Stereoselective S_N2-Substitutions using Polyfunctional Lithium Arylcuprates Prepared by an Iodine-Copper Exchange

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Supporting Information

General considerations

Unless otherwise indicated, all reactions were carried out with magnetic stirring and, if air or moisture sensitive, in flame-dried glassware under argon. Syringes used to transfer reagents and solvent were purged with argon prior to use. Reactions were monitored by gas chromotography (GC and GC-MS) or thin layer chromotography (TLC). Enantiomeric purity was determined by chiral HPLC or capillary GC analysis. In all cases, the analysis was calibrated with a sample of the racemate.

Chiral HPLC:

column A: Chiralcel OD-H, 0.46 cm x 25 cm

column B: Chiralcel OD, 0.46 cm x 25 cm

column C: Chiralcel AD, 0.46 cm x 25 cm

Chiral GC:

column A: TFA gamma-cyclodextrin, 30.0 m x 0.25 mm

method A: 40 °C (2 min), ramp of 20 °C/min to 150 °C (45 min)

method B: 130 °C (100 min).

method C: 150 °C (150 min).

Starting materials

(*R*)-2-Iodo-2-cyclohexen-1-ol and (*R*)-2-iodo-2-cyclopenten-1-ol are literature known.[1] and (1*S,* 2*Z*)-1-Butyl-2-butenyl-2,3,4,5,6-pentafluorobenzoate are literature known.[2]

Neophyllithium solutions were titrated using the method of Paquette.[3]

Preparation of lithium dineophylcuprate (Nphyl$_2$CuLi):[4]

A dry and argon flushed 500 mL round-bottom flask was charged with lithium dust (3.0 g, 432 mmol) and 2,2-dimethyl-2-phenylethyl chloride (14.0 mL, 86.9 mmol) in *n*-hexane (75 mL). The reaction mixture was refluxed overnight. After cooling to rt *n*-hexane was removed *in vacuo* and then dry diethyl ether was added. The resulting mixture was cannulated into a flame dried Schlenk tube and centrifuged (2000 rpm, 30 min). The clear solution of neophyllithium thus obtained was titrated before use with menthol using *o*-phenanthroline as indicator and could be stored at -30 °C for several days. Usaully 1.4 M/Et_2O solution of the lithium reagent is obtained.

A dry and argon flushed 25 mL flask was charged with CuCN (110 mg, 1.2 mmol). Dry diethyl ether (1 mL) was added and the resulting suspension was cooled to 0 °C. The freshly titrated solution of neophyllithium was then added slowly and the mixture was quickly warmed to rt and stirred for 10 min, until a clear yellow solution of the desired cuprate was obtained.

(*R*)-2-Iodo-2-cyclopenten-1-yl acetate (4a): [5]

(*R*)-2-Iodo-2-cyclopenten-1-ol (1.6 g, 7.6 mmol) was dissolved in pyridine (5.0 mL) and Ac_2O (2.5 mL). The resulting mixture was stirred for 12 h at 25 °C. It was diluted with Et_2O (50 mL) and washed with 2M HCl (50 mL) and brine (50 mL x 2). The organic phase was dried (Na_2SO_4). The solvent was removed and the crude product purified by column chromatography (SiO_2, pentane/diethyl ether = 6 : 1) to give 1.54 g (80 %) of **4a** as a colorless oil.

GC (column A, method A): t_R/min = 8.7 (major), 13.0 (minor); 96.6 % *ee*.

$[\alpha]_D^{20}$ + 33.8° (c 1.16, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.36 (m, 1H), 5.63 (m, 1H), 2.51-2.16 (m, 3H), 2.03 (s, 3H), 1.72-1.86 (m, 1H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 170.6, 145.7, 92.7, 83.8, 33.0, 29.9, 21.1.

IR (film): 1738 (vs), 1372 (m), 1233 (vs), 1034 (s), 926 (m), 808 (w).

MS (EI, 70 ev), *m/z* (%): 209 (4, M^+-CH_3CO), 192 (21), 125 (48), 83 (100), 66 (35), 65 (36), 55 (6).

Anal. calcd. for $C_7H_9IO_2$ (252.05): C 33.36, H 3.60; found: C 33.78, H 3.22.

(*R*)-2-Iodo-2-cyclohexen-1-yl ethyl acetate (4b):[5]

To a solution of (*R*)-2-iodo-cyclohexen-1-ol (3.7 g, 16.5 mmol) in 20 mL pyridine, acetic anhydride (8.5 g, 82.6 mmol) was added at rt. The resulting mixture was stirred at rt for 12 h and then diluted with 100 mL diethyl ether. The solution was washed with 2M HCL (100 mL) and brine (100 mL x 2). The organic phase was dried ($NaSO_4$) and concentrated in vacuum. The residue was purified by column chromatography (SiO_2, pentane/diethyl ether = 10 :1) to give 4.2 g (95%) of **4b** as a colorless oil.

GC (column A, method A): t_R/min = 10.24 (major), 11.04 (minor); 98 % *ee*.

$[\alpha]_D^{20}$ + 21.6 (c 1.08, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 6.65 (m 1H), 539 (m, 1H), 2.11 (s. 3H), 2.11-1.70 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 170.5, 143.9, 95.8, 73.8, 30.3, 29.5, 21.6, 17.8.

IR (film): 2944 (w), 1735 (vs), 1427 (w), 1371 (m), 1233 (vs), 977 (m), 917 (w), 730 (w).

MS (EI, 70 ev), *m/z* (%): 206 (4) $[M\text{-}AcO\text{-}H]^+$, 139 (85), 126 (15), 97 (100), 79 (47), 55 (4).

Anal. calcd. for $C_8H_{11}IO_2$ (252.05): C 36.11, H 4.17; found: C 33.38, H 4.06.

1-d-2-Iodo-2-cyclohexenyl acetate (4c):

To a solution of 2-iodo-2-cyclohex-1-one (1.11 g, 5 mmol) and $CeCl_3 \cdot 7H_2O$ (1.86 g, 5 mmol) in MeOH (8 mL) cooled at 0 ^oC, $NaBD_4$ was added in small portions. The resulting mixture was stirred at 25 ^oC for 3 h. The reaction mixture was poured into cold water and extracted with Et_2O (3 x 20 mL). The combined organic phase was washed with brine and dried (Na_2SO_4). The solvent was removed and the crude product was purified by column chromatography (SiO_2, pentane/diethyl ether = 5 :1) to give 856 mg (76 % yield) of 1-d-2-iodo-2-cyclohexenol as a colorless oil.

To a solution of 1-d-2-iodo-2-cyclohexenol (788 mg, 3.51 mmol) in pyridine (3.1 mL), Ac_2O (1.9 mL) was added. The resulting mixture was stirred at 25 ^oC for 2 h. The reaction mixture was quenched with 2 M HCl (5 mL) and extracted with Et_2O (3 x 20 mL). The combined organic phase was washed with H_2O, saturated aqueous $NaHCO_3$ solution, brine, and dried (Na_2SO_4). The solvent was removed and the crude product was purified by column chromatography (SiO_2 , pentane/diethyl ether = 10:1) to give 775 mg (83% yield) of **4c** as a colorless oil.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 6.65-6.50 (m, 1H), 2.08 - 1.64 (m, 9H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 169.6, 144.0, 95.8, 72.0, 30.3, 29.5, 21.6, 17.7.

IR (film): 2944 (m), 1738 (s), 1369 (m), 1264 (m), 1240 (s), 1013 (m), 922 (m).

MS (EI, 70 ev), *m/z* (%): 208 (3), 207 (5), 140 (79), 127 (10), 98 (100), 80 (33).

HRMS (EI): calcd. for C_6H_7DI $[M^+\text{- OAc}]$: 207.9732, found: 207.9733.

4-[(1*R*)-(2-Iodo-2-cyclopenten-1-yl)] phenyl methyl ether (5a):

Typical procedure A: A dry and argon flushed 25 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv). A solution of ethyl 4-iodoanisole (281 mg, 1.2 mmol) in THF (2 mL) was added over the solution of $Nphyl_2CuLi$, and the mixture was stirred at 0 °C until I/Cu-exchange was completed (30 min). The mixture was cooled at -40 °C and a solution of (*R*)-2-iodo-2-cyclopenten-1-yl acetate (**5a**) (252 mg, 1.0 mmol, 1.0 equiv) in THF (1.5 mL) was added. The resulting reaction mixture was allowed to warm to –20 ^{o}C and stirred at this temperature for 12 h. Saturated aqueous NH_4Cl sol. (20 mL) was added followed by 25 % aqueous ammonia solution (1 mL). The reaction mixture was stirred at 25 °C until the copper salts had dissolved and was extracted with Et_2O (3 x 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (SiO_2, pentane, then pentane:Et_2O = 30:1) afforded 213 mg (71 % yield) of **5a** as a colorless oil.

GC (column A, method C,): t_R/min = 18.3 (minor), 18.9 (major); 92.4 % *ee*.

$[\alpha]_D^{20}$ -26.7° (c 1.19, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.20-7.04 (m, 2H), 6.90-6.83 (m, 2H), 6.30 (m, 1H), 3.89-3.80 (m, 1H), 3.80 (s, 3H), 2.58-2.33 (m, 3H), 1.99-1.85 (m, 1H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 158.4, 140.8, 136.1, 128.7, 113.9, 100.9, 58.7, 55.2, 33.9, 33.0.

IR (film): 2934 (m), 1611 (m), 1511 (vs), 1464 (m), 1303 (w), 1248 (vs), 1176 (s), 1037 (s), 828 (m), 808 (m), 543 (w).

MS (EI, 70 ev), *m/z* (%): 300 (M^+,100), 269 (4), 173 (42), 158 (29), 145 (15), 128 (16), 115 (13), 102 (9), 91 (4), 77 (4).

HRMS (EI): calcd. for $C_{13}H_{13}IO$ [M^+]: 300.0011, found: 300.0036.

Ethyl 4-[(1R)-(2-iodo-2-cyclopenten-1-yl)] benzoate (5b):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), ethyl 4-iodobenzoate (0.331 g, 1.2 mmol, 1.2 equiv) and (*R*)-2-iodo-2-cyclopenten-1-yl acetate (252 mg, 1.0 mmol, 1.0 equiv). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 30 : 1) yielded 170 mg (50 % yield) of **5b** as a colorless oil.

GC (column A, method C,): t_R/min = 81.5 (minor), 86.4 (major); 97.0 % *ee*.

$[\alpha]_D^{20}$ -14.4° (c 1.03, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.96-7.90 (m, 2H), 7.19-7.11 (m, 2H), 6.29 (m, 1H), 4.30 (q, *J*= 7.1 Hz, 2H), 3.95-3.84 (m, 1H), 2.55-2.28 (m, 3H), 1.94-1.79 (m, 1H), 1.31 (t, *J*= 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 166.5, 149.2, 141.9, 129.9, 129.1, 127.7, 98.6, 60.8, 59.5, 34.1, 33.0, 14.3.

IR (film): 2935 (m), 1716 (vs), 1610 (m), 1418 (m), 1276 (vs), 1178 (m), 1102 (s), 1022 (m), 771 (m), 707 (m), 541 (w).

MS (EI, 70 ev), *m/z* (%): 342 (100) [M^+], 313 (8), 297 (55), 269 (45), 215 (64), 192 (11), 187 (9), 169 (10), 142 (50), 141 (55), 128 (24), 115 (32), 114 (11), 85 (6).

HRMS (EI): calcd. for $C_{14}H_{15}IO_2$ [M^+]: 342.0117, found: 342.0154.

Ethyl 4-[(1*S*)-2-iodocyclohex-2-en-1-yl]beozoate (5c):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), ethyl 4-iodobenzoate (331 mg, 1.2 mmol, 1.2 equiv) and (*R*)-2-iodo-cyclohex-2-enyl ester (266 mg, 1.0 mmol). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 10 : 1) yielded 274 mg (77 % yield) of **5c** as a colorless oil.

HPLC (column C, heptane : *i*PrOH = 99:1, 0.5 ml/min): t_R/min = 18.3 (minor), 19.8 (major); 98 % *ee*.

$[\alpha]_D^{20}$ + 12.1 (c 0.99, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.94 (d, *J* = 8.4 Hz, 2H), 7.20 (d, *J* = 8.4 Hz, 2H), 6.62 (m, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.68 (m, 1H), 2.09 - 1.53 (m, 6H), 1.32 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =149.8, 141.2, 130.1, 129.4, 128.7, 100.2, 61.2, 53.0, 33.9, 29.7, 18.1, 14.8.

IR (film): 3415 (w), 2937 (s), 1715 (vs), 1609 (m), 1444 (m), 1417 (m), 1366 (m), 1276 (vs), 1178 (s), 1102 (vs), 1021 (m), 769 (m), 707 (m).

MS (EI, 70 ev), *m/z* (%): 356 (100) [M^+], 311 (32), 229 (27), 206 (19), 183 (7), 155 (20), 129 (25), 115 (13), 91 (7).

HRMS (EI): calcd. For $C_{15}H_{17}IO_2$ [M^+]: 356.0273, found 356.0280.

4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzonitrile (5d):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 4-bromobenzonitrile (218 mg, 1.2 mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-cyclohex-2-enyl ester (266 mg, 1.0 mmol, 1.0equiv). The temperature for the Br/Cu-exchange

is rt. Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 15:1) yielded 204 mg (66 % yield) of **5d** as a colorless oil.

GC (column A, method B): t_R/min = 33.73 (minor), 34.98 (major); 97 % *ee*.

$[\alpha]_D^{20}$ + 18.5 (c 1.26, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.56 (d, *J* = 8.4 Hz, 2H), 7.24 (d, *J* = 8.4 Hz, 2H), 6.63 (m, 1H), 3.69 (m, 1H), 2.09 - 1.53 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 148.7, 140.4, 131.2, 128.1, 118.0, 109.6, 51.6, 32.4, 28.2, 16.6.

IR (film): 4306 (w), 2907 (m), 2229 (vs), 1604 (s), 1503 (s), 1411 (s), 975(s), 833 (vs), 690 (s), 563 (vs), 483 (w).

MS (EI, 70 ev), *m/z* (%): 309 (100) [M^+], 182 (41), 154 (63), 140 (26), 127 (19), 116 (57).

HRMS (EI): calcd. For $C_{13}H_{12}IN$ [M^+]: 309.0014, found 309.0008.

1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-4-(trifluoromethyl)benzene (5e):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 1-iodo-4-trifluoromethylbenzene (326 mg, 1.2 mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-cyclohex-2-enyl ester (266 mg, 1.0 mmol, 1.0 equiv). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 15:1) yielded 250 mg (70 % yield) of **5e** as a colorless oil.

GC (column A, method B): t_R/min = 24.56 (minor), 25.91 (major); 94 % *ee*.

$[\alpha]_D^{20}$ + 11.7 (c 1.36, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.52 (d, *J* = 8.0 Hz, 2H), 7.24 (d, *J* = 8.0 Hz, 2H), 6.62 (m, 1H), 3.68 (m, 1H), 1.53-2.12 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 148.5, 141.4, 129.5, 129.0, 125.7, 124 (q, *J* = 271 H_Z), 99.8, 73.3, 52.8, 33.9, 29.6 17.9.

IR (film): 2938 (s), 1618 (s), 1445 (m), 1418 (m), 1325 (vs), 1163 (vs), 1124 (vs), 1110 (vs), 985 (m), 834 (m), 606 (w).

MS (EI, 70 ev), *m/z* (%): 352 (100) [M^+], 333 (15), 225 (61), 197 (45), 177 (43), 158 (87), 128 (20).

HRMS (EI): calcd. For $C_{13}H_{12}F_3I$ [M^+]: 351.9936, found 351.9916.

1-Iodo-4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzene (5f):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 1,4-diiodobenzene (394 mg, 1.2 mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-

cyclohex-2-enyl ester (266 mg, 1.0 mmol). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 15:1) yielded 336 mg (82 % yield) of **5f** as a colorless oil.

GC (column A, method C): t_R/min = 78.77 (minor), 82.21 (major); 98 % *ee*.

$[\alpha]_D^{20}$ + 25.2 (c 1.58, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.58 (d, *J* = 8.4 Hz, 2H), 6.88 (d, *J* = 8.4 Hz, 2H), 6.58 (m, 1H), 3.57 (m, 1H), 2.14 - 1.46 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =142.5, 139.4, 136.1, 129.1, 98.8, 90.7, 50.9, 32.2, 28.0, 16.3.

IR (film): 2934 (s), 1627 (w), 1479 (s), 1400 (m), 1141 (w), 1060 (m), 1006 (s), 981 (m), 818 (s), 551 (w).

MS (EI, 70 ev), *m/z* (%): 410 (100) [M^+], 283 (23), 217 (26), 156 (36), 141 (19), 128 (37), 115 (17).

HRMS (EI): calcd. For $C_{12}H_{12}I_2$ [M^+]: 409.9028, found 409.9017.

1-Bromo-4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzene (5g):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 4-bromo-iodobenzene (339 mg, 1.2mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-cyclohex-2-enyl ester (266 mg, 1.0 mmol). Standard workup and purification by column chromatography (SiO_2, *n*-pentane) yielded 323 mg (89 % yield) of **5g** as a colorless oil.

CC (column A, method B): t_R/min = 117.23 (minor), 132.05 (major); 96% *ee*.

$[\alpha]_D^{20}$ +14.8 (c 1.43, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.38 (d, *J* = 8.4 Hz, 2H), 7.01 (d, *J* = 8.4 Hz, 2H), 6.58 (m, 1H), 3.61 (m, 1H), 1.50-2.14 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 143.6, 141.1, 131.9, 130.5, 120.9, 100.6, 52.5, 33.9, 29,7, 18.0.

IR (film): 2934 (vs), 1898 (w), 1628 (m), 1483 (vs), 1442 (s), 1404 (s9, 1073 (s), 1010 (vs), 984 (s), 895 (m), 820 (s),701 (m9, 552 (w).

MS (EI, 70 ev), *m/z* (%): 362 (45) [M^+], 235 (35), 206 (31), 169 (40), 156 (100), 141 (34), 128 (77), 115 (29), 77 (15).

HRMS (EI): calcd. For $C_{12}H_{12}BrI$ [M^+]: 361.9167, found 361.9153.

1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-4-methoxybenzene (5h):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 4-iodoanisole (291 mg, 1.2 mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-cyclohex-

2-enyl ester (266 mg, 1.0 mmol). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/Et_2O = 150 : 1) yielded 270 mg (85 %) of **5h** as a colorless oil.

GC (column A, method B): t_R/min = 96.5 (minor), 102.2 (major); 95 % *ee*.

$[\alpha]_D^{20}$ + 15.2 (c 1.04, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.04 (d, *J* = 8.4 Hz, 2H), 6.79 (d, *J* = 8.4 Hz, 2H), 6.56 (m, 1H), 3.73 (s, 3H), 3.57 (m, 1H), 2.12 - 1.54 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 158.7, 140.4, 136.7, 129.7, 114.1, 102.5, 55.6, 52.2, 34.1, 29.7, 18.2.

IR (film): 2933 (vs), 2832 (s), 1610 (s), 1510 (vs), 1463 (s), 1302 (m), 1249 (vs), 1176 (s), 1036 (s), 828 (m), 602 (w).

MS (EI, 70 ev), *m/z* (%): 314 (100) [M^+], 286 (4), 208 (18), 187 (31), 171(10), 159 (24), 144 (22), 121 (43), 108 (23), 77 (11).

HRMS (EI): calcd. For $C_{13}H_{15}IO$ [M^+]: 314.0168, found 314.0150.

1-{4-[(1*R*)-2-Iodocyclohex-2-en-1-yl]phenyl}ethanone (5i):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 4-iodo-acetobenzene (295 mg, 1.2 mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-cyclohex-2-enyl ester (266 mg, 1.0 mmol). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 10 : 1) yielded 218 mg (67 % yield) of **5i** as a colorless oil.

HPLC (column C, heptane : *i*PrOH = 99 : 1, 0.4 ml/min): t_R/min = 47.19 (minor), 51.78 (major); 89 % *ee*.

$[\alpha]_D^{20}$ +24.7 (c 1.43, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.87 (d, *J* = 8.4 Hz, 2H), 7.23 (d, *J* = 8.4 Hz, 2H), 6.63 (m, 1H), 3.69 (m, 1H), 2.53 (s, 3H), 2.12 - 1.57 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =198.1, 150.1, 141.3, 136.1, 129.0, 100.0, 53.0, 33.9, 29.7, 27.0, 18.1.

IR (film): 2935 (s), 1681 (vs), 1605 (s), 1412 (m), 1357 (s), 1268 (s), 938 (m), 830 (m), 589 (m), 553 (w).

MS (EI, 70 ev), *m/z* (%): 326 (100) [M^+], 311 (48), 206 (13), 199 (18), 154 (20), 128 (20), 115 (14), 77 (7).

HRMS (EI): calcd. For $C_{14}H_{15}IO$ [M^+]: 326.0168, found 326.0162.

1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-3-methoxybenzene (5j):

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), 3-iodoanisole (281 mg, 1.2 mmol, 1.2 equiv), and acetic acid (*R*)-2-iodo-cyclohex-2-enyl ester (266 mg, 1.0 mmol). Standard workup and purification by column chromatography (SiO_2, *n*-pentane/diethyl ether = 100 : 1) yielded 270 mg (86 % yield) of **5j** as a colorless oil.

HPLC (column A, heptane : *i*PrOH = 99 : 1, 0.2 ml/min): t_R/min = 31.52 (minor), 38.05 (major); 92 % *ee*.

$[\alpha]_D^{20}$ + 27.6 (c 1.27, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.28 (t, *J* = 8.4 Hz, 1H), 6.84-6.78 (m, 3H), 6.68 (m, 1H), 3.84 (s, 3H), 3.70 (m, 1H), 2.17-1.63 (m, 6H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ = 160.0, 146.2, 140.7, 129.7, 121.2, 114.8, 112.0, 101.4, 55.6, 53.0, 34.0, 29.1, 18.2.

IR (film): 2935 (vs), 2832 (w), 1660 (vs), 1583 (vs), 1464 (vs), 1485 (s), 1435 (s), 1347 (m), 1252 (vs), 1154 (s), 1052 (s), 985 (m), 779 (m), 700 (s), 568 (w).

MS (EI, 70 ev), *m/z* (%): 314 (100) [M^+], 187 (46), 172 (9), 159 (14), 144 (12), 121 (37), 115 (30), 79 (15).

HRMS (EI): calcd. For $C_{13}H_{15}IO$ [M^+]: 314.0168, found 314.0157.

Ethyl 4-(1-d-2-iodo-2-cyclohexen-1-yl)benzoate (5k)

The reaction was carried out according to typical procedure A with $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv), ethyl 4-iodobenzoate (331 mg, 1.2 mmol, 1.2 equiv) and 1-d-2-iodo-2-cyclohexenyl acetate (**4c**) (267 mg, 1.0 mmol, 1.0 equiv) in THF (1.5 mL). Standard workup and purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 100 : 1) yielded 189 mg (53 % yield) of **5k** as a colorless oil.

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.97-7.96 (m, 2H), 7.23-7.17 (m, 2H), 6.65-6.60 (m, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 2.18-2.04 (m, 3H), 1.76-1.64 (m, 1H), 1.62-1.50 (m, 2H), 1.31 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 149.7, 141.2, 130.1, 129.4, 128.7, 100.2, 61.2, 52.6, 33.9, 29.7, 18.1, 14.8.

IR (film): 2935 (m), 1716 (s), 1610 (m), 1276 (s), 1178 (m), 1104 (s), 1022 (m), 771 (m), 707 (m).

MS (EI, 70 ev), *m/z* (%): 357 [M^+], (100), 312 (37), 230 (23), 207 (31), 156 (28), 142 (15), 129 (48), 116 (14).

HRMS (EI): calcd.for $C_{15}H_{16}DIO_2$: 357.0335, found: 357.0334.

4-(2-Hex-1-ynylcyclohex-2-enyl)-benzoic acid ethyl ester (6a):

A flame-dried 25 mL flask equipped with a magnetic stirring bar, an argon inlet, and a septum was charged with $PdCl_2(PPh_3)_2$ (35 mg, 0.05 mmol), CuI (10 mg, 0.05 mmol) and dry THF (2 mL). A solution of ethyl 4 –[(1*R*)-(2-iodocyclohex-2-en-1-yl)] benzoate (**5c**) (335 mg, 1.0 mmol, 95% ee) in THF (2 mL) was added dropwise. The reaction mixture was stirred at 25 ^oC for 5 min, then dry Et_3N (304 mg, 3.0 mmol) and 1-hexyne (90 mg, 1.1 mmol) were added consecutively. The resulting yellow solution was stirred at 25 ^oC for 25 h. The reaction mixture was quenched with saturated aqueous NH_4Cl sol. (20 mL) and extracted with Et_2O (3 x 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (SiO_2, pentane/diethyl ether = 80 : 1) afforded 205 mg (70 % yield) of **6a** as a colorless oil.

$[\alpha]_D^{20}$ + 1.43° (c 0.70, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.92-7.86 (m, 2H), 7.24-7.18 (m, 2H), 6.22-6.17 (m, 1H), 4.30 (q, *J* = 7.1 Hz, 2H), 3.46-3.40 (m, 1H), 2.16-2.08 (m, 2H), 2.04-1.88 (m, 3H), 1.64-1.40 (m, 4H), 1.36-1.24 (m, 2H), 1.22-1.10 (m, 2H), 1.10 - 0.96 (m, 2H), 0.67 (t, *J* = 7.2 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.1, 150.8, 135.7, 129.7, 128.7, 123.2, 89.5, 81.9, 61.1, 45.8, 32.4, 31.1, 28.7, 26.1, 22.0, 19.5, 19.2, 14.7, 13.9.

IR (film): 2933 (m), 1719 (s), 1610 (m), 1275 (s), 1178 (m), 1102 (s), 1022 (m).

MS (EI, 70 ev), *m/z* (%): 310 [M^+], 100), 295 (7), 281 (23), 265 (44), 253 (19), 237 (42), 225 (12) 209 (12), 195 (43), 181 (51), 165 (72), 152 (33), 134 (28), 119 (29), 115 (29), 103 (35), 91 (41), 77 (17).

HRMS (EI): calcd. for $C_{21}H_{26}O_2$: 310.1933, found: 310.1946.

Ethyl 4-[2-(4-(benzoyloxy)phenyl)-2-cyclohexen-1-yl]benzoate (6b):

A flame-dried 25 mL flask equipped with a magnetic stirring bar, an argon inlet, and a septum was charged with benzoic acid 4-iodo phenyl ester (243 mg, 0.75 mmol) and dry THF (1 mL), and cooled to –20 ^oC. To the resulting solution, *i*-PrMgCl (1.45 M/THF, 0.8 mL) was added dropwise. The resulting mixture was stirred at –20 ^oC for 30 min. The solution of $ZnBr_2$ (1.5 M/THF, 1.5 mL) was added dropwise, and the reaction mixture was stirred at –20 ^oC for 15 min. Then the reaction mixture was warmed up to 25 ^oC for 30 min. The resulting solution was cannulated to the flame-dried 25 mL flask which was charged with $Pd(dba)_2$ (14 mg, 25 mmol), dppf (14 g, 25 mmol), ethyl 4 –[(1*R*)-(2-iodocyclohex-2-en-1-yl) benzoate (**5c**) (178 mg, 0.5

mmol, 95 % ee) and THF (3 mL). The reaction mixture was stirred at 25 ^{o}C for 16 h, quenched with saturated aqueous NH_4Cl sol. (20 mL) and extracted with Et_2O (3 x 20 mL). The combined extracts were washed with brine and dried (Na_2SO_4). Evaporation of the solvents and purification by column chromatography (SiO_2, pentane/diethyl ether = 10 : 1) afforded 160 mg (75 % yield) of **6b** as a white solid, mp = 128 ^{o}C.

$[\alpha]_D^{20}$ – 95.0° (c 0.60, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 8.10-8.04 (m, 2H), 7.88-7.82 (m, 2H), 7.58-7.50 (m, 1H), 7.44-7.36 (m, 2H), 7.24-7.18 (m, 4H), 6.98-6.92 (m, 2H), 6.38-6.32 (m, 1H), 4.26 (q, *J* = 7.1 Hz, 2H), 4.02 - 3.94 (m, 2H), 2.32-2.20 (m, 2H), 2.12 - 1.98 (m, 1H), 1.82-1.70 (m, 1H), 1.58-1.42 (m, 2H), 1.28 (t, *J* = 7.1 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 167.0, 165.5, 150.9, 149.9, 139.7, 137.0, 133.9, 130.5, 129.9, 129.0, 128.9, 128.7, 127.2, 121.6, 61.1, 43.2, 32.9, 26.4, 17.9, 14.7.

IR (film): 2934 (m), 1731 (s), 1720 (s), 1609 (m), 1506 (m), 1275 (s), 1205 (s), 1173 (s), 1102 (m), 1082 (m), 1065 (m), 1024 (m), 741 (s).

MS (EI, 70 ev), *m/z* (%): 426 (5, M^+), 115 (2), 106 (8), 105 (100), 78 (2), 77 (19), 51 (2).

HRMS (EI): calcd. for $C_{28}H_{26}O_4$: 426.1831, found: 426.1812.

anal. calcd. for $C_{28}H_{26}O_4$ (426.18): C 78.85, H 6.14; found: C 78.59, H 6.25.

Ethyl 4-[(1*S*)-2-butyl-2-cyclohexen-1-yl]benzoate (6c):

To Zn foil (690 mg, 10 mmol) previously activated with 1,2-dibromoethane (79 μL) and TMSCl (49 μL) in THF (1 mL) was added a solution of iodobutane (0.644 g, 3.5 mmol) in THF (1.5 mL). The reaction mixture was heated at 40 ^{o}C for 4 h. GC analysis of hydrolyzed reaction aliquot showed the complete formation of the zinc reagent.

A flame-dried 25 mL flask was charged with $Pd(dba)_2$ (14 mg, 0.025 mmol), dppf (14 mg, 0.025 mmol) and THF (1 mL). Then the solution of ethyl 4 [(1*R*)-(2-iodocyclohex-2-en-1-yl) benzoate (**5c**) (0.178 mg, 0.5 mmol, 95 % ee) in THF (2 mL) was added dropwise followed by addition of freshly prepared butylzinc iodide (1.4 M/THF, 1.5 mL). The reaction mixture was refluxed at 80 ^{o}C for 12 h. The reaction mixture was quenched with saturated aqueous NH_4Cl sol. (20 mL) and extracted with Et_2O (3 x 20 mL). The combined extracts were washed with brine and dried over Na_2SO_4. Evaporation of the solvents and purification by column chromatography (SiO_2, pentane/diethyl ether = 100 : 2) afforded 99 mg (69 % yield) of **6c** as a colorless oil.

$[\alpha]_D^{20}$ – 74.08° (c 1.25, CH_2Cl_2).

^{1}H-NMR ($CDCl_3$, 300 MHz): δ = 7.92-7.86 (m, 2H), 7.20-7.14 (m, 2H), 5.66-5.62 (m, 1H), 4.29 (q, *J* = 6.9 Hz, 2H), 3.36-3.28 (m, 1H), 2.08 - 1.96 (m, 2H), 1.94 - 1.82 (m, 1H), 1.80-1.00 (m, 12H), 0.74 (t, *J* = 6.9 Hz, 3H).

^{13}C-NMR ($CDCl_3$, 75 MHz): δ = 165.7, 150.2, 137.0, 128.4, 127.5, 127.2, 123.0, 59.7, 43.1, 34.6, 31.7, 28.9, 24.4, 21.4, 17.8, 13.4, 13.0.

IR (film): 2930 (m), 1720 (s), 1609 (m), 1276 (s), 1177 (m), 1102 (s), 1023 (m).

MS (EI, 70 ev), *m/z* (%): 286 [M^+], (100), 241 (34), 229 (91), 216 (24), 215 (24), 201 (12), 171 (39), 157 (31), 141 (32), 129 (60), 115 (28), 91 (24), 77 (14).

HRMS (EI): calcd. for $C_{19}H_{26}O_2$: 286.1933, found: 286.1915.

Ethyl 4-[(1*R*,2*E*)-1-methylhept-2-en-1-yl]benzoate (8):

A dry and argon flushed 15 mL flask, equipped with a magnetic stirrer and a septum, was charged with a solution of $Nphyl_2CuLi$ (1.2 mmol, 1.2 equiv). Ethyl 4-iodobenzoate (331 mg, 1.2 mmol, 1.2 equiv) was added at –78 °C. The resulting mixture was immediately warmed to 0 ^{o}C and kept stirring for 30 min. Then the reaction was cooled to –78 ^{o}C and the solution of $ZnBr_2$ in THF (1.5 M, 0.8 mL, 1.2 mmol) was added at this temperature. After 10 min, the solution of **7** (320 mg, 1.0 mmol) in THF (1.5 mL) was added at –40 ^{o}C. The mixture was allowed to warm to rt overnight. The reaction mixture was quenched with saturated aqueous NH_4Cl solution and poured into water (25 mL). The aqueous phase was extracted with diethyl ether (3 × 30 mL). The organic fractions were washed with brine, dried ($MgSO_4$) and concentrated *in vacuo*. Purification by flash chromatography (SiO_2, *n*-pentane/diethyl ether = 80:1) yielded 220 mg (85% yield) of **8** as a colorless oil

HPLC (column B, heptane : *i*PrOH = 99 : 1, 0.2 ml/min): t_R/min = 21.87 (major), 23.86 (minor); 95% *ee*.

$[\alpha]_D^{20}$ –35.4 (c 1.01, CH_2Cl_2)

^{1}H-NMR ($CDCl_3$, 300 MH_Z): δ = 7.85 (d, *J* = 8.4 Hz, 2H), 7.19 (d, *J* = 8.4 Hz, 2H), 5.48-5.41 (m, 2H), 4.29 (q, *J* = 7.07 Hz, 2H), 3.40 (m, 1H), 1.94 (m, 2H), 1.33-1.22 (m 10H), 0.80 (t, *J* = 7.07, 3H).

^{13}C-NMR ($CDCl_3$, 75 MH_Z): δ =167.1, 152.3, 134.4, 130.5, 130.1, 128.6, 127.5, 61.1, 42.7, 32.6, 32.0, 22.6, 21.7, 14.7, 14.1.

IR (film): 3409 (s), 2959 (s), 2932 (s), 1718 (vs), 1608 (w), 1465 (w), 1408 (w), 1367 (m), 1276 (vs), 1181 (m), 1107 (vs), 1019 (m), 856 (w), 771 (m), 707 (w).

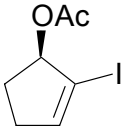
MS (EI, 70 ev), *m/z* (%): 260 (66) [M^+], 245 (9), 231 (12), 215 (50), 190 (91), 175 (20), 162 (41), 145 (66), 131 (100), 117 (41), 105 (12), 91 (15), 77 (7).

HRMS (EI): calcd. For $C_{17}H_{24}O_2$ [M^+]: 260.1776, found 260.1763.

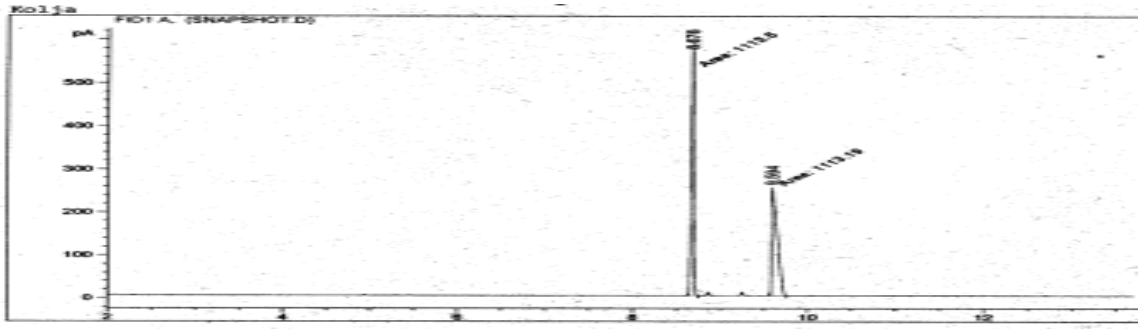
Appendix:

Determination of the enantiomer excess by chiral GC and chiral HPLC

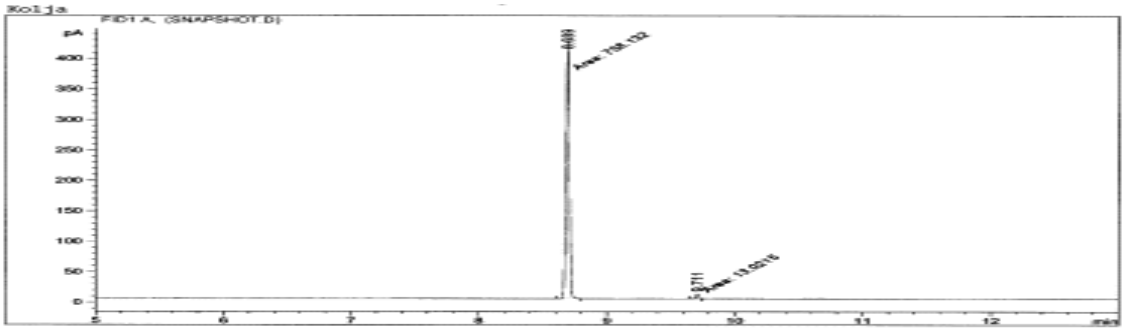
(*R*)-2-Iodo-2-cyclopenten-1-yl acetate(4a)
GC (40 °C (2 min), ramp of 20 °C/min to 150 °C (45 min); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 8.7 (*R*), 9.6 (*S*); 96.5 % *ee*.



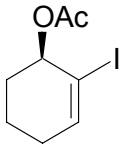
a) racemic



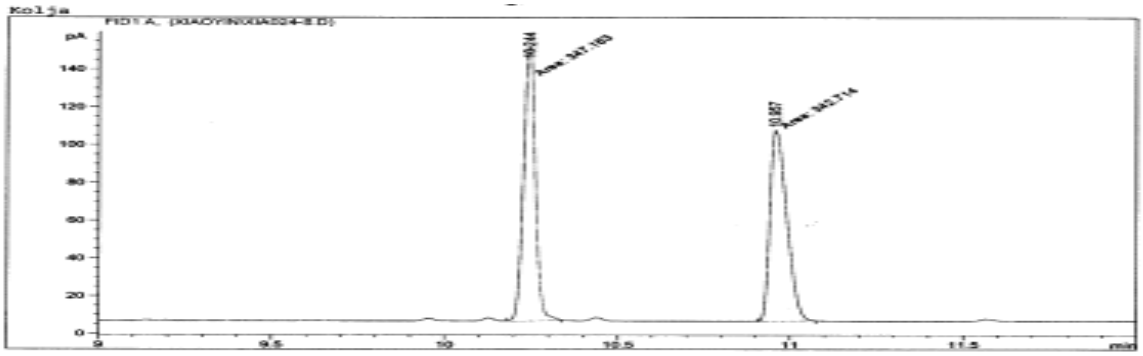
b)chiral



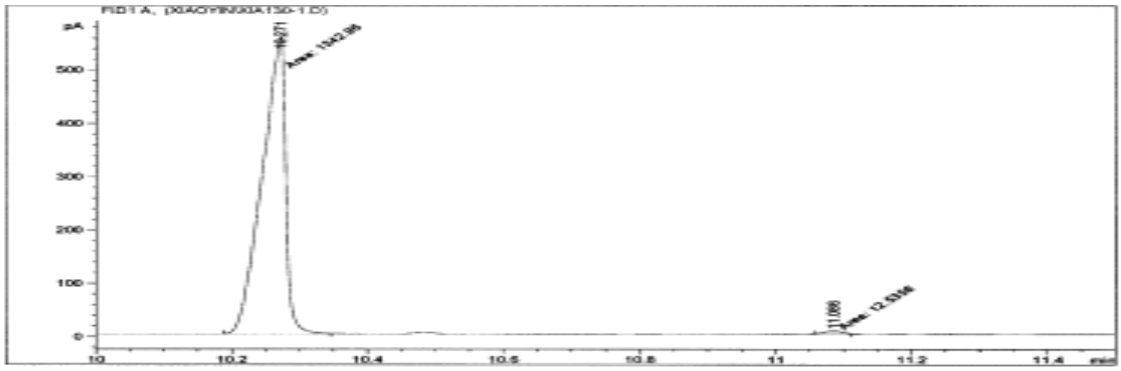
(*R*)-2-Iodo-2-cyclohexen-1-yl ethyl acetate (4b)
GC (40 °C (2 min), ramp of 20 °C/min to 150 °C (45 min); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 8.7 (*R*), 9.6 (*S*); 98 % *ee*.



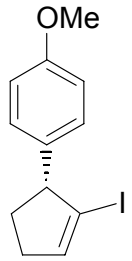
a): racemic



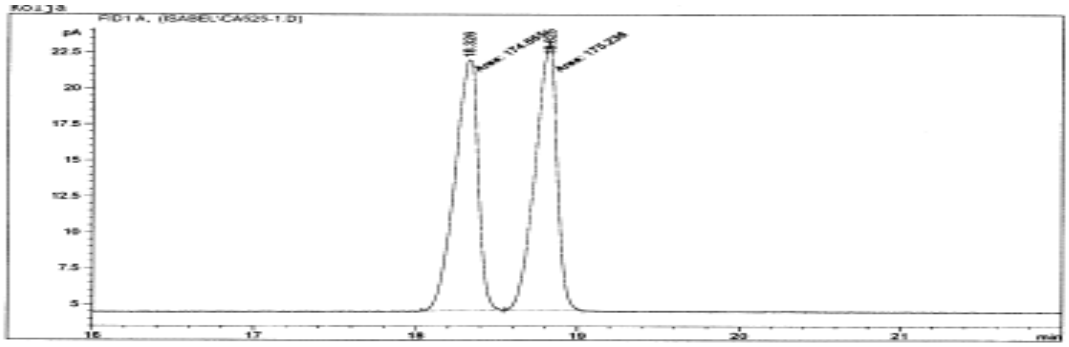
b)chiral



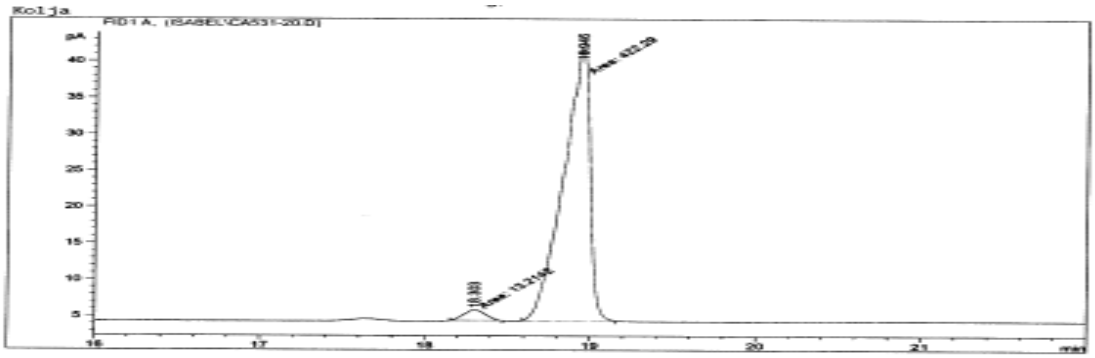
4-[(1*R*)-(2-Iodo-2-cyclopenten-1-yl)] phenyl methyl ether (5a)
GC (150 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 18.3 (*R*), 18.9 (*S*); 96 % *ee*.



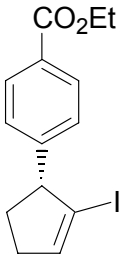
a) racemic



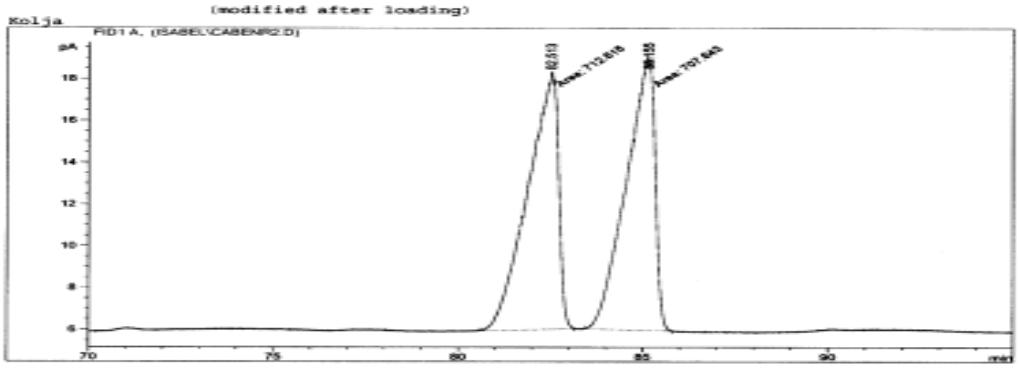
b) chiral



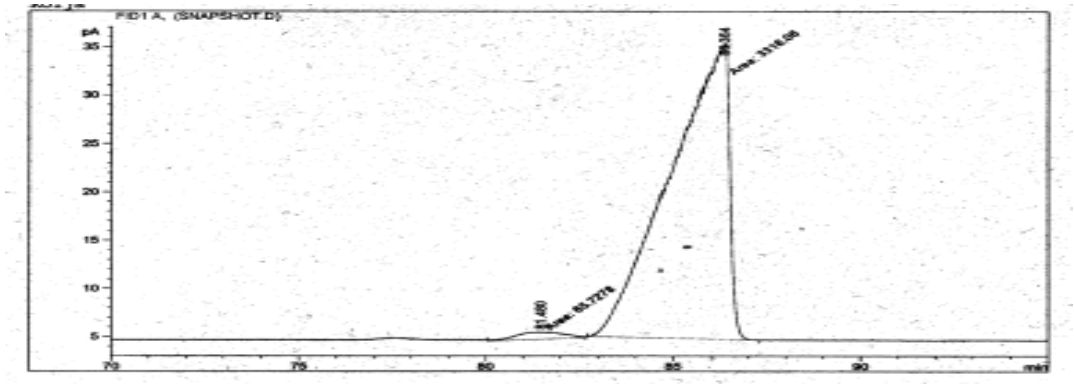
Ethyl 4-[(1*R*)-(2-iodo-2-cyclopenten-1-yl)] benzoate (5b):
GC (150 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 81.5 (*R*), 85.2 (*S*); 92 % *ee*.



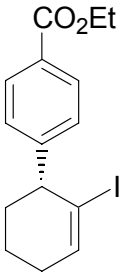
a) racemic



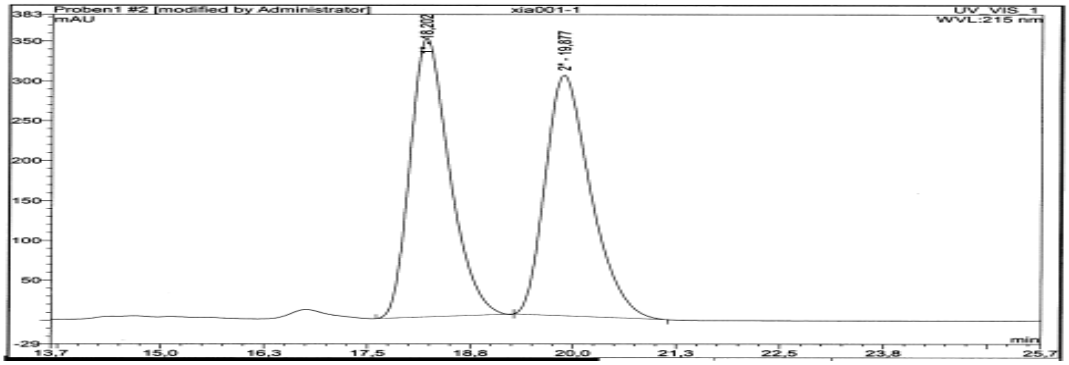
b) chiral



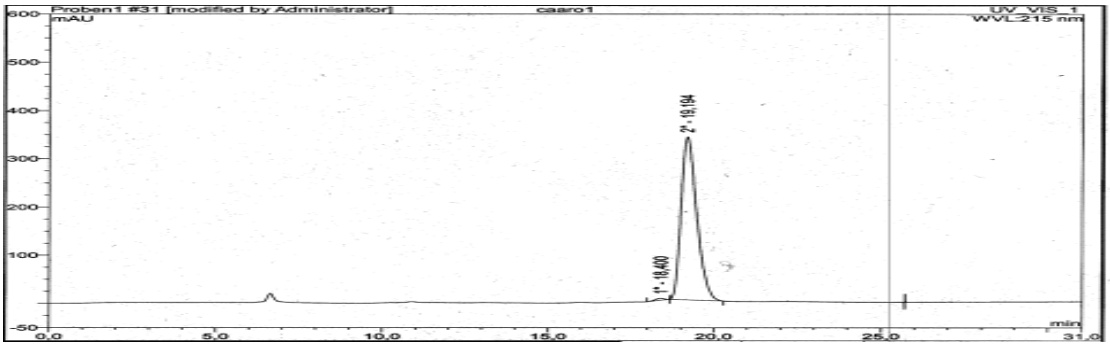
Ethyl 4-[(1*R*)-2-iodocyclohex-2-en-1-yl]beozoate (5c):
HPLC (Chiralcel AD, 0.46 cm x 25 cm; heptane : *i*PrOH = 99:1, 0.5 ml/min): t_R/min = 18.3 (*S*), 19.8 (*R*); 98 % *ee*.



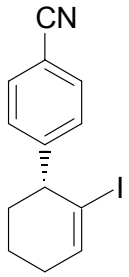
a): racemic



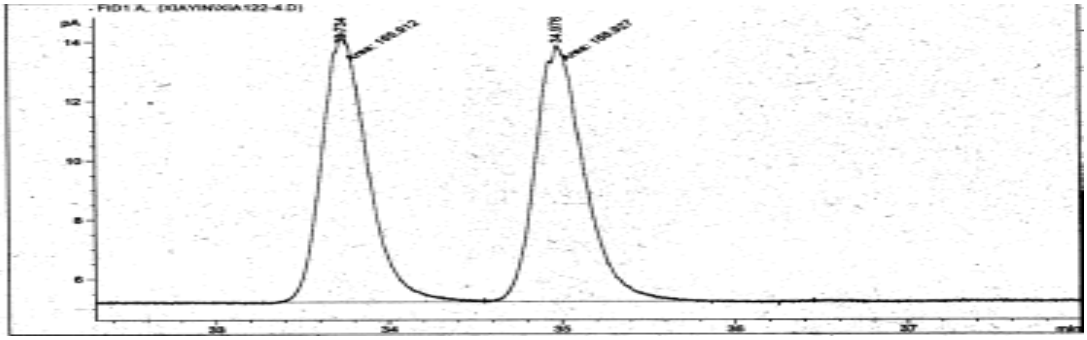
b) chiral



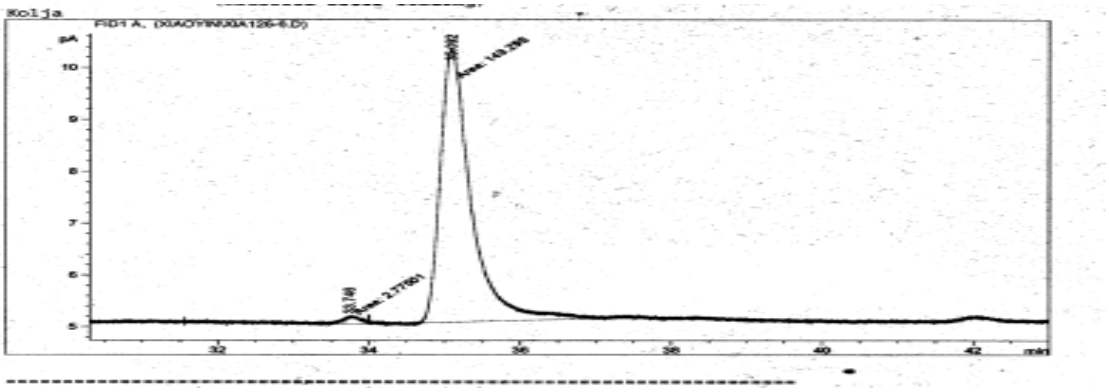
4-[(1*R*)-2-Iodocyclohex-2-en-1-yl]benzonitrile (5d):
GC (130 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 33.7 (*R*), 34.9 (*R*); 96% *ee*.



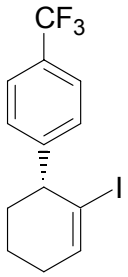
a) racemic



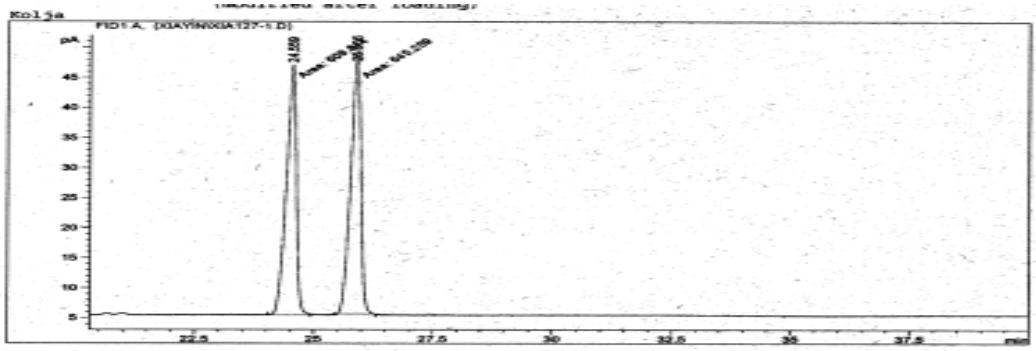
b) chiral



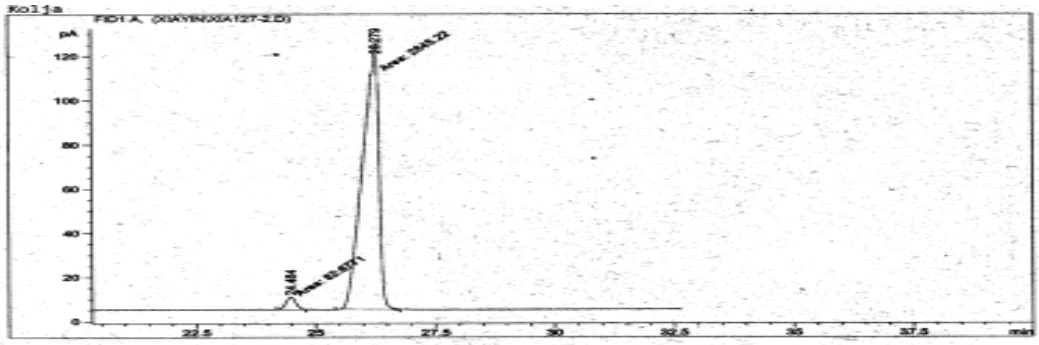
1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-4-(trifluoromethyl)benzene (5e):
GC (130 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 24.6 (*S*), 26.0 (*R*); 94 % *ee*.



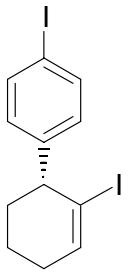
a) racemic



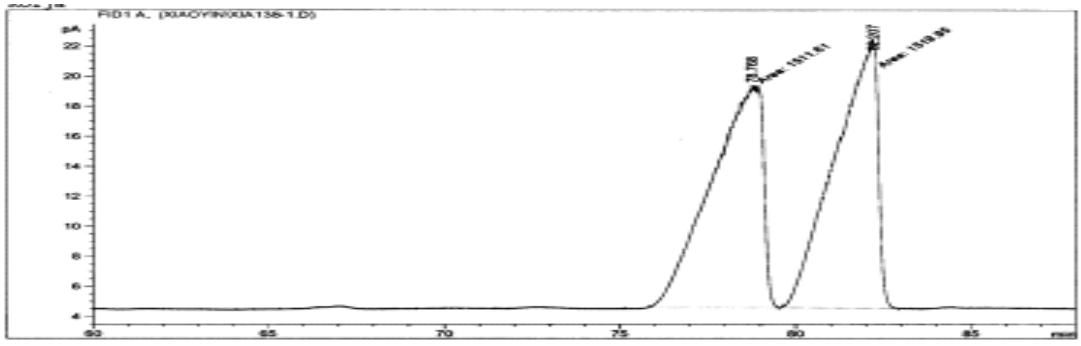
b) chiral



1-Iodo-4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzene (5f):
GC (150 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): *tR*/min 78.7 (*R*), 82.2 (*S*); 97 % *ee*.



a) racemic



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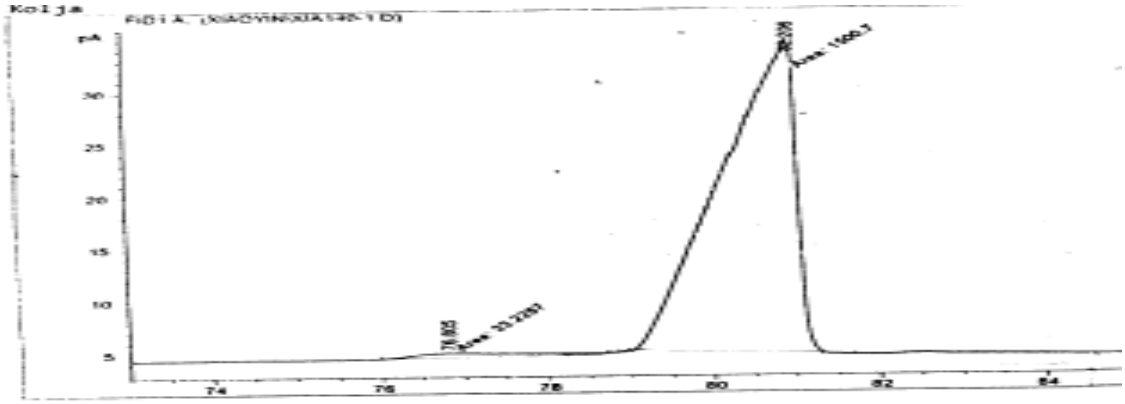
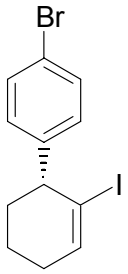
b) chiral



1-Bromo-4-[(1*R*)-2-iodocyclohex-2-en-1-yl]benzene (5g):
GC (130 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 123.7 (*S*), 133.6 (*R*); 96 % *ee*.



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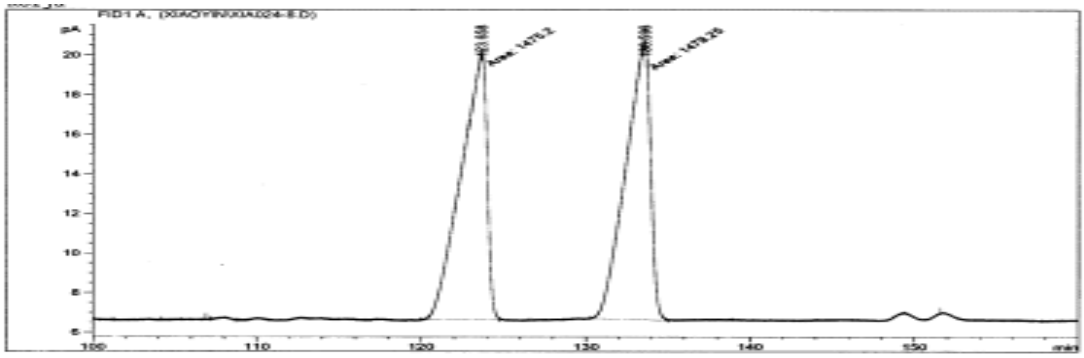

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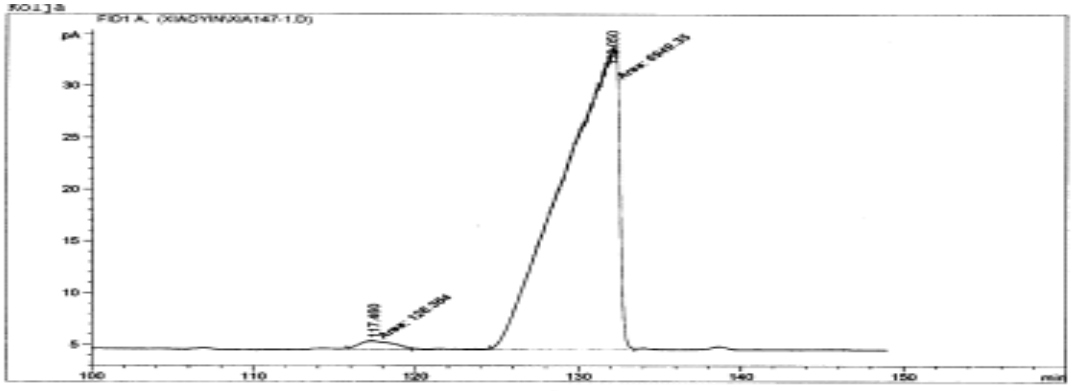
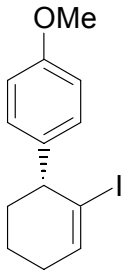


1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-4-methoxybenzene (5h):
GC (130 °C (100 min)); TFA gamma-cyclodextrin, 30.0 m x 0.25 mm): t_R/min 83.3 (*S*), 87.8 (*R*); 95 % *ee*.



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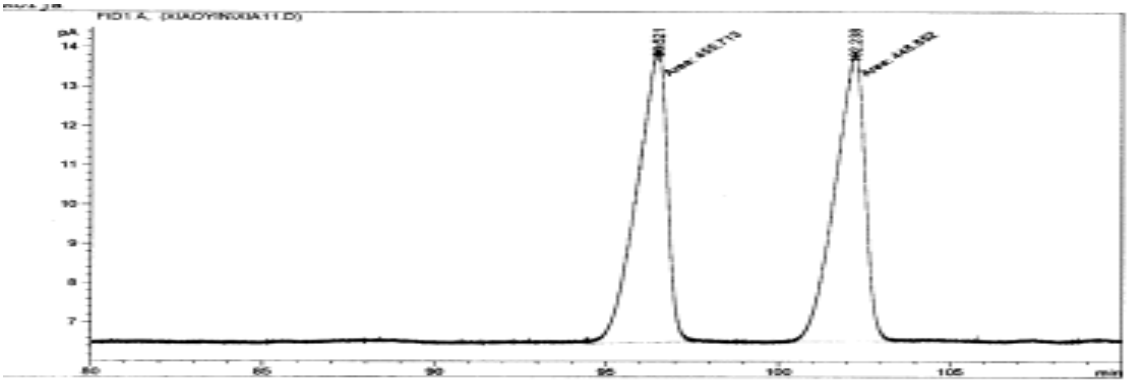

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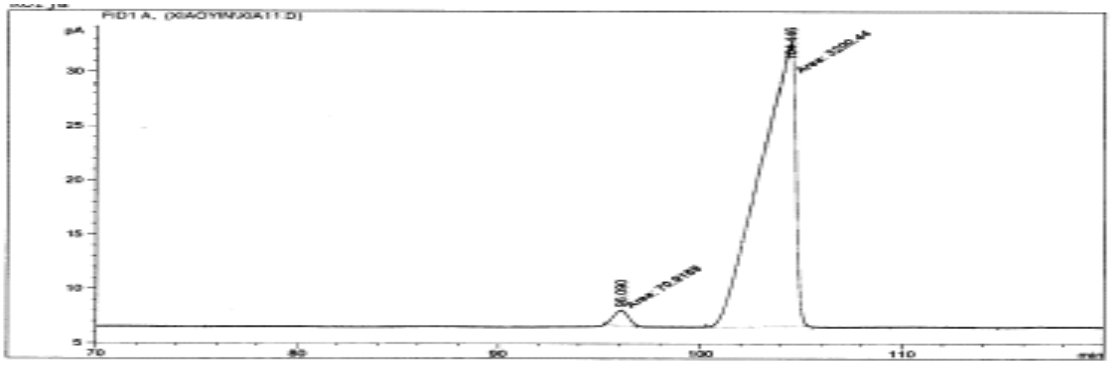
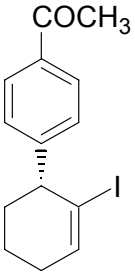


1-{4-[(1*R*)-2-Iodocyclohex-2-en-1-yl]phenyl}ethanone (5i):
HPLC (Chiralcel AD, 0.46 cm x 25 cm; heptane : *i*PrOH = 99:1, 0.4 ml/min): t_R/min = 37.4 (*S*), 43.3 (*R*); 89 % *ee*.



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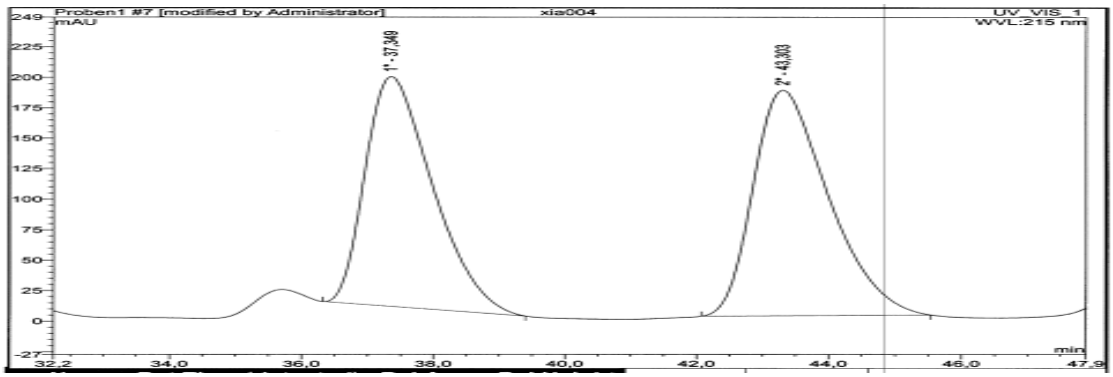

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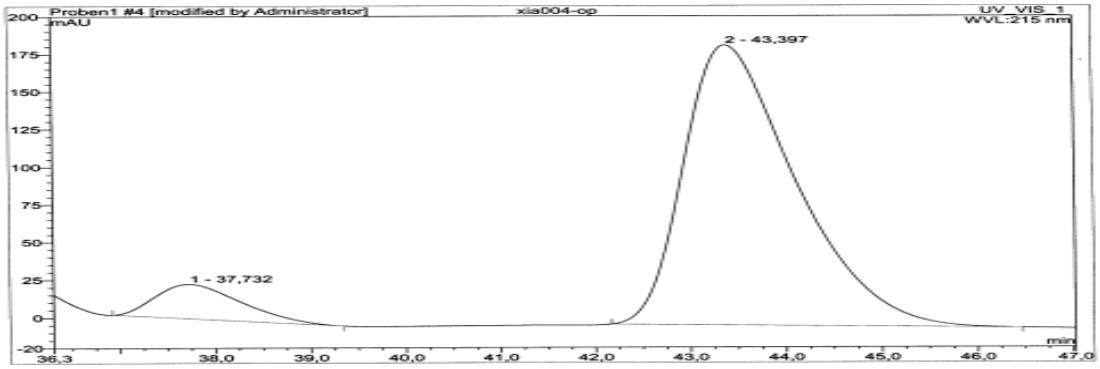
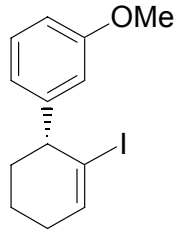


1-[(1*R*)-2-Iodocyclohex-2-en-1-yl]-3-methoxybenzene (5j):
HPLC (Chiralcel OD-H, 0.46 cm x 25 cm; heptane : *i*PrOH = 99:1, 0.2 ml/min): t_R/min = 31.5 (*S*), 38.1 (*R*); 92 % *ee*.



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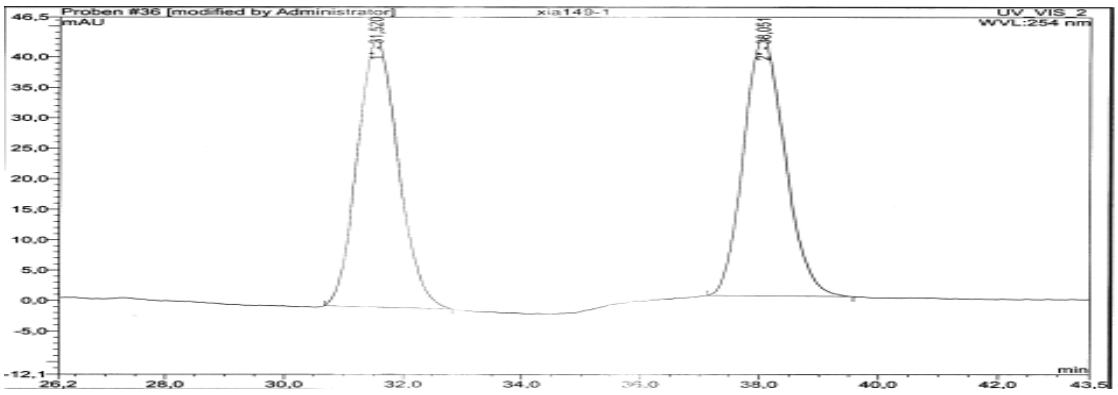

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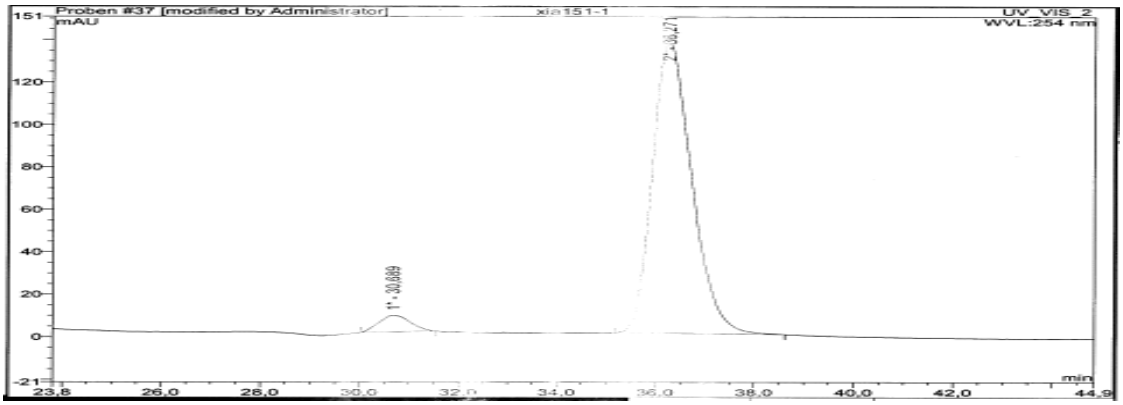
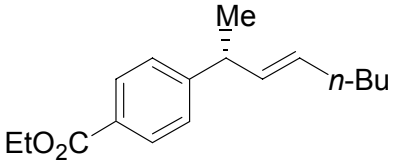


Ethyl 4-[(1*R*,2*E*)-1-methylhept-2-en-1-yl]benzoate (8):
HPLC (OD, 0.46 cm x 25 cm; heptane : *i*PrOH = 99:1, 0.2 ml/min): t_R/min = 21.8 (*R*), 23.8 (*S*); 95 % *ee*.



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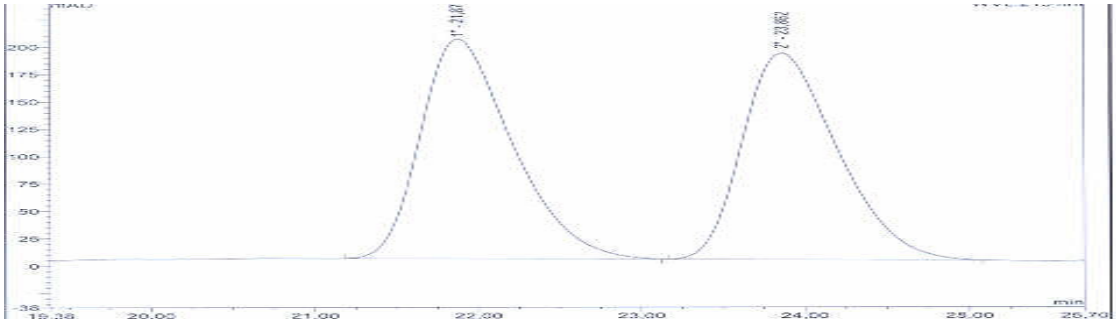

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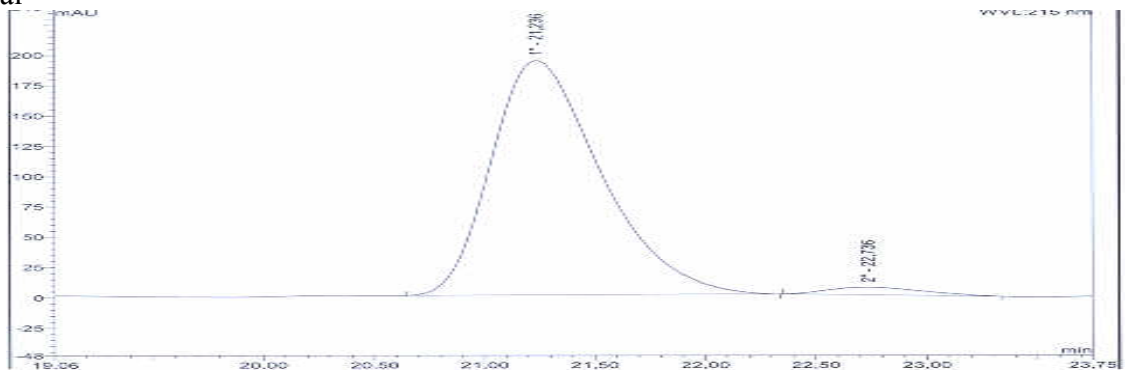

Reference:
[1] Demay, S.; Harms, K.; Knochel, P. *Tetrahedron Lett.* **1999**, *40*, 4981.
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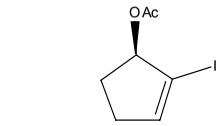
[4] (a) Cano, A.; Cuenca, T.; Galakov, M.; Rodríguez, G. M.; Royo, P.; Cardin, C. J.; Convery, M. A. *J. Organomet. Chem.* **1995**, *493*, 17. (b) Negishi, E.; Swanson, D. R.; Rousset, C. J. *J. Org. Chem*. **1990**, *55*, 5406.
[5] Zhdanov, R. I.; Zhenodarova, S. M. *synthesis*, **1975**, 222.



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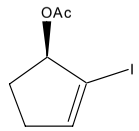

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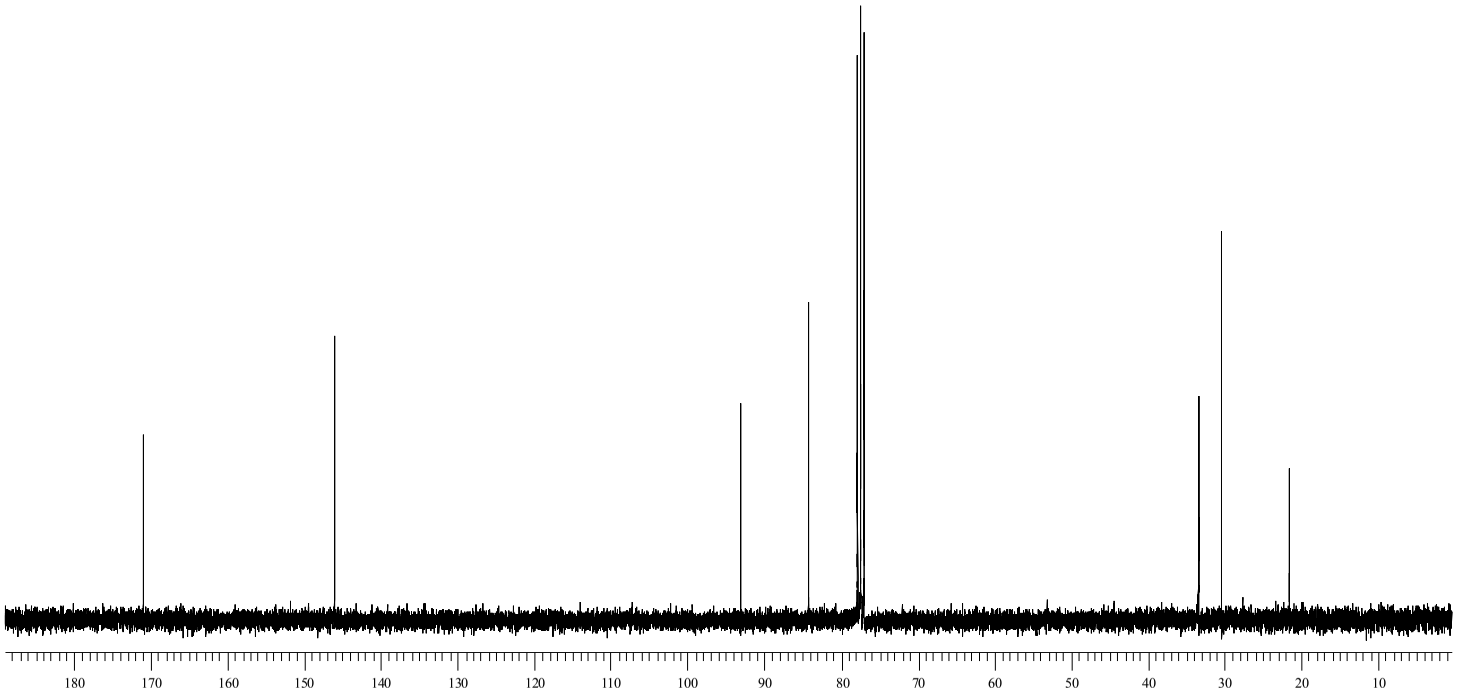

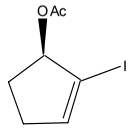

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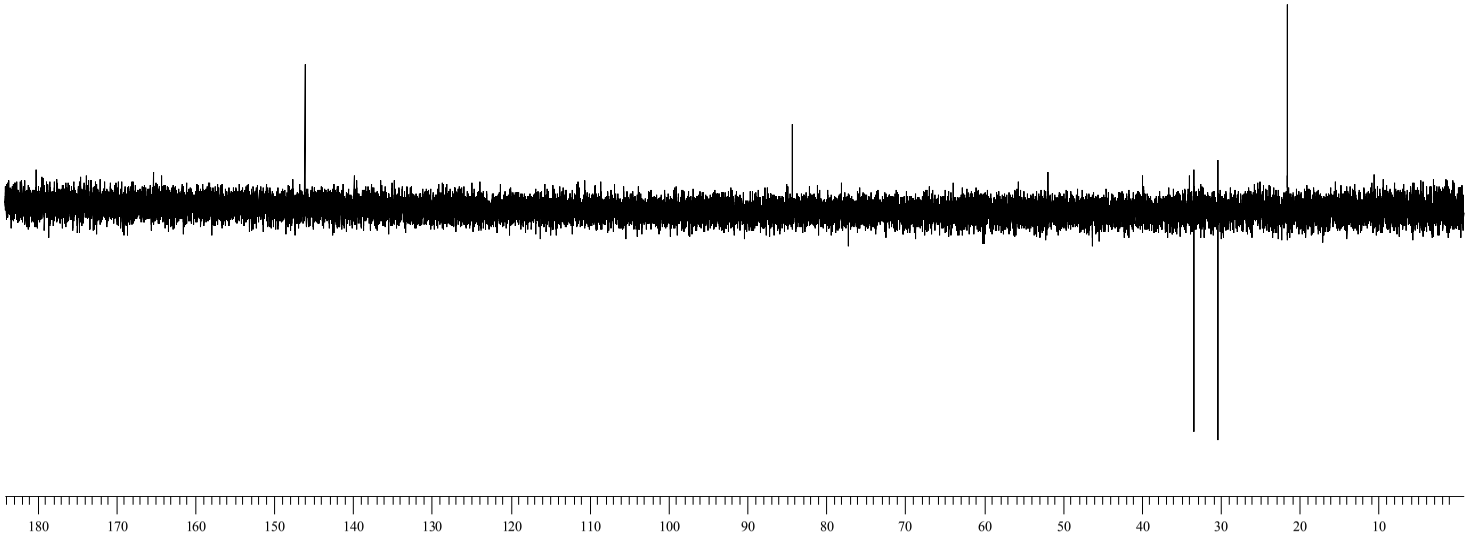

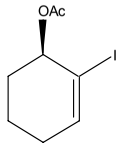

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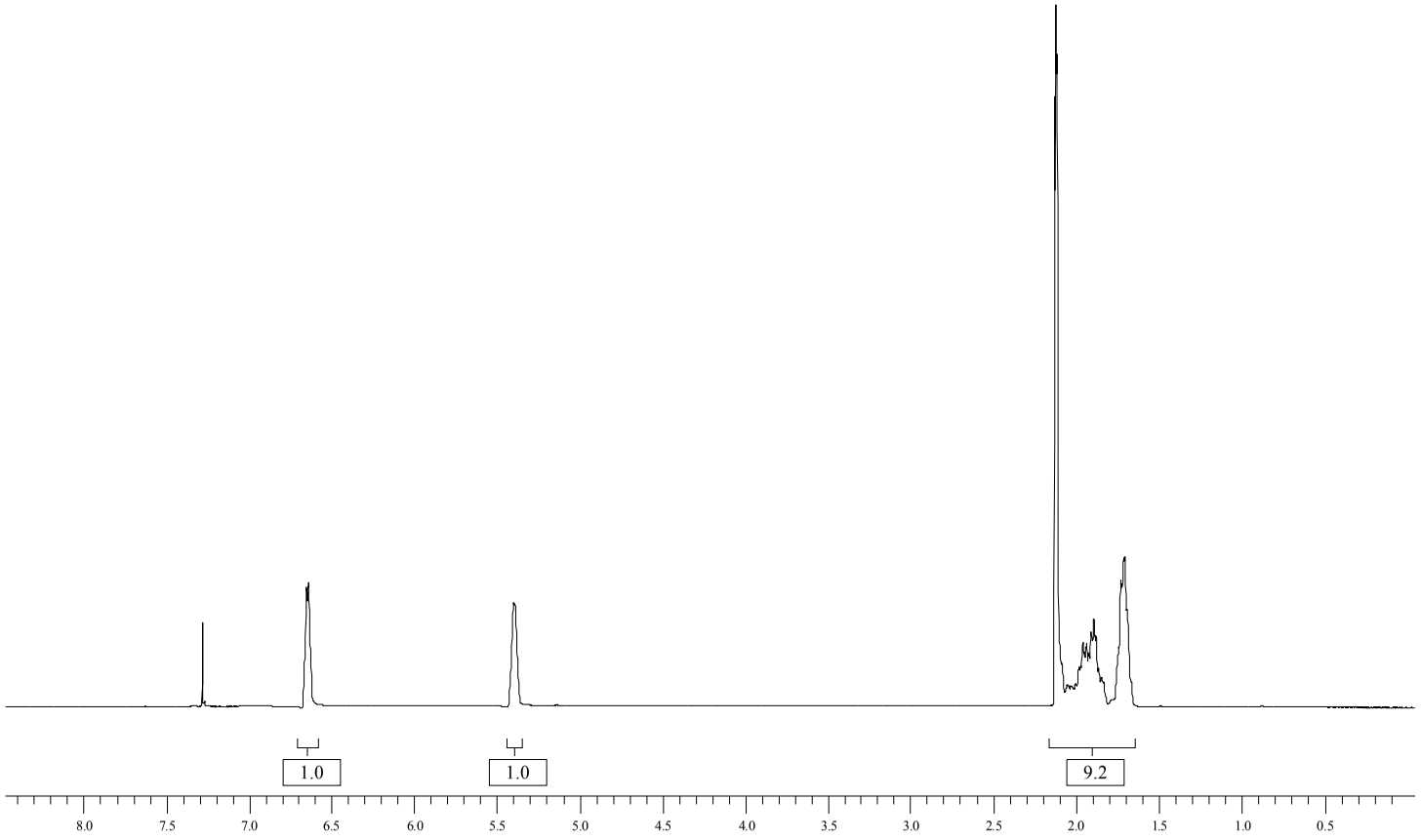

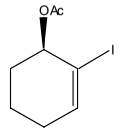
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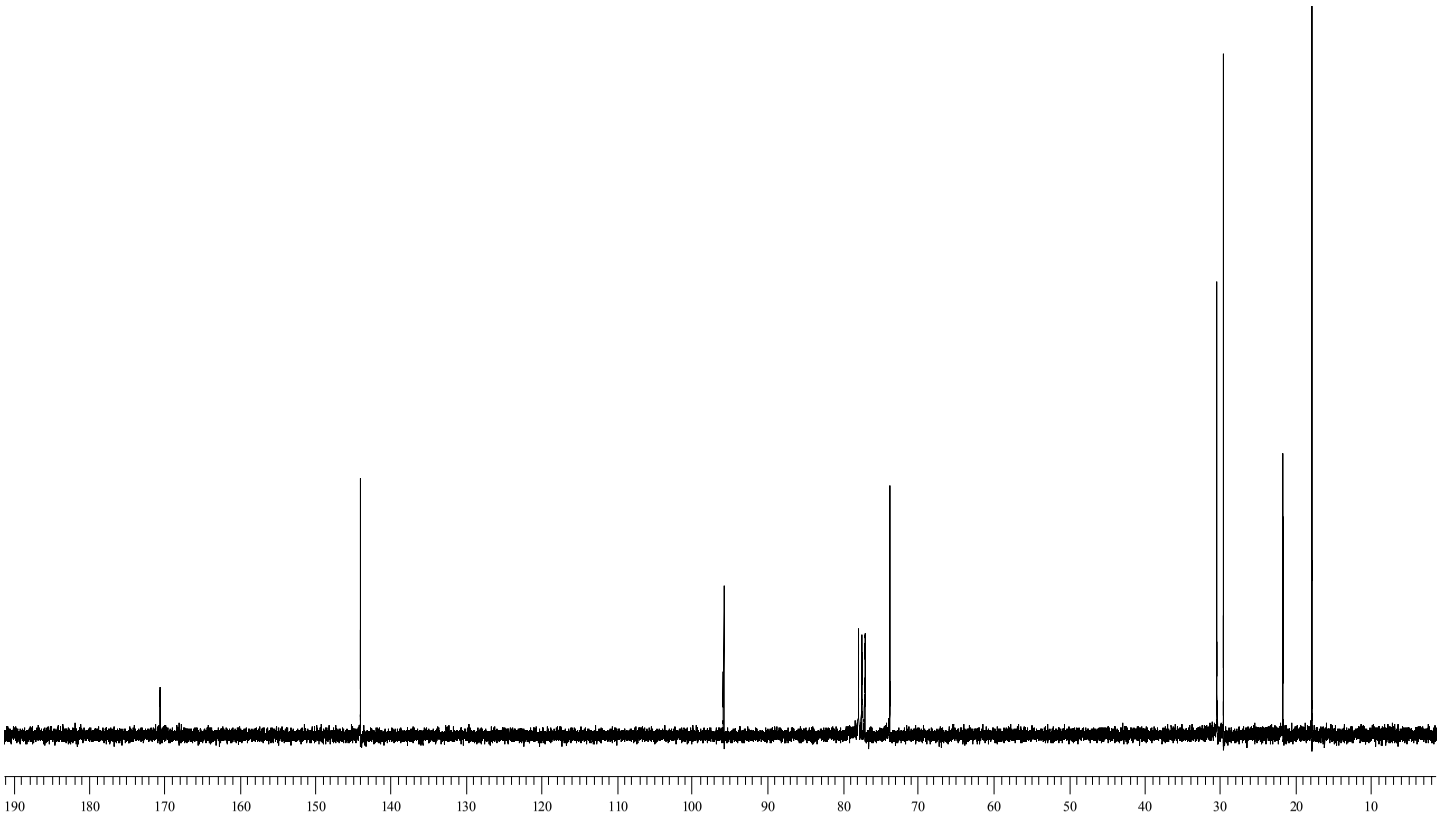
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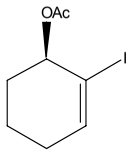

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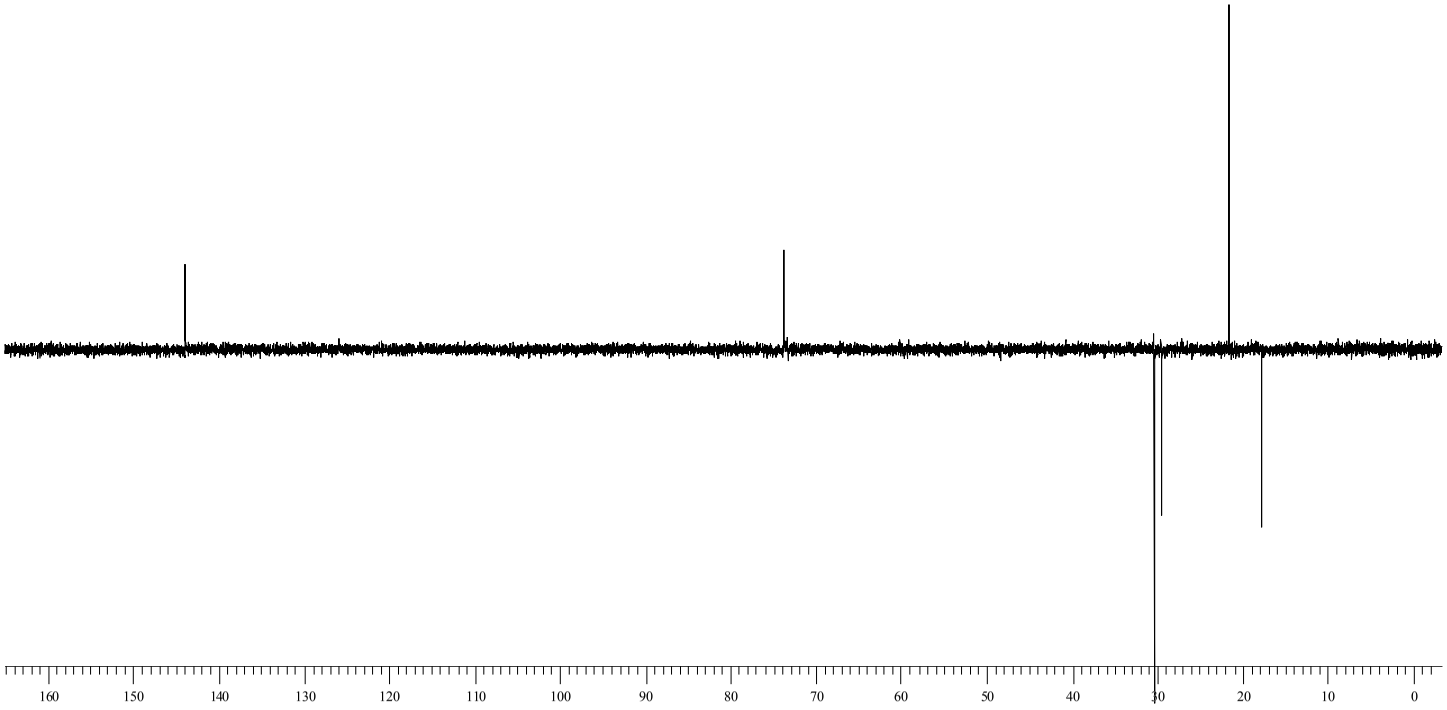

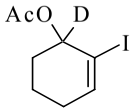

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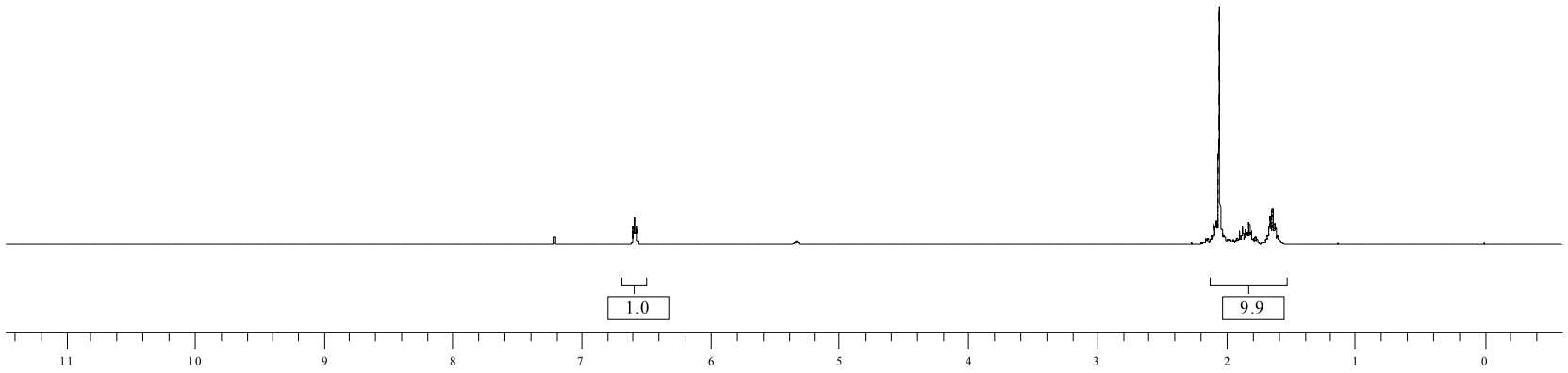

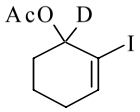

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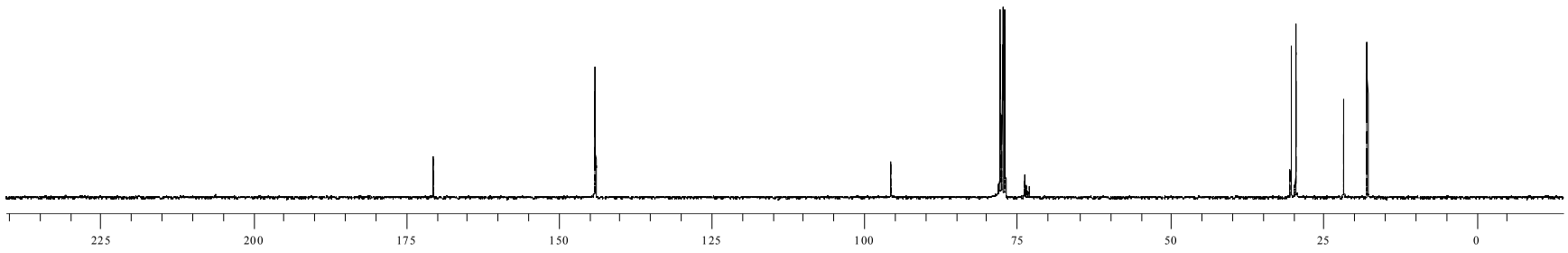

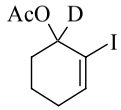

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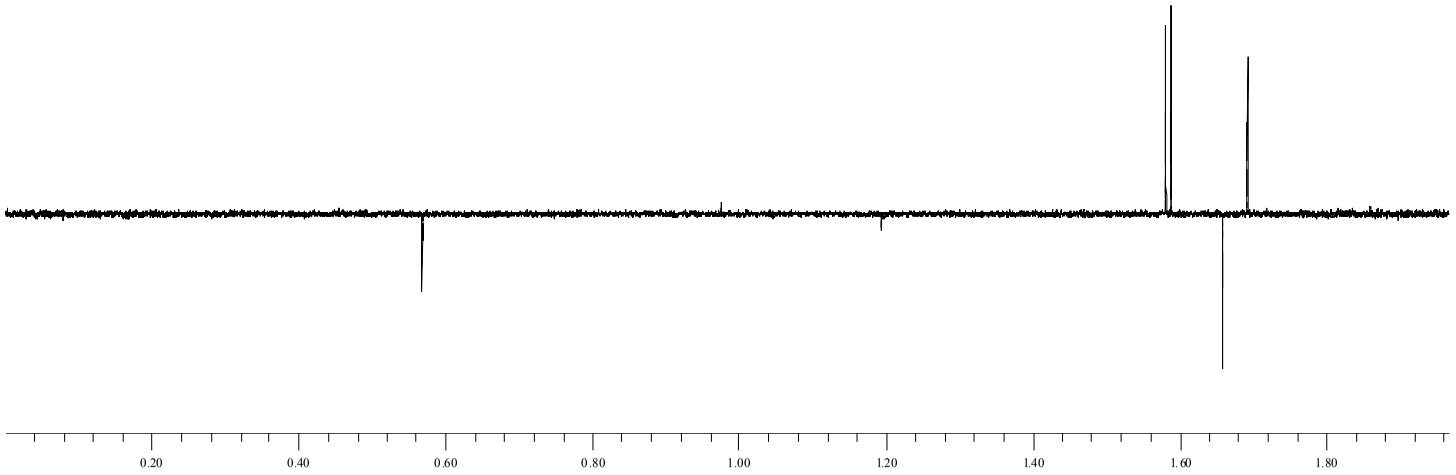

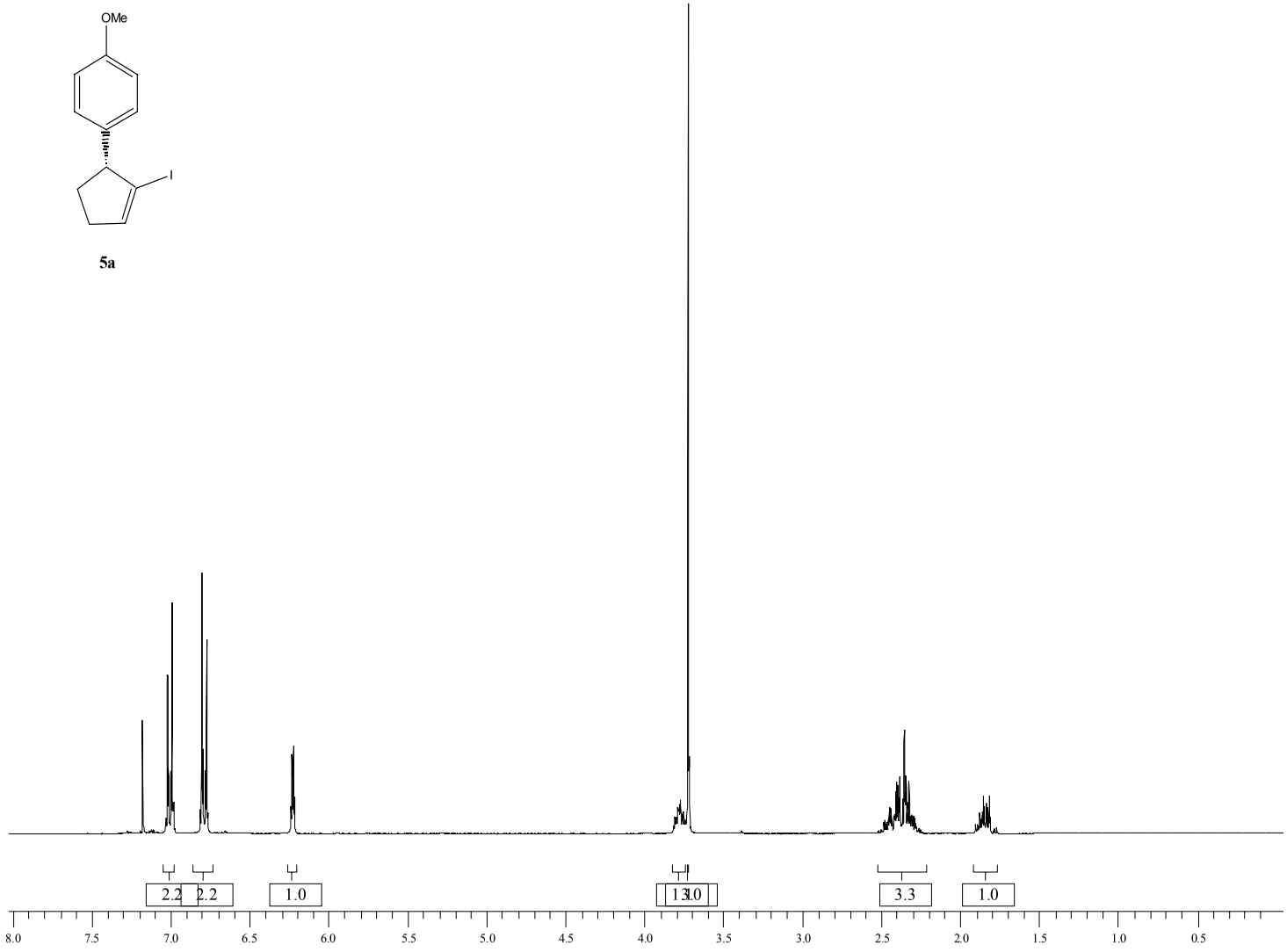
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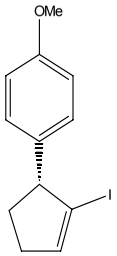

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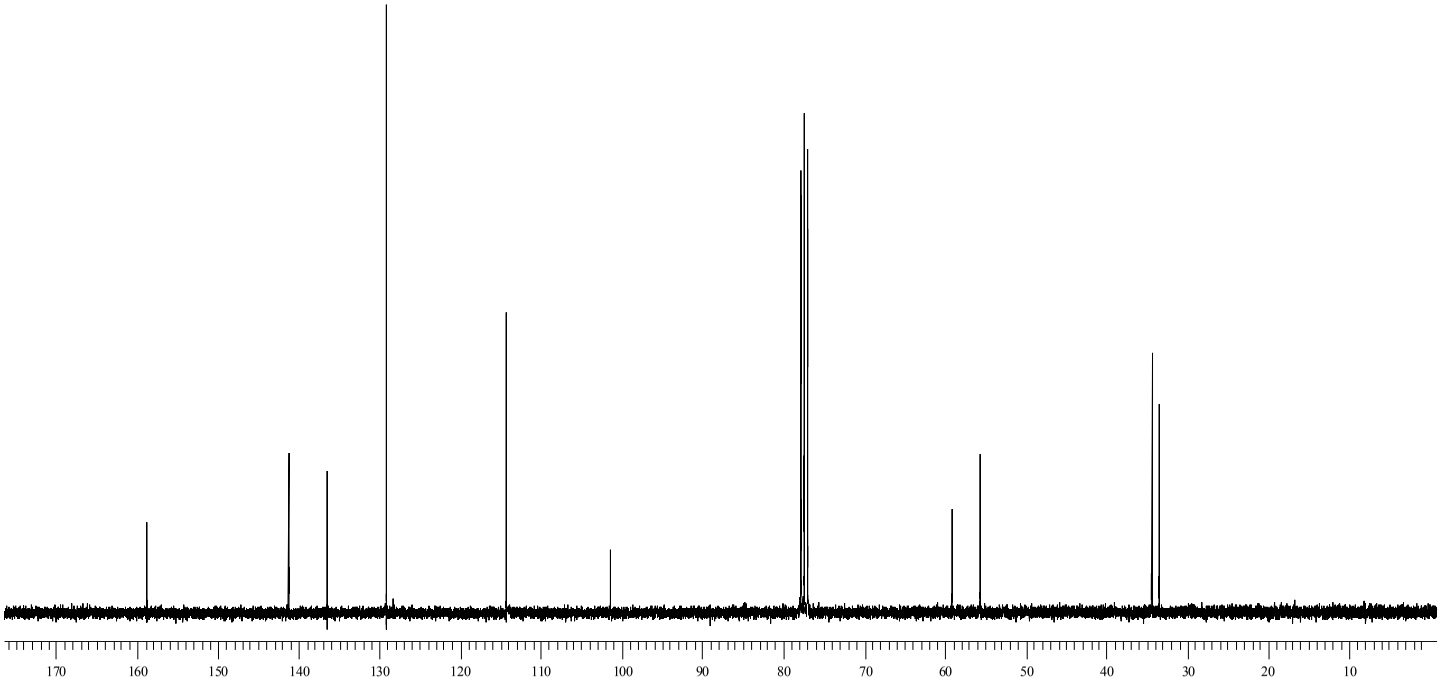

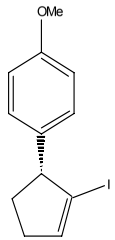

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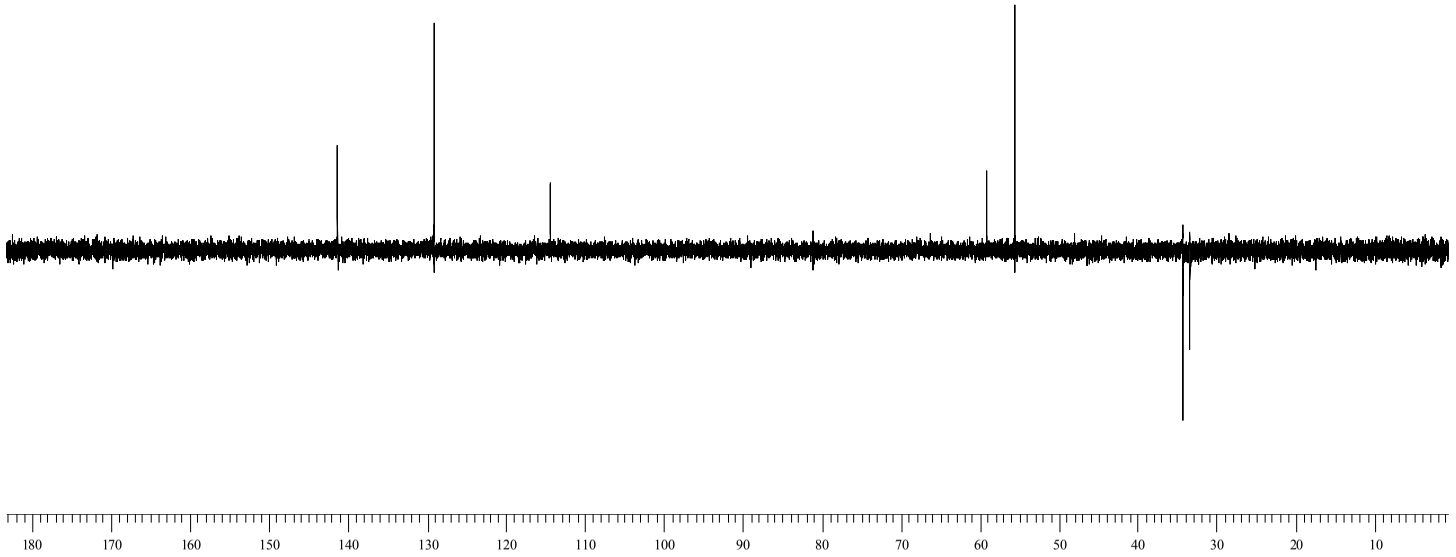

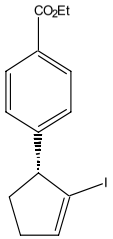
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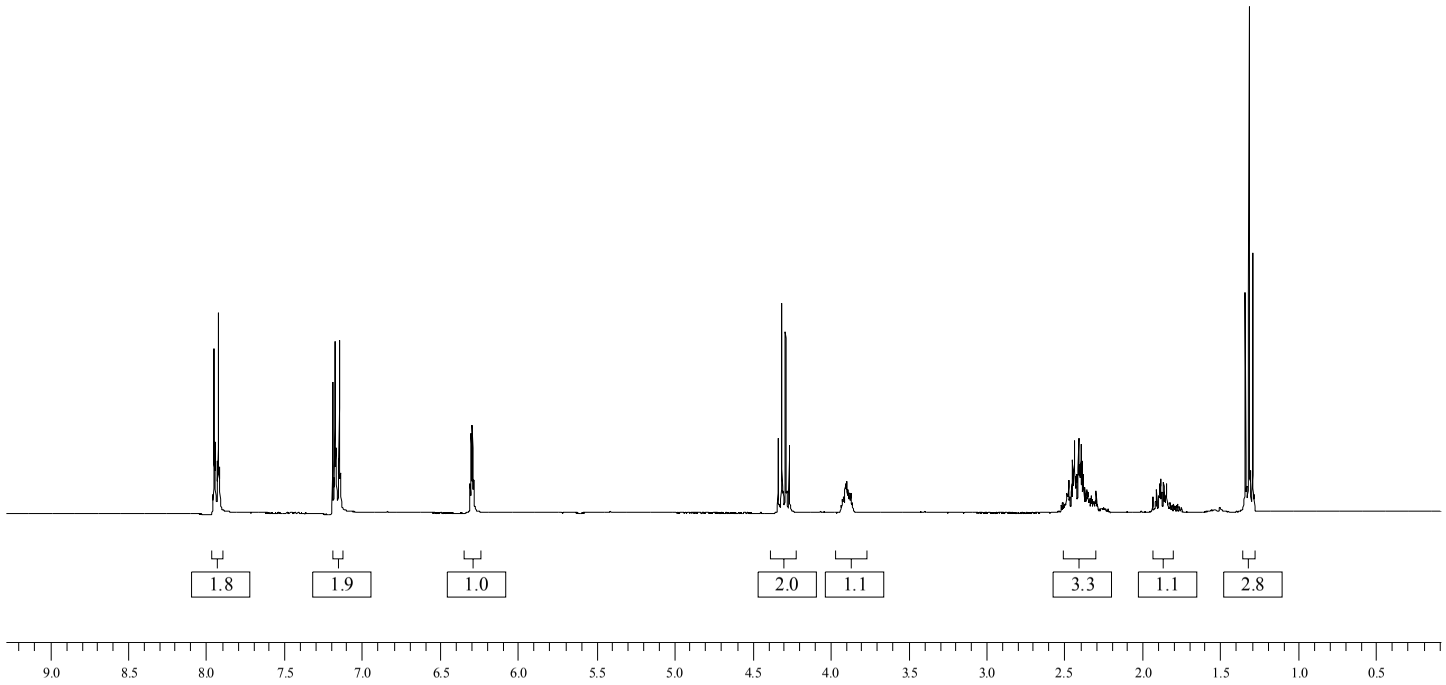
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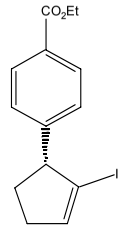
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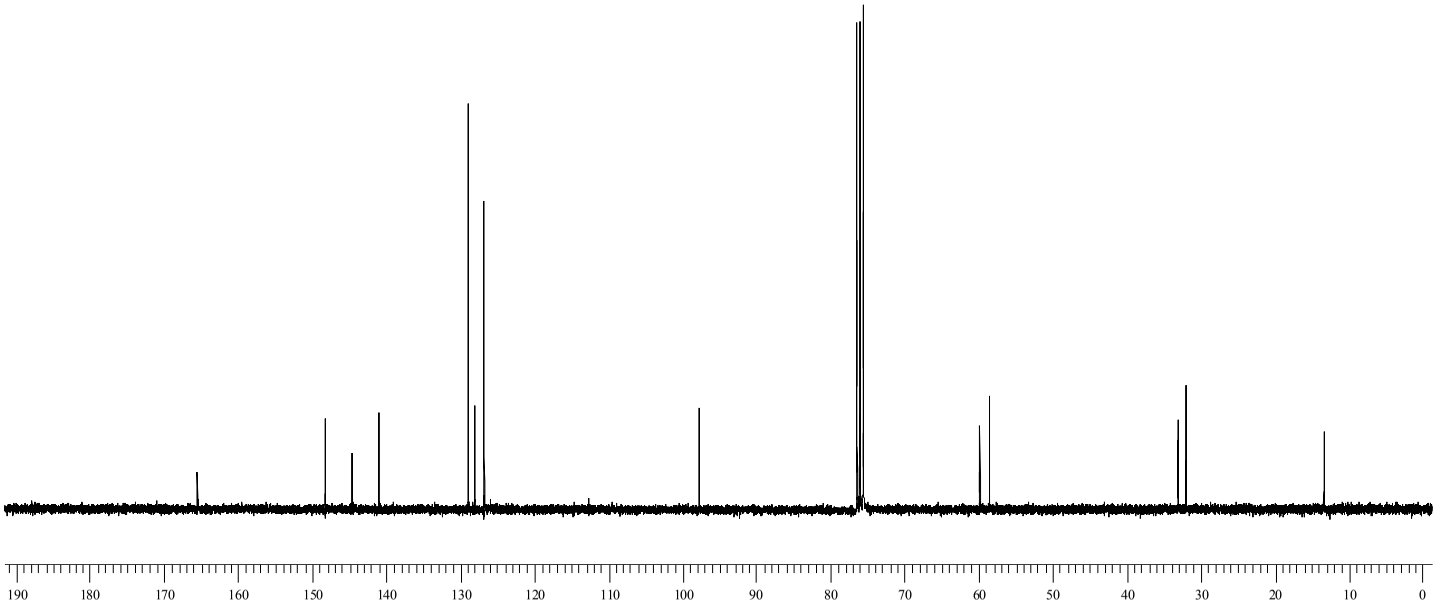
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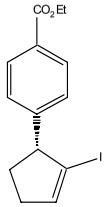

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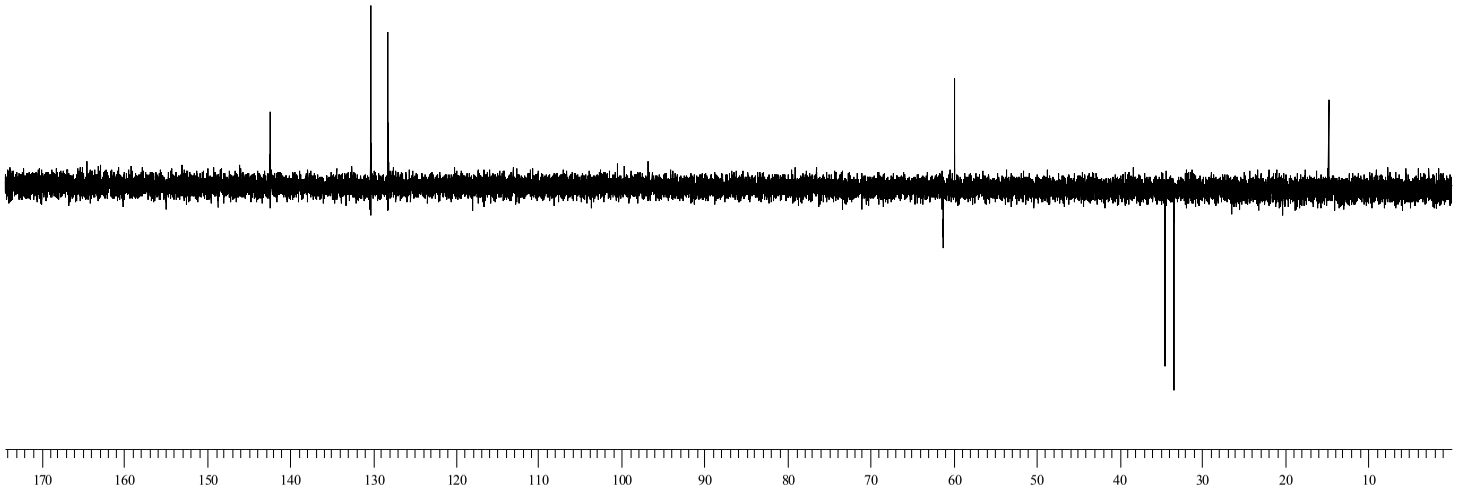

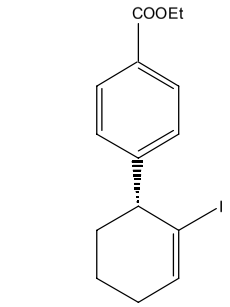
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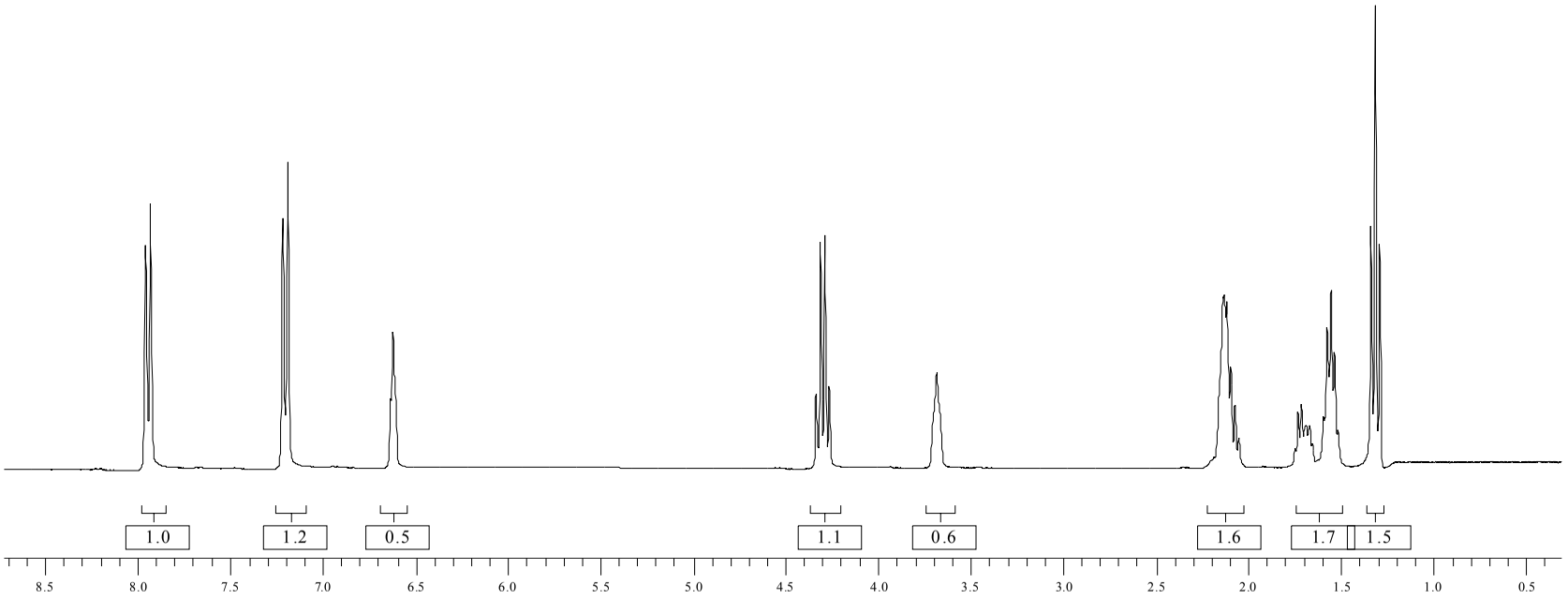
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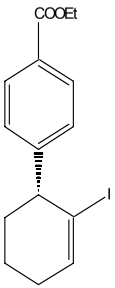
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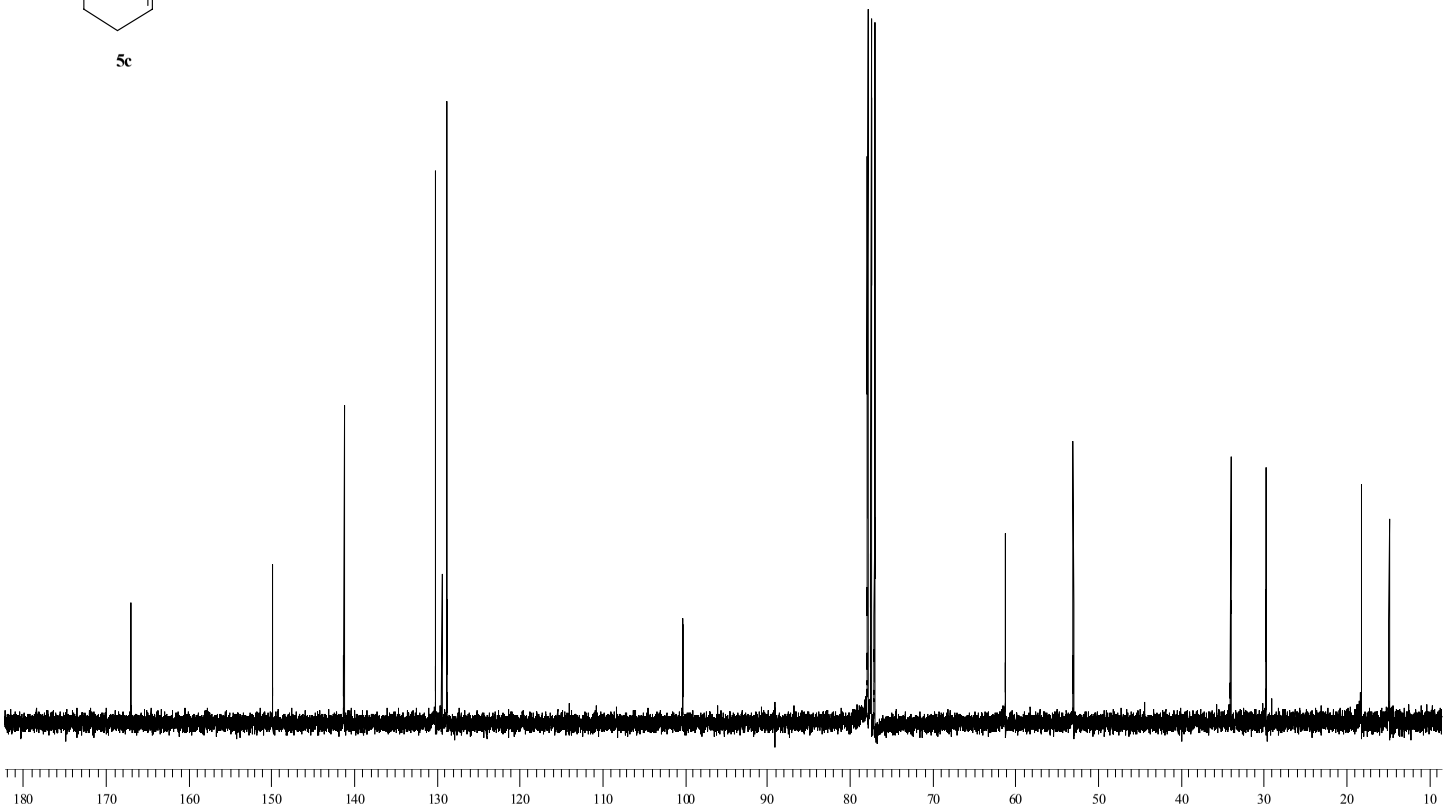
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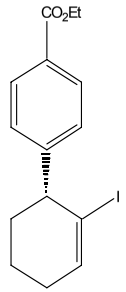
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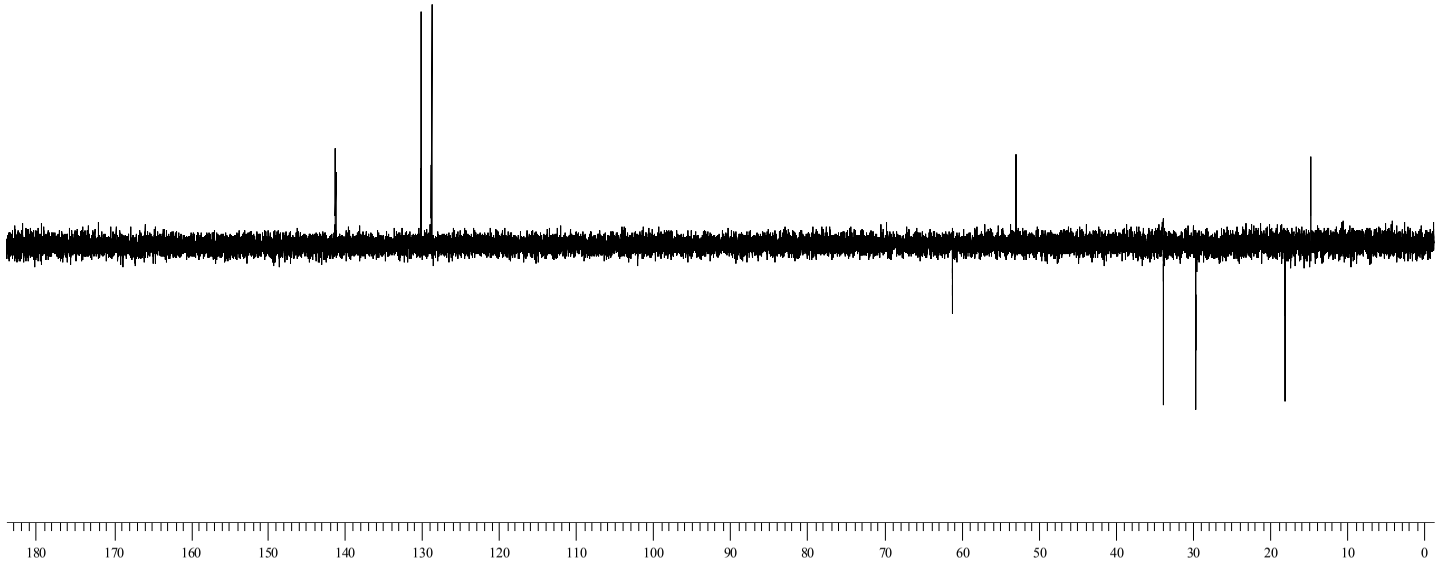
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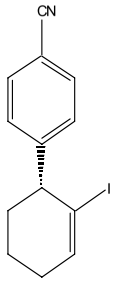

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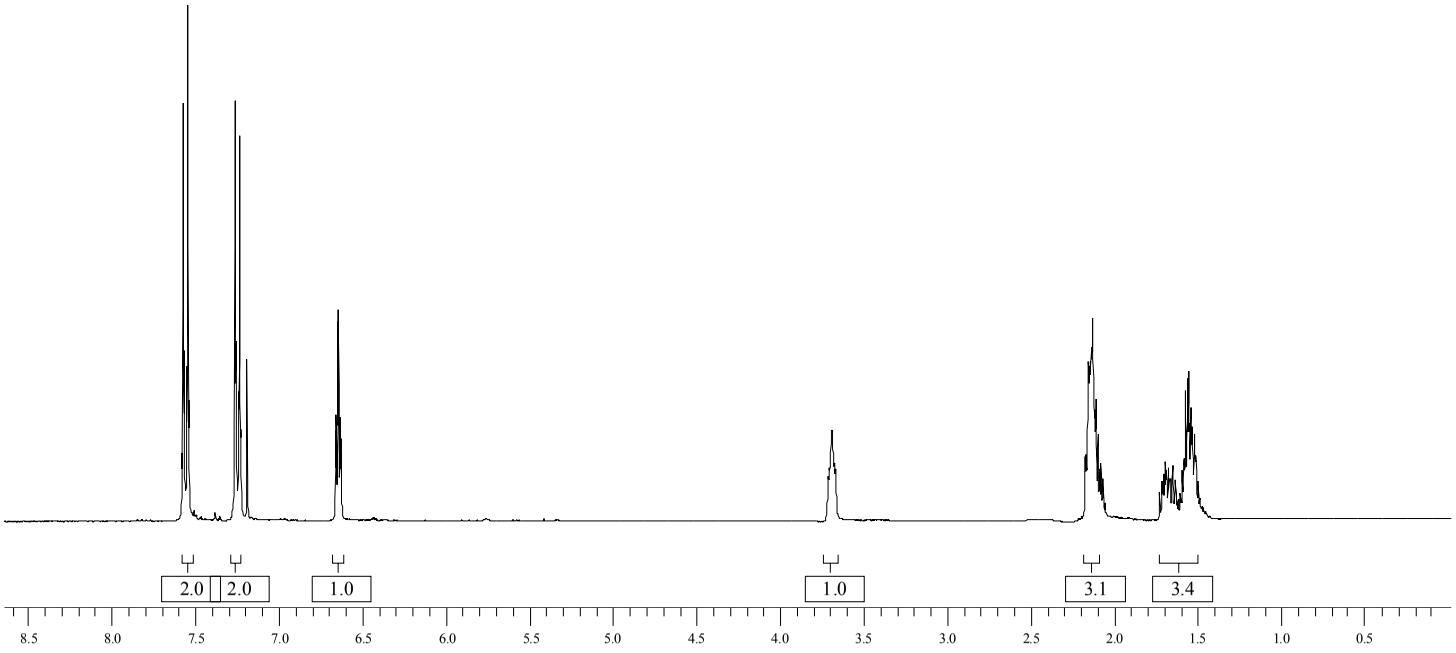

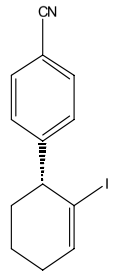

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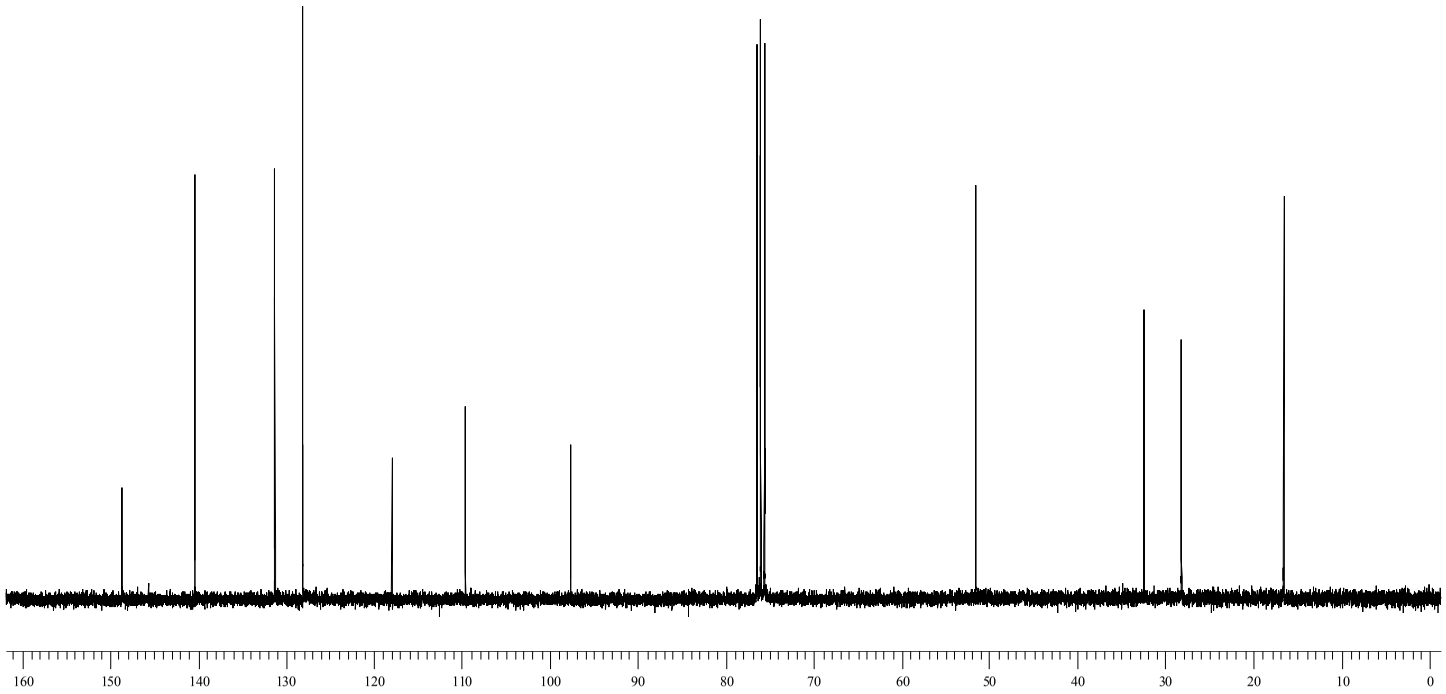

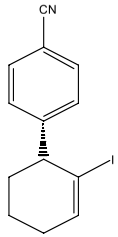

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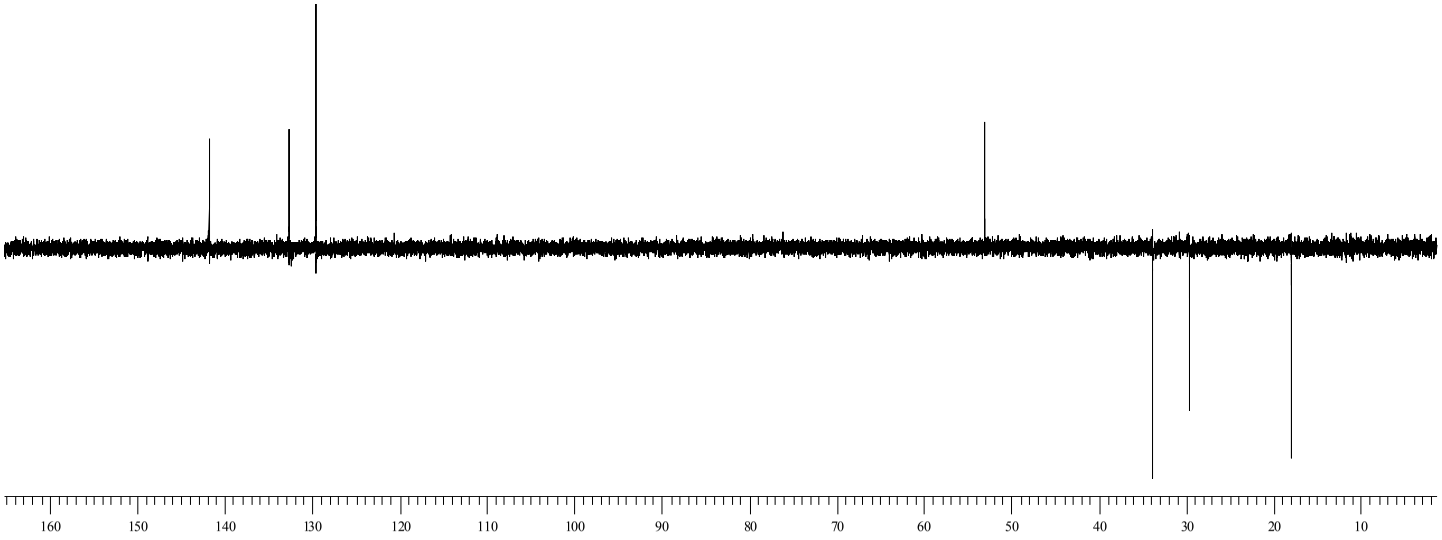

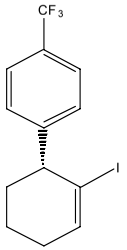
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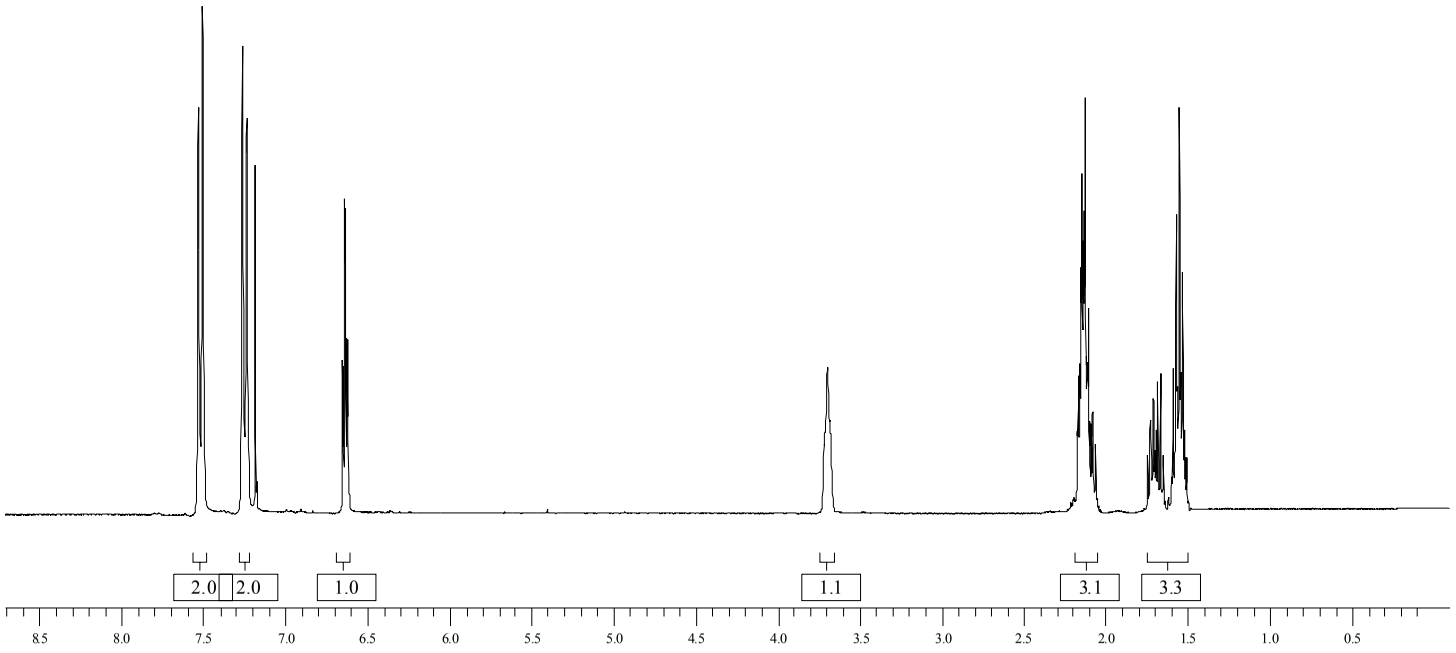
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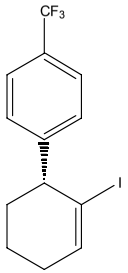

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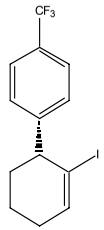

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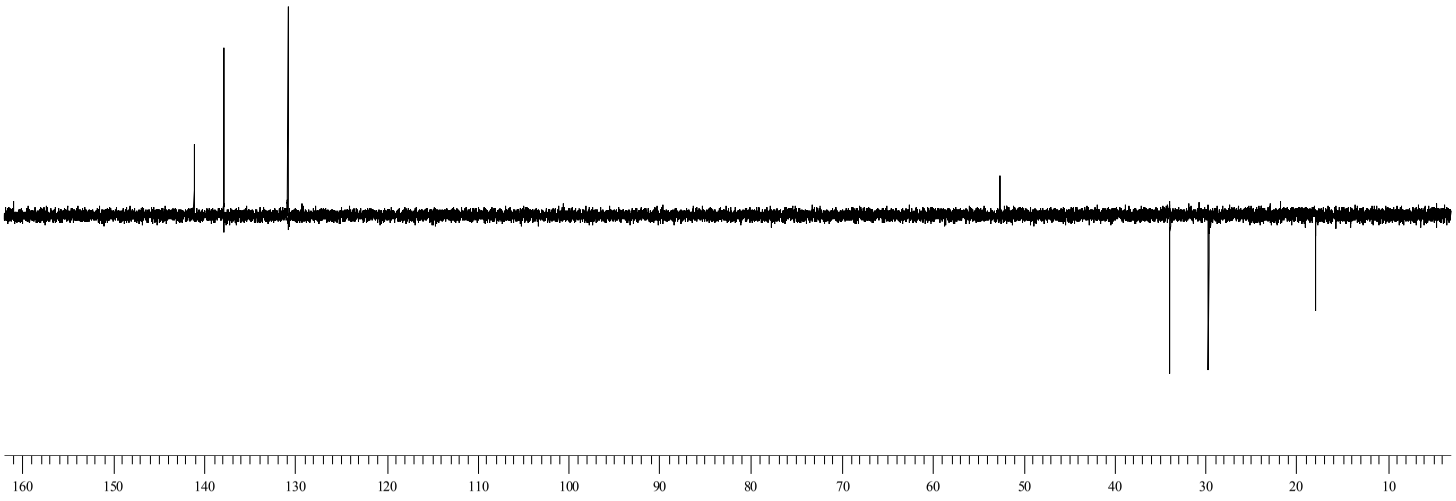

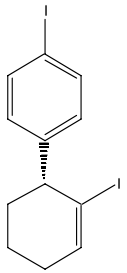

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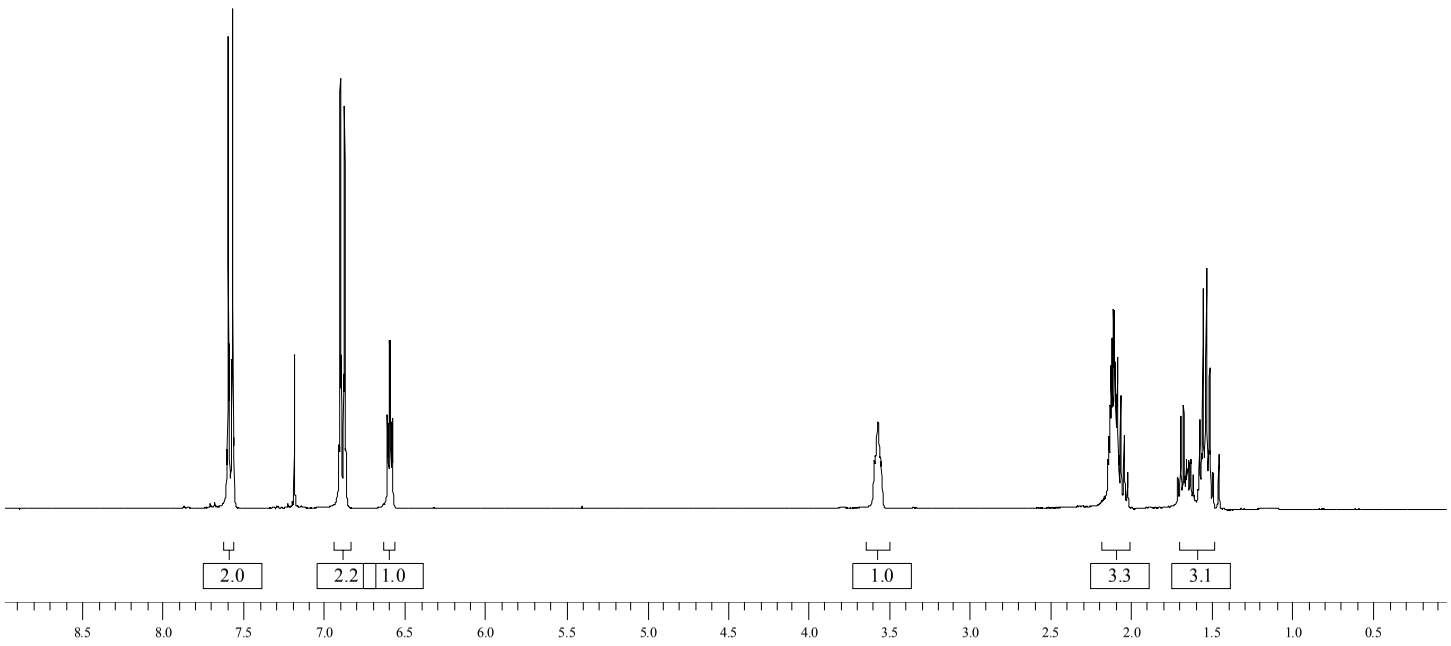

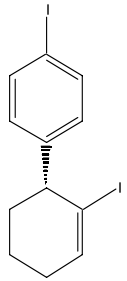

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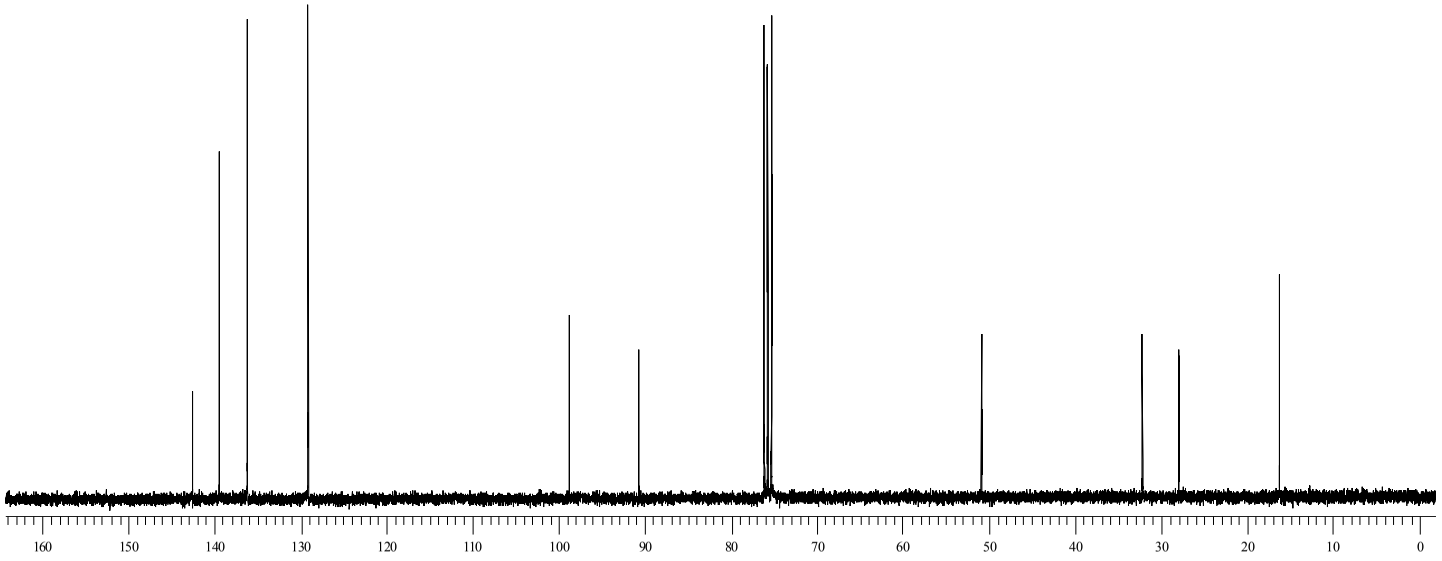

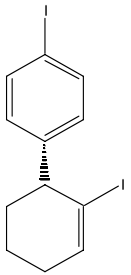

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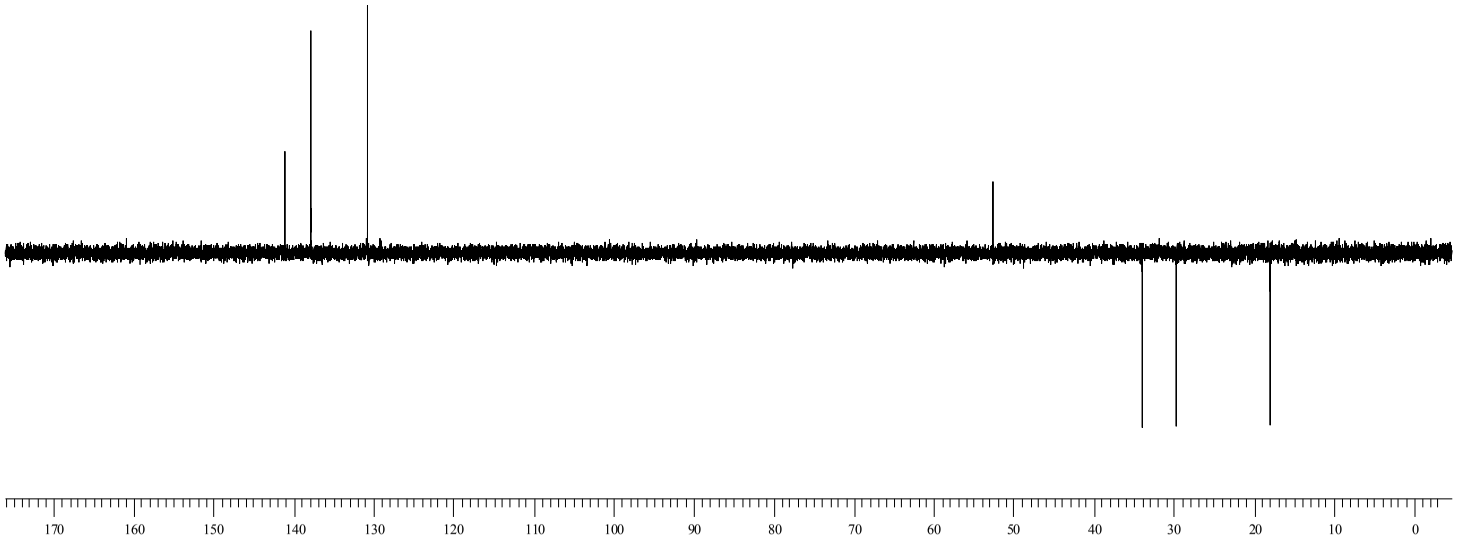

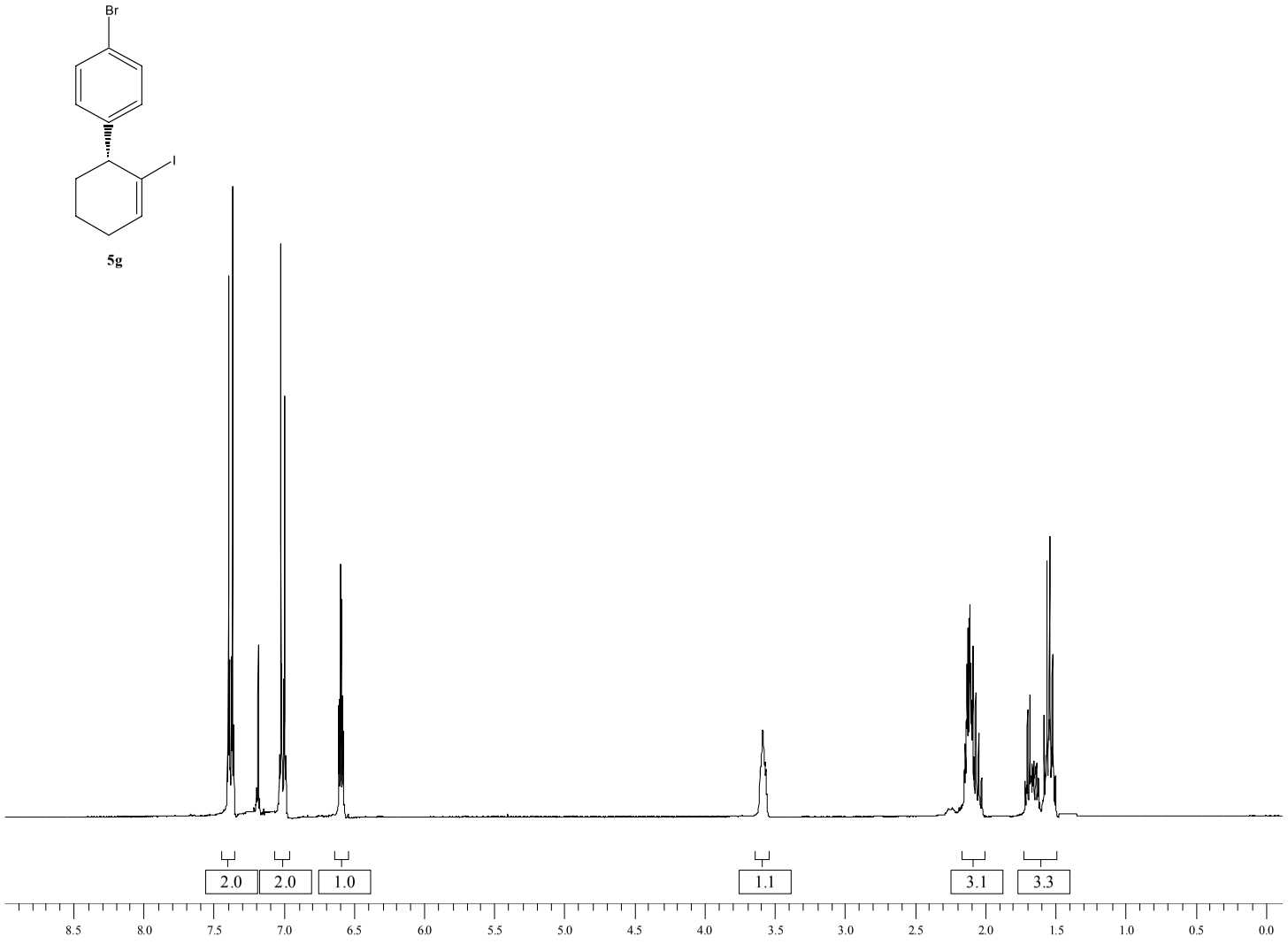
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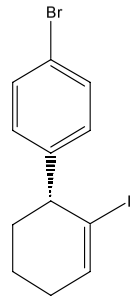

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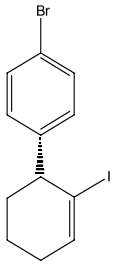

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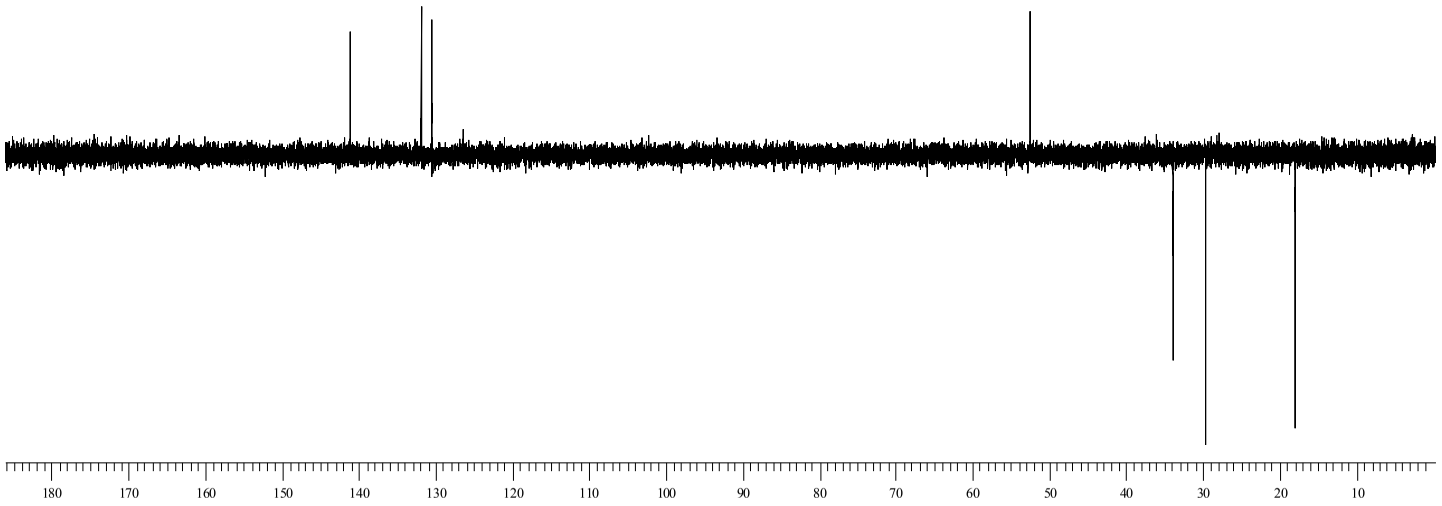

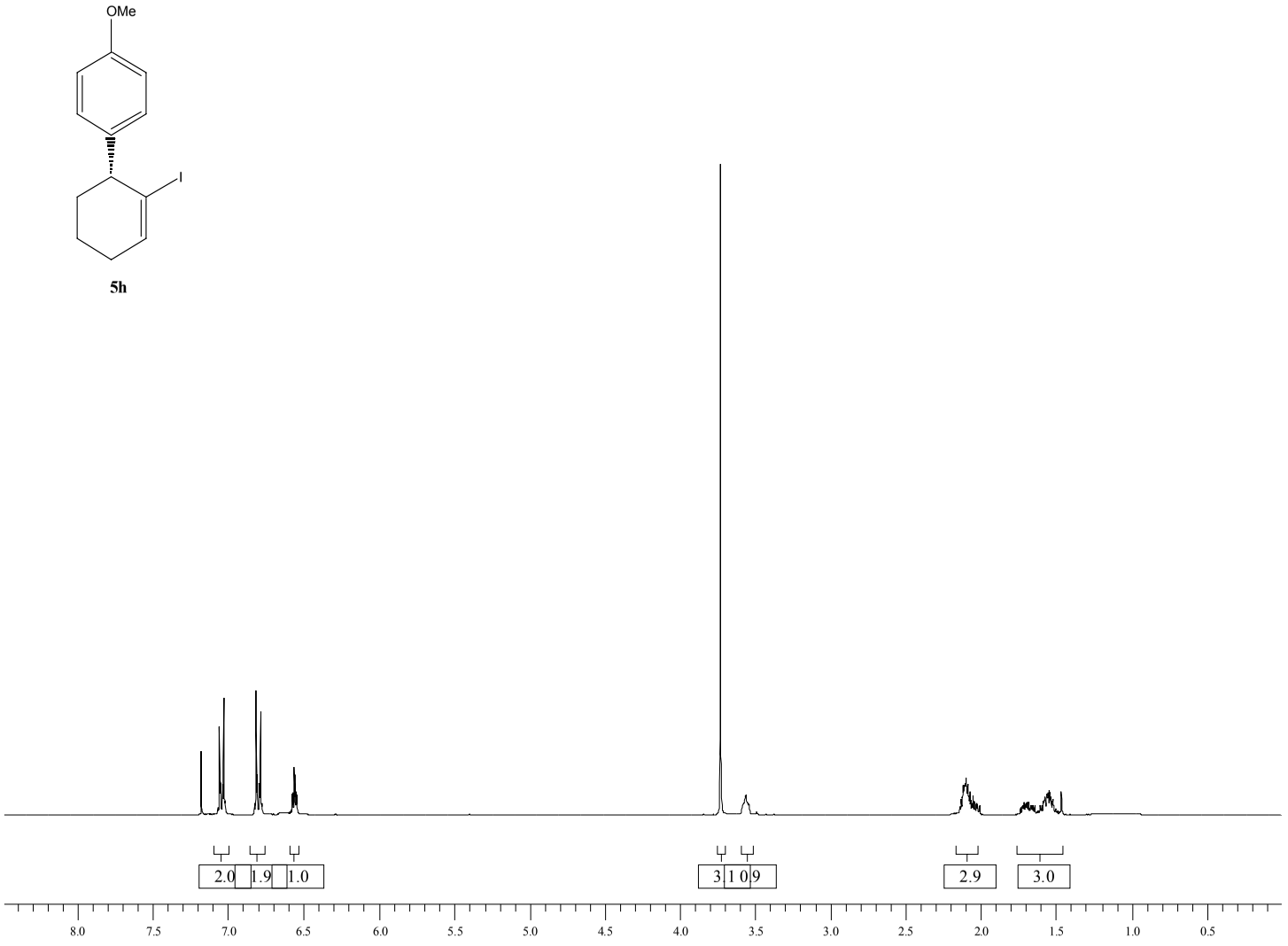
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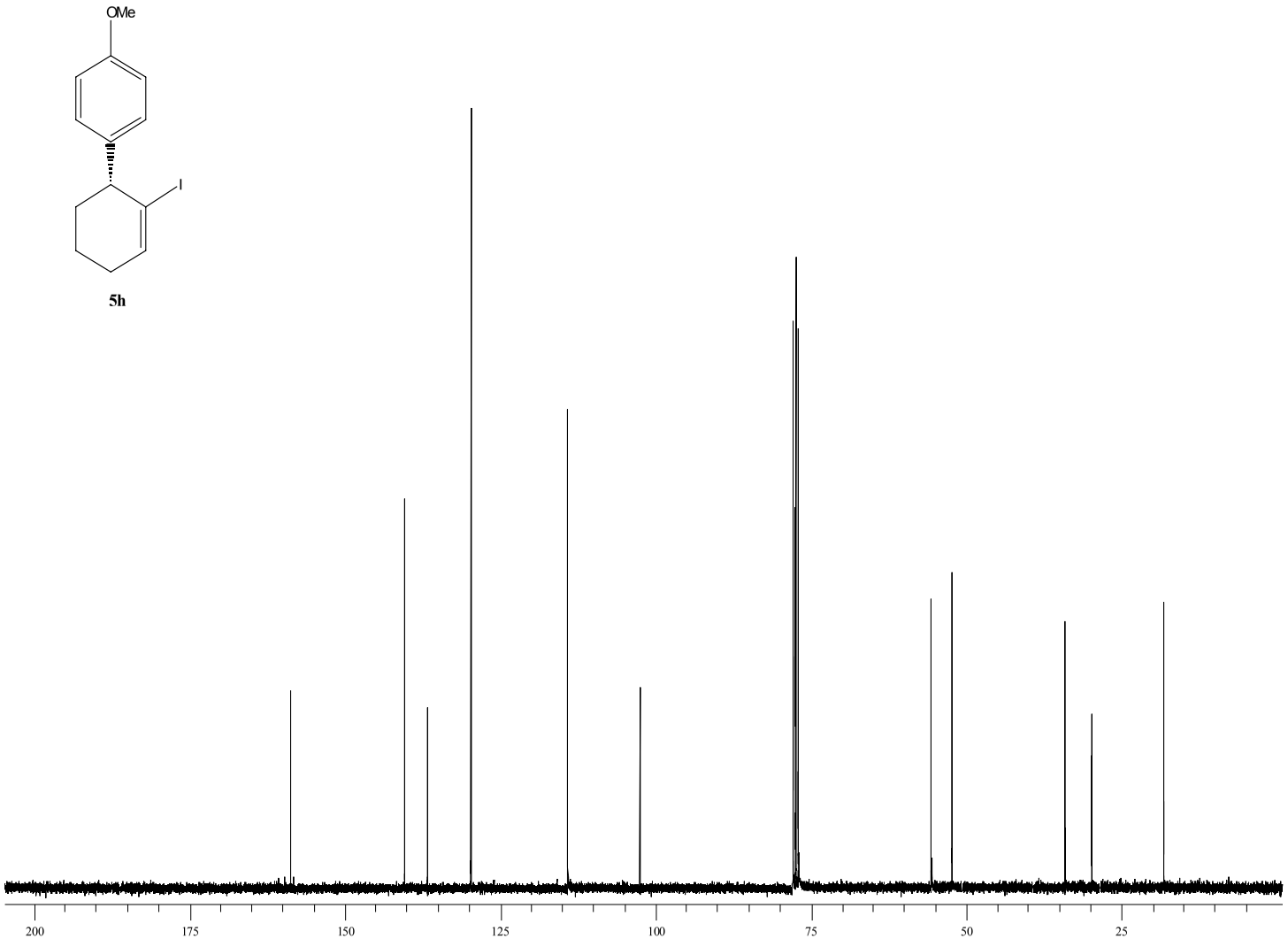

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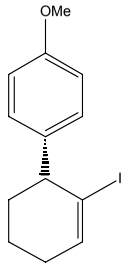

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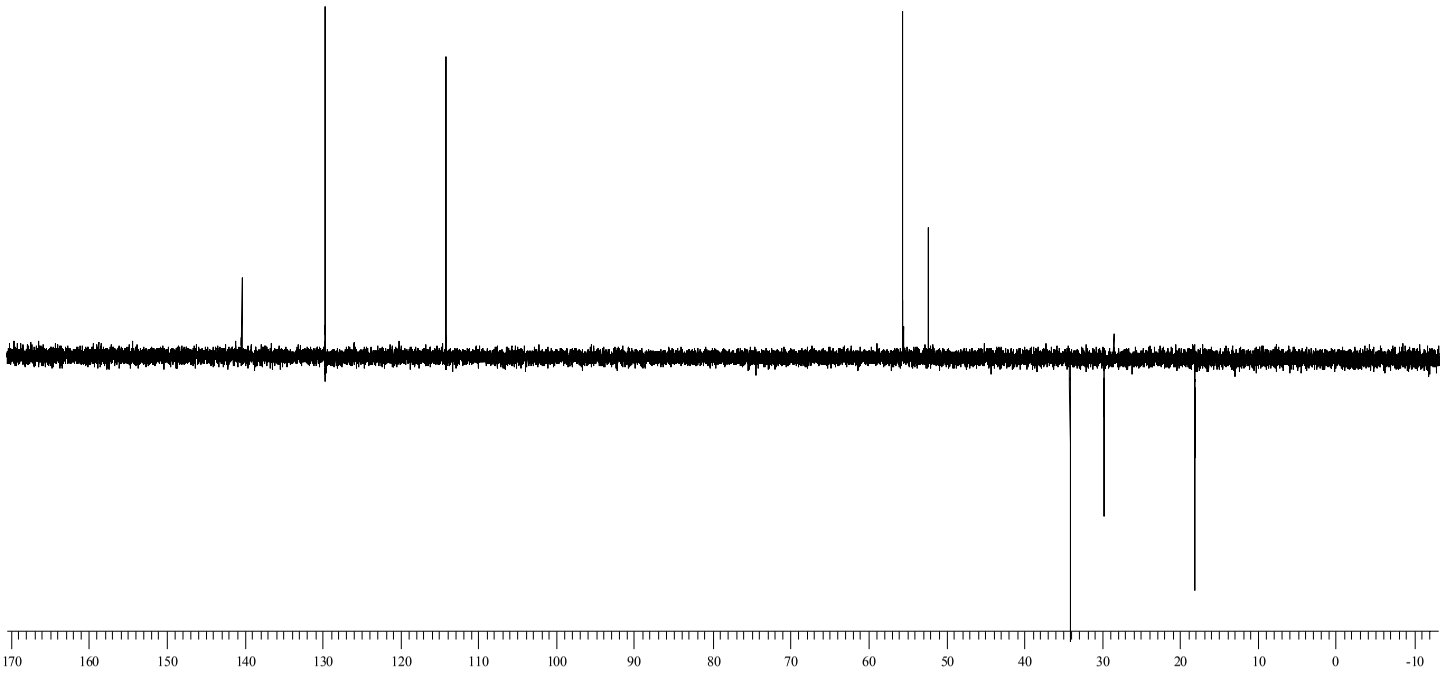

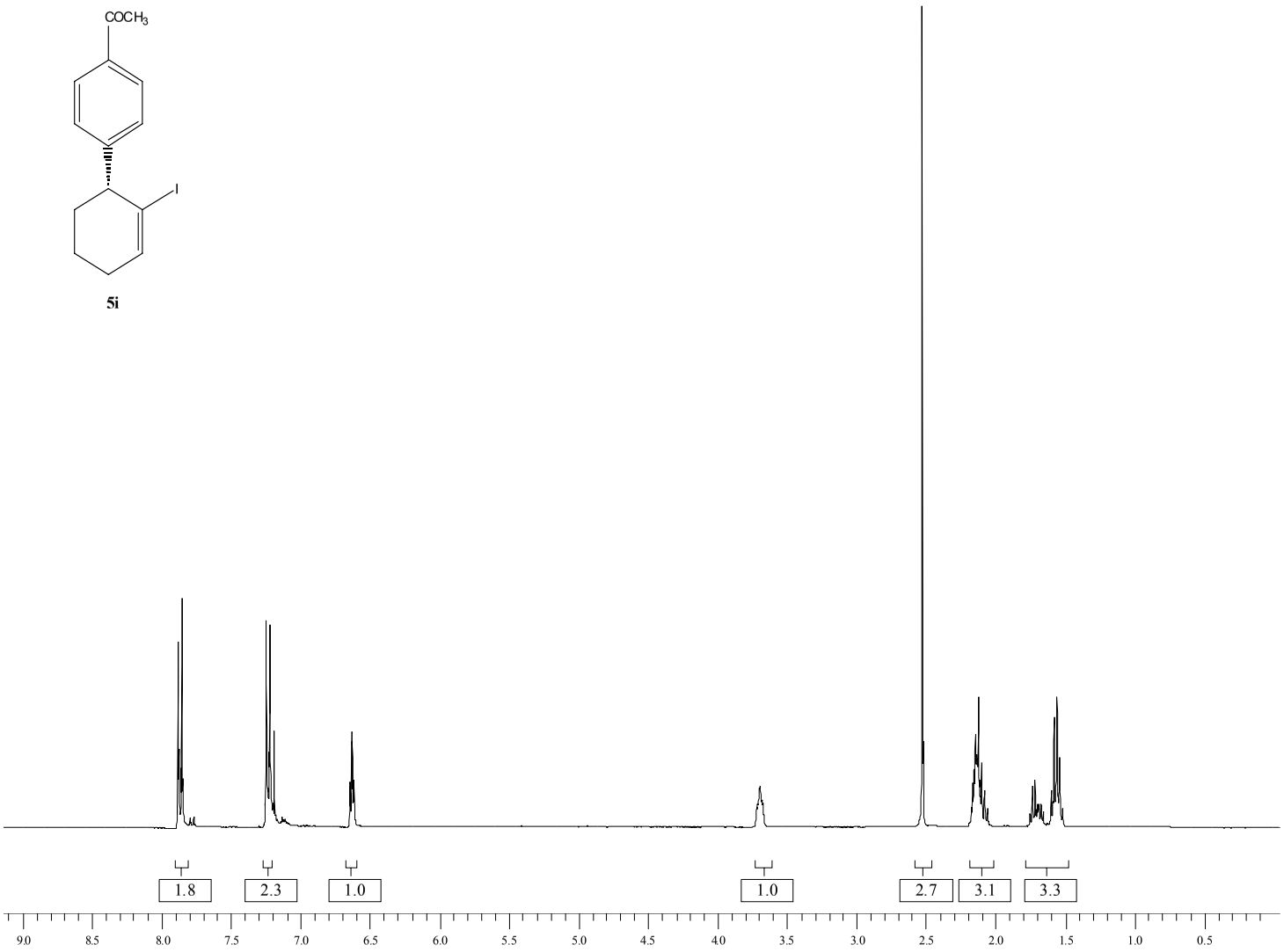
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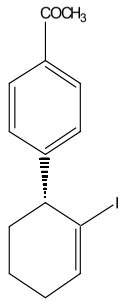
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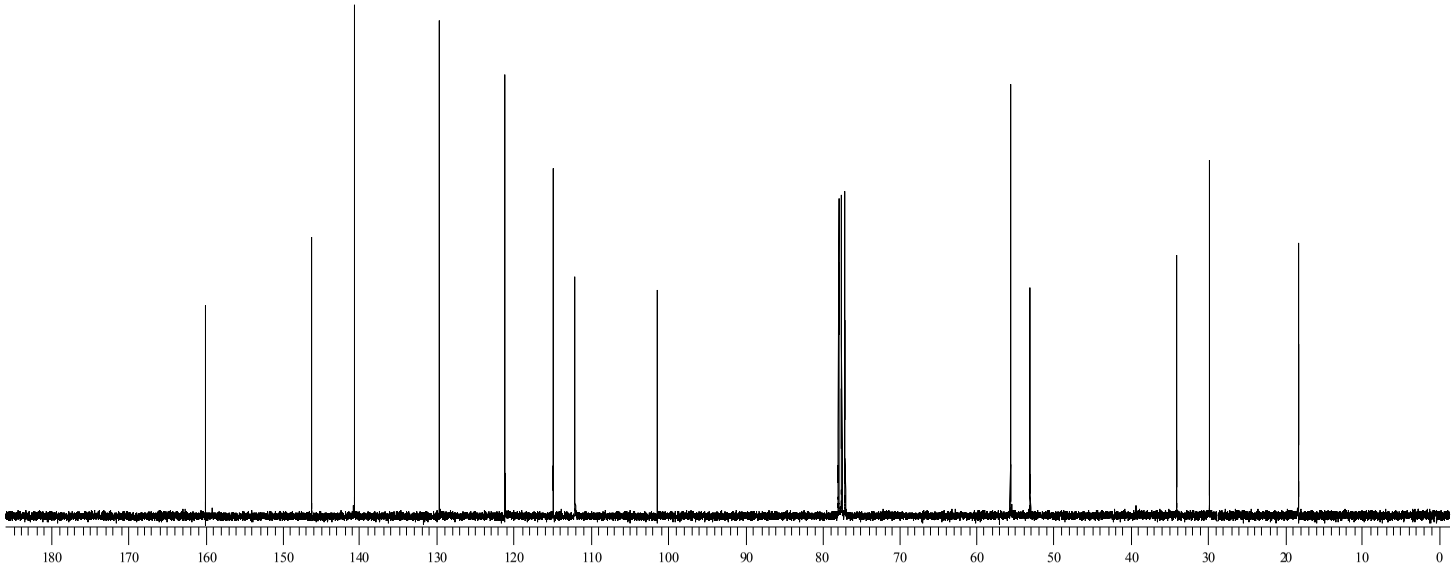
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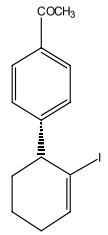

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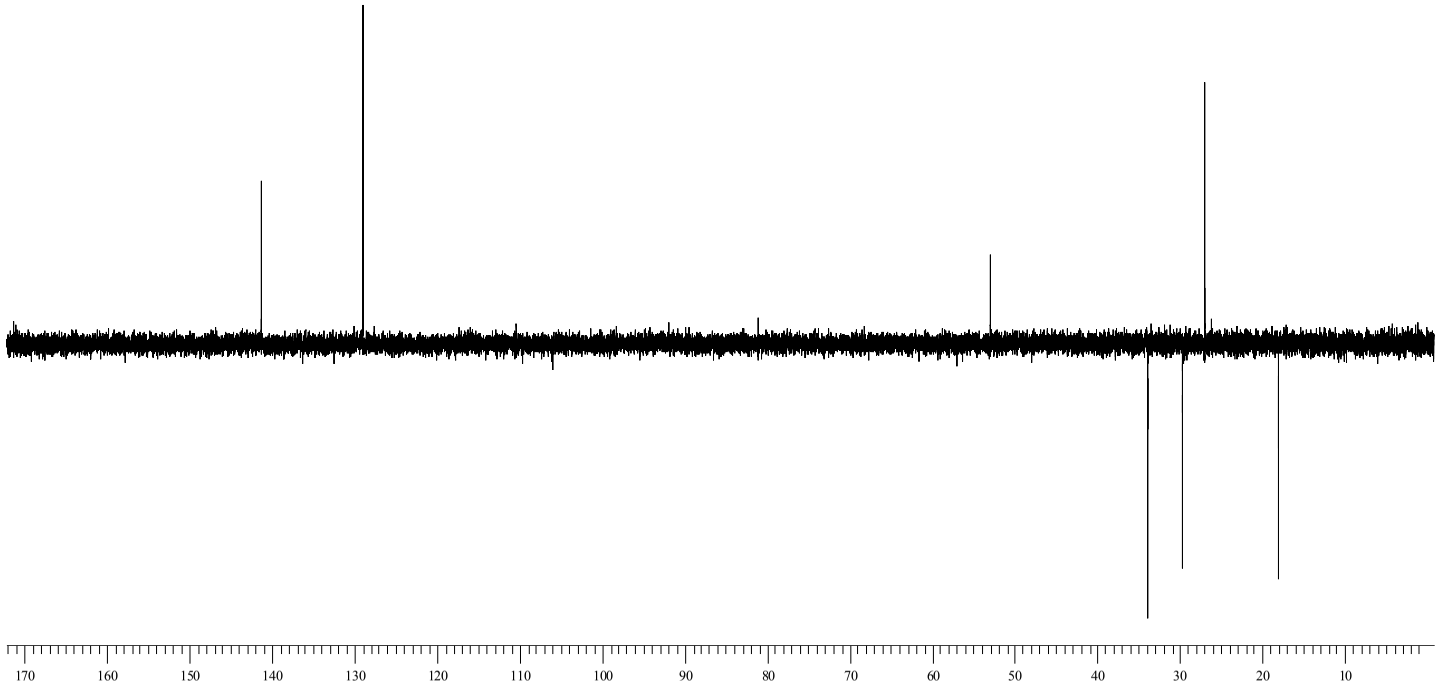

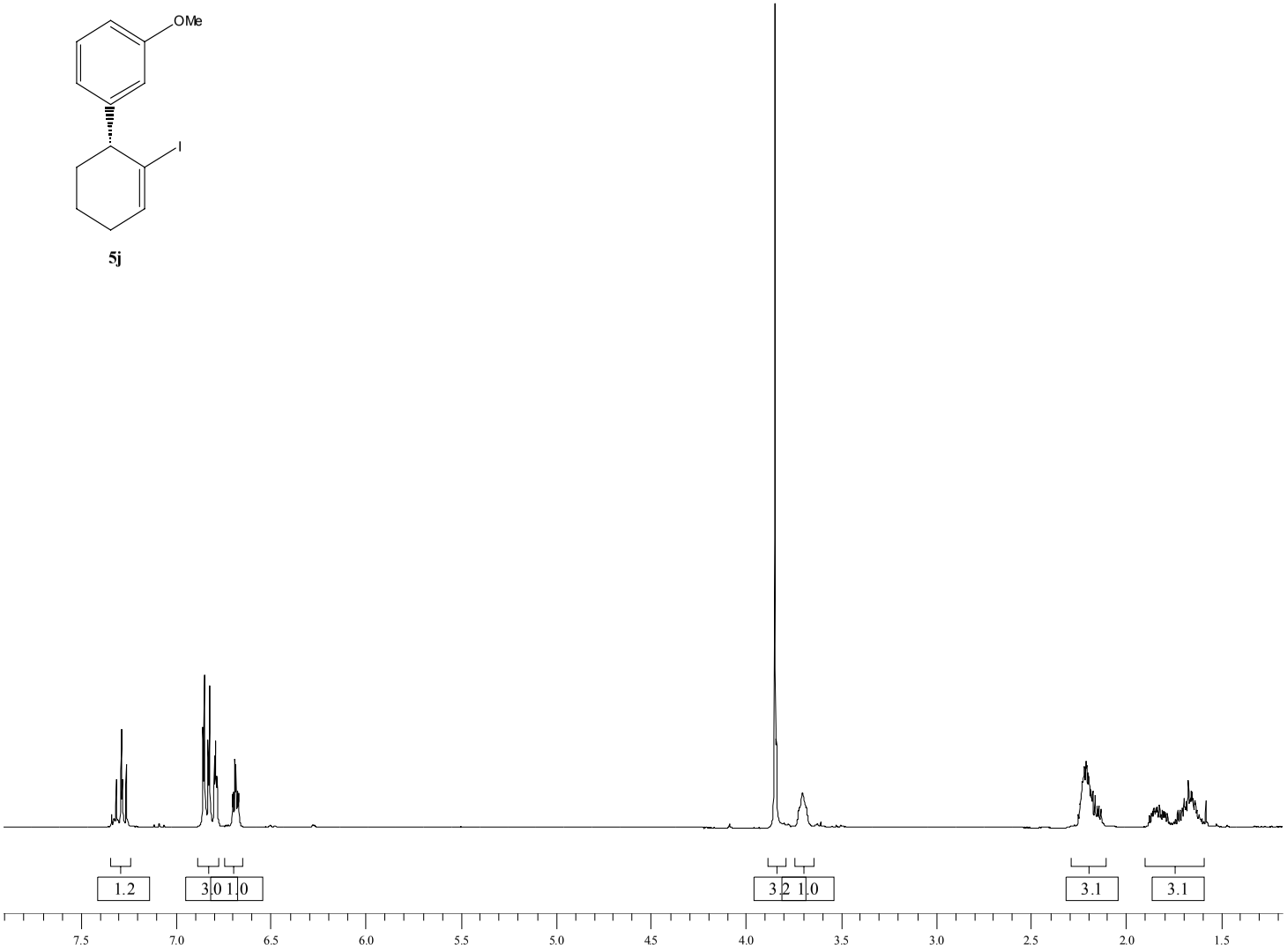
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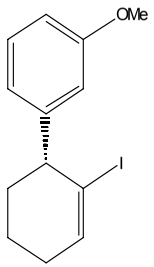
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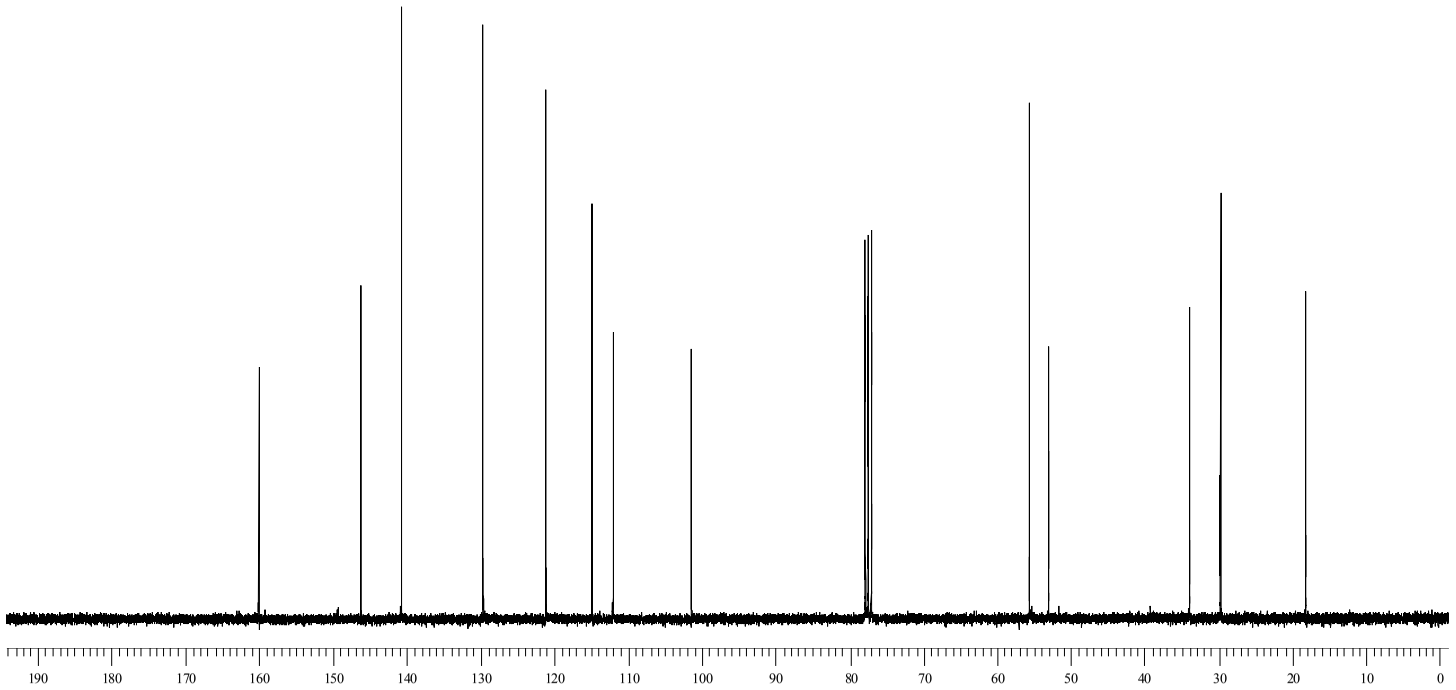
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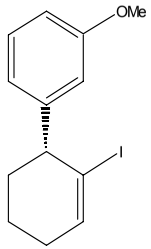

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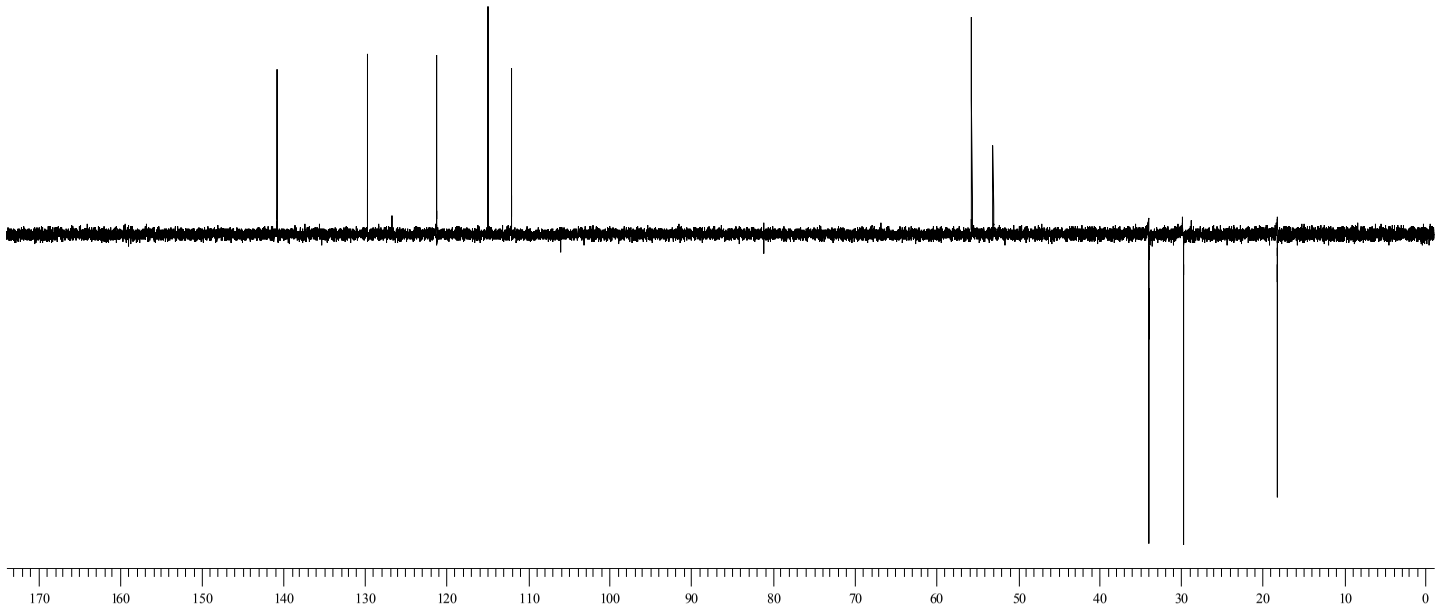

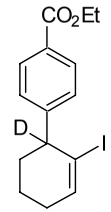

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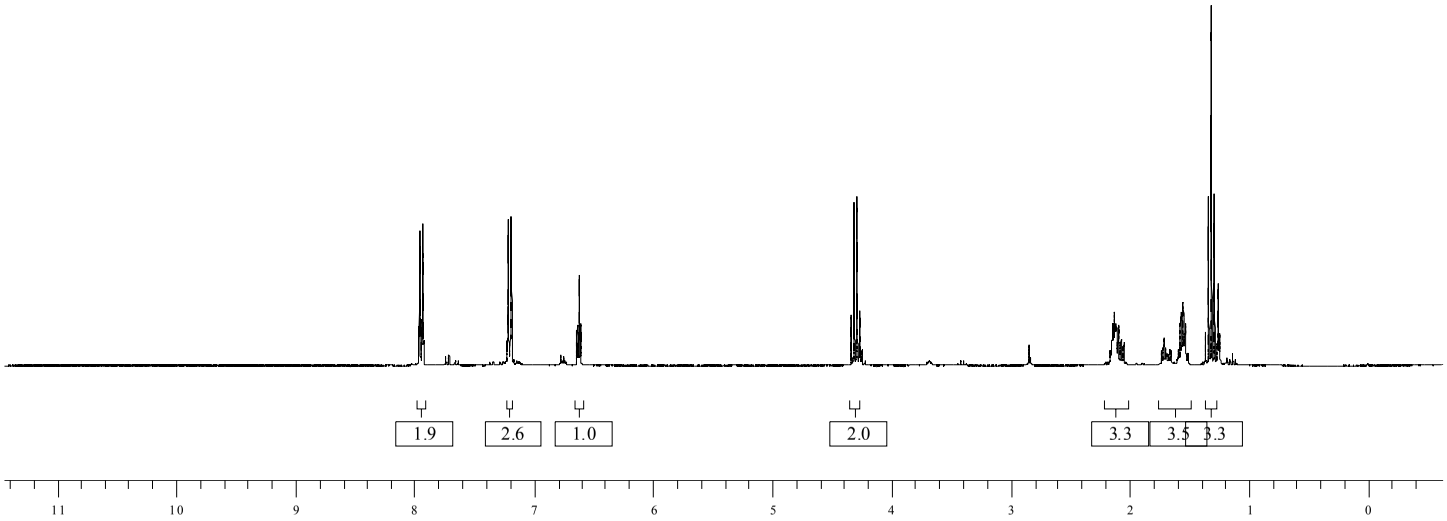

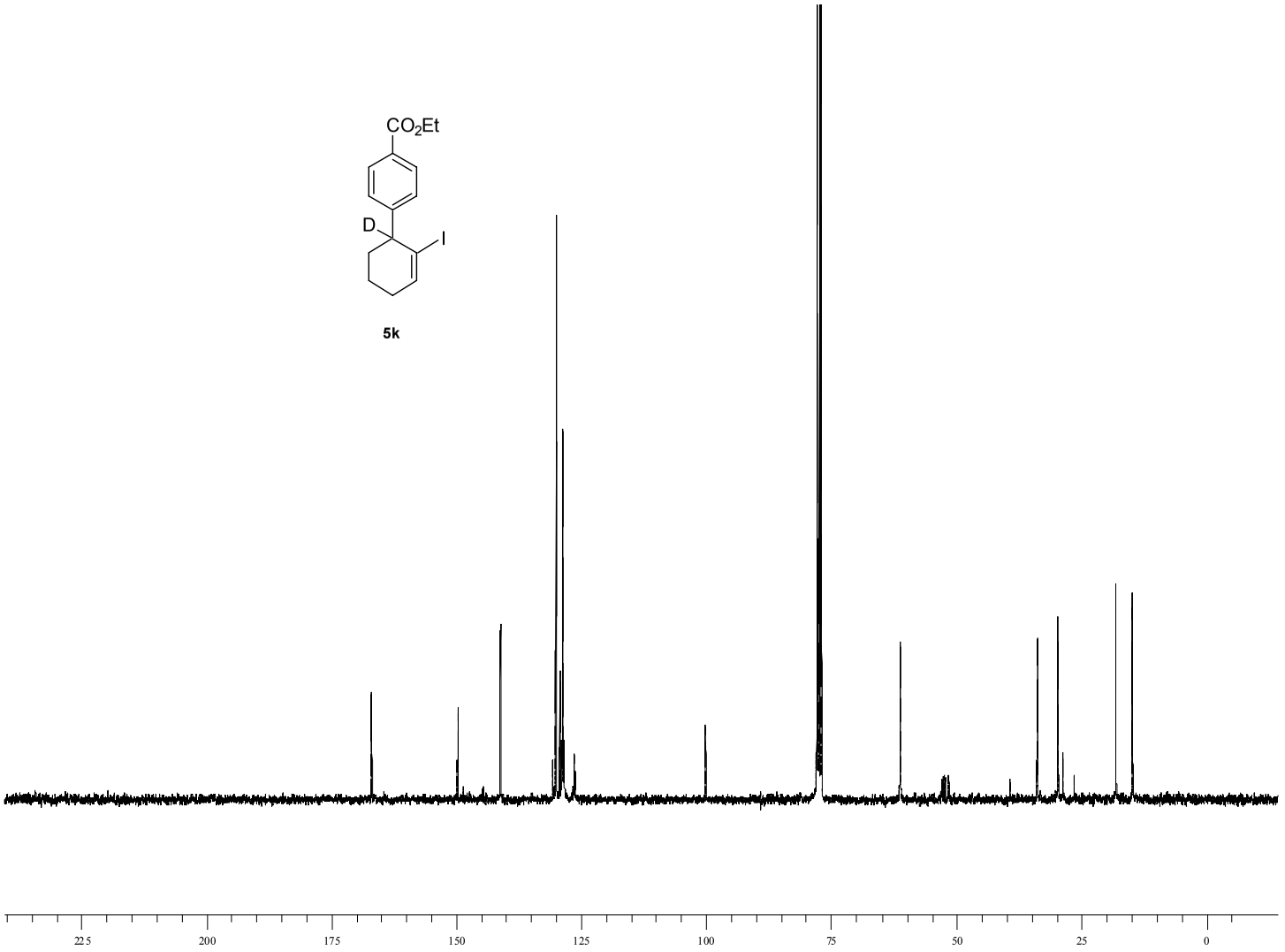
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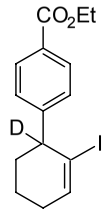

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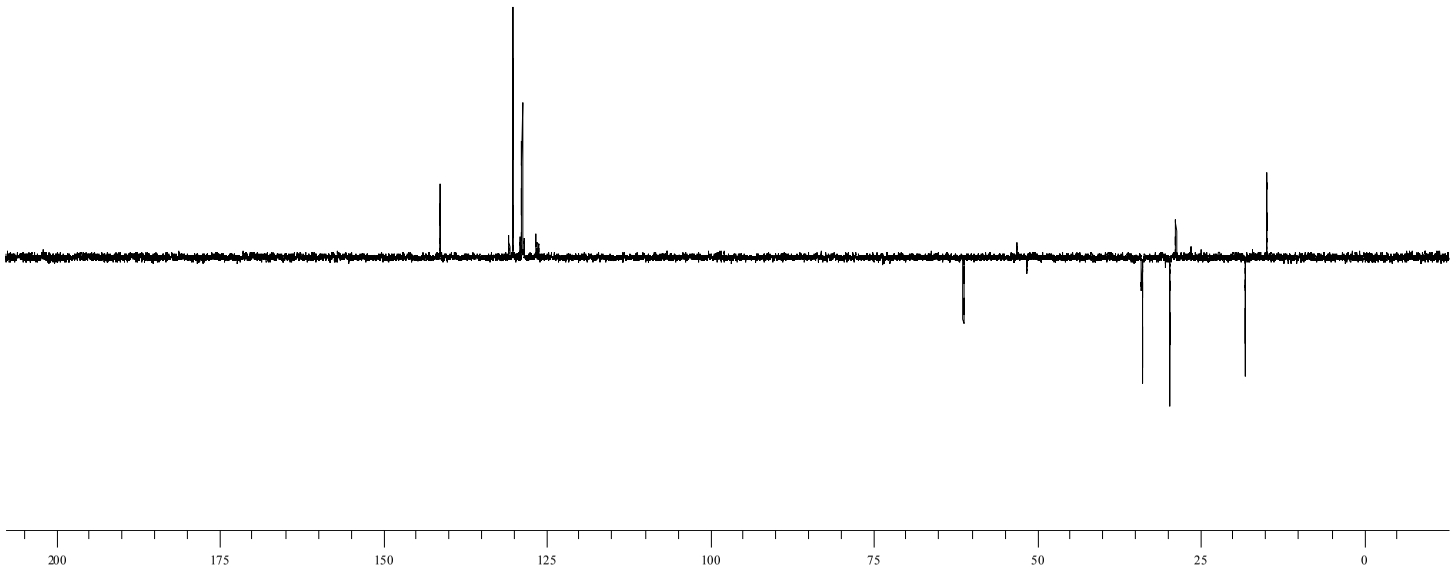

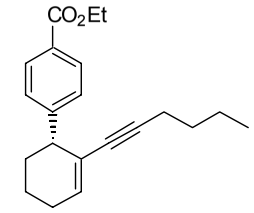
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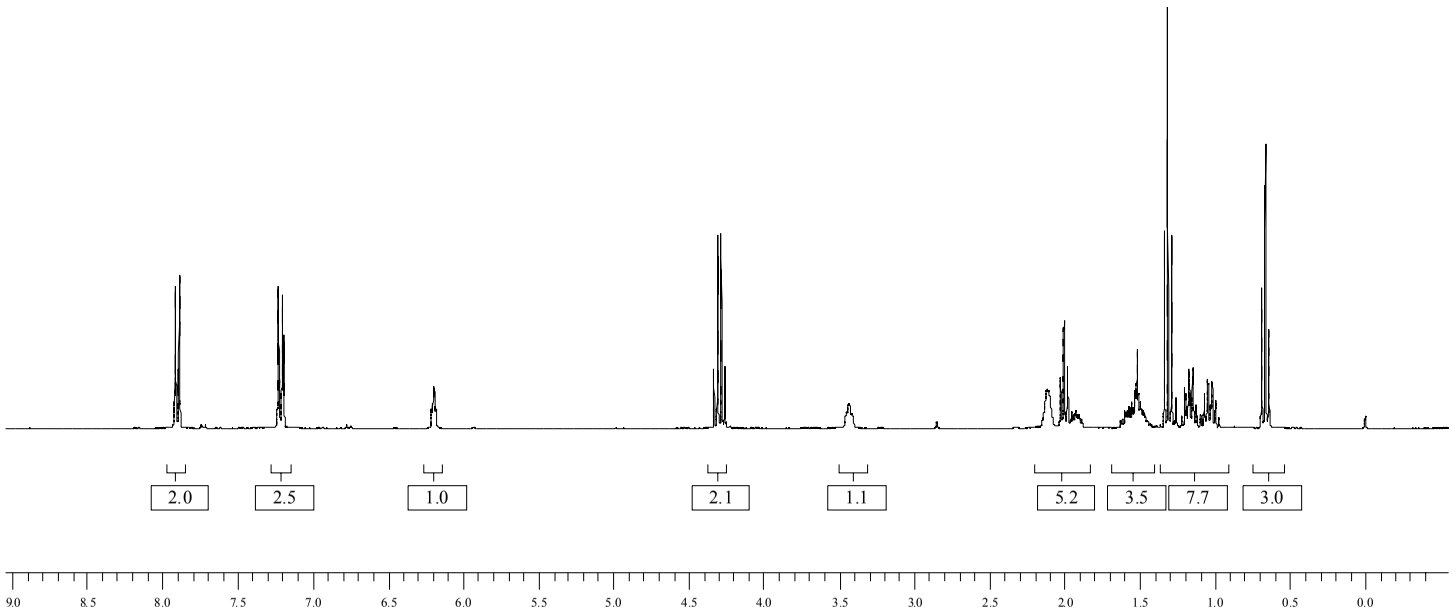
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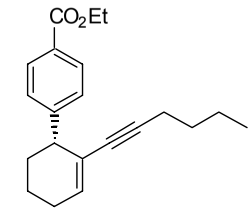

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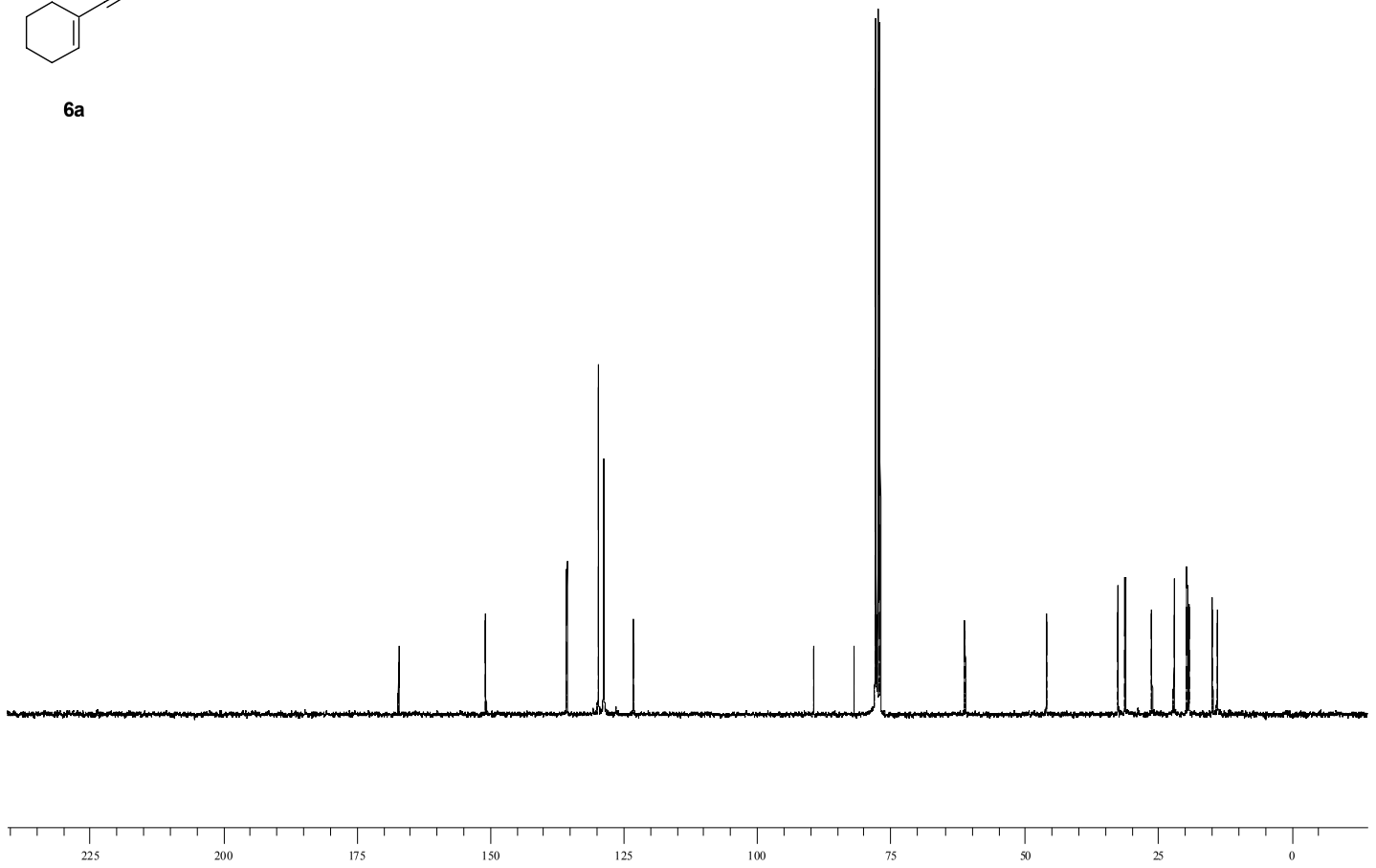

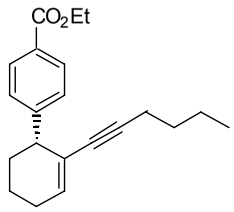

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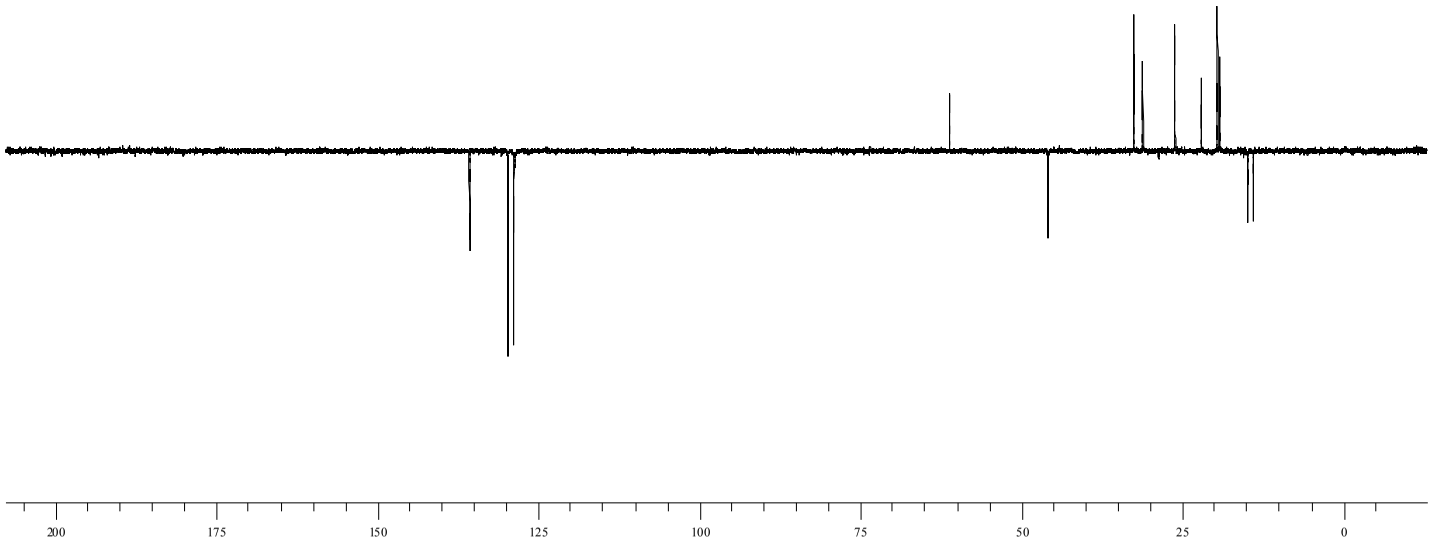

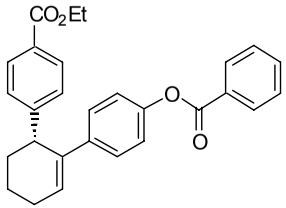
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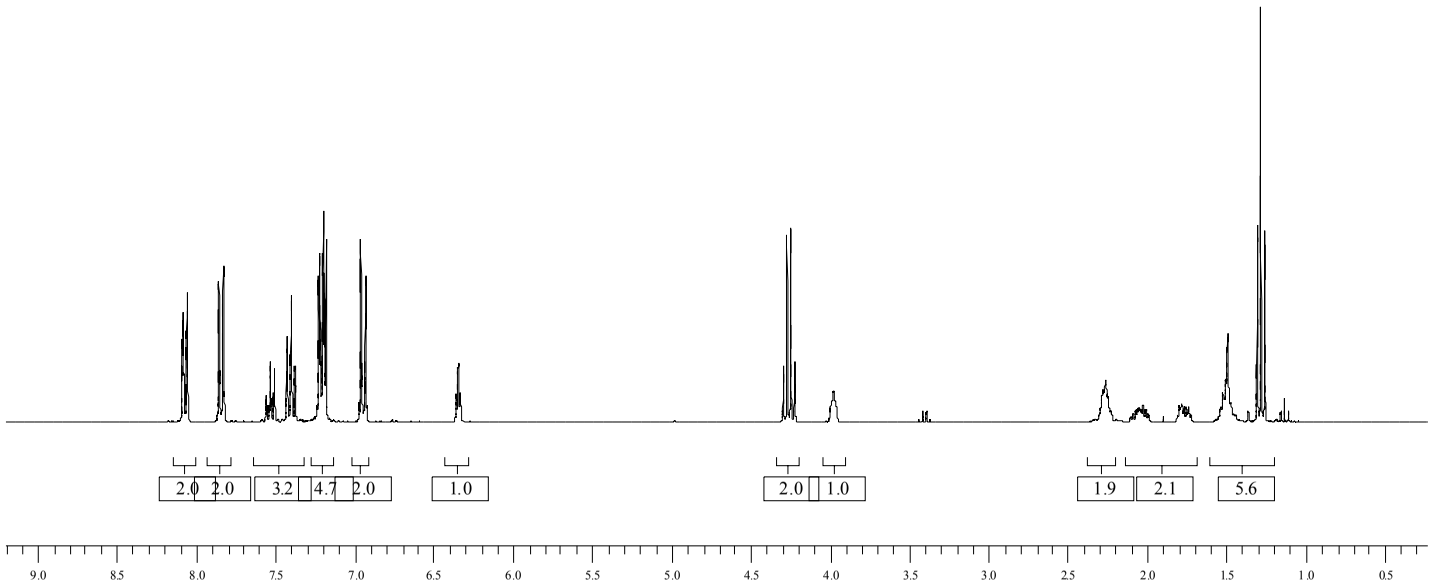
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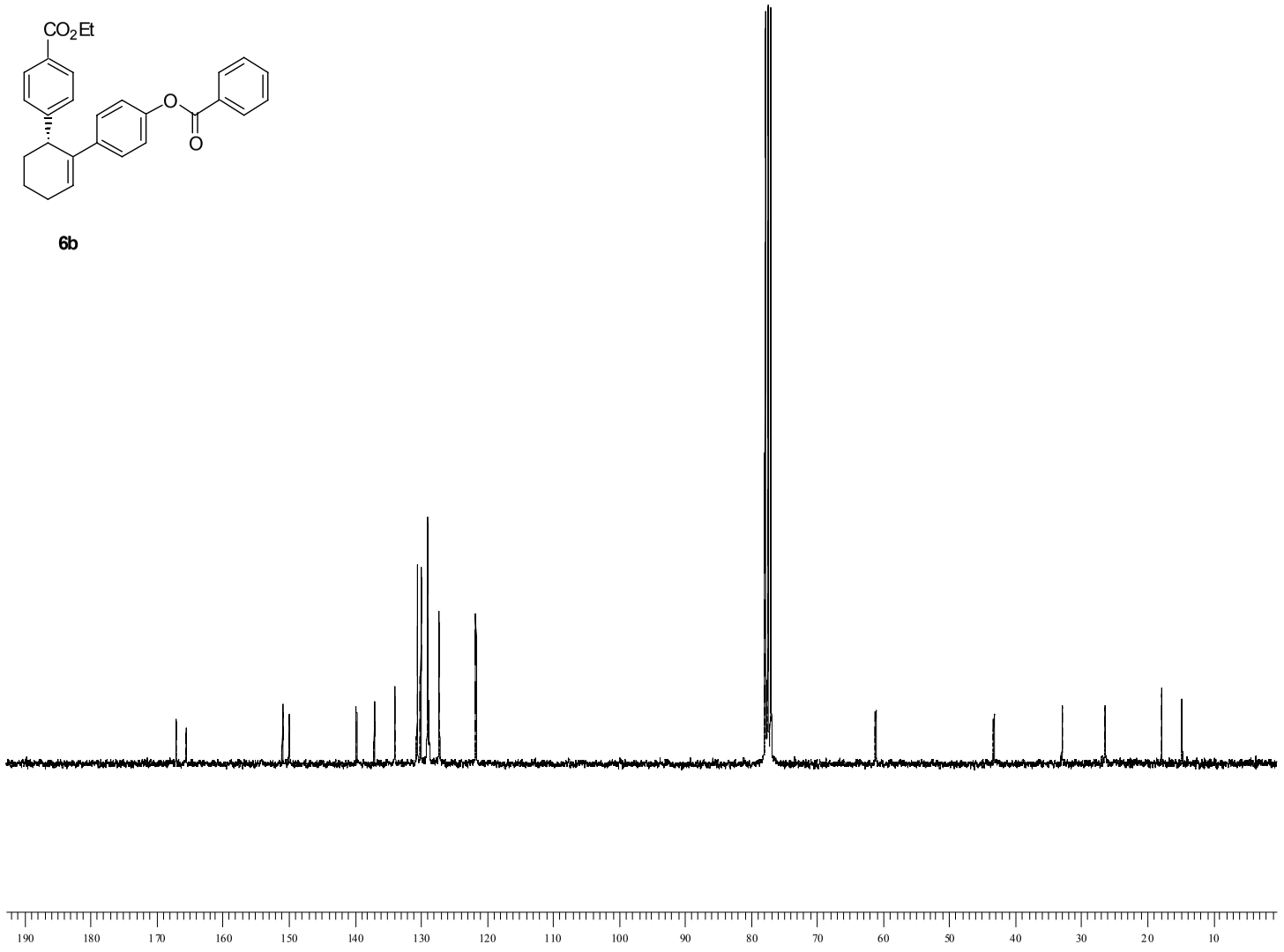
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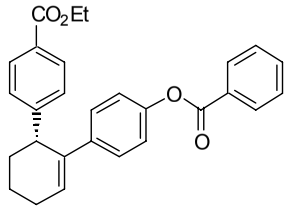

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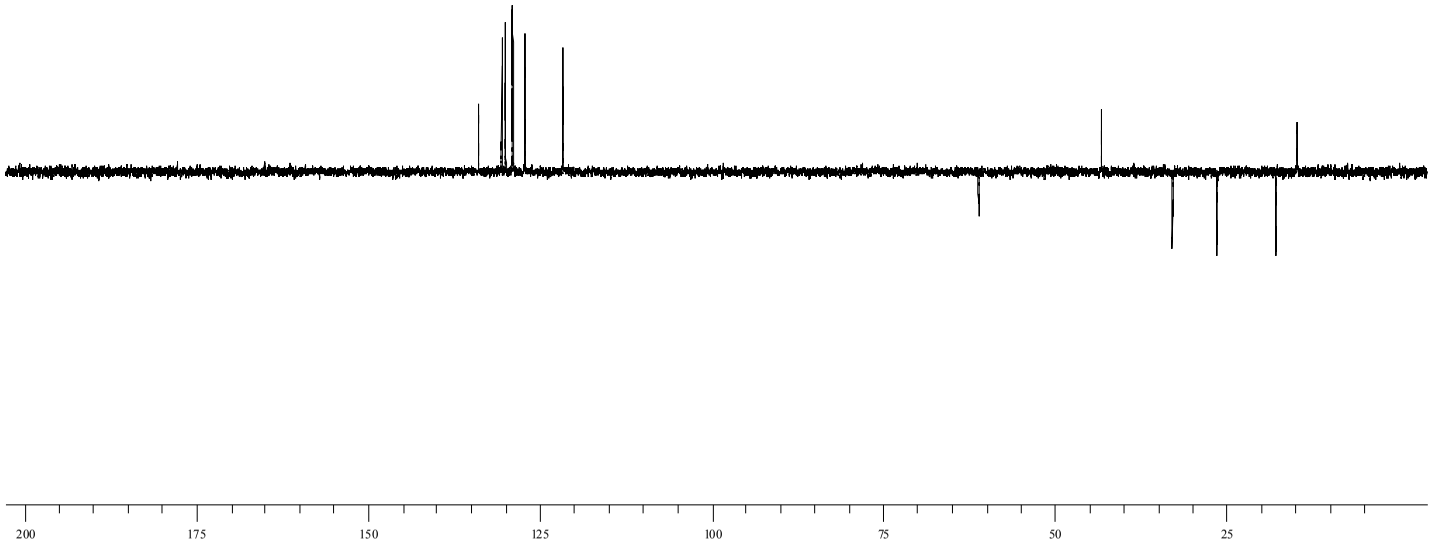
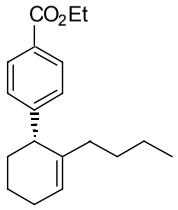
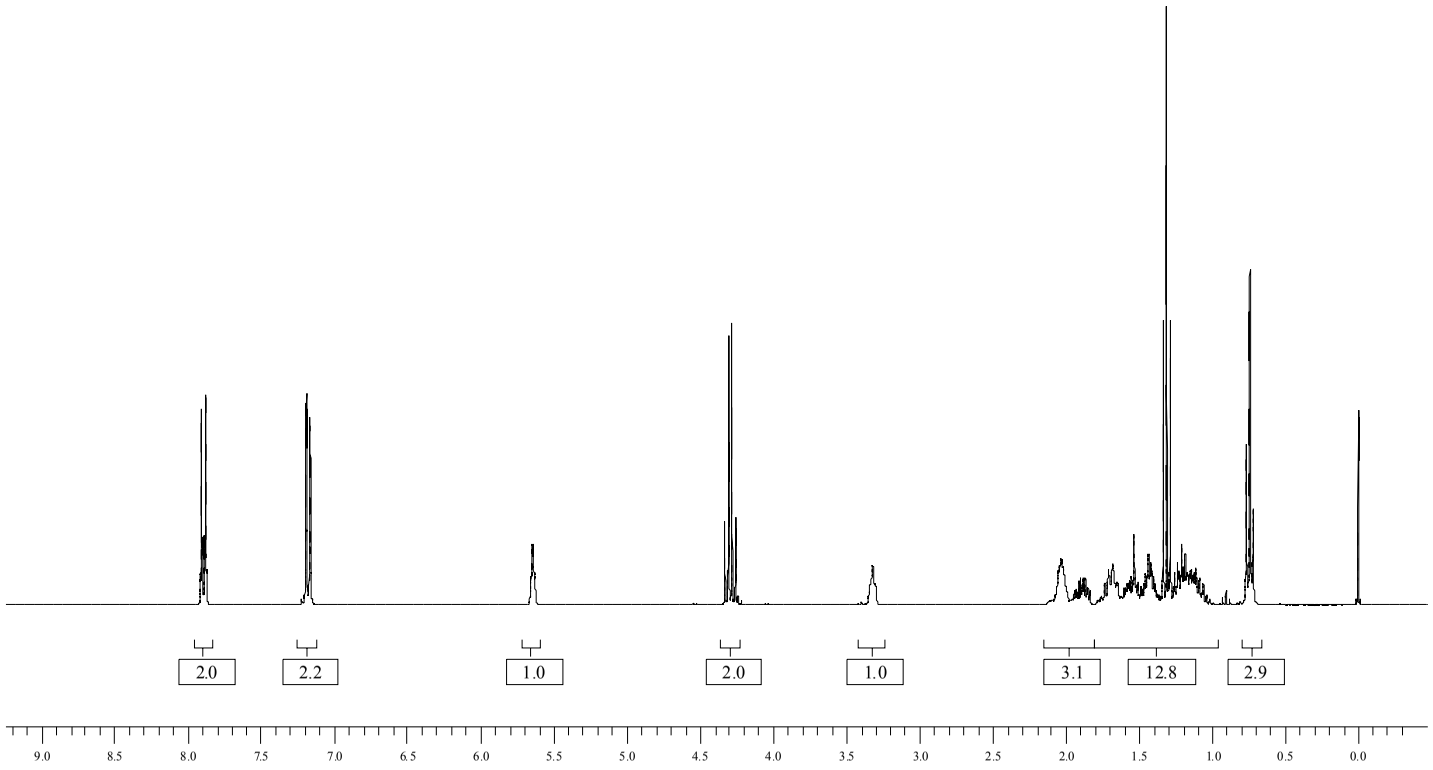
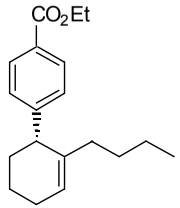


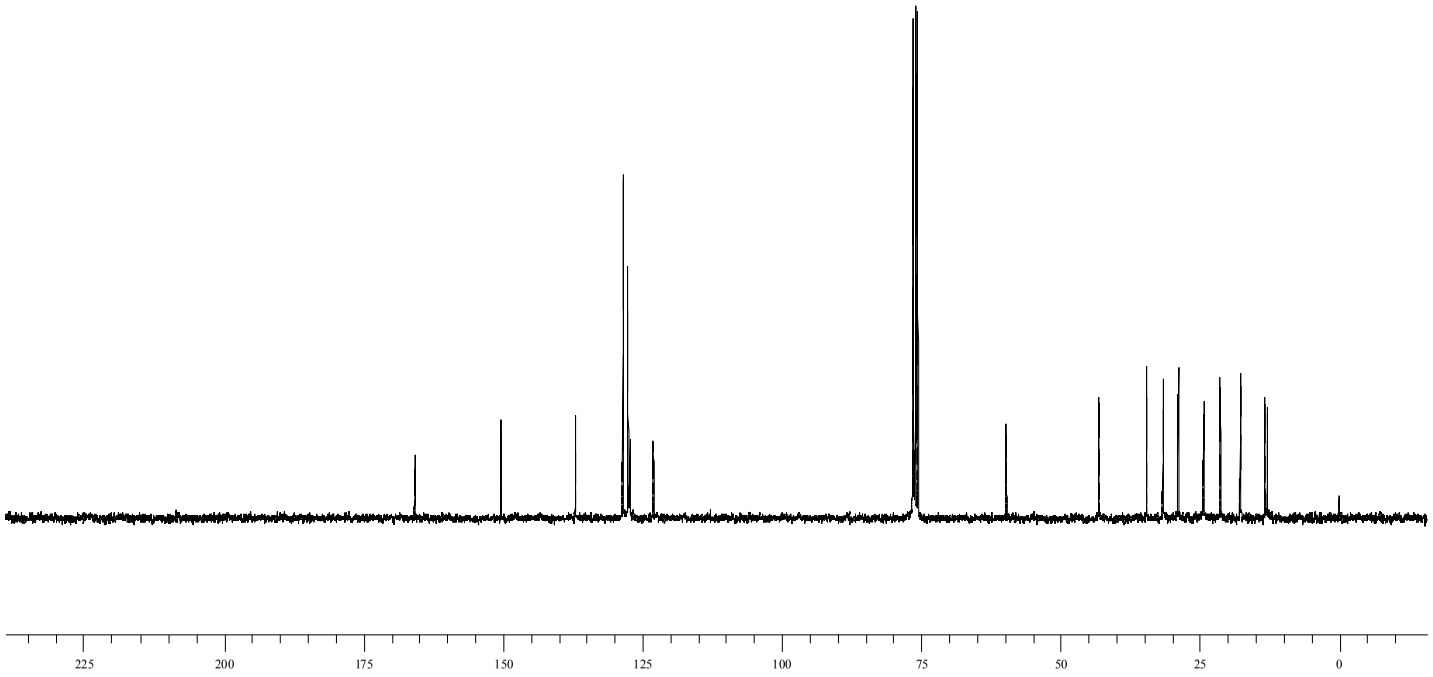

CO2Et

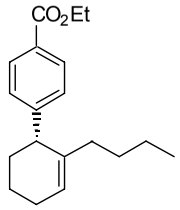
6c


2.0
2.2
1.0
2.0
1.0
3.1
12.8
2.9
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0

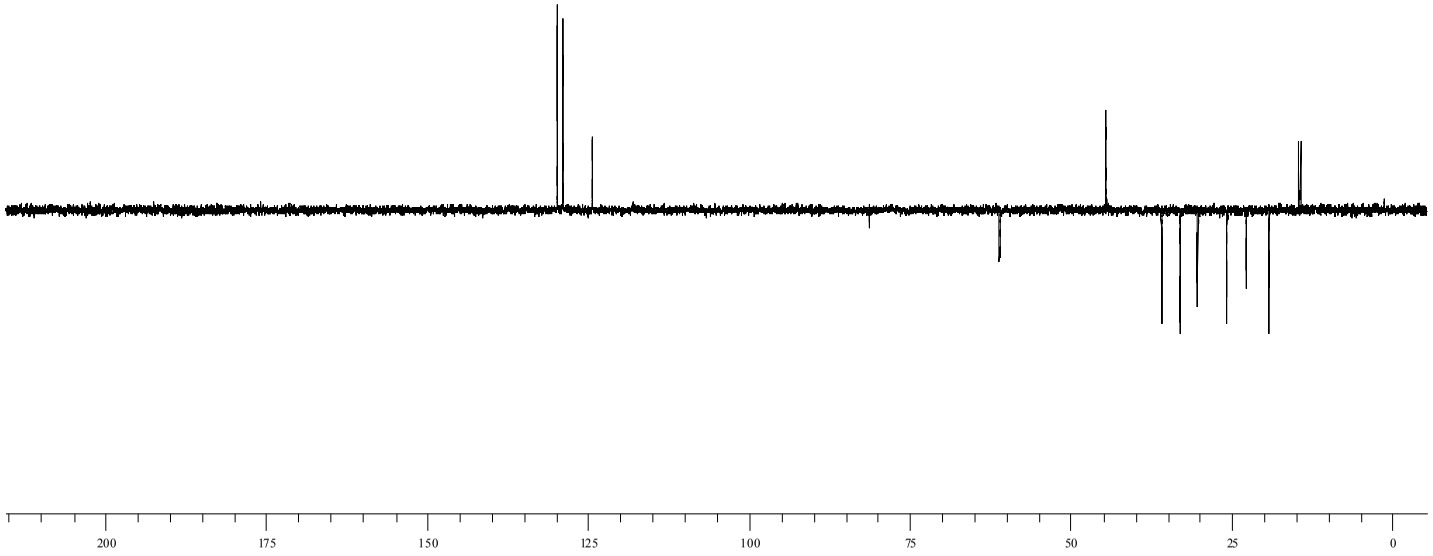


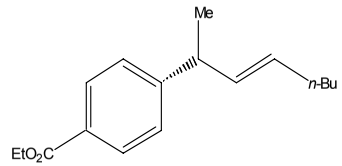
6c



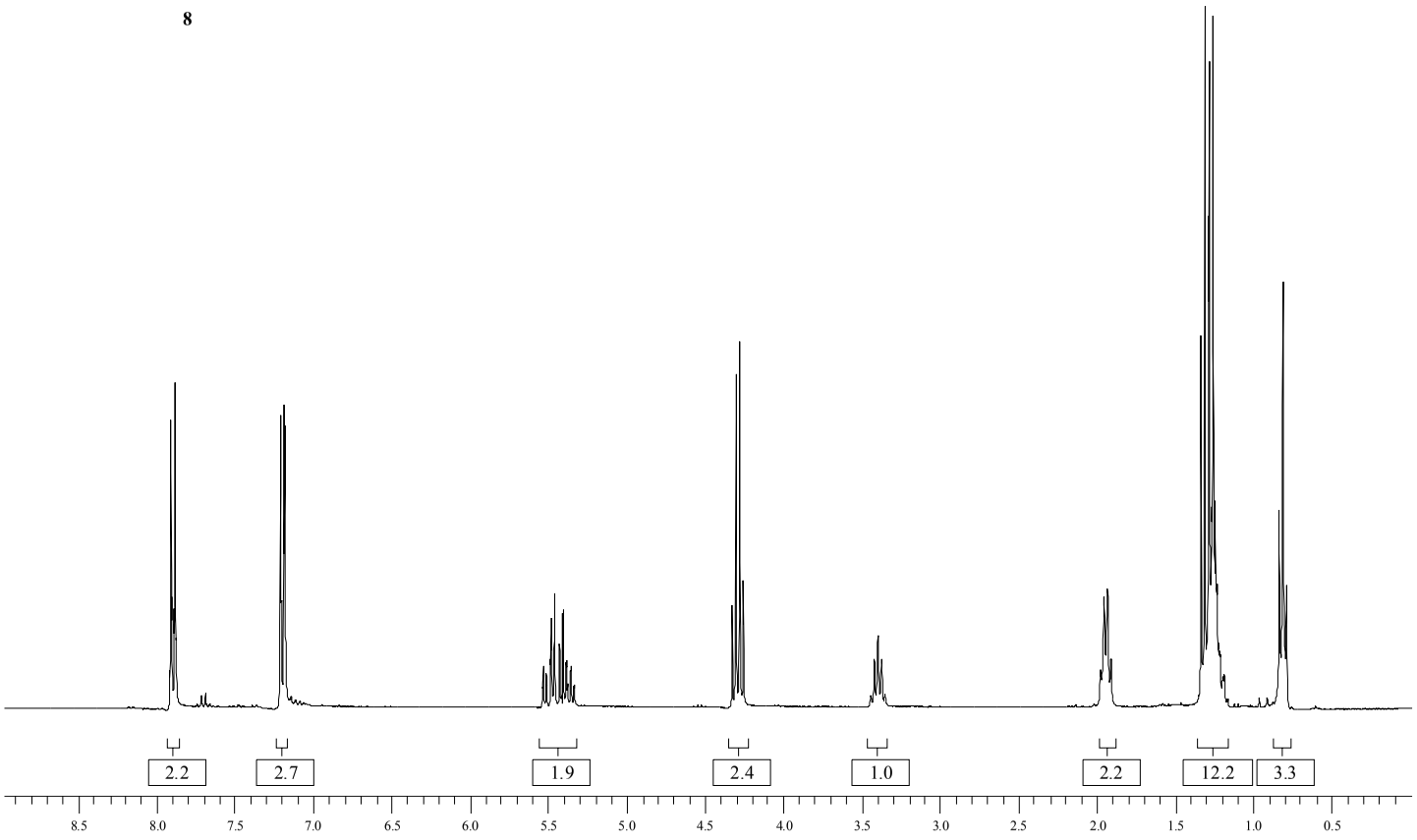


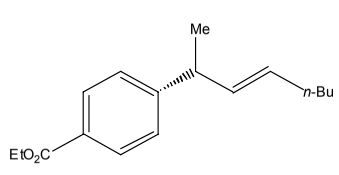
6c




Me
n-Bu
EtO2C

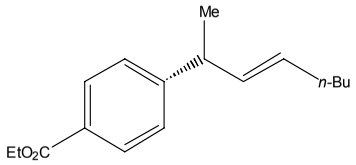
8


2.2
2.7
1.9
2.4
1.0
2.2
12.2
3.3
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5


Me
n-Bu
EtO2C

8

180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0



8