1 h. 2-Bromobenzaldehyde was added to this solution by portion and the mixture was warmed to room temperature and stirred for another 6 h. After the reaction, mixture was quenched by saturated NH_4Cl aq., and the solution was extracted with CH_2Cl_2 (10 ml X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was passed through a short column chromatography with hexane/ethyl acetate (50:1) to give 1-bromo-2-(2-methoxyvinyl)benzene (**S1**) as an E/Z mixture (8.5 mmol, 85% isolated yield).

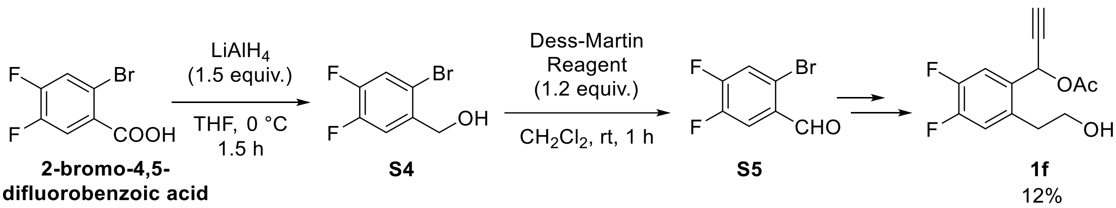
In a 50 mL Schlenk flask were placed **S1** (8.00 mmol) and anhydrous THF (20 mL) under N_2 atmosphere. The solution was cooled down to -78 °C. *n*BuLi (1.57 M in hexane, 7.60 mL, 12.0 mmol) was added dropwise and the mixture was stirred at 0 °C for 1 h. Anhydrous DMF (1.20 mL, 16.0 mmol) was added to the solution, and the mixture was warmed to room temperature and stirred for another 2 h. After the reaction, mixture was quenched by saturated NH_4Cl aq., and the solution was extracted with CH_2Cl_2 (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography with hexane/EtOAc (50:1-30:1) to give 2-(2-methoxyvinyl)benzaldehyde (**S2**) as an E/Z mixture (6.10 mmol, 76% isolated yield).

To a solution of **S2** (6.00 mmol) in anhydrous THF (15 mL) was added ethynylmagnesium bromide (0.5 M in THF, 18.0 mL, 9.00 mmol) at 0 °C and the mixture was stirred for 1 h. Acetic anhydride (1.10 mL, 12.0 mmol) was added to the solution and the mixture was allowed to warm to room temperature. After stirring for 2 h, the mixture was quenched by saturated NH_4Cl aq., and the solution was extracted with CH_2Cl_2 (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was dissolved in 10 mL acetone, and 6M HCl (2.00 mL, 12.0 mmol) was added to the solution at room temperature. The reaction was monitored by TLC until the starting material vanished. After the reaction, the solution was diluted by H_2O and extracted with CH_2Cl_2 (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography with hexane/EtOAc (20:1-10:1) to give 1-(2-(2-oxoethyl)phenyl)prop-2-yn-1-yl acetate (**S3a**) as a yellow oil (4.90 mmol, 82% isolated yield).

S3a (865 mg, 4.00 mmol) was dissolved in 10 mL MeOH, and the solution was cooled down to 0 °C. $NaBH_4$ (182 mg, 4.80 mmol) was added to the solution and the mixture was stirred for 1 h at 0 °C. After the reaction, the solution was diluted by H_2O and extracted with CH_2Cl_2 (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography with hexane/EtOAc (10:1-4:1) to give 1-(2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate (**1a**) as a pale yellow oil (3.5 mmol, 88% isolated yield). ^{1}H NMR δ 7.62 (d, J = 7.2 Hz, 1H), 7.27-7.20 (m, 3H), 6.61 (d, J = 2.4 Hz, 1H), 3.78 (t, J = 6.8 Hz, 2H), 3.01-2.90 (m, 3H), 2.65 (d, J = 2.4 Hz, 1H), 2.04 (s, 3H). ^{13}C NMR δ 169.6, 136.5, 134.8, 130.3, 129.0, 128.1, 126.7, 80.2, 75.5, 62.80, 62.77, 35.3, 20.7. HRMS (FAB) Calcd. for $C_{13}H_{14}NaO_3$ [M+Na]: 241.0841. Found: 241.0840.

Substrates **1b, 1c, 1d, 1e**, **1g**, **1h**, **1i**, **1k, 1l, 1m** were synthesized by using various substituted halogen benzaldehydes, as a similar method as the synthesis of **1a.**

Scheme S2 Preparation of propargylic acetate **1f**

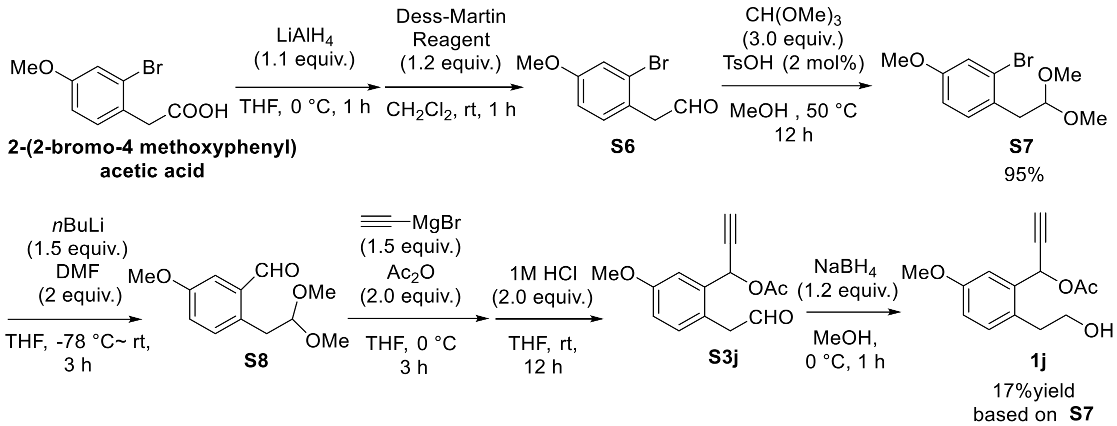


In a 50 mL Schlenk flask were placed 2-bromo-4,5-difluorobenzoic acid (1.19 g, 5.00 mmol) anhydrous THF (20 mL) under N_2 atmosphere. The solution was cooled down to 0 °C. $LiAlH_4$ (285 mg, 7.50 mmol) was added by portion and the mixture was stirred at 0 °C for 1.5 h. The mixture was quenched saturated NH_4Cl aq., and the suspension was filtered through a celite pad. Then the filtrate was extracted with EtOAc (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. Crude (2-bromo-4,5-difluoro) benzylic alcohol (**S4**) was used to the next step without further purification.

To a solution of **S4** in 20 mL CH_2Cl_2, Dess-Martin periodinane (2.54 g, 6.00 mmol) was added. The mixture was stirred for 1 h at room temperature. After the reaction, the solution was diluted by H_2O and extracted with CH_2Cl_2 (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified by column chromatography with hexane/ethyl acetate (50:1-40:1) to give the corresponding 2-bromo-4,5-difluorobenzaldehyde (**S5**).

1f was synthesized from **S5**, as a similar method as the synthesis of **1a** (0.60 mmol, 12% total yield). A pale yellow oil. ^{1}H NMR δ 7.46 (dd, J = 11.2 Hz, 8.0 Hz, 1H), 7.07 (dd, J = 11.2 Hz, 8.0 Hz, 1H), 6.54 (d, J = 2.0 Hz, 1H), 3.84 (t, J = 6.4 Hz, 2H), 3.00-2.82 (m, 2H), 2.65 (d, J = 2.0 Hz, 1H), 2.10 (s, 3H), 1.79 (br, 1H). ^{13}C NMR δ 169.5, 150.3 (dd, $^1J_{C-F}$ = 250 Hz and $^2J_{C-F}$ = 12.4 Hz), 149.0 (dd, $^1J_{C-F}$ = 250 Hz and $^2J_{C-F}$ = 12.4 Hz), 133.8 (dd, $^3J_{C-F}$ = 5.7 Hz and $^4J_{C-F}$ = 3.8 Hz), 132.0 (t, $^3J_{C-F}$ = $^4J_{C-F}$ = 4.3 Hz), 119.0 (d, $^2J_{C-F}$ = 17.1 Hz), 117.3 (d, $^2J_{C-F}$ = 18.1 Hz), 79.7, 75.9, 62.8, 61.9, 34.7, 20.8. HRMS (EI) Calcd. for $C_{13}H_{12}F_2O_3$ [M]: 254.0755. Found: 254.0760.

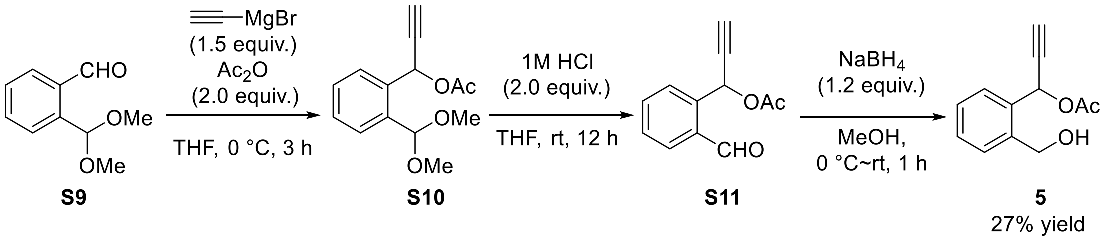
Scheme S3 Preparation of propargylic acetate **1j**



2-(2-Bromo-4-methoxyphenyl)acetaldehyde (**S6**) was synthesized from the 2-(2-bromo-4 methoxyphenyl)acetic acid as a similar method as the synthesis of **S5**. To the solution of crude **S6** (5.00 mmol) in 30 mL MeOH, trimethyl orthoformate (1.60 mL, 15.0 mmol) and TsOH.H_2O (19.0 mg, 0.10 mmol) were added. The mixture was stirred at 50 °C for 3 h. After the reaction, the resulting mixture was evaporated in vacuo and the residue was purified by silica gel column to give 2-bromo-1-(2,2-dimethoxyethyl)-4-methoxybenzene **S7** (4.75 mmol, 95% yield).

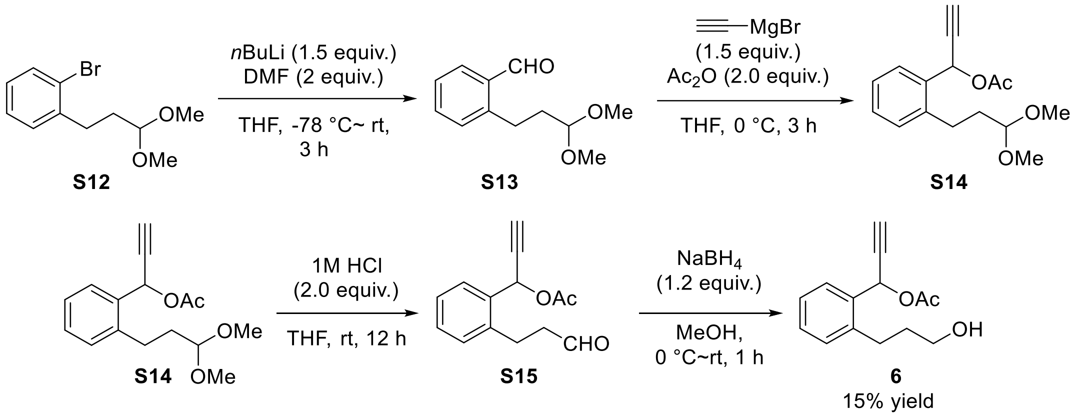
1-(2-(2-hydroxyethyl)-5-methoxyphenyl)prop-2-yn-1-yl acetate **1j** was synthesized from **S7** as a similar method as the synthesis of **1a** (0.80 mmol, 17% total yield from **S7**). A pale yellow oil. ^{1}H NMR δ 7.19 (d, J = 2.8 Hz, 1H), 7.15 (d, J = 9.0 Hz, 1H), 6.87 (dd, J = 9.0 Hz, 2.8 Hz, 1H), 6.59 (d, J = 2.4 Hz, 1H), 3.83-3.79 (m, 5H), 2.98-2.84 (m, 2H), 2.64 (d, J = 2.4 Hz, 1H), 2.10 (s, 3H), 2.00 (br, 1H). ^{13}C NMR δ 169.6, 158.4, 136.2, 131.6, 128.4, 114.7, 113.6, 80.3, 75.5, 63.3, 62.9, 55.3, 34.8, 20.9. HRMS(EI) Calcd. for $C_{14}H_{16}O_4$ [M]: 248.1049. Found: 248.1052.

Scheme S4 Preparation of propargylic acetate **5**



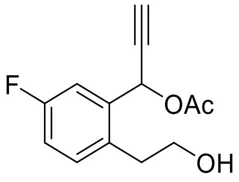
1-(2-(hydroxymethyl)phenyl)prop-2-yn-1-yl acetate **5** was synthesized from **S9**[s4] (6.00 mmol) as a similar method as the synthesis of **1a** (1.60 mmol, 27% total yield). A pale yellow oil.^{1}H NMR δ 7.73-7.70 (m, 1H), 7.44-7.31 (m, 3H), 5.69-5.68 (m, 1H), 5.35 (d, J = 12.8 Hz, 1H), 5.26 (d, J = 12.8 Hz, 1H), 3.31 (d, J = 5.4 Hz, 1H), 2.67 (d, J = 2.4 Hz, 1H), 2.08 (s, 3H). ^{13}C NMR δ 171.0, 138.3, 133.4, 129.9, 128.8, 128.7, 127.4, 83.1, 75.0, 63.7, 61.8, 20.9. HRMS (EI) Calcd. for $C_{12}H_{12}O_3$ [M]: 204.0786. Found: 204.0784.

Scheme S5 Preparation of propargylic acetate **6**



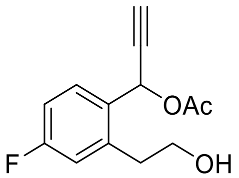
1-(2-(3-Hydroxypropyl)phenyl)prop-2-yn-1-yl acetate **6** was synthesized from **S12**[s5] (6.00 mmol) according to a similar method as the synthesis of **1a** (0.90 mmol, 15% total yield). ^{1}H NMR δ 7.63 (dd, J = 7.2 Hz, 1.2 Hz, 1H), 7.32-7.19 (m, 3H), 6.63 (d, J = 2.2 Hz, 1H), 3.67 (t, J = 6.4 Hz, 2H), 2.85-2.77 (m, 2H), 2.62 (d, J = 2.2 Hz, 1H), 2.10 (s, 3H), 2.00 (br, 1H). 1.91-1.82 (m, 2H). ^{13}C NMR δ 169.7, 139.8, 134.4, 129.8, 129.2, 128.2, 126.5, 80.5, 75.3, 62.7, 61.9, 34.0, 28.3, 21.0. HRMS (EI) Calcd. for $C_{14}H_{16}O_3$ [M]: 232.1099. Found: 232.1091.

Spectroscopic Data of Other Propargylic Acetates



1b

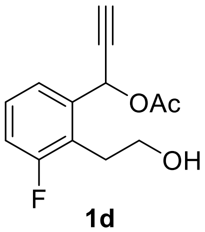
1-(5-fluoro-2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate (1b) : a pale yellow oil. ^{1}H NMR δ 7.33 (dd, J = 9.6 Hz, 2.6Hz, 1H), 7.18 (dd, J = 8.2 Hz, 6.0 Hz, 1H), 6.98 (td, J = 8.2 Hz, 2.6 Hz, 1H), 6.56 (d, J = 2.4 Hz, 1H), 3.78 (t, J = 6.8 Hz, 2H), 2.96-2.84 (m, 2H), 2.64 (d, J = 2.4 Hz, 1H), 2.42 (br, 1H), 2.08 (s, 3H). ^{13}C NMR δ 169.6, 161.5 (d, $^1J_{C-F}$ = 244 Hz), 137.1 (d, $^3J_{C-F}$ = 6.7 Hz), 132.1 (d, $^4J_{C-F}$ = 2.9 Hz), 132.0 (d, $^3J_{C-F}$ = 6.6 Hz), 116.0 (d, $^2J_{C-F}$ = 21 Hz), 114.8 (d, $^2J_{C-F}$ = 23 Hz), 79.8, 75.8, 62.9, 62.3, 34.8, 20.8. HRMS (EI) Calcd. for $C_{13}H_{13}FO_3$ [M]: 236.0849. Found: 236.0857.



1c

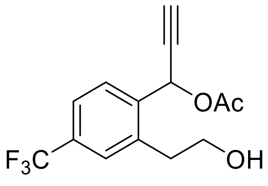
1-(4-fluoro-2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate (1c) : a pale yellow oil. ^{1}H NMR δ 7.64 (dd, J = 9.6 Hz, 5.6 Hz, 1H), 7.00-6.95 (m, 2H), 6.60 (d, J = 2.4 Hz, 1H), 3.89 (t, J =

6.4 Hz, 2H), 3.06-2.93 (m, 2H), 2.65 (d, J = 2.4 Hz, 1H), 2.11 (s, 3H), 1.69 (br, 1H). ^{13}C NMR δ 169.7, 162.9 (d, $^{1}J_{C-F}$ = 247 Hz), 139.5 (d, $^{3}J_{C-F}$ = 7.7 Hz), 131.1 (d, $^{4}J_{C-F}$ = 1.9 Hz), 130.5 (d, $^{3}J_{C-F}$ = 8.6 Hz), 117.0 (d, $^{2}J_{C-F}$ = 21 Hz), 113.9 (d, $^{2}J_{C-F}$ = 22 Hz), 80.3, 75.6, 62.8, 62.4, 35.4, 20.9. HRMS (EI) Calcd. for $C_{13}H_{13}FO_3$ [M]: 236.0849. Found: 236.0844.



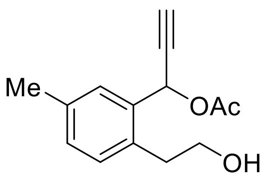
1d

1-(3-fluoro-2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate (1d): a pale yellow oil. ^{1}H NMR δ 7.44 (d, J = 8.0 Hz, 1H), 7.31-7.24 (m, 1H), 7.07 (t, J = 9.0 Hz, 1H), 6.66 (d, J = 2.2 Hz, 1H), 3.87 (t, J= 6.8 Hz, 2H), 3.11-3.04 (m, 2H), 2.66 (d, J = 2.2 Hz, 1H), 2.13 (s, 3H), 1.75 (br, 1H). ^{13}C NMR δ 169.6, 161.5 (d, $^{1}J_{C-F}$ = 244 Hz), 137.8 (d, $^{3}J_{C-F}$ = 3.8 Hz), 128.2 (d, $^{3}J_{C-F}$ = 9.5 Hz), 124.4 (d, $^{2}J_{C-F}$ = 16.2 Hz), 123.8 (d, $^{4}J_{C-F}$ = 2.9 Hz), 116.0 (d, $^{2}J_{C-F}$ = 22.9 Hz), 80.1, 75.7, 62.8 (d, $^{4}J_{C-F}$ = 3.8 Hz), 62.3, 28.8, 21.0. HRMS (EI) Calcd. for $C_{13}H_{13}FO_3$ [M]: 236.0849. Found: 236.0842.



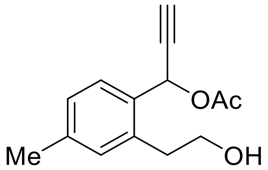
1e

1-(2-(2-hydroxyethyl)-4-(trifluoromethyl)phenyl)prop-2-yn-1-yl acetate (1e): a pale yellow oil. ^{1}H NMR δ 7.75 (d, J = 7.6 Hz, 1H), 7.54-7.50 (m, 2H), 6.67 (s, 1H), 3.88 (t, J = 6.8 Hz, 2H), 3.13-3.00 (m, 2H), 2.67 (d, J = 2.0 Hz, 1H), 2.30 (br, 1H), 2.11 (s, 3H). ^{13}C NMR δ 169.6, 139.1 137.7, 131.2 (q, $^{2}J_{C-F}$ = 32 Hz), 128.5, 127.2 (q, $^{3}J_{C-F}$ = 3.8 Hz), 123.8 (q, $^{3}J_{C-F}$ = 3.8 Hz), 123.8 (q, $^{1}J_{C-F}$ = 271 Hz), 79.7, 76.1, 62.7, 62.4, 35.4, 20.8. HRMS (FAB) Calcd. for $C_{14}H_{13}F_3NaO_3$ [M+Na]: 309.0714. Found: 309.0715.



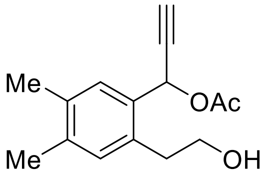
1g

1-(2-(2-hydroxyethyl)-5-methylphenyl)prop-2-yn-1-yl acetate (1g): a pale yellow oil. ^{1}H NMR δ 7.44 (s, 1H), 7.12 (s, 2H), 6.60 (d, J = 2.0 Hz, 1H), 3.80 (t, J = 6.4 Hz, 2H), 3.03-2.87 (m, 2H), 2.64 (d, J = 2.0 Hz, 1H), 2.34 (s, 3H), 2.30 (br, 1H), 2.09 (s, 3H). ^{13}C NMR δ 169.6, 136.6, 134.7, 133.4, 130.4, 129.9, 128.8, 80.5, 75.4, 63.2, 62.9, 35.1, 20.9. HRMS (EI) Calcd. for $C_{14}H_{16}O_3$ [M]: 232.1099. Found: 232.1099.



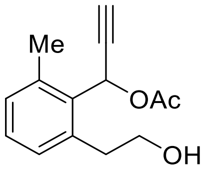
1h

1-(2-(2-hydroxyethyl)-4-methylphenyl)prop-2-yn-1-yl acetate (1h): a pale yellow oil. ^{1}H NMR δ 7.54 (d, J = 7.6 Hz, 1H), 7.10 (d, J = 7.6 Hz, 1H), 7.07 (s, 1H), 6.61 (d, J = 2.2 Hz, 1H), 3.85 (t, J = 6.4 Hz, 2H), 3.06-2.88 (m, 2H), 2.63 (d, J = 2.2 Hz, 1H), 2.34 (s, 3H), 2.09 (br, 4H). ^{13}C NMR δ 169.7, 139.1, 136.4, 132.2, 131.1, 128.4, 127.8, 80.6, 75.3, 63.3, 62.9, 35.5, 21.0, 20.9. HRMS (FAB) Calcd. for $C_{14}H_{16}NaO_3$ [M+Na]: 255.0997. Found: 255.0998.



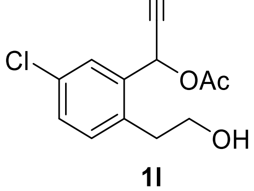
1i

1-(2-(2-hydroxyethyl)-4,5-dimethylphenyl)prop-2-yn-1-yl acetate (1i): a pale yellow oil. ^{1}H NMR δ 7.42 (s, 1H), 7.03 (s, 1H), 6.60 (d, J = 2.2 Hz, 1H), 3.82 (t, J = 6.8 Hz, 2H), 3.04-2.86 (m, 2H), 2.66 (d, J = 2.2 Hz, 1H), 2.42 (br, 1H), 2.26 (s, 3H), 2.25 (s, 3H), 2.10 (s, 3H). ^{13}C NMR δ 169.6, 137.7, 135.2, 133.7, 132.2, 131.7, 129.5, 80.6, 75.2, 63.2, 62.8, 35.0, 20.8, 19.3, 19.1. HRMS (EI) Calcd. for $C_{15}H_{18}O_3$ [M]: 246.1256. Found: 246.1263.



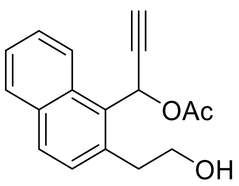
1k

1-(2-(2-hydroxyethyl)-6-methylphenyl)prop-2-yn-1-yl acetate (1k): a pale yellow oil. ^{1}H NMR δ 7.20 (t, J = 7.2 Hz, 1H), 7.12-7.08 (m, 2H), 6.90 (d, J = 2.2 Hz, 1H), 3.93-3.83 (m, 2H), 3.30-3.24 (m, 1H), 3.10-3.03 (m, 1H), 2.61 (d, J = 2.2 Hz, 1H), 2.58 (s, 3H), 2.09 (s, 3H), 1.86 (br, 1H). ^{13}C NMR δ 169.6, 138.0, 137.5, 133.3, 130.0, 128.9, 128.8, 80.2, 75.0, 63.6, 61.2, 36.7, 20.9, 20.4. HRMS (FAB) Calcd. for $C_{14}H_{16}NaO_3$ [M+Na]: 255.0997. Found: 255.0992.



1l

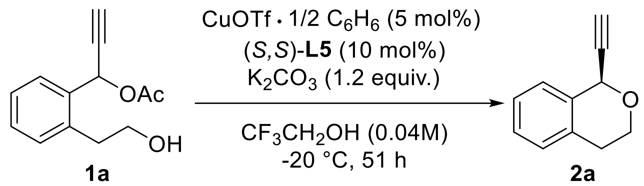
1-(5-chloro-2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate (1l): a pale yellow oil. ^{1}H NMR δ 7.63 (d, J = 2.2 Hz, 1H), 7.28 (dd, J = 8.4 Hz, 2.2 Hz, 1H), 7.19 (d, J = 8.4 Hz, 1H), 6.59 (d, J = 2.2 Hz, 1H), 3.84 (t, J = 2.4 Hz, 2H), 3.02-2.90 (m, 2H), 2.67 (d, J = 2.2 Hz, 1H), 2.13 (s, 3H), 2.01 (br, 1H). ^{13}C NMR δ 169.6, 137.0, 135.0, 132.8, 131.8, 129.2, 128.1, 79.8, 75.9, 63.0, 62.3, 35.0, 20.9. HRMS (FAB) Calcd. for $C_{13}H_{13}ClO_3$ [M]: 252.0553. Found: 252.0557.



1m

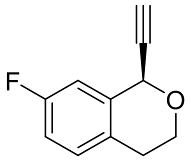
1-(2-(2-hydroxyethyl)naphthalen-1-yl)prop-2-yn-1-yl acetate (1m): a pale yellow oil. ^{1}H NMR δ 8.66 (d, J = 8.8 Hz, 1H), 7.83 (d, J = 8.0 Hz, 1H), 7.79 (d, J = 8.8 Hz, 1H), 7.60-7.55 (m, 1H), 7.50-7.45 (m, 1H), 7.35-7.29 (m, 2H), 3.93 (t, J = 6.4 Hz, 2H), 3.44-3.39 (m, 1H), 3.20-3.10 (m, 1H), 2.67 (d, J = 2.4 Hz, 1H) 2.21 (br, 1H), 2.06 (s, 3H). ^{13}C NMR δ 169.8, 135.5, 133.2, 131.1, 130.0, 129.9, 128.52, 128.48, 126.2, 125.7, 125.4, 80.8, 75.8, 63.4, 61.2, 37.3, 20.8. HRMS (EI) Calcd. for $C_{17}H_{16}O_3$ [M]: 268.1099. Found: 268.1093.

Enantioselective Intramolecular Propargylic Etherification of Propargylic Acetates.



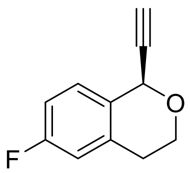
A typical experimental procedure for the reaction of 1-(2-(2-hydroxyethyl)phenyl)prop-2-yn-1-yl acetate (**1a**) is described below. In an oven dried 20 mL Schlenk flask were placed CuOTf.1/2C_6H_6 (1.3 mg, 0.005 mmol) and (*S,S*)-Ph-pybox (**L5**) (3.7 mg, 0.01 mmol) under N_2. Anhydrous methanol (1.0 mL) was added, and then the mixture was magnetically stirred at 60 °C for 1 h. After the solution was cooled to -20 °C, **1a** (21.8 mg, 0.10 mmol) in anhydrous methanol (1.5 mL) and K_2CO_3 (17 mg, 0.12 mmol) were added under N_2, and the reaction mixture was kept at -20 °C for 51 h. The mixture was diluted by H_2O (10 mL) and extracted with CH_2Cl_2 (10 mL X 3). The combined organic layers were dried over anhydrous Na_2SO_4 and concentrated under reduced pressure *with caution*. The residue was purified by the column chromatography (SiO_2) with hexane/Et_2O (50:1-40:1) to give 1-ethynylisochromane (**2a**) as a pale yellow oil (14.1 mg, 0.089 mmol, 89% isolated yield). ^{1}H NMR δ 7.27-7.18 (m, 3H), 7.15-7.10 (m, 1H), 5.55 (s, 1H), 4.26-4.20 (m, 1H), 4.01-3.95 (m, 1H), 2.94-2.80 (m, 2H), 2.56 (s, 1H). ^{13}C NMR δ 134.3, 132.7, 129.0, 127.3, 126.4, 125.8, 82.8, 73.8, 66.4, 62.4, 27.9. HRMS (EI) Calcd. for $C_{11}H_{10}O$ [M]: 158.0732. Found: 158.0731. $[\alpha]^{21}_D$ = +26.6 (c = 0.50, $CHCl_3$). The enantiomeric excess of **2a** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 18.6 min (major) and 26.0 min (minor), 93% ee.

Spectroscopic Data and Isolated Yields of Other Products.



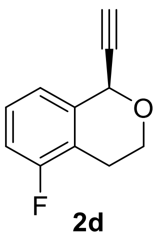
2b

1-ethynyl-7-fluoroisochromane (2b): Isolated yield 90%. A pale yellow oil. ^{1}H NMR δ 7.08 (dd J = 8.6 Hz, 6.0 Hz, 1H), 6.98 (dd J = 9.2 Hz, 2.4 Hz, 1H), 6.27 (td, J = 8.6 Hz, 2.4 Hz, 1H), 5.50 (s, 1H), 4.24-4.17 (m, 1H), 4.01-3.93 (m, 1H), 2.90-2.75 (m, 2H), 2.57 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ 161.2 (d, $^{1}J_{C-F}$ = 246 Hz), 136.0 (d, $^{3}J_{C-F}$ = 6.7 Hz), 130.4 (d, $^{3}J_{C-F}$ = 6.6 Hz), 128.3 (d, $^{4}J_{C-F}$ = 2.9 Hz), 114.7 (d, $^{2}J_{C-F}$ = 21 Hz), 112.5 (d, $^{2}J_{C-F}$ = 23 Hz), 82.1, 74.2, 66.3, 62.6, 27.2. HRMS (EI) Calcd. for $C_{11}H_9FO$ [M]: 176.0637. Found: 176.0636. $[\alpha]^{22}_{D}$ = +49.6 (c = 0.32, $CHCl_3$). The enantiomeric excess of **2b** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 17.3 min (major) and 18.5 min (minor), 87% ee.



2c

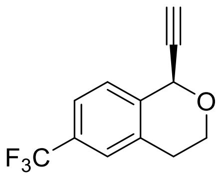
1-ethynyl-6-fluoroisochromane (2c): Isolated yield 75%. A pale yellow oil. ^{1}H NMR δ 7.22 (dd, J = 8.3 Hz, 5.2 Hz, 1H), 6.92 (td, J = 8.3Hz, 2.6 Hz, 1H), 6.81 (dd, J = 9.6 Hz, 2.6 Hz, 1H), 5.50 (s, 1H), 4.24-4.17 (m, 1H), 4.00-3.93 (m, 1H), 2.95-2.77 (m, 2H), 2.57 (d, J = 2.0 Hz, 1H). ^{13}C NMR δ 161.8 (d, $^{1}J_{C-F}$ = 245 Hz), 135.0 (d, $^{3}J_{C-F}$ = 7.6 Hz), 130.0 (d, $^{4}J_{C-F}$ = 2.9 Hz), 127.5 (d, $^{3}J_{C-F}$ = 8.6 Hz), 115.3 (d, $^{2}J_{C-F}$ = 22 Hz), 113.7 (d, $^{2}J_{C-F}$ = 22 Hz), 82.6, 74.1, 66.1, 62.0, 28.0. HRMS (EI) Calcd. for $C_{11}H_9FO$ [M]: 176.0637. Found: 176.0630. $[\alpha]^{21}_{D}$ = +47.7 (c = 0.27, $CHCl_3$). The enantiomeric excess of **2c** was determined by HPLC analysis; DAICEL Chiralpak OZ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 9.9 min (major) and 10.6 min (minor), 94% ee.



2d

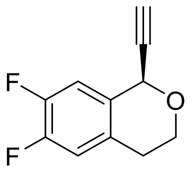
1-ethynyl-5-fluoroisochromane (2d): Isolated yield 65%. A pale yellow oil. ^{1}H NMR δ 7.20 (dd J = 13.2 Hz, 8.1 Hz, 1H), 7.06 (d, J = 8.1 Hz, 1H), 6.95 (t, J = 8.1 Hz, 1H), 5.53 (s, 1H), 4.27-4.19 (m, 1H), 4.04-3.97 (m, 1H), 2.83 (t, J = 6.0, 2H), 2.58 (d, J = 2.8 Hz, 1H). ^{13}C NMR δ 160.3 (d, $^{1}J_{C-F}$ = 244 Hz), 136.4 (d, $^{3}J_{C-F}$ = 4.8 Hz), 127.2 (d, $^{3}J_{C-F}$ = 8.5 Hz), 121.2 (d, $^{4}J_{C-F}$ = 2.9 Hz), 120.7 (d, $^{2}J_{C-F}$ = 19 Hz), 113.6 (d, $^{2}J_{C-F}$ = 21 Hz), 82.2, 74.3, 65.9 (d, $^{4}J_{C-F}$ = 2.8 Hz), 61.6, 21.3 (d, $^{3}J_{C-F}$ =

2.9 Hz). HRMS (EI) Calcd. for $C_{11}H_9FO$ [M]: 176.0637. Found: 176.0640. $[\alpha]^{22}_{D}$ = +34.1 (c = 0.57, $CHCl_3$). The enantiomeric excess of **2d** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 17.8 min (major) and 19.2 min (minor), 89% ee.



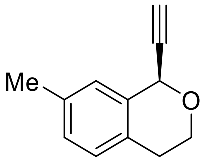
2e

1-ethynyl-6-(trifluoromethyl)isochromane (2e): Isolated yield 87%. A pale yellow oil. ^{1}H NMR δ 7.47 (d, J = 7.6 Hz, 1H), 7.40-7.36 (m, 2H), 5.57 (s, 1H), 4.28-4.21 (m, 1H), 4.05-3.98 (m, 1H), 3.02-2.83 (m, 2H), 2.59 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ 138.2, 133.6, 129.7 (d, $^{2}J_{C\text{-}F}$ = 32 Hz), 126.4, 126.0 (d, $^{3}J_{C\text{-}F}$ = 3.8 Hz), 123.9 (d, $^{1}J_{C\text{-}F}$ = 272 Hz), 123.2 (d, $^{3}J_{C\text{-}F}$ = 3.9 Hz), 82.0, 74.6, 66.3, 62.0, 27.8. HRMS (EI) Calcd. for $C_{12}H_9F_3O$ [M]: 226.0605. Found: 226.0601. $[\alpha]^{22}_{D}$ = +27.5 (c = 0.50, $CHCl_3$). The enantiomeric excess of **2e** was determined by HPLC analysis; DAICEL Chiralpak OZ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 9.09 min (major) and 9.94 min (minor), 93% ee.



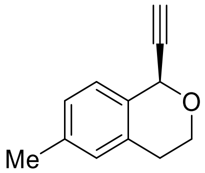
2f

1-ethynyl-6,7-difluoroisochromane (2f): Isolated yield 51%. A pale yellow oil. ^{1}H NMR δ 7.08 (dd, J = 10.4 Hz, 7.6 Hz, 1H), 6.93 (dd, J = 10.4 Hz, 7.6 Hz, 1H), 5.46 (s, 1H), 4.23-4.15 (m, 1H), 4.00-3.92 (m, 1H), 2.89-2.73 (m, 2H), 2.59 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ 149.6 (dd, $^{1}J_{C\text{-}F}$ = 247 Hz and $^{2}J_{C\text{-}F}$ = 12 Hz), 148.9 (dd, $^{1}J_{C\text{-}F}$ = 247 Hz and $^{2}J_{C\text{-}F}$ = 11 Hz), 130.6 (t, $^{3}J_{C\text{-}F}$ = $^{4}J_{C\text{-}F}$ = 4.8 Hz), 129.3 (t, $^{3}J_{C\text{-}F}$ = $^{4}J_{C\text{-}F}$ = 5.7 Hz), 117.2 (d, ^{2}J = 17.1 Hz), 114.6 (d, ^{2}J = 18.1Hz), 81.9, 74.5, 65.8, 62.1, 27.2. HRMS (EI) Calcd. for $C_{11}H_8F_2O$ [M]: 194.0543. Found: 194.0544. $[\alpha]^{20}_{D}$ = +34.5 (c = 0.35, $CHCl_3$). The enantiomeric excess of **2f** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 18.6 min (minor) and 19.6 min (major), 92% ee.



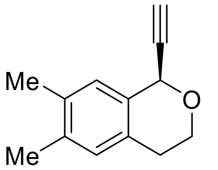
2g

1-ethynyl-7-methylisochromane (2g): Isolated yield 75%. A pale yellow oil. ^{1}H NMR δ 7.08-7.00 (m, 3H), 5.52 (d, J = 2.0 Hz, 1H), 4.24-4.19 (m, 1H), 4.01-3.94 (m, 1H), 2.89-2.75 (m, 2H), 2.56 (d, J = 2.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR δ 136.0, 134.0, 129.6, 128.8, 128.2, 126.1, 83.0, 73.7, 66.4, 62.5, 27.5, 21.1. HRMS (EI) Calcd. for $C_{12}H_{12}O$ [M]: 172.0888. Found: 172.0894. $[\alpha]^{22}_{D}$ = +78.1 (c = 0.44, $CHCl_3$). The enantiomeric excess of **2g** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 14.6 min (major) and 17.9 min (minor), 88% ee.



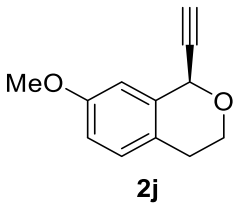
2h

1-ethynyl-6-methylisochromane (2h): Isolated yield 90%. A pale yellow oil. ^{1}H NMR δ 7.15 (d, J = 7.5 Hz, 1H), 7.03 (d, J = 7.8 Hz, 1H), 6.94 (s, 1H), 5.52 (s, 1H), 4.25-4.18 (m, 1H), 4.00-3.92 (m, 1H), 2.93-2.73 (m, 2H), 2.54 (d, J = 2.4 Hz, 1H), 2.32 (s, 3H). ^{13}C NMR δ 137.0, 132.5, 131.4, 129.4, 127.3, 125.7, 83.0, 73.7, 66.4, 62.4, 27.9, 21.1. HRMS (EI) Calcd. for $C_{12}H_{12}O$ [M]: 172.0888. Found: 172.0885. $[\alpha]^{21}_{D}$ = +42.0 (c = 0.37, $CHCl_3$). The enantiomeric excess of **2h** was determined by HPLC analysis; DAICEL Chiralpak OZ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 9.67 min (major) and 10.8 min (minor), 91% ee.



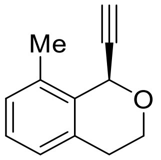
2i

1-ethynyl-6,7-dimethylisochromane (2i): Isolated yield 66%. A pale yellow oil. ^{1}H NMR δ 7.02 (s, 1H), 6.90 (s, 1H), 5.50 (s, 1H), 4.24-4.17 (m, 1H), 3.99-3.92 (m, 1H), 2.92-2.70 (m, 2H), 2.55 (d, J = 2.4 Hz, 1H), 2.24 (s, 3H), 2.23 (s, 3H). ^{13}C NMR δ 135.8, 134.8, 131.6, 130.0, 129.9, 126.6, 83.2, 73.6, 66.2, 62.5, 27.4, 19.42, 19.40. HRMS (EI) Calcd. for $C_{13}H_{14}O$ [M]: 186.1045. Found: 186.1051. $[\alpha]^{23}_{D}$ = +84.9 (c = 0.42, $CHCl_3$). The enantiomeric excess of **2i** was determined by HPLC analysis; DAICEL Chiralpak OZ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 9.41 min (major) and 10.6 min (minor), 87% ee.



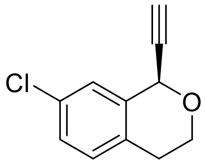
2j

1-ethynyl-7-methoxyisochromane (2j): Isolated yield 72%. A pale yellow oil. ^{1}H NMR δ 7.06-7.02 (m, 1H), 6.82-6.77 (m, 2H), 5.51 (s, 1H), 4.24-4.17 (m, 1H), 4.00-3.94 (m, 1H), 3.80 (s, 3H), 2.89-2.72 (m, 2H), 2.56 (d, J = 2.0 Hz, 1H). ^{13}C NMR δ 158.0, 135.2, 129.9, 124.7, 113.9, 110.4, 82.7, 73.8, 66.6, 62.7, 55.3, 27.1. HRMS (EI) Calcd. for $C_{12}H_{12}O_2$ [M]: 188.0837. Found: 188.0833. $[\alpha]^{22}_{D}$ = +45.0 (c = 0.47, $CHCl_3$). The enantiomeric excess of **2j** was determined by HPLC analysis; DAICEL Chiralpak OZ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 12.7 min (major) and 13.6 min (minor), 93% ee.



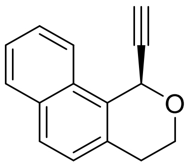
2k

1-ethynyl-8-methylisochromane (2k): Isolated yield 75%. A pale yellow oil. ^{1}H NMR δ 7.14 (t, J = 7.3 Hz, 1H), 7.02 (d, J =7.3 Hz, 1H), 6.98 (d, J = 7.3 Hz, 1H), 5.50 (d, J = 2.0 Hz, 1H), 4.33-4.22 (m, 1H), 4.10-4.04 (m, 1H), 3.14-3.04 (m, 1H), 2.72-2.62 (m, 1H), 2.53 (d, J = 2.0 Hz, 1H), 2.33 (s, 3H). ^{13}C NMR δ 134.3, 132.7, 132.4, 128.3, 127.2, 126.9, 81.8, 74.1, 64.3, 60.7, 27.9, 18.4. HRMS (EI) Calcd. for $C_{12}H_{12}O$ [M]: 172.0888. Found: 172.0884. $[\alpha]^{20}_{D}$ = +18.6 (c = 0.60, $CHCl_3$). The enantiomeric excess of **2k** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 13.2 min (major) and 14.9 min (minor), 80% ee.



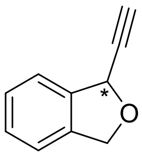
2l

7-chloro-1-ethynylisochromane (2l): Isolated yield 85%. A pale yellow oil. ^{1}H NMR δ 7.26 (s, 1H), 7.19 (dd, J = 8.4 Hz, 2.4 Hz, 1H), 7.06 (d, J = 8.4 Hz, 1H), 5.50 (s, 1H), 4.24-4.17 (m, 1H), 4.00-3.93 (m, 1H), 2.92-2.75 (m, 2H), 2.59 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ 136.0, 131.9, 131.2, 130.3, 127.6, 125.8, 82.1, 74.4, 66.1, 62.3, 27.3. HRMS (EI) Calcd. for $C_{11}H_9ClO$ [M]: 192.0342. Found: 192.0346. $[\alpha]^{22}_{D}$ = +152.6 (c = 0.27, $CHCl_3$). The enantiomeric excess of **2l** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 17.7 min (major) and 20.4 min (minor), 80% ee.



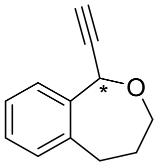
2m

1-ethynyl-3,4-dihydro-1H-benzo[h]isochromene (2m): Isolated yield 57%. A pale yellow oil. ^{1}H NMR δ 7.97 (d, J = 8.4, 1H), 7.82 (d, J = 8.4, 1H), 7.73 (d, J = 8.6, 1H), 7.58-7.52 (m, 1H), 7.47 (td, J = 8.0 Hz, 1.2 Hz, 1H), 7.23 (d, J = 8.6 Hz, 1H), 6.05 (s, 1H), 4.46-4.36 (m, 1H), 4.21-4.15 (m, 1H), 3.27-3.20 (m, 1H), 2.83-2.75 (m, 1H), 2.58 (d, J = 2.0 Hz, 1H). ^{13}C NMR δ 132.3, 130.4, 129.4, 128.9, 128.7, 127.9, 127.4, 126.5, 125.4, 122.4, 82.5, 74.7, 64.0, 60.7, 28.3. HRMS (EI) Calcd. for $C_{15}H_{12}O$ [M]: 208.0888. Found: 208.0882. $[\alpha]^{22}_{D}$ = +83.3 (c = 0.51, $CHCl_3$). The enantiomeric excess of **2m** was determined by HPLC analysis; DAICEL Chiralpak OZ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 9.96 min (major) and 11.8 min (minor), 83% ee.



7

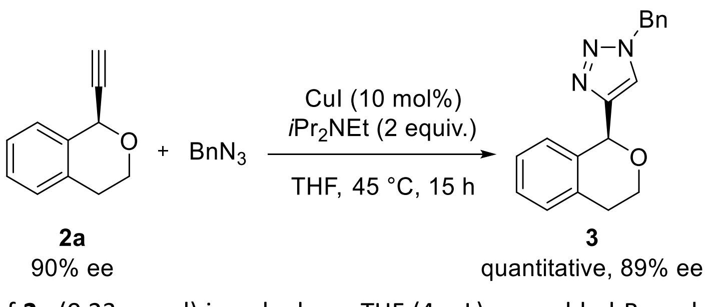
1-ethynyl-1,3-dihydroisobenzofuran (7): Isolated yield 36% (with **L2**). A pale yellow oil. ^{1}H NMR δ 7.39-7.31 (m, 3H), 7.27-7.22 (m, 1H), 5.88 (s, 1H), 5.26 (dd, J = 12.2 Hz, 2.0 Hz, 1H), 5.10 (d, J = 12.2, 1H), 2.60 (d, J = 2.4 Hz, 1H). ^{13}C NMR δ 138.8, 138.6, 128.3, 127.8, 121.7, 121.1, 82.0, 74.2, 73.1, 73.0. HRMS (EI) Calcd. for $C_{10}H_8O$ [M]: 144.0575. Found: 144.0582. $[\alpha]^{21}_{D}$ = +119.2 (c = 0.14, $CHCl_3$). The enantiomeric excess of **7** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time:20.8 min (major) and 27.5 min (minor), 68% ee.



8

1-ethynyl-1,3,4,5-tetrahydrobenzo[c]oxepine (8): Isolated yield 40% (with **L5**). A pale yellow oil. ^{1}H NMR δ 7.57-7.49 (m, 1H), 7.24-7.15 (m, 3H), 5.50 (d, J = 2.2 Hz, 1H), 4.45-4.39 (m, 1H), 4.04-3.97 (m, 1H), 3.15-3.11 (m, 1H), 3.03-2.95 (m, 1H), 2.81 (d, J = 2.2 Hz, 1H), 1.89-1.79 (m, 2H). ^{13}C NMR δ 141.6, 138.7, 129.7, 128.4, 127.4, 126.3, 80.1, 77.5, 72.6, 72.4, 34.6, 29.8. HRMS (EI) Calcd. for $C_{12}H_{12}O$ [M]: 172.0888. Found: 172.0884. $[\alpha]^{22}_{D}$ = -2.40 (c = 0.15, $CHCl_3$). The enantiomeric excess of **8** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/*i*PrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time:43.1 min (minor) and 52.5 min (major), 29% ee.

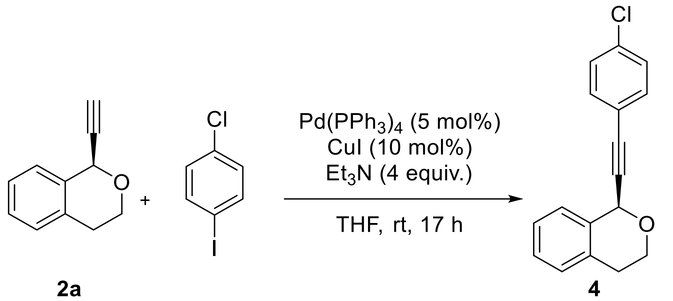
Preparation of (*S*)-1-benzyl-4-(isochroman-1-yl)-1H-1,2,3-triazole (3)



To a solution of **2a** (0.23 mmol) in anhydrous THF (4 mL) was added Benzyl azide (37.0 µL, 0.28 mmol), CuI (4.40 mg, 0.023 mmol), *i*Pr_2NEt (64.0 µL, 0.46 mmol). The mixture was stirred at 45 °C for 15 h. The mixture was concentrated under reduced pressure and purified by column chromatography with hexane/EtOAc (5:1-3:1) to give (*S*)-1-benzyl-4-(isochroman-1-yl)-1H-1,2,3-triazole **3** as a white solid (65.0 mg, 0.23 mmol, 98% isolated yield). ^{1}H NMR δ 7.36-7.00 (m, 10H), 6.05 (s, 1H), 5.51 (d, J = 14.8 Hz, 1H), 5.44 (d, J = 14.8 Hz, 1H), 4.16-4.10 (m, 1H), 3.96-3.88 (m, 1H), 3.05-2.96 (m, 1H), 2.84-2.76 (m, 1H). ^{13}C NMR δ 150.0, 135.7, 134.4, 133.4, 129.0, 128.8, 128.7, 128.1, 126.9, 126.3, 126.1, 122.0, 71.7, 63.6, 54.2, 28.5. HRMS (EI) Calcd.

for $C_{18}H_{17}N_3O$ [M]: 291.1372. Found: 291.1383. $[\alpha]^{24}_D$ = +71.3 (c = 0.50, $CHCl_3$). The enantiomeric excess of **3** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/*i*PrOH = 70/30, flow rate = 0.5 mL/min, λ = 220 nm, retention time: 28.6 min (major) and 52.7 min (minor), 89% ee.

Preparation of (*R*)-1-((4-chlorophenyl)ethynyl)isochromane (4)

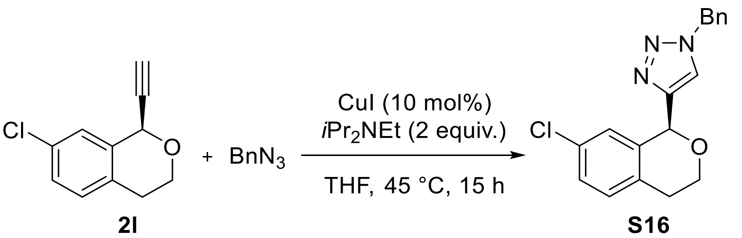


2a
90% ee

4
92%, 92.5% ee

To a solution of **2a** (0.17 mmol) in anhydrous THF (4 mL) was added 1-chloro-4-iodobenzene (80.0 mg, 0.34 mmol), $Pd(PPh_3)_4$ (9.80 mg, 0.0085 mmol), CuI (3.20 mg, 0.017 mmol), Et_3N (95.0 µL, 0.68 mmol) at room temperature and the mixture was stirred for 17 h. The mixture was concentrated under reduced pressure and purified by column chromatography with hexane/EtOAc (100:0-25:1) to give (*R*)-1-((4-chlorophenyl)ethynyl)isochromane **4** as a yellow oil (42 mg, 0.156 mmol, 92% isolated yield). ^{1}H NMR δ 7.39-7.10 (m, 8H), 5.76 (s, 1H), 4.32-4.24 (m, 1H), 4.05-3.98 (m, 1H), 2.98-2.83 (m, 2H). ^{13}C NMR δ 134.6, 134.5, 133.1, 132.8, 129.0, 128.6, 127.3, 126.4, 125.9, 121.0, 89.1, 84.5, 67.2, 62.7, 28.0. HRMS (EI) Calcd. for $C_{17}H_{13}ClO$ [M]: 268.0655. Found: 268.0648. $[\alpha]^{24}_D$ = +1.43 (c = 0.55, $CHCl_3$). The enantiomeric excess of **4** was determined by HPLC analysis; DAICEL Chiralpak OJ-H, hexane/iPrOH = 95/5, flow rate = 0.5 mL/min, λ = 220 nm, retention time:24.1 min (minor) and 30.8 min (major), 92.5% ee.

Preparation of (*S*)-1-benzyl-4-(7-chloroisochroman-1-yl)-1H-1,2,3-triazole (S16)



2l
80% ee

S16
75% yield

(*S*)-1-benzyl-4-(7-chloroisochroman-1-yl)-1H-1,2,3-triazole **S16** was synthesized from **2l** (0.6 mmol) as a similar method as the synthesis of **3** from **2a**. Recrystallization from CH_2Cl_2 gave crystals of **S16** suitable for X-ray analysis (0.45 mmol, 75% yield). A white solid. ^{1}H NMR δ 7.39-7.32 (m, 4H), 7.29-7.23 (m, 2H), 7.14 (dd, J = 8.0 Hz, 1.6 Hz, 1H), 7.09-7.03 (m, 2H), 5.98 (s, 1H), 5.56 (d, J = 15.0 Hz, 1H), 5.47 (d, J = 15.0 Hz, 1H), 4.18-4.10 (m, 1H), 3.94-3.86 (m, 1H), 3.02-2.92 (m, 1H), 2.82-2.72 (m, 1H). ^{13}C NMR δ 149.2, 137.4, 134.3, 131.8, 131.7, 130.2, 129.1, 128.8, 128.1, 127.2, 126.3, 122.0, 71.4, 63.5, 54.2, 27.9. HRMS (EI) Calcd. for $C_{18}H_{16}N_3O$ [M]: 325.0982. Found: 325.0979.

X-ray diffraction studies of S16

Diffraction data for (*S*)-1-benzyl-4-(7-chloroisochroman-1-yl)-1H-1,2,3-triazole (**S16**, CCDC 1910939) were collected for the 2ϑ range of 4 to 55° at –100 °C on a Rigaku R-AXIS RAPID imaging plate diffractometer with graphite-monochromated Mo-Kα radiation (λ = 0.71075 Å) with VariMax optics. Intensity data were corrected for Lorentz and polarization effects and for empirical absorptions (ABSCOR),[S6] whereas structure solutions and refinements were carried out by using *CrystalStructure* package.[S7] Positions of non-hydrogen atoms were determined by direct methods (SHELXD Version 2013/2)[S8] and subsequent Fourier syntheses SHELXL Version 2016/6),[S9] and were refined on F_o^2 with all the unique reflections by full-matrix least squares with anisotropic thermal parameters. All the hydrogen atoms were placed at the calculated positions with fixed isotropic parameters. Anomalous dispersion effects were included in F_c,[S10] and mass attenuation coefficients, values for $\Delta f'$ and $\Delta f''$, and neutral atom scattering factors were taken from references.[S11–S13] Refinement of the Flack parameter (0.09(3)) using 1202 Parsons' quotients demonstrates that the absolute configuration of **S16** is (*S*).[S14] Details of the crystal and data collection parameters of **S16** are summarized in **Table S1**. ORTEP drawing of **S16** is shown in **Figure S1**.

Table S1. Crystallographic Data for **S16**.

compound	**S16**
CCDC number	1910939
chemical formula	$C_{18}H_{16}ClN_3O$
formula weight	325.80
crystal size (mm^3)	0.48 × 0.11 × 0.07
color, habit	colorless, needle
temperature (°C)	–100
crystal system	monoclinic
space group	$P2_1$ (no. 4)
a (Å)	12.1916(6)
b (Å)	5.5082(3)
c (Å)	12.3900(6)
α (deg)	90
β (deg)	102.989(7)
γ (deg)	90
V (Å^3)	810.74(8)
Z	2
d_{calcd} (g cm^{-3})	1.334
F(000)	340
μ (cm^{-1})	2.430
transmission factors range	0.840 – 0.983
number of measured reflections	7587
number of unique reflections	3593
R_{int}	0.0258
number of refined parameters	208
$R1$ ($I > 2\sigma(I)$) [a]	0.0485
$wR2$ (all data) [b]	0.0965
GOF [c]	1.000
maximum and minimum residual peaks (e Å^{-3})	+0.55 / –0.44
Flack parameter	0.09(3)

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$. [b] $wR2 = [\Sigma\{w(F_o^2 - F_c^2)^2\}/\Sigma w(F_o^2)^2]^{1/2}$, $w = 1/[\sigma^2(F_o^2) + rP]$, $P = (\mathrm{Max}(F_o^2, 0) + 2F_c^2)/3$ [r = 0.5080]. [c] GOF = $[\Sigma w(F_o^2 - F_c^2)^2/(N_o - N_{params})]^{1/2}$.

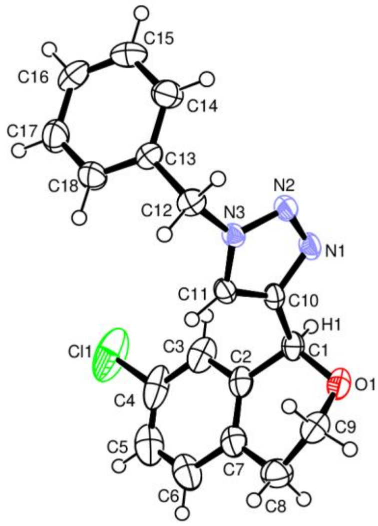


Figure S1. ORTEP drawing of **S16**. Thermal ellipsoids are given at the 50% probability level. Hydrogen atom labels except for H1 are omitted for clarity.

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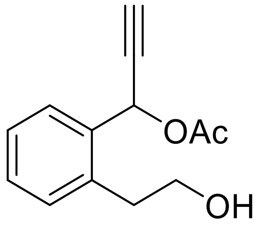
^{1}H and ^{13}C NMR Spectra



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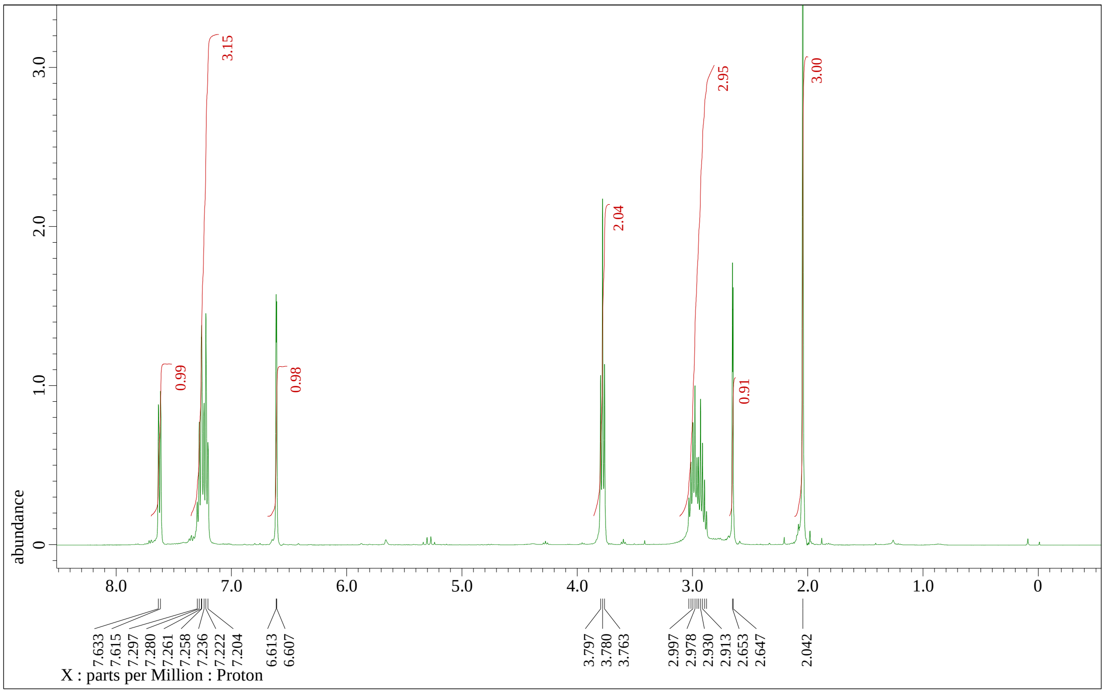

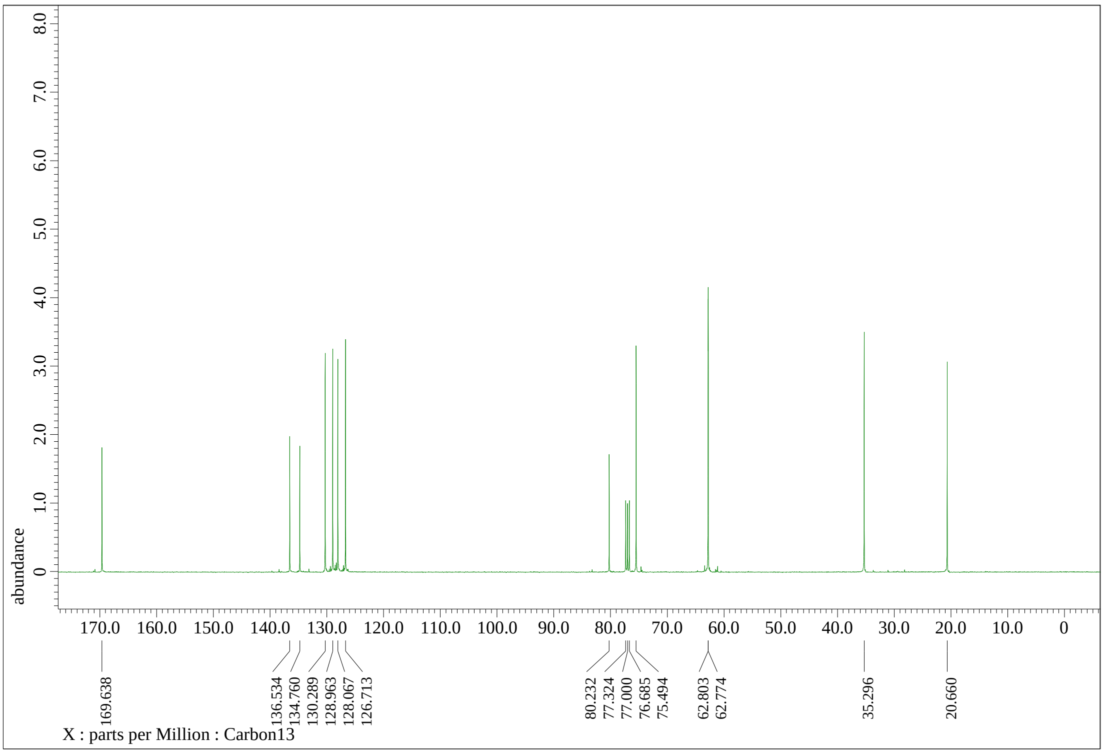

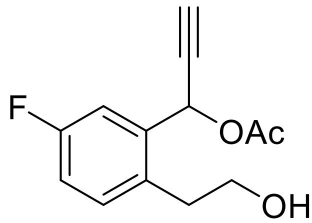
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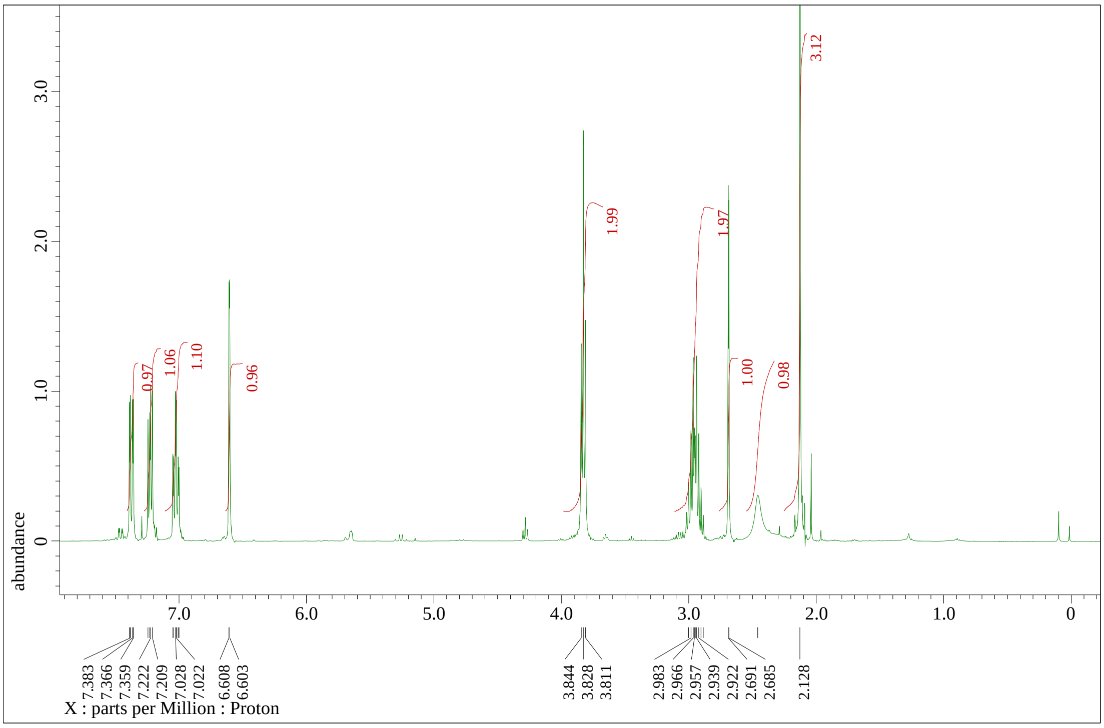
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1.10
0.96
1.99
1.97
1.00
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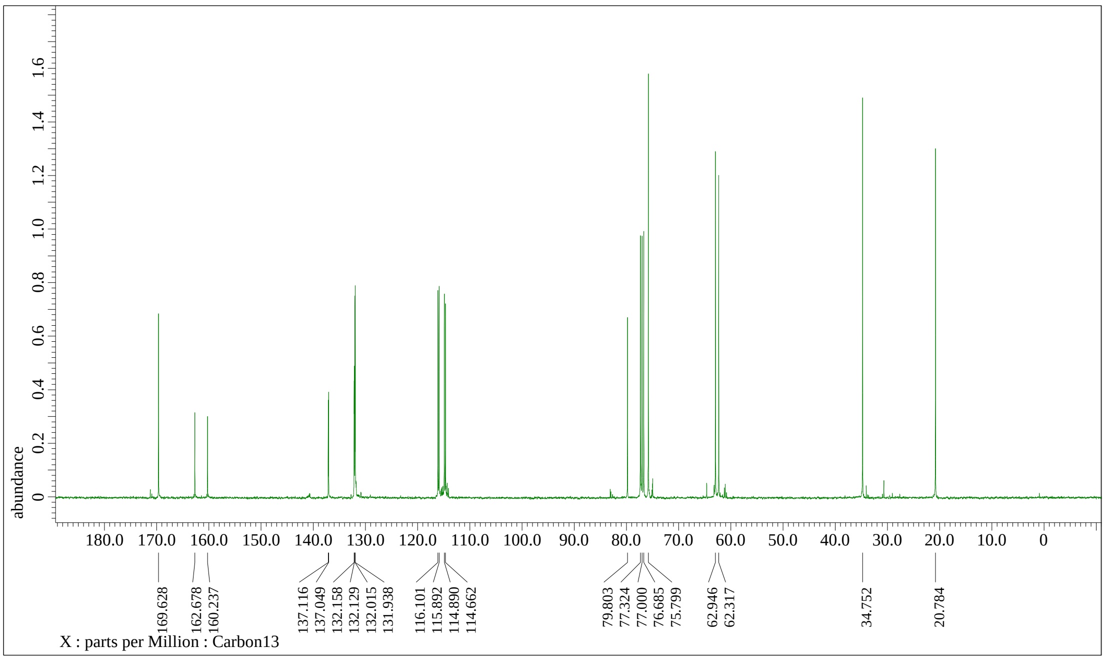
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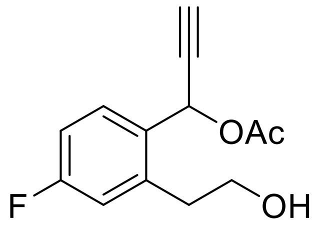

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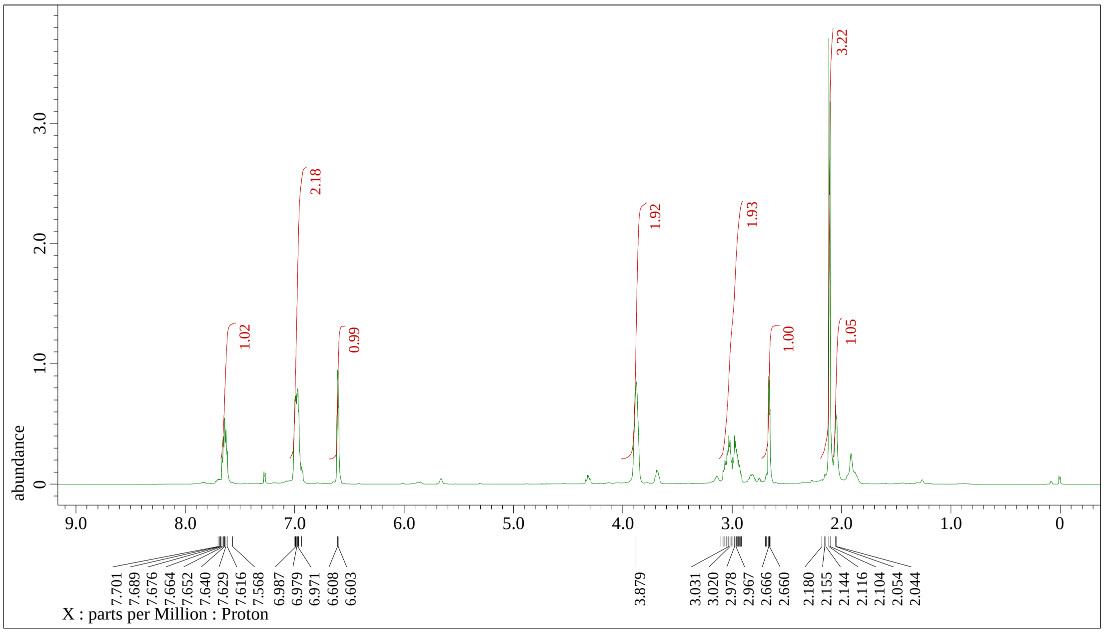

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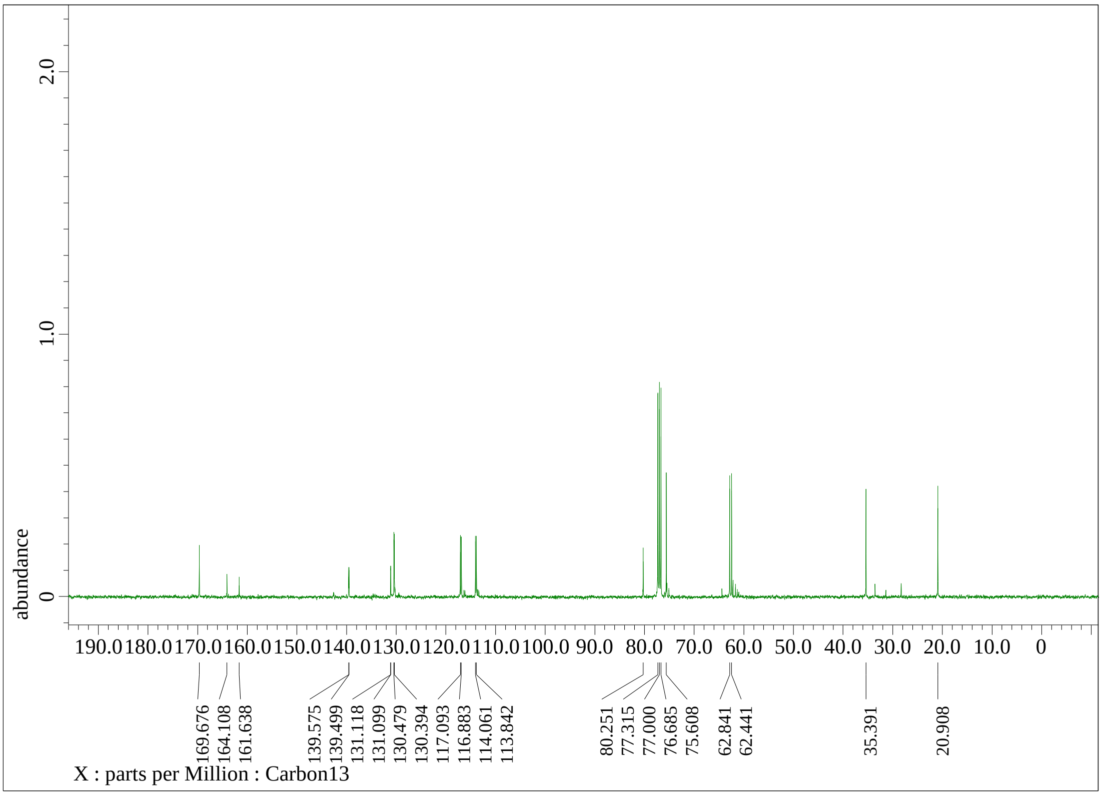

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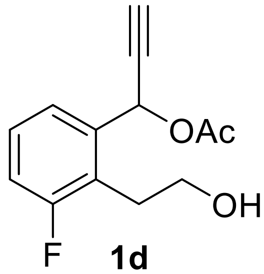
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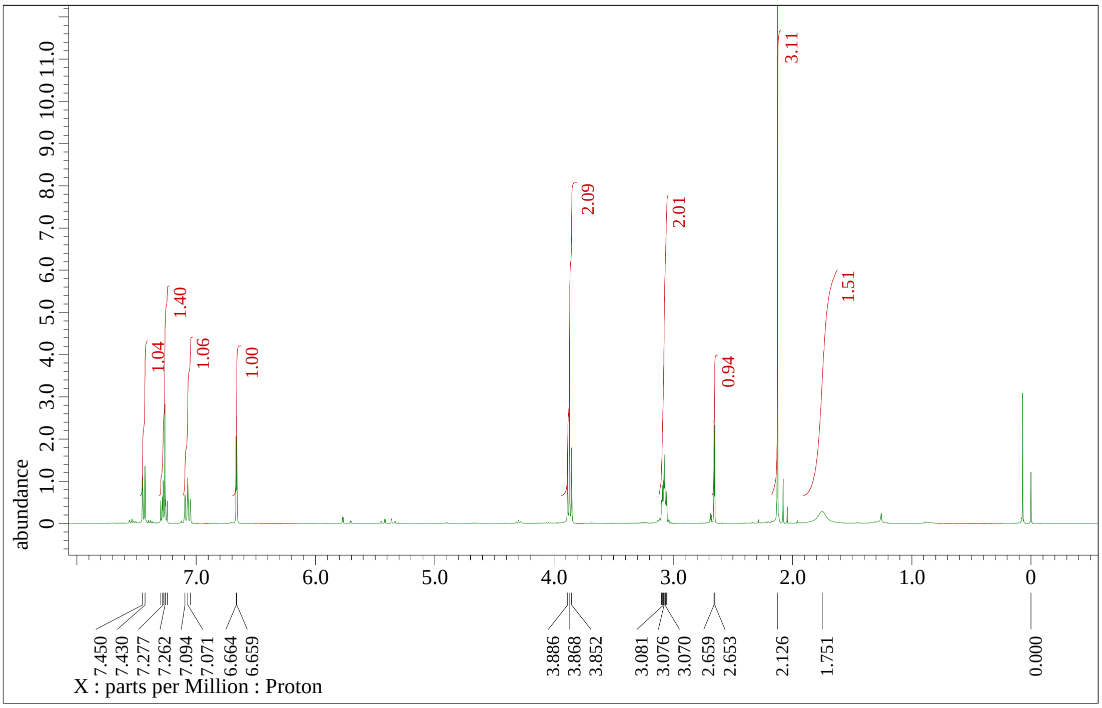
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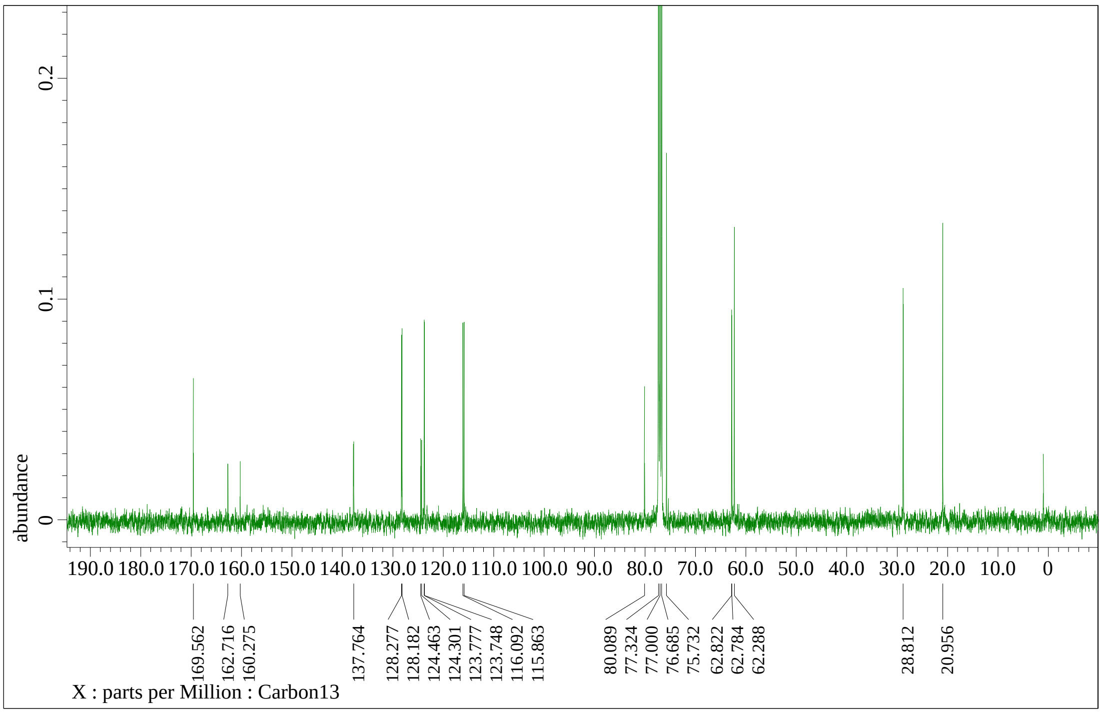
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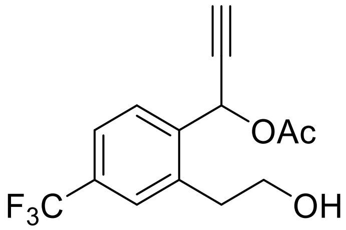
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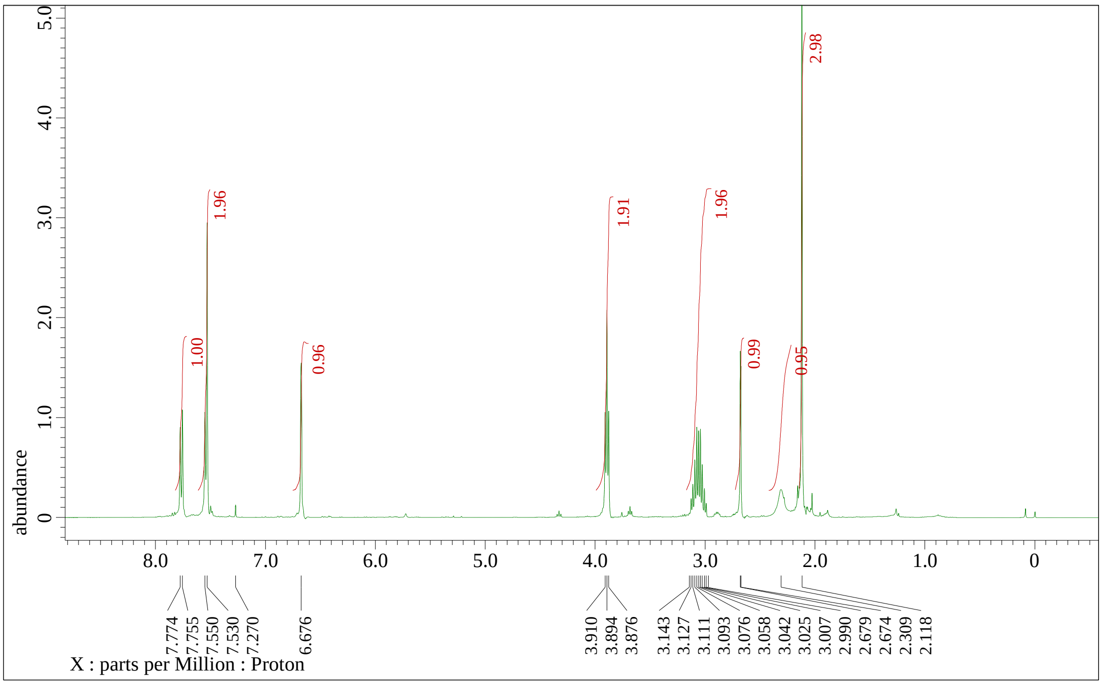
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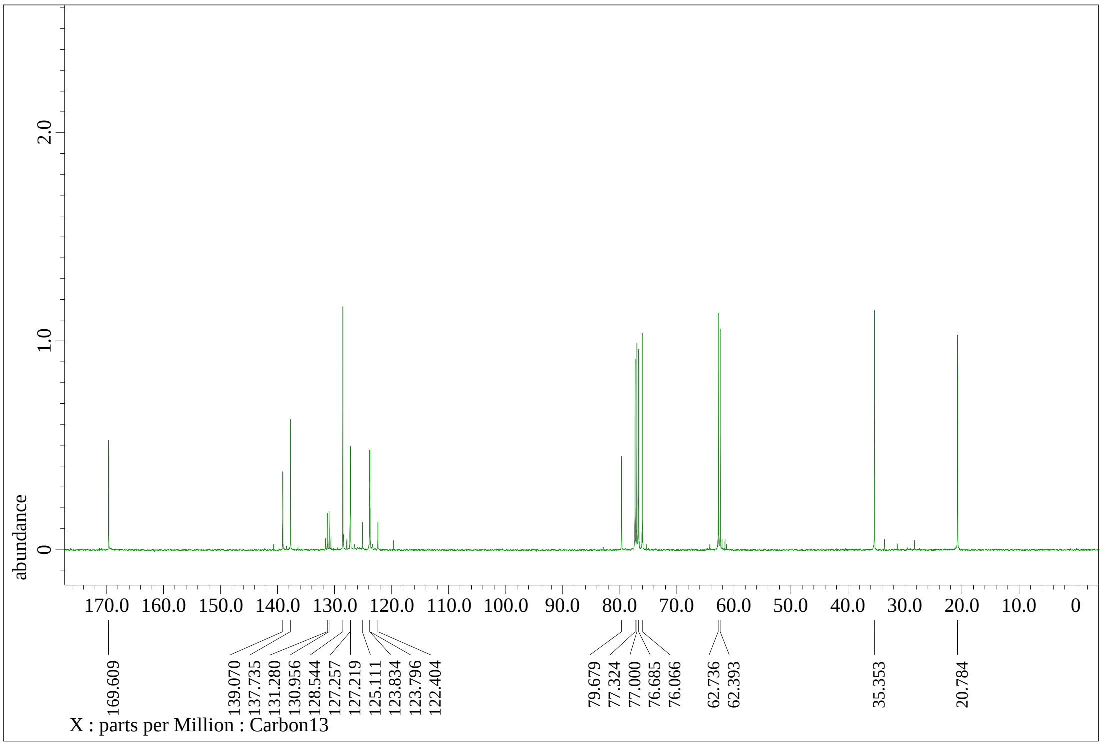
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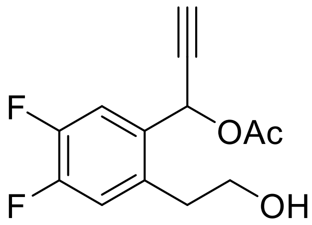
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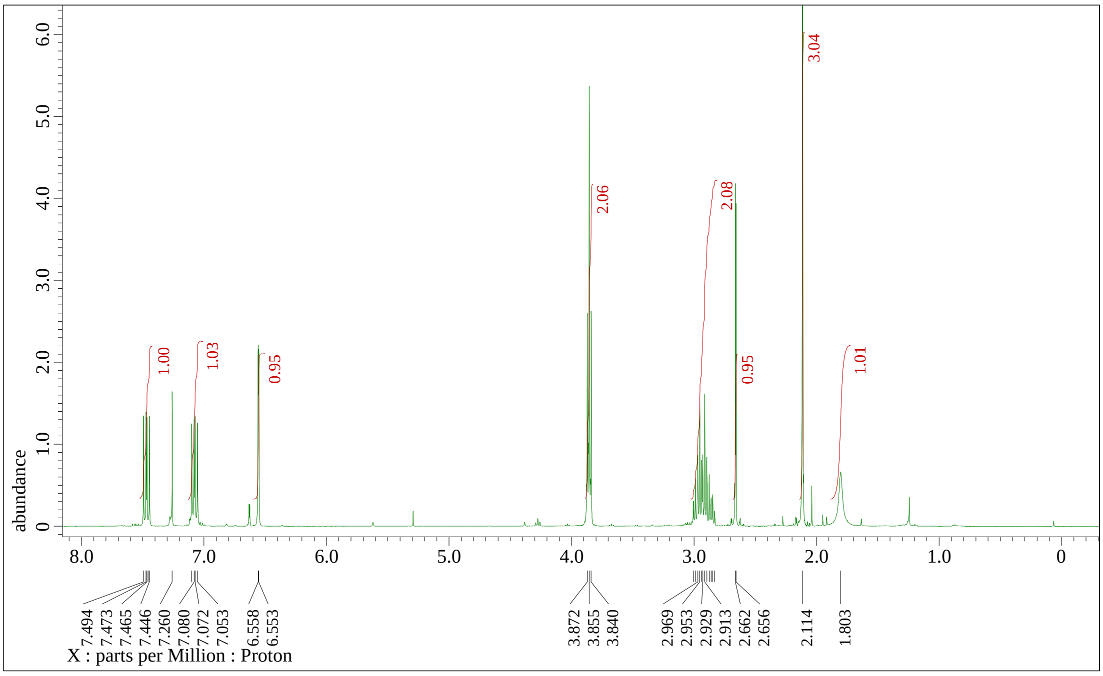
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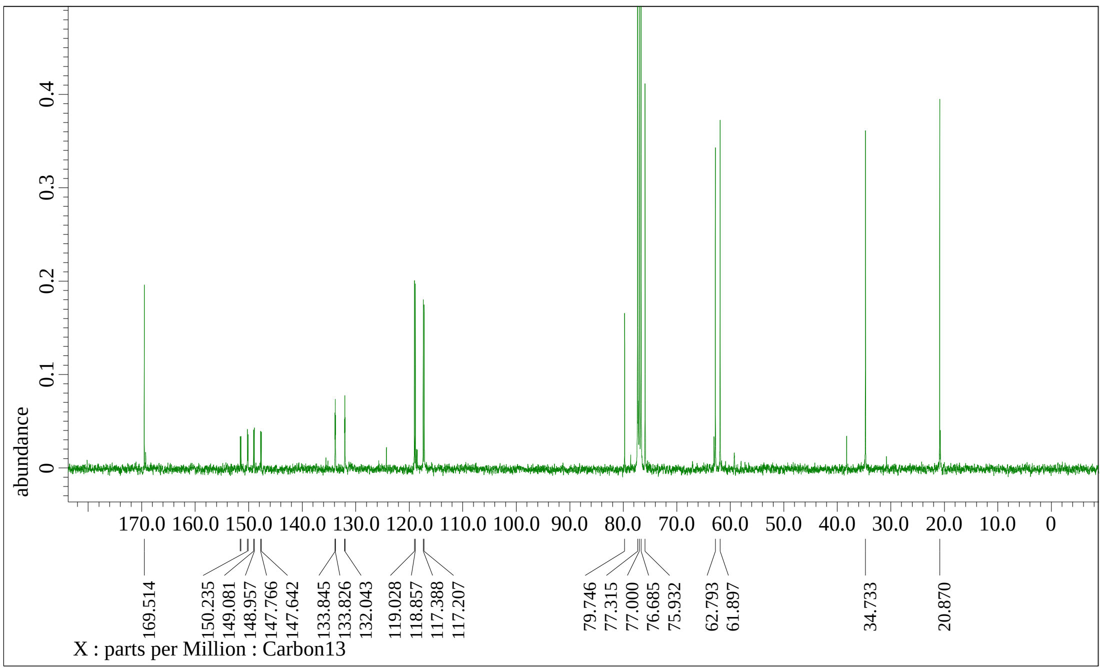
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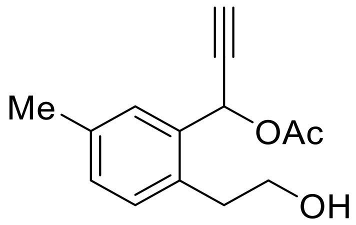
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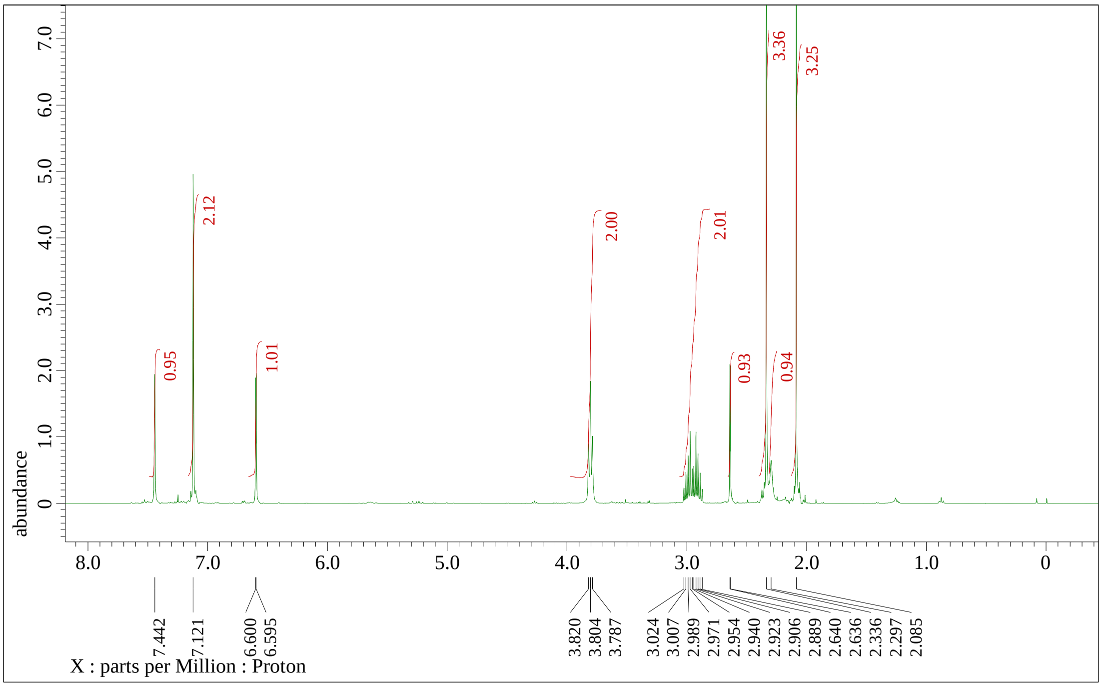
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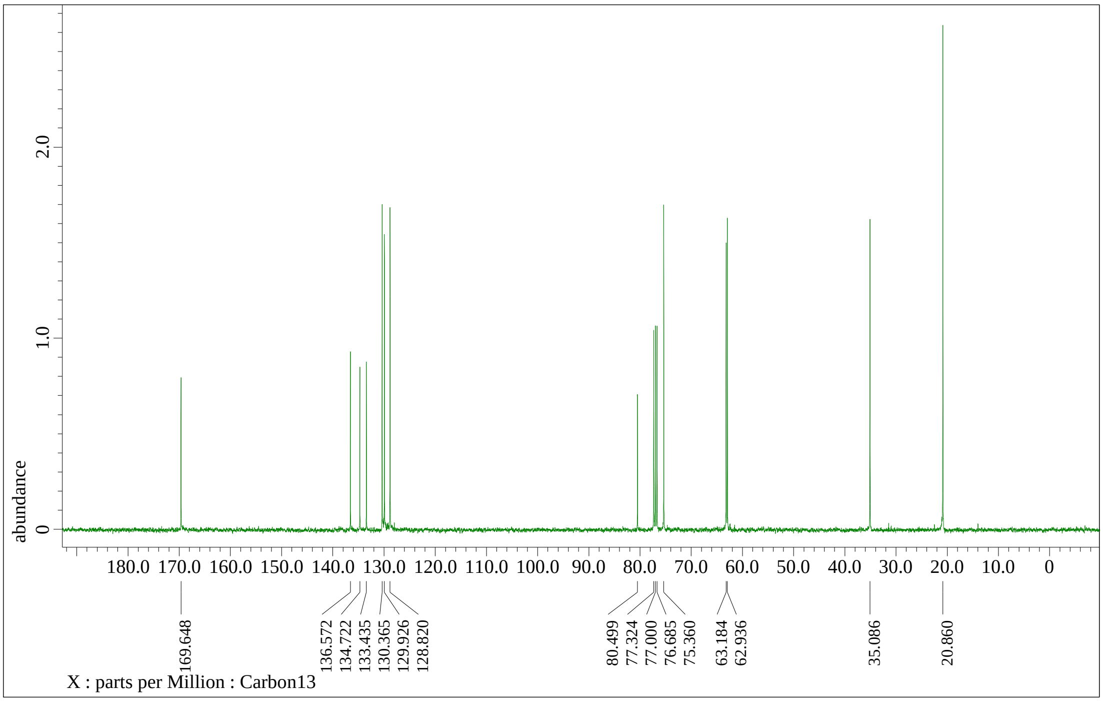
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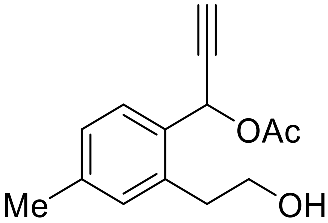
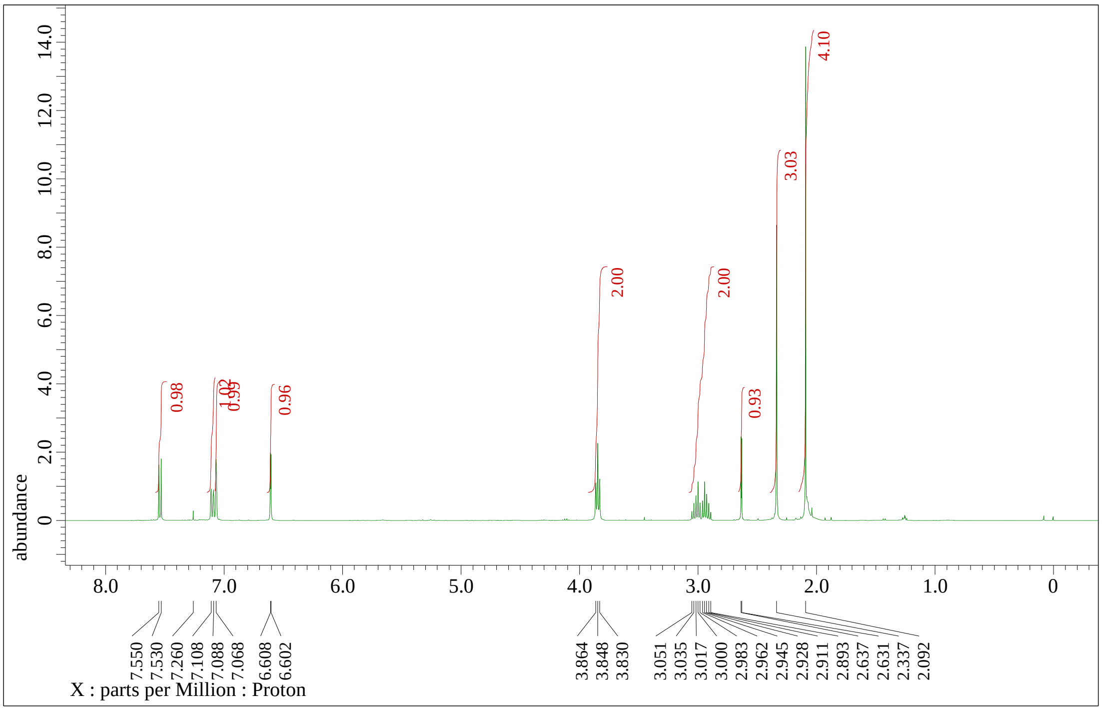
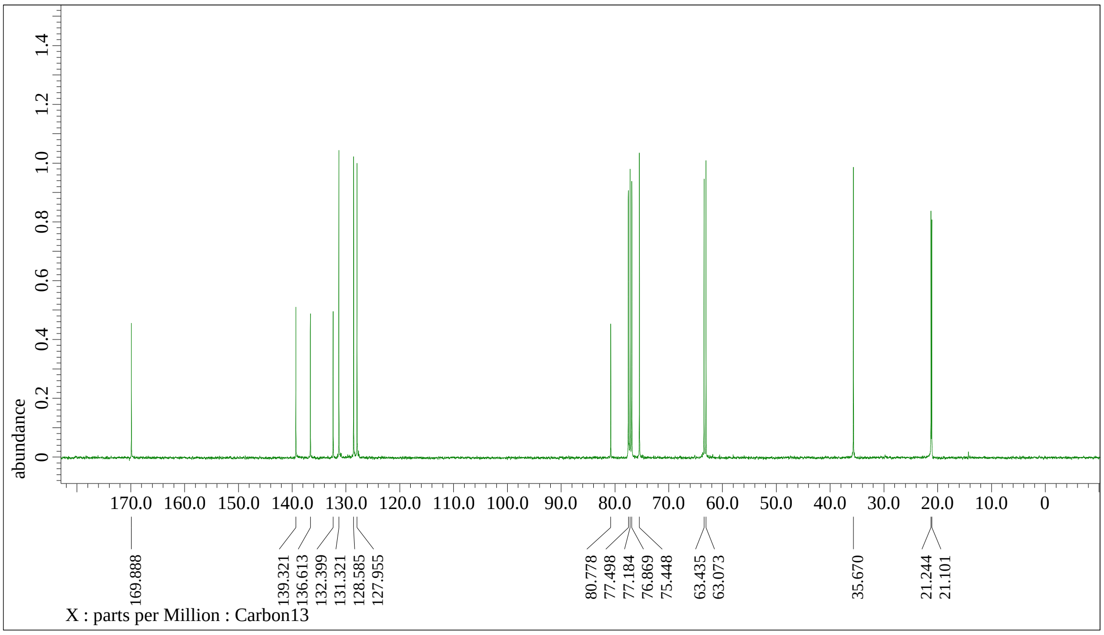
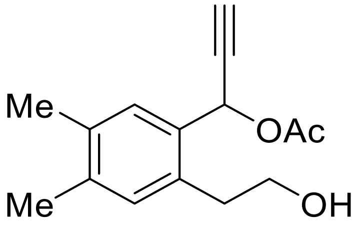
62.936
35.086
20.860


OAc
Me
OH

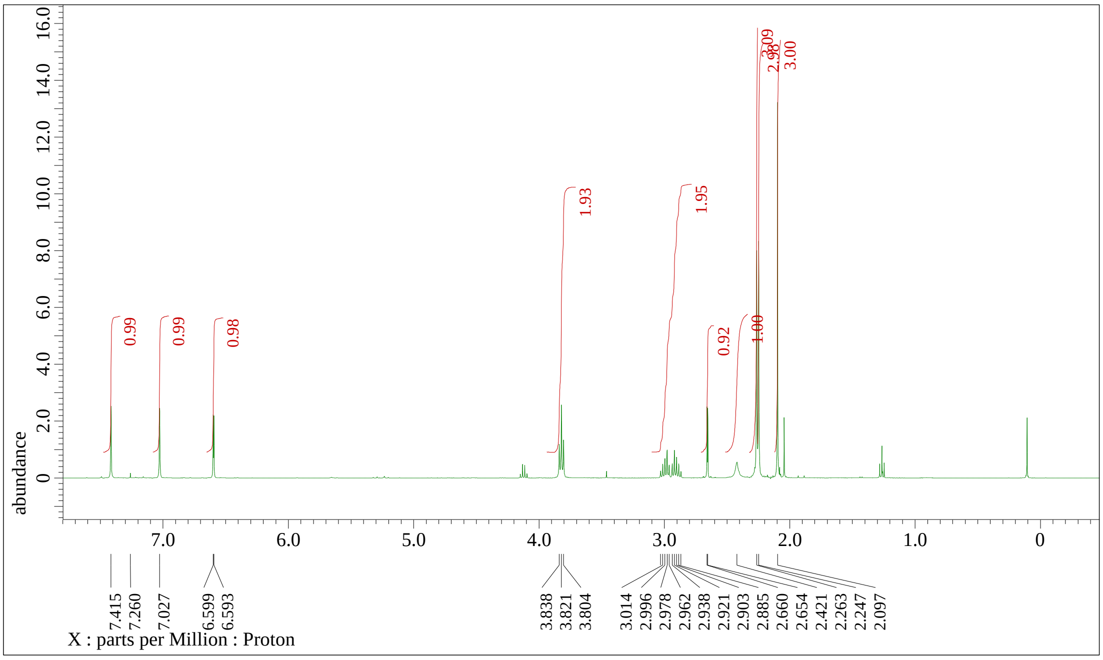
1h

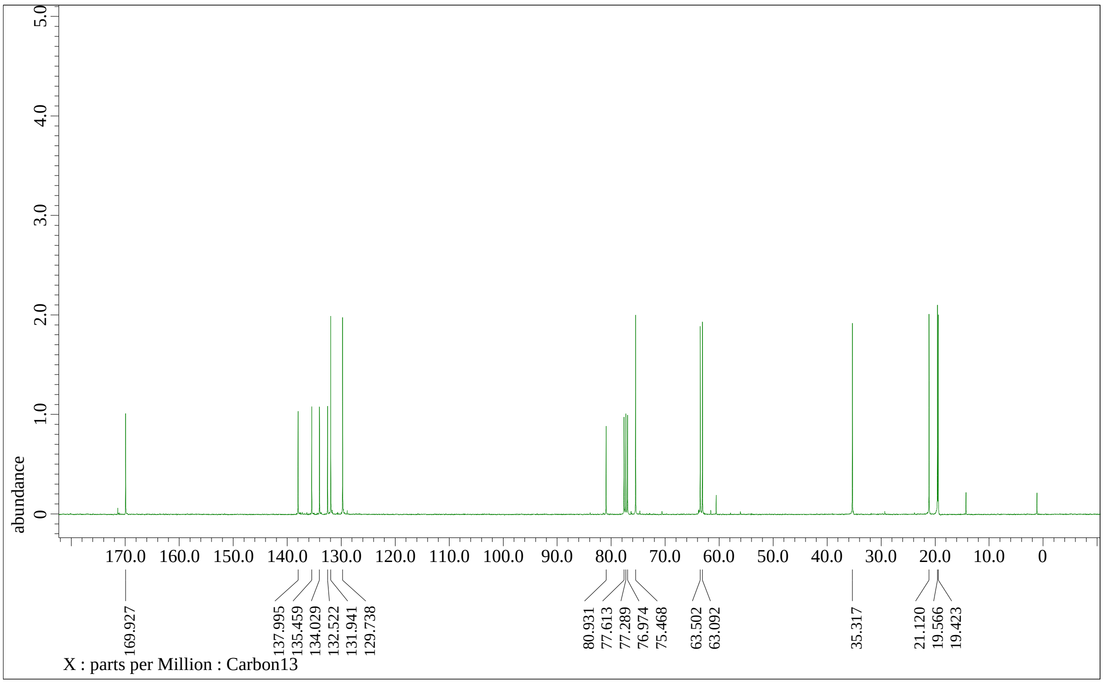

abundance
0.98
1.02
0.99
0.96
2.00
2.00
0.93
3.03
4.10
7.550
7.530
7.260
7.108
7.088
7.068
6.608
6.602
3.864
3.848
3.830
3.051
3.035
3.017
3.000
2.983
2.962
2.945
2.928
2.911
2.893
2.637
2.631
2.337
2.092
X : parts per Million : Proton

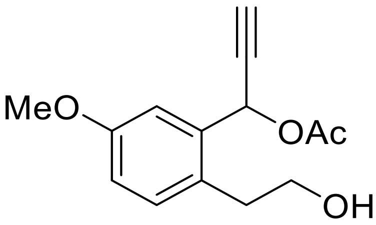

abundance
169.888
139.321
136.613
132.399
131.321
128.585
127.955
80.778
77.498
77.184
76.869
75.448
63.435
63.073
35.670
21.244
21.101
X : parts per Million : Carbon13


Me
Me
OAc
OH

1i

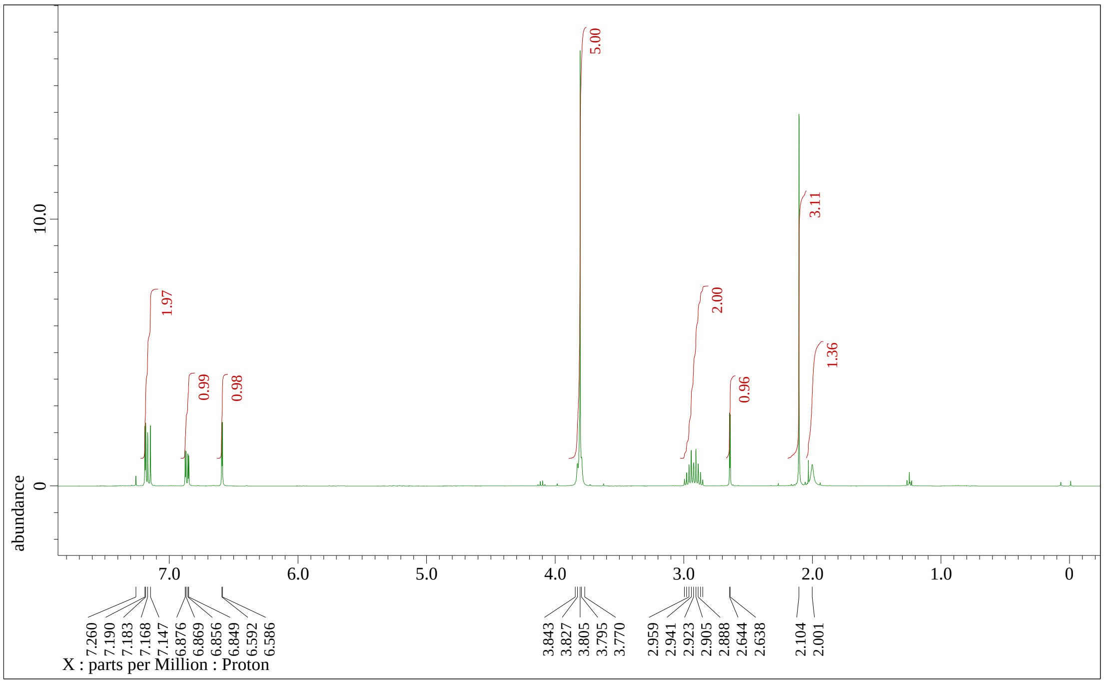

abundance
0.99
0.99
0.98
1.93
1.95
0.92
1.00
3.09
2.98
3.00
7.415
7.260
7.027
6.599
6.593
3.838
3.821
3.804
3.014
2.996
2.978
2.962
2.938
2.921
2.903
2.885
2.660
2.654
2.421
2.263
2.247
2.097
X : parts per Million : Proton


abundance
169.927
137.995
135.459
134.029
132.522
131.941
129.738
80.931
77.613
77.289
76.974
75.468
63.502
63.092
35.317
21.120
19.566
19.423
X : parts per Million : Carbon13

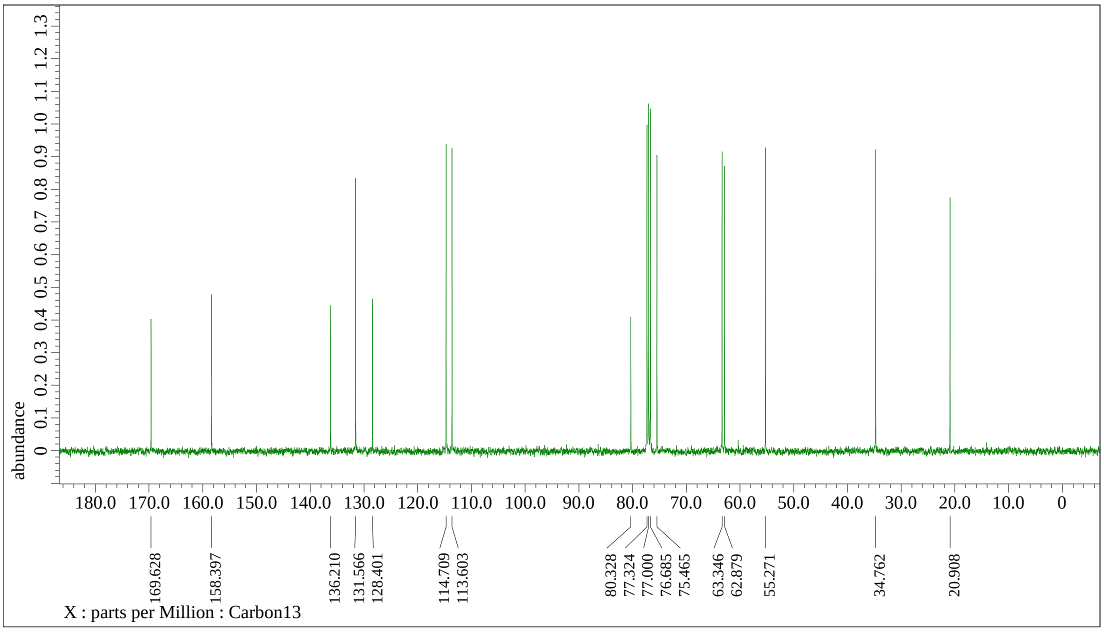


MeO
OAc
OH

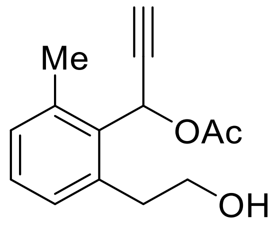
1j



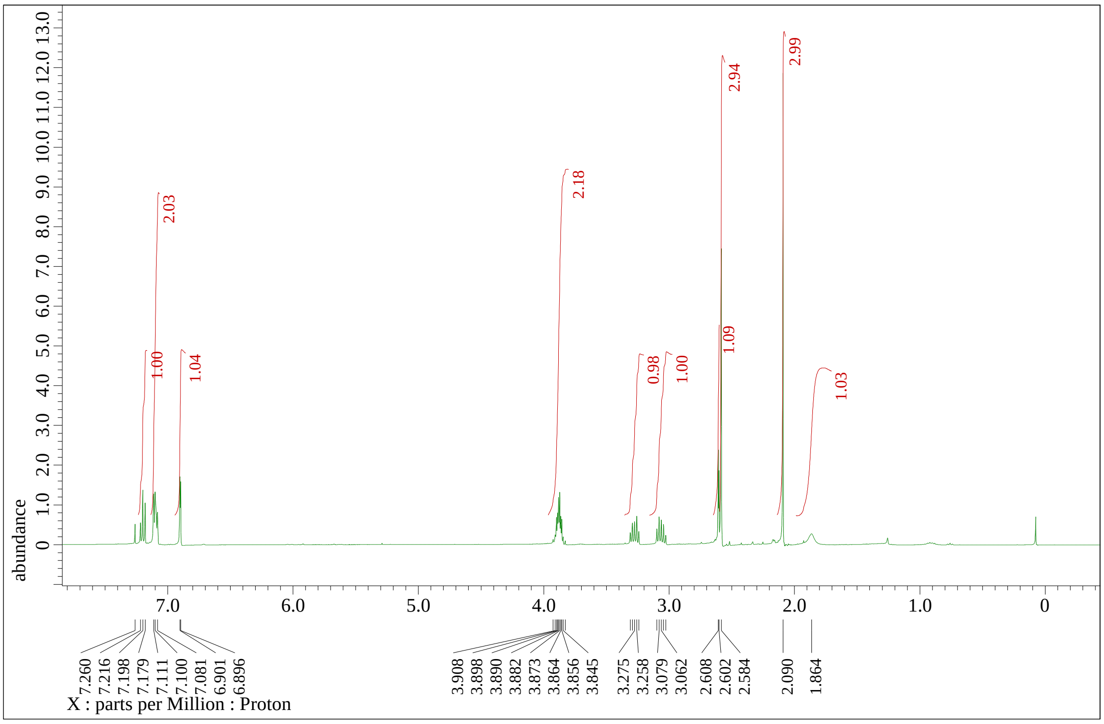
abundance
X : parts per Million : Proton



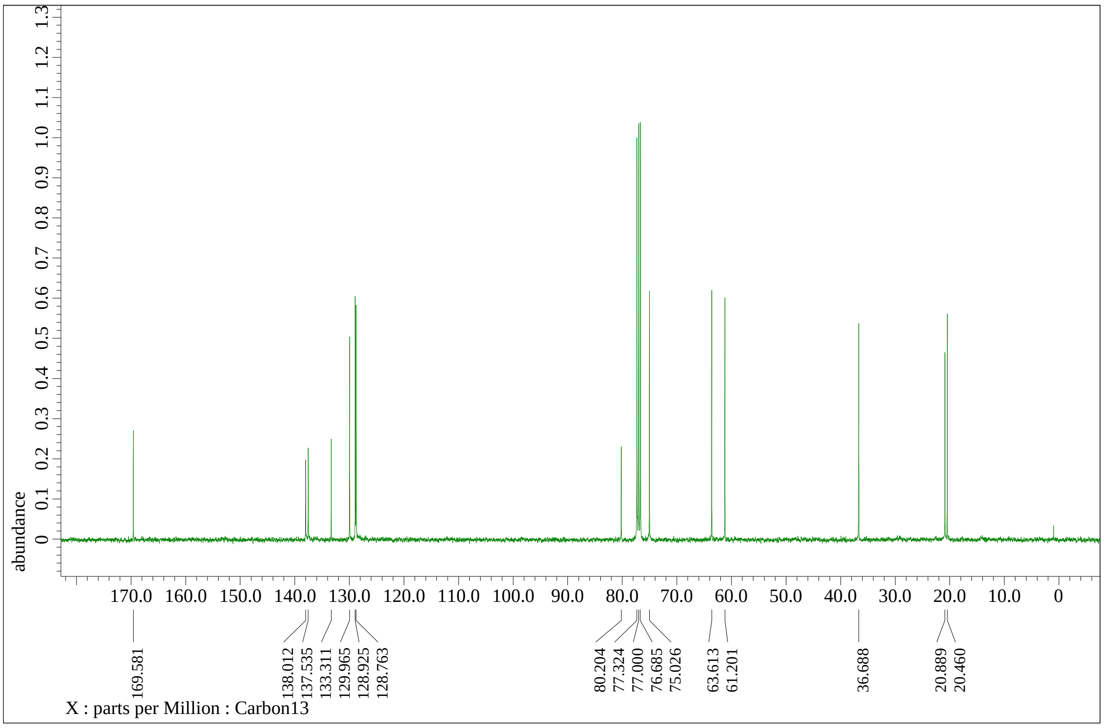
abundance
X : parts per Million : Carbon13



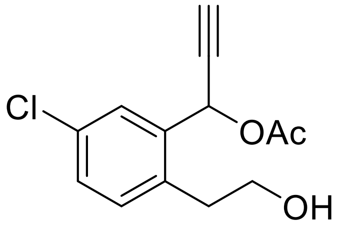
1k



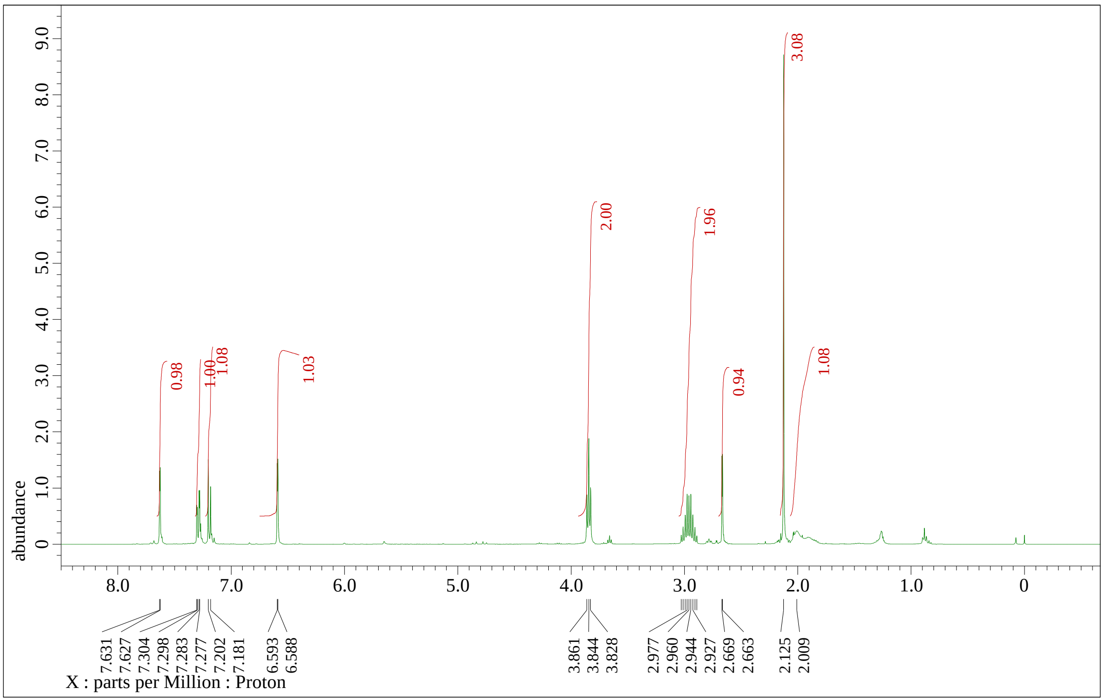
abundance
X : parts per Million : Proton



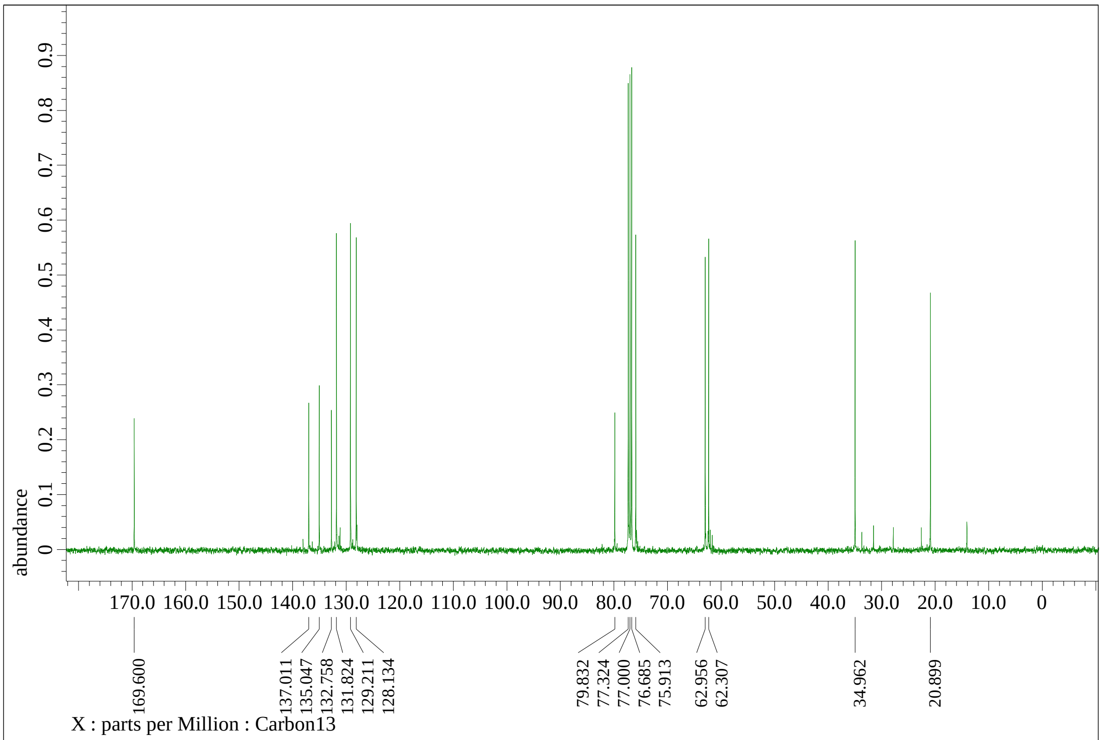
abundance
X : parts per Million : Carbon13



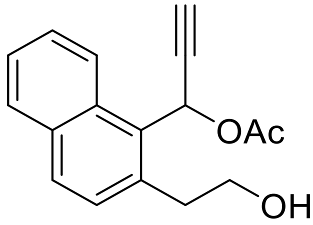
1l



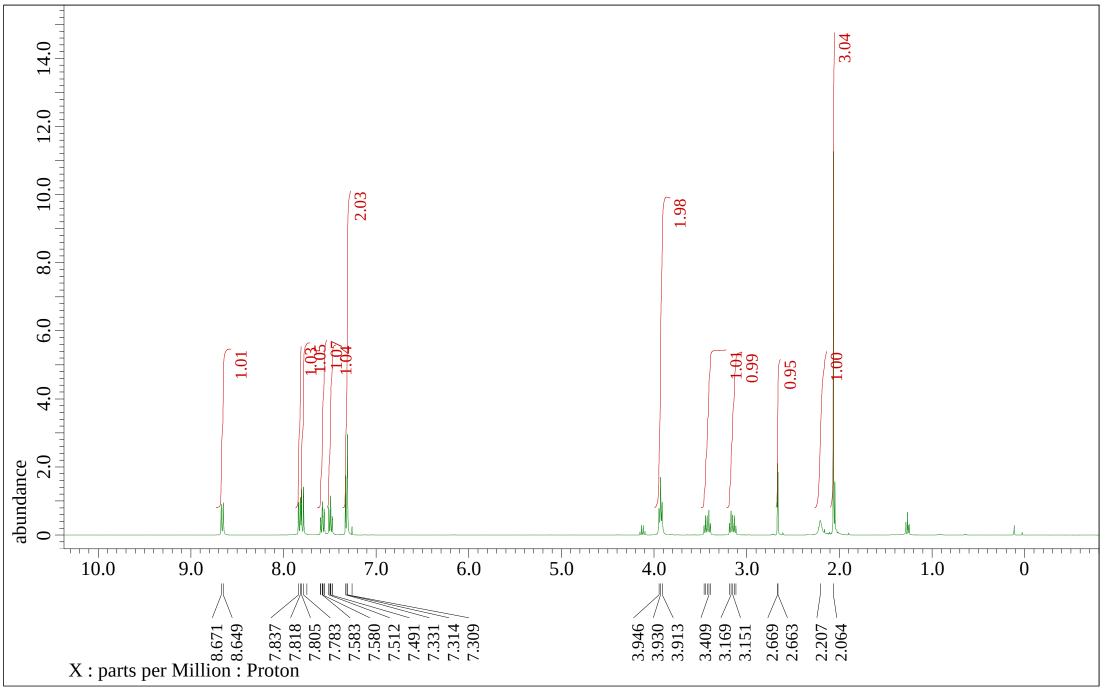
abundance
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
0.98
1.00
1.08
1.03
2.00
1.96
0.94
3.08
1.08
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.631
7.627
7.304
7.298
7.283
7.277
7.202
7.181
6.593
6.588
3.861
3.844
3.828
2.977
2.960
2.944
2.927
2.669
2.663
2.125
2.009
X : parts per Million : Proton



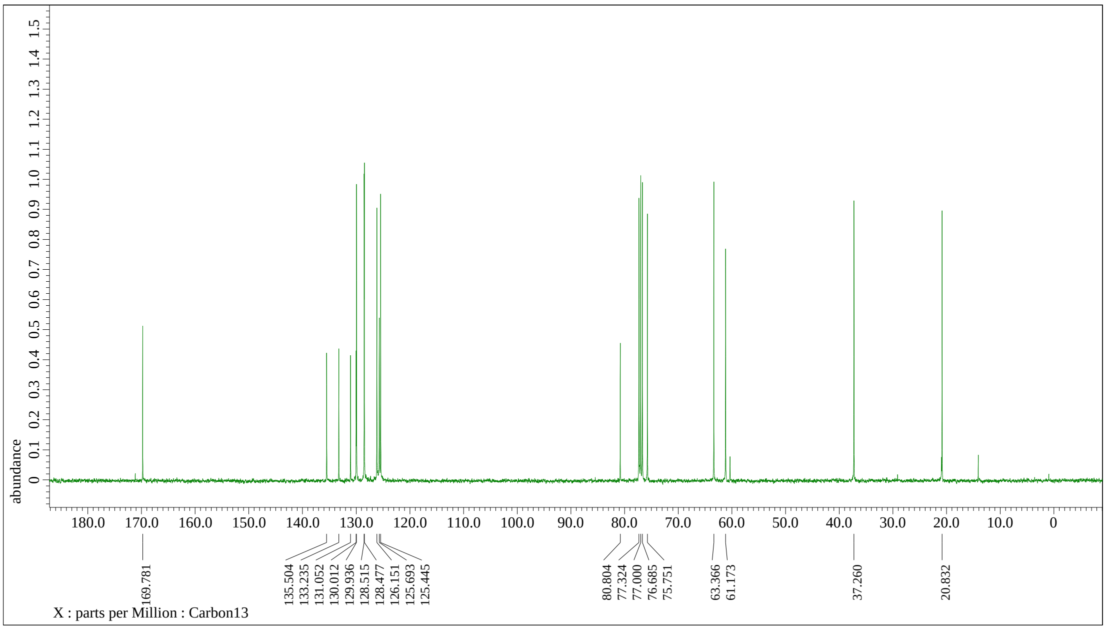
abundance
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
169.600
137.011
135.047
132.758
131.824
129.211
128.134
79.832
77.324
77.000
76.685
75.913
62.956
62.307
34.962
20.899
X : parts per Million : Carbon13



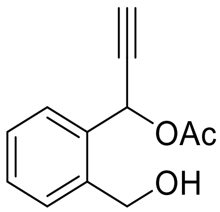
1m



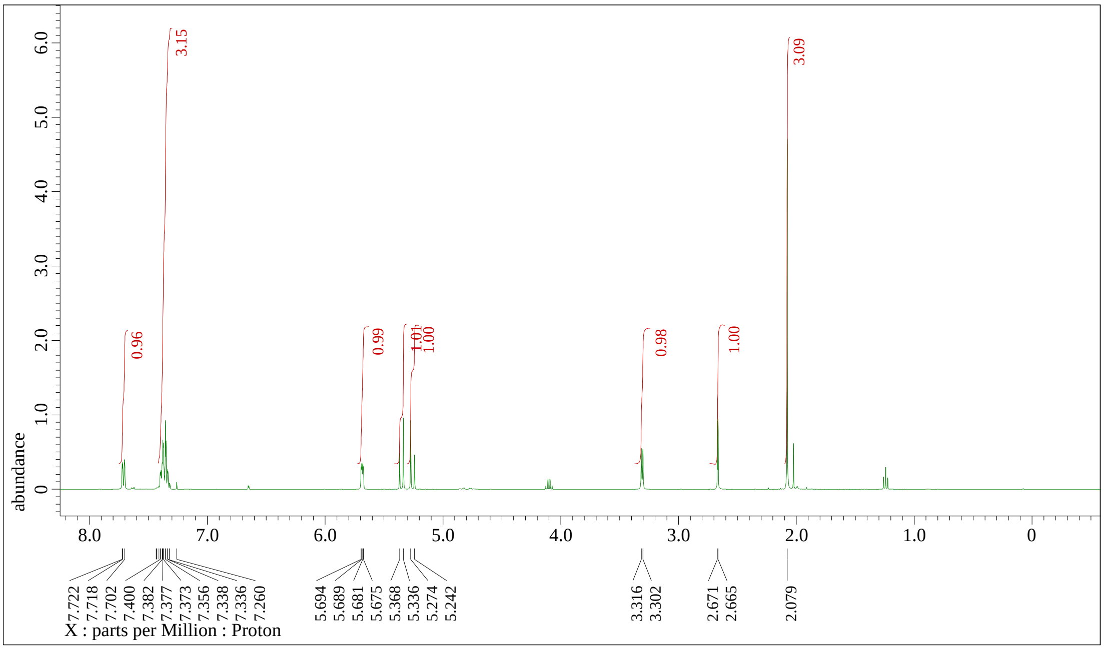
abundance
1.01
1.03
1.05
1.07
1.04
2.03
1.98
1.01
0.99
0.95
1.00
3.04
8.671
8.649
7.837
7.818
7.805
7.783
7.583
7.580
7.512
7.491
7.331
7.314
7.309
3.946
3.930
3.913
3.409
3.169
3.151
2.669
2.663
2.207
2.064
X : parts per Million : Proton

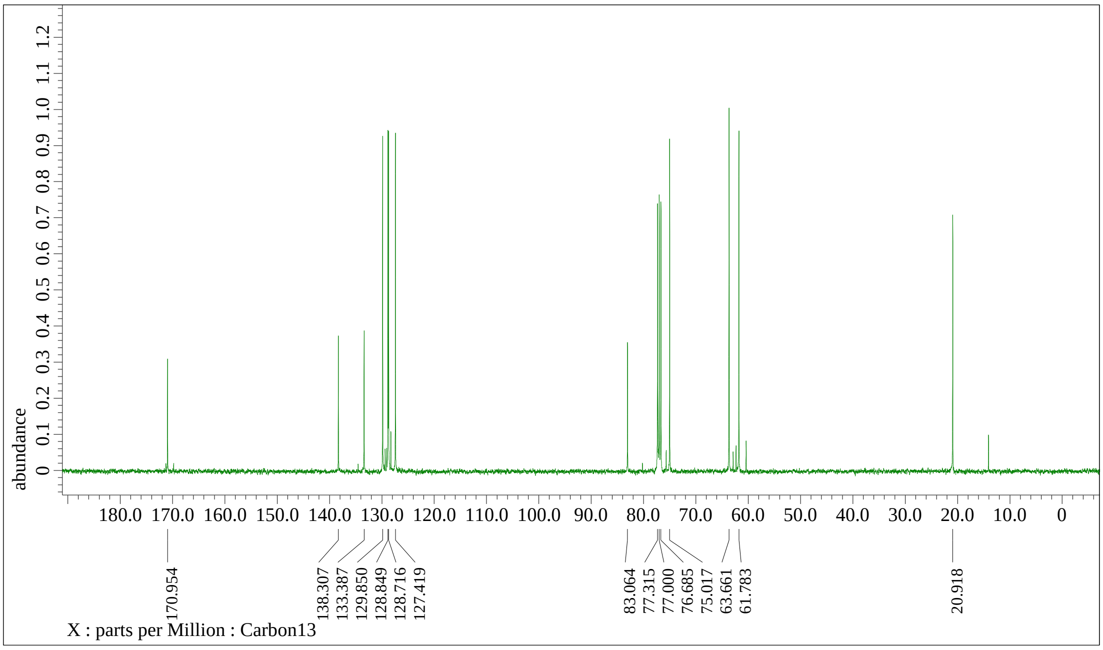


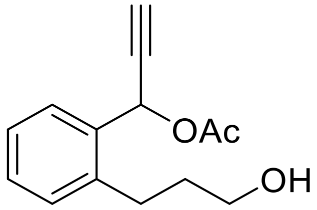
abundance
169.781
135.504
133.235
131.052
130.012
129.936
128.515
128.477
126.151
125.693
125.445
80.804
77.324
77.000
76.685
75.751
63.366
61.173
37.260
20.832
X : parts per Million : Carbon13


OAc
OH

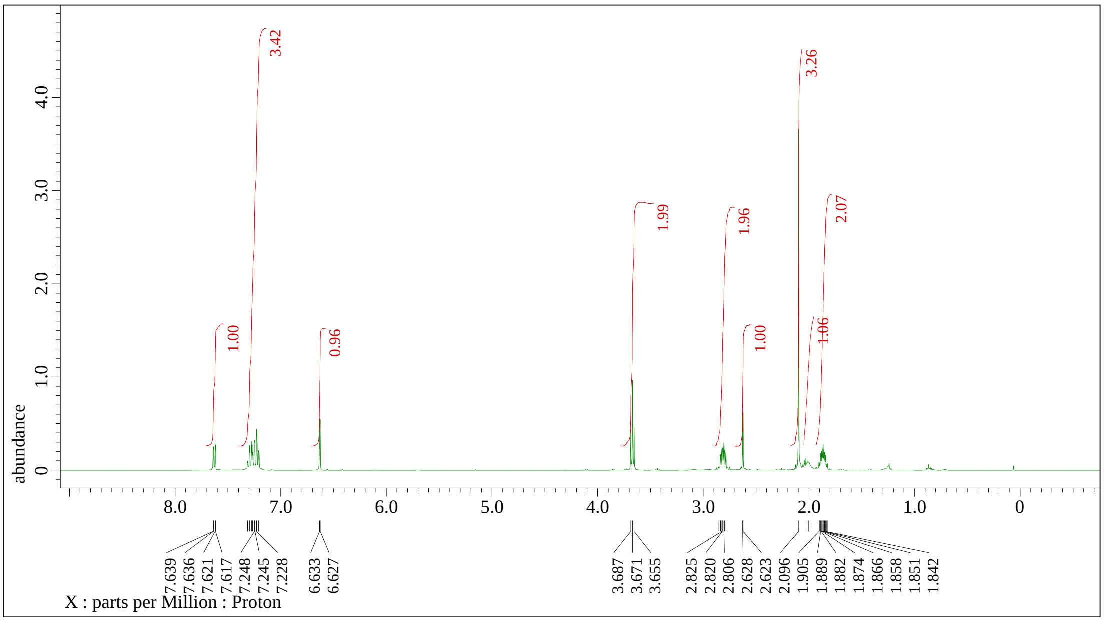
5

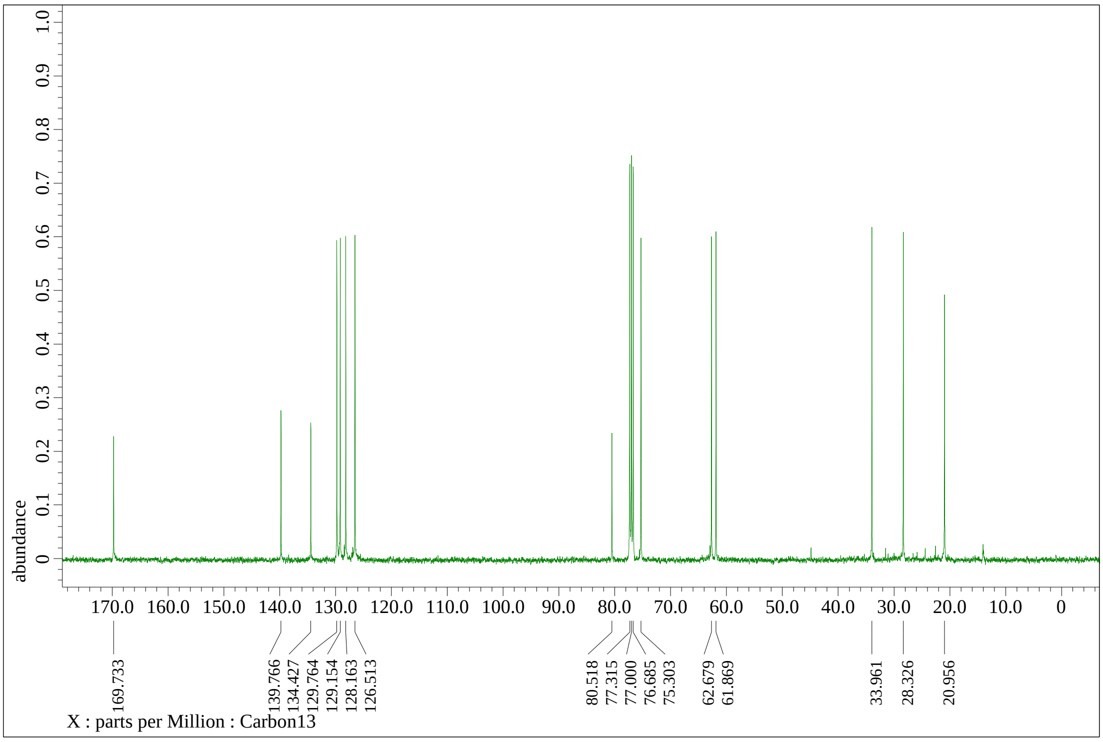

abundance
3.15
3.09
0.96
0.99
1.01
1.00
0.98
1.00
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0
7.722 7.718 7.702 7.400 7.382 7.377 7.373 7.356 7.338 7.336 7.260
5.694 5.689 5.681 5.675 5.368 5.336 5.274 5.242
3.316 3.302
2.671 2.665
2.079
X : parts per Million : Proton

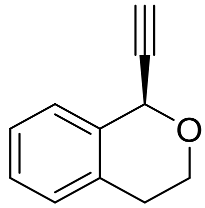

abundance
180.0 170.0 160.0 150.0 140.0 130.0 120.0 110.0 100.0 90.0 80.0 70.0 60.0 50.0 40.0 30.0 20.0 10.0 0
170.954
138.307 133.387 129.850 128.849 128.716 127.419
83.064 77.315 77.000 76.685 75.017 63.661 61.783
20.918
X : parts per Million : Carbon13


OAc
OH

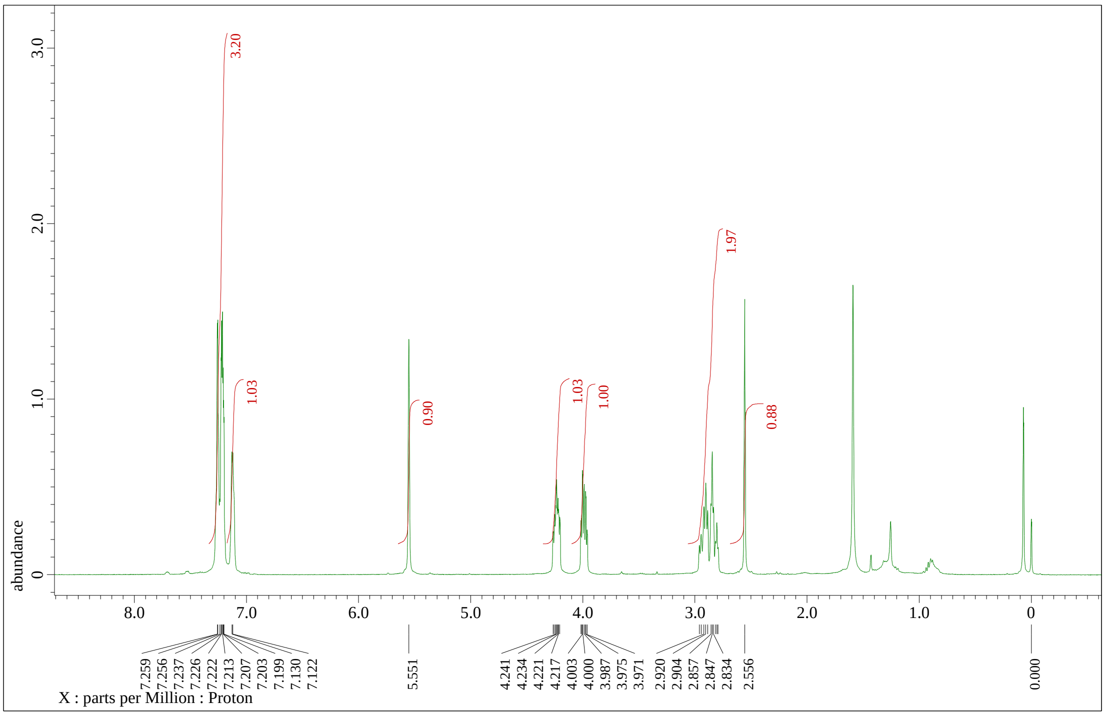
6


abundance
X : parts per Million : Proton
3.42
3.26
1.99
1.96
2.07
1.00
0.96
1.00
1.06
7.639
7.636
7.621
7.617
7.248
7.245
7.228
6.633
6.627
3.687
3.671
3.655
2.825
2.820
2.806
2.628
2.623
2.096
1.905
1.889
1.882
1.874
1.866
1.858
1.851
1.842

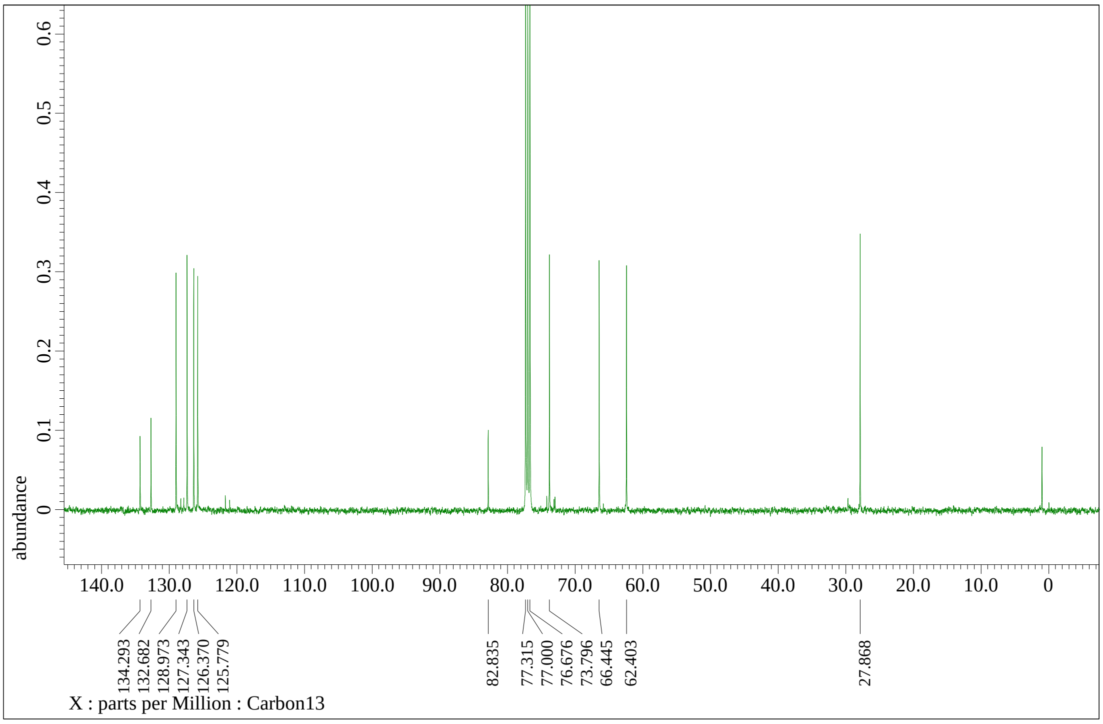

abundance
X : parts per Million : Carbon13
169.733
139.766
134.427
129.764
129.154
128.163
126.513
80.518
77.315
77.000
76.685
75.303
62.679
61.869
33.961
28.326
20.956



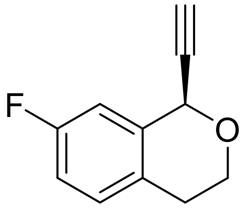
2a



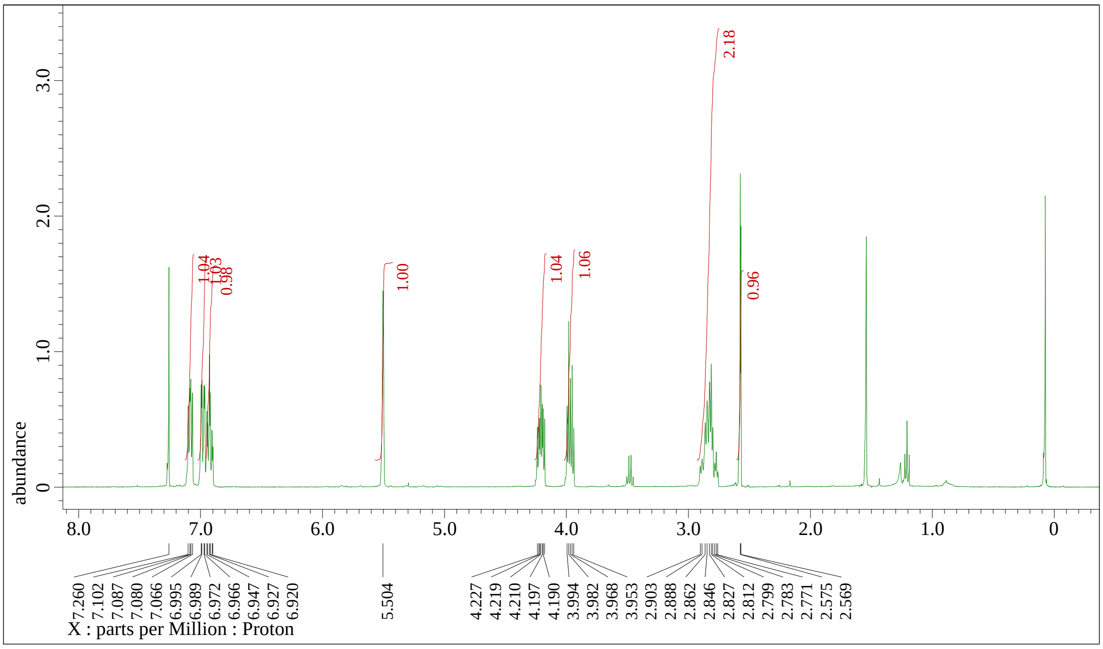
3.20
1.03
0.90
1.03
1.00
1.97
0.88
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.259
7.256
7.237
7.226
7.222
7.213
7.207
7.203
7.199
7.130
7.122
5.551
4.241
4.234
4.221
4.217
4.003
4.000
3.987
3.975
3.971
2.920
2.904
2.857
2.847
2.834
2.556
0.000
X : parts per Million : Proton



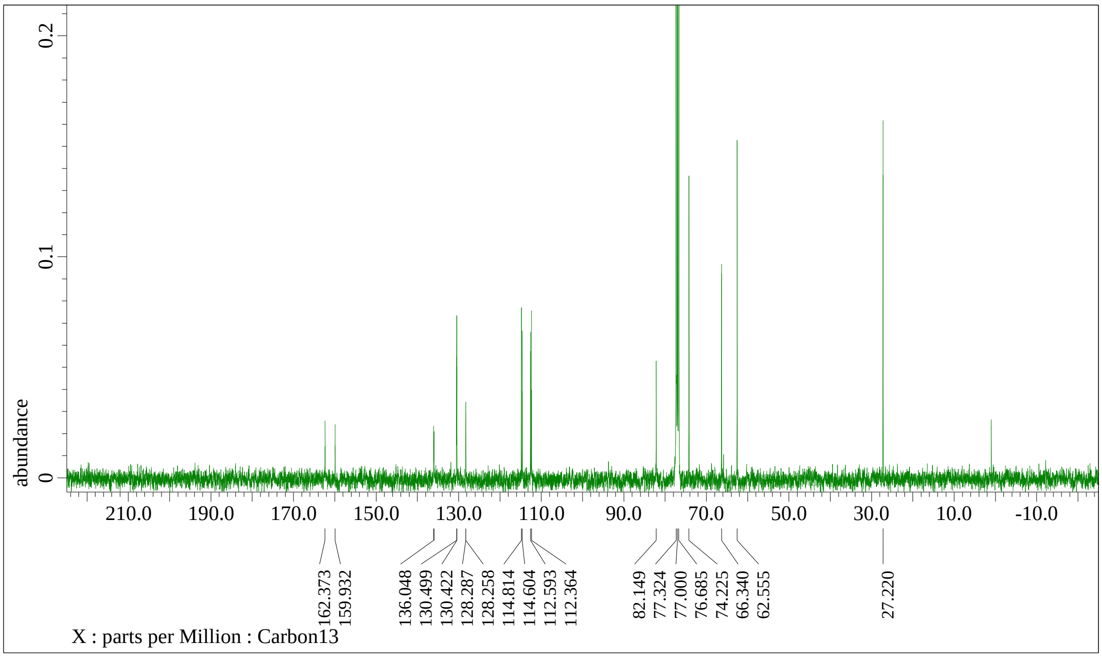
abundance
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
134.293
132.682
128.973
127.343
126.370
125.779
82.835
77.315
77.000
76.676
73.796
66.445
62.403
27.868
X : parts per Million : Carbon13



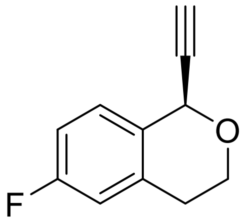
2b



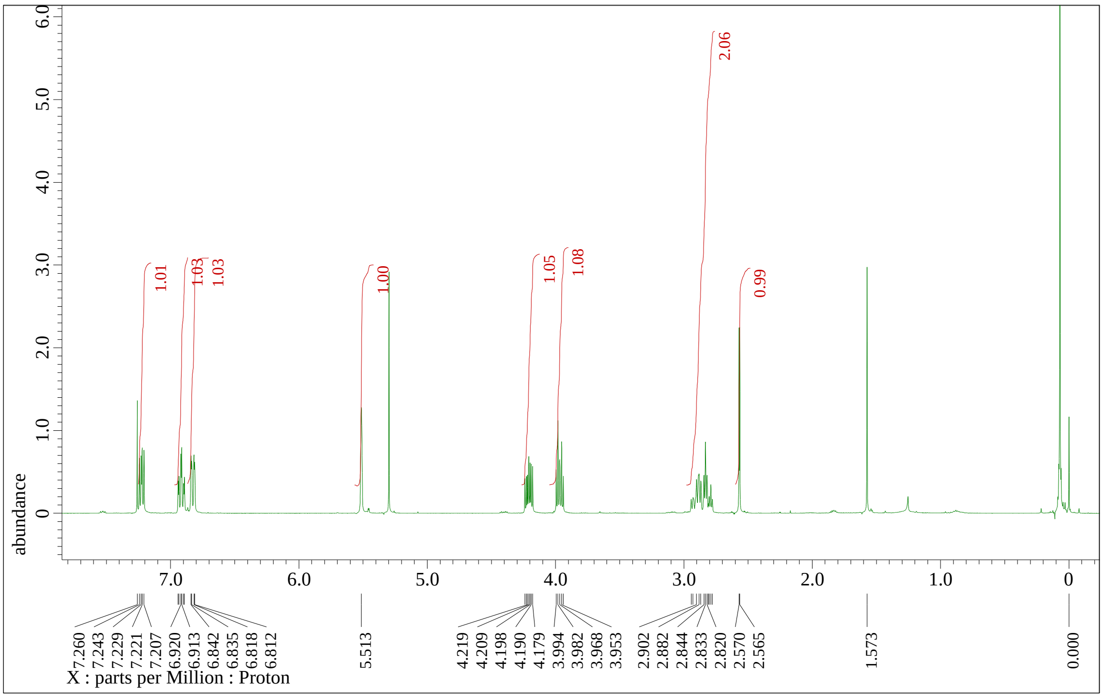
abundance
3.0
2.0
1.0
0
1.04
1.03
0.98
1.00
1.04
1.06
2.18
0.96
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.260
7.102
7.087
7.080
7.066
6.995
6.989
6.972
6.966
6.947
6.927
6.920
5.504
4.227
4.219
4.210
4.197
4.190
3.994
3.982
3.968
3.953
2.903
2.888
2.862
2.846
2.827
2.812
2.799
2.783
2.771
2.575
2.569
X : parts per Million : Proton



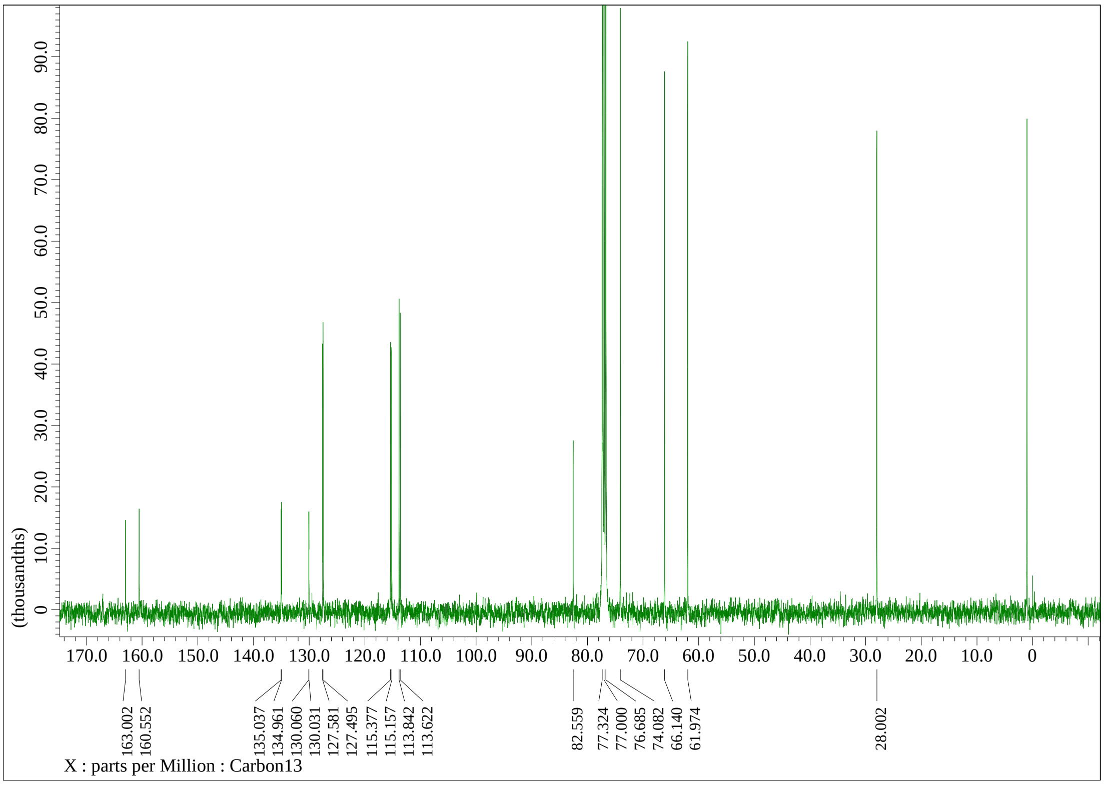
abundance
0.2
0.1
0
210.0
190.0
170.0
150.0
130.0
110.0
90.0
70.0
50.0
30.0
10.0
-10.0
162.373
159.932
136.048
130.499
130.422
128.287
128.258
114.814
114.604
112.593
112.364
82.149
77.324
77.000
76.685
74.225
66.340
62.555
27.220
X : parts per Million : Carbon13



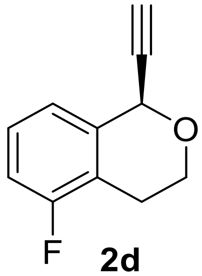
2c



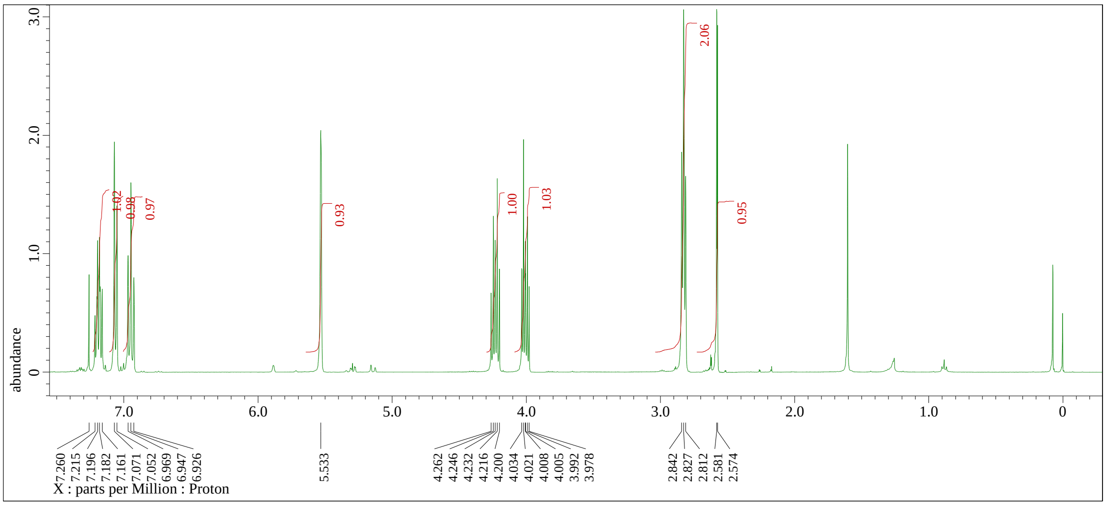
abundance
X : parts per Million : Proton

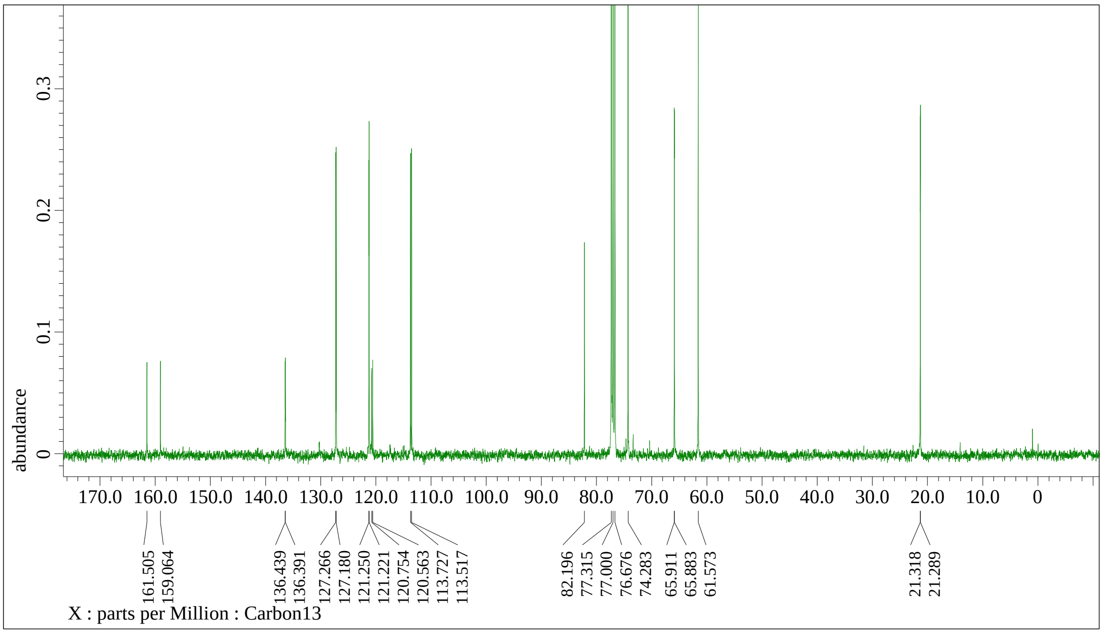


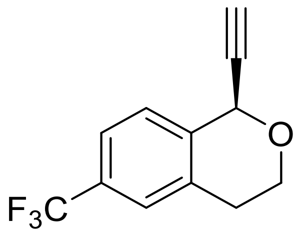
(thousandths)
X : parts per Million : Carbon13


O
F

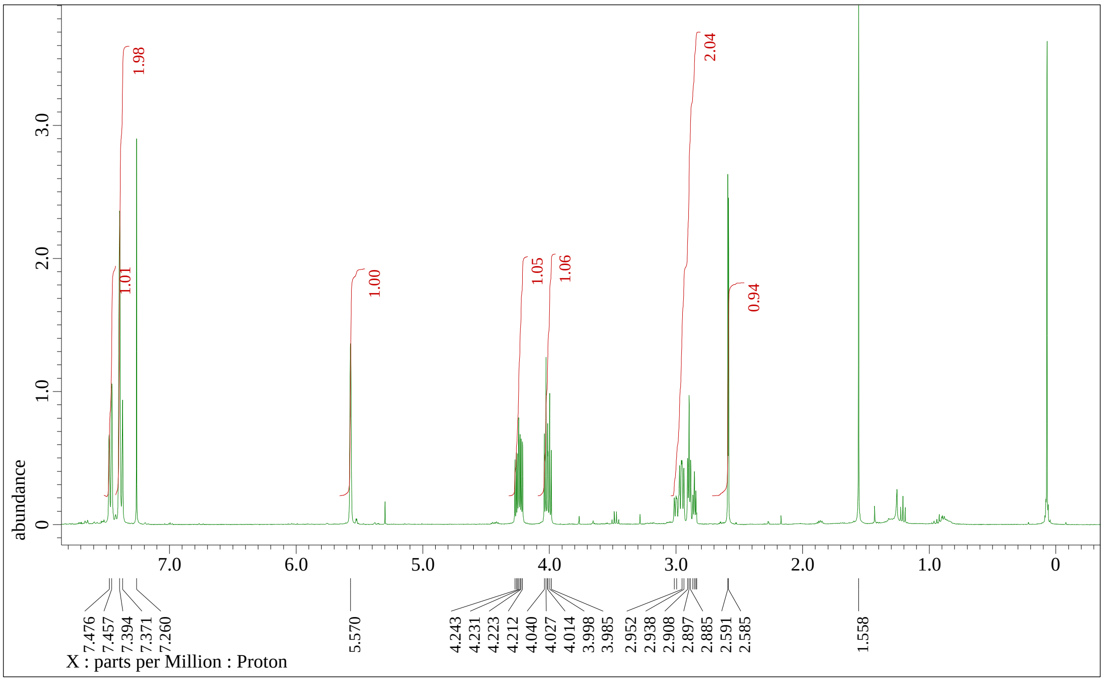
2d

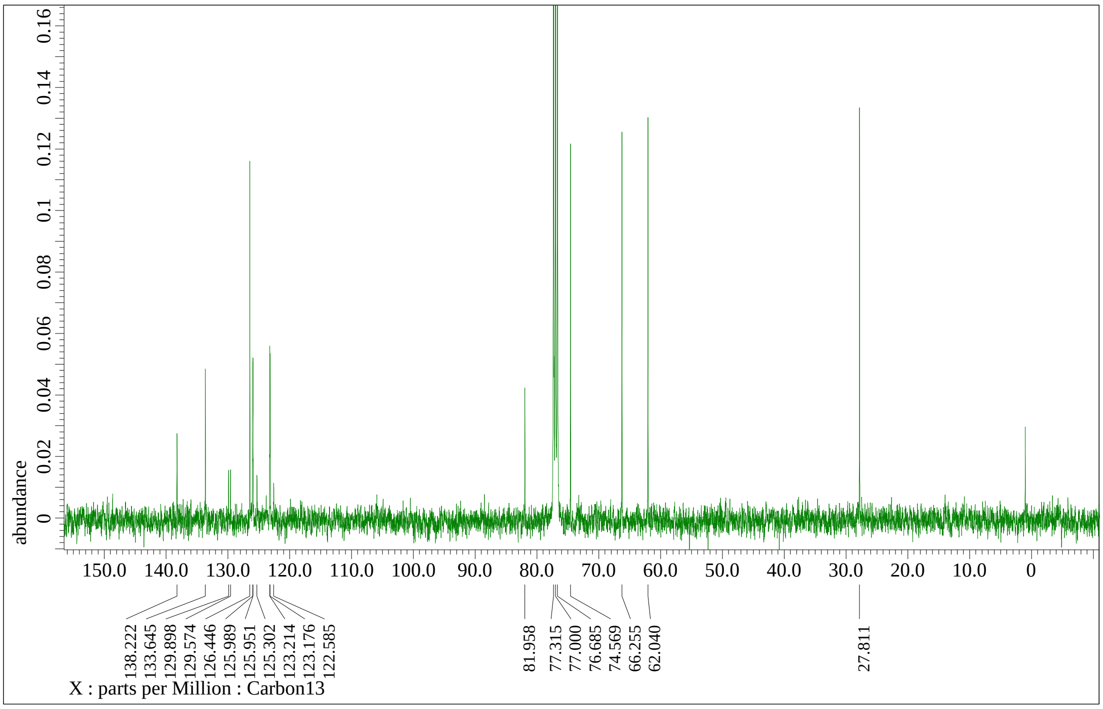

abundance
3.0
2.0
1.0
0
1.02
0.98
0.97
0.93
1.00
1.03
2.06
0.95
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.260
7.215
7.196
7.182
7.161
7.071
7.052
6.969
6.947
6.926
5.533
4.262
4.246
4.232
4.216
4.200
4.034
4.021
4.008
4.005
3.992
3.978
2.842
2.827
2.812
2.581
2.574
X : parts per Million : Proton

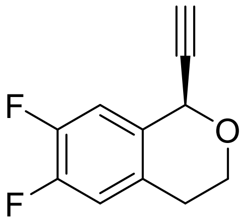

abundance
0.3
0.2
0.1
0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
161.505
159.064
136.439
136.391
127.266
127.180
121.250
121.221
120.754
120.563
113.727
113.517
82.196
77.315
77.000
76.676
74.283
65.911
65.883
61.573
21.318
21.289
X : parts per Million : Carbon13


O
F3C

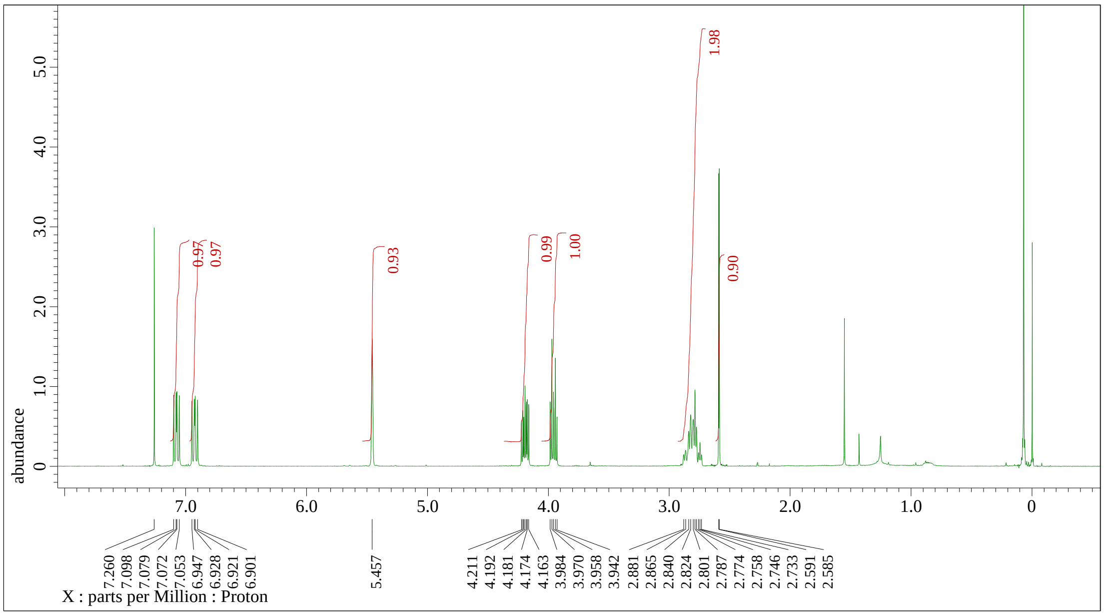
2e

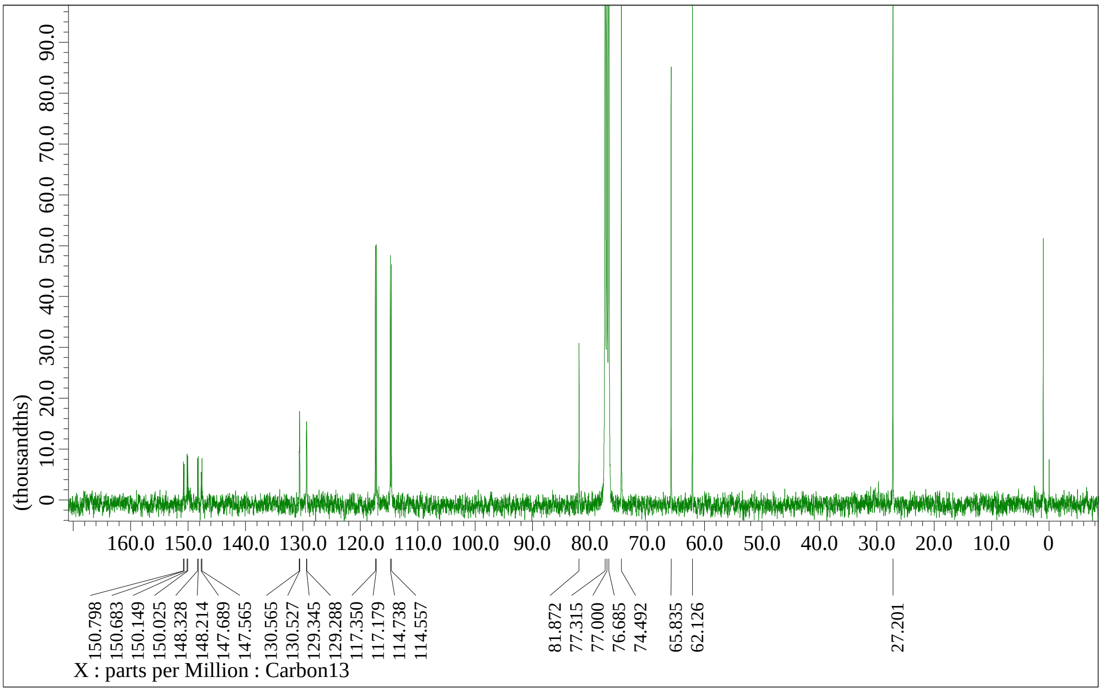

1.98
1.01
1.00
1.05
1.06
2.04
0.94
abundance
0
1.0
2.0
3.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.476
7.457
7.394
7.371
7.260
5.570
4.243
4.231
4.223
4.212
4.040
4.027
4.014
3.998
3.985
2.952
2.938
2.908
2.897
2.885
2.591
2.585
1.558
X : parts per Million : Proton

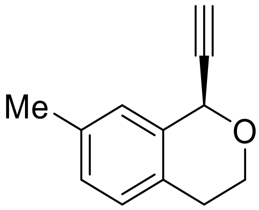

abundance
0
0.02
0.04
0.06
0.08
0.1
0.12
0.14
0.16
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
138.222
133.645
129.898
129.574
126.446
125.989
125.951
125.302
123.214
123.176
122.585
81.958
77.315
77.000
76.685
74.569
66.255
62.040
27.811
X : parts per Million : Carbon13


F
F
O

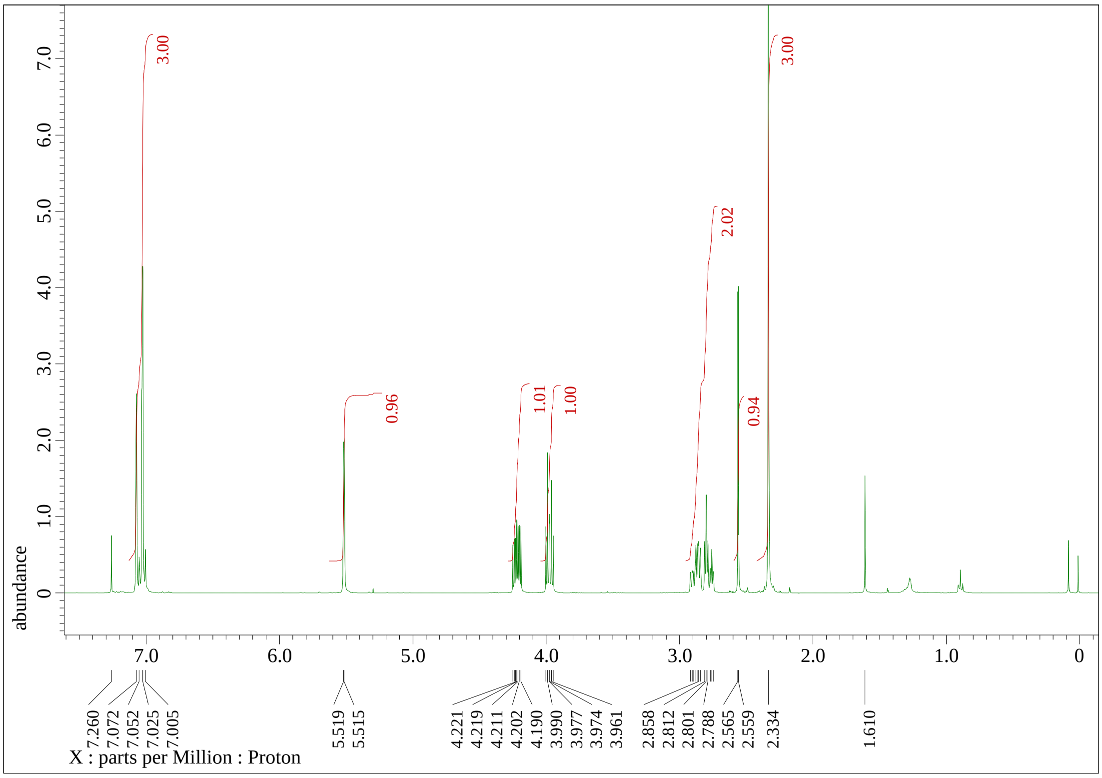
2f

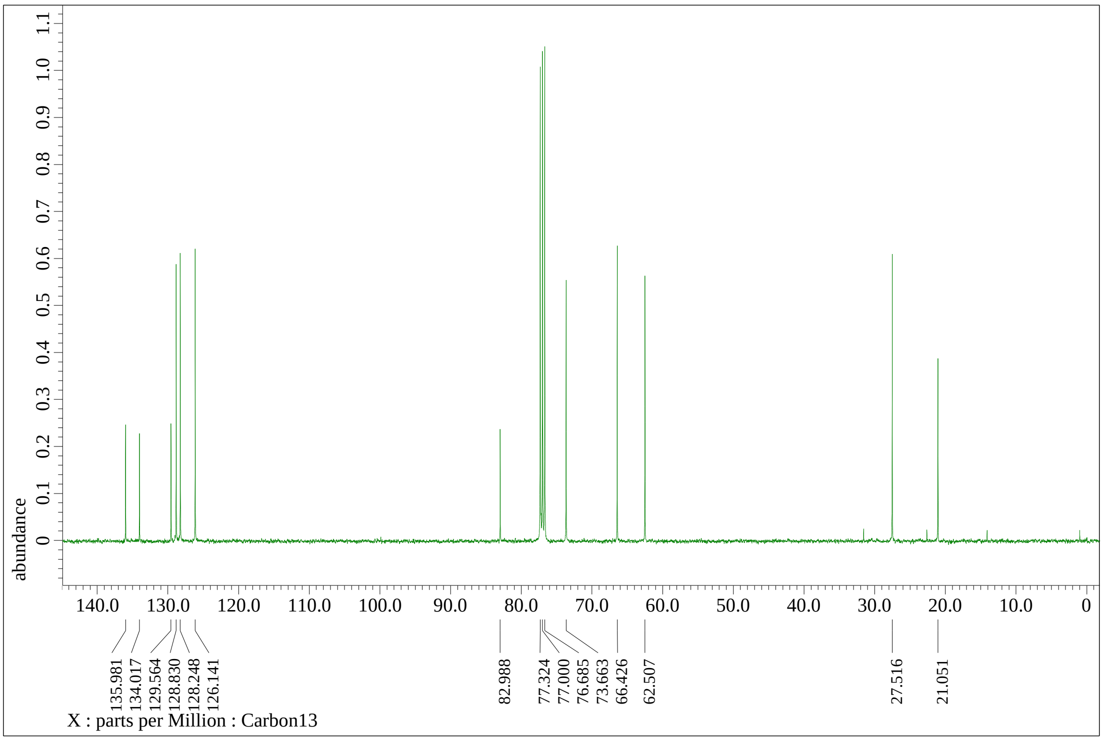

abundance
0.97
0.97
0.93
0.99
1.00
0.90
1.98
7.260
7.098
7.079
7.072
7.053
6.947
6.928
6.921
6.901
5.457
4.211
4.192
4.181
4.174
4.163
3.984
3.970
3.958
3.942
2.881
2.865
2.840
2.824
2.801
2.787
2.774
2.758
2.746
2.733
2.591
2.585
X : parts per Million : Proton

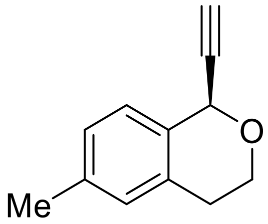

(thousandths)
150.798
150.683
150.149
150.025
148.328
148.214
147.689
147.565
130.565
130.527
129.345
129.288
117.350
117.179
114.738
114.557
81.872
77.315
77.000
76.685
74.492
65.835
62.126
27.201
X : parts per Million : Carbon13


Me
O

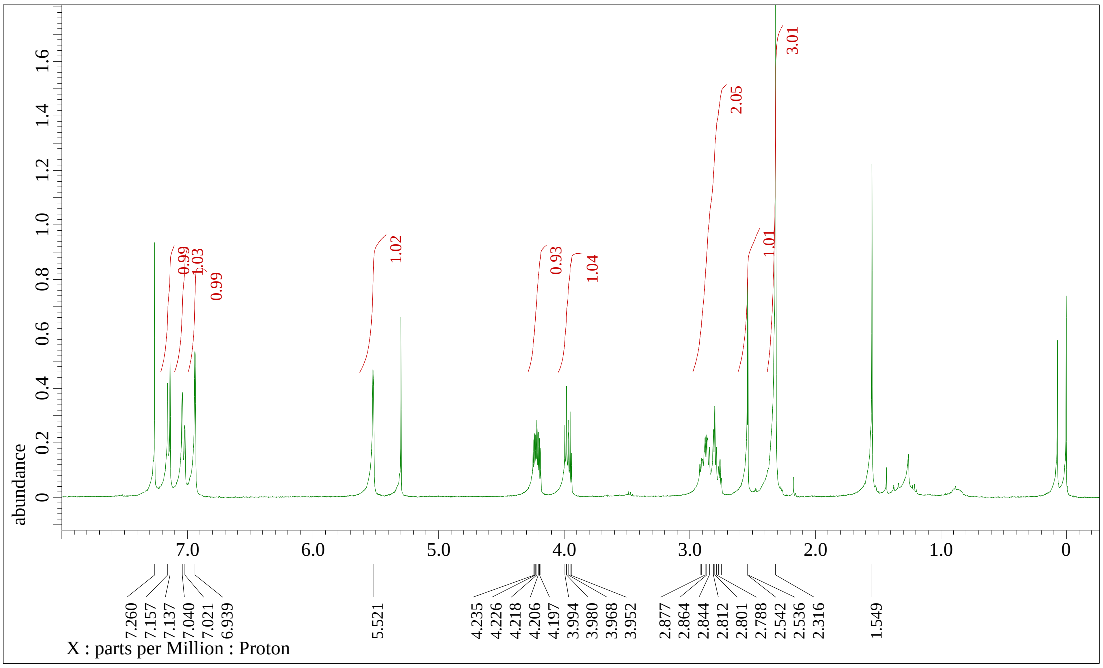
2g

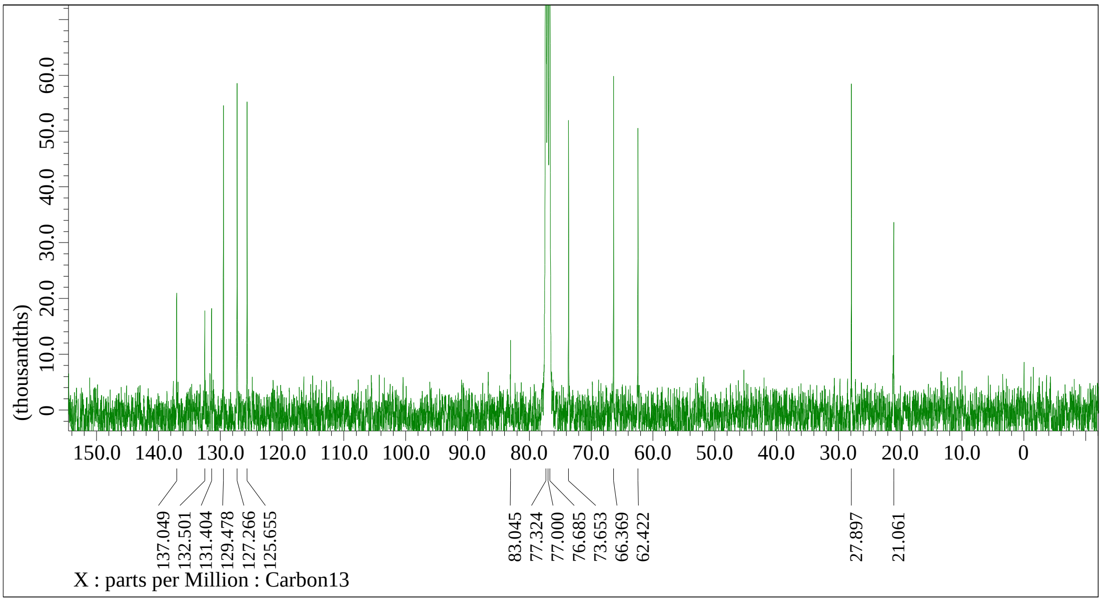

7.260
7.072
7.052
7.025
7.005
5.519
5.515
4.221
4.219
4.211
4.202
4.190
3.990
3.977
3.974
3.961
2.858
2.812
2.801
2.788
2.565
2.559
2.334
1.610
3.00
0.96
1.01
1.00
2.02
0.94
3.00
abundance
X : parts per Million : Proton

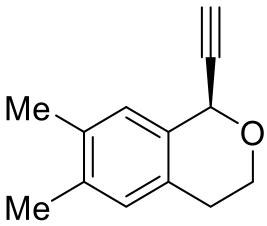

135.981
134.017
129.564
128.830
128.248
126.141
82.988
77.324
77.000
76.685
73.663
66.426
62.507
27.516
21.051
abundance
X : parts per Million : Carbon13


O
Me

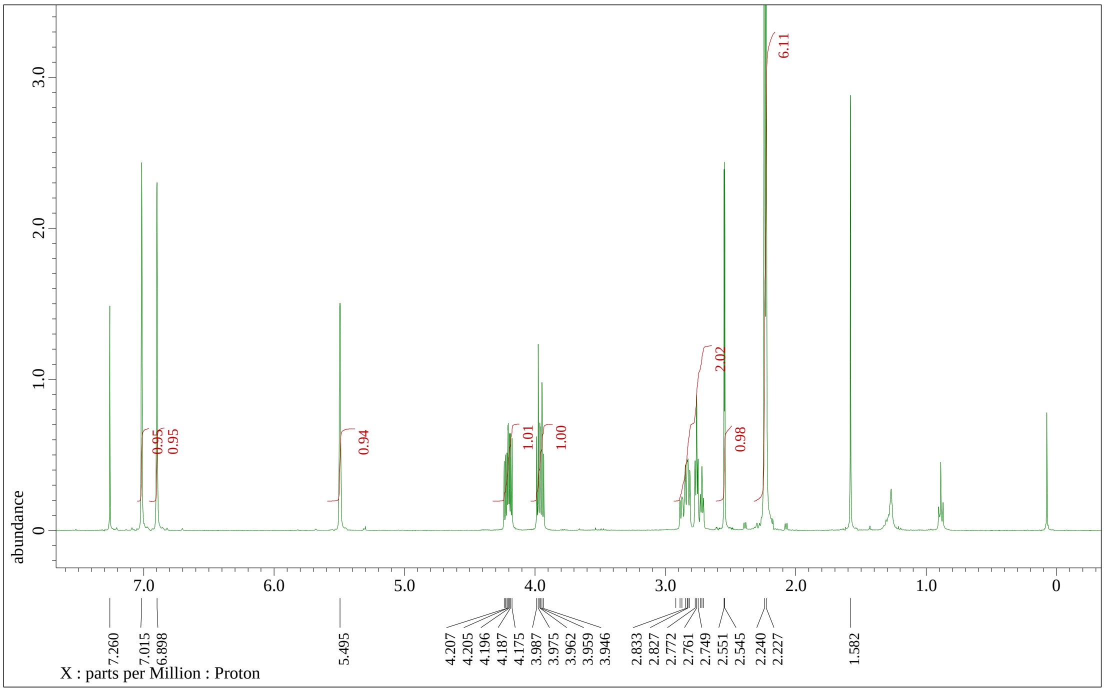
2h

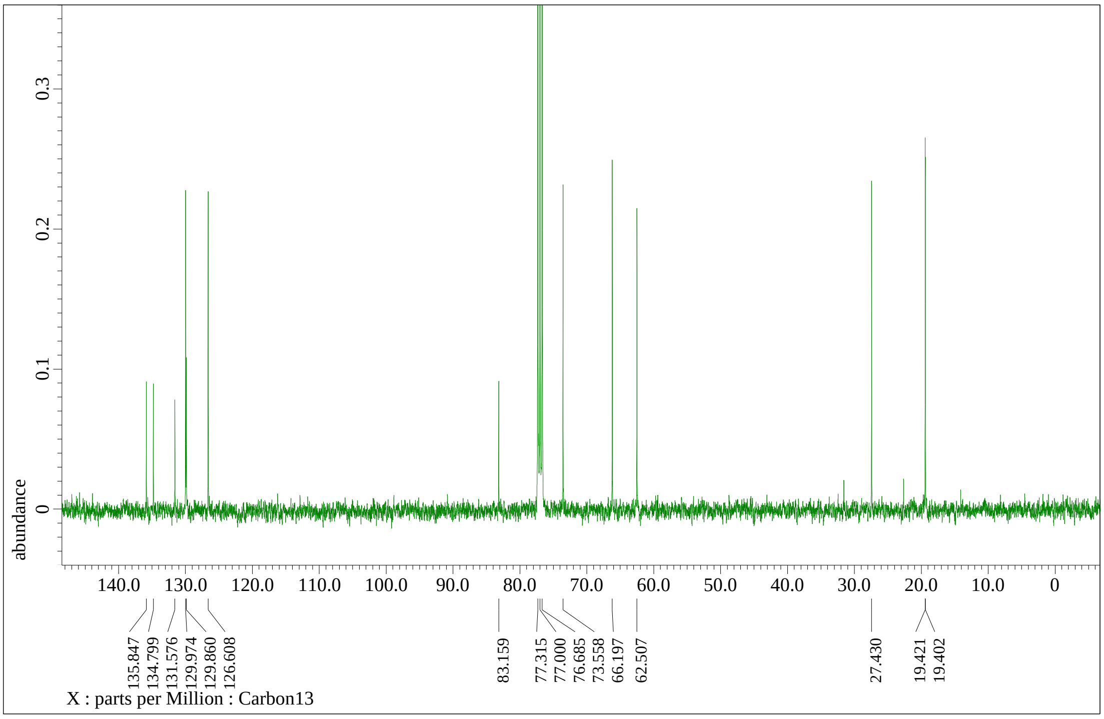

abundance
X : parts per Million : Proton
7.260
7.157
7.137
7.040
7.021
6.939
5.521
4.235
4.226
4.218
4.206
4.197
3.994
3.980
3.968
3.952
2.877
2.864
2.844
2.812
2.801
2.788
2.542
2.536
2.316
1.549
0.99
1.03
0.99
1.02
0.93
1.04
2.05
1.01
3.01

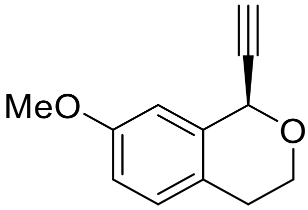

(thousandths)
X : parts per Million : Carbon13
137.049
132.501
131.404
129.478
127.266
125.655
83.045
77.324
77.000
76.685
73.653
66.369
62.422
27.897
21.061


Me
Me
O

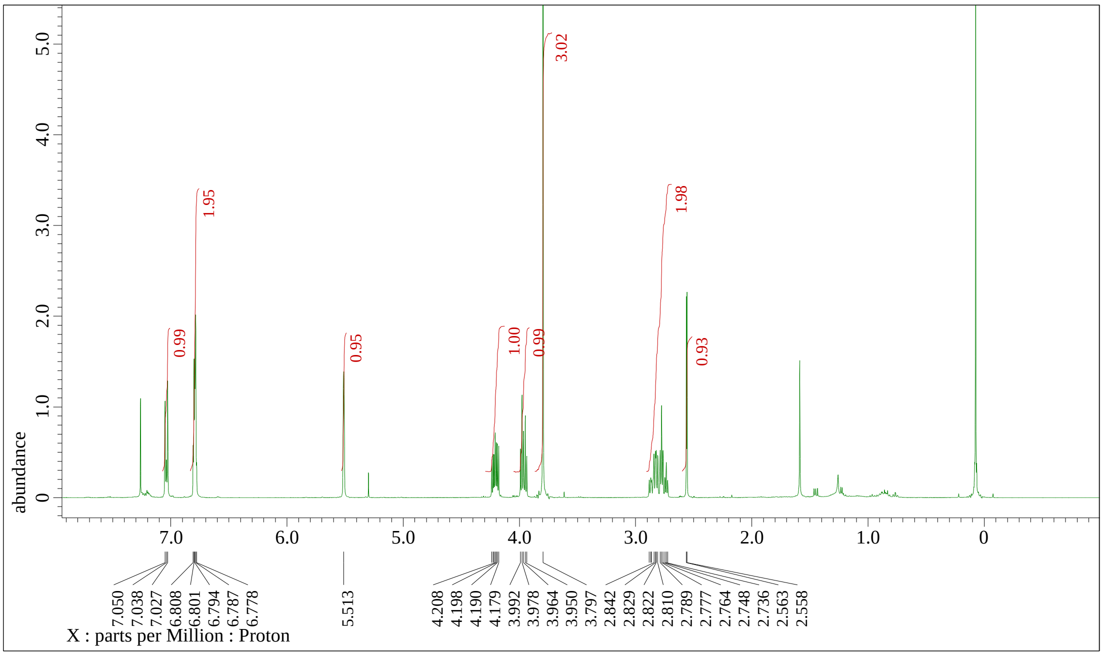
2i

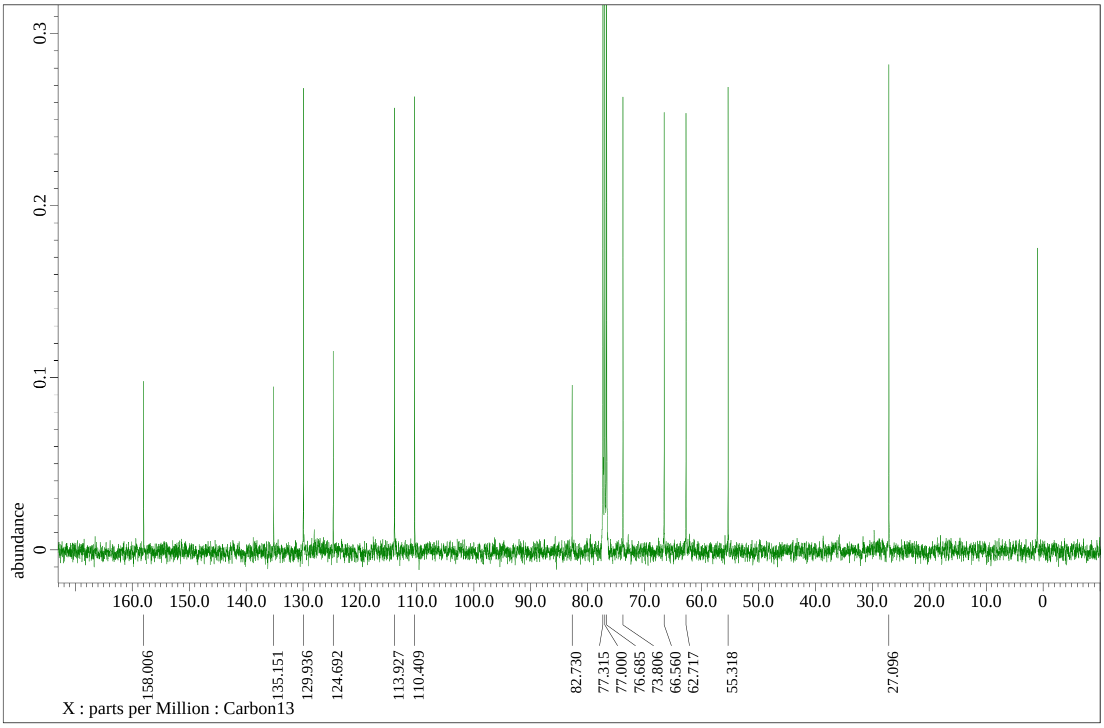

abundance
0
1.0
2.0
3.0
0.95
0.95
0.94
1.01
1.00
2.02
0.98
6.11
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.260
7.015
6.898
5.495
4.207
4.205
4.196
4.187
4.175
3.987
3.975
3.962
3.959
3.946
2.833
2.827
2.772
2.761
2.749
2.551
2.545
2.240
2.227
1.582
X : parts per Million : Proton

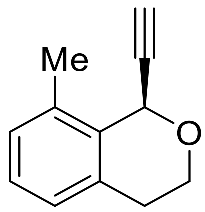

abundance
0
0.1
0.2
0.3
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
135.847
134.799
131.576
129.974
129.860
126.608
83.159
77.315
77.000
76.685
73.558
66.197
62.507
27.430
19.421
19.402
X : parts per Million : Carbon13


MeO
O

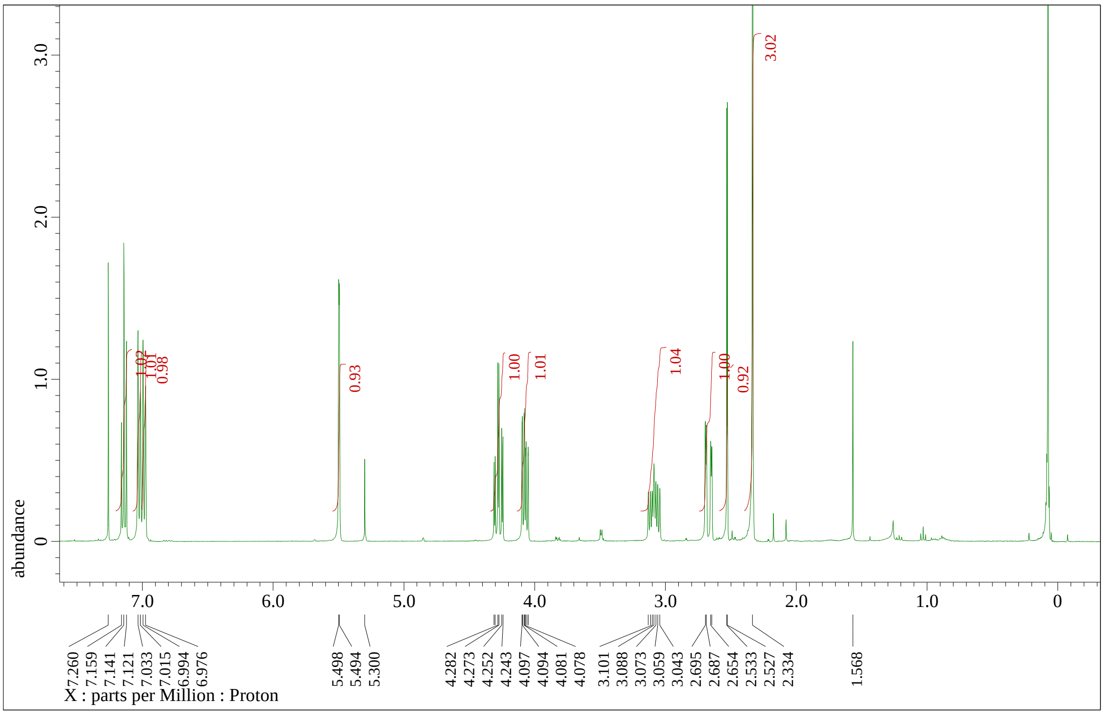
2j

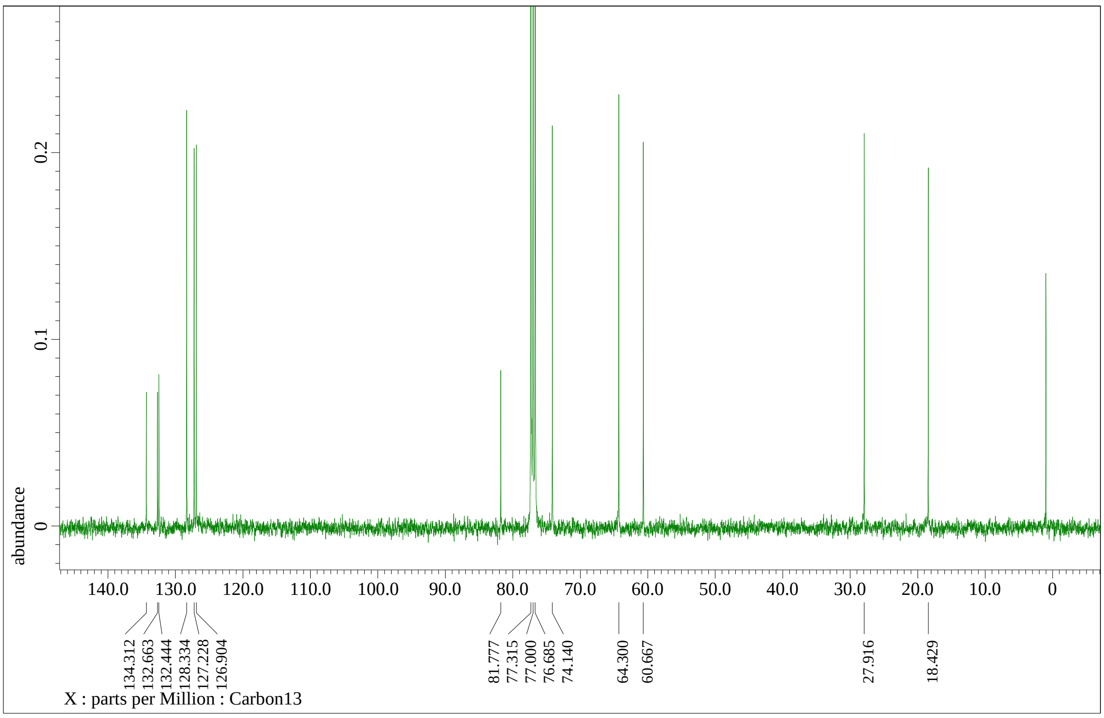

abundance
X : parts per Million : Proton

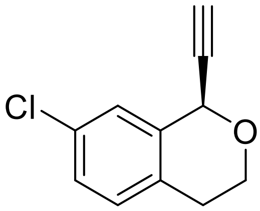

abundance
X : parts per Million : Carbon13


Me
O

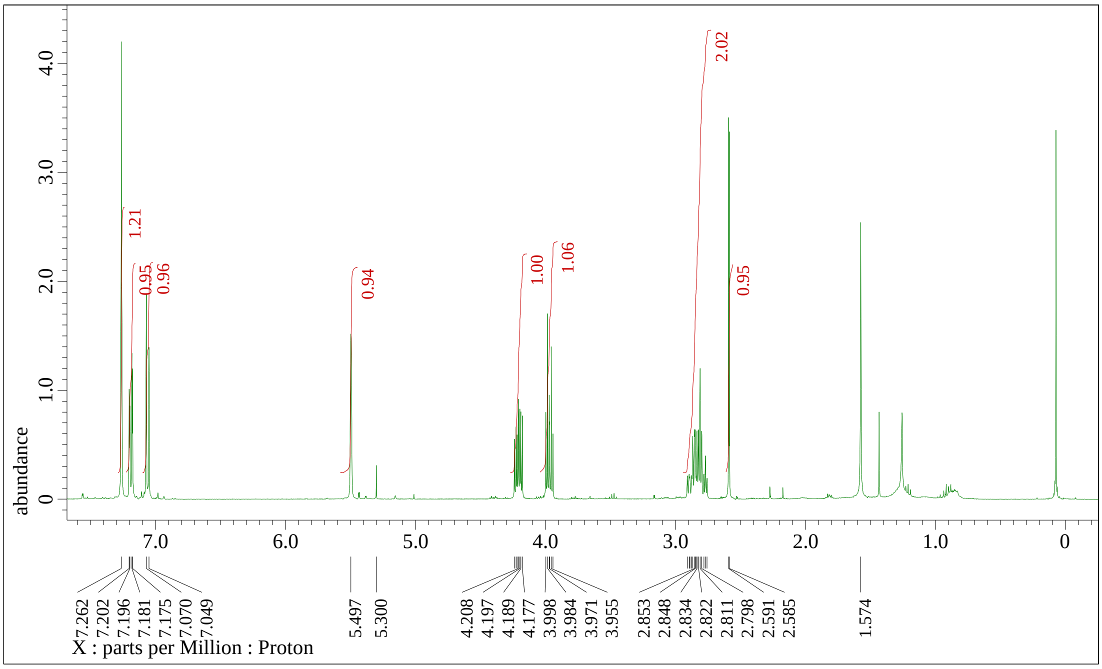
2k


abundance
X : parts per Million : Proton
7.260
7.159
7.141
7.121
7.033
7.015
6.994
6.976
5.498
5.494
5.300
4.282
4.273
4.252
4.243
4.097
4.094
4.081
4.078
3.101
3.088
3.073
3.059
3.043
2.695
2.687
2.654
2.533
2.527
2.334
1.568
1.02
1.01
0.98
0.93
1.00
1.01
1.04
1.00
0.92
3.02

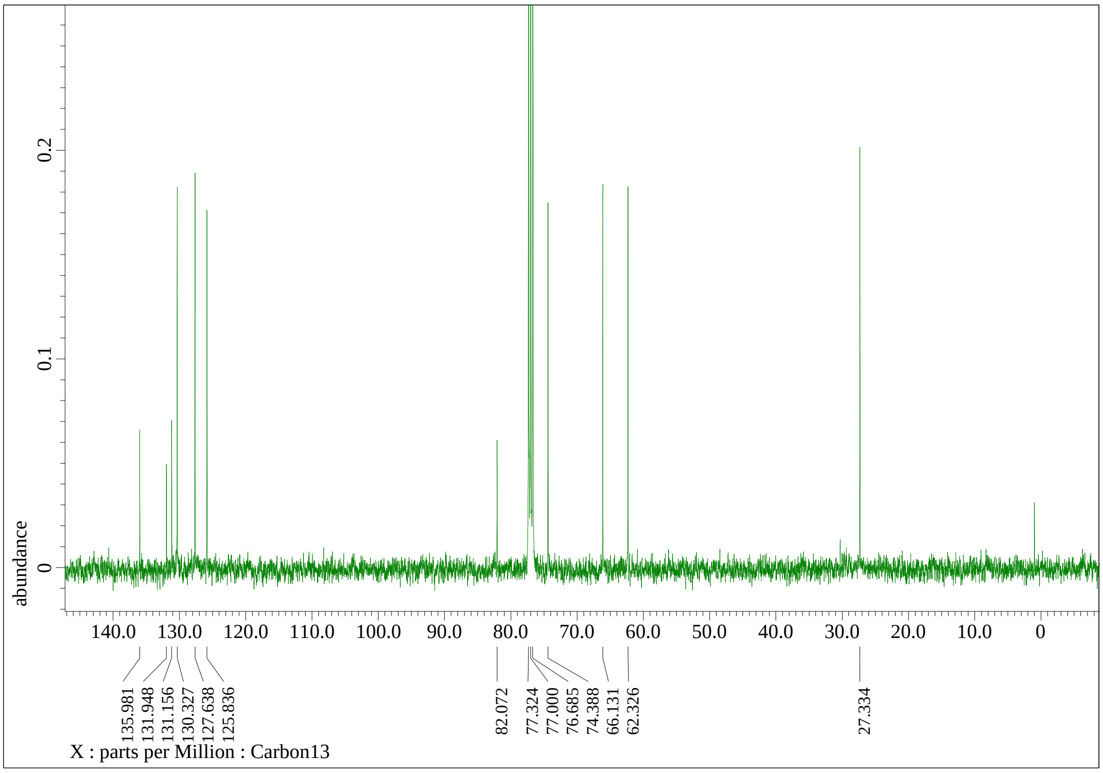

abundance
X : parts per Million : Carbon13
134.312
132.663
132.444
128.334
127.228
126.904
81.777
77.315
77.000
76.685
74.140
64.300
60.667
27.916
18.429



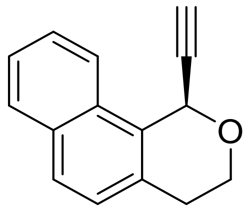
2l



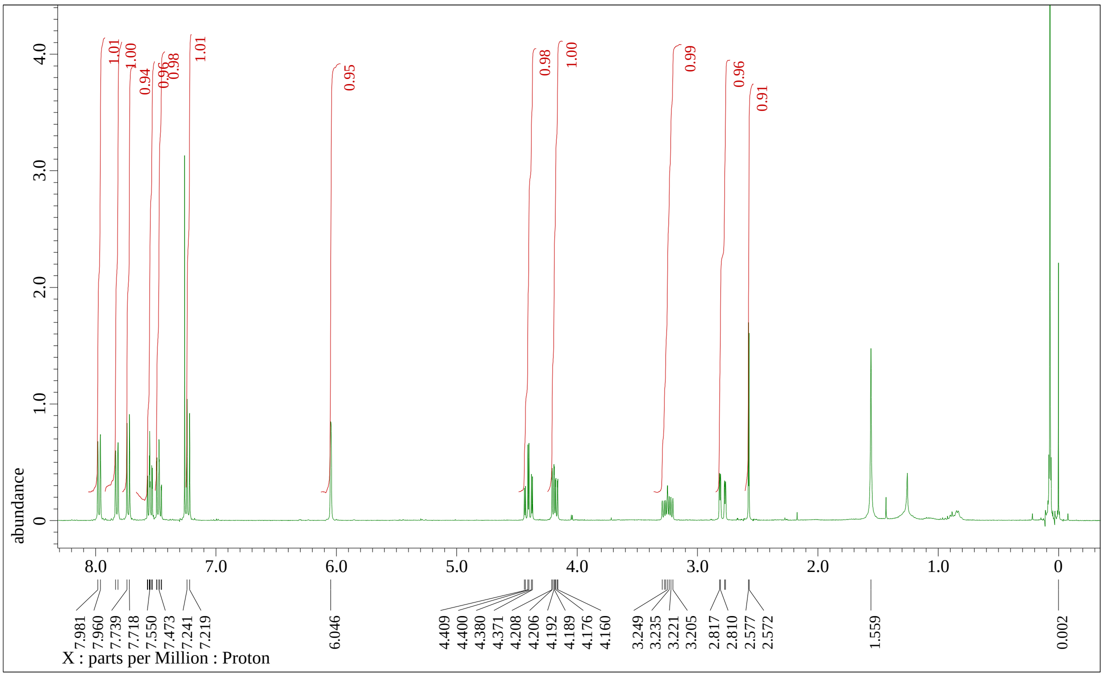
abundance
X : parts per Million : Proton
7.262
7.202
7.196
7.181
7.175
7.070
7.049
5.497
5.300
4.208
4.197
4.189
4.177
3.998
3.984
3.971
3.955
2.853
2.848
2.834
2.822
2.811
2.798
2.591
2.585
1.574
1.21
0.95
0.96
0.94
1.00
1.06
2.02
0.95

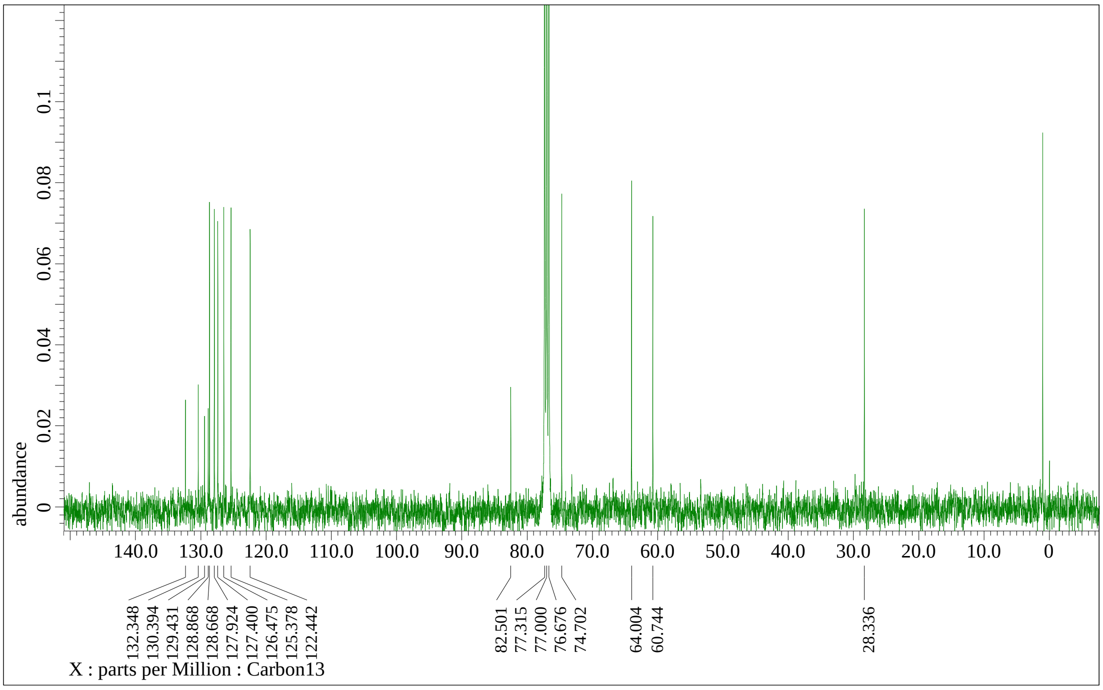


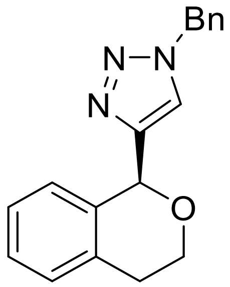
abundance
X : parts per Million : Carbon13
135.981
131.948
131.156
130.327
127.638
125.836
82.072
77.324
77.000
76.685
74.388
66.131
62.326
27.334



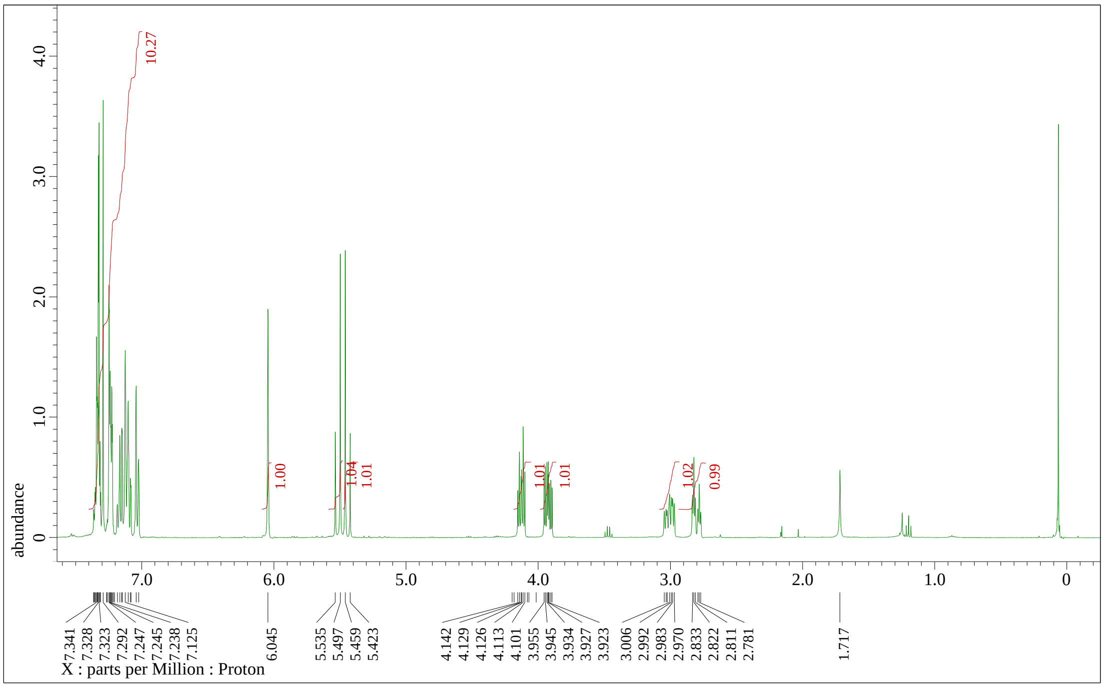
2m

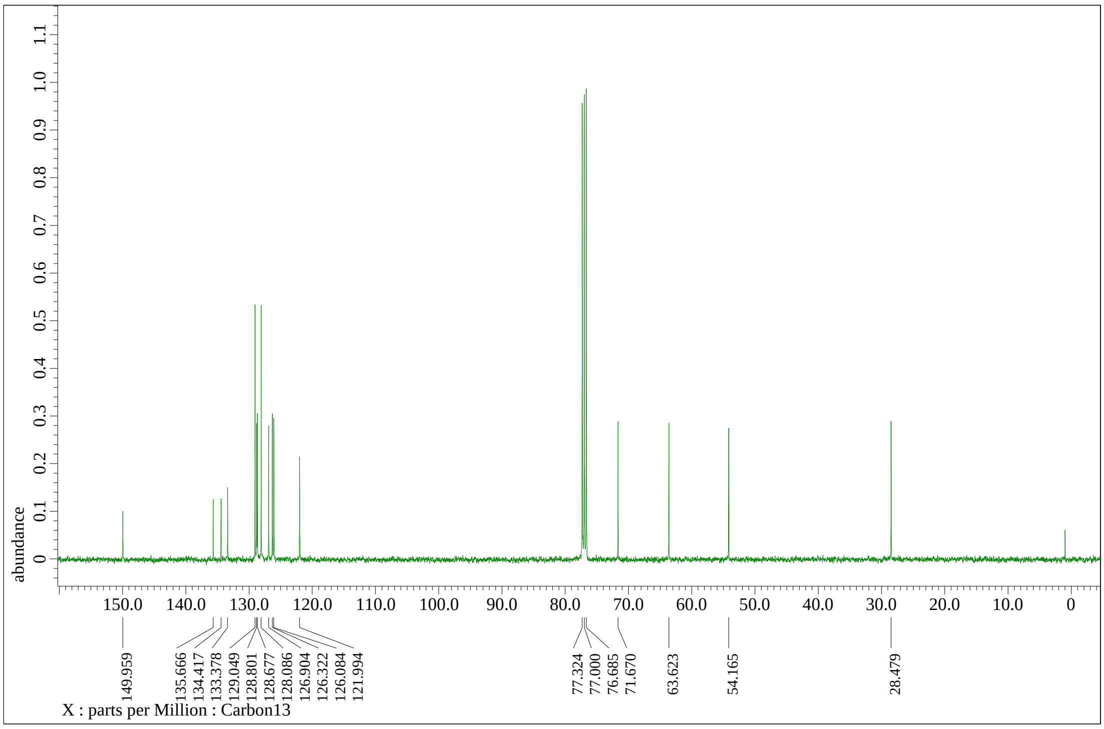

abundance
X : parts per Million : Proton
7.981
7.960
7.739
7.718
7.550
7.473
7.241
7.219
6.046
4.409
4.400
4.380
4.371
4.208
4.206
4.192
4.189
4.176
4.160
3.249
3.235
3.221
3.205
2.817
2.810
2.577
2.572
1.559
0.002

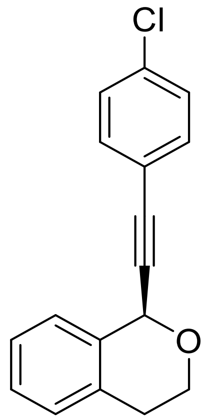

abundance
X : parts per Million : Carbon13
132.348
130.394
129.431
128.868
128.668
127.924
127.400
126.475
125.378
122.442
82.501
77.315
77.000
76.676
74.702
64.004
60.744
28.336


Bn
N
N
N
O

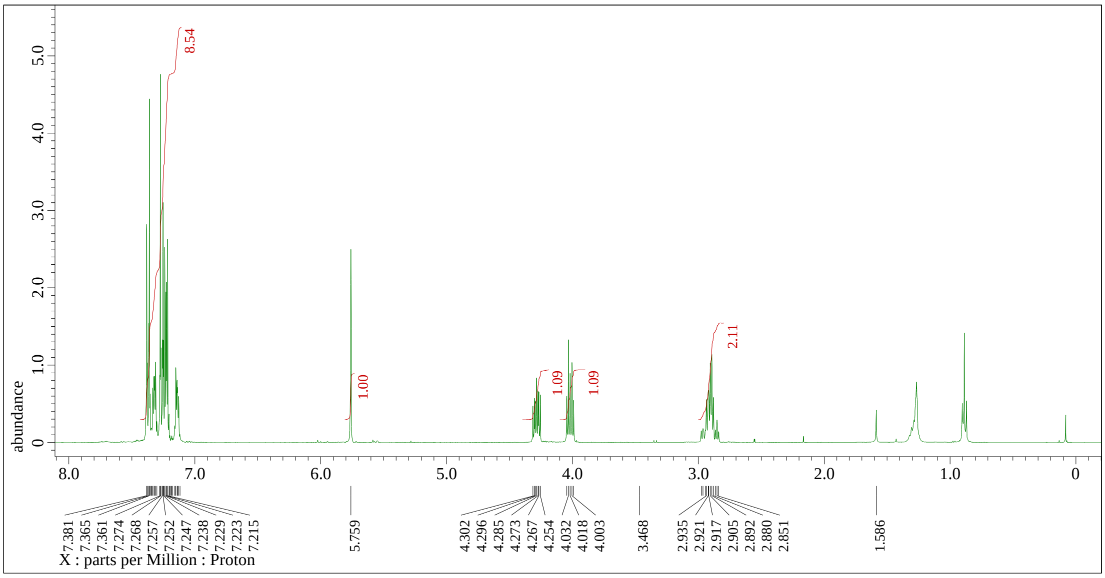
3


abundance
4.0
3.0
2.0
1.0
0
10.27
1.00
1.04
1.01
1.01
1.01
1.02
0.99
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.341
7.328
7.323
7.292
7.247
7.245
7.238
7.125
6.045
5.535
5.497
5.459
5.423
4.142
4.129
4.126
4.113
4.101
3.955
3.945
3.934
3.927
3.923
3.006
2.992
2.983
2.970
2.833
2.822
2.811
2.781
1.717
X : parts per Million : Proton

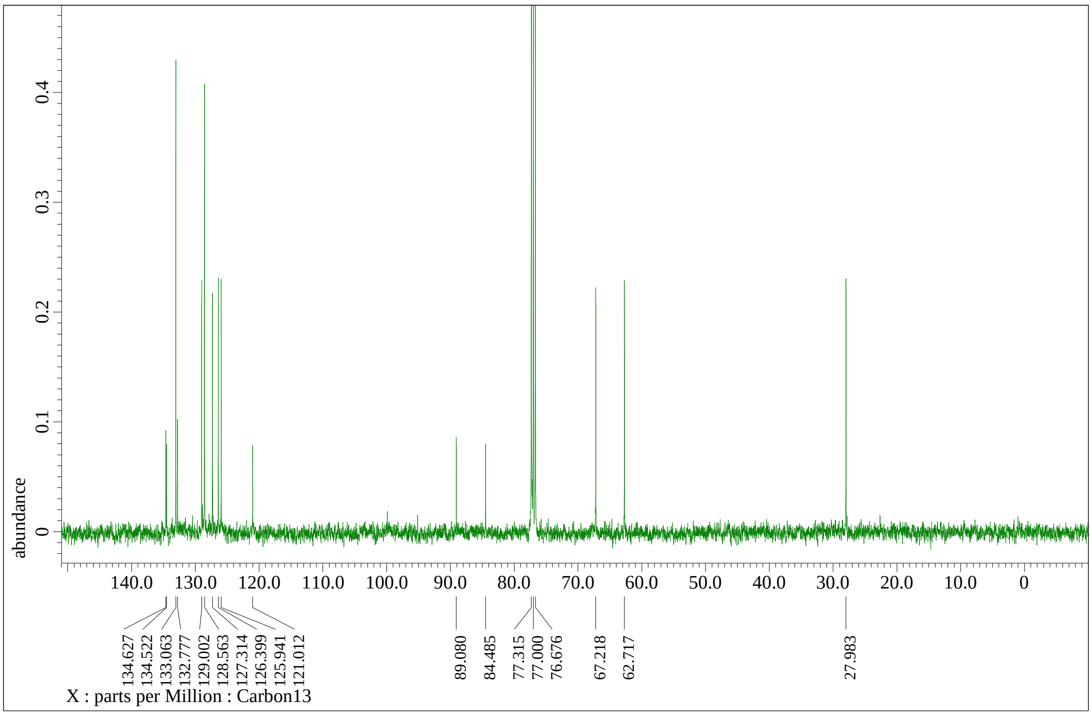

abundance
1.1
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
149.959
135.666
134.417
133.378
129.049
128.801
128.677
128.086
126.904
126.322
126.084
121.994
77.324
77.000
76.685
71.670
63.623
54.165
28.479
X : parts per Million : Carbon13



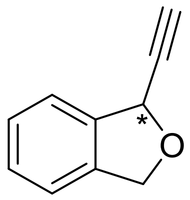
4



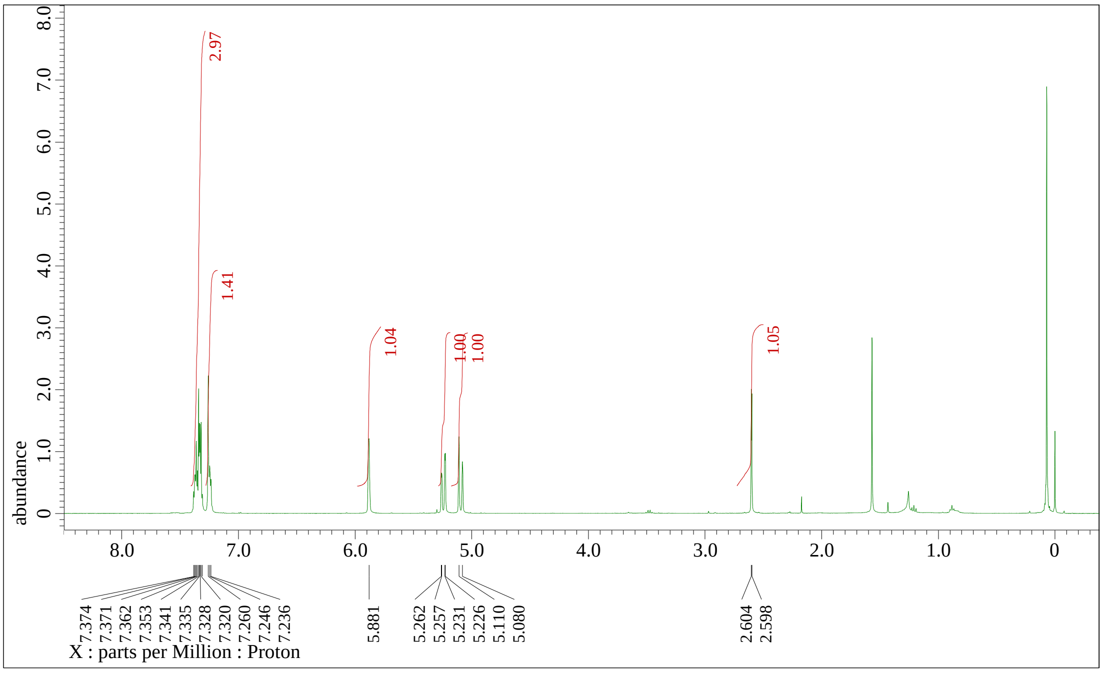
8.54
1.00
1.09
1.09
2.11
abundance
5.0
4.0
3.0
2.0
1.0
0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
7.381 7.365 7.361 7.274 7.268 7.257 7.252 7.247 7.238 7.229 7.223 7.215
5.759
4.302 4.296 4.285 4.273 4.267 4.254 4.032 4.018 4.003
3.468
2.935 2.921 2.917 2.905 2.892 2.880 2.851
1.586
X : parts per Million : Proton



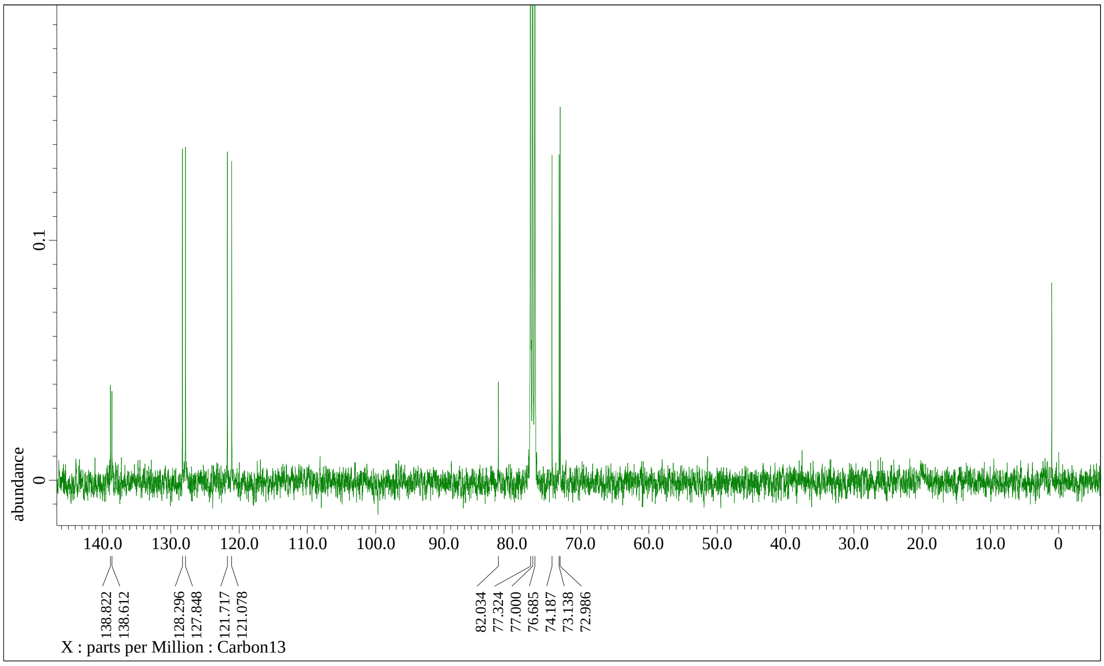
abundance
0.4
0.3
0.2
0.1
0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
134.627 134.522 133.063 132.777 129.002 128.563 127.314 126.399 125.941 121.012
89.080
84.485
77.315 77.000 76.676
67.218
62.717
27.983
X : parts per Million : Carbon13



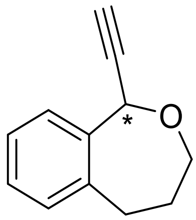
7



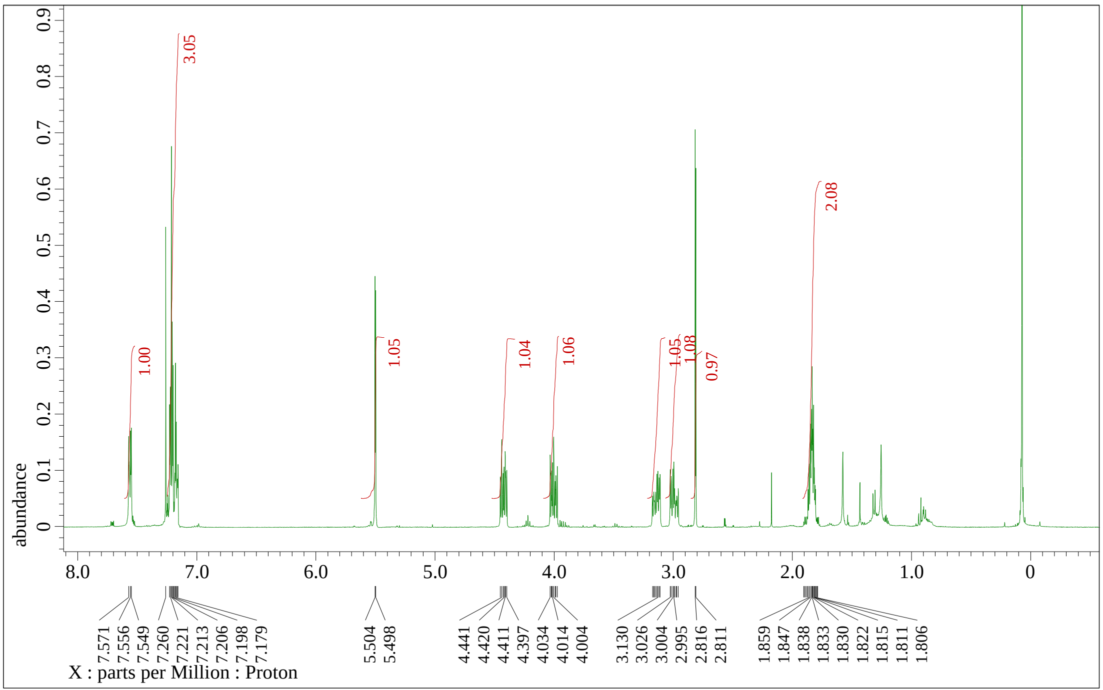
abundance
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
2.97
1.41
1.04
1.00
1.00
1.05
7.374
7.371
7.362
7.353
7.341
7.335
7.328
7.320
7.260
7.246
7.236
5.881
5.262
5.257
5.231
5.226
5.110
5.080
2.604
2.598
X : parts per Million : Proton

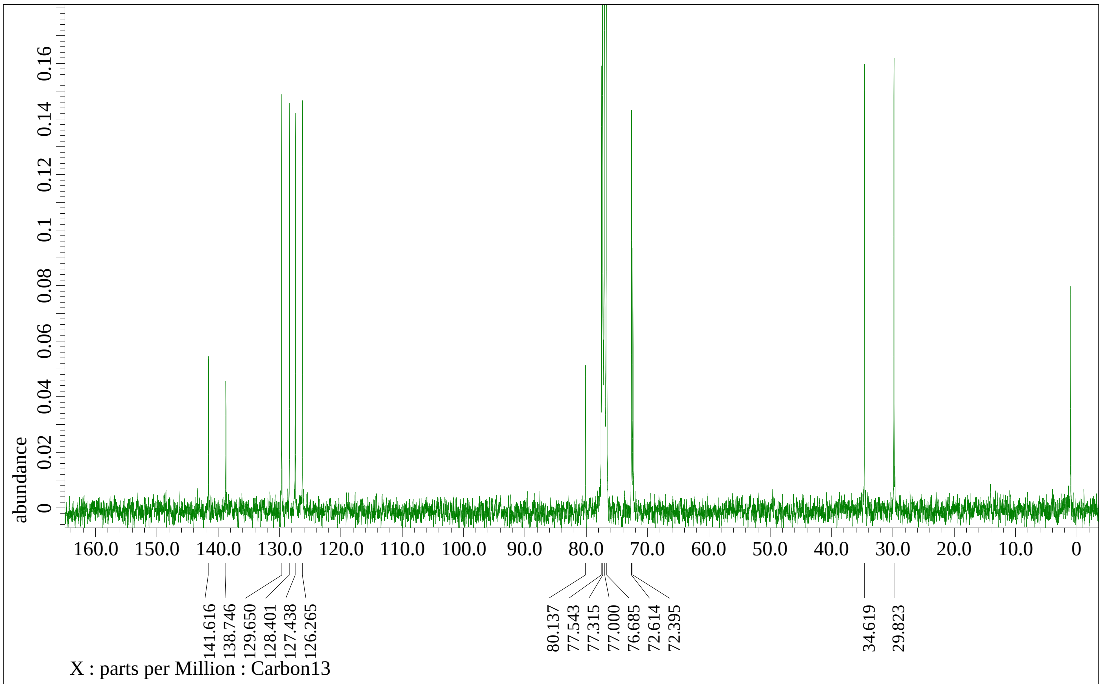


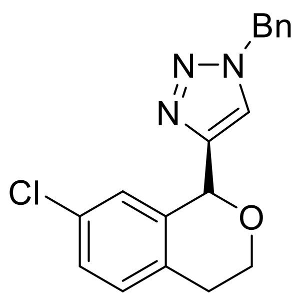
abundance
0.1
0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
138.822
138.612
128.296
127.848
121.717
121.078
82.034
77.324
77.000
76.685
74.187
73.138
72.986
X : parts per Million : Carbon13



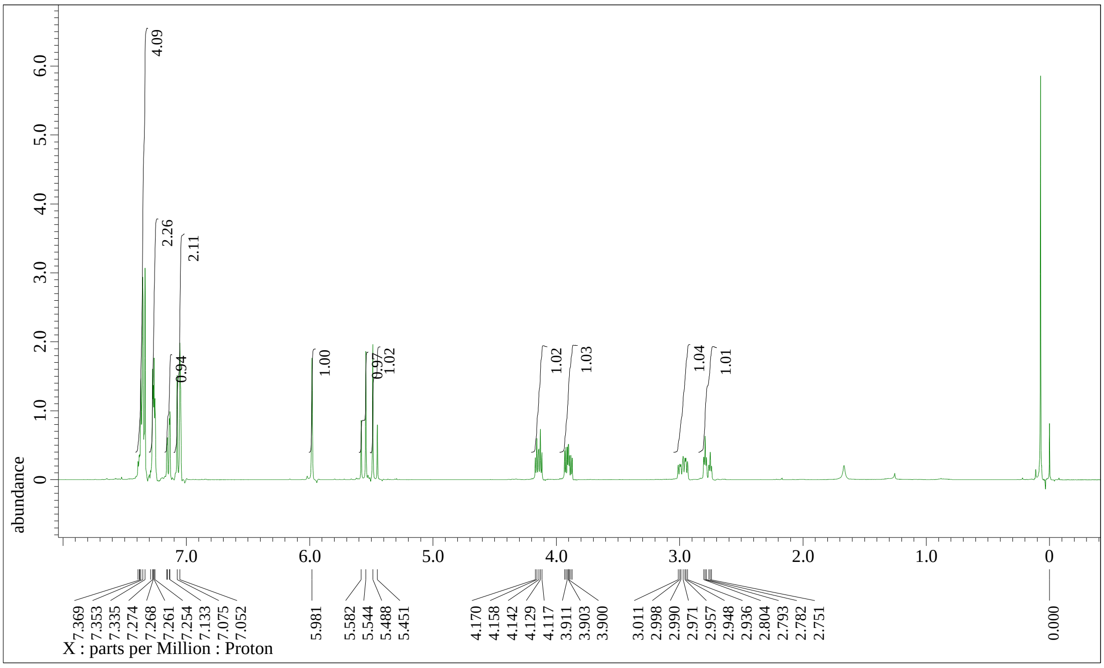
8

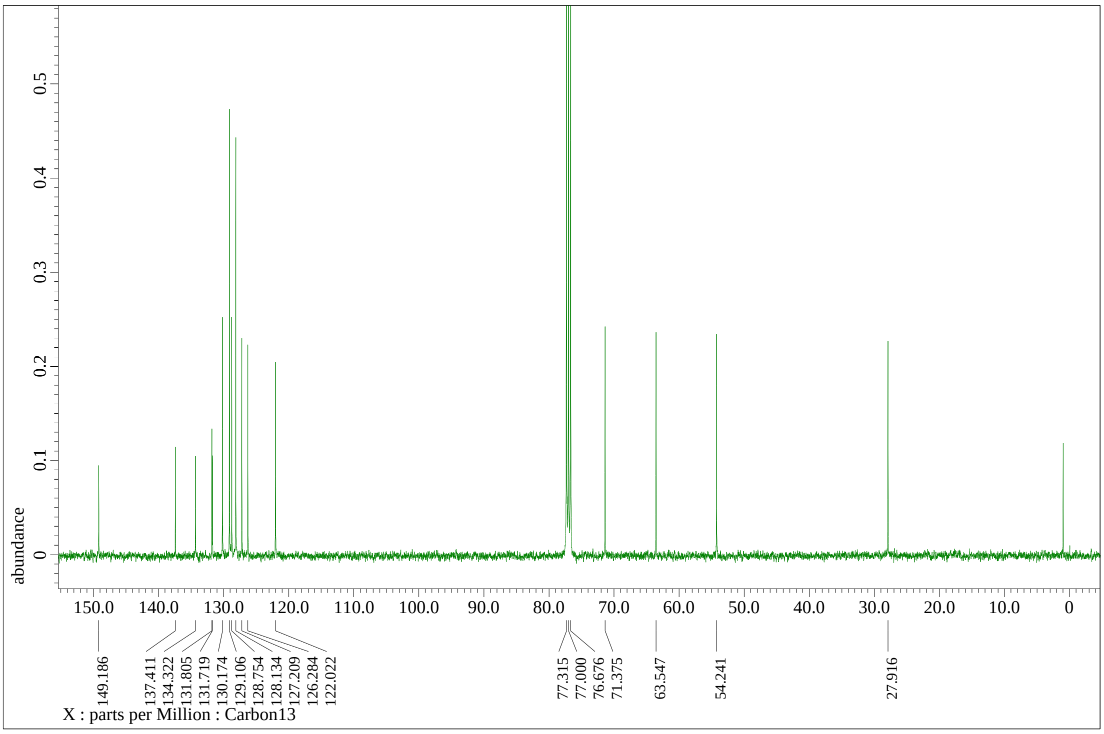

abundance
X : parts per Million : Proton
7.571
7.556
7.549
7.260
7.221
7.213
7.206
7.198
7.179
5.504
5.498
4.441
4.420
4.411
4.397
4.034
4.014
4.004
3.130
3.026
3.004
2.995
2.816
2.811
1.859
1.847
1.838
1.833
1.830
1.822
1.815
1.811
1.806
1.00
3.05
1.05
1.04
1.06
1.05
1.08
0.97
2.08


abundance
X : parts per Million : Carbon13
141.616
138.746
129.650
128.401
127.438
126.265
80.137
77.543
77.315
77.000
76.685
72.614
72.395
34.619
29.823


Bn
N
N
N
Cl
O

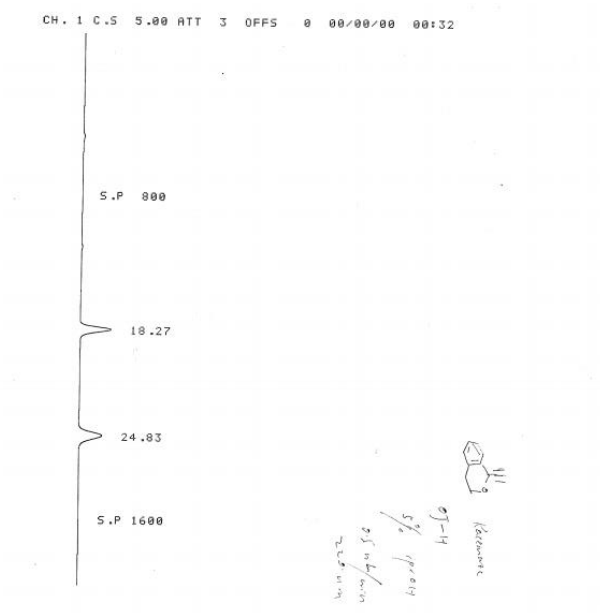
S16


abundance
X : parts per Million : Proton
4.09
2.26
2.11
0.94
1.00
0.97
1.02
1.02
1.03
1.04
1.01
7.369
7.353
7.335
7.274
7.268
7.261
7.254
7.133
7.075
7.052
5.981
5.582
5.544
5.488
5.451
4.170
4.158
4.142
4.129
4.117
3.911
3.903
3.900
3.011
2.998
2.990
2.971
2.957
2.948
2.936
2.804
2.793
2.782
2.751
0.000


abundance
X : parts per Million : Carbon13
149.186
137.411
134.322
131.805
131.719
130.174
129.106
128.754
128.134
127.209
126.284
122.022
77.315
77.000
76.676
71.375
63.547
54.241
27.916

HPLC Chart

2a (rac)



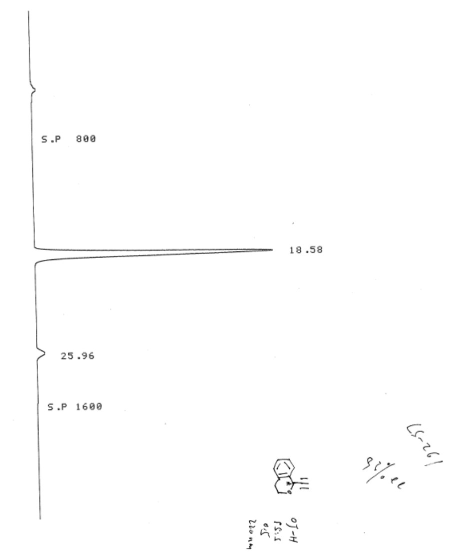
D-2500 00/00/00 00:32

METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	18.27	10856	49.816	BB
2	24.83	10936	50.184	BB
TOTAL		21792	100.000	
PEAK REJ :		0		

2a (chiral)



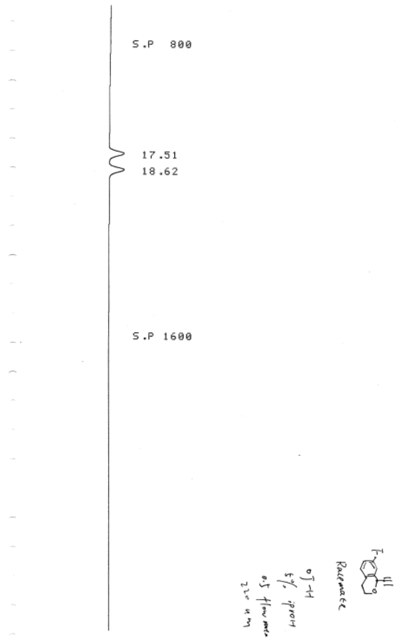
D-2500 00/00/00 01:4

METHOD: TAG: 3 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	18.58	26854	96.549	BB
2	25.96	960	3.451	BB
TOTAL		27814	100.000	
PEAK REJ :		0		

2b (rac)



D-2500 00/00/00

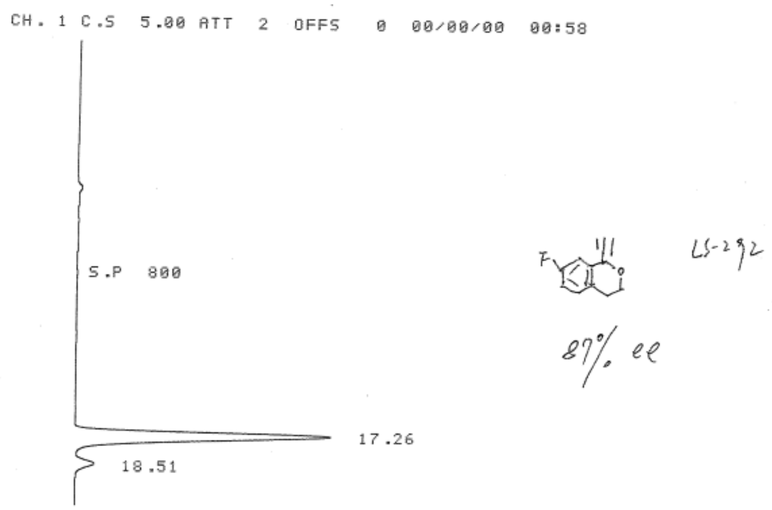
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	17.51	5642	49.409	BB
2	18.62	5777	50.591	BB
TOTAL		11419	100.000	

PEAK REJ : 0

2b (chiral)



D-2500 00/00/00 00:58

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	17.26	34900	93.405	BB
2	18.51	2464	6.595	BB
TOTAL		37364	100.000	

PEAK REJ : 0

2c (rac)

CH. 1 C.S 5.00 ATT 3 OFFS 0 00/00/00 01:42

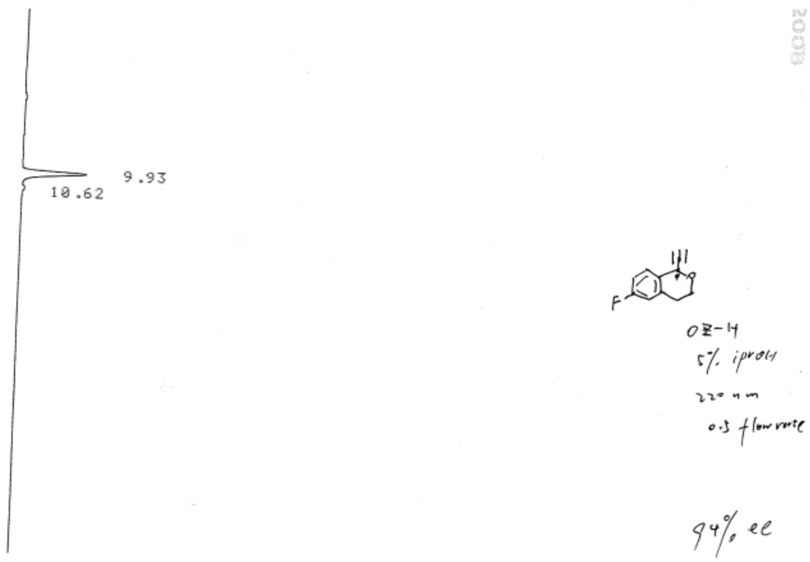
D-2500 00/00/00 01:42

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	9.93	7991	50.701	BB
2	10.60	7770	49.299	BB
TOTAL		15761	100.000	
PEAK REJ :		0		

2c (chiral)



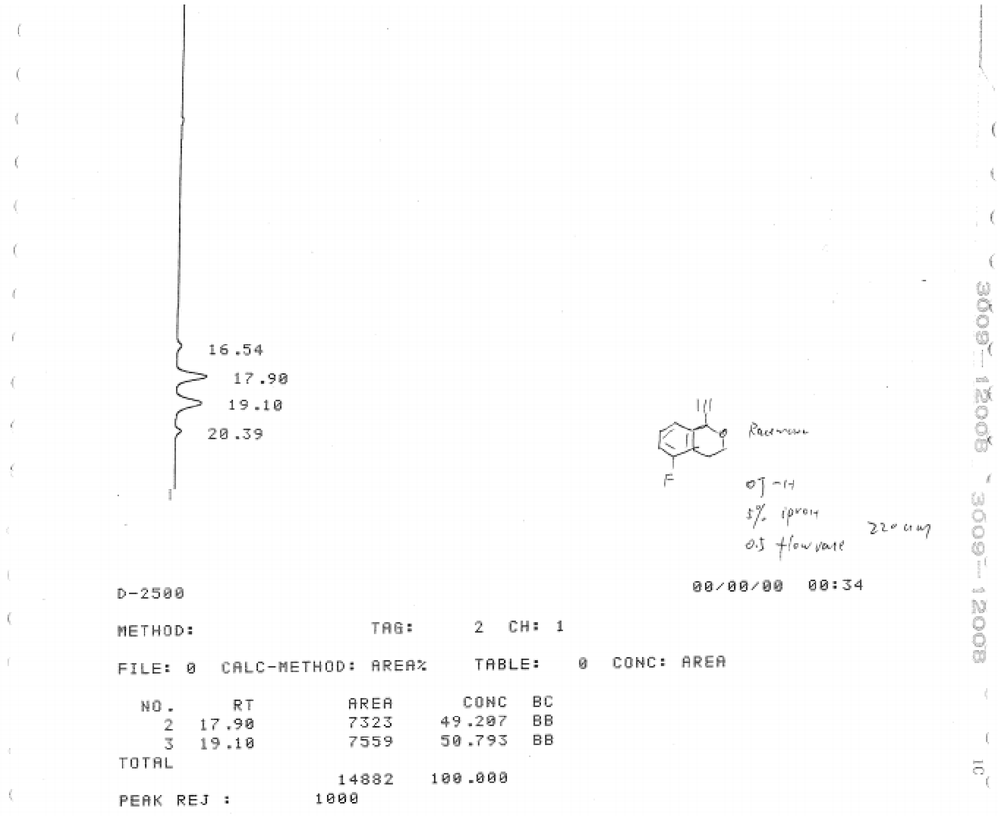
D-2500 00/00/00 00:50

METHOD: TAG: 1 CH: 1

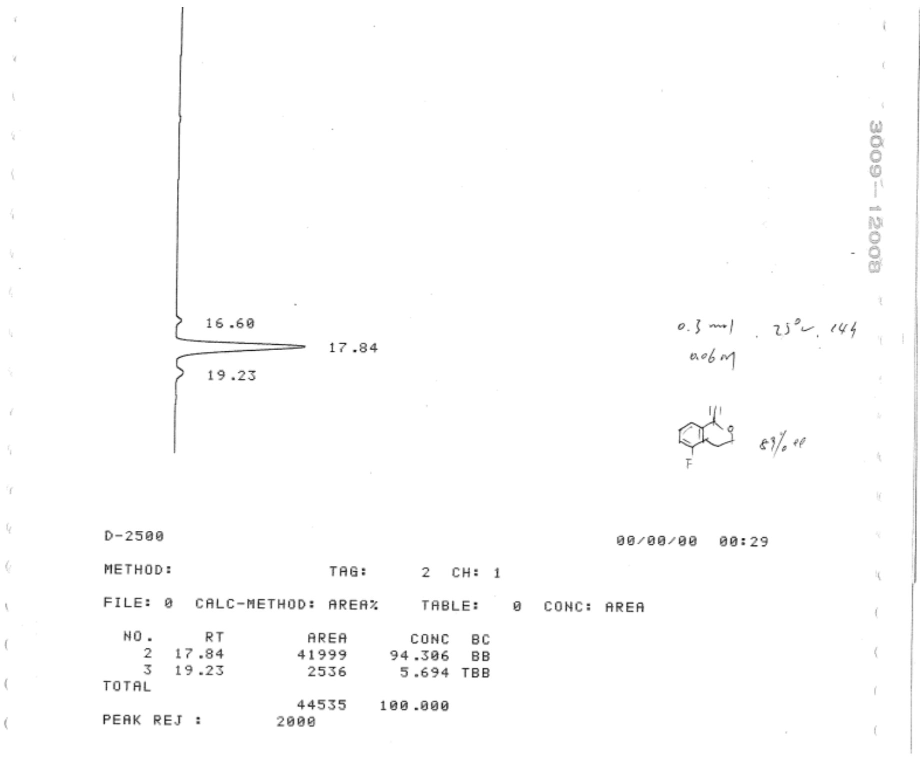
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	9.93	10312	96.936	BB
2	10.62	326	3.064	TBB
TOTAL		10638	100.000	
PEAK REJ :		0		

2d (rac)

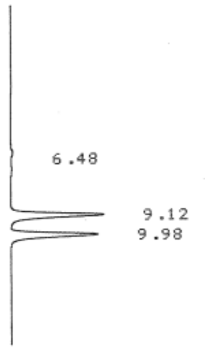


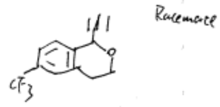
2d (chiral)



2e (rac)

CH. 1 C.S 5.00 ATT 3 OFFS 0 00/00/00 04:02





OZ-H
5% iproH
220 nm
0.5 flowrate

D-2500 00/00/00 04:02

METHOD: TAG: 4 CH: 1

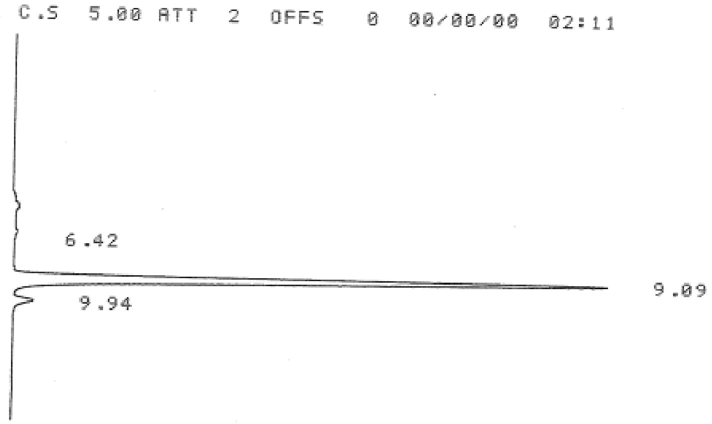
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

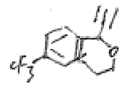
NO.	RT	AREA	CONC	BC
2	9.12	12734	50.278	BB
3	9.98	12593	49.722	BB
TOTAL		25327	100.000	

PEAK REJ : 5000

2e (chiral)

CH. 1 C.S 5.00 ATT 2 OFFS 0 00/00/00 02:11





93% ee

D-2500 00/00/00 02:11

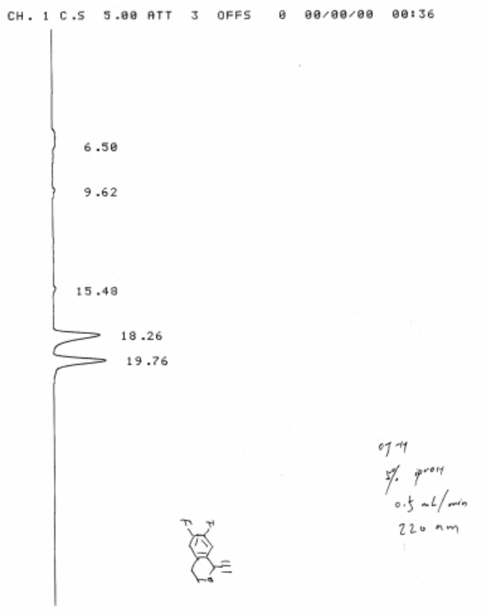
METHOD: TAG: 4 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	9.09	35509	96.618	BB
3	9.94	1243	3.382	BB
TOTAL		36752	100.000	

PEAK REJ : 500

2f (rac)



D-2500 00/00/00 00:36

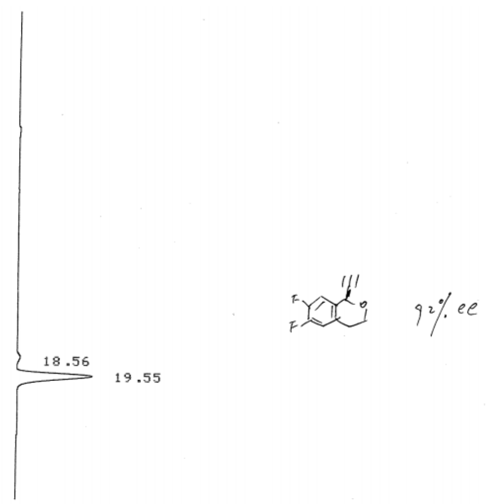
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
4	18.26	19276	49.272	BB
5	19.76	19846	50.728	BB
TOTAL		39122	100.000	

PEAK REJ : 5000

2f (chiral)



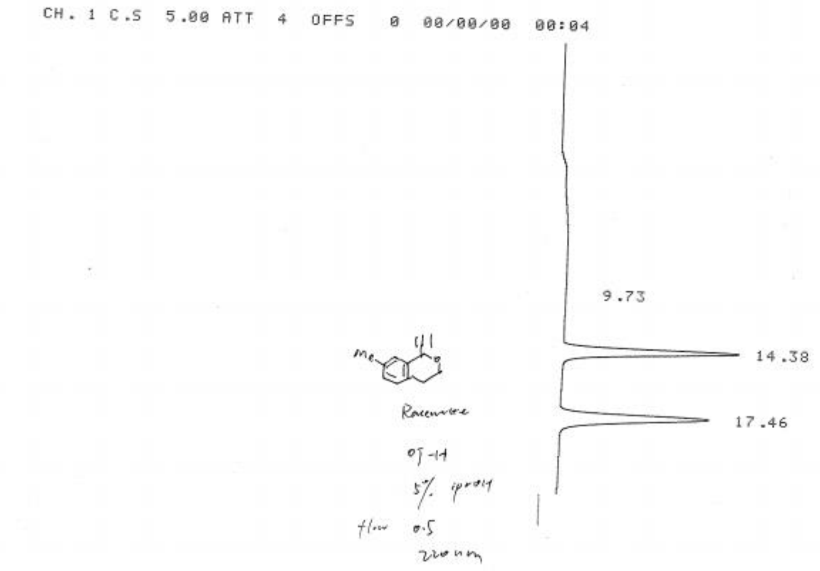
D-2500 00/00/00 02:16

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	18.56	948	3.880	BB
2	19.55	23488	96.120	BB
TOTAL		24436	100.000	

2g (rac)



D-2500 00/00/00 00:04

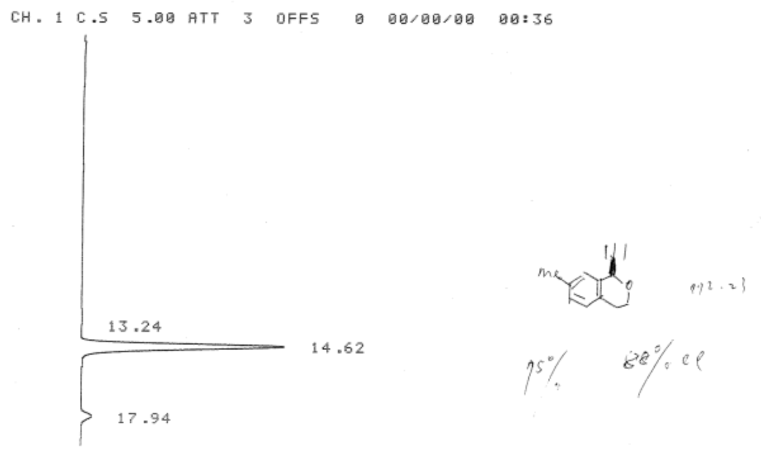
METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	14.38	78488	49.033	BB
3	17.46	81583	50.967	BB
TOTAL		160071	100.000	

PEAK REJ : 20000

2g (chiral)



D-2500 00/00/00 00:36

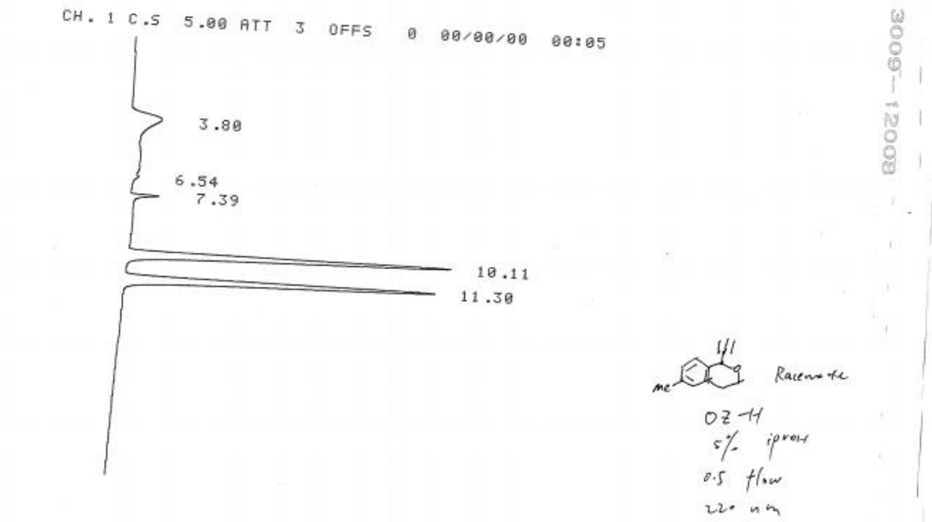
METHOD: TAG: 4 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	14.62	44736	93.833	BB
3	17.94	2940	6.167	BB
TOTAL		47676	100.000	

PEAK REJ : 2000

2h (rac)



D-2500 00/00/00 00:05

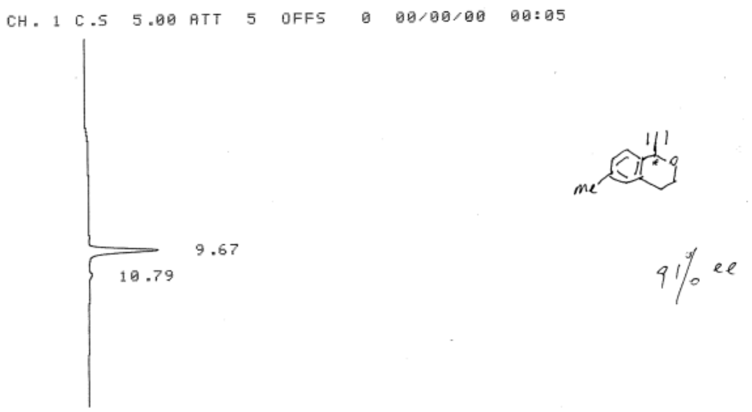
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
4	10.11	48578	49.254	BB
5	11.30	50049	50.746	BB
TOTAL		98627	100.000	

PEAK REJ : 30000

2h (chiral)



D-2500 00/00/00 00:05

METHOD: TAG: 1 CH: 1

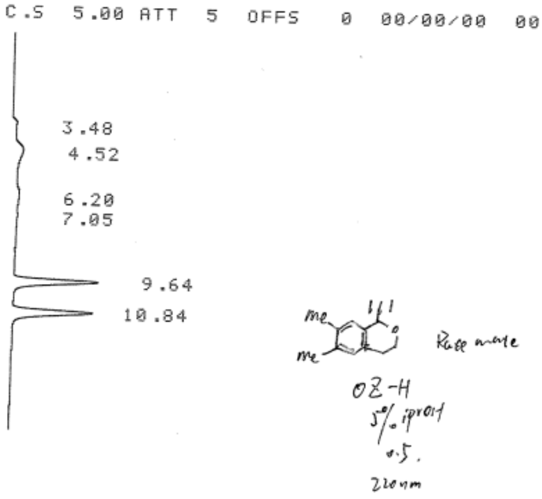
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	9.67	41232	95.619	BB
2	10.79	1889	4.381	TBB
TOTAL		43121	100.000	

PEAK REJ : 0

2i (rac)

CH. 1 C.S 5.00 ATT 5 OFFS 0 00/00/00 00:04



D-2500 00/00/00 00:04

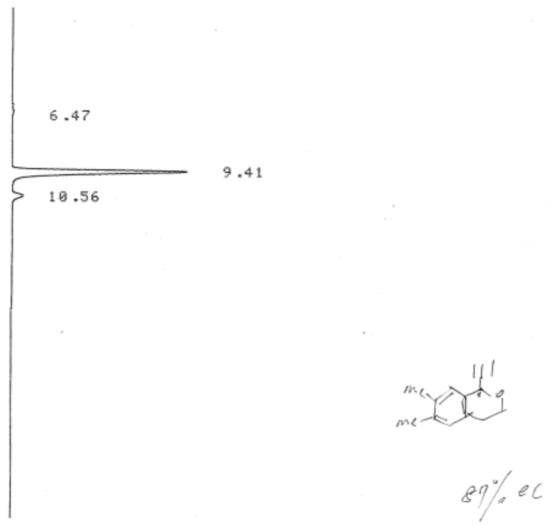
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
5	9.64	41159	49.541	BB
6	10.84	41922	50.459	BB
TOTAL		83081	100.000	

PEAK REJ : 10000

2i (chiral)



D-2500 00/00/00 01:13

METHOD: TAG: 1 CH: 1

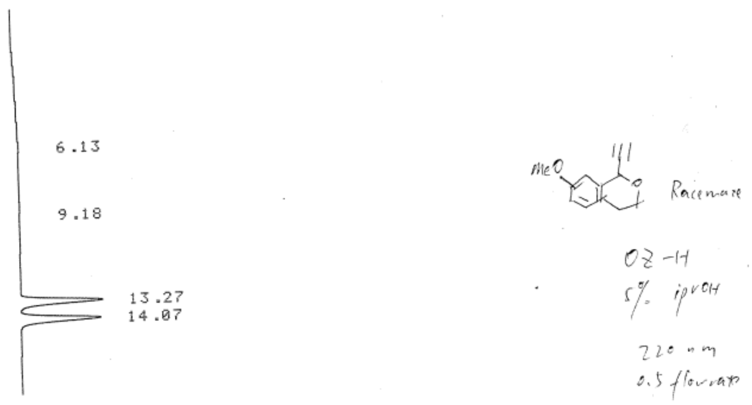
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	9.41	55516	93.617	BB
3	10.56	3785	6.383	BB
TOTAL		59301	100.000	

PEAK REJ : 500

2j (rac)

CH. 1 C.S 5.00 ATT 5 OFFS 0 00/00/00 00:04



D-2500

00/00/00 00:04

METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
3	13.27	55966	49.690	BV
4	14.07	56664	50.310	VB
TOTAL		112630	100.000	

PEAK REJ : 10000

2j (chiral)

D-2500

00/00/00 00:58

METHOD: TAG: 1 CH: 1

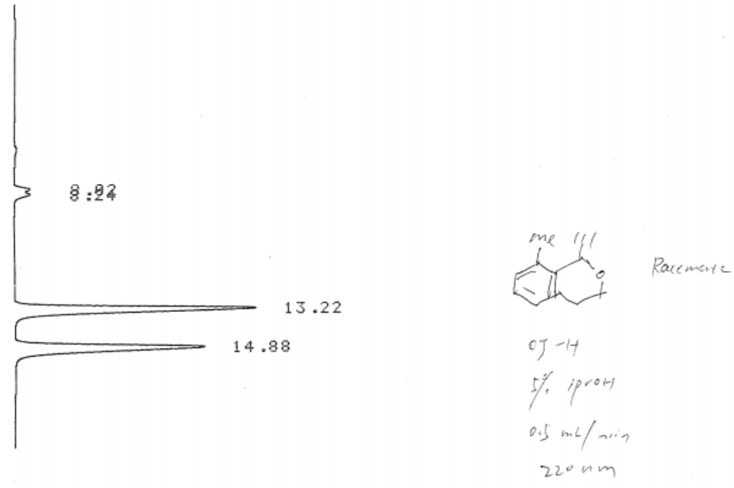
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	12.74	15176	96.270	BB
3	13.62	588	3.730	TBB
TOTAL		15764	100.000	

PEAK REJ : 400

2k (rac)

CH. 1 C.S 5.00 ATT 3 OFFS 0 00/00/00 00:30



D-2500 00/00/00 00:30

METHOD: TAG: 1 CH: 1

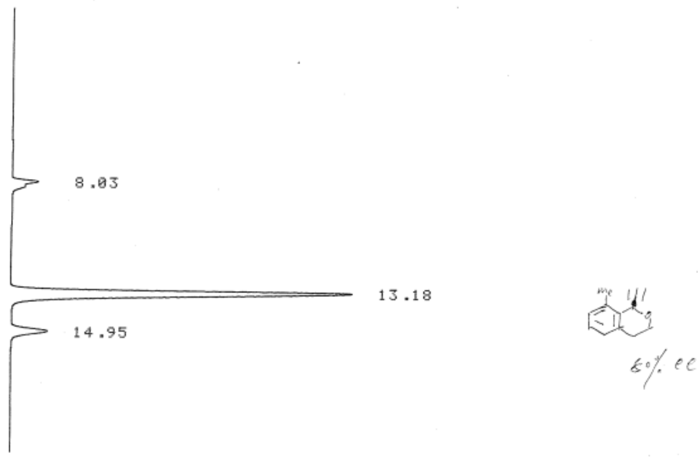
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
3	13.22	45208	53.318	BB
4	14.88	39582	46.682	BB
TOTAL		84790	100.000	

PEAK REJ : 5000

2k (chiral)

CH. 1 C.S 5.00 ATT 3 OFFS 0 00/00/00 00:38



D-2500 00/00/00 00:38

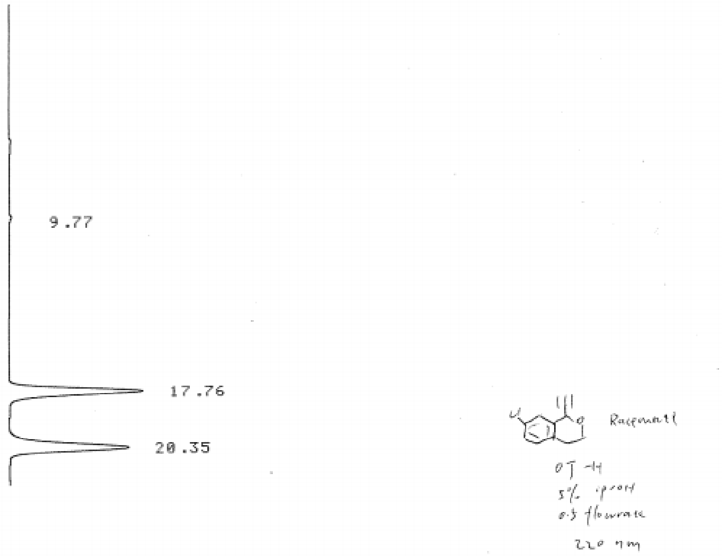
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	13.18	71827	90.100	BB
3	14.95	7892	9.900	BB
TOTAL		79719	100.000	

PEAK REJ : 6000

2l (rac)



D-2500 00/00/00 00:54

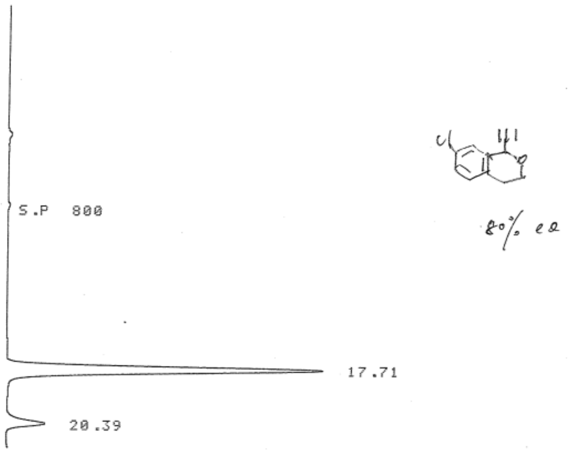
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	17.76	33856	49.812	BB
3	20.35	34112	50.188	BB
TOTAL		67968	100.000	

PEAK REJ : 500

2l (chiral)



D-2500 00/00/00 01:20

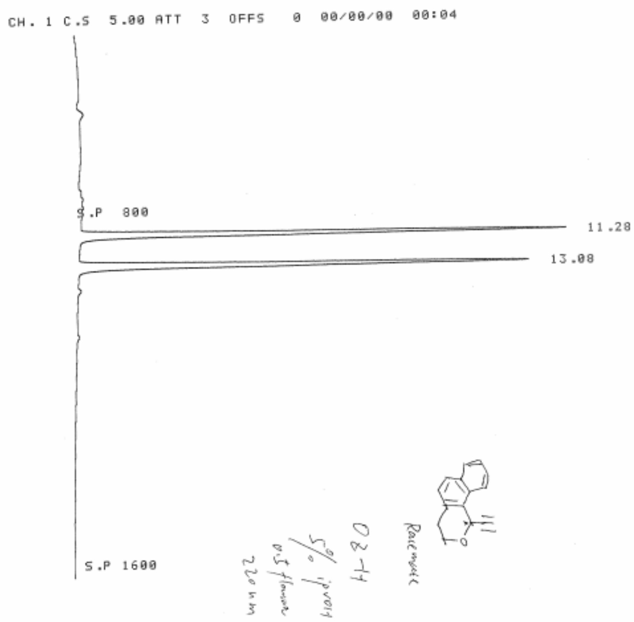
METHOD: TAG: 3 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	17.71	42720	89.871	BB
2	20.39	4815	10.129	BB
TOTAL		47535	100.000	

PEAK REJ : 0

2m (rac)



D-2500 00/00/00 00:04

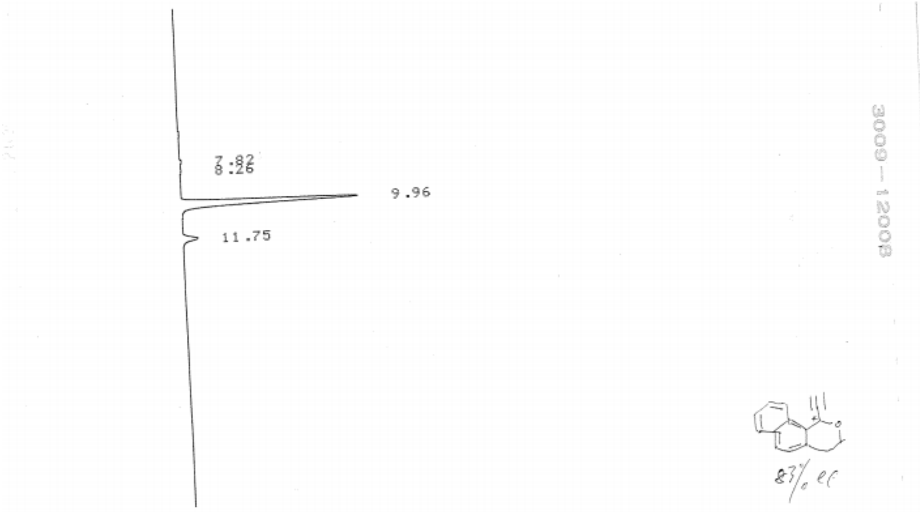
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	11.28	90416	49.533	BB
2	13.08	92120	50.467	BB
TOTAL		182536	100.000	

PEAK REJ : 0

2m (chiral)



D-2500 00/00/00 01:01

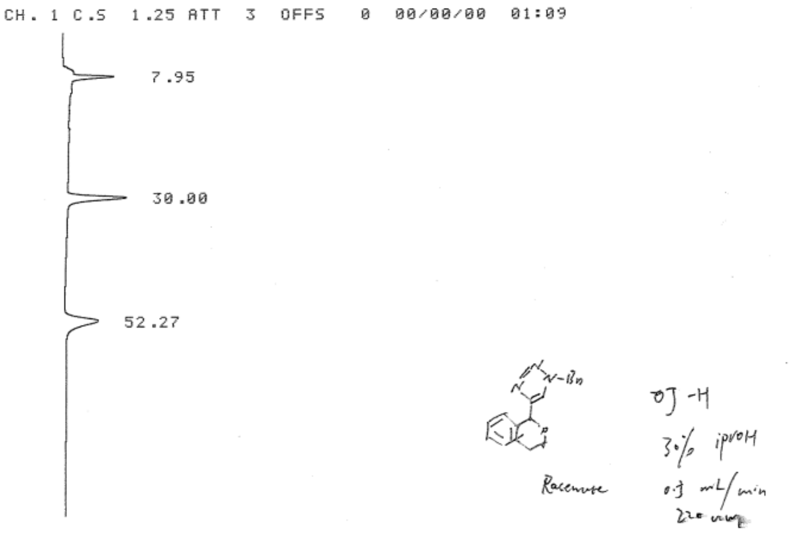
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
3	9.96	127596	91.612	BB
4	11.75	11682	8.388	BB
TOTAL		139278	100.000	

PEAK REJ : 10000

3 (rac)



D-2500 00/00/00 01:09

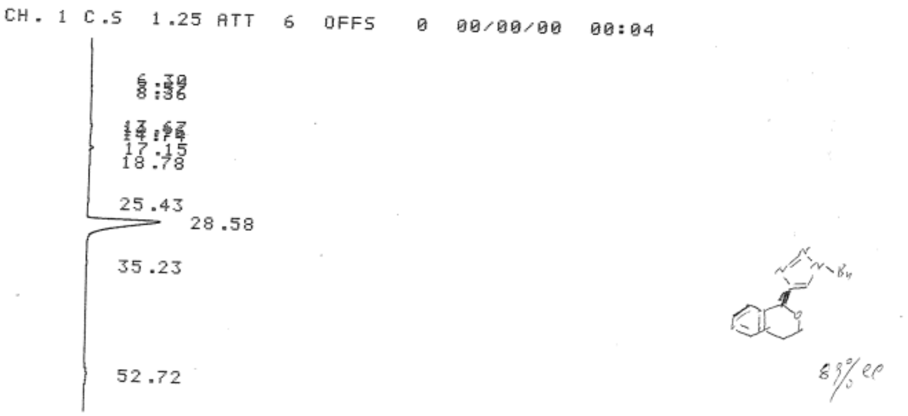
METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
2	30.00	35600	49.267	BB
3	52.27	36660	50.733	BB
TOTAL		72260	100.000	

PEAK REJ : 20000

3 (chiral)



D-2500 00/00/00 00:04

METHOD: TAG: 1 CH: 1

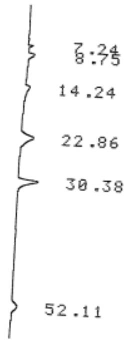
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

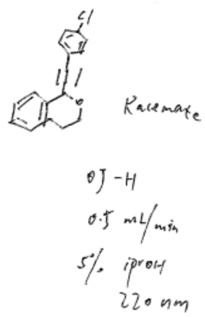
NO.	RT	AREA	CONC	BC
10	28.58	411885	94.699	BB
12	52.72	23056	5.301	BB
TOTAL		434941	100.000	

PEAK REJ : 20000

4 (rac)

CH. 1 C.S 1.25 ATT 5 OFFS 0 00/00/00 00:06





D-2500 00/00/00 00:06

METHOD: TAG: 1 CH: 1

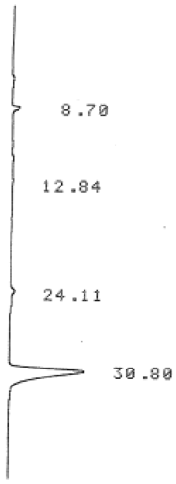
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

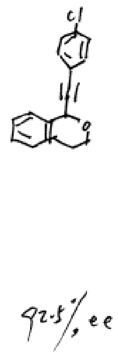
NO.	RT	AREA	CONC	BC
4	22.86	43763	49.874	BB
5	30.38	43984	50.126	BB
TOTAL		87747	100.000	

PEAK REJ : 20000

4 (chiral)

CH. 1 C.S 2.50 ATT 3 OFFS 0 00/00/00 01:16





D-2500 00/00/00 01:16

METHOD: TAG: 2 CH: 1

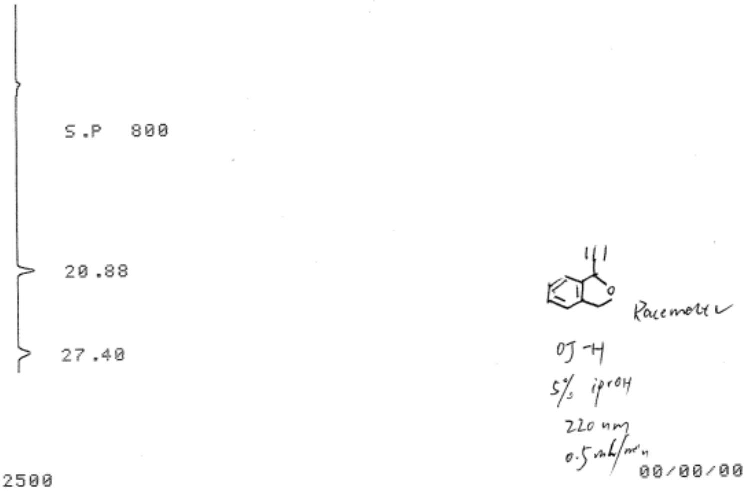
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
3	24.11	1496	3.706	BB
4	30.80	38873	96.294	BB
TOTAL		40369	100.000	

PEAK REJ : 1400

7 (rac)

CH. 1 C.S 2.50 ATT 2 OFFS 0 00/00/00 00:54



D-2500 00/00/00 00:54

METHOD: TAG: 2 CH: 1

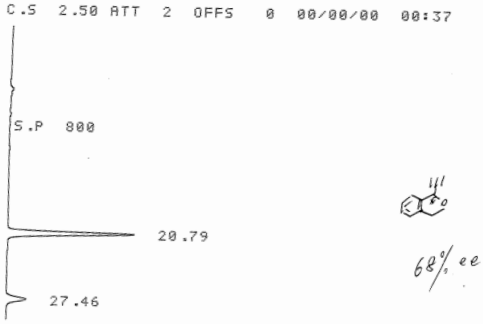
FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	20.88	1685	48.940	BB
2	27.40	1758	51.060	BB
TOTAL		3443	100.000	

PEAK REJ : 0

7 (chiral)

CH. 1 C.S 2.50 ATT 2 OFFS 0 00/00/00 00:37



D-2500 00/00/00 00:37

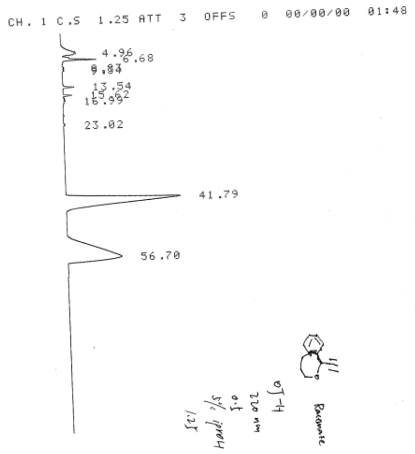
METHOD: TAG: 1 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	20.79	18616	83.973	BB
2	27.46	3553	16.027	BB
TOTAL		22169	100.000	

PEAK REJ : 0

8 (rac)



D-2500 00/00/00

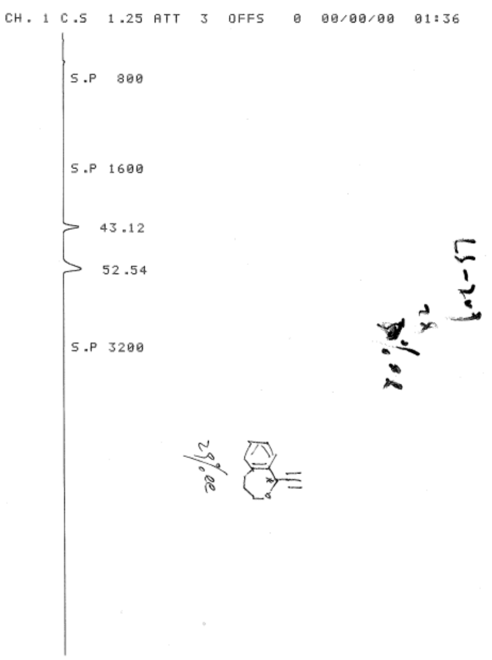
METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
9	41.79	190720	50.759	BB
10	56.70	185017	49.241	BB
TOTAL		375737	100.000	

PEAK REJ : 100000

8 (chiral)



D-2500 00/00/00 01:

METHOD: TAG: 2 CH: 1

FILE: 0 CALC-METHOD: AREA% TABLE: 0 CONC: AREA

NO.	RT	AREA	CONC	BC
1	43.12	10350	35.322	BB
2	52.54	18952	64.678	BB
TOTAL		29302	100.000	

PEAK REJ : 1000