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Construction of C-S Bonds with a Quaternary Stereocenter through a Formal Michael Reaction. Asymmetric Synthesis of Tertiary Mercaptans

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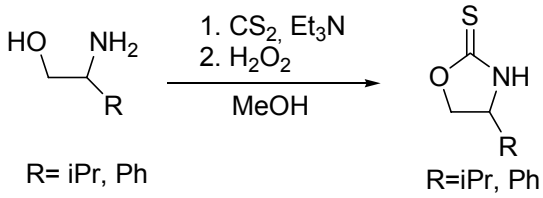
General Procedures.

All non-aqueous reactions were carried out under a nitrogen atmosphere in oven-dried (120ºC) glassware. Melting points were determined with capillary apparatus and are uncorrected. Proton nuclear magnetic resonance (200, 300 or 500 MHz) spectra and ^{13}C spectra (50, 75 or 125 MHz) were recorded at room temperature for $CDCl_3$ solutions, unless otherwise stated. All chemical shifts are reported as δ values (ppm) relative to residual $CHCl_3$ $^{\delta}H$ (7.27 ppm) and $CHCl_3$ $^{\delta}C$ (77.0 ppm) as internal standards, respectively. Optical rotations were measured at 25 ± 0.2ºC in a Perkin-Elmer 243 B instrument. HPLC analyses were performed on analytical columns (25cm, phase Lichrosorb-si 60) and (25 cm, phase Chiralcel OD) with flow rates using 1mL/min and 0.5mL/min respectively, using a DAD. TLC analyses were taken in Merck aluminium sheets, silica gel 60 F254, plates. Flash chromatography was executed with Merck Kiesegel 50 (230-400 mesh) using mixtures of ethyl acetate and hexane as eluants. Non acid silica gel was prepared by thorough stirring of silicagel with saturated solution of sodium bicarbonate (300mL of solution for 100g of silicagel) and evaporation of water in an oven at 80ºC for 72 hours. Et_2O and THF were distilled from sodium metal/benzophenone ketyl. Methylene chloride was shaken with concentrated sulfuric acid, dried over potassium carbonate and distilled from calcium hydride. All others reagents and solvents were commercial and used as it.

Preparation of oxazolidine- 2-thiones



(Adapted from: Li, G.; Ohtani, T.; *Heterocycles* **1997**,*45*, 2471-2474).

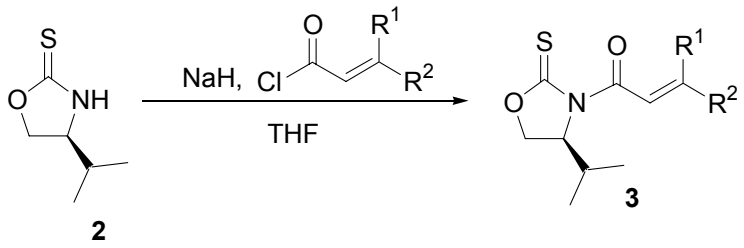
A solution of (*S*)-valinol (5.57 mL, 50.0 mmol) in methanol (50mL), was treated successively with triethylamine (6.95 mL, 50.0 mmol) and carbon disulfide (4.51 mL, 75.0 mmol), with ice cooling under a nitrogen atmosphere. The resulting solution was stirred at room temperature for 0.5 h after which hydrogen peroxide (30%, 8-10mL, 75-100mmol) was added at such a rate that reflux of the solvent was observed until the upper solution of the reaction mixture no longer became cloudy by addition of extra hydrogen peroxide. The reaction mixture was then cooled down to room temperature, filtered, and concentrated under reduced pressure. An aqueous 1M sodium hydroxide

[#] (Crystal structure analysis) the Organisch-chemisches Institut der Universität Zürich, Winterthurerstrasse 190, CH-8057, Zürich, Switzerland.

solution (20 mL) was added to this residue to free the triethylamine, and the volatiles were removed in vacuo. Same operation was repeated twice. The mixture was finally neutralized (pH 7) with 6M hydrochloric acid (6M). Methylene chloride (50 mL) was added and the resulting solution washed with brine (50 mL) and evaporated under reduced pressure to dryness. Purification of crude material was carried out by flash column chromatography on silica gel (eluent ethyl acetate:hexane).

The same procedure was employed to prepare 4-(*R*)-phenyl-1,3-oxazolidine-2-thione, starting from (*R*)-phenylglycinol. (Compound described in *J. Org. Chem.* **1995**, *60*, 6604).

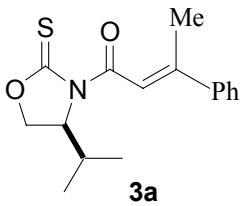
General Procedure for the acylation of oxazolidine-2-thione.



2 **3**

A solution of *NH*-oxazolidine-2-thione (5.0 mmol) in THF (5.0 mL) was added dropwise to a suspension of NaH (60% dispersion in mineral oil, 0.3 g, 7.5 mmol) in THF (10 mL) cooled to 0ºC, under a nitrogen atmosphere. The resulting mixture was stirred at 0ºC for 45 min and then a solution of the corresponding acid chloride[1] (6.0 mmol) in THF (2 mL) was added slowly at the same temperature. The mixture was stirred at 0ºC until disappearance of the starting oxazolidine-2-thione as monitored by TLC (typically 8-12 h). The reaction mixture was then quenched with a saturated solution of ammonium chloride (30 mL) and the organic solvent was eliminated in the rotary evaporator. The mixture was then extracted with methylene chloride (3 x 50 mL), the organic phase washed with a saturated solution of sodium bicarbonate (2 x 100 mL) and brine (100 mL), dried over $MgSO_4$, and the solvent evaporated under reduced pressure. The crude material was purified by flash chromatography using a neutralized silica gel (see General Procedures) and a mixture of ethyl acetate and hexane as eluent.

Preparation of (*S*)-*N*-[3-phenyl-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3a)



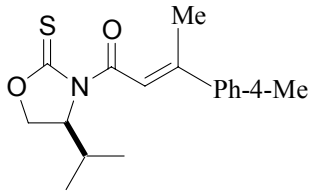
3a

The indicated compound (**3a**) was prepared according to the general procedure to provide the pure product as an oil in 76 % yield after flash chromatography using non acid silica gel

[1] Configurationally pure (*E*)-β,β-disubstituted enoyl chlorides were obtained from the corresponding carboxylic acids, the latter obtained through Horner-Wadsworth-Emmons olefination of the respective aryl methyl ketone (for compounds **3a-h** and **6**) or propiophenone (for compound **3i**) with diethyl carboxymethanephosphonate and purification of *E* isomer via crystallization (adapted from P. Coutrot, M. Snoussi, P. Savignac *Synthesis* **1978**, 133). Alternatively, the required *E*-configured carboxylic acid for compound **3j** was obtained by conjugate addition of butyl cuprate to methyl phenylpropinoate and subsequent hydrolysis (adapted from R. J. Anderson, V. L. Corbin, G. Cotterrell, G. R. Cox, C. A. Henrick, F. Schaub *J. Am. Chem. Soc.* **1975**, *97*, 1197).

(EtOAc/Hexane, 1/9); [α]$_D$ +198.6 (c=1.04, CH_2Cl_2); IR (film) 2970, 1684, 1614, 1456 cm^{-1}; ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.75 (d, J=1.2 Hz, 1H), 7.62-7.67 (m, 2H), 7.39-7.48 (m, 3H), 4.72-4.82 (m, 1H), 4.40-4.51 (m, 2H), 2.54 (s, 3H), 2.42-2.53 (m, 1H), 0.96 (d, J=12.3Hz, 3H), 0.94 (d, J=12 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 186.3, 166.3, 154.6, 141.8, 129.2, 128.5, 126.6, 118.7, 67.9, 63.1, 28.9, 18.6, 18.2, 14.9.

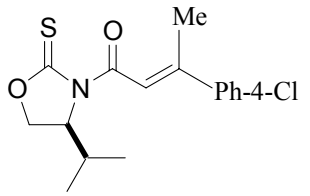
Preparation of (*S*)-*N*-[3-(4-methylphenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3b)



3b

The indicated compound (**3b**) was prepared according to the general procedure to provide the pure product as a white solid in 74 % yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/9); mp 60-64 °C; [α]$_D$ +204.5 (c=1.06, CH_2Cl_2); IR (KBr) 2970, 1684, 1614, 1210 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.75 (s, 1H), 7.56 (d, J=7.8 Hz, 1H), 7.22 (d, J=7.8Hz, 2H), 4.77-4.79 (m, 1H), 4.46 (t, 8.8Hz, 1H), 4.42 (dd, J=9.3 Hz, J'=3.1 Hz, 1H), 2.50 (s, 3H), 2.45-2.49 (m, 1H), 2.4 (s, 3H), 0.97 (d, J=7.3 Hz, 3H), 0.93 (d, J=6.8 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 186.4, 166.3, 154.9, 139.5, 138.9, 129.2, 126.5, 117.8, 67.8, 63.1, 28.9, 21.2, 18.5, 18.2, 14.9; elemetal analysis calc. for $C_{17}H_{21}NO_2S$, C 67.29, H 6.98, N 4.62, S 10.57, found C 68.40 H 6.90 N 4.74 S 10.32.

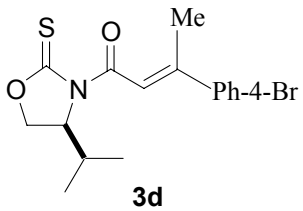
Preparation of (*S*)-*N*-[3-(4-chlorophenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3c)



3c

The indicated compound (**3c**) was prepared according to the general procedure to provide the pure product as a white solid in 60% yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/9); mp 64-67 °C; [α]$_D$ +185.6 (c=1.12, CH_2Cl_2); IR (KBr) 2970, 1667, 1614, 1193 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.70 (s, 1H), 7.58 (d, J=8.3 Hz, 2H), 7.38 (d, J=8.3 Hz, 2H), 4.77-4.79 (m, 1H), 4.48 (t, J=9.3 Hz, 1H), 4.43 (dd, J=3.9 Hz, J'=9.3Hz, 1H), 2.50 (s, 3H), 2.45-2.47 (m, 1H), 0.96 (d, J=20Hz, 3H), 0.95 (d, J=20Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 186.4, 166.2, 152.8, 140.3, 135.3, 128.8, 127.9, 119.2, 67.9, 63.1, 28.9, 18.4, 18.2, 15.0; elemental analysis calc. for $C_{16}H_{18}NO_2SCl$, C 59.34, H 5.60, N 4.34, S 9.90, found C 60.05 H 5.58 N 4.48 S 9.91.

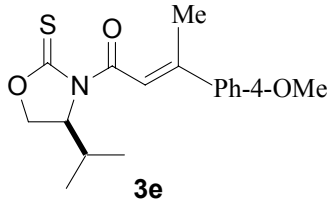
Preparation of (*S*)-*N*-[3-(4-bromophenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3d)



3d

The indicated compound (**3d**) was prepared according to the general procedure to provide the pure product as an oil in 66% yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/20); $[\alpha]_D$ +146.0 (c=0.62, CH_2Cl_2); IR (film) 2964, 1678, 1367, 1196 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.70 (d, J=1.6 Hz, 1H), 7.52 (m, 4H), 4.78 (m, 1H), 4.47 (t, J=9.3 Hz, 1H), 4.42 (dd, J=3.8 and 2.2 Hz, 1H), 2.49 (d, J=1.0 Hz, 3H), 2.46 (m, 1H), 0.97 (d, J=7.4 Hz, 3H), 0.93 (d, J=6.9 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 186.3, 166.0, 152.5, 140.6, 131.6, 128.0, 123.4, 119.1, 67.9, 63.0, 28.8, 18.3, 18.1, 14.9.

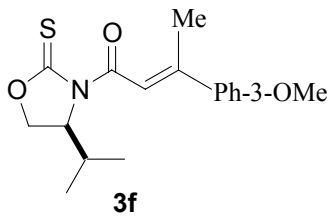
Preparation of (*S*)-*N*-[3-(4-methoxyphenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3e)



3e

The indicated compound (**3e**) was prepared according to the general procedure to provide the pure product as an oil in 68% yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/9); $[\alpha]_D$ +214.9 (c=1.01, CH_2Cl_2); IR (film) 2959, 1677, 1597, 1503, 1362, 1324, 1292, 1249, 1179, 1023 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.74 (s, 1H) 7.64 (d, J=8.8 Hz, 2H), 6.94 (d, J=8.8 Hz, 2H), 4.77-4.80 (m, 1H), 4.47 (t, J=8.8 Hz, 1H), 4.42 (dd, J=9.3 Hz, J'=3.9 Hz, 1H), 3.85 (s, 3H), 2.53 (s, 3H), 2.44-2.50 (m, 1H), 0.95 (d, J=18.6 Hz, 3H), 0.94 (d, J=18.6 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 186.4, 166.3, 160.7, 154.7, 134.1, 128.1, 116.7, 113.0, 67.8, 63.1, 55.3, 28.9, 18.4, 18.2, 14.9.

Preparation of (*S*)-*N*-[3-(3-methoxyphenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3f)

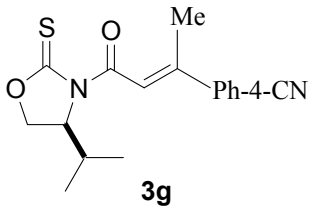


3f

The indicated compound (**3f**) was prepared according to the general procedure to provide the pure product as an oil in 64 % yield after flash chromatography using non acid silica gel

(EtOAc/Hexane, 1/9); [α]$_D$ +181.7 (c=1.06, CH_2Cl_2); IR (film) 2963, 1678, 1607, 1577, 1380, 1361, 1330, 1288, 1218, 1194 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.93 (d, J=6.5 Hz, 3H), 0.97 (d, J=7.0 Hz, 3H), 2.43-2.50 (m, 1H), 2.51 (s, 3H), 3.85 (s, 3H), 4.42 (dd, J=9.5, 4.0 Hz, 1H), 4.47 (t, J=9.0 Hz, 1H), 4.76-4.80 (m, 1H), 6.92 (dd, J=17.5, 3.5 Hz, 1H), 7.20-7.25 (m, 2H), 7.32 (t, J=8.0 Hz, 1H), 7.74 (s, 1H); ^{13}C (125 MHz, $CDCl_3$) δ 186.4, 166.2, 159.6, 154.5, 143.4, 129.5, 119.0, 118.9, 114.9, 112.0, 67.9, 63.1, 55.2, 28.9, 18.6, 18.2, 14.9.

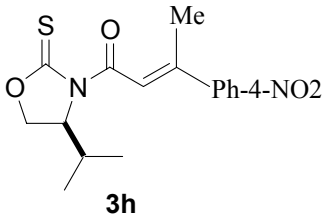
Preparation of (*S*)-*N*-[3-(4-cyanophenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3g)



3g

The indicated compound (**3g**) was prepared according to the general procedure to provide the pure product as an white solid in 72 % after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/9); mp 128-131°C; [α]$_D$ +189.7 (c=0.136, CH_2Cl_2); IR (film) 2978, 2237, 1682, 1621, 1367, 1198 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71 (m, 5H), 4.78 (m, 1H), 4.49 (t, J=9.3 Hz, 1H), 4.46 (dd, J=9.2, 3.3 Hz, 1H), 2.48 (s, 3H), 2.46(m, 1H), 0.98 (d, J=7.4 Hz, 3H), 0.94 (d, J=6.9 Hz, 3H) ; ^{13}C (125 MHz, $CDCl_3$) δ 186.5, 166.0, 150.8, 146.4, 132.5, 127.3, 121.5, 118.6, 112.6, 68.3, 63.2, 29.0, 18.4, 18.3, 15.1; elemetal analysis calc. for $C_{17}H_{18}N_2O_2S$, C 64.94, H 5.77, N 8.91, S 10.20, found C 65.02, H 5.81, N 8.62, S 10.35.

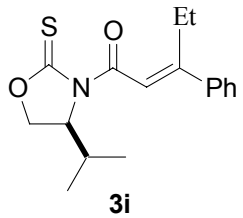
Preparation of (*S*)-*N*-[3-(4-nitrophenyl)-2-(*E*)-butenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3h)



3h

The indicated compound (**3h**) was prepared according to the general procedure to provide the pure product as a solid in 47 % yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/3); mp 114-117 °C; [α]$_D$ + 91.9 (c=0.62, CH_2Cl_2); IR (film) 2968, 1678, 1593, 1341, 1188, 1145, 857 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.95 (d, J=7.0 Hz, 3H), 0.99 (d, J=6.5 Hz, 3H), 2.44-2.50 (m, 1H), 2.51 (s, 3H), 4.46 (dd, J=9.5 Hz, J'=4.0 Hz, 1H), 4.50 (t, J=9.5 Hz, 1H), 4.78-4.81 (m, 1H), 7.71 (s, 1H), 7.79 (d, J=9.0 Hz, 2H), 8.27 (d, J=8.5 Hz, 2H);^{13}C (125 MHz, $CDCl_3$) δ 186.4, 165.9, 150.0, 148.1, 147.9, 127.9, 127.4, 123.8, 123.5, 121.9, 68.2, 63.1, 28.9, 18.4, 18.2, 14.9; elemetal analysis calc. for $C_{16}H_{18}N_2O_4S$, C 57.47, H 5.43, N 8.38, S 9.59, found C 57.61, H 5.48, N 8.55, S 9.78.

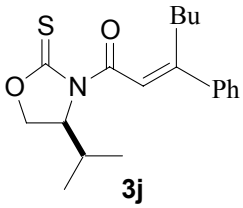
Preparation of (*S*)-*N*-[3-phenyl-2-(*E*)-pentenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3i)



3i

The indicated compound (**3i**) was prepared according to the general procedure to provide the pure product as a white solid in 81 % yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/10); mp 78-80 °C; $[\alpha]_D$ +196.1 (c=1.01, CH_2Cl_2); IR (KBr) 2970, 1684, 1596, 1210 cm^{-1}; ^1H NMR (300 MHz, $CDCl_3$) δ 7.60-7.64 (m, 2H), 7.59 (s, 1H), 7.37-7.44 (m, 3H), 4.76-4.81 (m, 1H), 4.46 (t, J=15.5 Hz, 1H), 4.42 (dd, J=16.0 Hz, J'=7.5 Hz, 1H), 2.91-3.11 (m, 2H), 2.42-2.53 (m, 1H), 1.15 (t, J=12.5 Hz, 3H), 0.97 (d, J=17.8 Hz, 3H), 0.95 (d, J=17.8 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 186.3, 166.0, 160.6, 140.6, 129.1, 128.5, 126.9, 118.4, 67.8, 63.1, 28.9, 24.7, 18.2, 14.9, 13.6; elemetal analysis calc. for $C_{17}H_{21}NO_2S$, C 67.29, H 6.97, N 4.62, S 10.57, found C 67.25 H 7.59 N 4.69 S 10.79.

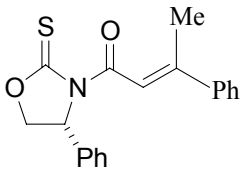
Preparation of (*S*)-*N*-[3-phenyl-2-(*E*)-heptenoyl]-4-isopropyl-1,3-oxazolidine-2-thione (3j)



3j

The indicated compound (**3j**) was prepared according to the general procedure to provide the pure product as an oil in 40 % yield after flash chromatography using non acid silica gel (EtOAc/Hexane, 1/9); $[\alpha]_D$ +74.1 (c= 0.86, CH_2Cl_2); IR (film) 2960, 1679, 1605, 1370, 1331, 1195 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.61 (d, J=6.7 Hz, 2H), 7.53 (s, 1H), 7.40 (s, 1H), 4.78 (m, 1H), 4.47 (t, J=9.2 Hz, 1H), 4.42 (dd, J=9.3, 4.10 Hz, 1H), 3.05 (m, 1H), 2.97 (m, 1H), 2.47 (m, 1H), 1.45 (m, 2H), 1.38 (m, 2H), 0.97 (d, J=6.8 Hz, 3H), 0.88 (t, J=7.4 Hz, 3H) ; ^{13}C (125 MHz, $CDCl_3$) δ 186.3, 166.2, 159.2, 141.0, 129.0, 128.5, 126.9, 119.2, 67.8, 63.1, 31.1, 31.0, 28.9, 22.7, 18.2, 15.9, 13.8.

Preparation of (*R*)-*N*-[3-phenyl-2-(*E*)-butenoyl]-4-phenyl-1,3-oxazolidine-2-thione (6)



6

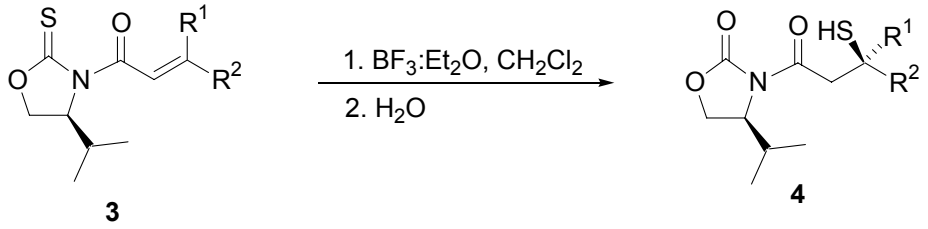
The indicated compound (**6**) was prepared according to the general procedure to provide the pure product as a white syrup in 94 % yield after flash chromatography using non acid silica gel

(EtOAc/Hexane, 1/9); [α]$_D$ –140.3 (c=1, CH_2Cl_2); IR (film) 3062, 1682, 1608, 1367, 1341, 1193, cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.71 (s, 1H), 7.53 (d, J=6.5 Hz, 2H), 7.42-7.30 (m, 8H), 5.76 (dd, J= 8.5, 4.5 Hz, 1H), 4.86 (t, J=9.0 Hz, 1H), 4.45 (dd, J=9.0, 5.0 Hz, 1H), 2.46 (s, 3H); ^{13}C (50 MHz, $CDCl_3$) δ 185.9, 165.7, 155.5, 141.8, 138.3, 129.4, 129.3, 129.1, 128.8, 128.6, 126.6, 126.0, 118.6, 74.2, 62.2; elemental analysis calc. for $C_{19}H_{17}NO_2S$, C 70.56, H 5.30, N 4.33, S 9.91, found C 70.59, H, 5.27, N 4.40, S, 9.58.

Preparation of *E/Z* mixtures of variable compositions for compounds 4d, 4g, 4h, and 6

E/Z mixtures of variable composition for compounds **4d**, **4g**, **4h**, and **6** were obtained through chromatographic enrichment of the original *E/Z* mixture, the latter obtained by acylation of the corresponding oxazolidinethione with a *E/Z* mixture of the respective acid chloride. The *E/Z* mixture of acid chlorides was obtained in each case starting from the original mixture of *E* and *Z* isomers of the respective α,β-unsaturated carboxylic acid resulted from either olefination or conjugate addition step as described above.

Reaction of *N*-enoyl oxazolidinone-2-thiones 3 with $BF_3{\cdot}Et_2O$.



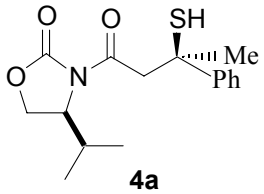
3 **4**

To a solution of the corresponding *N*-enoyl oxazolidinone-2-thione (**3**) (0.5 mmol) in methylene chloride (8 mL) at –30ºC (bath temperature) or at the corresponding temperature (see Table 1), under a nitrogen atmosphere, was added dropwise via syringe BF_3-Et_2O (1.0 mmol, 0.127 mL) and the mixture was stirred at that temperature until completion as monitored by ^1H NMR. The mixture was then poured into a saturated solution of sodium bicarbonate (20 mL) and the layers were separated. The organic layer was washed with brine (50 mL), dried over $MgSO_4$, and the solvent evaporated under reduced pressure. The crude material was purified by silica gel chromatography using a mixture of ethyl and hexane (10:90) as eluent**.**

When other Lewis acids were used for the same reaction, the above protocol was followed employing the corresponding Lewis acids instead of BF_3:Et_2O.

Example at 3.0 mmol scale: BF_3-Et_2O (6.0 mmol, 0.762 mL) was added dropwise via syringe to a solution of **6** (*E:Z* 100:0) (3.0 mmol, 969 mg) in methylene chloride (50 mL) under a nitrogen atmosphere at –30ºC (bath temperature). The resulting mixture was stirred at the same temperature until no peak of starting material was observable by ^1H NMR of aliquots (48 hours). The mixture was then poured into a saturated solution of sodium bicarbonate (80 mL) and the layers were separated. The organic layer was washed with brine (100 mL), dried over $MgSO_4$, and the solvent evaporated under reduced pressure. The crude material was purified by silica gel chromatography using a mixture of ethyl acetate and hexane (10:90) as eluent to give 634 mg (62%) of **7**. For characterization data of **7**, see below.

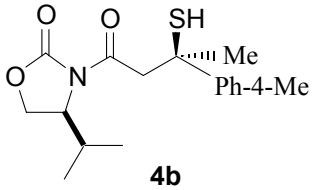
(*S*)-*N*-[(3*R*)-3-phenyl-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4a)



4a

The indicated compound (**4a**) was prepared according to the general procedure to provide the pure product (d.r 99:1) as an oil in 80 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ + 61.57 (c=1.34, CH_2Cl_2); IR (film) 2976, 1776, 1701, 1390, 1362, 1305, 1207 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.59 (d, J=7.8 Hz, 2H), 7.33(t, J=7.8 Hz, 2H), 7.23(t, J=7.4 Hz, 1H), 4.35-436 (m, 1H), 4.12-4.23 (m, 2H), 3.84 (d, J=17.5 Hz, 2H), 2.84 (s, 1H), 2.06-2.25 (m, 1H), 1.94 (s, 3H), 0.84 (d, J=7.4 Hz, 3H), 0.79 (d, J=6.8 Hz, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 169.8, 153.9, 146.1, 128.1, 126.7, 125.6, 63.3, 58.3,49.2, 47.3, 32.0, 28.4, 17.8,14.6.

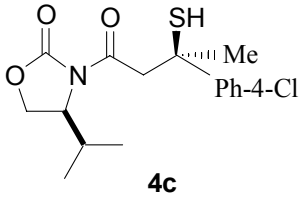
(*S*)-*N*-[(3*R*)-3-(4-methylphenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4b)



4b

The indicated compound (**4b**) was prepared according to the general procedure to provide the pure product (d.r 97:3) as an oil in 77 % yield after flash chromatography (EtOAc/Hexane, 1/9); IR (film) 2971, 1772, 1702, 1386, 1368, 1210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.47 (d, J=8.3 Hz, 2H), 7.14 (d, J=7.8 Hz, 2H), 4.30-4.38 (m, 1H), 4.15-4.24 (m, 2H), 3.95 (d, J=17.1 Hz, 1H) (minor), 3.84 (d, J=17.5 Hz, 2H) (major), 3.79 (d, J=17 Hz, 2H) (major), 3.66 (d, J=17.2 Hz, 1H) (minor), 2.85 (s, 1H) (minor), 2.82 (s, 1H) (major), 2.32 (s, 3H), 2.18-2.29 (m, 1H), 1.92 (s, 3H), 0.85 (d, J=6.8 Hz, 3H), 0.79 (d, J=6.8 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 169.7 (major), 169.6 (minor), 153.8, 143.2 (minor), 143.1 (major), 136.1, 128.8 (minor), 128.7 (major), 125.4, 63.2 (major), 63.0 (minor), 58.3 (minor), 58.2 (major), 49.1, 47.0 (major), 46.9 (minor), 31.9 (major), 31.7 (minor), 28.2 (major), 28.1 (minor) , 20.8 (minor), 20.7 (major), 17.7 (major), 17.6 (minor), 14.5 (minor), 14.4 (major).

(*S*)-*N*-[(3*R*)-3-(4-chlorophenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4c)

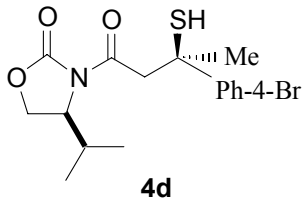


4c

The indicated compound (**4c**) was prepared according to the general procedure to provide the pure product (d.r 92:8) as an oil in 72 % yield after flash chromatography (EtOAc/Hexane, 1/9); IR (film) 2970, 1772, 1702, 1384,1368, 1245, 1210 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.55 (d,

J=8.3 Hz, 2H), 7.31 (d, J=8.8 Hz, 2H), 4.38-4.36 (m, 1H), 4.25-4.18 (m, 2H), 3.99 (d, J=17.1 Hz, 1H) (minor), 3.86 (d, J=17.6 Hz, 2H)(major), 3.81 (d, J=17.6 Hz, 2H)(major), 3.66 (d, J=17.1 Hz, 1H) (minor), 2.91 (s, 1H) (minor), 2.86 (s, 1H) (major), 2.20-2.23 (m, 1H), 1.92 (s, 3), 0.84 (dd, J=28.4 Hz, J'=27.9 Hz, 6H); ^{13}C (125 MHz, $CDCl_3$) δ 169.5, 153.9, 144.8, 132.5, 128.2, 127.2, 63.3, 58.3, 49.2, 46.9, 32.1 (major), 32.0 (minor), 28.3, 17.8.

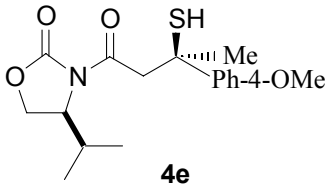
(*S*)-*N*-[(3*R*)-3-(4-bromophenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4d)



4d

The indicated compound (**4d**) was prepared according to the general procedure to provide the pure product (d.r 98:2) as an oil in 76 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ +52.6 (c=0.5, CH_2Cl_2); IR (film) 2964, 1786, 1383, 1197cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.45 (m, 4H), 4.35 (m, 1H), 4.23 (t, J=8.6 Hz, 1H), 4.18 (dd, J=9.1 and 3.4 Hz, 1H), 3.81 (apt, J=22.1 Hz, 2H), 2.87 (s, 1H) (min), 2.83 (s, 1H), 2.22 (m, 1H), 1.89 (s, 3H), 0.85 (d, J=7.3 Hz, 3H), 0.80 (d, J=7.4 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 169.6, 154.0, 145.4, 131.3, 127.6, 120.8, 63.4, 58.4, 49.3, 47.0, 32.2, 28.4, 17.9, 14.6.

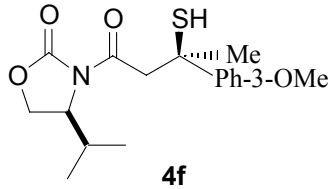
(*S*)-*N*-[(3*R*)-3-(4-methoxyphenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4e)



4e

The indicated compound (**4e**) was prepared according to the general procedure to provide the pure product (d.r 52:48) as an oil in 65 % yield after flash chromatography (EtOAc/Hexane, 1/9); ^1H NMR (500 MHz, $CDCl_3$) δ 7.50 (d, J=8.8 Hz, 2H), 6.85 (d, J=8.8 Hz, 2H), 4.35 (m, 1H), 4.20 (m, 2H), 3.64-3.94 (m, 5H), 2.85 (s, 1H, minor), 2.81 (s, 1H, major), 2.23 (m, 1H), 1.93 (s, 3H, major), 1.92 (s, 3H, minor), 0.78-0.87 (m, 6H); ^{13}C (75 MHz, $CDCl_3$) δ 169.9 (major), 169.8 (minor), 158.2, 153.9, 138.4 (minor), 138.2 (major)126.9, 113.5, 63.3, 58.5 (minor), 58.4 (major), 55.2, 49.3, 47.0 (major), 46.9 (minor), 32.2 (major), 32.0 (minor), 28.4, 17.9, 14.7 (minor), 14.6 (major).

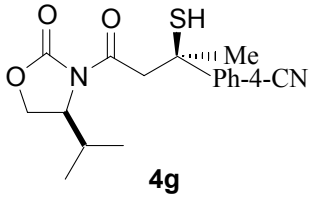
(*S*)-*N*-[(3*R*)-3-(3-methoxyphenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4f)



4f

The indicated compound (**4f**) was prepared according to the general procedure to provide the pure product (d.r 93:7) as an oil in 83 % yield after flash chromatography (EtOAc/Hexane, 1/9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 0.81 (d, J=6.5 Hz, 3H), 0.86 (d, J=6.5 Hz, 3H), 1.93 (s, 3H), 2.20-2.30 (m, 1H), 2.85 (s, 1H) (major), 2.90 (s, 1H) (minor), 3.65-4.05 (m, 5H), 4.15-4.18 (m, 1H), 4.21 (t, J=9.0 Hz, 1H), 4.34-4.40 (m, 1H), 6.78 (d, J=7.5 Hz, 1H), 7.12-7.20 (m, 2H), 7.25 (t, J=7.5 Hz, 1H);^{13}C (125 MHz, $CDCl_3$) δ 169.7 (major), 169.6 (minor), 159.4, 153.9, 147.9, 129.1, 117.8, 112.2, 111.8, 63.3, 58.4, 55.1, 49.1, 47.3, 32.0 (major), 31.9 (minor), 28.4, 17.8 (major), 17.7 (minor), 14.6.

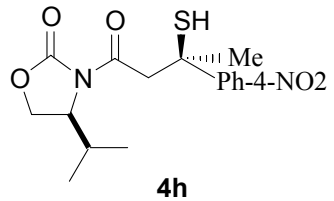
(*S*)-*N*-[(3*R*)-3-(4-cyanophenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4g)



4g

The indicated compound (**4g**) was prepared according to the general procedure to provide the pure product (d.r 92:8) as an oil in 73 % yield after flash chromatography (EtOAc/Hexane, 1/9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.71(d, J=8.3 Hz, 2H), 7.62 (d, J=8.3 Hz, 2H), 4.34 (m, 1H), 4.25 (t, J=9.3 Hz, 1H), 4.19 (dd, J=9.1, 3.3 Hz, 1H), 4.03 (d, J=18.0 Hz, 1H) (minor), 3.87 (m, 2H), 3.67(d, J=18.0 Hz, 1H) (minor), 2.89 (s, 1H) (minor), 2.84 (s, 1H), 2.22 (m, 1H), 1.89 (s, 3H), 0.97 (d, J=6.7 Hz, 3H) (minor), 0.93 (d, J=6.7 Hz, 3H) (minor), 0.85 (d, J=6.6 Hz, 3H), 0.81 (d, J=6.6 Hz, 3H), 0.81 (d, J=6.6 Hz, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 169.4, 154.0, 151.9, 132.1, 126.6, 118.6, 110.6, 63.6, 58.4, 49.4, 47.1, 32.1, 28.4, 17.8, 14.7.

(*S*)-*N*-[(3*R*)-3-(4-nitrophenyl)-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (4h)

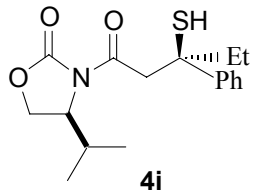


4h

The indicated compound (**4h**) was prepared according to the general procedure to provide the pure product (d.r 91:9) as an oil in 70 % yield after flash chromatography (EtOAc/Hexane, 1/9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 8.18 (d, J=8.7 Hz, 2H), 7.76 (d, J=8.7 Hz, H), 4.35 (m, 1H), 4.26 (t, J=8.8 Hz, 1H), 4.20 (dd, J=9.1, 3.4 Hz, 1H), 3.90 (s, 2H), 2.92 (s, 1H) (minor), 2.88 (s, 1H), 2.23 (m, 1H), 1.91 (s, 3H), 0.98 (d, J=10.9 Hz, 3H) (minor), 0.94 (d, J=10.9 Hz, 3H) (minor), 0.85 (d,

J=7.4 Hz, 3H), 0.81 (d, J=6.8 Hz, 3H);^{13}C (125 MHz, $CDCl_3$) δ 169.3, 154.0, 146.4, 126.8, 123.4, 63.5, 58.3, 49.5, 47.0, 32.2, 28.3, 17.8, 14.6.

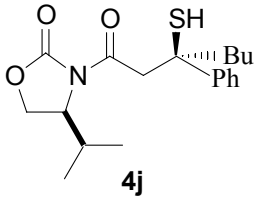
(*S*)-*N*-[(3*R*)-3-phenyl-3-mercaptopentanoyl]-4-isopropyloxazolidin-2-one (4i)



4i

The indicated compound (**4i**) was prepared according to the general procedure to provide the pure product (d.r 98:2) as an oil in 77 % yield after flash chromatography (EtOAc/Hexane, 1/9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J=7.85 Hz, 2H), 7.34-7.31 (m, 2H), 7.24-7.21 (m, 1H), 4.33-4.30 (m, 1H), 4.16-4.15 (m, 2H), 4.11 (d, J=17.1 Hz, 1H) (minor), 3.99 (d, J=17.1 Hz, 1H) (major), 3.71 (d, J=17.1 Hz, 1H) (major), 3.60 (d, J=17.6 Hz, 1H) (minor), 2.87 (s, 1H) (minor), 2.82 (s, 1H) (major), 2.27-2.32 (m, 1H), 2.10-2.25 (m, 2H), 0.83-0.87 (m, 9H); ^{13}C (75 MHz, $CDCl_3$) δ 170.1, 154.0, 144.0, 128.0, 126.5, 63.3, 58.4, 52.4, 47.2 (major), 46.9 (minor), 37.5 (major), 37.3 (minor), 28.4, 17.8, 14.7, 9.1.

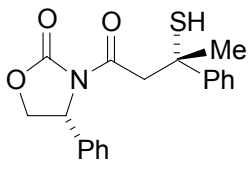
(*S*)-*N*-[(3*R*)- 3-phenyl-3-mercaptoheptenoyl]-4-isopropyloxazolidin-2-one (4j)



4j

The indicated compound (**4j**) was prepared according to the general procedure to provide the pure product (d.r 96:4) as an oil in 68 % yield after flash chromatography (EtOAc/Hexane, 1/9); ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.57 (d, J=8.3 Hz, 2H), 7.32 (t, J= 7.3 Hz, 2H), 7.22 (t, J=7.3 Hz, 1H), 4.31 (m, 1H), 4.15 (m, 2H), 4.00 (d, J=17.8 Hz, 1H), 3.71 (d, J=17.5 Hz, 1H), 2.93 (s, 1H) (minor) 2.88 (s, 1H) (major), 2.29 (m, 1H), 2.09 (m, 2H), 1.27 (m. 3H), 1.15 (m, 1H), 0.85 (m, 9H); ^{13}C (125 MHz, $CDCl_3$) δ 170.1, 154.1, 144.9, 128.0, 126.5, 126.4, 63.4, 58.5, 51.9, 47.6, 44.6, 28.4, 26.8, 22.8, 17.9, 14.7, 13.8.

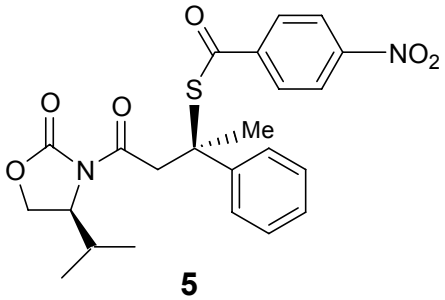
(*S*)-*N*-[(3*R*)-3-phenyl-3-mercaptobutanoyl]-4-isopropyloxazolidin-2-one (7)



7

The indicated compound (**7**) was prepared from **6** according to the general procedure to provide the pure product (d.r 98:2) as an oil in 62 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ - 39 (c=0.69, CH_2Cl_2); IR (film) 2978, 1777, 1708, 1385, 1199 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.54 (d, J=7.5 Hz, 2H), 7.35-7.29 (m, 5H), 7.24-7.20 (m, 1H), 7.16 (d, J=7.5 Hz, 2H), 5.37 (dd, J=8.0, 3.5 Hz, 1H), 4.62 (t, J=9.0 Hz, 1H), 4.22 (dd, J= 8.5, 4.0 Hz, 1H), 3.93 (d, J=16.5 Hz, 1H), 3.77 (d, J=16.5 Hz, 1H), 2.79 (s, 1H), 1.87 (s, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 171.7, 146.0, 138.6, 129.0, 128.5, 128.1, 128.2, 126.7, 125.6, 125.5, 69.7, 57.4, 49.2, 47.3, 31.7.

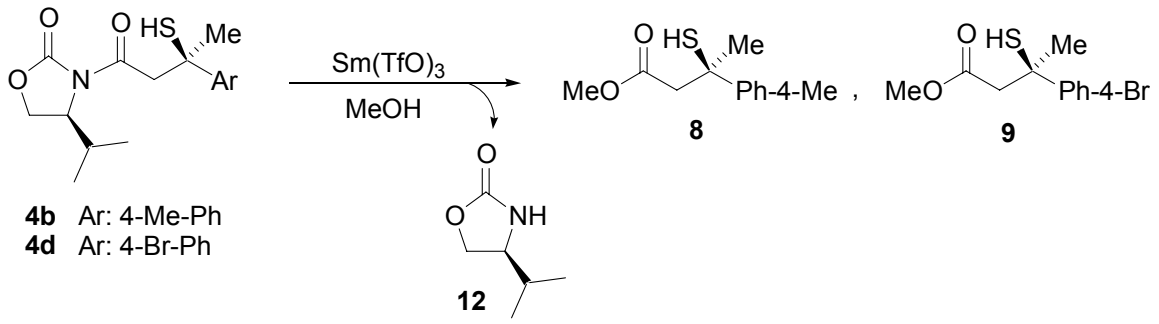
(*S*)-*N*-[(*3*R)-3-(4-nitrobenzoylthio)-3-phenylbutanoyl]-4-isopropyloxazolidin-2-one (5)



5

To a solution of **4a** (0.097 g, 0.32 mmol) in CH_2CL_2 (10 mL) were added successively triethylamine (0.07 mL, 0.47 mmol), a catalytic amount of DMAP, and, dropwise, a solution of 4-nitrobenzoylchloride (0.087 g, 0.47 mmol) in CH_2CL_2 (2 mL). The resulting solution was stirred at 0°C for 4h and then at room temperature for 20 additional hours. Then a saturated solution of ammonium chloride (30 mL) was added and the layers were separated. The organic layer was washed with a saturated solution of $NaHCO_3$ (3x30mL), brine (30 mL), dried over MgSO4 and the solvent evaporated under reduced pressure to give the title compound , wich was recrystallized from a mixture of CH_2Cl_2 and hexane; m.p. 103-106; $[\alpha]_D$ +54.7 (c=1.0, CH_2Cl_2); IR (KBr) 2970, 1772, 1772, 1702, 1667, 1596, 1526 cm^1; ^1H NMR (500 MHz, $CDCl_3$) δ 8.25 (d, J=8.8 Hz, 2H), 8.06 (d, J=8.3 Hz, 2H), 7.61 (d, J=7.8 Hz, 2H), 7.36 (t, J=7.4 Hz, 2H), 7.27 (m, 1H), 4.40 (d, J=17.1 Hz, 1H), 4.32 (m, 1H), 4.19(t, J=8.8 Hz, 1H), 4.12-4.16 (m, 1H), 4.08 (d, J=17.1 Hz, 1H), 2.34 (s, 3H), 2.05 (m, 1H), 0.78 (d, J=6.8 Hz, 3H), 0.68 (d, J=6.8 Hz, 3H); ^{13}C (75MHz, $CDCl_3$) δ 189.6, 169.2, 153.8, 150.2, 142.2, 141.9, 128.3, 128.1, 127.6, 126.4, 123.7, 63.2, 58.3, 55.3, 43.9, 28.3, 25.1, 17.7,14.5.

Conversion of adducts 4b/4d into the β-mercapto methyl esters 8/9.



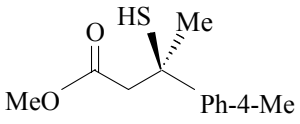
4b Ar: 4-Me-Ph
4d Ar: 4-Br-Ph

8 , **9** , **12**

(Adapted from: Lee, E.; Jeong, E.-J.; Kang, E.-J.; Sung, L.-T.; Hong, S.- K.; *J. Am. Chem . Soc.* **2001**, 123, 10131- 10132).

To a solution of the corresponding adduct **4b/4d** (0.5 mmol) in MeOH (5 mL) under a nitrogen atmosphere was added samarium (III) triflate (0.5g, 0.75 mmol) at room temperature. The mixture was stirred at room temperature until completion of the reaction as monitored by TLC (26-72h)**.** Water (10 mL) was then added and the mixture was extracted with ethyl acetate (3 x 10mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, and concentrated under vacuum. The product was purified by silica gel chromatography using a mixture of ethyl acetate and hexane (1:9) as eluent.

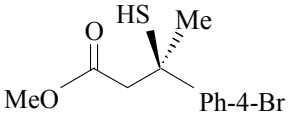
(3*R*)-3-Mercapto-3-(4-methylphenyl) butyric acid methyl ester (8)



8

The indicated compound (**8**) was prepared according to the general procedure to provide the pure product as an oil in 58 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ +20.8 (c=1.04, CH_2Cl_2); IR (film) 2941, 1737, 1175, 1070, 825 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.43 (d, J= 8.3 Hz, 2H), 7.14 (d, J=8.3 Hz, 2H), 3.61 (s, 3H), 3.11 (s, 2H), 2.76 (s, 1H), 2.33 (s, 3H), 1.93 (s, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 170.8, 142.9, 136.6, 128.9, 125.5, 51.5, 49.9, 46.7, 31.5.

(3*R*)-3-Mercapto-3-(4-bromophenyl) butyric acid methyl ester (9)

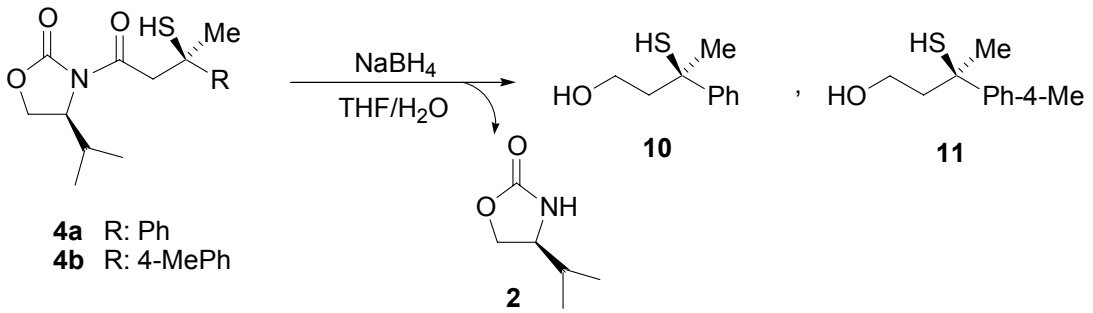


9

The indicated compound (**9**) was prepared according to the general procedure to provide the pure product as an oil in 87 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ +10.0 (c=1.0, CH_2Cl_2); IR (film) 2946, 1732, 1009, 827 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (m, 4H)

3.60 (s, 3H), 3.10 (m, 2H), 2.79 (s, 1H), 1.91 (s, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 170.4, 145.0, 131.3, 127.6, 121.0, 51.6, 49.7, 46.5, 31.5.

Reduction of adducts 4a/4b to the β-mercapto alcohols 10/11.

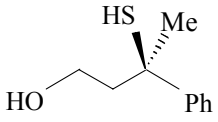


4a R: Ph
4b R: 4-MePh

(Adapted from Prashad, M.; Har, D.; Kim, H.-Y.; Repic, O. *Tetrahedron Lett.* **1998**, *39*, 7067).

To a solution of the corresponding adduct **4a** or **4b** (0.8 mmol) in THF (2.4 mL) at 20-25ºC (bath temperature) was added dropwise a solution of sodium borohydride (0.12 g, 3.2 mmol) in water (0.8 mL). The mixture was stirred at room temperature until completion as monitored by TLC (18h). To the reaction mixture was added 2N HCl (3 mL) at a rate to maintain the temperature at 20-25ºC. The reaction mixture was then extracted with ethyl acetate (3 x 10mL). The combined organic layers were washed with brine (20 mL), dried over $MgSO_4$, and concentrated under vacuum. Silica gel chromatography, using a mixture of ethyl and hexane (1:5) as eluent, led to the corresponding 1,2-mercapto alcohol **10** or **11** in the first fractions and to the corresponding oxazolidinone in the subsequent fractions.

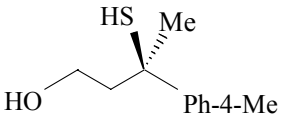
(3*R*)-3-mercapto-3-phenylbutan-1-ol (10)



10

The indicated compound (**10**) was prepared according to the general procedure to provide the pure product as an oil in 66 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ + 48.4 (c=2.1, CH_2Cl_2); 96% ee; IR (film) 3353, 2931, 1447, 1042, 698 cm^{-1}; ^{1}H NMR (500 MHz, $CDCl_3$) δ 7.56 (m, 2H), 7.35 (m, 2H), 7.25 (m, 1H), 3.68 (m, 2H), 2.36 (m, 2H), 2.22 (s, 1H), 1.87 (s, 3H); ^{13}C (75 MHz, $CDCl_3$) δ 141.4,128.4,126.8, 125.8, 60.2, 48.7, 48.5, 32.4.

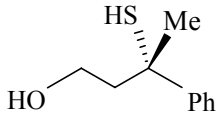
(3*R*)-3-mercapto-3-(4-methylphenyl)butan-1-ol (11)



11

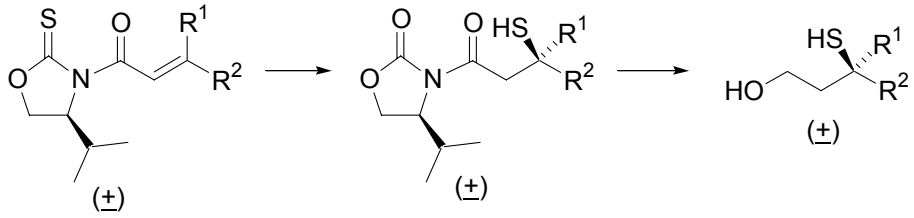
The indicated compound (**11**) was prepared according to the general procedure to provide the pure product as an oil in 78 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ +43.01 (c=0.46, CH_2Cl_2); 94% ee; IR (film) 3357, 2941, 1508, 1456, 1368, 1053, 816 cm^{-1}; ^1H NMR (500 MHz, $CDCl_3$) δ 7.44 (d, J=8.3 Hz, 2H), 7.16 (d, J=8.3 Hz, 2H), 3.62-3.72 (m, 2H), 2.31-2.39 (m, 2H), 2.34 (s, 3H), 2.20(s, 1H), 1.84 (s, 3H); ^{13}C (125 MHz, $CDCl_3$) δ 143.4, 136.5, 129.0, 125.7, 60.2, 48.7, 48.3, 32.4, 20.9.

(*3S*)-3-mercapto-3-phenylbutan-1-ol



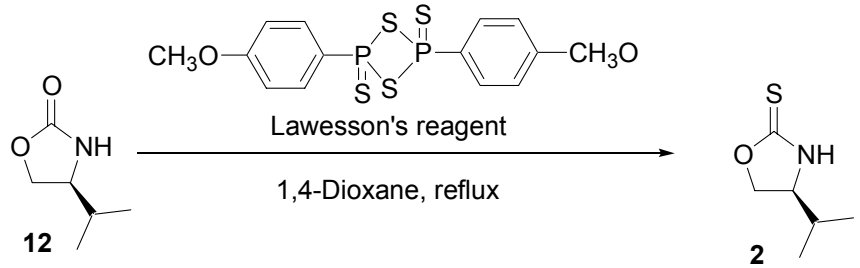
The indicated compound was prepared according to the general procedure starting from **7** to provide the pure product as an oil in 54 % yield after flash chromatography (EtOAc/Hexane, 1/9); $[\alpha]_D$ –45.6 (c=0.25, CH_2Cl_2); 96% ee.

Preparation of racemic mercapto alcohols.



Racemic β-mercapto alcohols were obtained following the same reaction sequence described above starting from D,L-valinol.

Regeneration of oxazolidine-2-thione 2 from 2-oxazolidinone 12.



(Adapted from Lakshmikantham, M. V.; Chen, W.; Cava, M. P. *J. Org. Chem.* **1989**, 54, 4746-4750).

To a solution of 2-oxazolidinone **12** (65.8 mg, 0.5 mmol) in 1,4-dioxane (10 mL) was added Lawesson's reagent (313 mg, 0.75 mmol) and the mixture was stirred at reflux. Additional two portions of the Lawesson's reagent (0.75 mmol each) were successively added to the reaction mixture at 4 and at 6 h, respectively, and stirring continued until disappearance of the starting oxazolidinone (7 h total). The reaction mixture was then cooled to room temperature, the solvent

removed under reduced pressure, and the crude product was purified by column chromatography. Compound **2** was obtained in 75% yield.

Determination of diastereomeric ratios of adducts 4.

^{13}C NMR of each crude product was taken and two sets of peaks could be identified for adduct **4e**. For adducts **4a**, **4b**, **4c**, **4d, 4f, 4g** and **4h** only the peak corresponding to the methyl group attached to the quaternary carbon split out. For **4i** and **4j** only the methylene in the ethyl group split out (see examples enclosed).

^{1}H NMR of each crude product was taken and two sets of peaks corresponding to the SH and methylene group could be identified for each compound **4**.

Determination of enantiomeric purities of mercapto alcohols 10 and 11.

HPLC chromatograms were taken of compounds **10** and **11**, respectively, and compared with those obtained from the corresponding racemic samples, the latter prepared as mentioned above. HPLC analysis conditions: Chiralcel OD capilary column, flow rates of 0.5 mL/min, at 25ºC, using mixtures of 2-propanol/hexane 5:95 as eluent.

Determination of the enantiomeric purity of mercapto methyl esters 8 and 9.

Due to the unsatisfactory degree of resolution obtained by chiral HPLC analysis of esters **8** and **9**, the ee values were determined on the alcohol products obtained from their reduction. HPLC chromatograms were taken of the reduced products and compared with those obtained from racemic samples, as mentioned above.

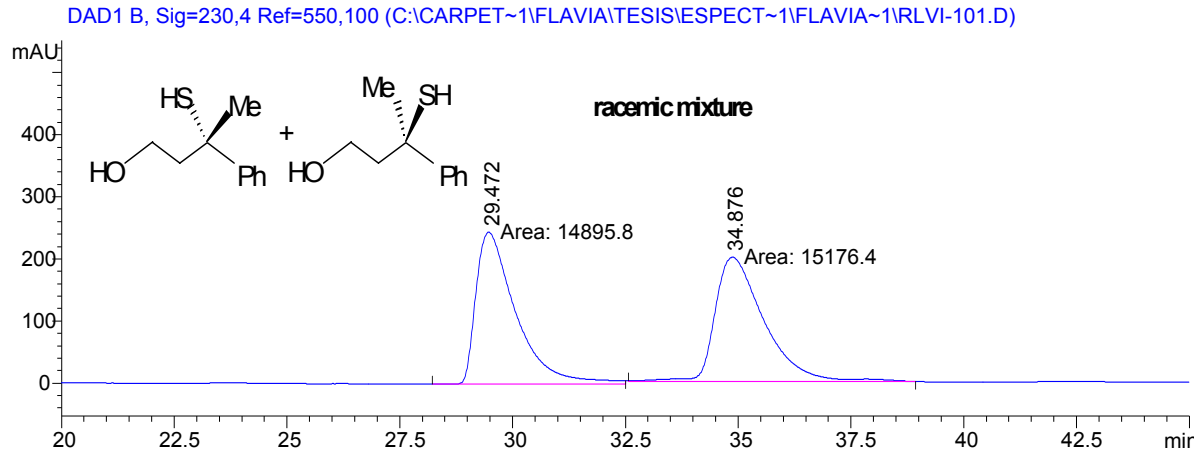
Reduction conditions for **8**:

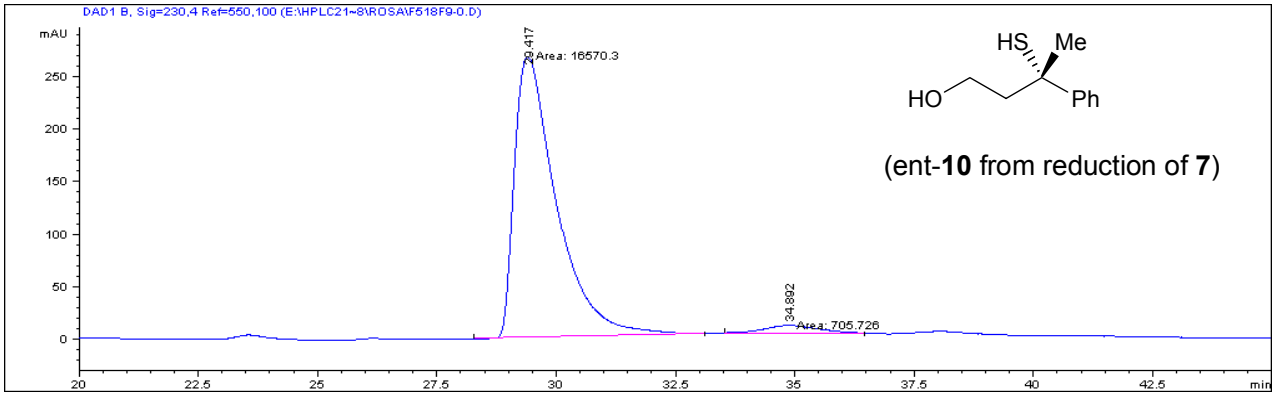
$LiAlH_4$ (0.29mmol) was suspended in 5mL of dried diethyl ether and a solution of **8** (0.076mmol) in diethyl ether (5mL) was added dropwise. The reaction mixture was stirred for 7h at room temperature. After the reaction completion, the excess $LiAlH_4$ was destroyed by careful addition of a mixture of ice and water. The water phase was extracted with diethyl ether (3 x 30 mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated. The obtained sample was submitted to chiral HPLC analysis. 96% ee.

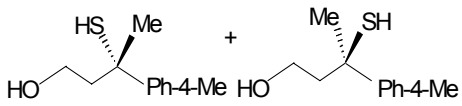
Reduction conditions for **9**:

To a solution of **9** (53mg, 0.18mmol) in dry toluene (2mL), a solution of DIBAL in hexane (0.6mmol) was added dropwise at –78ºC for 1h, and then the temperature was allowed to up to room temperature. After 18h, to the reaction mixture was added water (20mL). The water phase was extracted with diethyl ether (3x 30mL) and the combined organic extracts were dried ($MgSO_4$) and concentrated. The obtained sample was submitted to chiral HPLC analysis. 97% ee.

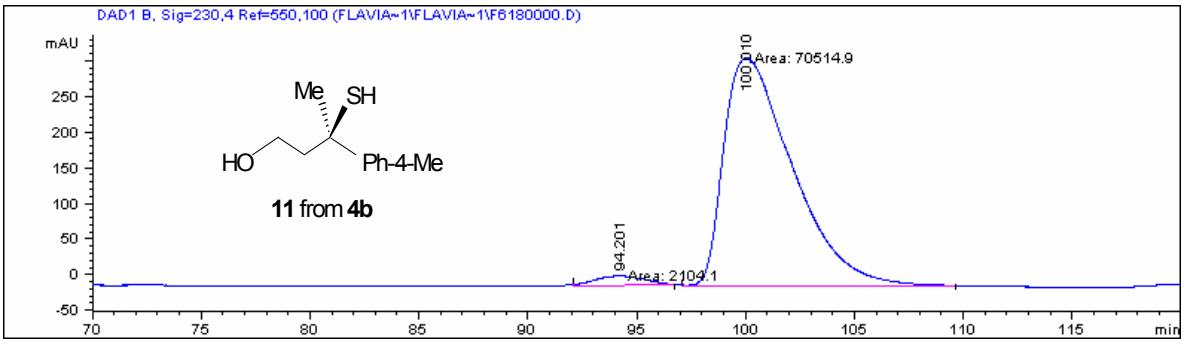
HPLC cromatograms of mercapto alcohols obtained from reduction of adducts 7 and 4b.



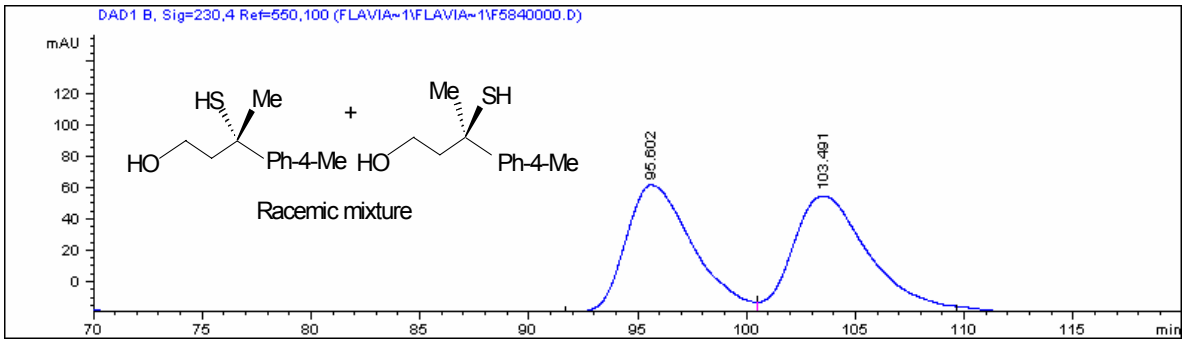


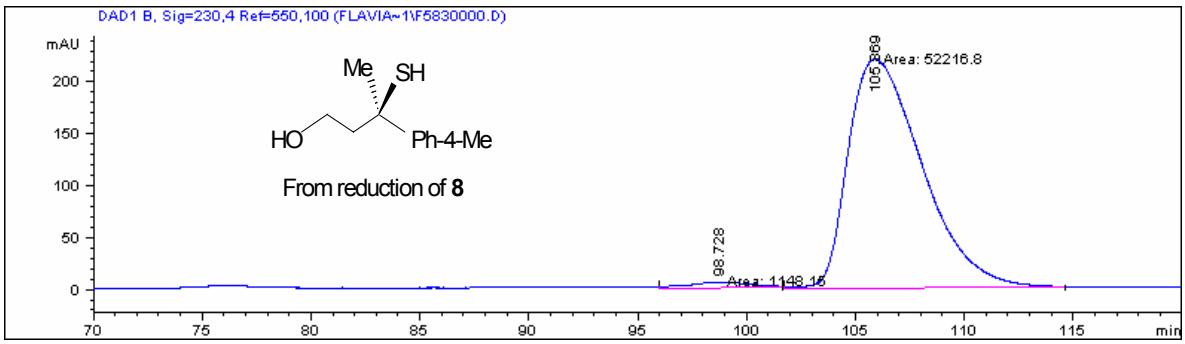


Racemic mixture

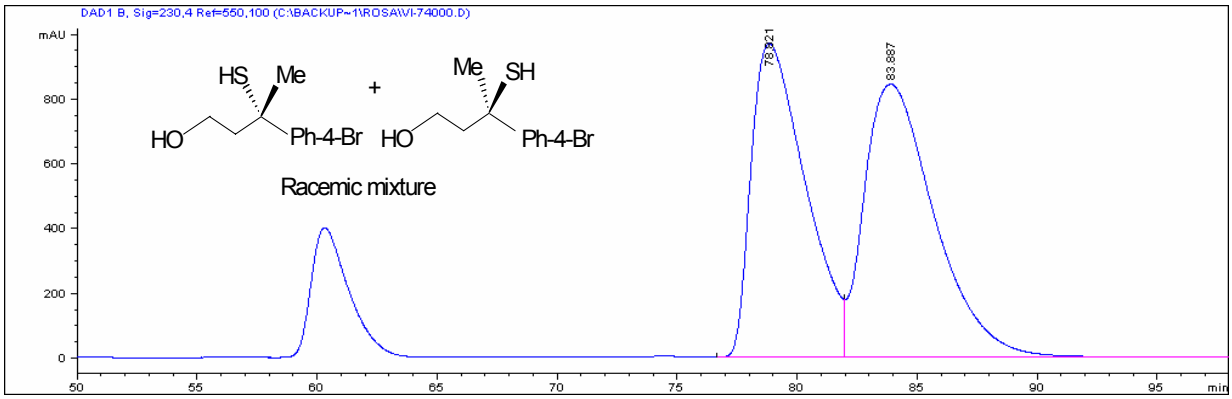


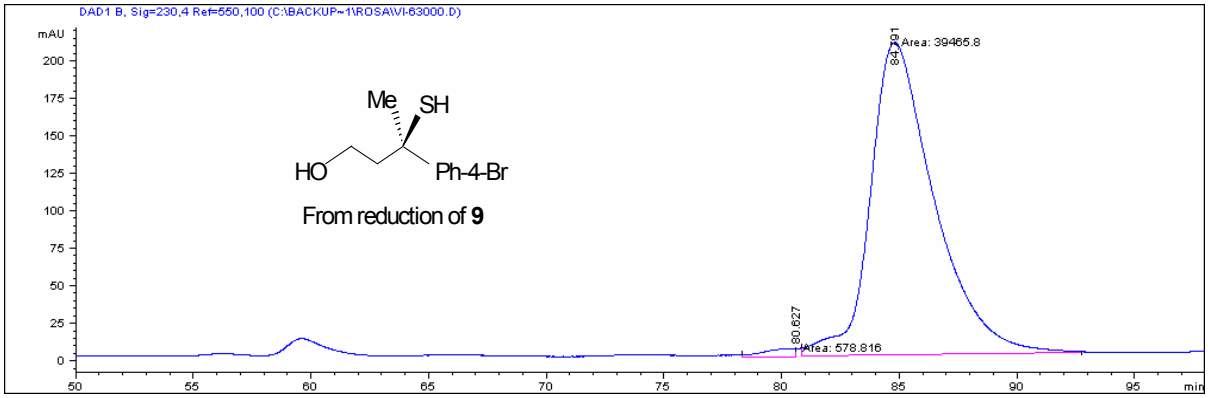
HPLC cromatograms of mercapto alcohols obtained from reduction of ester 8



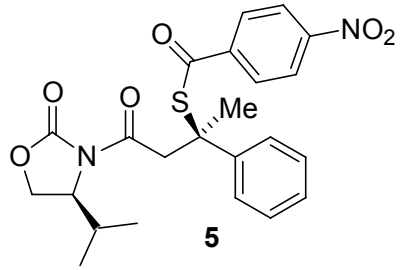


HPLC cromatograms of mercapto alcohols obtained from reduction of ester 9

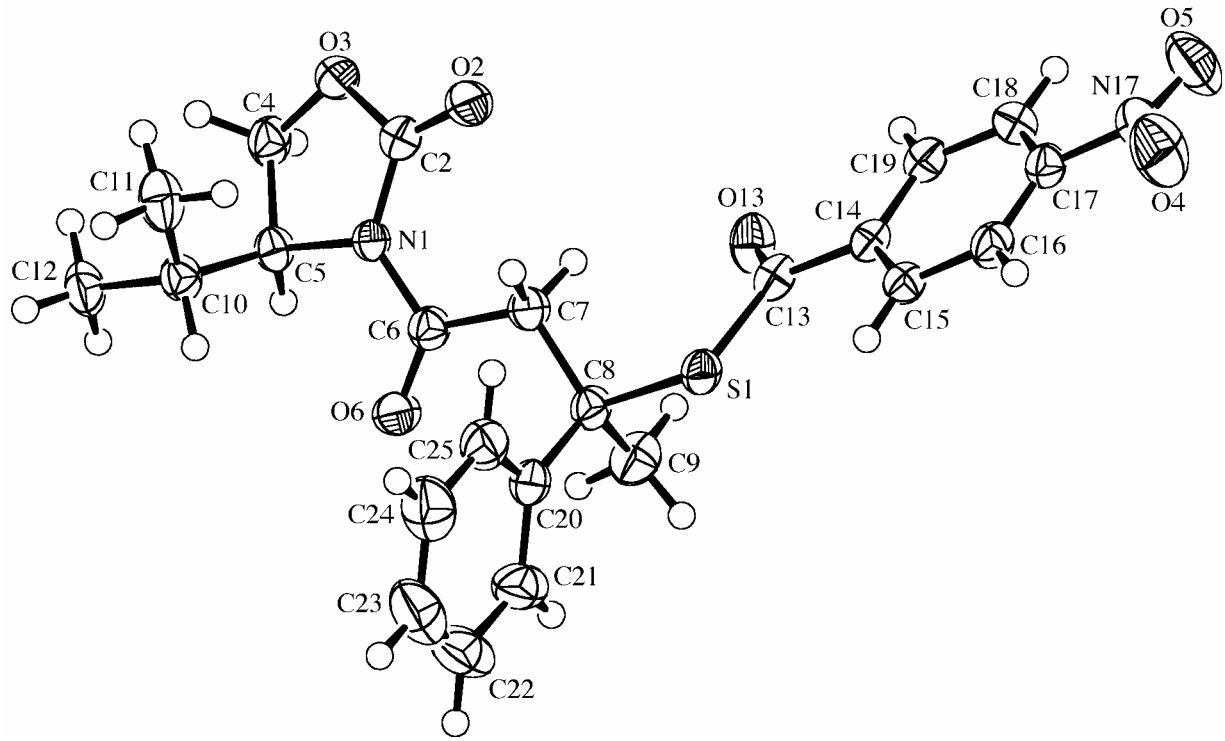


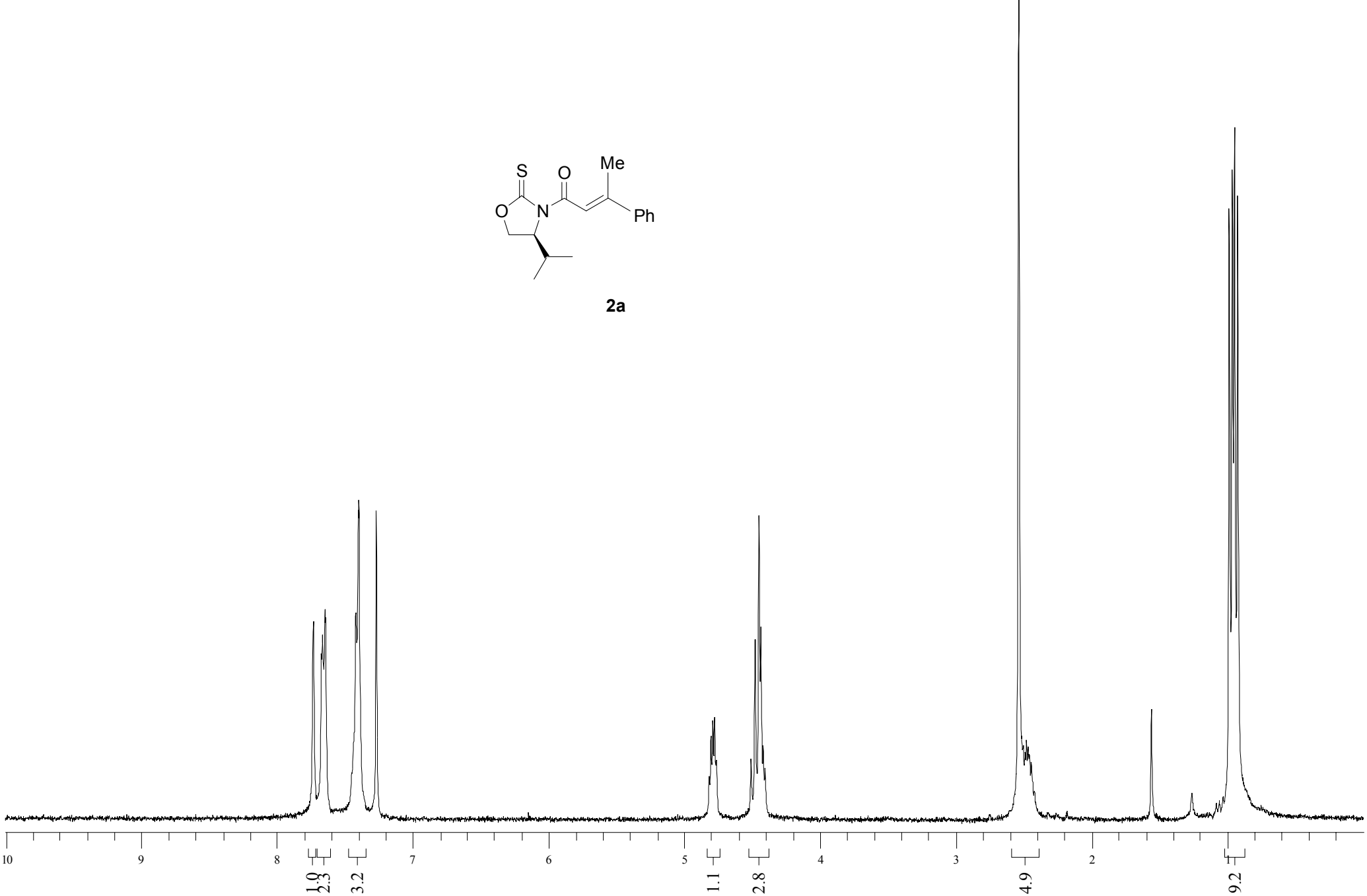


ORTEP diagram of 5



5





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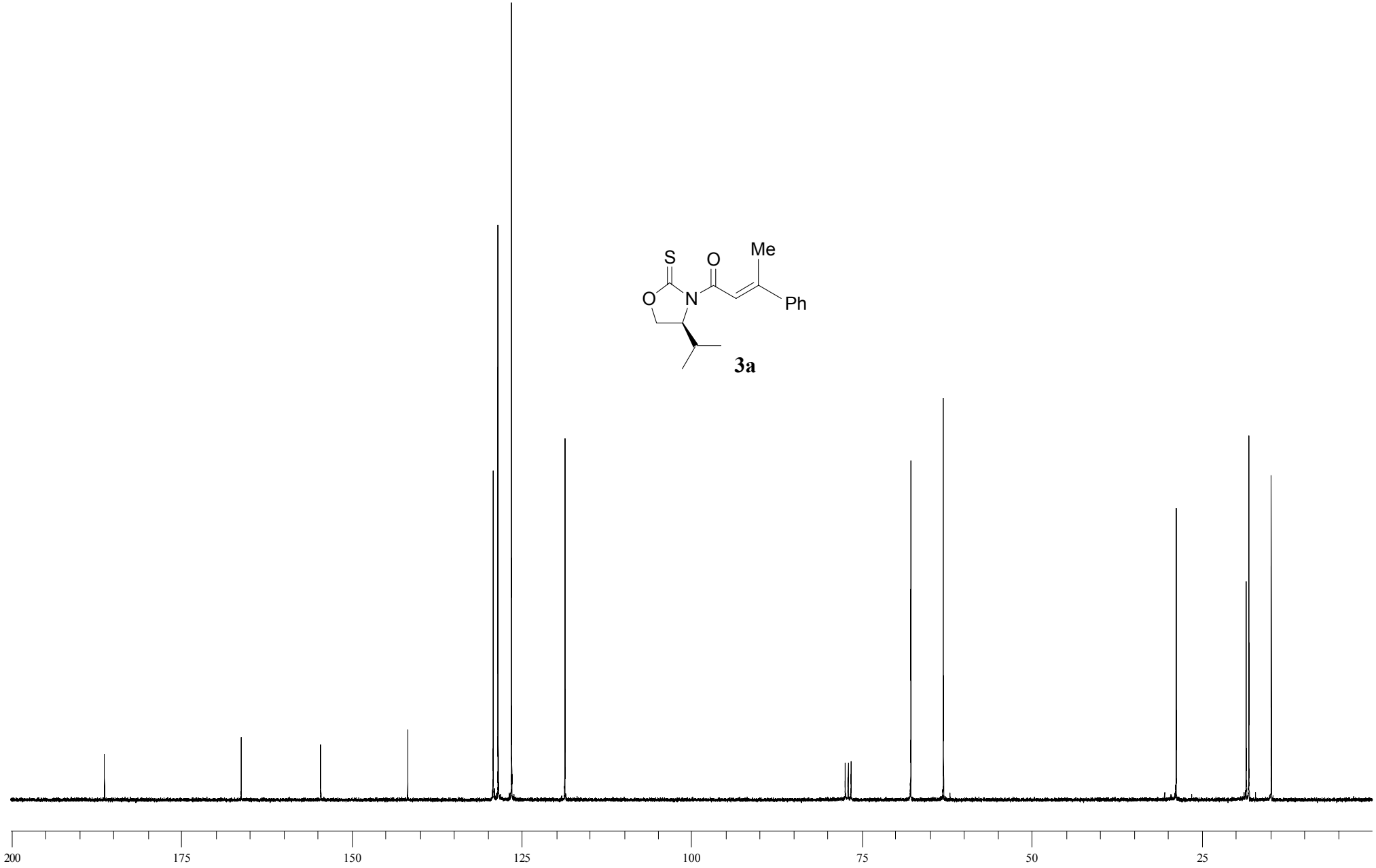
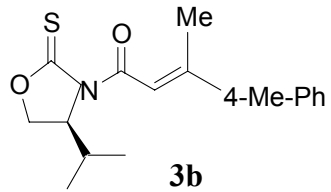


3a



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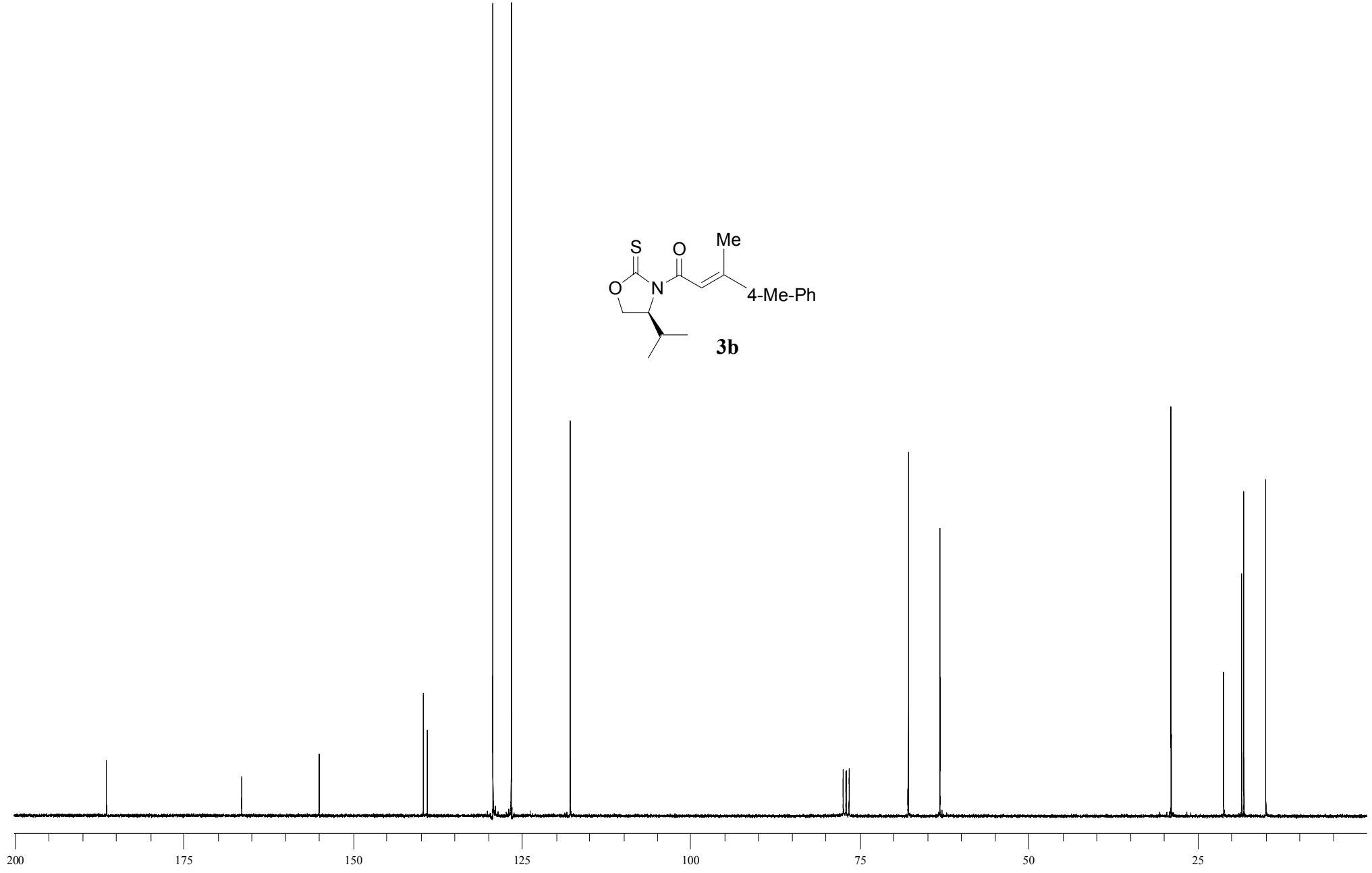
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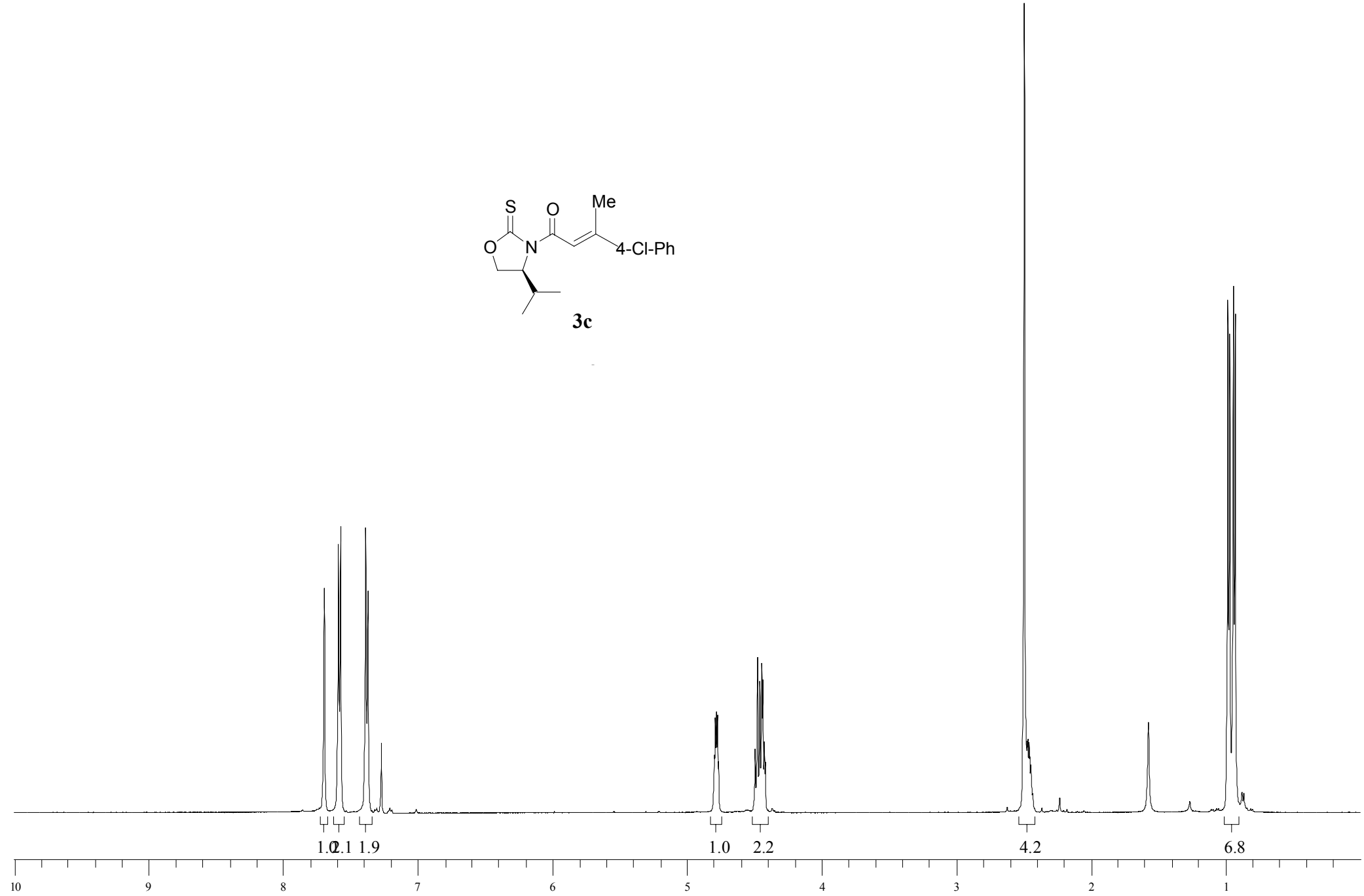

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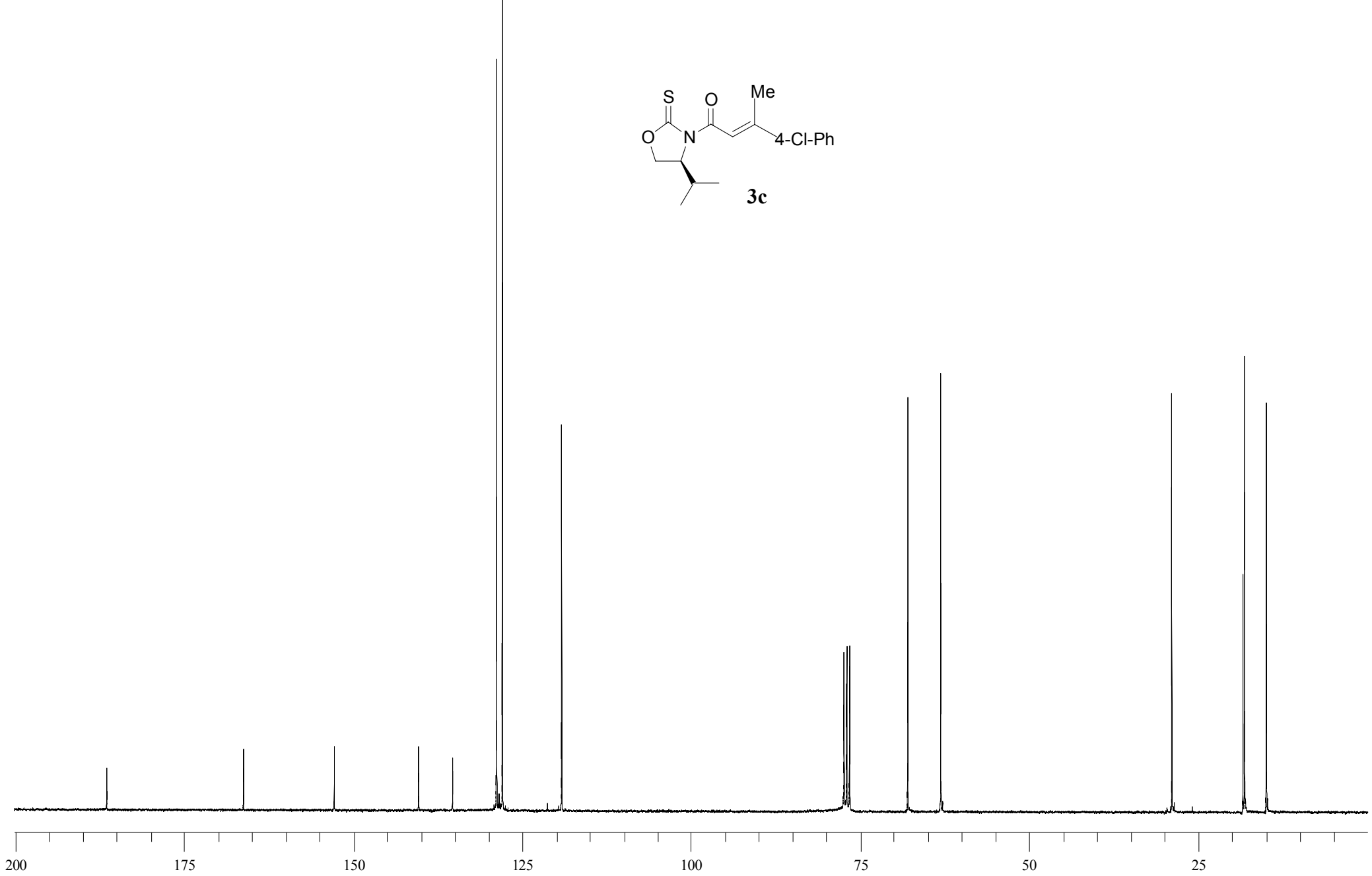

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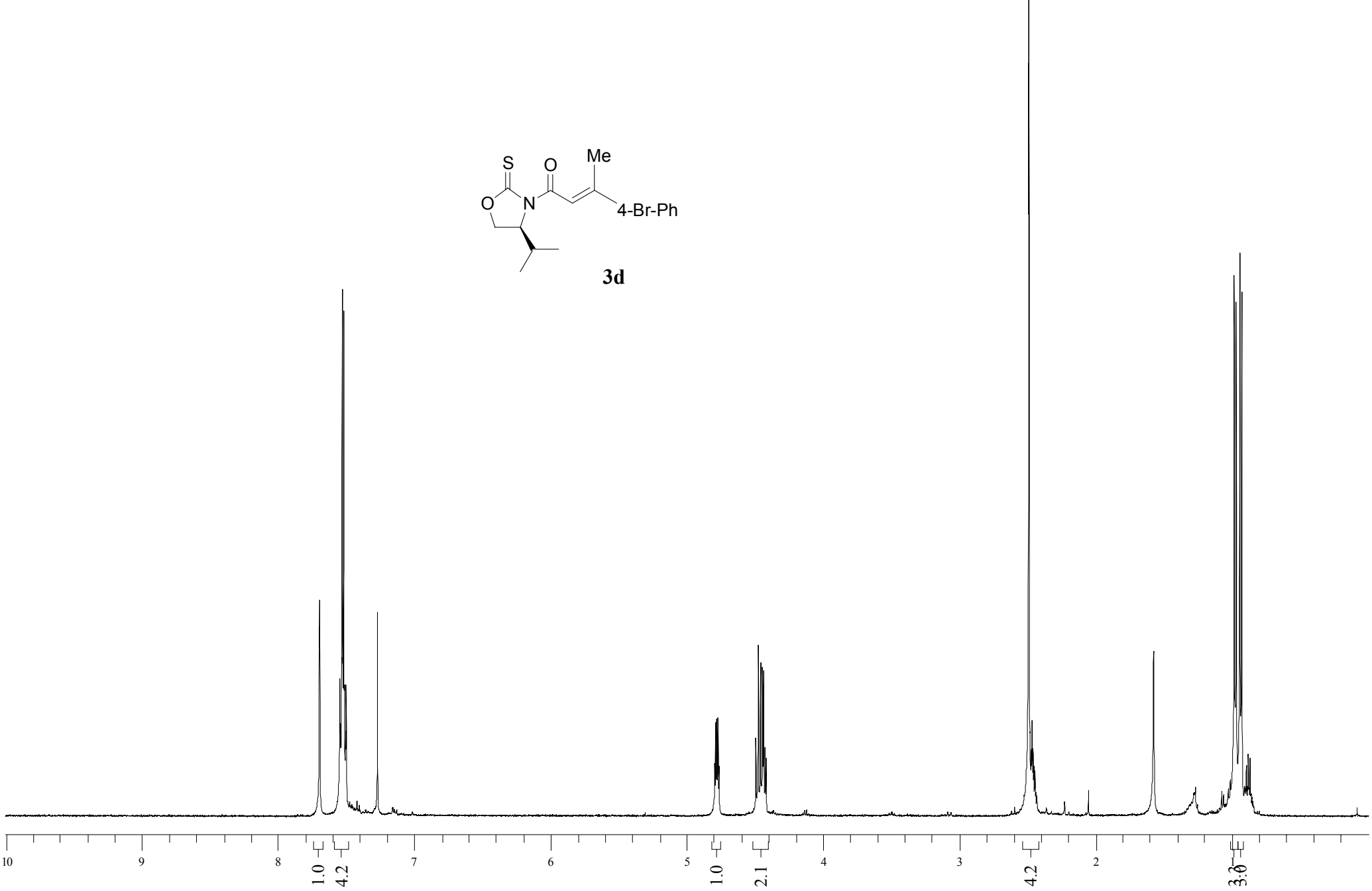

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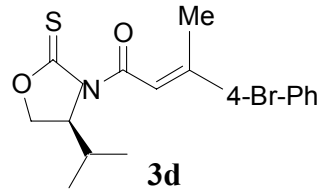

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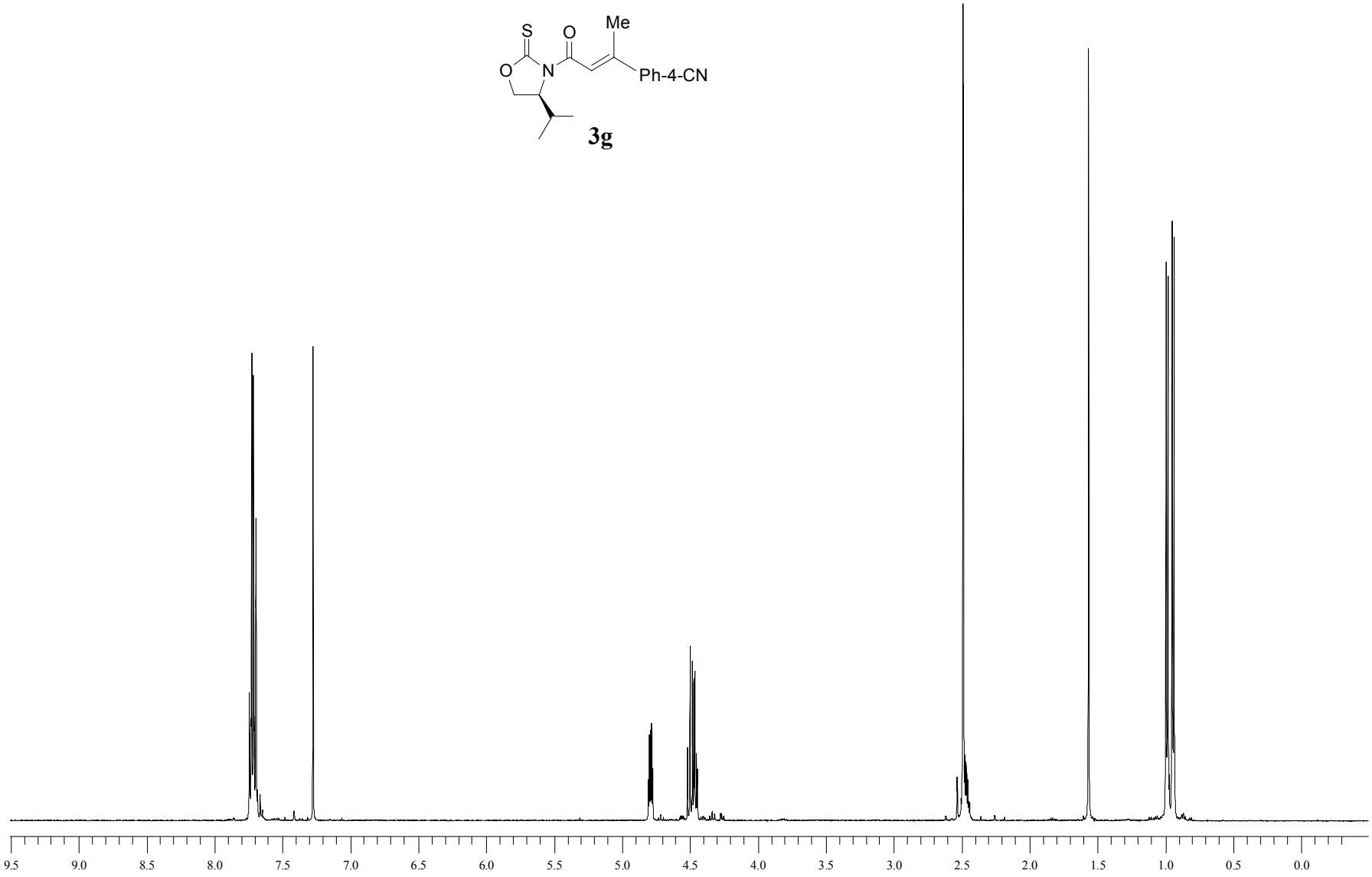
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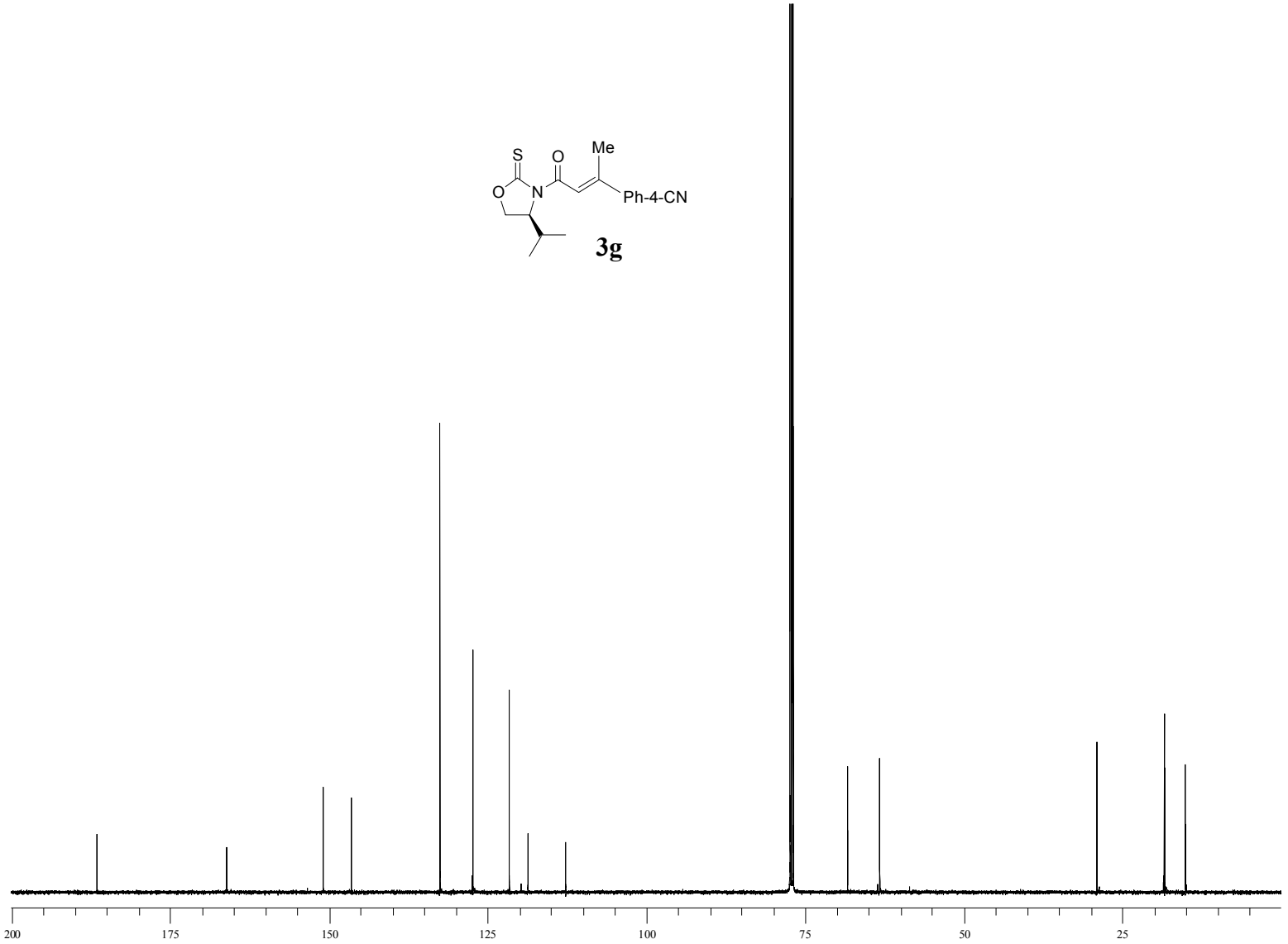

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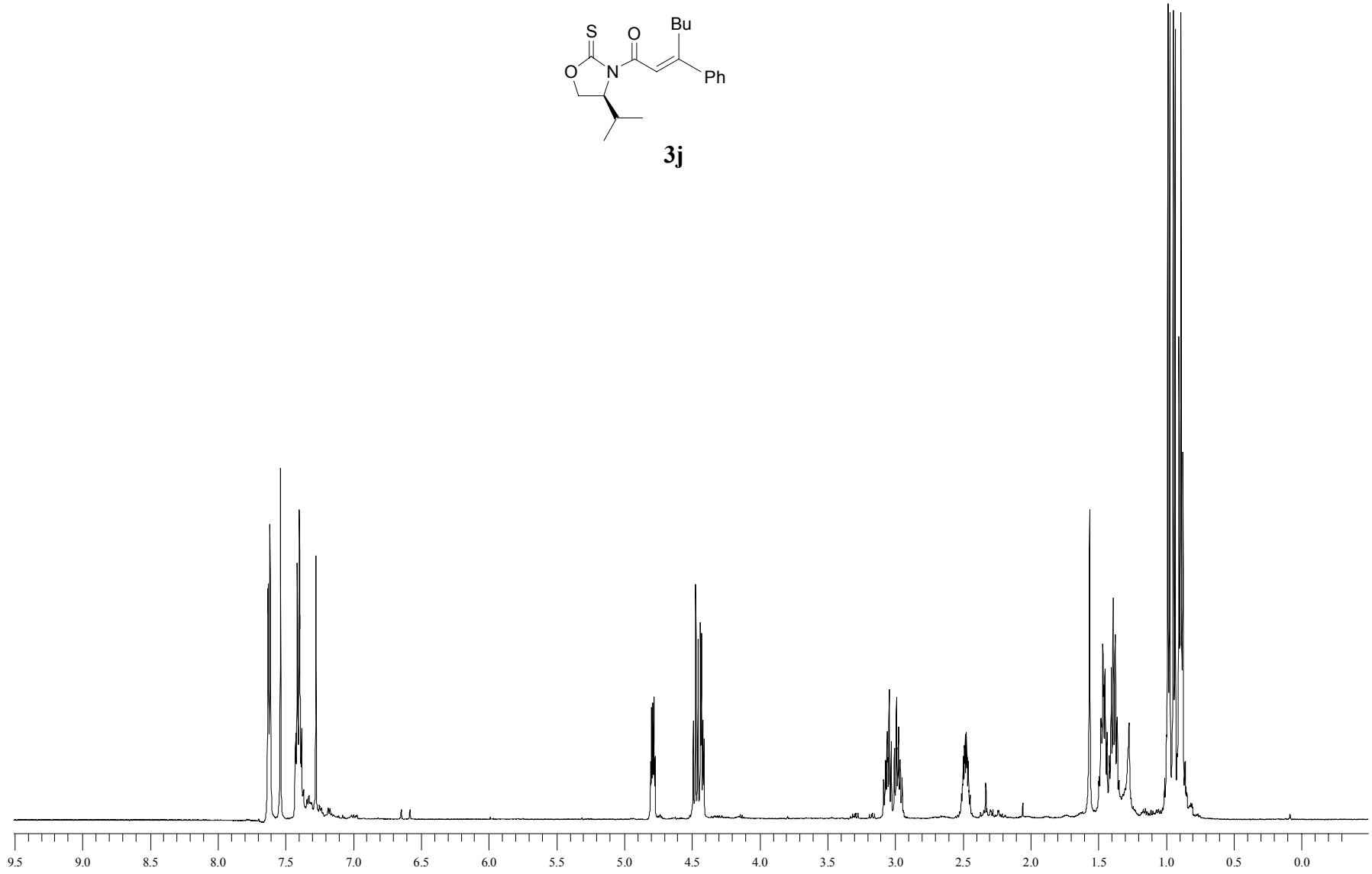

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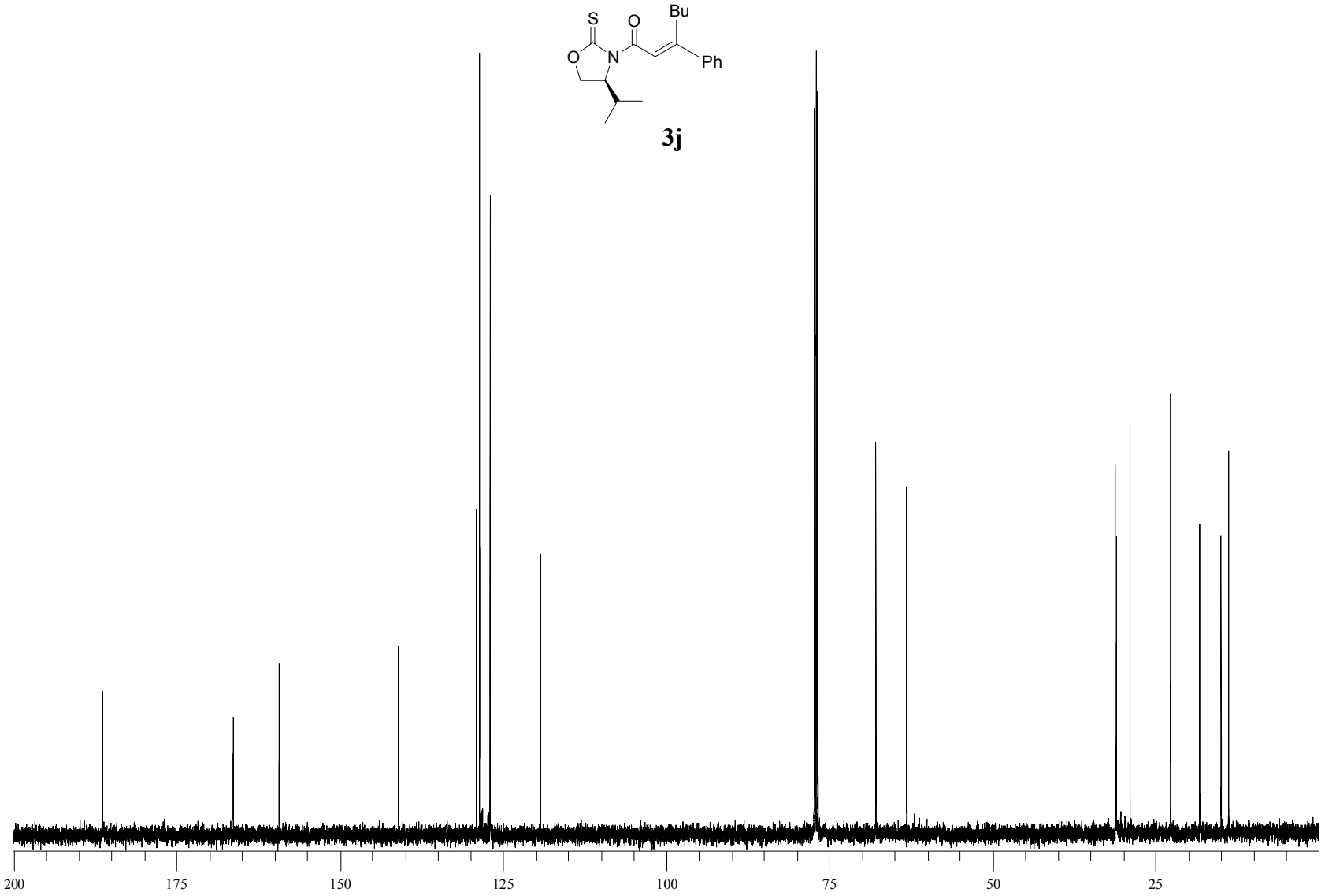

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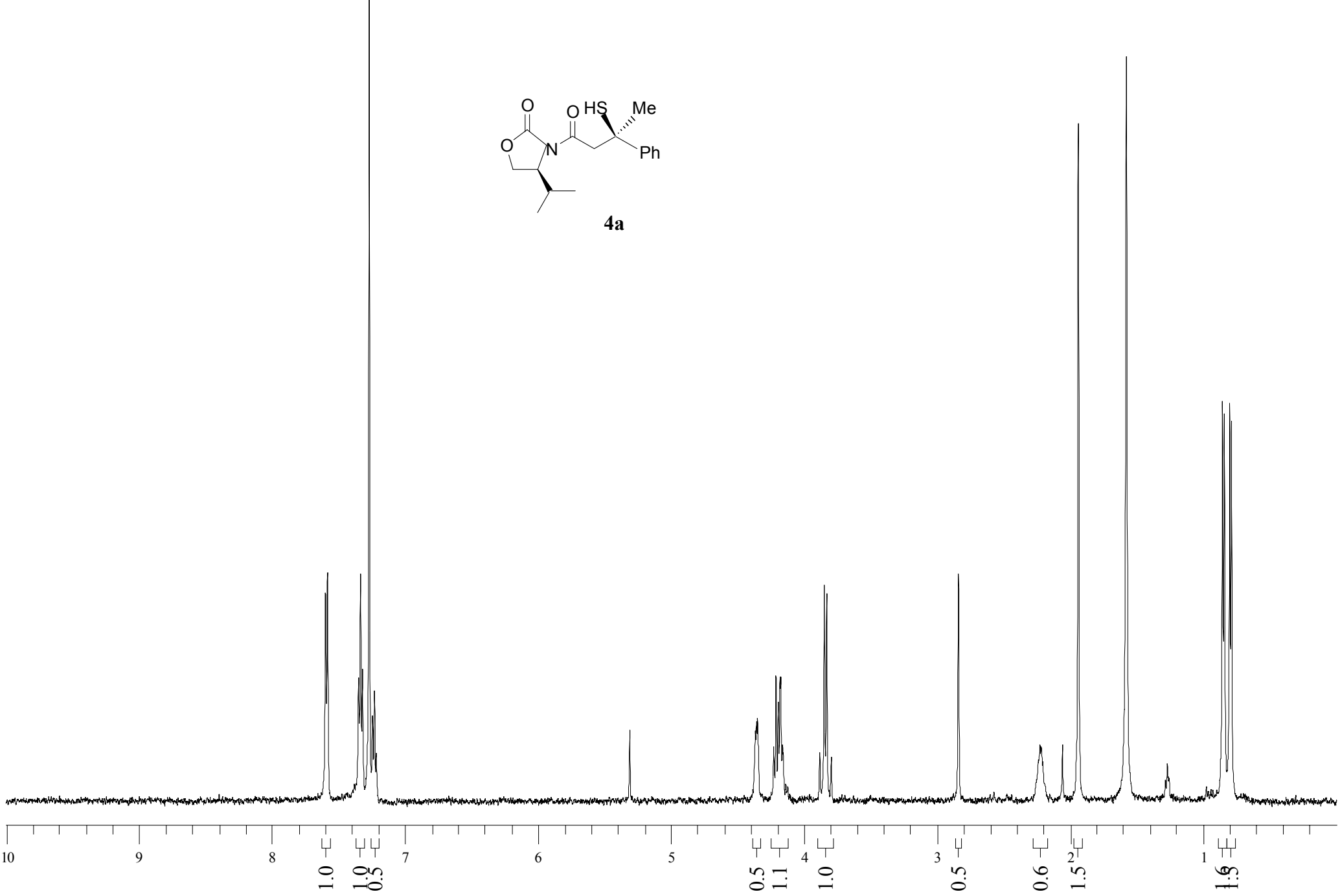
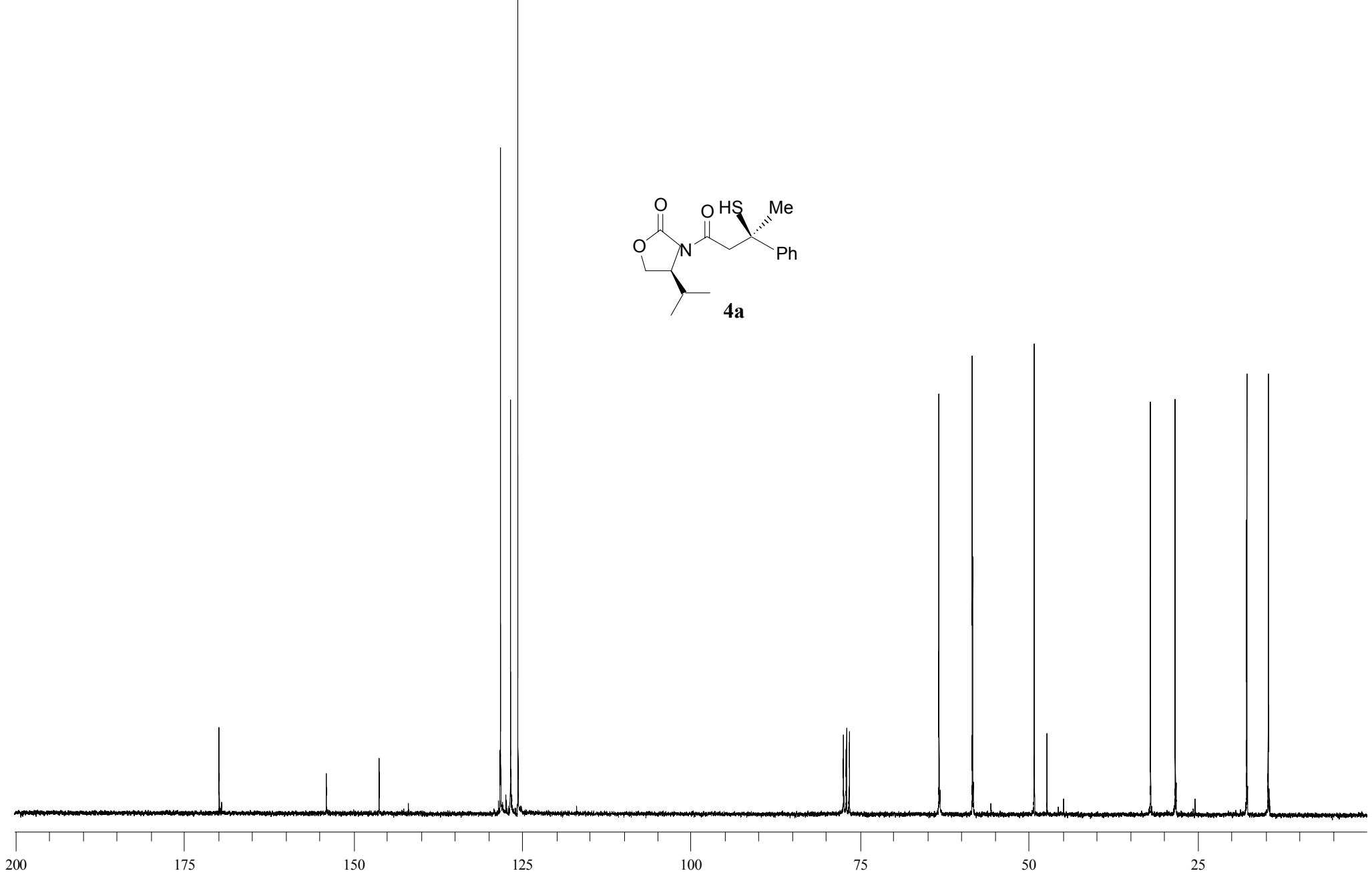


4a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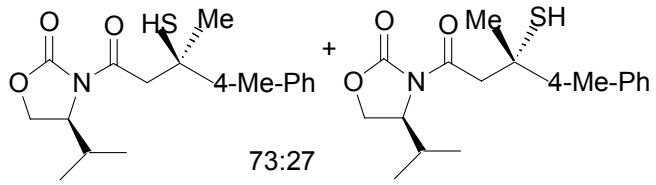
25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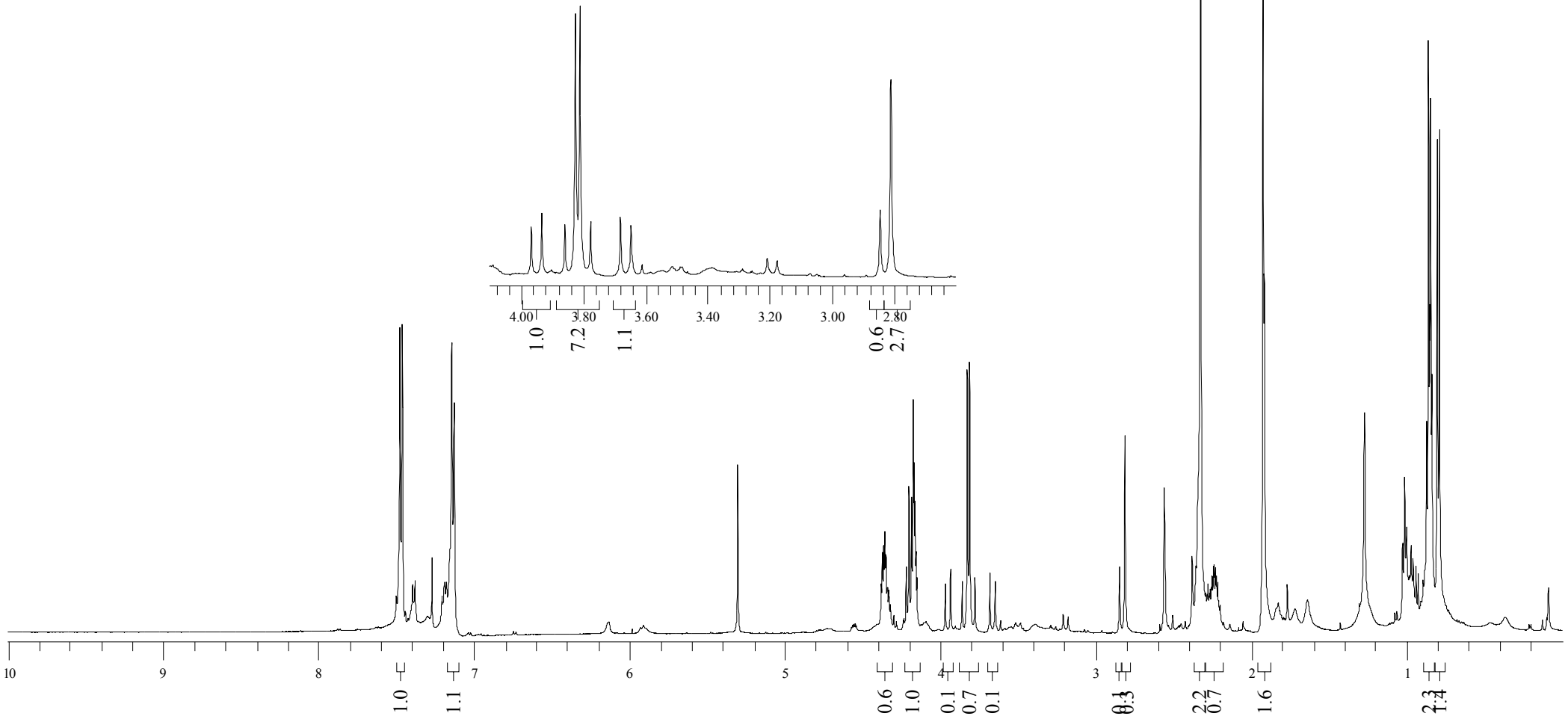
73:27

4b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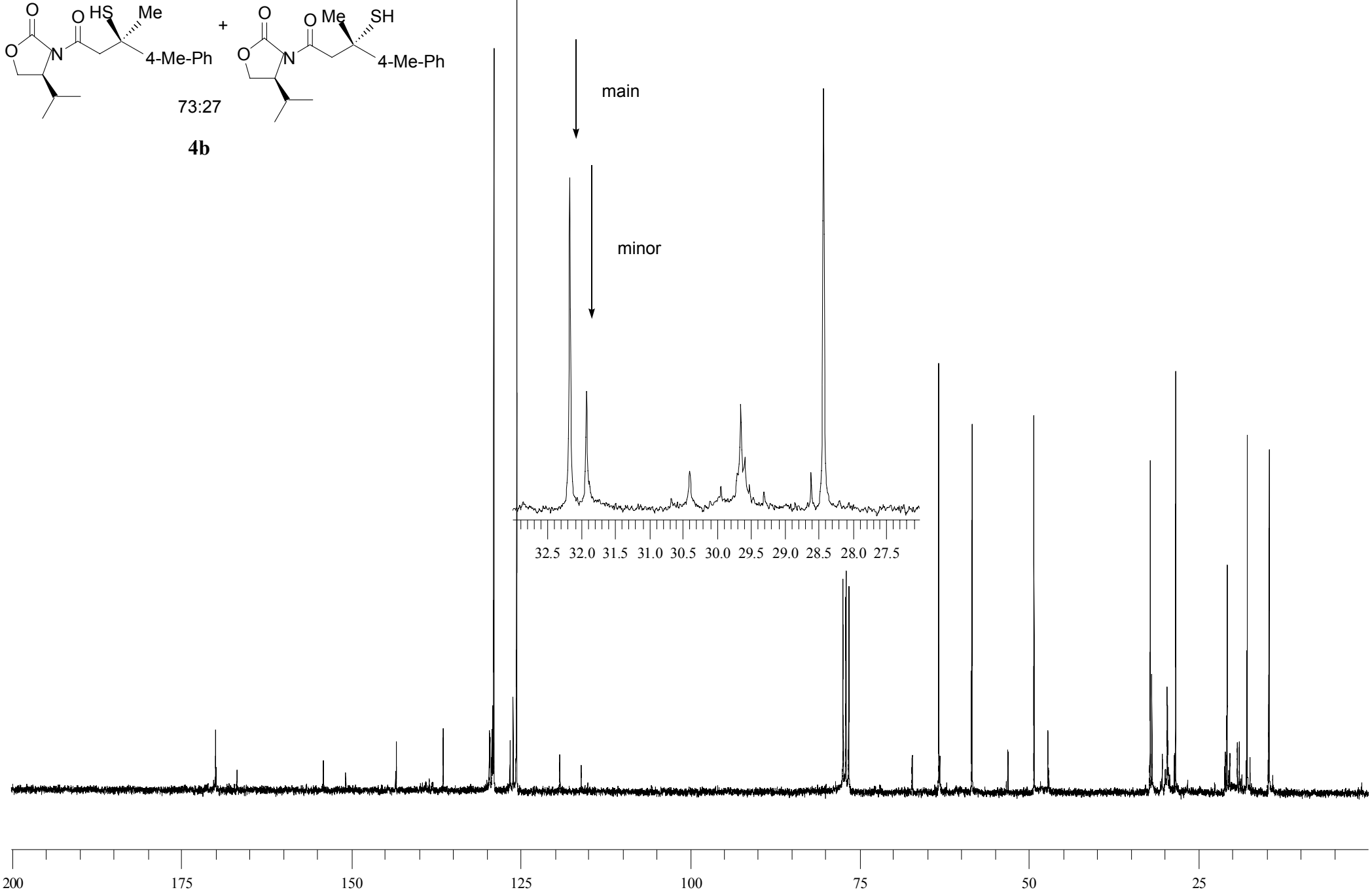
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Me
SH
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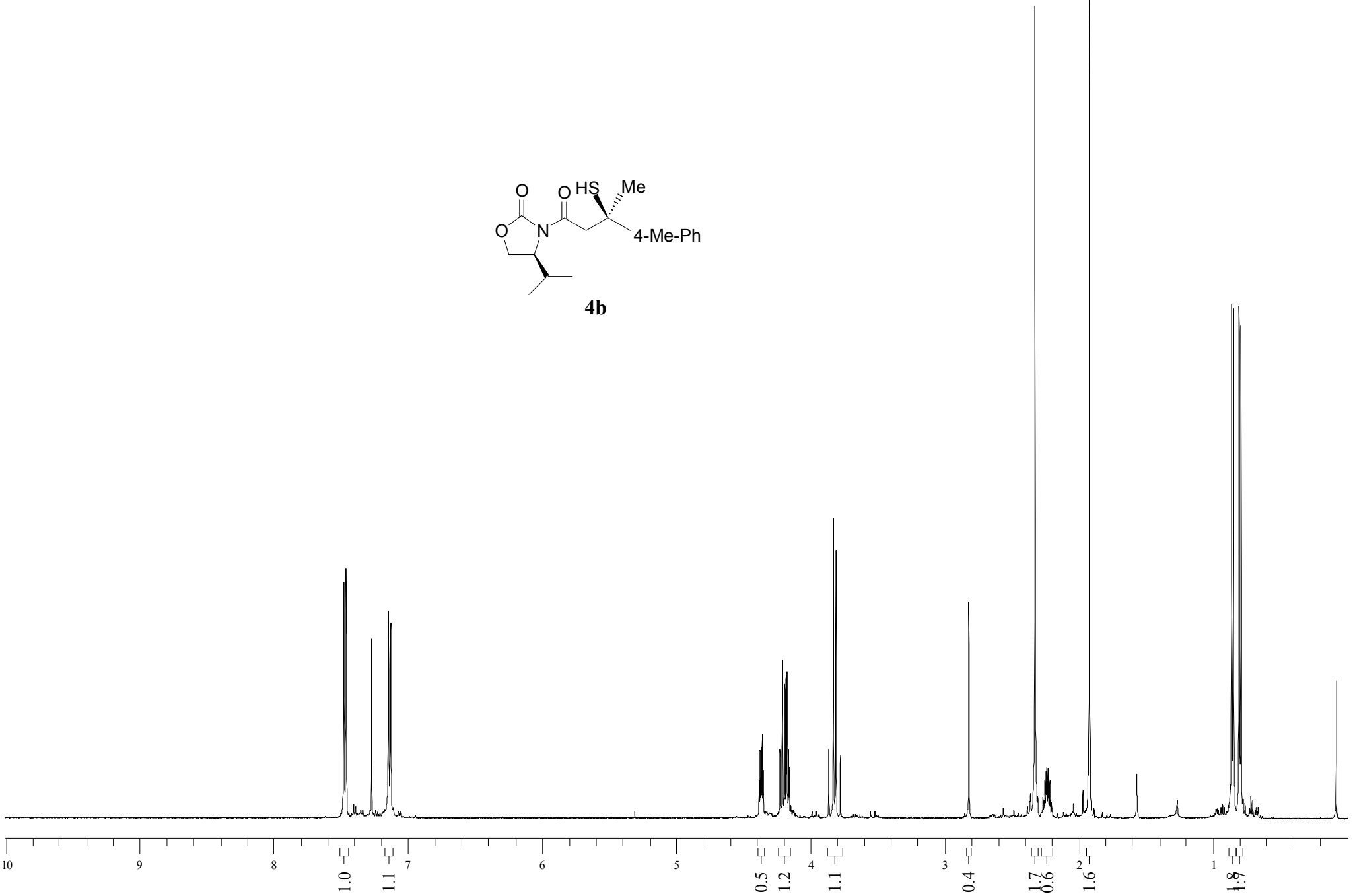
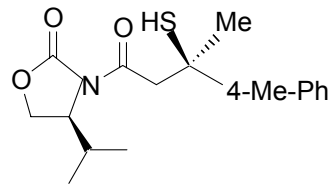
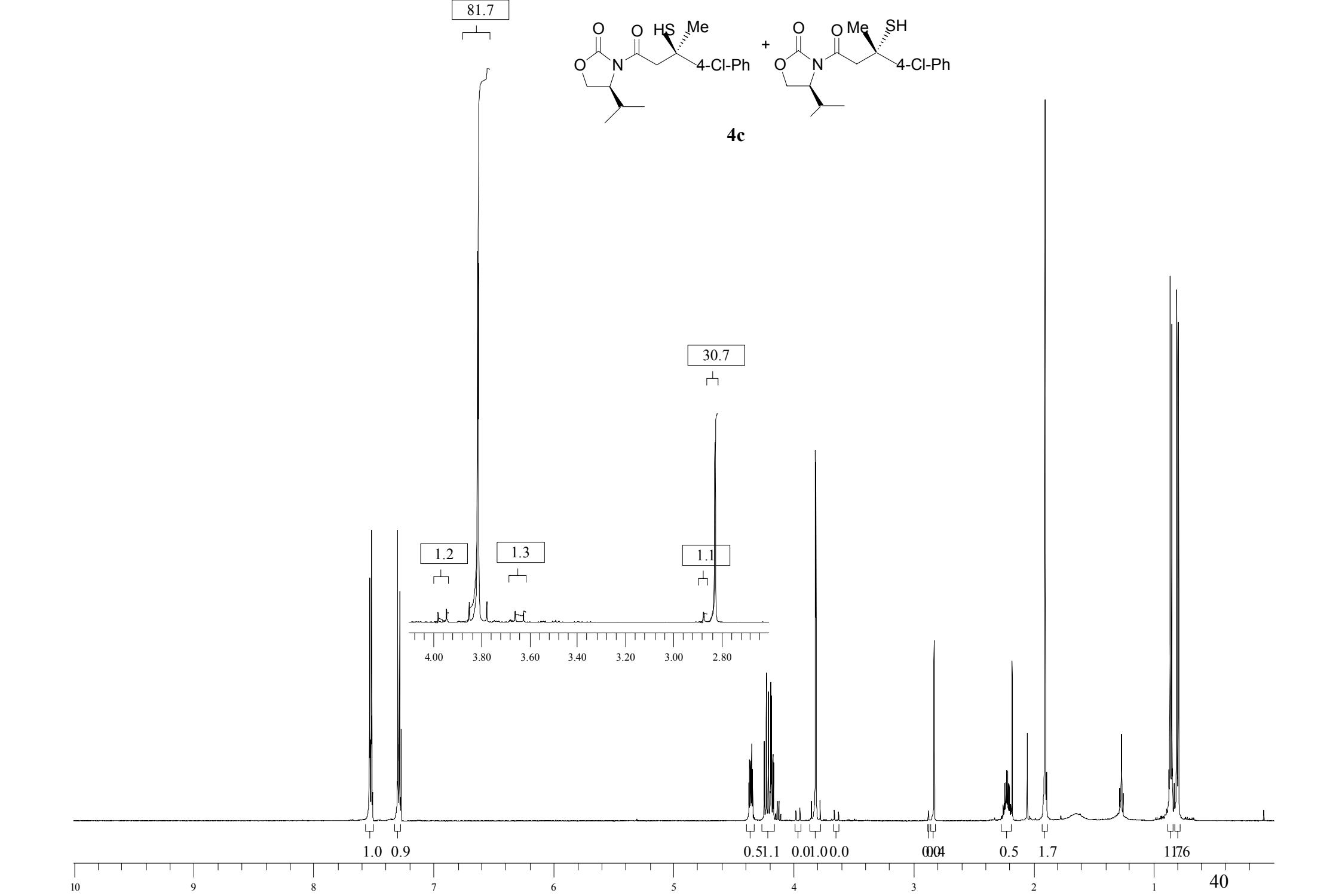
75
50
25



4b



4b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0.5
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1.7
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10
9
8
7
6
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+
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Me
SH
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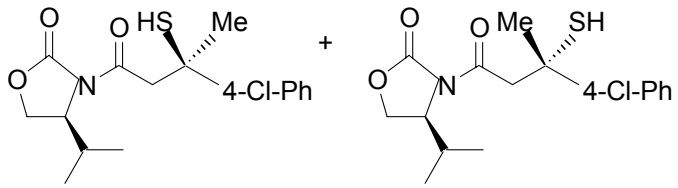
4c


O
O
HS
Me
O
N
4-Cl-Ph
+
O
O
Me
SH
O
N
4-Cl-Ph

4c

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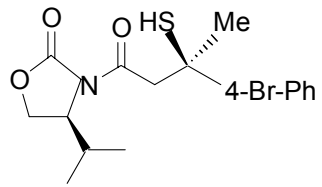
200
175
150
125
100
75
50
25



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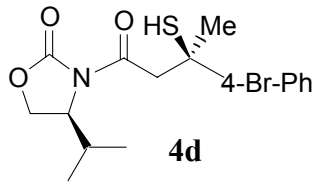

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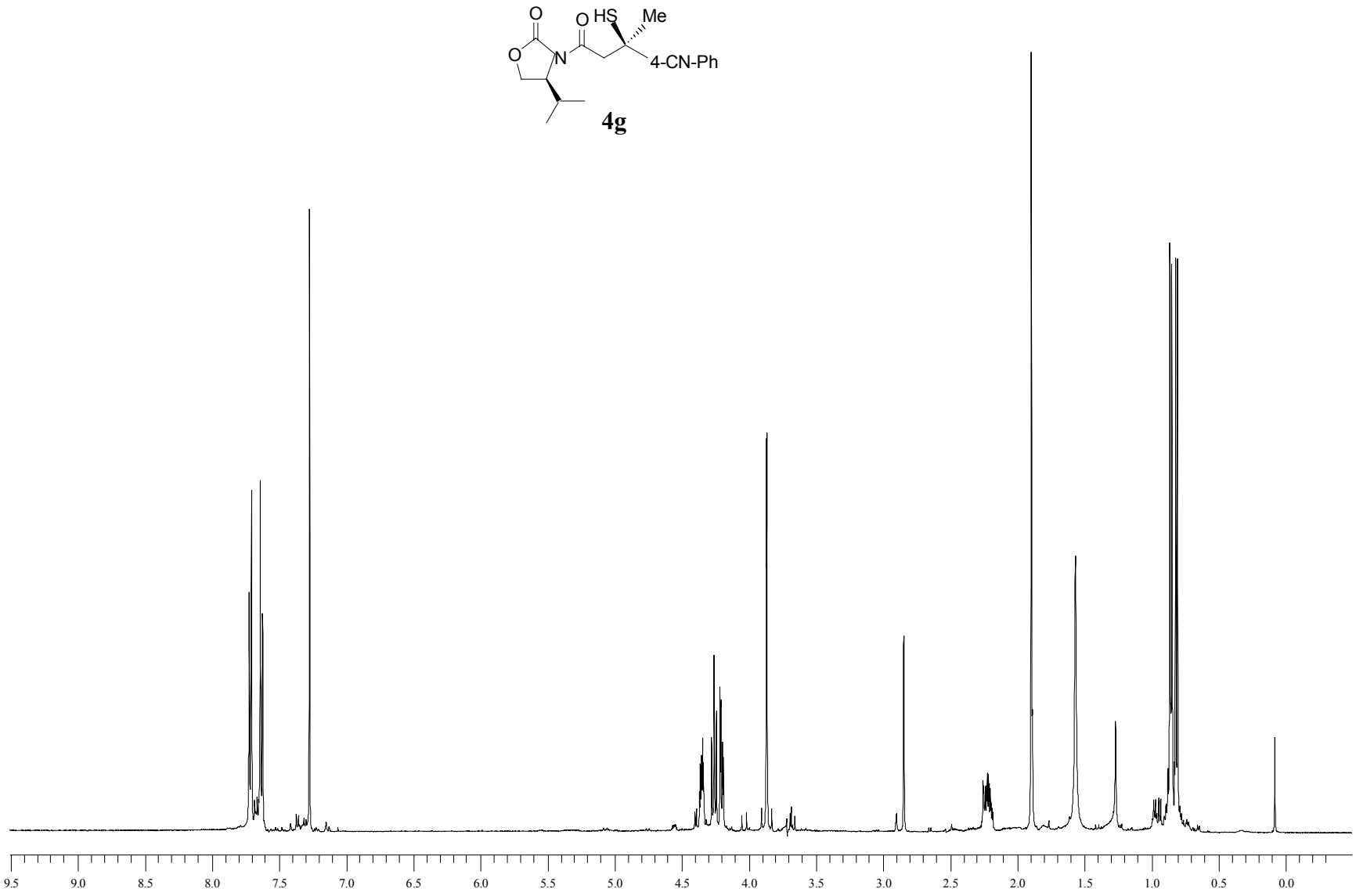
O
O
HS
Me
O
N
4-CN-Ph
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
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4.0
3.5
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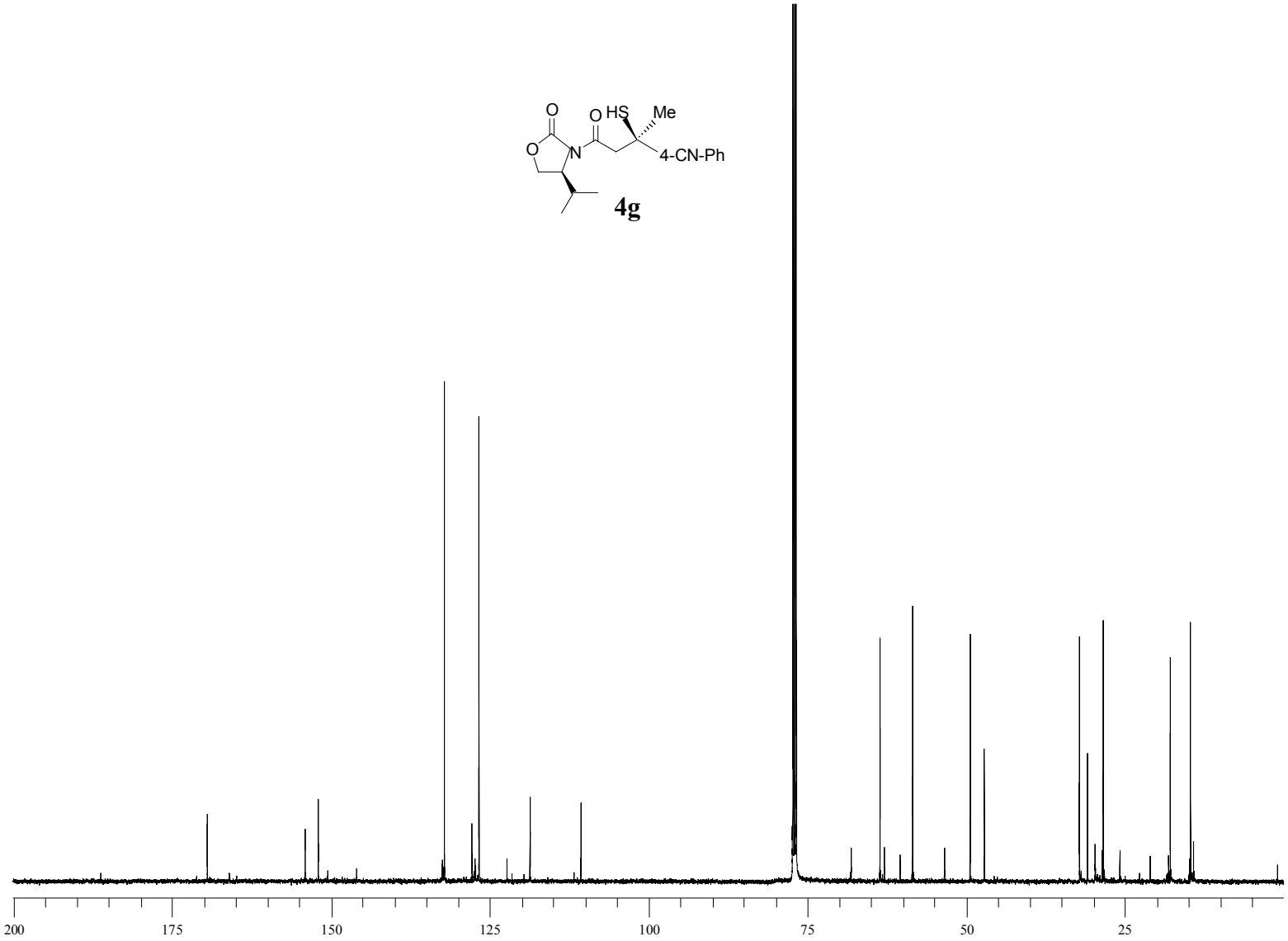
1.5
1.0
0.5
0.0

4g



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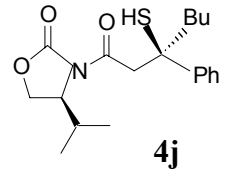
O
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HS
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9.5
9.0
8.5
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7.5
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6.0
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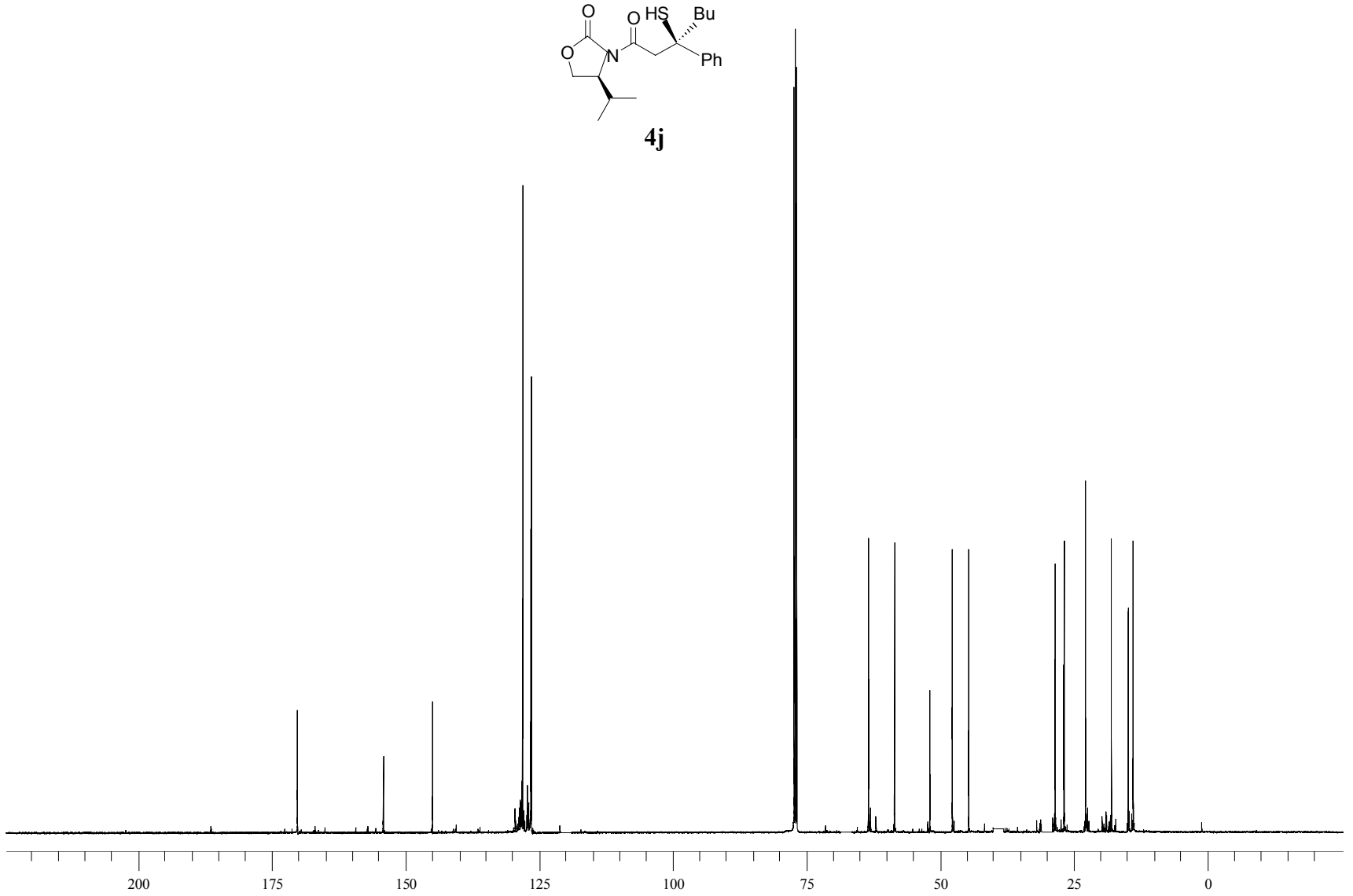

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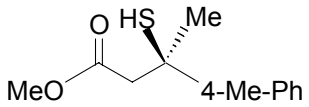

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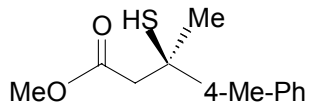

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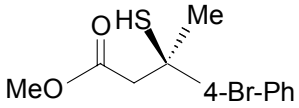

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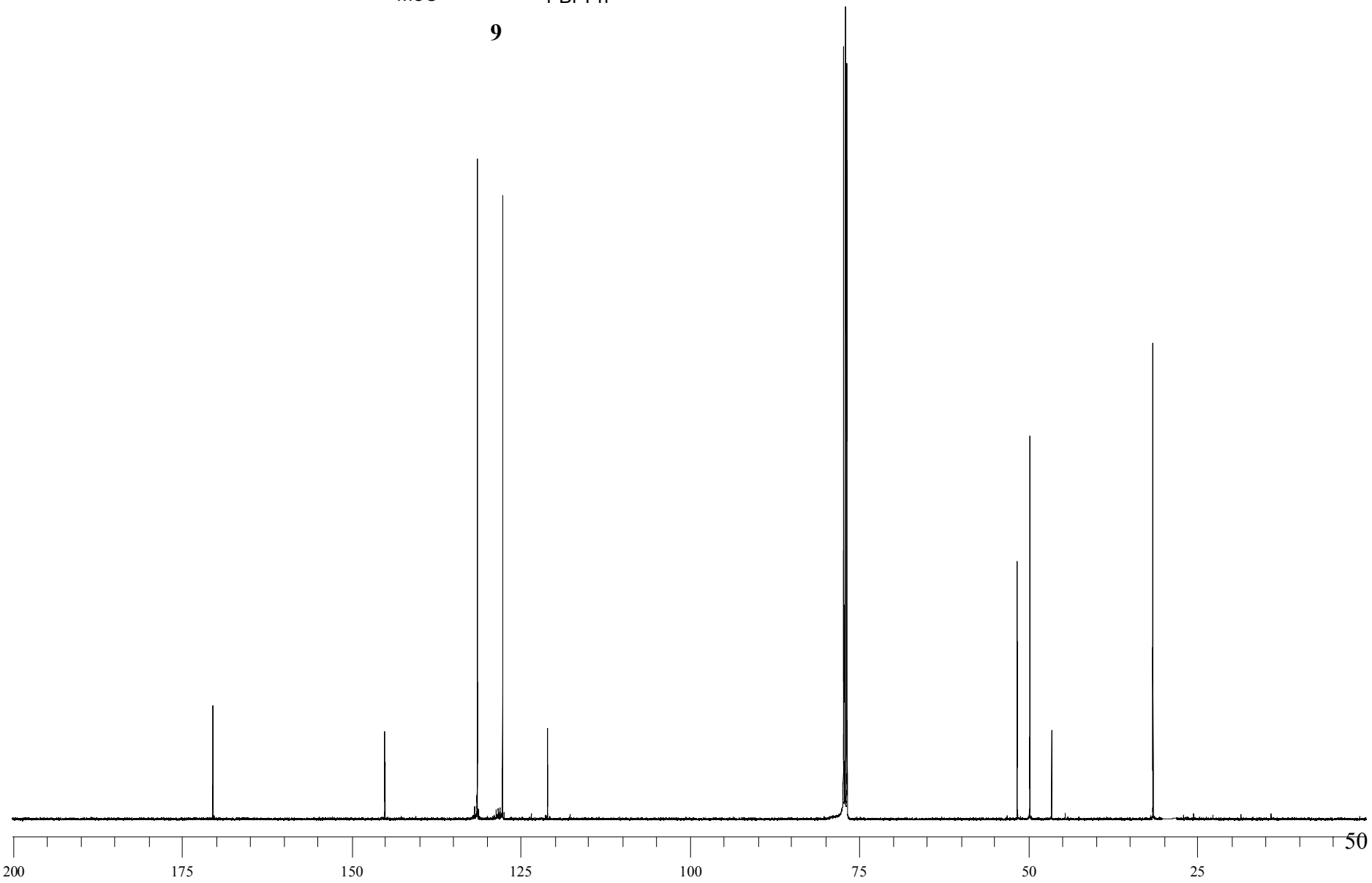

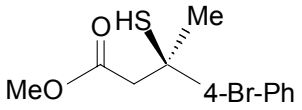

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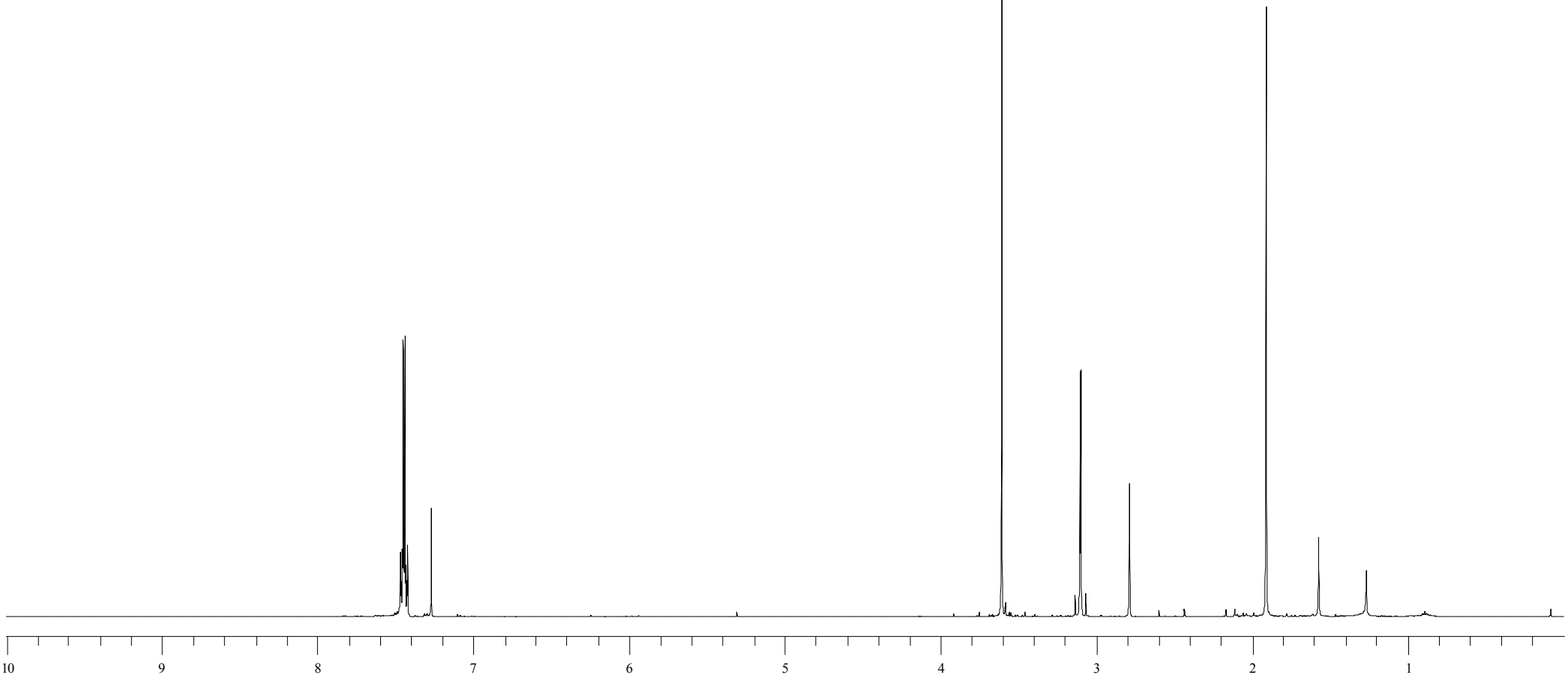

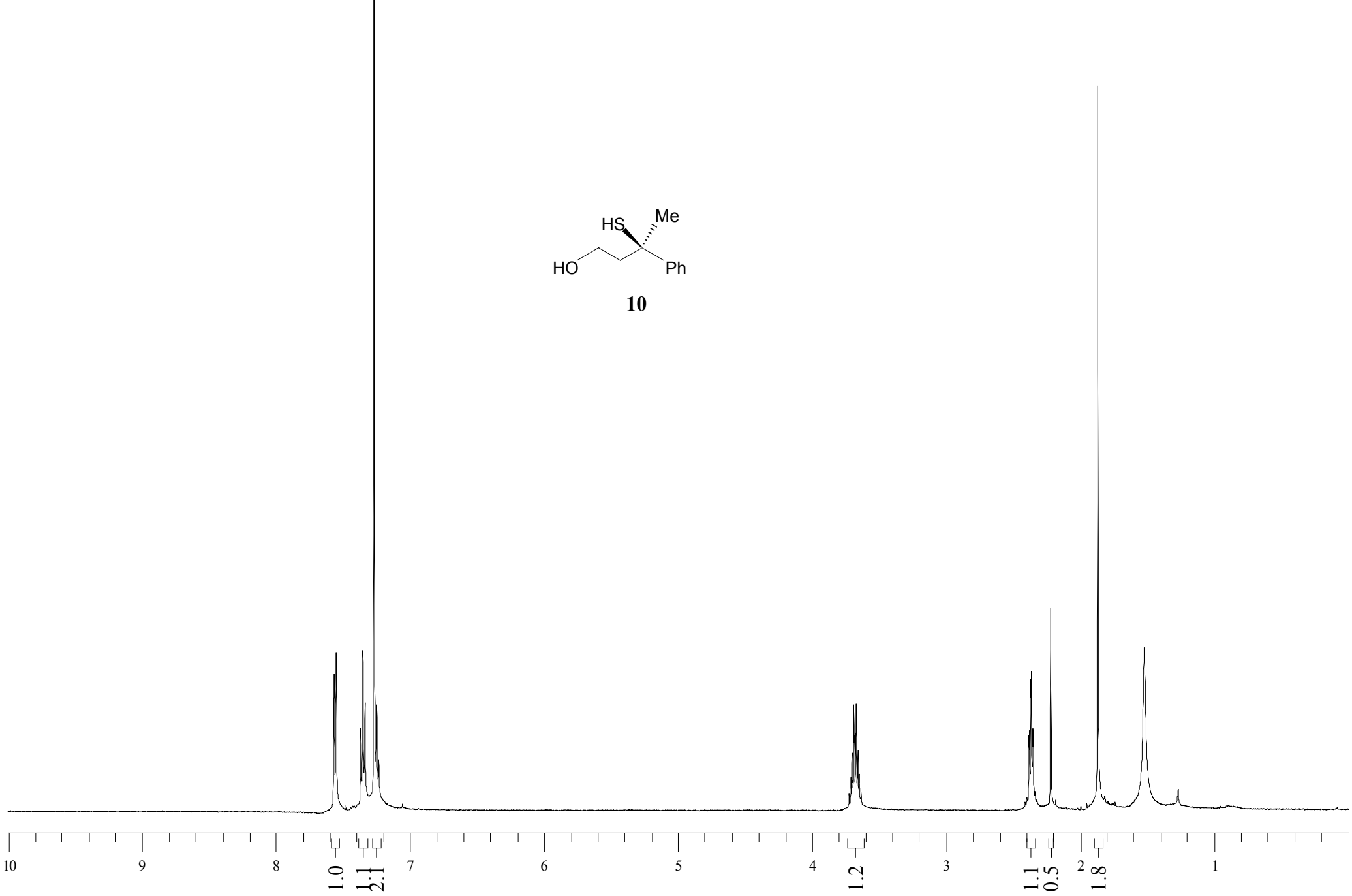
HS
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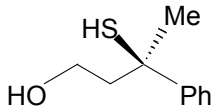
0.5
1.8



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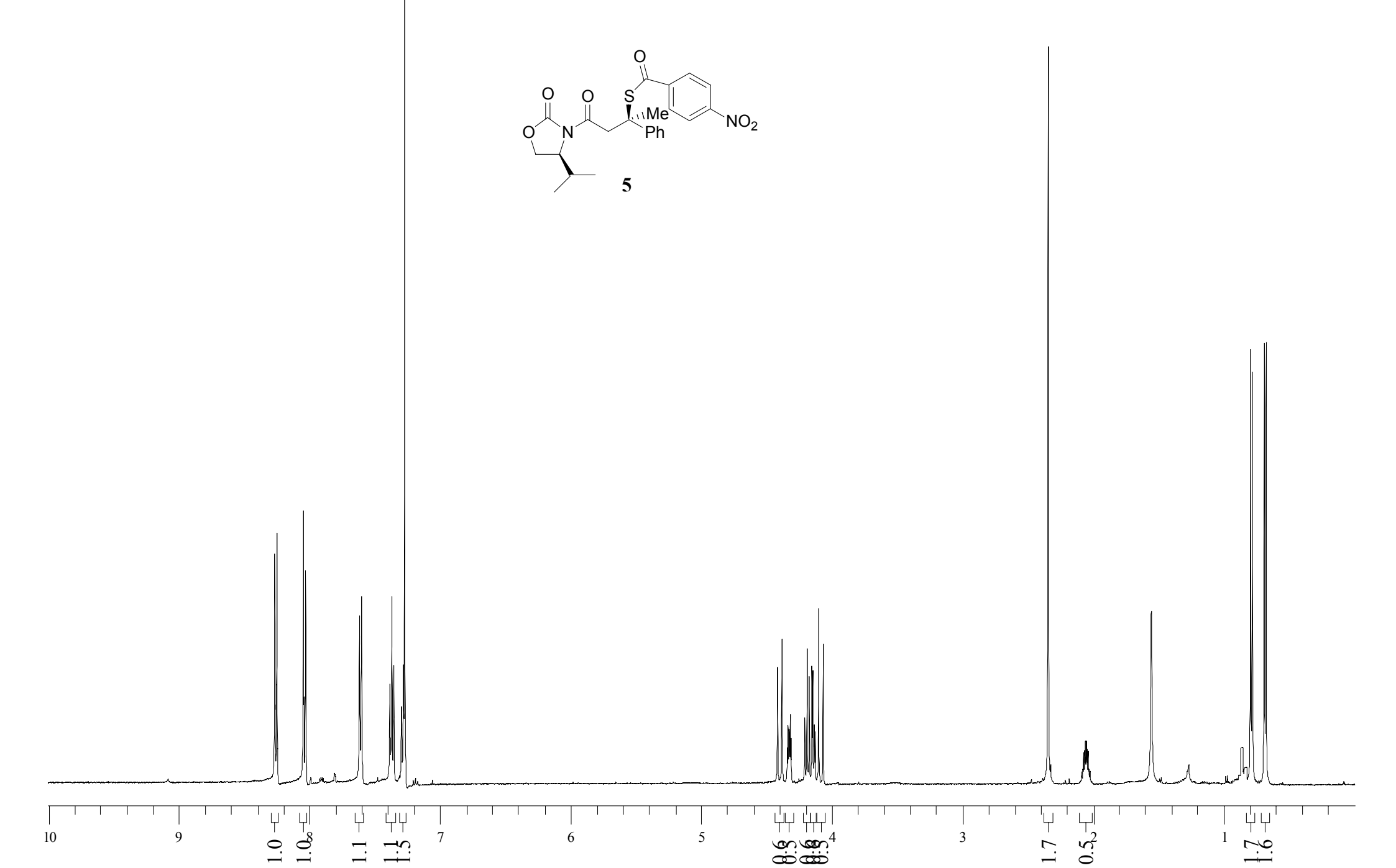
O
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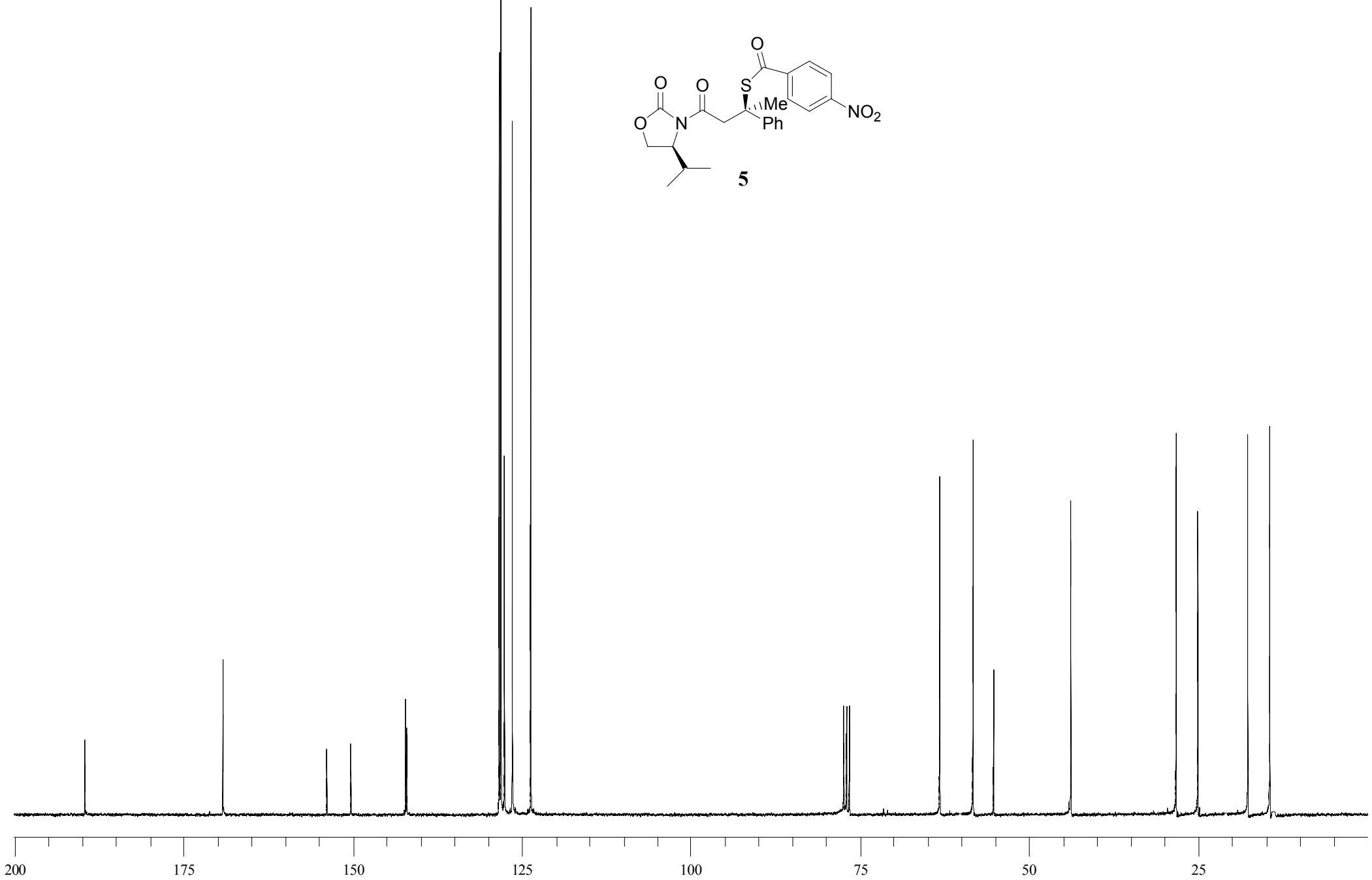
0.5
1.7
1.6



5