Supplementary Material (ESI) for Chemical Communications

SUPPORTING INFORMATION

One-Pot Approach for the Synthesis of *trans*-Cyclopropyl Compounds from Aldehydes. Application to the Synthesis of GPR40 Receptor Agonists

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GENERAL INFORMATION

Unless otherwise noted, all non-aqueous reactions were run under an inert atmosphere (argon) with rigid exclusion of moisture from reagents and glassware using standard techniques for manipulating air-sensitive compounds.[1] All glassware was stored in the oven and/or was flame dried prior to use under an inert atmosphere of gas. The solvents were dried using standard methods prior to use. Analytical thin-layer chromatography (TLC) was performed on precoated, glass-backed silica gel (Merck 60 F254). Visualization of the developed chromatogram was performed by UV absorbance, aqueous cerium molybdate, ethanolic phosphomolybdic acid, iodine, or aqueous potassium permanganate. Flash column chromatography was performed using 230-400 mesh silica (EM Science or Silicycle) of the indicated solvent system according to standard technique.[2] Melting points were obtained on a Buchi melting point apparatus and are uncorrected. Infrared spectra were taken on a Perkin Elmer Spectrum One FTIR and are reported in reciprocal centimeters (cm^{-1}). Only the most important and relevant frequencies are reported. Nuclear magnetic resonance spectra (^{1}H, ^{13}C, DEPT 135, COSY, HMQC, NOESY) were recorded either on a Bruker AV 300, AMX 300, AV 400 or ARX 400 spectrometer (300, 300, 400 et 400 MHz respectively) in deuterochloroform, unless otherwise noted. Chemical shifts for ^{1}H NMR spectra are recorded in parts per million (ppm) on the δ scale relative to an internal standard of residual solvent (chloroform, δ7.26 ppm). Data are reported as follows: chemical shift, multiplicity (s = singlet, d = doublet, t = triplet, q = quartet, qn = quintet, m = multiplet and br = broad), coupling constant in Hz, integration, and assignment. Chemical shifts for 13C NMR spectra are recorded in parts per million from tetramethylsilane using the central peak of deuterochloroform (77.00 ppm) as the internal standard. All spectra were obtained with complete proton decoupling. When ambiguous, proton and carbon assignments were established using COSY, HMQC and DEPT experiments. High resolution mass spectra were performed by the Centre régional de spectroscopie de masse de l'Université de Montréal. Combustion analyses were performed by the Laboratoire d'analyse élémentaire de l'Université de Montréal. Copper(I) iodide CuI was purchased from Strem. The commercially available aldehydes were purified using standard methods prior to use. Triphenylphosphine was received from Aldrich Chemical Co and used without further purification.

CAUTION!!! Diazo compounds are toxic and potentially explosive. They should be stored in refrigerator and handled with caution in a fume hood. Ethyl diazoacetate is commercially available from Aldrich, but was prepared from ethyl glycinate hydrochloride according to the literature.[3] Diazomethane was prepared as a solution in dichloromethane (C = 0.30 to 0.50M).[4] Other diazo compounds methyl diazoacetate and *tert*-butyldiazoacetate,[5] diazoacetophenone,[6] *N*,*N*-dimethyl diazoacetamide and *N*-methoxy-*N*-methyl diazoacetamide,[7] dimethyl (diazomethyl)phosphonate[8] were prepared following literature procedure.

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1 Shriver, D. F.; Drezdzon, M. A. *The manipulation of air-sensitive compounds*; 2nd Edition ed.; Wiley: New York, 1986.

2 Still, W. C.; Kahn, M.; Mitra, A. *J. Org. Chem.* **1978**, *43*, 2923.

3 Searle N. E. *Org. Synth.* Coll. Vol. IV, **1963**, 424.

4 de Boer T. J.; Backer, H. J. *Org. Synth.* Coll. Vol. IV, **1963**, 250.

5 Regitz, M.; Hocker, J.; Liedhegener A. *Org. Synth.* Coll. Vol. V, **1973**, 179.

6 Bridson, J.N.; Hooz J. *Org. Synth.* Coll. Vol. VI, **1988**, 386.

7 Bartlett, P.A.; Carruthers, N.I.; Winter, B. M.; Long, K.P. *J. Org. Chem.* **1982**, *47*, 1284-91.

8 Ohira, S. *Synth. Commun.* **1989**, *19*, 561-564.

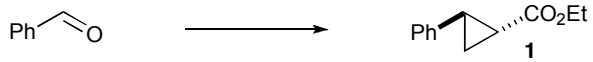
GENERAL PROCEDURES

Method A: Catalytic one-pot process in dichloromethane.
CuI (10 mg, 0.050 mmol) and triphenylphosphine (262 mg, 1.00 mmol) were placed in a vessel which was backfilled with argon. Dichloromethane (4.0 mL) was added and the resulting solution was stirred for 5 minutes until the solution became clear. The aldehyde (1.00 mmol) was then added and the mixture was heated under reflux. After 5 minutes, ethyl diazoacetate (2.00 mmol) was added in one portion and the reaction was stirred until the reaction reached completion as gauged by GC, ^{1}H NMR or TLC analysis. The mixture was cooled first to rt, then to -78 °C. $Pd_2(dba)_3$ (5 mg, 0.005 mmol) was added and a freshly prepared solution of diazomethane was slowly added (about 0.2 mL/min) until the reaction was completed. The conversion of the reaction was monitored either by NMR ^{1}H or by GC/MS. The solvent was removed under reduced pressure and the crude cyclopropane was purified by flash chromatography on silica gel.

Method B: Catalytic one-pot process in toluene.
CuI (10 mg, 0.050 mmol) and triphenylphosphine (262 mg, 1.00 mmol) were placed in a vessel which was backfilled with argon. Toluene (4.0 mL) was added and the resulting solution was stirred for 5 minutes until the solution became clear. The aldehyde (1.00 mmol) was then added and the mixture was heated at 80 °C. After 5 minutes, ethyl diazoacetate (2.00 mmol) was added in one portion and the reaction was stirred until the reaction reached completion as gauged by GC, ^{1}H NMR or TLC analysis. The mixture was cooled first to rt then to -78 °C. $Pd(OAc)_2$ (2 mg, 0.01 mmol) was added and a freshly prepared solution of diazomethane was slowly added (about 0.2 mL/min) until the reaction was completed. The conversion of the reaction was monitored either by NMR ^{1}H or by GC/MS. The solvent was removed under reduced pressure and the crude cyclopropane was purified by flash chromatography on silica gel.

Method C: Catalytic one-pot process in dichloroethane.
CuI (10 mg, 0.050 mmol) and triphenylphosphine (262 mg, 1.00 mmol) were placed in a vessel which was backfilled with argon. Dichloroethane (4 mL) was added and the resulting solution was stirred for 5 minutes until the solution became clear. The aldehyde (1.00 mmol) was then added and the mixture is heated at 80 °C. After 5 minutes, ethyl diazoacetate (2.00 mmol) was added in one portion and the reaction was stirred until the reaction reached completion as gauged by GC, ^{1}H NMR or TLC analysis. The mixture was first to rt, then to -78 °C. $Pd_2(dba)_3$ (5 mg, 0.005 mmol) was added and a freshly prepared solution of diazomethane was slowly added (about 0.2 mL/min) until the reaction was completed. The conversion of the reaction was monitored either by NMR ^{1}H or by GC/MS. The solvent was removed under reduced pressure and the crude cyclopropane was purified by flash chromatography on silica gel.

CHARACTERIZATION OF PRODUCTS



1

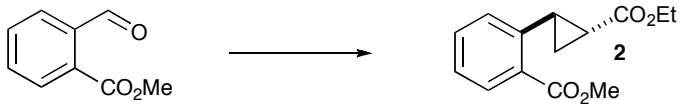
(1*R,2*R**)-Ethyl 2-phenylcyclopropanecarboxylate (1).**[9] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **1** (161 mg, 85%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.24 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.30-7.17 (M, 3H), 7.11-7.09 (M, 2H), 4.17 (q, J = 7 Hz, 2H), 2.55-2.48 (m, 1H), 1.93-1.87 (m, 1H), 1.63-1.57 (m, 1H), 1.34-1.27 (m, 1H), 1.28 (t, J = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3,

[9] Huang, L.; Chen, Y.; Gao, G.-Y.; Zhang, X. P. *J. Org. Chem.* **2003**, *68*, 8179 - 8184.

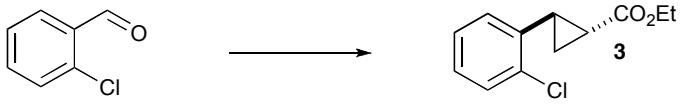
140.0, 128.4, 126.4, 126.1, 60.6, 26.1, 24.1, 17.0, 14.2. IR (neat) 3060, 1662, 1600, 1283, 1223, 1012 cm^{-1}.

(1*R,2*R**)-Ethyl 2-phenylcyclopropanecarboxylate (1).** The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 6.00 mmol of diazomethane. The desired cyclopropane **1** (131 mg, 69%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes).

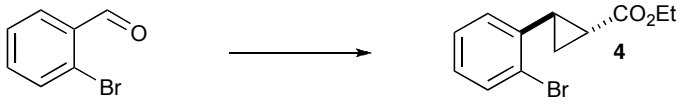
(1*R,2*R**)-Ethyl 2-phenylcyclopropanecarboxylate (1).** The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **C** using 6.00 mmol of diazomethane. The desired cyclopropane **1** (146 mg, 77%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes).



Methyl 2-((1*R,2*R**)-2-(ethoxycarbonyl)cyclopropyl)benzoate (2).** The title compound was prepared from methyl 2-formylbenzoate[10] (164 mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **2** (221 mg, 89%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.20 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.87 (dd, *J* = 8, 1 Hz, 1H), 7.44-7.40 (m, 1H), 7.30-7.26 (m, 1H), 7.13 (d, *J* = 8 Hz, 1H), 4.20 (q, *J* = 7 Hz, 2H), 3.88 (s, 3H), 3.14-3.09 (m, 1H), 1.78-1.73 (m, 1H), 1.63-1.58 (m, 1H), 1.36-1.31 (m, 1H), 1.30 (t, *J* = 7 Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 167.9, 140.5, 131.9, 131.4, 130.5, 127.2, 126.6, 60.5, 52.1, 25.4, 23.3, 15.6, 14.3; IR (neat) 2955, 1726, 1451, 1295, 1260, 1184 cm^{-1}; HRMS (FAB) calcd for $C_{14}H_{17}O_4$ $[M+H]^+$: 249.1121. Found 249.1120.



(1*R,2*R**)-Ethyl 2-(2-chlorophenyl)cyclopropanecarboxylate (3).**[11] The title compound was prepared from 2-chlorobenzaldehyde (113 μL, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **3** (157 mg, 70%) was obtained as a light yellow oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.25 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.38-7.35 (m, 1H), 7.19-7.15 (m, 2H), 7.02-6.99 (m, 1H), 4.20 (q, *J* = 7 Hz, 2H), 2.78-2.71 (m, 1H), 1.84-1.78 (m, 1H), 1.65-1.59 (m, 1H), 1.35-1.28 (m, 1H), 1.29 (t, *J* = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 137.4, 135.6, 129.3, 127.8, 127.0, 126.7, 60.7, 24.2, 22.9, 15.5, 14.2; IR (neat) 2981, 1726, 1445, 1408, 1326, 1182 cm^{-1}.

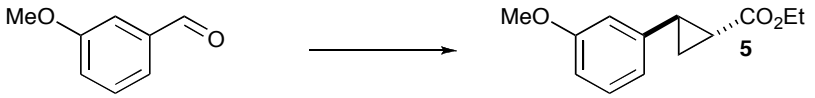


(1*R,2*R**)-Ethyl 2-(2-bromophenyl)cyclopropanecarboxylate (4).** The title compound was prepared from 2-bromobenzaldehyde (117 μL, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **4** (180 mg, 67%) was obtained as a light yellow oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.27 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.56 (dd, *J* = 8, 1 Hz, 1H), 7.26-7.20 (m, 1H), 7.11-7.00 (m, 2H), 4.21 (q, J = 7 Hz, 2H), 2.74-2.67 (m, 1H), 1.82-1.76 (m, 1H), 1.65-1.59 (m, 1H), 1.36-1.28 (m, 1H), 1.29 (t, *J* = 7 Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.2, 139.0, 132.5, 128.1, 127.4, 127.3, 126.2, 60.7, 26.9, 23.1, 15.6,

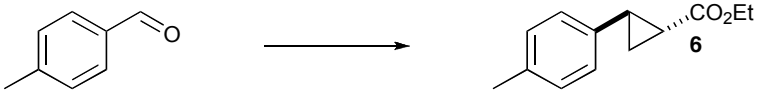
[10] This compound was prepared from 2-carboxybenzaldehyde: Ye, B.-H.; Naruta, Y. *Tetrahedron*, **2003**, *59*, 3593-3601.

[11] Kaiser, C.; Lester, B. M.; Zirkle, C. L.; Burger, A.; Davis, C. S.; Delia, T. J.; Zirngibl, L. *J Med. Chem*. **1962**, *5*, 1243-65.

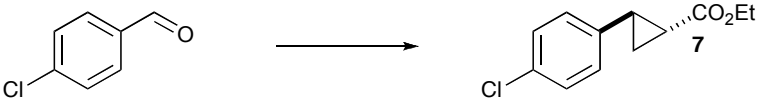
14.3. IR (neat) 2980, 1725, 1444, 1407, 1324, 1181 cm^{-1} ; HRMS (FAB) calcd for $C_{12}H_{14}BrO_2$ $[M+H]^+$: 269.0171. Found 269.0175.



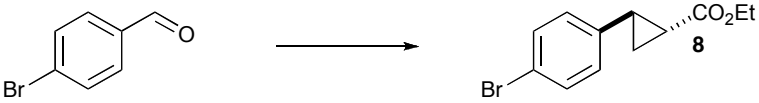
(1*R,2*R**)-Ethyl 2-(3-methoxyphenyl)cyclopropanecarboxylate (5).**[12] The title compound was prepared from *m*-anisaldehyde (122 μL, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **5** (202 mg, 92%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.46 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.19 (t, *J* = 8 Hz, 1H), 6.74 (d, *J* = 8 Hz, 1H), 6.68 (d, *J* = 8 Hz, 1H), 6.64 (s, 1H), 4.16 (q, *J* = 7 Hz, 2H), 3.79 (s, 3H), 2.51-2.46 (m, 1H), 1.92-1.87 (m, 1H), 1.61-1.56 (m, 1H), 1.32-1.27 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.3, 159.6, 141.7, 129.4, 118.4, 112.0, 111.6, 60.7, 55.1, 26.1, 24.1, 17.0, 14.2; IR (neat) 2980, 2835, 1722, 1603, 1407, 1181 cm^{-1}; HRMS (FAB) calcd for $C_{13}H_{17}O_3$ $[M+H]^+$: 221.1168. Found 221.1172.



(1*R,2*R**)-Ethyl 2-*p*-tolylcyclopropanecarboxylate (6).**[9] The title compound was prepared from *p*-tolualdehyde (118 μL, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **6** (163 mg, 80%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.18 (5% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.09 (d, *J* = 8 Hz, 2H), 6.99 (d, *J* = 8 Hz, 2H), 4.16 (q, *J* = 7 Hz, 2H), 2.52-2.45 (m, 1H), 2.31 (s, 3H), 1.89-1.83 (m, 1H), 1.60-1.53 (m, 1H), 1.31-1.14 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 137.0, 136.0, 129.1, 126.0, 60.6, 25.9, 24.0, 20.9, 16.9, 14.2; IR (neat) 2981, 1725, 1405, 1331, 1182 cm^{-1}.



(1*R,2*R**)-Ethyl 2-(4-chlorophenyl)cyclopropanecarboxylate (7).**[13] The title compound was prepared from 4-chlorobenzaldehyde (140 mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **7** (169 mg, 75%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.32 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.23 (d, *J* = 8 Hz, 2H), 7.02 (d, *J* = 8 Hz, 2H), 4.17 (q, *J* = 7 Hz, 2H), 2.50-2.45 (m, 1H), 1.88-1.83 (m, 1H), 1.62-1.57 (m, 1H), 1.29-1.24 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.0, 138.6, 132.1, 128.5, 127.5, 60.7, 25.4, 24.1, 17.0, 14.2; IR (neat) 2981, 1722, 1496, 1328, 1185 cm^{-1}.

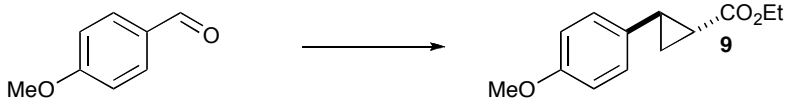


(1*R,2*R**)-Ethyl 2-(4-bromophenyl)cyclopropanecarboxylate (8).**[12] The title compound was prepared from 4-bromobenzaldehyde (185 mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **8** (193 mg, 72%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.35 (10% EtOAc/hexanes). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.39 (d, *J* = 8 Hz, 2H), 6.96 (d, *J* = 8 Hz, 2H), 4.16 (q, *J* = 7 Hz, 2H), 2.50-2.43 (m, 1H),

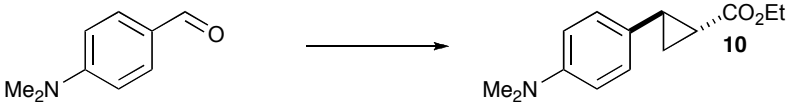
12 Hixson, S. S.; Franke, L. A.; Gere, J. A.; Xing, Y. D. *J. Am. Chem. Soc.* **1988**, *110*, 3601-10.

13 Niimi, T.; Uchida, T.; Irie, R.; Katsuki, T. *Adv. Synth. Catal.* **2001**, *343*, 79-88.

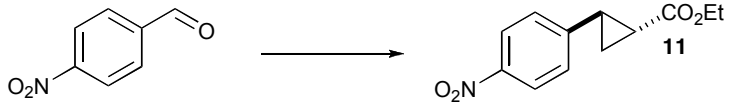
1.89-1.83 (m, 1H), 1.63-1.56 (m, 1H), 1.29-1.23 (m, 1H), 1.27 (t, J = 7Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.1, 139.1, 131.4, 127.8, 120.1, 60.8, 25.5, 24.1, 17.0, 14.2; IR (neat) 2984, 1720, 1495, 1408, 1328, 1183 cm^{-1}.



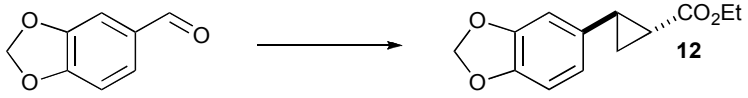
(1*R,2*R**)-Ethyl 2-(4-methoxyphenyl)cyclopropanecarboxylate (9).**[9] The title compound was prepared from *p*-anisaldehyde (121 μL, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **9** (168 mg, 76%) was obtained as a light yellow solid after flash chromatography (10% EtOAc/Hexanes). R_f 0.38 (20% EtOAc/hexanes). M.p. 83 °C (litt. 85 °C).[14] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.03 (d, J = 8 Hz, 2H), 6.82 (d, J = 8 Hz, 2H), 4.16 (q, J = 7 Hz, 2H), 3.78 (s, 3H), 2.51-2.44 (m, 1H), 1.85-1.79 (m, 1H), 1.58-1.52 (m, 1H), 1.28-1.22 (m, 1H), 1.27 (t, J = 7Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.5, 158.2, 132.0, 127.3, 113.8, 60.6, 55.2, 25.6, 23.8, 16.7, 14.2. IR (neat) 2982, 1721, 1606, 1408, 1180 cm^{-1}.



(1*R,2*R**)-Ethyl 2-(4-(dimethylamino)phenyl)cyclopropanecarboxylate (10).** The title compound was prepared from 4-dimethylaminobenzaldehyde (149 mg, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **10** (147 mg, 63%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.34 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.99 (d, J = 8 Hz, 2H), 6.67 (d, J = 8 Hz, 2H), 4.15 (q, J = 7 Hz, 2H), 2.91 (s, 6H), 2.47-2.42 (m, 1H), 1.82-1.77 (m, 1H), 1.54-1.50 (m, 1H), 1.27-1.22 (m, 1H), 1.27 (t, J = 7Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 149.4, 127.8, 127.0, 112.8, 60.5, 40.7, 25.7, 23.7, 16.5, 14.2; IR (neat) 2979, 2903, 1713, 1520, 1335, 1176 cm^{-1}; HRMS (FAB) calcd for $C_{14}H_{20}NO_2$ $[M+H]^+$: 234.1483. Found 234.1488.



(1*R,2*R**)-Ethyl 2-(4-nitrophenyl)cyclopropanecarboxylate (11).**[15] The title compound was prepared from 4-nitrobenzaldehyde (151 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **11** (139 mg, 59%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.45 (20% EtOAc/hexanes); m.p. 52 °C (litt.: 50 °C); ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.14 (d, J = 9 Hz, 2H), 7.20 (d, J = 9 Hz, 2H), 4.18 (q, J = 7 Hz, 2H), 2.62-2.56 (m, 1H), 2.02-1.96 (m, 1H), 1.75-1.69 (m, 1H), 1.41-1.34 (m, 1H), 1.28 (t, J = 7Hz, 3H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.4, 148.1, 146.5, 126.6, 123.7, 61.0, 25.6, 25.1, 17.8, 14.2; IR (neat) 2982, 1721,1517, 1343, 1177 cm^{-1}.



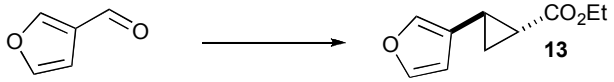
(1*R,2*R**)-Ethyl 2-(benzo[d][1,3]dioxol-6-yl)cyclopropanecarboxylate (12).**[16] The title compound was prepared from piperonal (150 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **12** (171 mg, 73%) was obtained as a light yellow oil

[14] Herbert O. House, H.O.; McDaniel, W. C.; Sieloff, R. F.;Vanderveer D. *J. Org. Chem.* **1978**, *43*, 4316-4323.

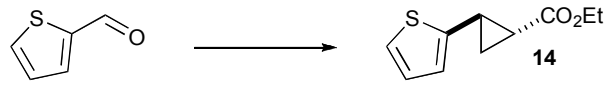
[15] Rasmussen, T.; Jensen, J. F.; Oestergaard, N.; Tanner, D.; Ziegler, T.; Norrby, P.-O. *Chem. Eur. J.* **2002**, *8*, 177-184.

[16] Yamashita, M.; Okuyama, K.; Ohhara, T.; Kawasaki, I.; Sakai, K. *Chem. Pharm. Bull.* **1995**, *43*, 2075-2081.

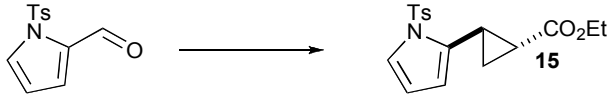
after flash chromatography (10% EtOAc/Hexanes). R_f 0.40 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 6.71 (d, *J* = 10 Hz, 1H), 6.60 (dd, *J* = 10, 2 Hz, 1H), 6.56 (d, *J* = 2 Hz, 1H), 5.91 (s, 2H), 4.16 (q, *J* = 10 Hz, 2H), 2.48-2.42 (m, 1H), 1.83-1.77 (m, 1H), 1.56-1.50 (m, 1H), 1.27 (t, *J* = 10 Hz, 3H) 1.26-1.19 (m, 1H) ; ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.4, 147.7, 146.1, 133.8, 119.6, 108.1, 106.6, 100.9, 60.6, 26.0, 23.9, 16.7, 14.2; IR (neat) 2890, 1487, 1245, 1039 cm^{-1}.



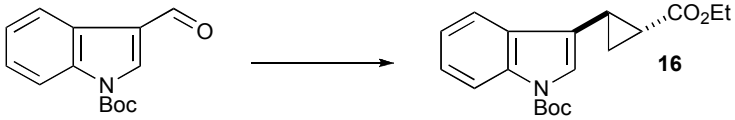
(1*R,2*R**)-Ethyl 2-(furan-3-yl)cyclopropanecarboxylate (13).** The title compound was prepared from 3-furfuraldehyde (86 μL mg, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropane **13** (128 mg, 71%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.15 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.32 (s, 1H), 7.28 (s, 1H), 6.15 (s, 1H), 4.15 (q, *J* = 7 Hz, 2H), 2.35-2.30 (m, 1H), 1.77-1.73 (m, 1H), 1.51-1.47 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H) 1.14-1.09 (m, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 143.1, 139.1, 124.7, 108.9, 60.6, 22.6, 17.1, 16.1, 14.2; IR (neat) 2981, 2933, 1721, 1323, 1181 cm^{-1}; HRMS (FAB) calcd for $C_{10}H_{13}O_3$ $[M+H]^+$: 181.0865. Found 181.0866.



(1*R,2*R**)-Ethyl 2-(thiophen-2-yl)cyclopropanecarboxylate (14).**[16] The title compound was prepared from 2-thiophenecarboxaldehyde (93 μL, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **14** (125 mg, 77%) was obtained as colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.35 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.09 (d, *J* = 5 Hz, 1H), 6.90 (dd, *J* = 5, 4 Hz, 1H), 6.82 (d, *J* = 4 Hz, 1H), 4.17 (q, *J* = 7 Hz, 2H), 2.72-2.67 (m, 1H), 1.95-1.90 (m, 1H), 1.64-1.59 (m, 1H), 1.34-1.28 (m, 1H), 1.28 (t, *J* = 7 Hz, 3H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.8, 144.1, 126.8, 123.8, 123.0, 60.7, 24.9, 21.4, 17.9, 14.2; IR (neat) 2980, 1721, 1404, 1178, 1045 cm^{-1}.



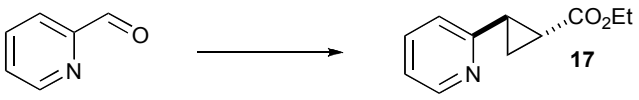
(1*R,2*R**)-Ethyl 2-(1-tosyl-1H-pyrrol-2-yl)cyclopropanecarboxylate (15).** The title compound was prepared from 1-tosyl-1H-pyrrole-2-carbaldehyde[17] (249 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **15** (273 mg, 82%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.29 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.65 (d, *J* = 8 Hz, 2H), 7.26-7.21 (m, 3H), 6.10 (t, *J* = 3Hz, 1H), 5.83 (s, 1H), 4.15 (q, *J* = 7 Hz, 2H), 2.57-2.52 (m, 1H), 2.36 (s, 3H), 1.58-1.54 (m, 1H), 1.39-1.33 (m, 1H), 1.26 (t, *J* = 7 Hz, 3H), 1.06-1.01 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 172.7, 144.8, 136.1, 133.6, 129.9, 127.0, 122.9, 111.3, 110.7, 60.7, 23.3, 21.6, 18.2, 15.1, 14.2; IR (neat) 2981, 2923, 1721, 1366, 1175, 1154, 1055 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{20}NO_4S$ $[M+H]^+$: 334.1107. Found 334.1101.



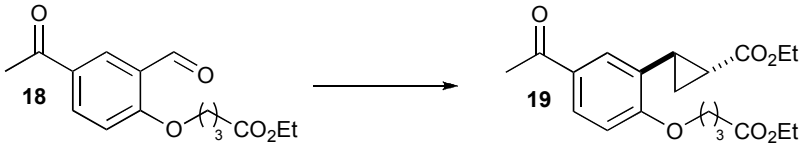
***tert*-Butyl 3-(1*R**,2*R**)-2-(ethoxycarbonyl)cyclopropyl)-1H-indole-1-carboxylate (16).** The title compound was prepared from *tert*-butyl 3-formyl-1H-indole-1-carboxylate[18] (245 mg, 1.00 mmol)

[17] Masquelin, T.; Broger, E.; Mueller, K.; Schmid, R.; Obrecht, D. *Helv. Chim. Acta*, **1994**, *77*, 1395-1411.
[18] Davies, J. R.; Kane, P. D.; Moody, C. J.; Slawin, A. M. Z. *J. Org. Chem.* **2005**, *70*, 5840-5851.

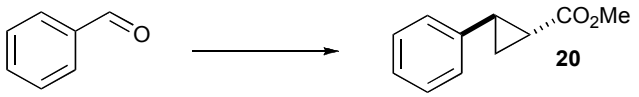
according to the general procedure **A** using 10.50 mmol of diazomethane. The desired cyclopropane **16** (227 mg, 69%) was obtained as a light yellow oil after an oxidative work-up and a flash chromatography (5% EtOAc/Hexanes). R_f 0.43 (20% EtOAc/hexanes). The oxidative work-up proceeded as follow: The crude product was dissolved in dichloromethane (10 mL) and cooled to −78°C. The solution was treated with ozone until the solution was blue. Oxygen was then bubbled into the mixture until the blue color had disappeared. Methyl sulfide (1 mL) was added at −78°C and left to warm to room temperature overnight. The solution was concentrated under reduced pressure and the residue was purified by column chromatography. ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J = 7 Hz, 1H), 7.61 (d, J = 8 Hz, 1H), 7.35-7.23 (m, 3H), 4.21 (q, J = 7 Hz, 2H), 2.57-2.50 (m, 1H), 1.92-1.87 (m, 1H), 1.66 (s, 9H), 1.62-1.55 (m, 2H), 1.31 (t, J = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.6, 149.5, 135.4, 130.4, 124.6, 122.5, 121.9, 120.2, 118.9, 115.2, 83.6, 60.7, 28.1, 21.7, 17.1, 15.3, 14.2. IR (neat) 2976, 1743, 1365, 1150 cm^{-1}; HRMS (FAB) calcd for $C_{19}H_{24}NO_4$ $[M+H]^+$: 330.1699. Found 330.1695.



(1*R,2*R**)-Ethyl 2-(pyridin-2-yl)cyclopropanecarboxylate (17).**[10] The title compound was prepared from 2-pyridinecarboxaldehyde (95 μL mg, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **17** (117 mg, 61%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.25 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.43-8.41 (m, 1H), 7.56-7.50 (m, 1H), 7.20 (d, J = 8 Hz, 1H), 7.08-7.03 (m, 1H), 4.14 (q, J = 7 Hz, 2H), 2.59-2.52 (m, 1H), 2.25-2.19 (m, 1H), 1.63-1.54 (m, 2H), 1.25 (t, J = 7 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.3, 158.8, 149.3, 135.9, 122.4, 121.2, 60.6, 27.1, 24.2, 17.2, 14.1; IR (neat) 2981, 1721, 1595, 1475, 1329, 1178 cm^{-1}.



(1*R,2*R**)-Ethyl 2-(2-(3-(ethoxycarbonyl)propoxy)-5-acetylphenyl) cyclopropanecarboxylate (19).** The title compound was prepared from ethyl 4-(4-acetyl-2-formylphenoxy)butanoate **18**[19] (278 mg, 1.00 mmol) according to the general procedure **A** using 7.50 mmol of diazomethane. The desired cyclopropanes **19** (188 mg, 52%) was obtained as a light yellow oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.43 (20% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.80 (dd, J = 12, 3 Hz, 1H), 7.58 (d, J = 3 Hz, 1H), 6.84 (d, J = 12 Hz, 1H), 4.23-4.08 (m, 6H), 2.68-2.61 (m, 1H), 2.52 (s, 3H), 2.51 (t, J = 10 Hz, 2H), 2.19-2.10 (m, 2H), 1.81-1.75 (m, 1H), 1.59-1.53 (m, 1H), 1.40-1.33 (m, 1H), 1.28 (t, J = 10 Hz, 3H), 1.24 (t, J = 10 Hz, 3H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 196.7, 173.5, 172.9, 161.5, 129.8, 129.2, 128.6, 126.7, 110.1, 67.1, 60.6, 60.4, 30.4, 26.2, 24.4, 22.4, 21.2, 14.9, 14.2, 14.1. IR (neat) 2980, 1725, 1676, 1601, 1259, 1182; HRMS (FAB) calcd for $C_{20}H_{27}O_6$ $[M+H]^+$: 363.1802. Found 363.1812.

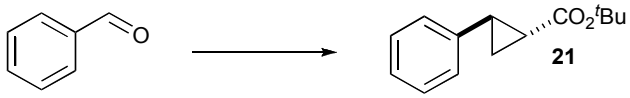


(1*R,2*R**)-Methyl 2-phenylcyclopropanecarboxylate (20).**[20] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **A** using 6.00 mmol of diazomethane. The desired cyclopropane **20** (143 mg, 81%) was obtained as a colorless oil after flash

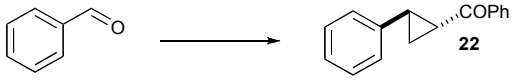
[19] Kahnberg, P.; Lee, C. W.; Grubbs, R. H.; Sterner, O. *Tetrahedron* **2002**, *58*, 5203-5208.

[20] Walser, P.; Renold, P.; N'Goka, V.; Hosseinzadeh, F.; Tamm, C. *Helv. Chim. Acta* **1991**, *74*, 1941-1952.

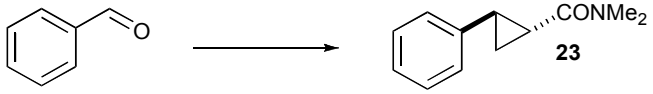
chromatography (5% EtOAc/Hexanes). R_f 0.29 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.22-7.20 (m, 1H), 7.11-7.09 (m, 2H), 3.72 (s, 3H), 2.56-2.51 (m, 1H), 1.93-1.89 (m, 1H), 1.63-1.58 (m, 1H), 1.35-1.30 (m, 1H) ; ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.8, 139.9, 128.4, 126.4, 126.1, 51.8, 26.2, 23.9, 16.9; IR (neat) 3029, 2951, 1724, 1440, 1197, 1171 cm^{-1}.



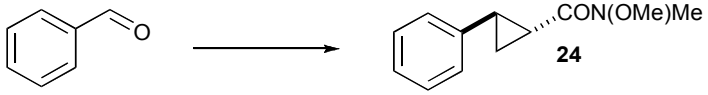
(1*R,2*R**)-*tert*-Butyl 2-phenylcyclopropanecarboxylate (21).**[21] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **C** using 6.00 mmol of diazomethane. The desired cyclopropane **21** (161 mg, 74%) was obtained as a colorless oil after flash chromatography (5% EtOAc/Hexanes). R_f 0.34 (10% EtOAc/hexanes). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.29-7.26 (m, 2H), 7.21-7.17 (m, 1H), 7.10-7.08 (m, 2H), 2.46-2.41 (m, 1H), 1.85-1.81 (m, 1H), 1.55-1.50 (m, 1H), 1.46 (s, 9H), 1.25-1.21 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.5, 140.5, 128.4, 126.2, 126.0, 80.5, 28.1, 25.7, 25.2, 17.0; IR (neat) 2977, 1705, 1637, 1328, 1314, 1148 cm^{-1}.



Phenyl((1*R,2*R**)-2-phenylcyclopropyl)methanone (22).**[22] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 6.00 mmol of diazomethane. The desired cyclopropane **22** (162 mg, 73%) was obtained as a yellow solid after flash chromatography (5% EtOAc/Hexanes). R_f 0.53 (20% EtOAc/hexanes); m.p. 44 °C (litt. 45-47 °C);[23] ^{1}H NMR (400 MHz, $CDCl_3$) δ 8.00 (d, J = 7 Hz, 2H), 7.58-7.54 (m, 1H), 7.48-7.44 (m, 2H), 7.33-7.30 (m, 2H), 7.26-7.17 (m, 3H), 2.93-2.89 (m, 1H), 2.73-2.68 (m, 1H), 1.95-1.91 (m, 1H), 1.59-1.54 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 198.5, 140.4, 137.7, 132.8, 128.5 (2C), 128.0, 126.5, 126.2, 29.9, 29.2, 19.2; IR (neat) 2980, 1711, 1627, 1272, 1164 cm^{-1}.



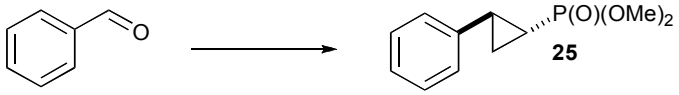
(1*R,2*R**)-*N*,*N*-dimethyl-2-phenylcyclopropanecarboxamide (23).**[24] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 4.50 mmol of diazomethane. The desired cyclopropane **23** (155 mg, 82%) was obtained as a colorless solid after flash chromatography (50% EtOAc/Hexanes). R_f 0.19 (50% EtOAc/hexanes); m.p. 59 °C (litt. 61 °C);[10] ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.31-7.12 (m, 5H), 3.14 (s, 3H), 3.00 (s, 3H), 2.52-2.45 (m, 1H), 2.03-1.97 (m, 1H), 1.68-1.61 (m, 1H), 1.30-1.24 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 171.8, 141.0, 128.4, 126.1, 126.0, 37.2, 35.8, 25.4, 23.1, 16.2.; IR (neat) 3028, 2930, 1634, 1496, 1417, 1139 cm^{-1}.



(1*R,2*R**)-*N*-methoxy-*N*-methyl-2-phenylcyclopropanecarboxamide (24).**[25] The title compound was prepared from benzaldehyde (102μL, 1.00 mmol) according to the general procedure **C** using 4.50 mmol of diazomethane. The desired cyclopropane **24** (181 mg, 88%) was obtained as a pale yellow oil after flash chromatography (50% EtOAc/Hexanes). R_f 0.22 (80% EtOAc/hexanes). M.p. 59 °C. ^{1}H

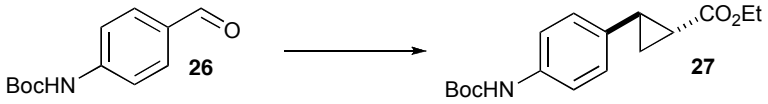
[21] Lyle, M. P. A.; Wilson, P. D. *Org. Lett.* **2004**, *6*, 855-858.
[22] Pyne, S. G.; Dong, Z.; Skelton, B. W.; White, A. H. *J. Org. Chem.* **1997**, *62*, 2337-2343.
[23] Wessig, P.; Muhling, O. *Helv. Chim. Acta*, **2003**, *86*, 865-893.
[24] Doyle, M. P.; Loh, K.-L.; DeVries, K. M.; Chinn, M. S. *Tetrahedron Lett.* **1987**, *28*, 833-836.
[25] Woo, J. C. S.; Fenster, E.; Dake, G. R. *J. Org. Chem.* **2004**, *69*, 8984-8986.

NMR (300 MHz, $CDCl_3$) δ 7.30-7.12 (m, 5H), 3.69 (s, 3H), 3.23 (s, 3H), 2.53-2.39 (m, 2H), 1.66-1.60 (m, 1H), 1.34-1.27 (m, 1H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 173.0, 140.7, 128.4, 126.26, 126.20, 61.7, 32.5, 25.9, 21.5, 16.5; IR (neat) 2936, 2241, 1650, 1437, 1274, 1176, 1119, 995, 910, 728 cm^{-1}.

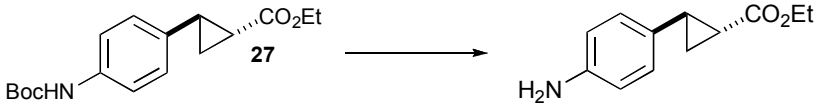


(1*R,2*R**)-Dimethyl 2-phenylcyclopropylphosphonate (25).**[26] The title compound was prepared from benzaldehyde (102 μL, 1.00 mmol) according to the general procedure **B** using 4.50 mmol of diazomethane. The desired cyclopropane **25** (156 mg, 69%) was obtained as a yellow oil after flash chromatography (80% EtOAc/Hexanes). R_f 0.31 (100% EtOAc). ^1H NMR (400 MHz, $CDCl_3$) δ 7.30-7.26 (m, 2H), 7.22-7.18 (m, 1H), 7.11 (d, *J* = 7 Hz, 2H), 3.79 (d, *J* = 8 Hz, 3H), 3.76 (d, *J* = 8 Hz, 3H), 2.53-2.44 (m, 1H), 1.54-1.45 (m, 1H), 1.30-1.22 (m, 1H), 1.16-1.10 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 139.8 (d, *J* = 3 Hz), 128.5, 126.6, 126.1, 52.7 (d, *J* = 8 Hz), 20.9 (d, *J* = 5 Hz), 13.8 (d, *J* = 192 Hz), 12.4 (d, *J* = 6 Hz); ^{31}P NMR (121 MHz, $CDCl_3$) δ 23.1; IR (neat) 2952, 2851, 1459, 1244, 1027 cm^{-1}.

SYNTHESIS OF CYCLOPROPANECARBOXYLIC ACID 31.



***tert*-Butyl 4-((1*R**,2*R**)-2-(ethoxycarbonyl)cyclopropyl)phenylcarbamate (27).** The title compound was prepared from 4-(*tert*-butoxycarbonylamino)benzaldehyde (**26**)[27] (221 mg, 1.00 mmol) according to the general procedure **A** using 4.50 mmol of diazomethane. The desired cyclopropane **27** (256 mg, 84%) was obtained as a colorless oil after flash chromatography (10% EtOAc/Hexanes). R_f 0.26 (20% EtOAc/hexanes). ^1H NMR (400 MHz, $CDCl_3$) δ 7.26 (d, *J* = 8 Hz, 2H), 7.01 (d, *J* = 8 Hz, 2H), 6.44 (s(br), 1H), 4.15 (q, *J* = 7 Hz, 2H), 2.49-2.44 (m, 1H), 1.85-1.80 (m, 1H), 1.57-1.53 (m, 1H), 1.50 (s, 9H), 1.29-1.25 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 152.6, 136.7, 134.6, 126.7, 118.6, 80.4, 60.6, 28.3, 25.7, 23.9, 16.8, 14.2; IR (neat) 3265, 2974, 1728, 1518, 1155 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{23}NO_4Na$ $[M+Na]^+$: 328.1519. Found 328.1514.



(1*R,2*R**)-Ethyl 2-(4-aminophenyl)cyclopropanecarboxylate.** To a solution of **27** (200 mg, 0.65 mmol) in DCM (4 mL) at 0 °C, was added TFA (2 mL). The resulting mixure was warmed at RT and stirred for 2 hours. The mixture was diluted with DCM (10 mL) then washed with 10% aqueous K_2CO_3 (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (5% MeOH/DCM). R_f 0.32 (20% MeOH/DCM). The free amine was obtained as a yellow oil (113 mg, 85%). ^1H NMR (400 MHz, $CDCl_3$) δ 6.90 (d, *J* = 9 Hz, 2H), 6.60 (d, *J* = 9 Hz, 2H), 4.15 (q, *J* = 7 Hz, 2H), 3.60 (s (br), 2H), 2.45-2.40 (m, 1H), 1.81-1.76 (m, 1H), 1.54-1.49 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H), 1.25-1.20 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.6, 144.9, 129.8, 127.2, 115.1, 60.5, 25.8, 23.7, 16.5, 14.2; IR (neat) 3352, 2943, 1679, 1501, 1247 cm^{-1}; HRMS (FAB) calcd for $C_{12}H_{16}NO_2$ $[M+H]^+$: 206.1175. Found 206.1174.

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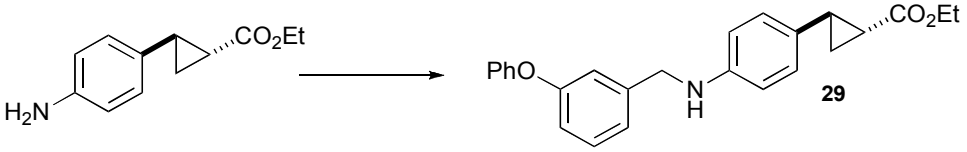
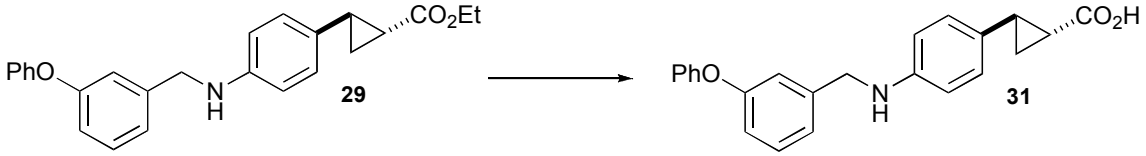
[26] Charette, A.B.C.; Bouchard, J.-E. *Can. J. Chem.* **2005**, *83*, 533-542.

[27] Niimi, T.; Orita, M.; Okazawa-Igarashi, M.; Sakashita, H.; Kikuchi, K.; Ball, E.; Ichikawa, A.; Yamagiwa, Y.; Sakamoto, S.; Tanaka, A.; Tsukamoto, S.; Fujita, S.; Tatsuta, K.; Maeda, Y.; Chikauchi, K. *J. Med. Chem.* **2001**, *44*, 4737-4740.

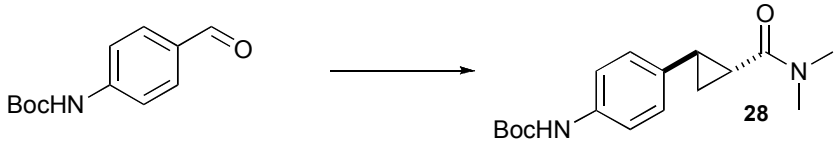


(1*R,2*R**)-Ethyl 2-(4-(3-phenoxybenzylamino)phenyl)cyclopropanecarboxylate (29).** A mixture of (1*R**,2*R**)-ethyl 2-(4-aminophenyl)cyclopropanecarboxylate (80 mg, 0.39 mmol) and 3-(phenyloxy)benzaldehyde (93 mg, 0.47 mmol) in DCE (4 mL) was heated at 80 °C for 2 hours then cooled to RT. Acetic acid (1 drop) and $NaHB(OAc)_3$ (123 mg, 0.58 mmol) were added and the reaction was stirred until the reaction was completed by TLC analysis. The mixture was diluted with DCM (10 mL) and washed with water (20 mL), dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (25% EtOAc/hexane). R_f 0.44 (50% EtOAc/hexane). The desired product was obtained as a yellow oil (117 mg, 77%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.35-7.28 (m, 3H), 7.12-6.87 (m, 8H), 6.53 (d, *J* = 8 Hz, 2H), 4.29 (s, 2H), 4.15 (q, *J* = 7 Hz, 2H), 4.02 (br, 1H), 2.46-2.39 (m, 1H), 1.80-1.75 (m, 1H), 1.54-1.48 (m, 1H), 1.27 (t, *J* = 7 Hz, 3H), 1.25-1.19 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.7, 157.5, 156.9, 146.5, 141.5, 129.8, 129.7, 128.8, 127.2, 123.2, 122.0, 118.9, 117.6, 117.4, 112.9, 60.5, 48.0, 25.8, 23.7, 16.5, 14.2; IR (neat) 2930, 1685, 1494, 1255 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{26}NO_3$ $[M+H]^+$: 388.1899. Found 388.1907.



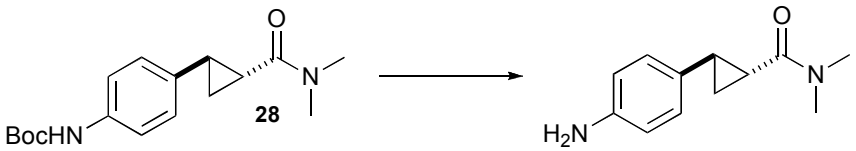
(1*R,2*R**)-2-(4-(3-Phenoxybenzylamino)phenyl)cyclopropanecarboxylic acid (31).** To solution of **29** (90 mg, 0.23 mmol) in MeOH (10 mL), was added a 25% aqueous NaOH solution (1 mL). The resulting mixture was heated under reflux overnight. The solution was diluted with water (5 mL) and the pH was adjusted to 3-4 with a saturated $NaHSO_3$ solution. The mixture was washed with DCM (10 mL) and the organic layer was dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (10% MeOH/DCM). R_f 0.29 (20% MeOH/DCM). The desired product **31** was obtained as a gum (77 mg, 93%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.27 (m, 3H), 7.12-7.01 (m, 2H), 7.01-6.98 (m, 3H), 6.94-6.88 (m, 3H), 6.54 (d, *J* = 9 Hz, 2H), 4.29 (s, 2H), 2.54-2.49 (m, 1H), 1.80-1.76 (m, 1H), 1.60-1.56 (m, 1H), 1.35-1.30 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 179.6, 157.5, 156.9, 146.7, 141.4, 129.9, 129.7, 128.3, 127.3, 123.2, 122.0, 118.9, 117.6, 117.4, 112.9, 48.0, 26.8, 23.5, 17.0; IR (neat) 2922, 1691, 1488, 1248, 1218, 735 cm^{-1}; HRMS (FAB) calcd for $C_{23}H_{22}NO_3$ $[M+H]^+$: 360.1585. Found 360.1594.

SYNTHESIS OF CYCLOPROPANECARBOXAMIDE 30.

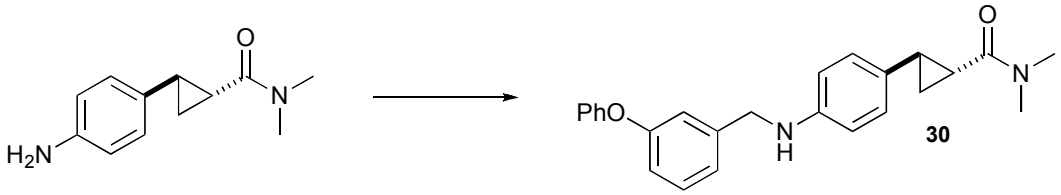


***tert*-Butyl 4-(*(1R*,2R*)*-2-(dimethylcarbamoyl)cyclopropyl)phenylcarbamate (28).** The title compound was prepared from 4-(*tert*-butoxycarbonylamino)benzaldehyde[27] according to the general procedure **C** using 9.00 mmol of diazomethane. The desired cyclopropane **28** (219 mg, 72%) was obtained as a colorless oil after flash chromatography (50% EtOAc/hexane). R_f 0.15 (10% EtOAc/DCM). ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.26 (d, *J* = 9 Hz, 2H), 7.03 (d, *J* = 9 Hz, 2H), 6.47 (br, 1H), 3.11 (s, 3H), 2.98 (s, 3H), 2.45-2.38 (m, 1H), 1.94-1.88 (m, 1H), 1.63-1.57 (m, 1H), 1.50 (s, 9H), 1.25-1.18 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 173.4, 152.6, 136.7, 134.6, 126.7, 118.6, 80.4, 60.6,

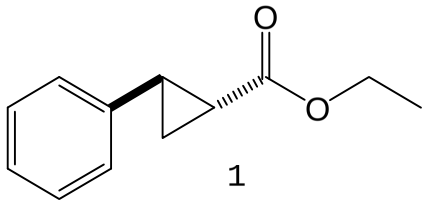
28.3, 25.7, 23.9, 16.8, 14.2; IR (neat) 3283, 2980, 1721, 1631, 1527, 1162 cm^{-1}; HRMS (FAB) calcd for $C_{17}H_{25}N_2O_3$ $[M+H]^+$: 304.1786. Found 304.1852.

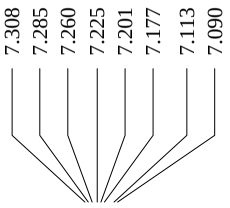


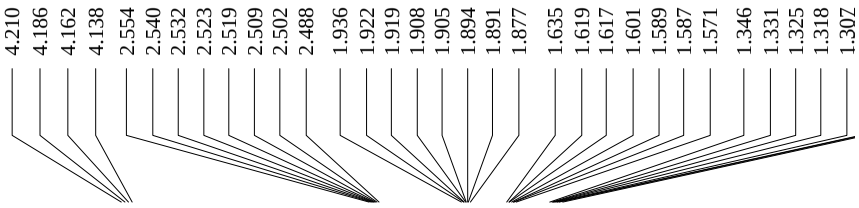
(1*R,2*R**)-2-(4-aminophenyl)-*N,N*-dimethylcyclopropanecarboxamide.** To a solution of **28** (88 mg, 0.29 mmol) in DCM (2 mL) at 0 °C, was added TFA (1 mL). The resulting mixture was warmed at RT and stirred for 2 hours. The mixture was diluted with DCM (10 mL), then washed with 10% aqueous K_2CO_3 (10 mL), water (10 mL) and brine (10 mL). The organic layer was dried over $MgSO_4$ and concentrated under reduced pressure. The residue was purified by flash chromatography on silica gel (10% MeOH/DCM). R_f 0.46 (20% MeOH/DCM). The free amine was obtained as a yellow oil (56 mg, 94%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.93 (d, *J* = 8 Hz, 2H), 6.61 (d, *J* = 8 Hz, 2H), 3.58 (s (br), 2H), 3.12 (s, 3H), 2.98 (s, 3H), 2.41-2.35 (m, 1H), 1.90-1.84 (m, 1H), 1.58-1.52 (m, 1H), 1.20-1.14 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 144.6, 130.9, 127.1, 115.1, 37.2, 35.8, 25.0, 22.7, 15.6; IR (neat) 3341, 3228, 3006, 2929, 1622, 1519, 1285, 1141 cm^{-1}; HRMS (FAB) calcd for $C_{12}H_{17}N_2O$ $[M+H]^+$: 205.1337. Found 205.1340.

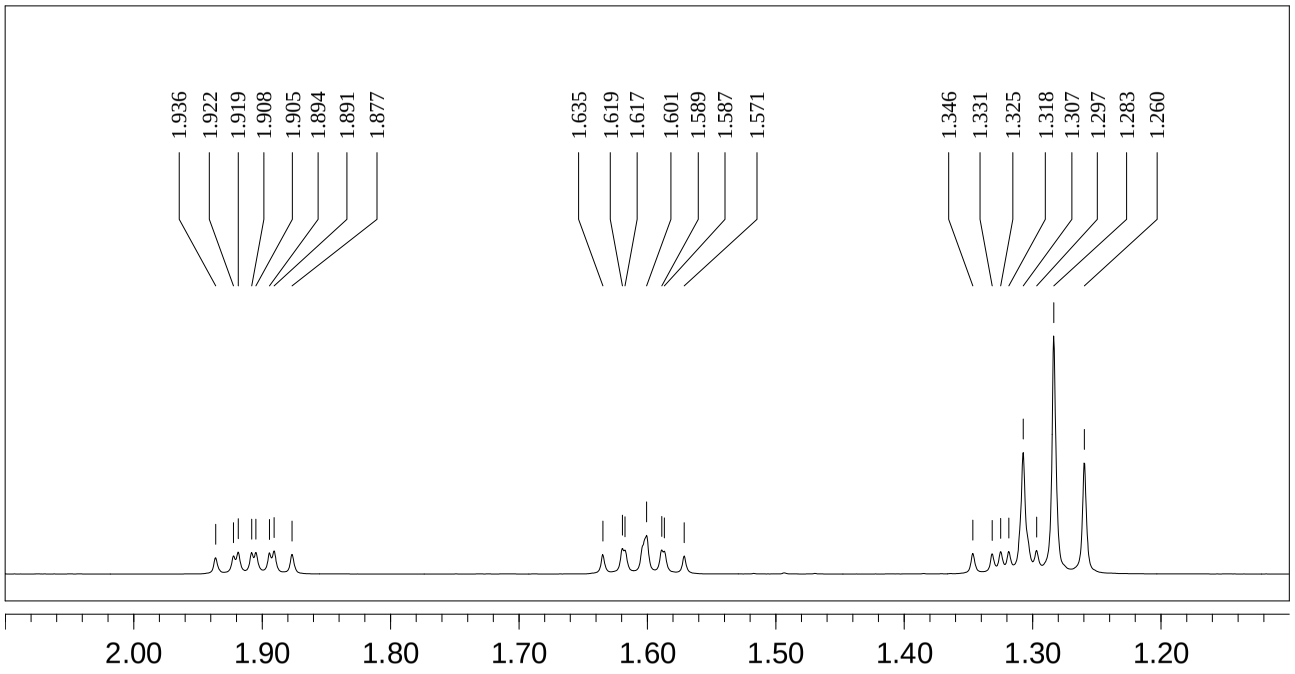


(1*R,2*R**)-2-(4-(3-phenoxybenzylamino)phenyl)-*N,N*-dimethylcyclopropanecarboxamide (30).** To a mixture of (1*R**,2*R**)-2-(4-aminophenyl)-*N,N*-dimethylcyclopropanecarboxamide (80 mg, 0.39 mmol), 3-(phenyloxy)benzaldehyde (93 mg, 0.47 mmol) and acetic acid (1 drop) in DCE (4 mL) was added $NaHB(OAc)_3$ (123 mg, 0.58 mmol). The reaction was stirred at RT until the reaction was completed by TLC analysis (2 hours). The mixture was diluted with DCM (10 mL) then washed with water (20 mL), dried over $MgSO_4$, filtrated and concentrated. The residue was purified by flash chromatography on silica gel (10% MeOH/DCM). R_f 0.32 (20% MeOH/DCM). The desired product **30** was obtained as a yellow oil (128 mg, 85%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.34-7.26 (m, 3H), 7.13-7.08 (m, 2H), 7.02-6.88 (m, 6H), 6.54 (d, *J* = 8 Hz, 2H), 4.28 (s, 2H), 4.05 (br, 1H), 3.11 (s, 3H), 2.98 (s, 3H), 2.40-2.35 (m, 1H), 1.89-1.85 (m, 1H), 1.58-1.53 (m, 1H), 1.20-1.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$) δ 172.2, 157.5, 156.9, 146.3, 141.5, 129.9, 129.8, 129.7, 127.1, 123.2, 122.0, 118.8, 117.6, 117.4, 112.9, 48.1, 37.2, 35.8, 25.0, 22.6, 15.6; IR (neat) 3336, 2926, 1615, 1523, 1486, 1247 cm^{-1}; HRMS (FAB) calcd for $C_{25}H_{27}N_2O_2$ $[M+H]^+$: 387.2079. Found 387.2072.

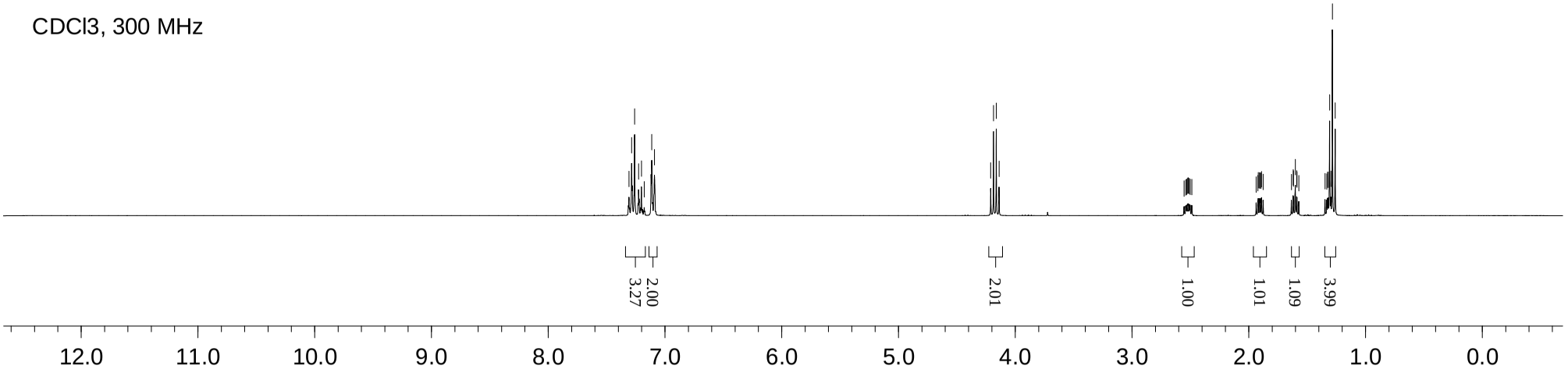




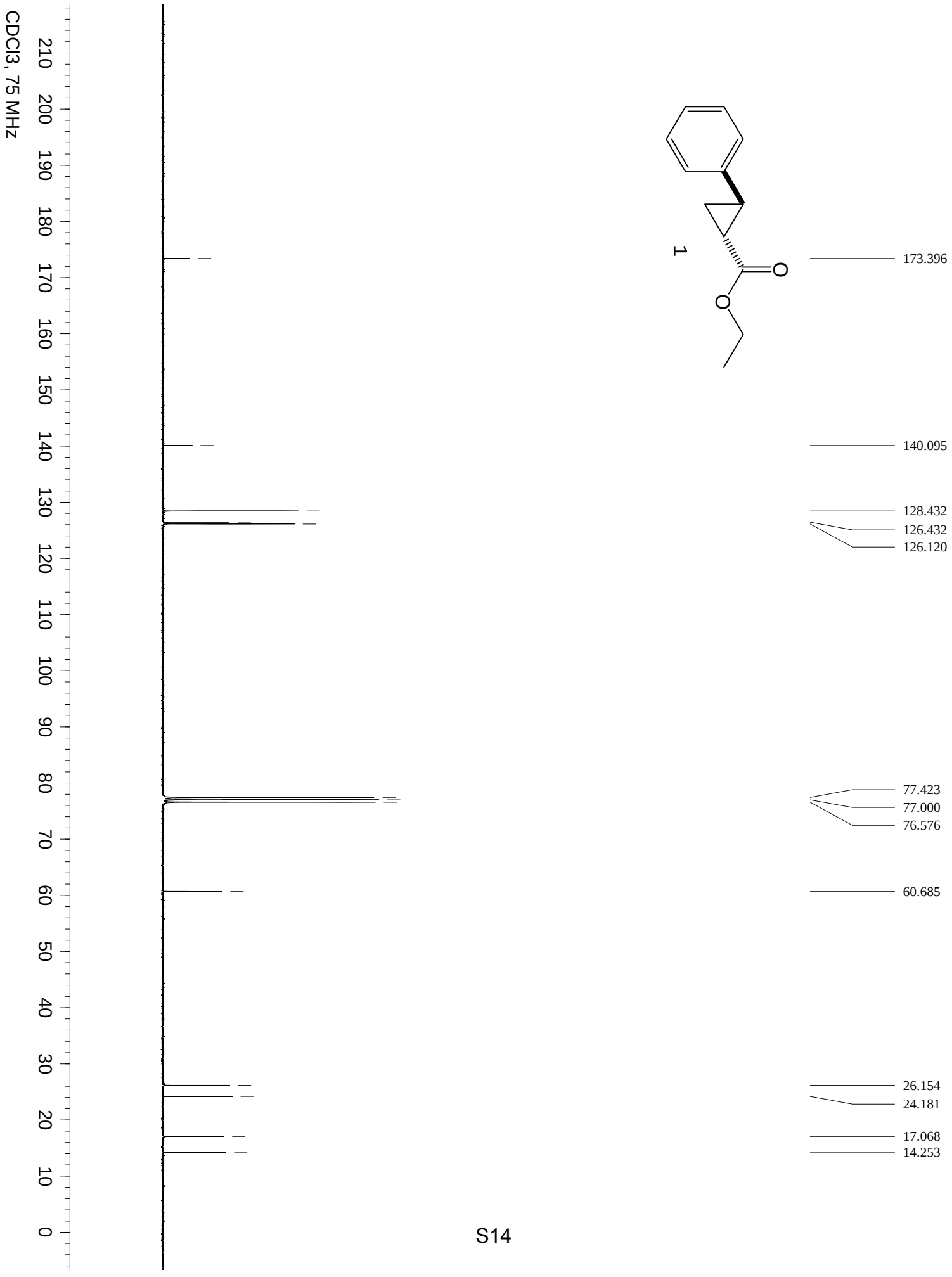


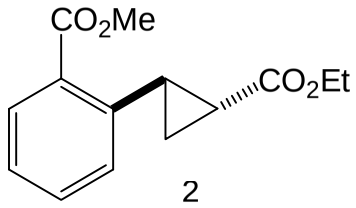


CDCl3, 300 MHz

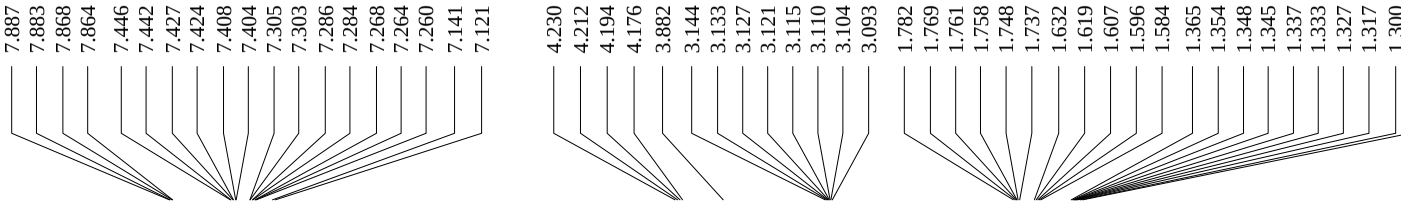


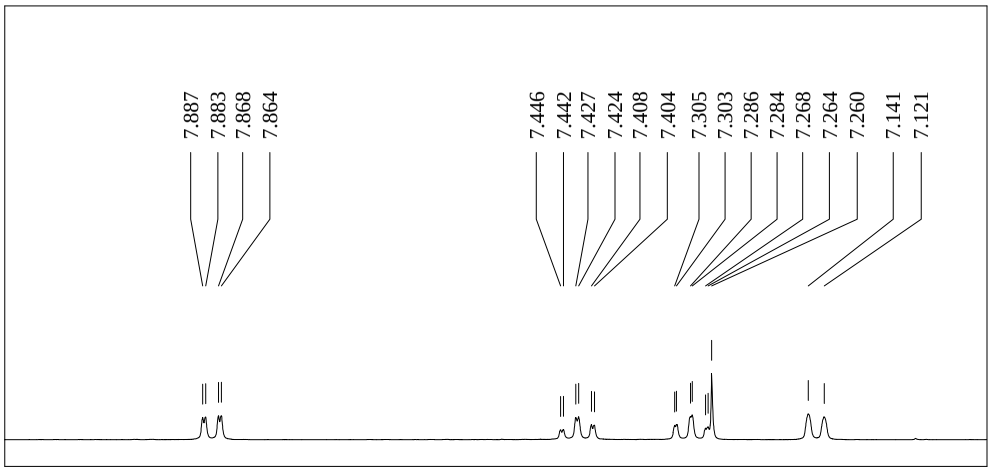
CDCl3, 300 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
1
O
O
173.396
140.095
128.432
126.432
126.120
77.423
77.000
76.576
60.685
26.154
24.181
17.068
14.253

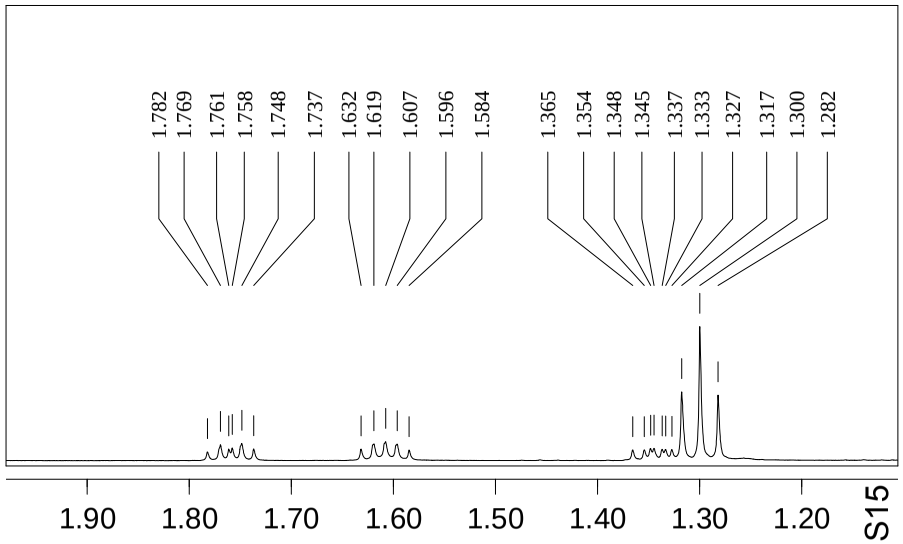


2

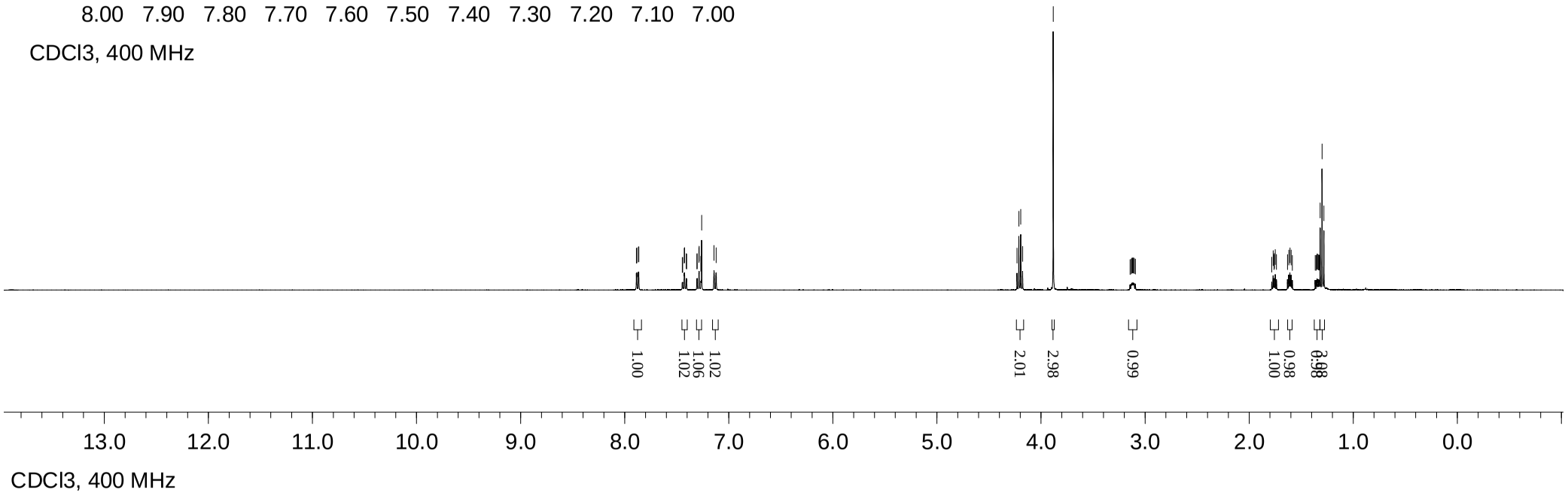




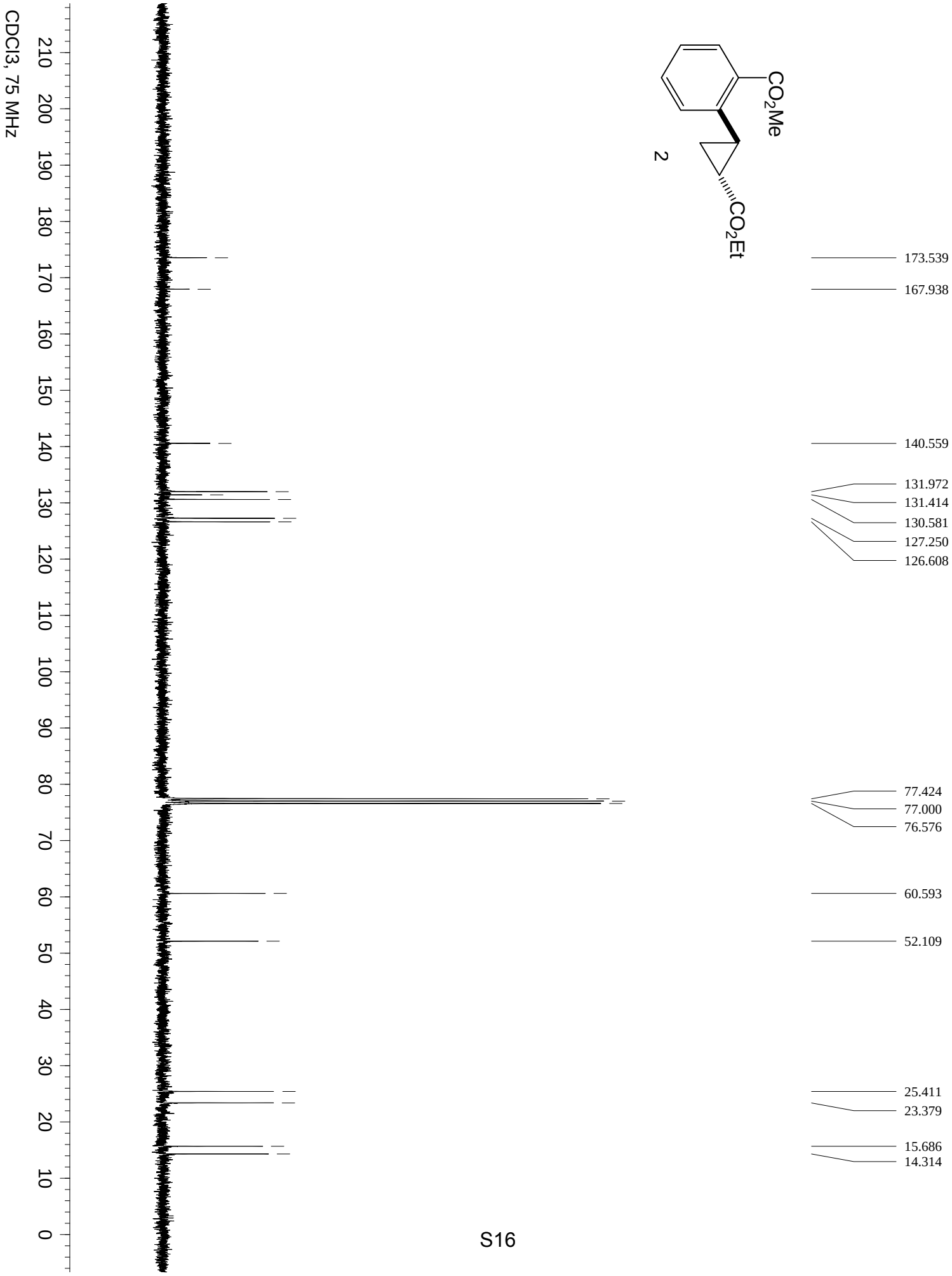
CDCl3, 400 MHz



CDCl3, 400 MHz



CDCl3, 400 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
CO2Me
2
CO2Et
173.539
167.938
140.559
131.972
131.414
130.581
127.250
126.608
77.424
77.000
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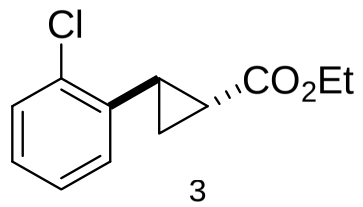
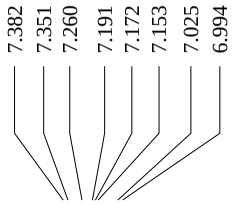
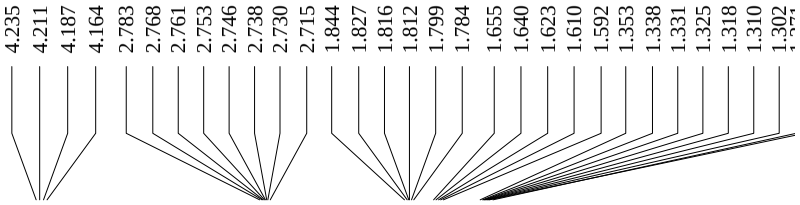
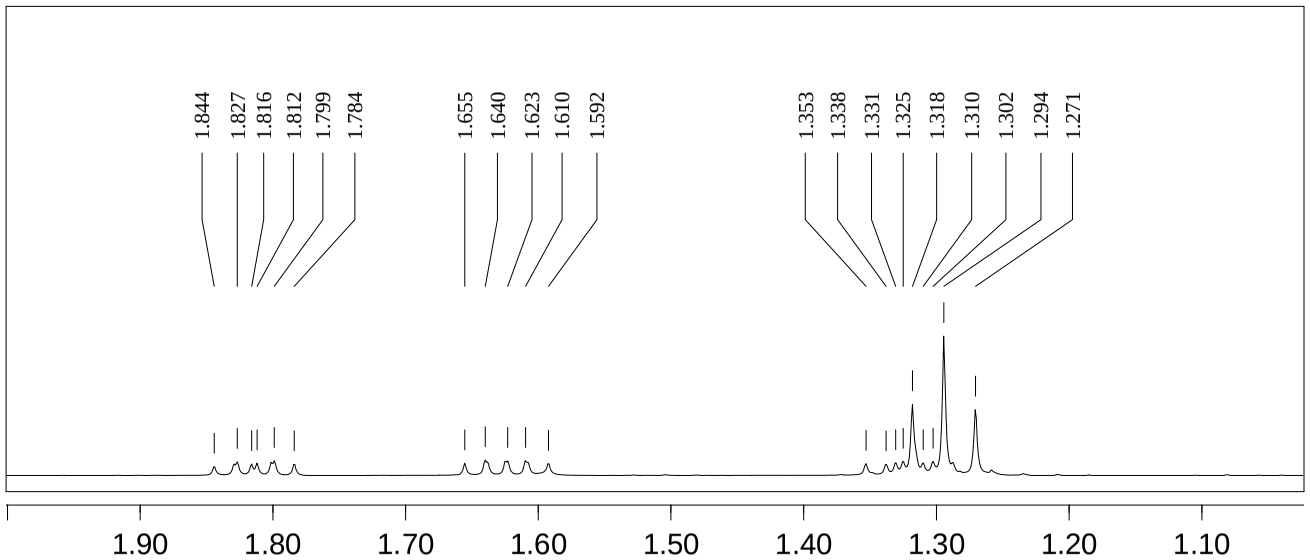
60.593
52.109
25.411
23.379
15.686
14.314



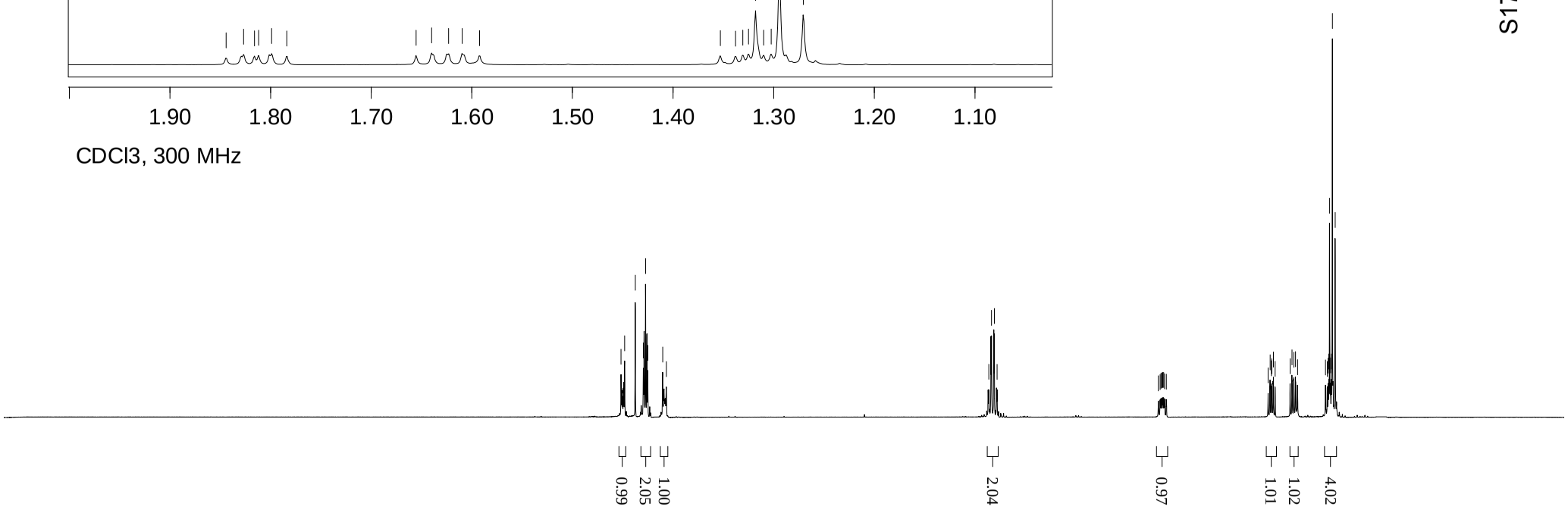
3



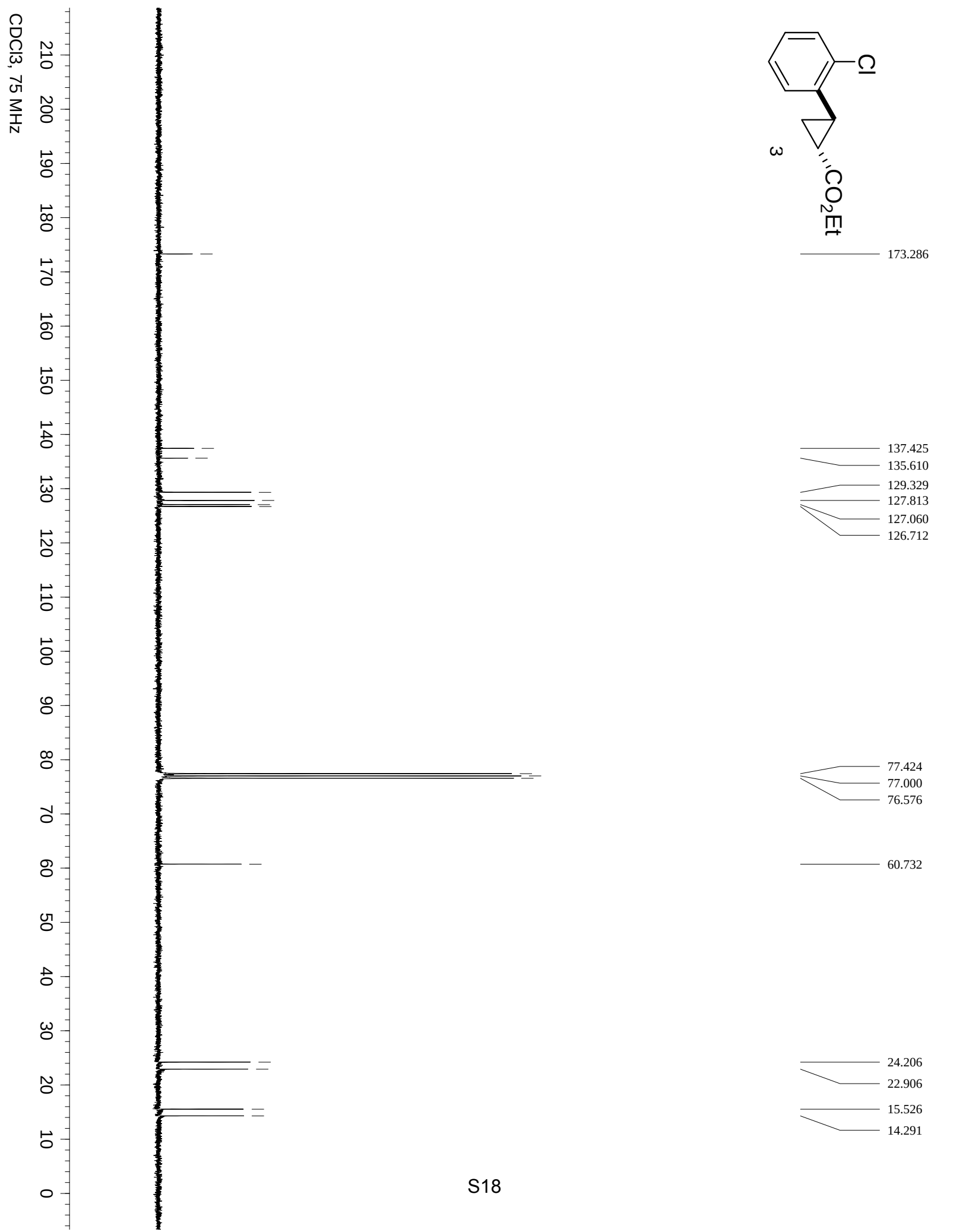


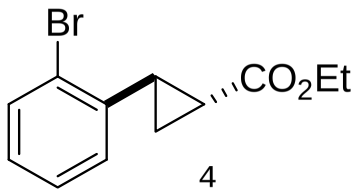


CDCl3, 300 MHz



CDCl3, 300 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Cl
CO2Et
3
173.286
137.425
135.610
129.329
127.813
127.060
126.712
77.424
77.000
76.576
60.732
24.206
22.906
15.526
14.291



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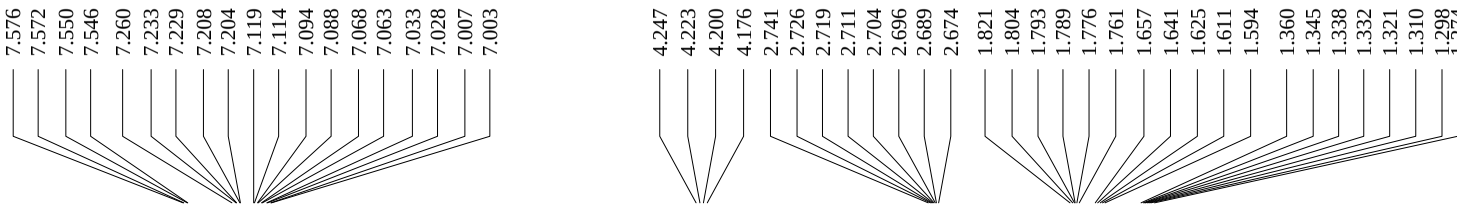
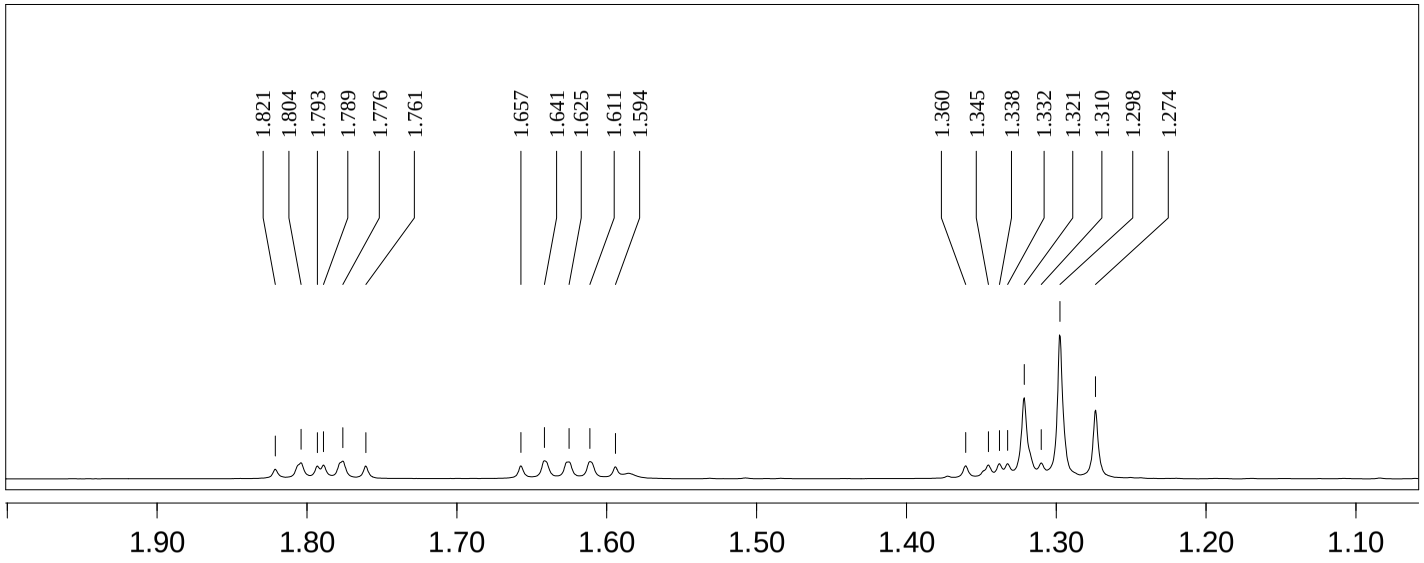
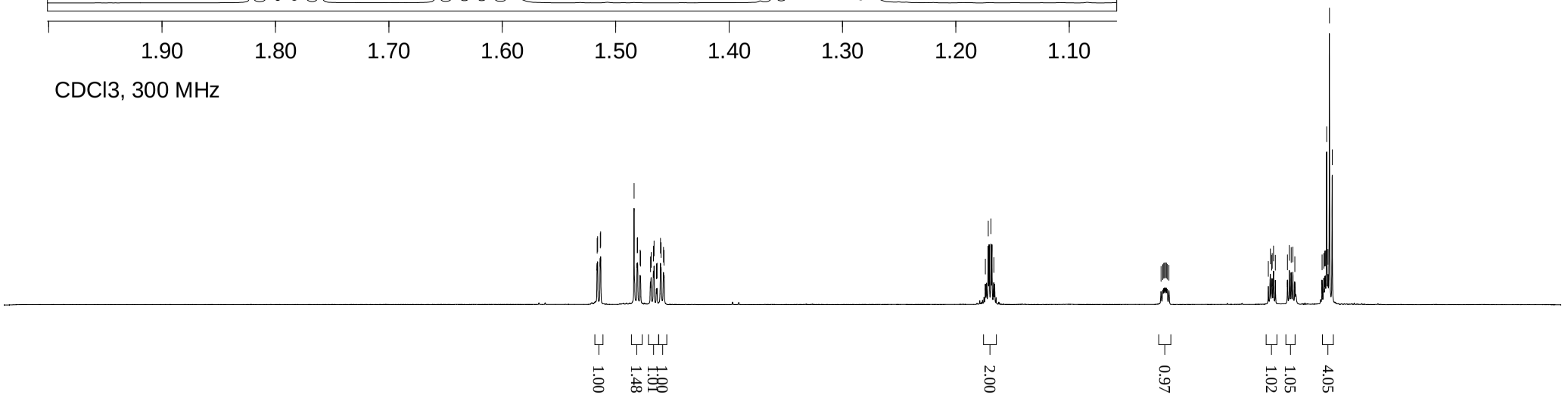
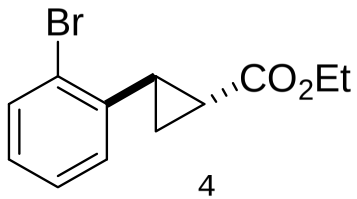




CDCl3, 300 MHz



CDCl3, 300 MHz

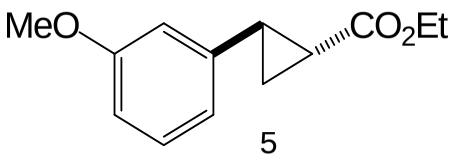


4

173.270
139.044
132.592
128.158
127.490
127.332
126.261
77.423
77.000
76.576
60.720
26.989
23.142
15.685
14.327

210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

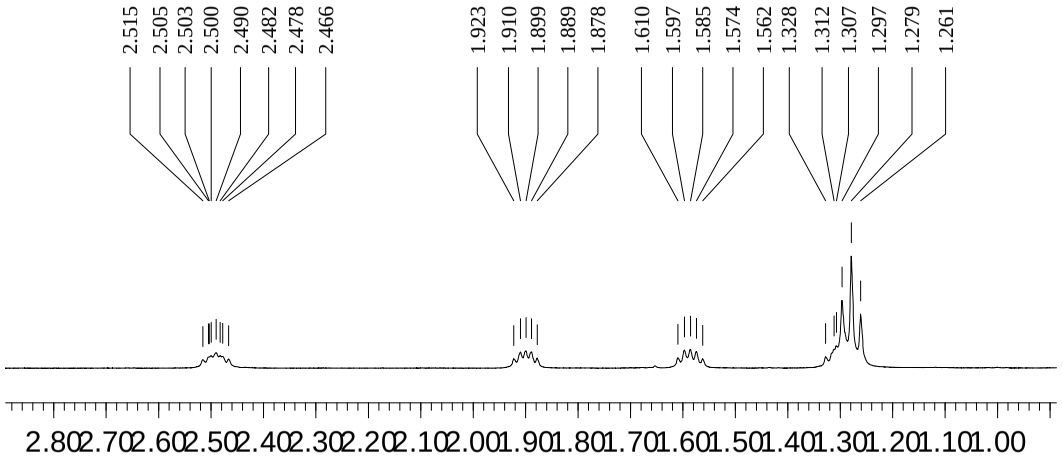
CDCl3, 75 MHz



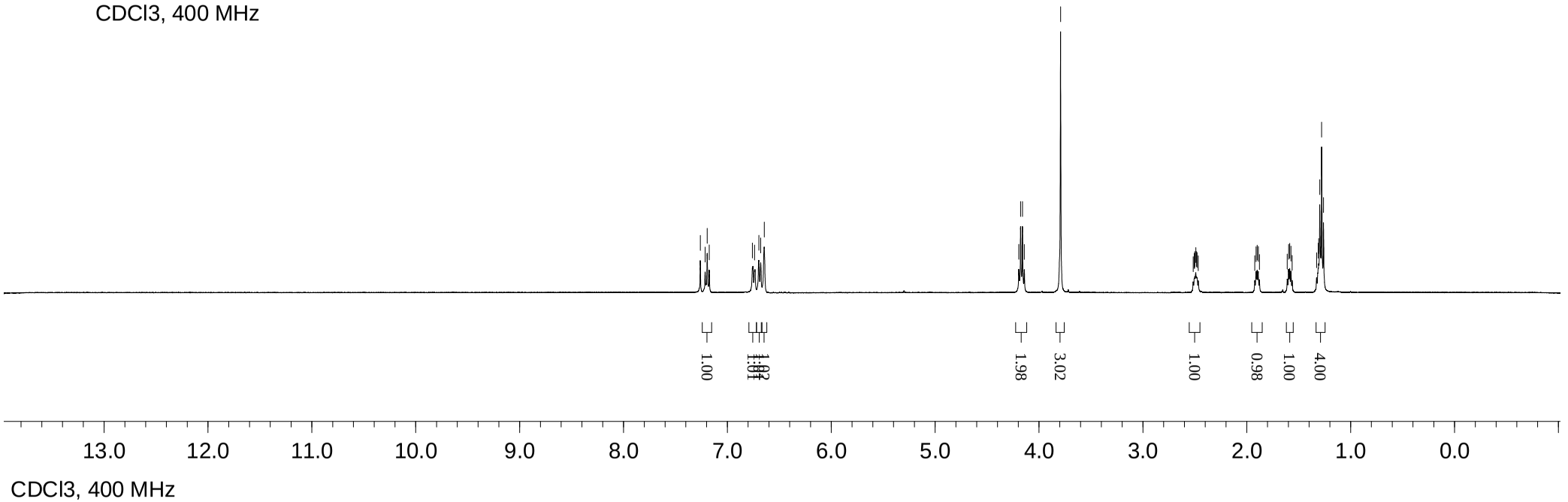
5

7.260 7.213 7.194 7.174 6.758 6.738 6.697 6.678 6.645

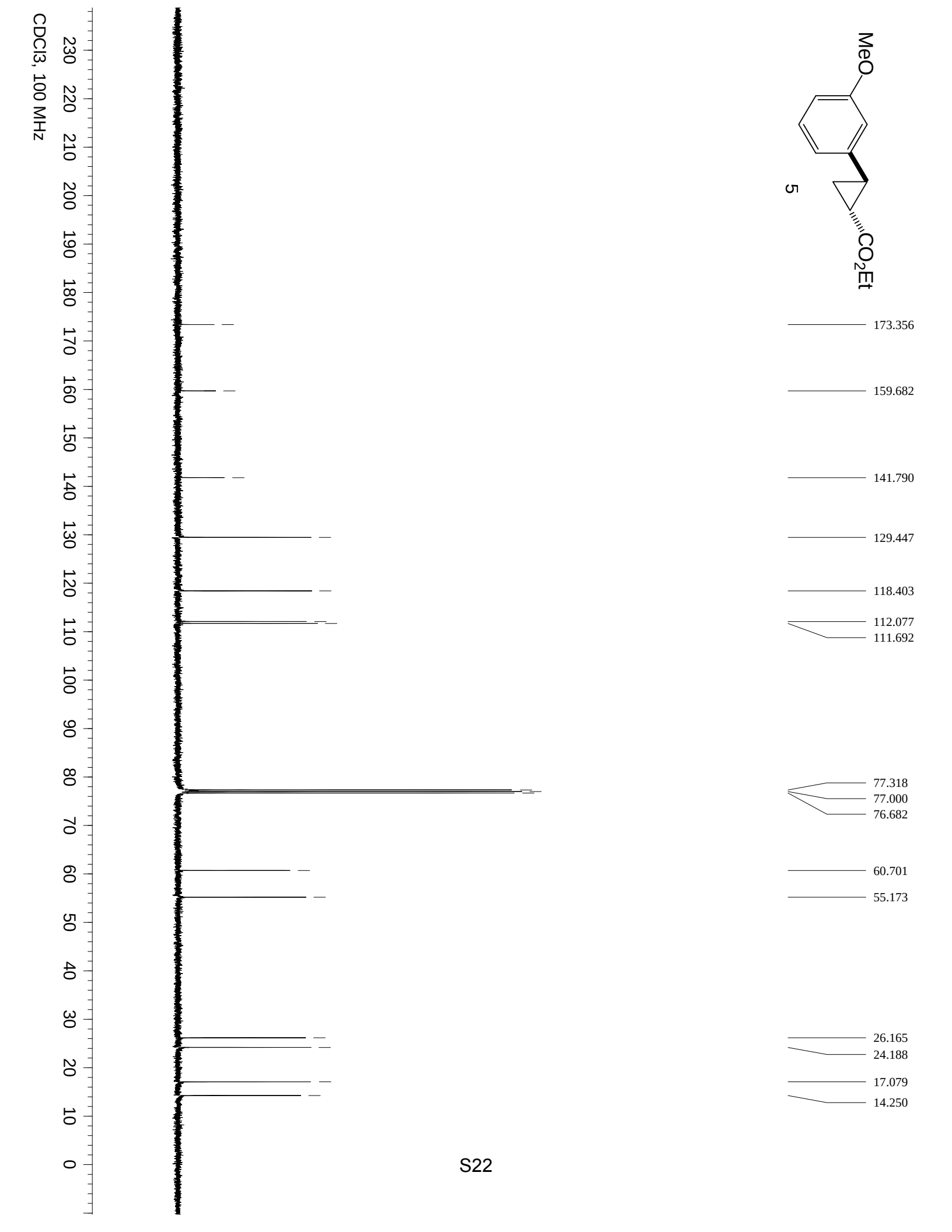
4.194 4.177 4.159 4.141 3.792 2.515 2.505 2.503 2.500 2.490 2.482 2.478 2.466 1.923 1.910 1.899 1.889 1.878 1.610 1.597 1.585 1.574 1.562 1.328 1.312 1.307 1.297 1.279 1.261

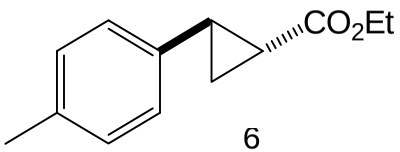


CDCl3, 400 MHz

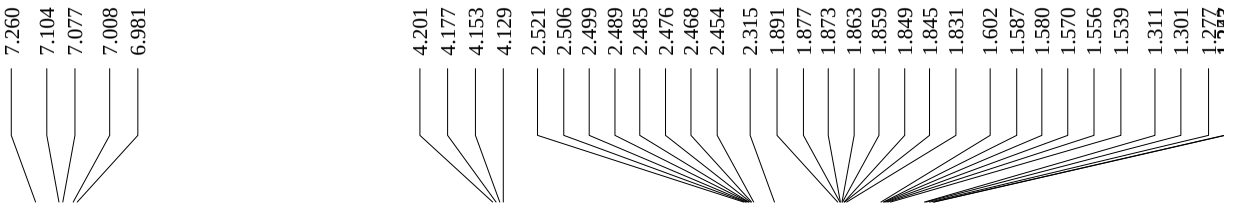


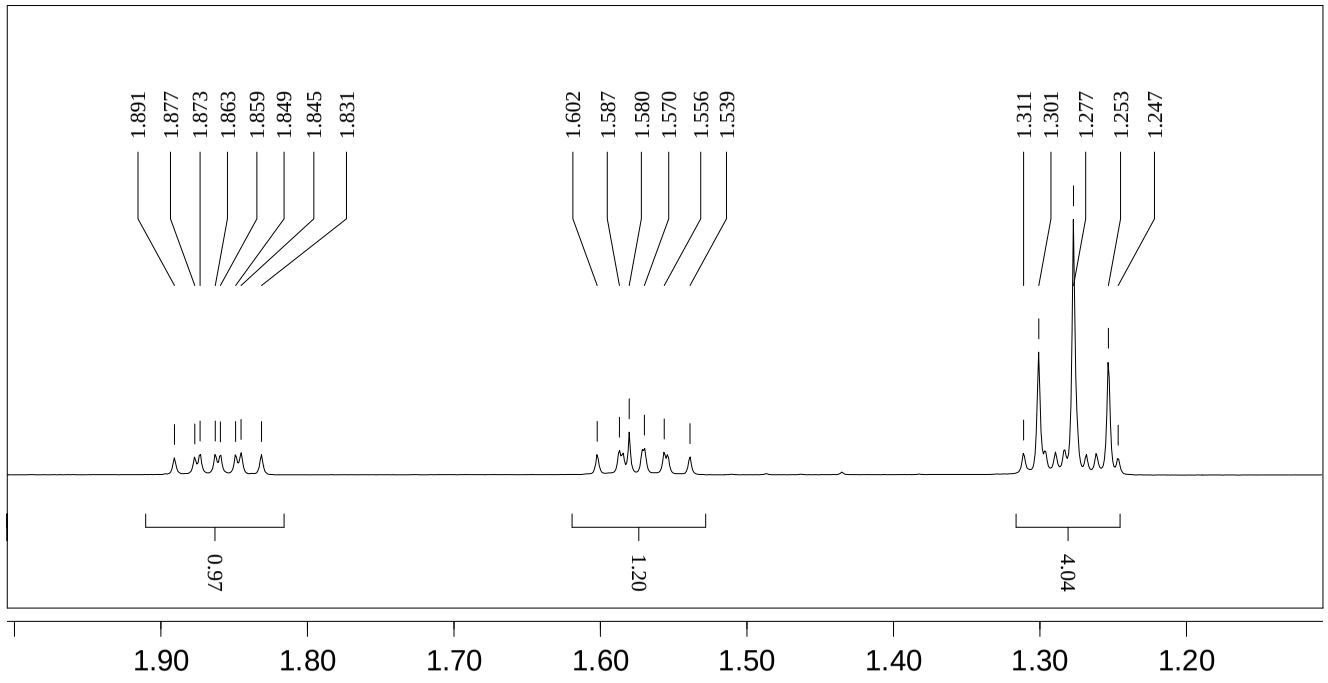
CDCl3, 400 MHz


CDCl3, 100 MHz
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
MeO
5
CO2Et
173.356
159.682
141.790
129.447
118.403
112.077
111.692
77.318
77.000
76.682
60.701
55.173
26.165
24.188
17.079
14.250

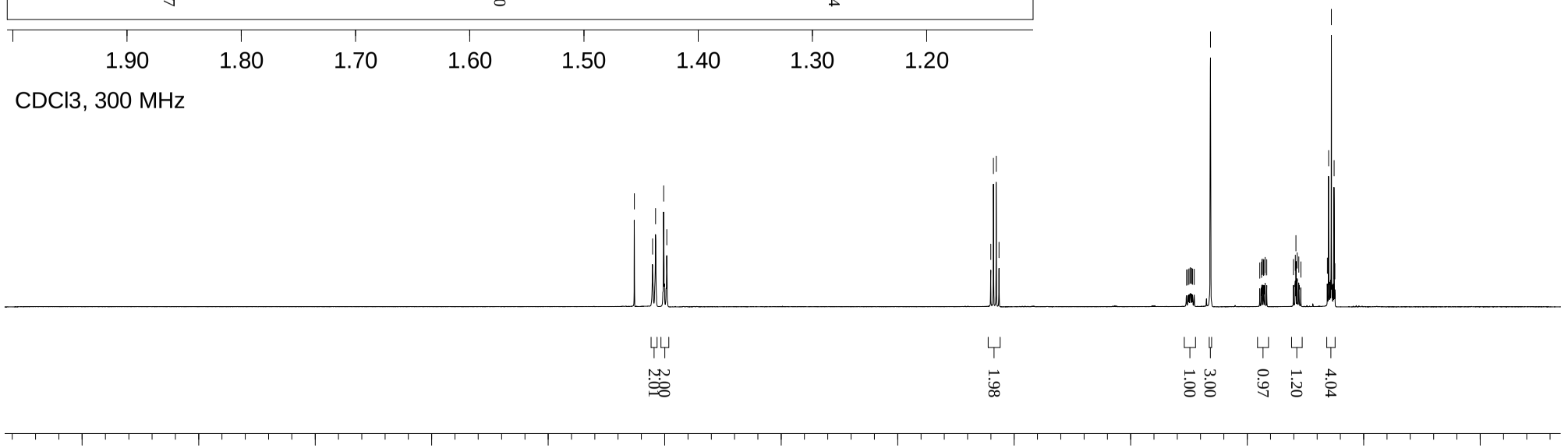


6

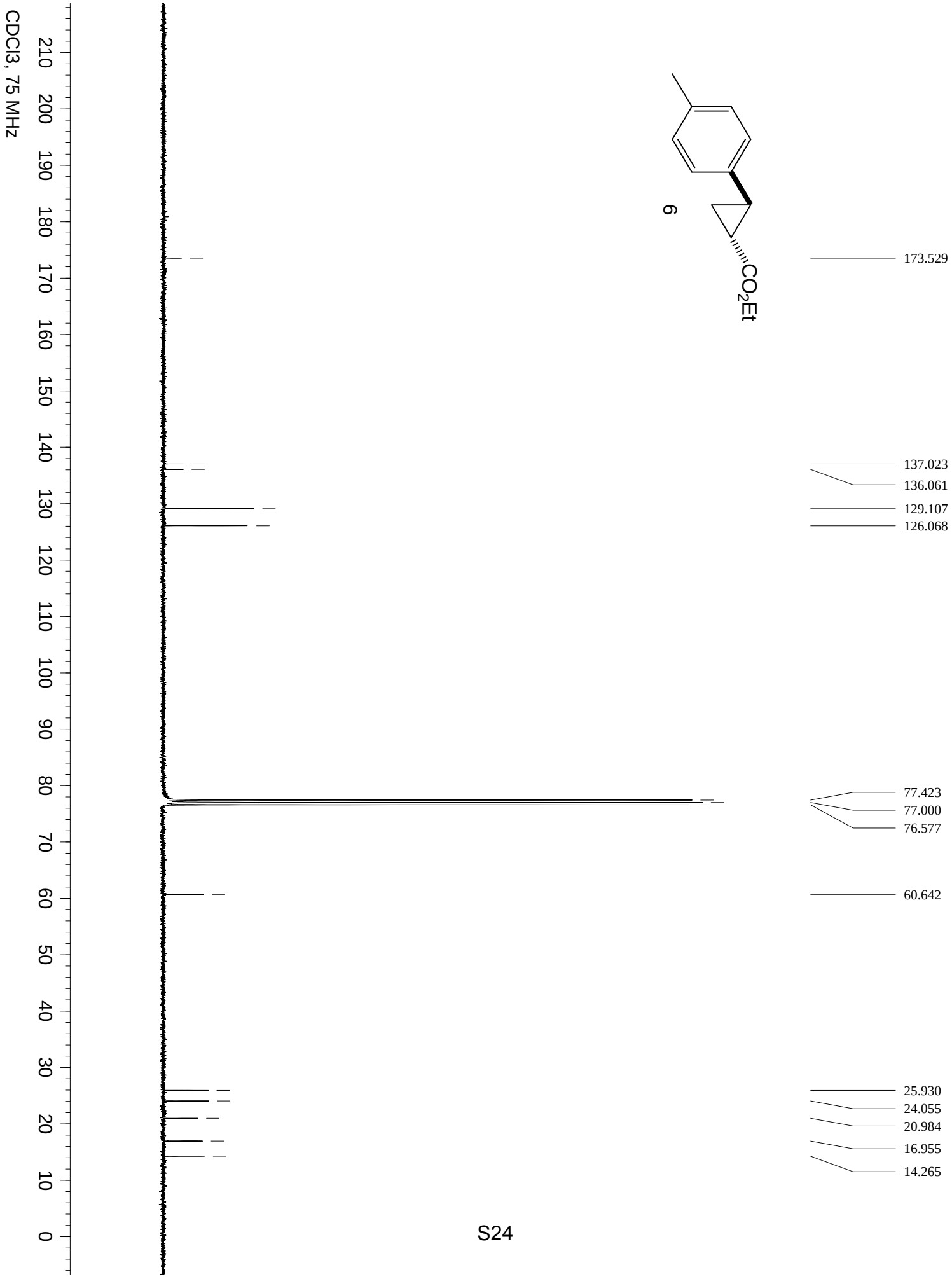


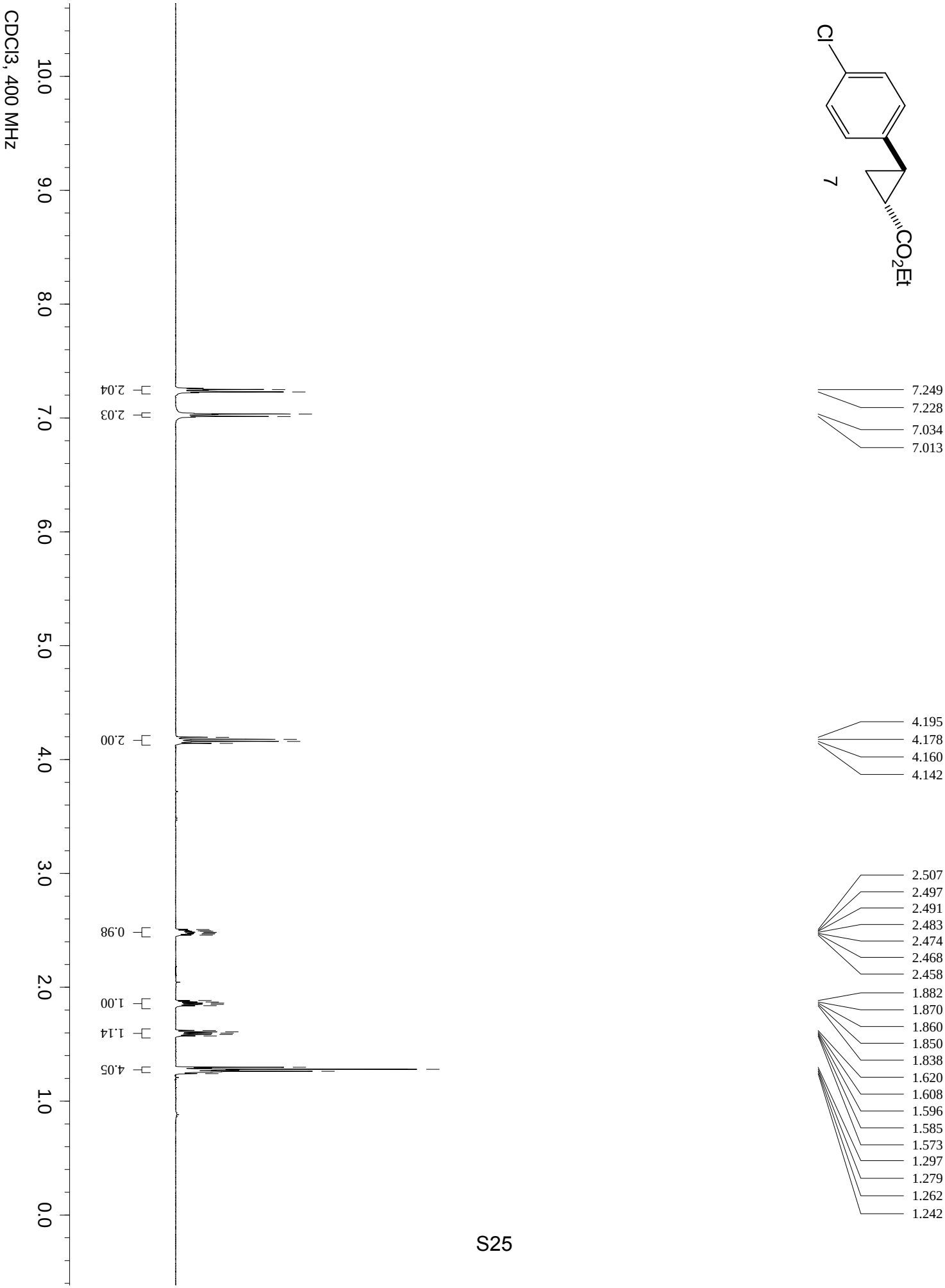


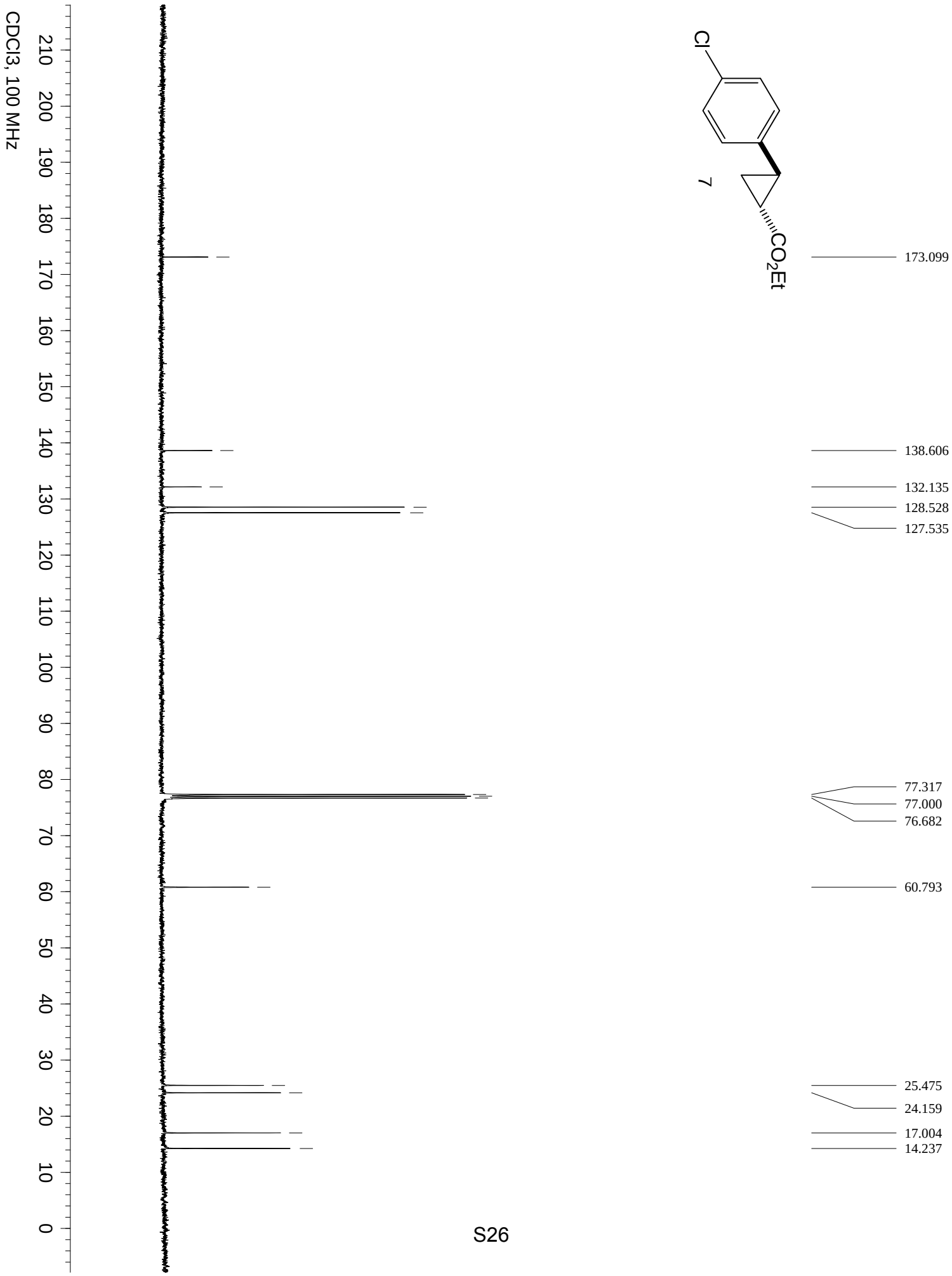
CDCl3, 300 MHz

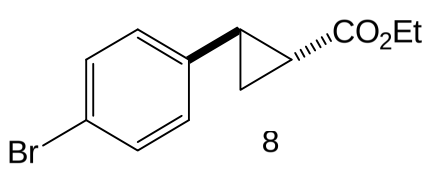


CDCl3, 300 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
6
CO2Et
173.529
137.023
136.061
129.107
126.068
77.423
77.000
76.577
60.642
25.930
24.055
20.984
16.955
14.265

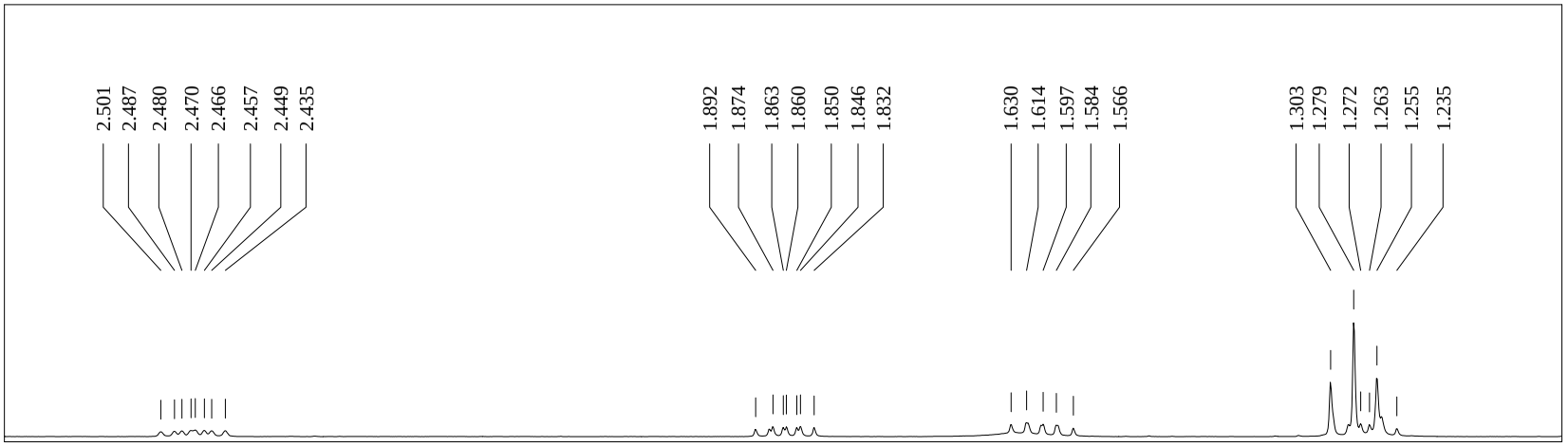

CDCl3, 400 MHz
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
2.04
2.03
2.00
0.98
1.00
1.14
4.05
Cl
7
CO2Et
7.249
7.228
7.034
7.013
4.195
4.178
4.160
4.142
2.507
2.497
2.491
2.483
2.474
2.468
2.458
1.882
1.870
1.860
1.850
1.838
1.620
1.608
1.596
1.585
1.573
1.297
1.279
1.262
1.242


CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Cl
7
CO2Et
173.099
138.606
132.135
128.528
127.535
77.317
77.000
76.682
60.793
25.475
24.159
17.004
14.237

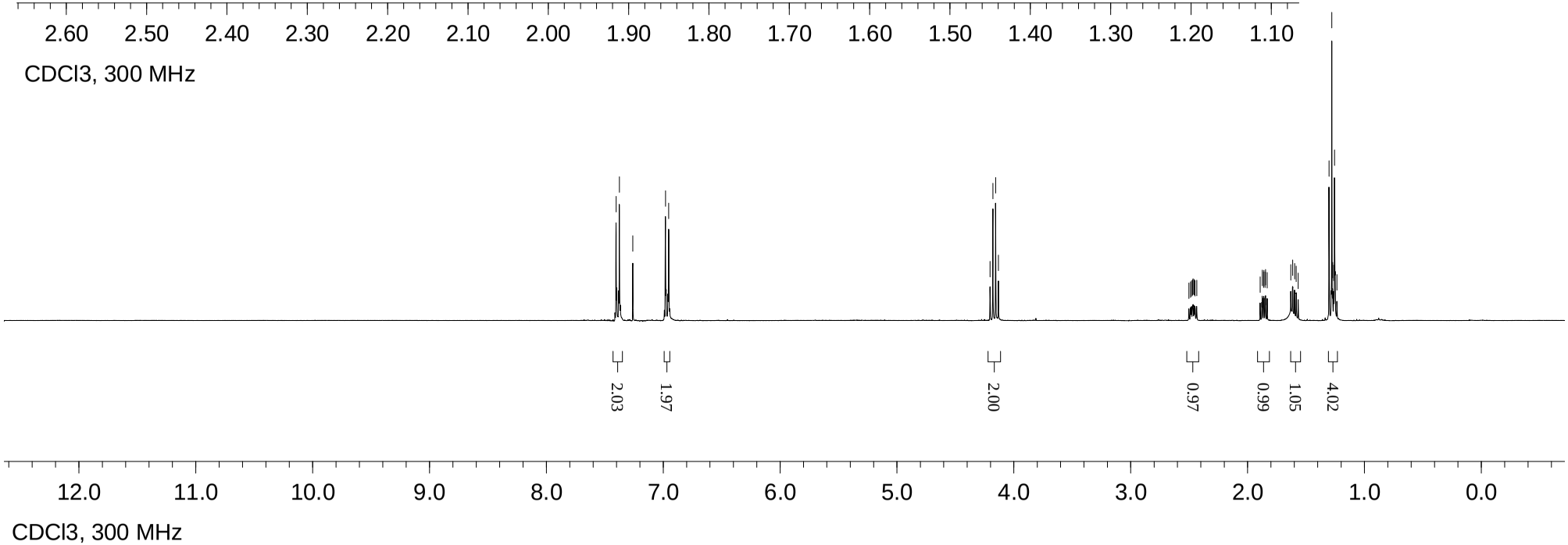


7.403 7.375 7.260 6.981 6.953

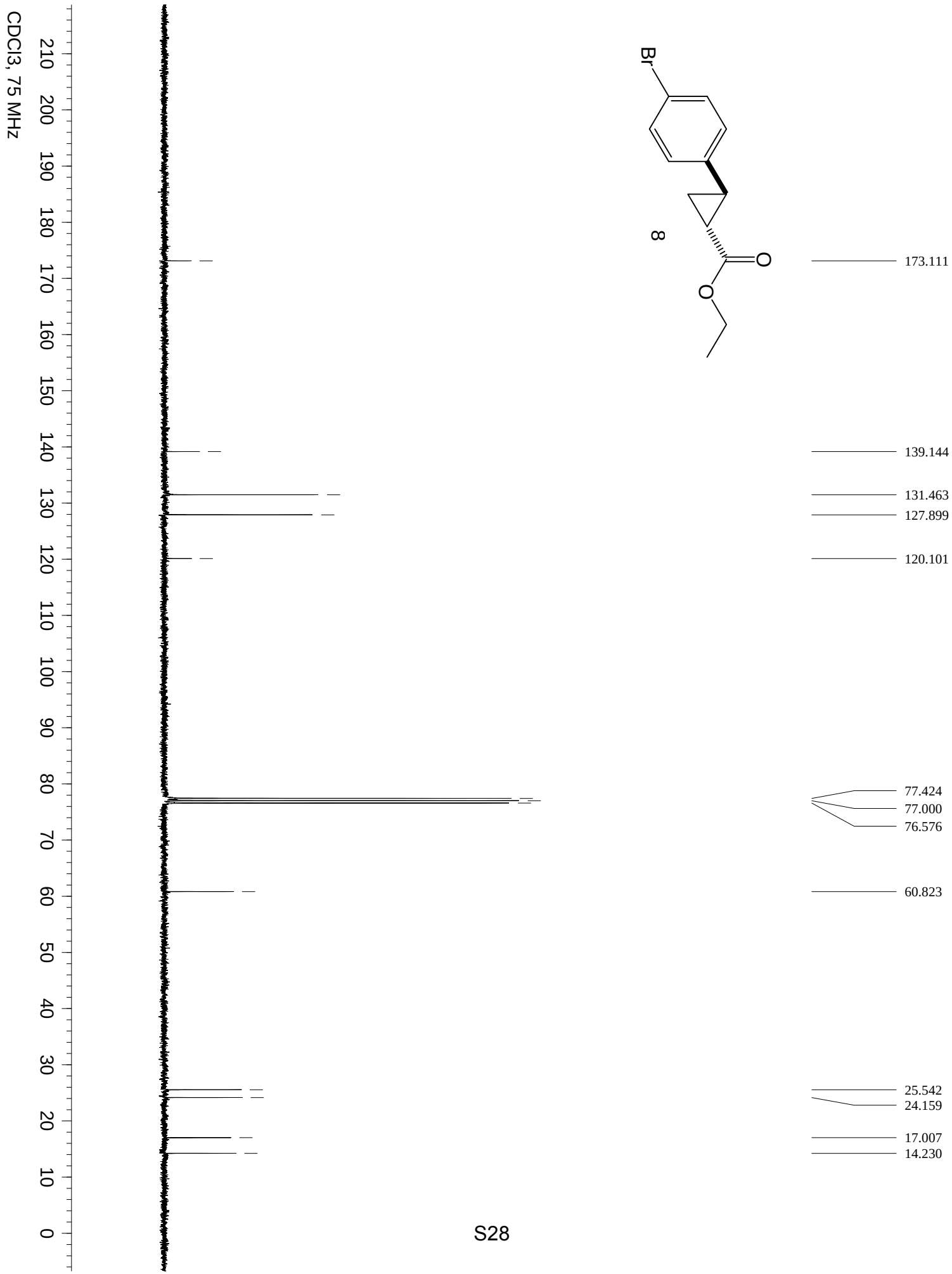
4.203 4.179 4.155 4.131 2.501 2.487 2.480 2.470 2.466 2.457 2.449 2.435 1.892 1.874 1.863 1.860 1.850 1.846 1.832 1.630 1.614 1.597 1.584 1.566 1.303 1.279 1.272 1.263 1.255

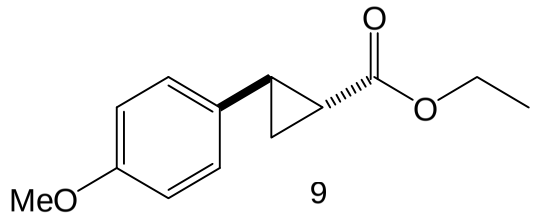


CDCl3, 300 MHz

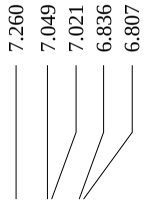


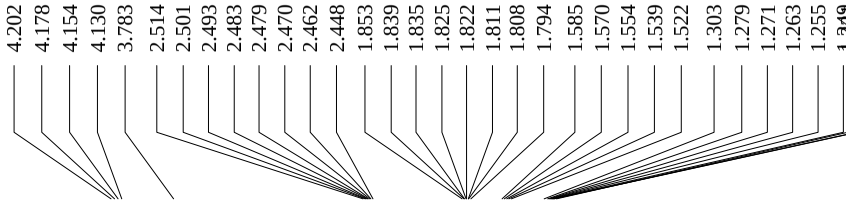
CDCl3, 300 MHz

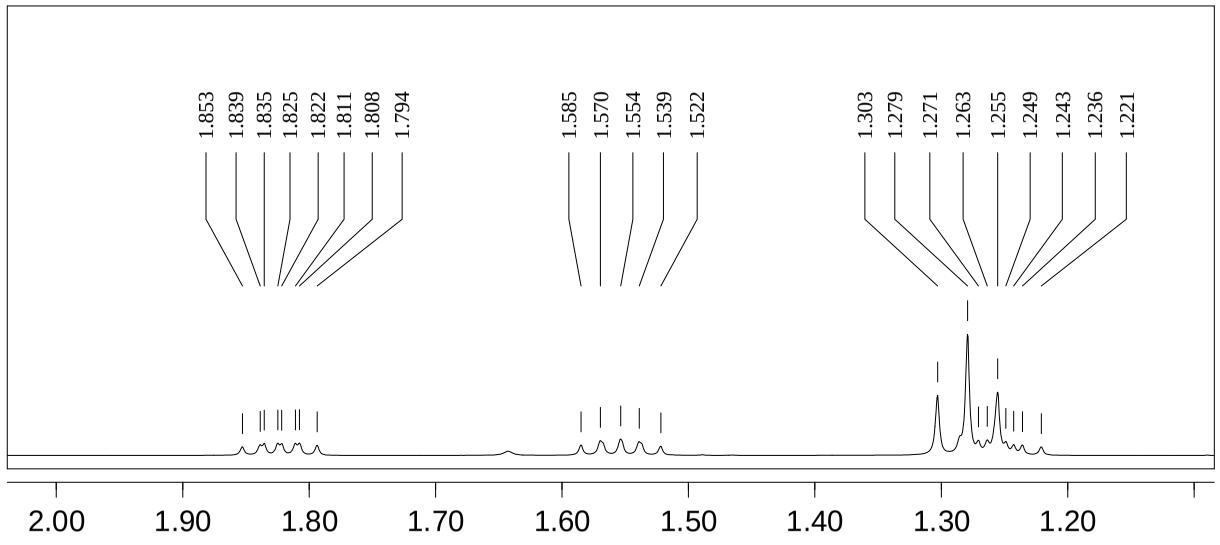

CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
Br
8
O
O
173.111
139.144
131.463
127.899
120.101
77.424
77.000
76.576
60.823
25.542
24.159
17.007
14.230



9

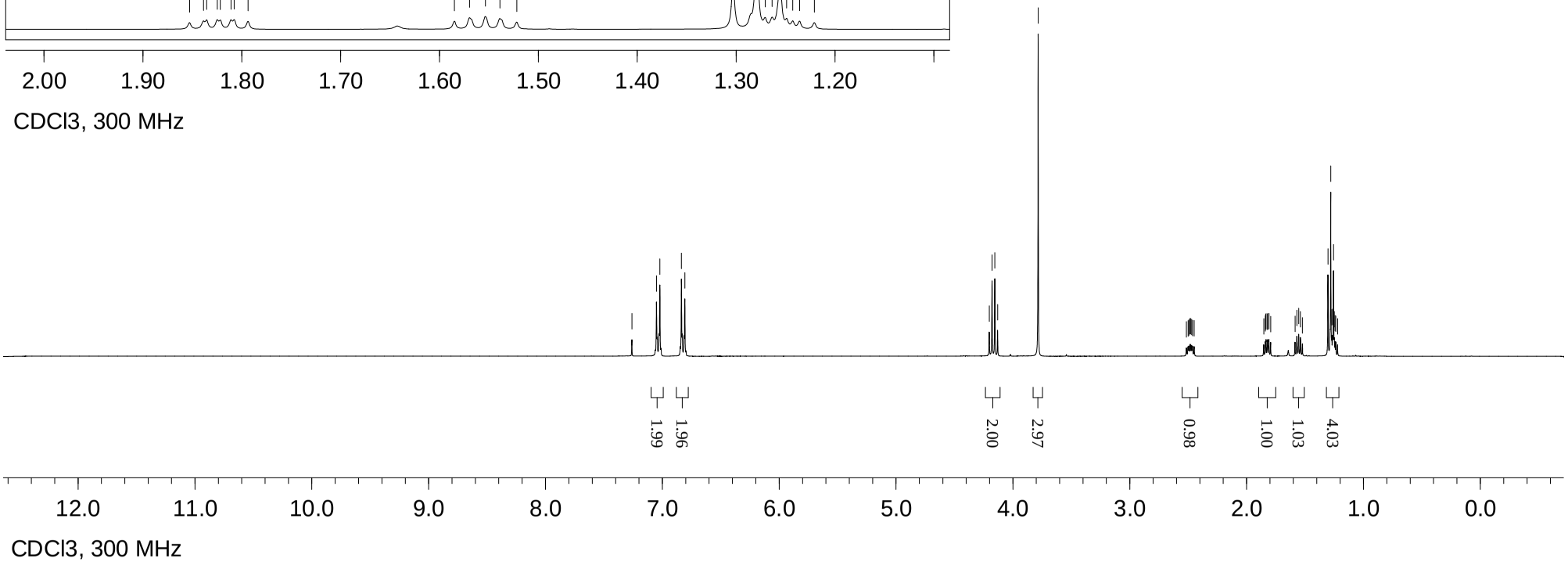




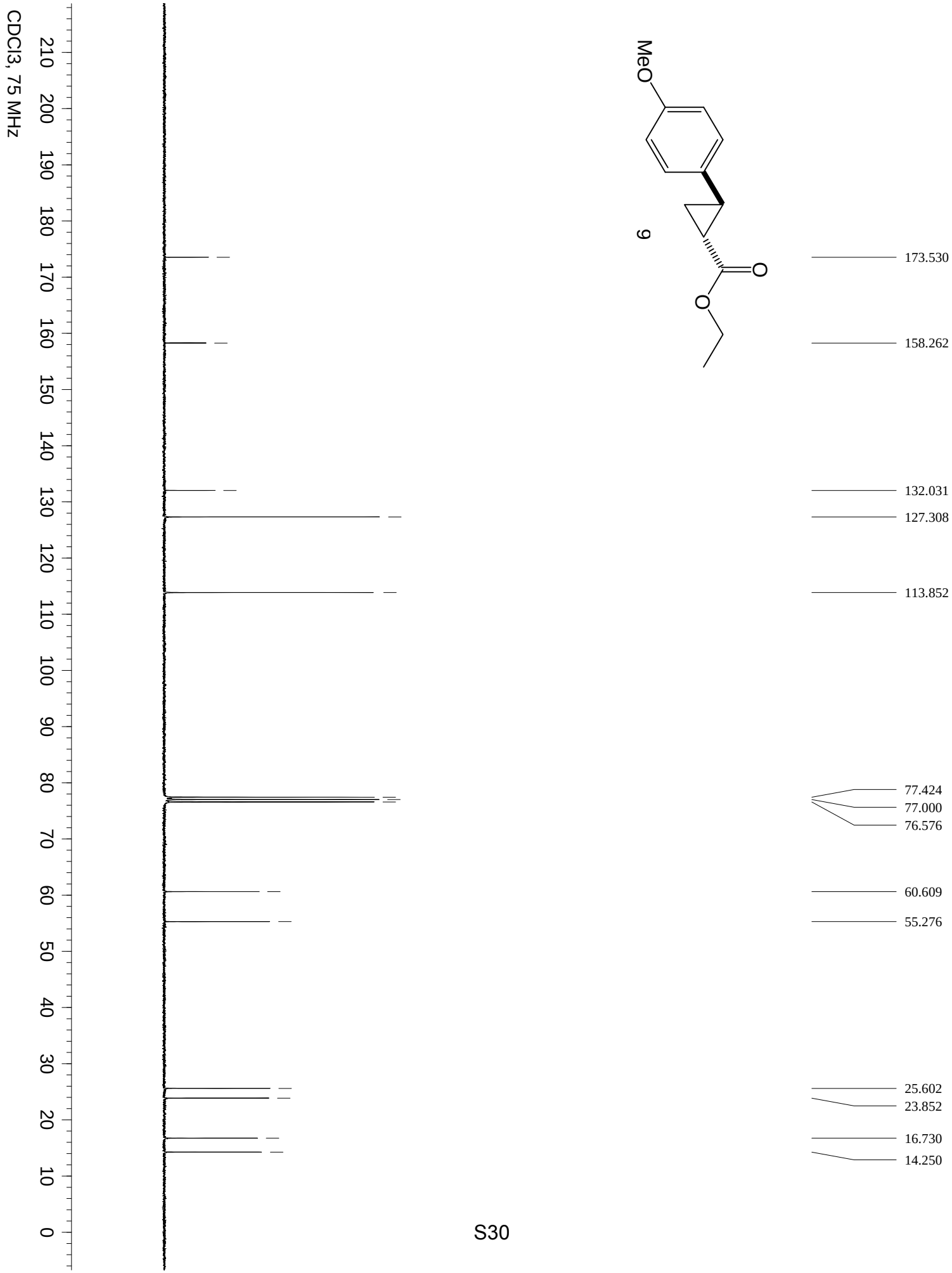


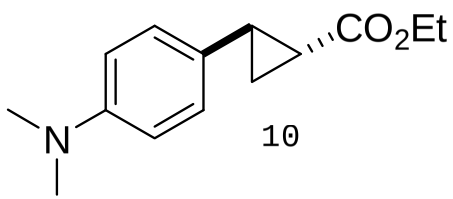
CDCl3, 300 MHz

S29



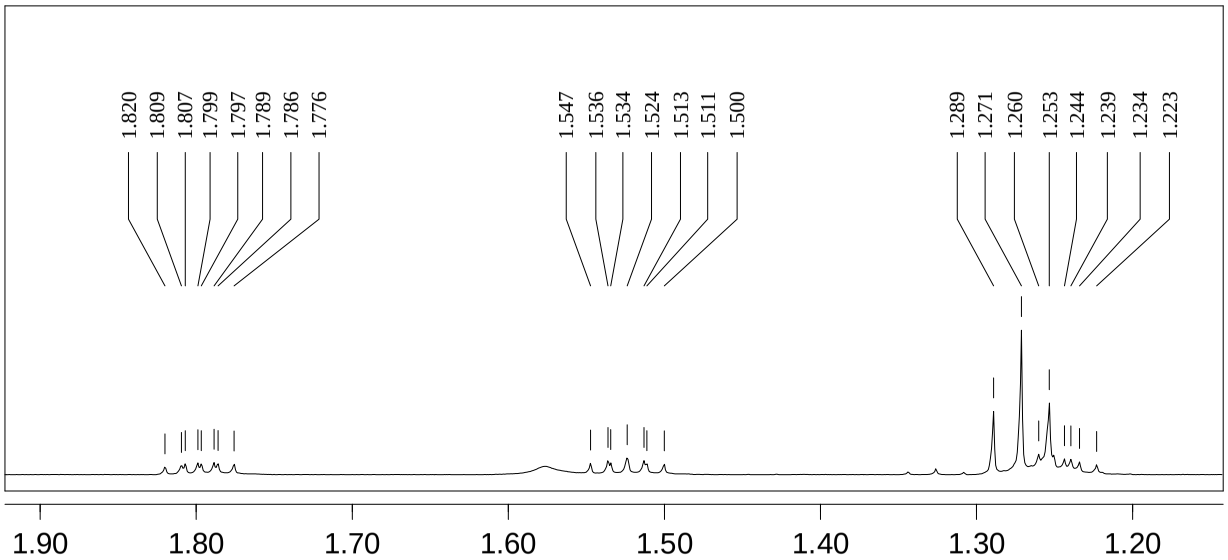
CDCl3, 300 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
MeO
O
O
9
173.530
158.262
132.031
127.308
113.852
77.424
77.000
76.576
60.609
55.276
25.602
23.852
16.730
14.250



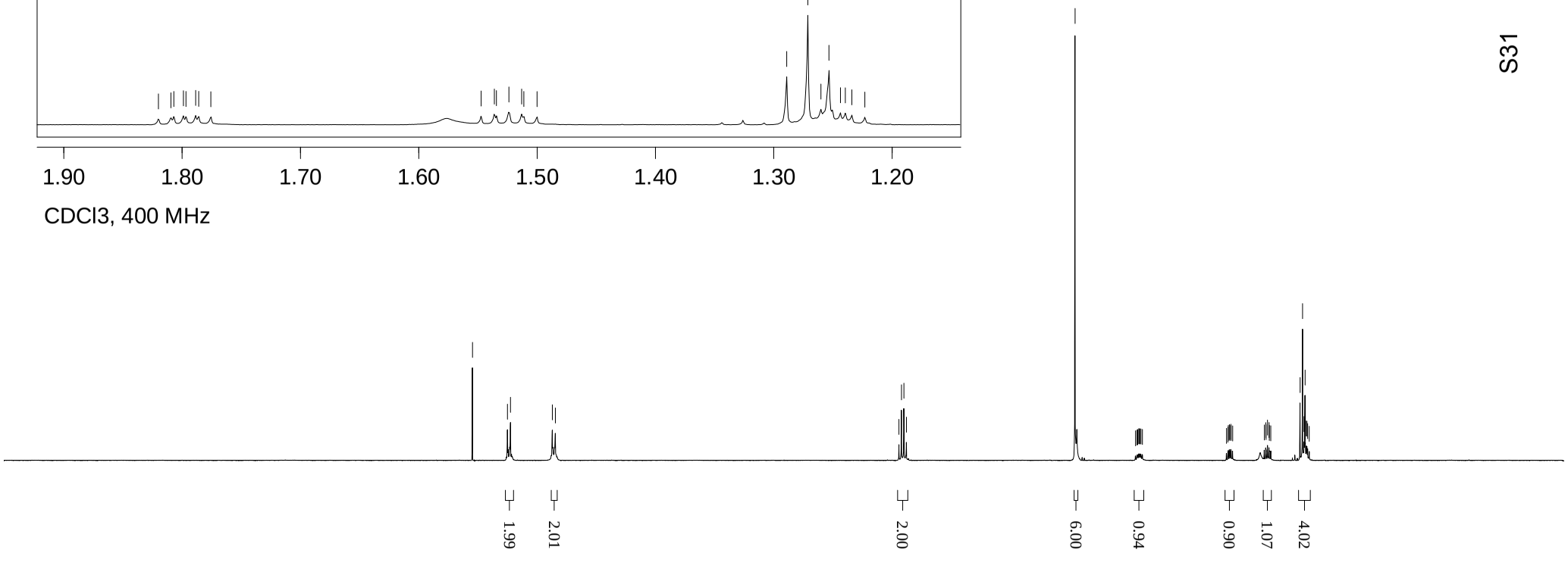
7.260 7.007 6.986 6.684 6.663

4.183 4.165 4.147 4.129 2.913 2.476 2.466 2.460 2.453 2.450 2.443 2.437 2.427 1.820 1.809 1.807 1.799 1.797 1.789 1.786 1.776 1.547 1.536 1.534 1.524 1.513 1.511 1.500 1.289 1.271 1.260 1.253 1.244 1.239 1.234

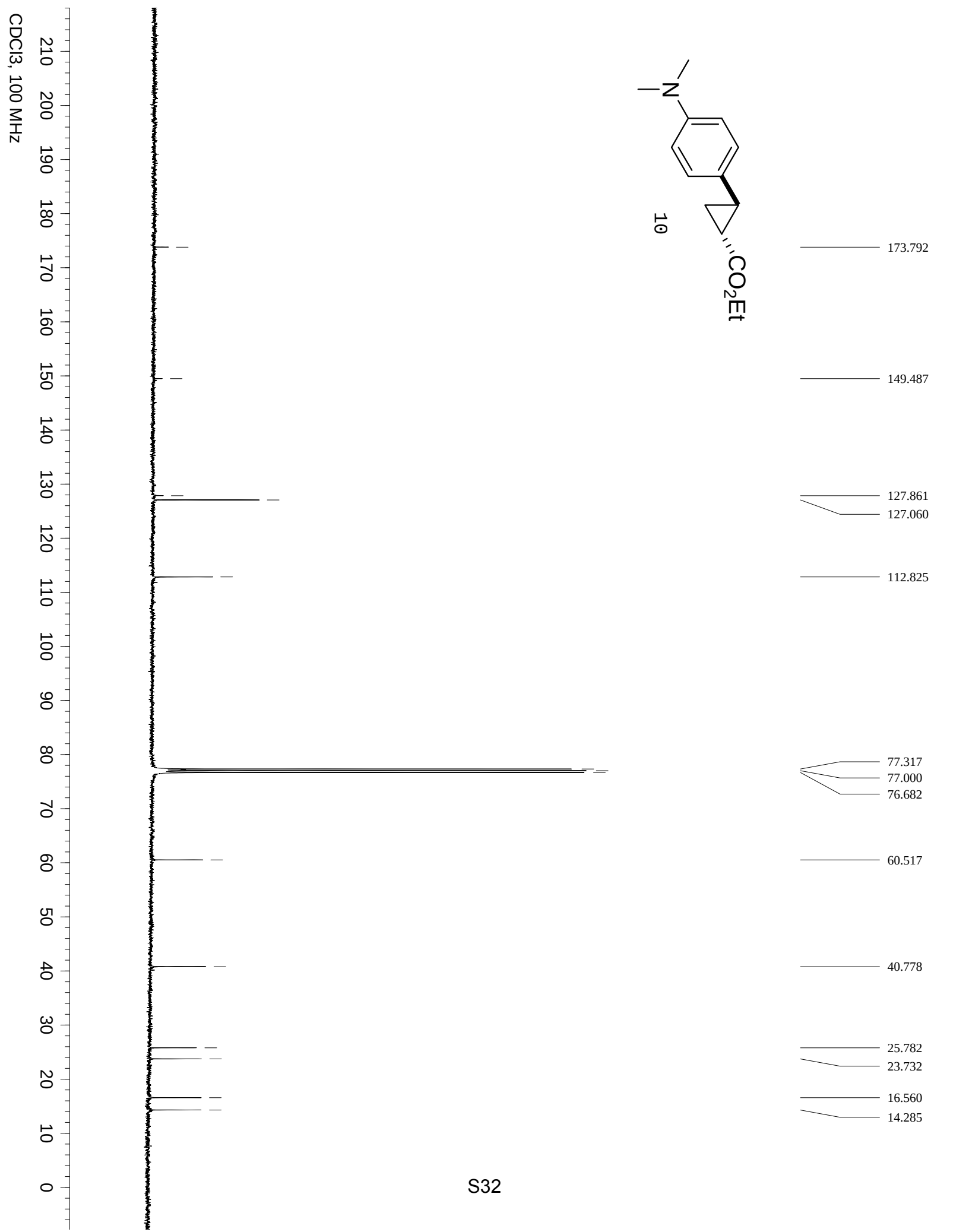


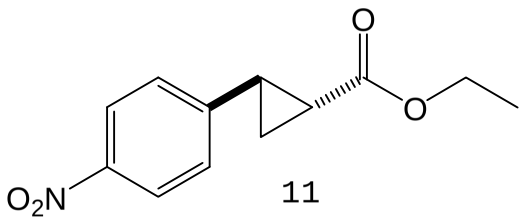
CDCl3, 400 MHz

S31



CDCl3, 400 MHz

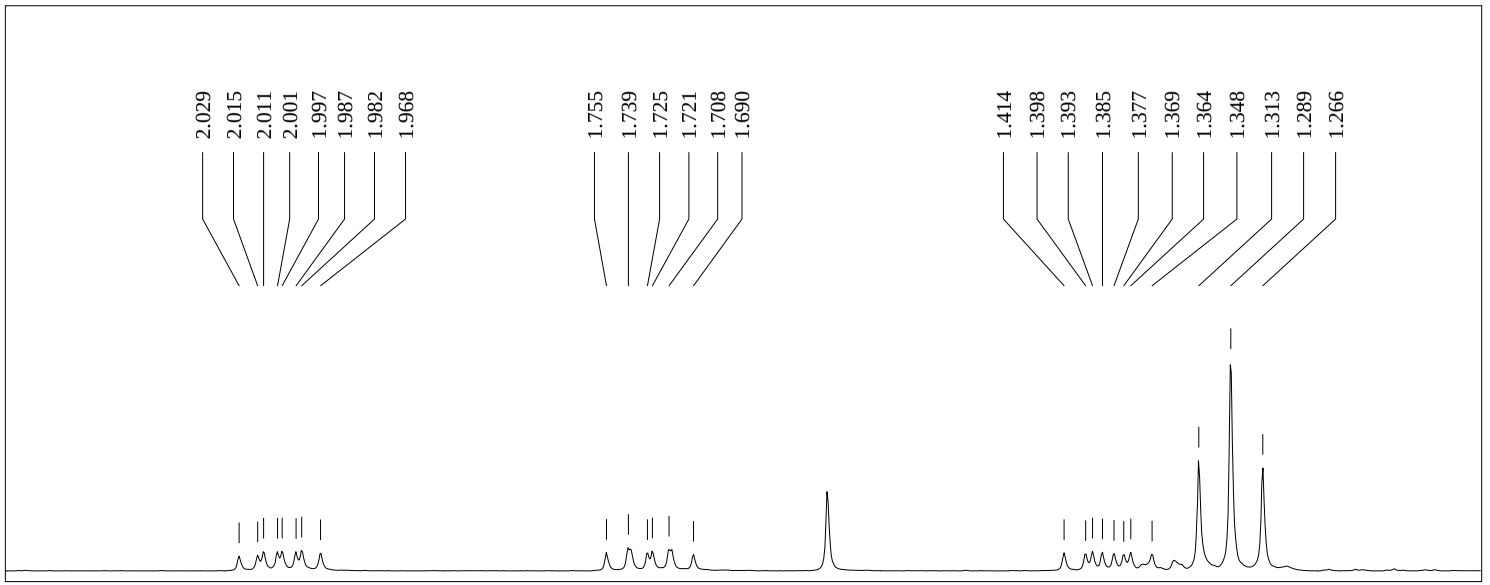

CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
N
10
CO2Et
173.792
149.487
127.861
127.060
112.825
77.317
77.000
76.682
60.517
40.778
25.782
23.732
16.560
14.285



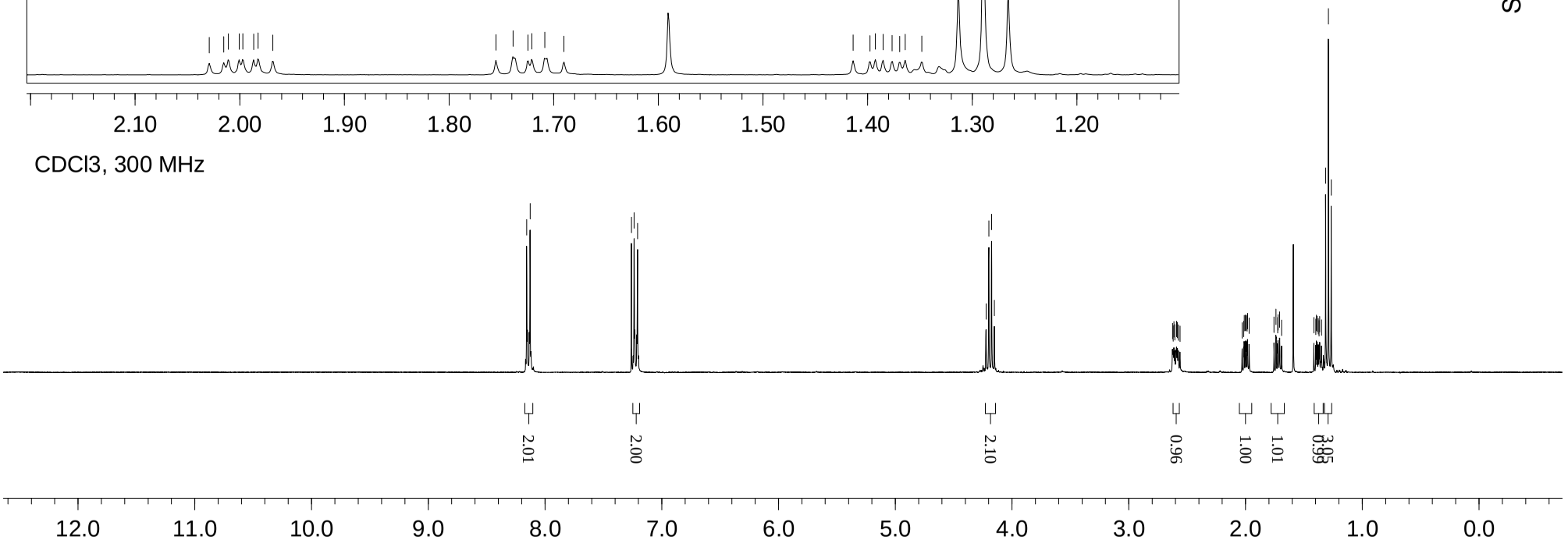
11

8.157 8.127 7.260 7.236 7.207

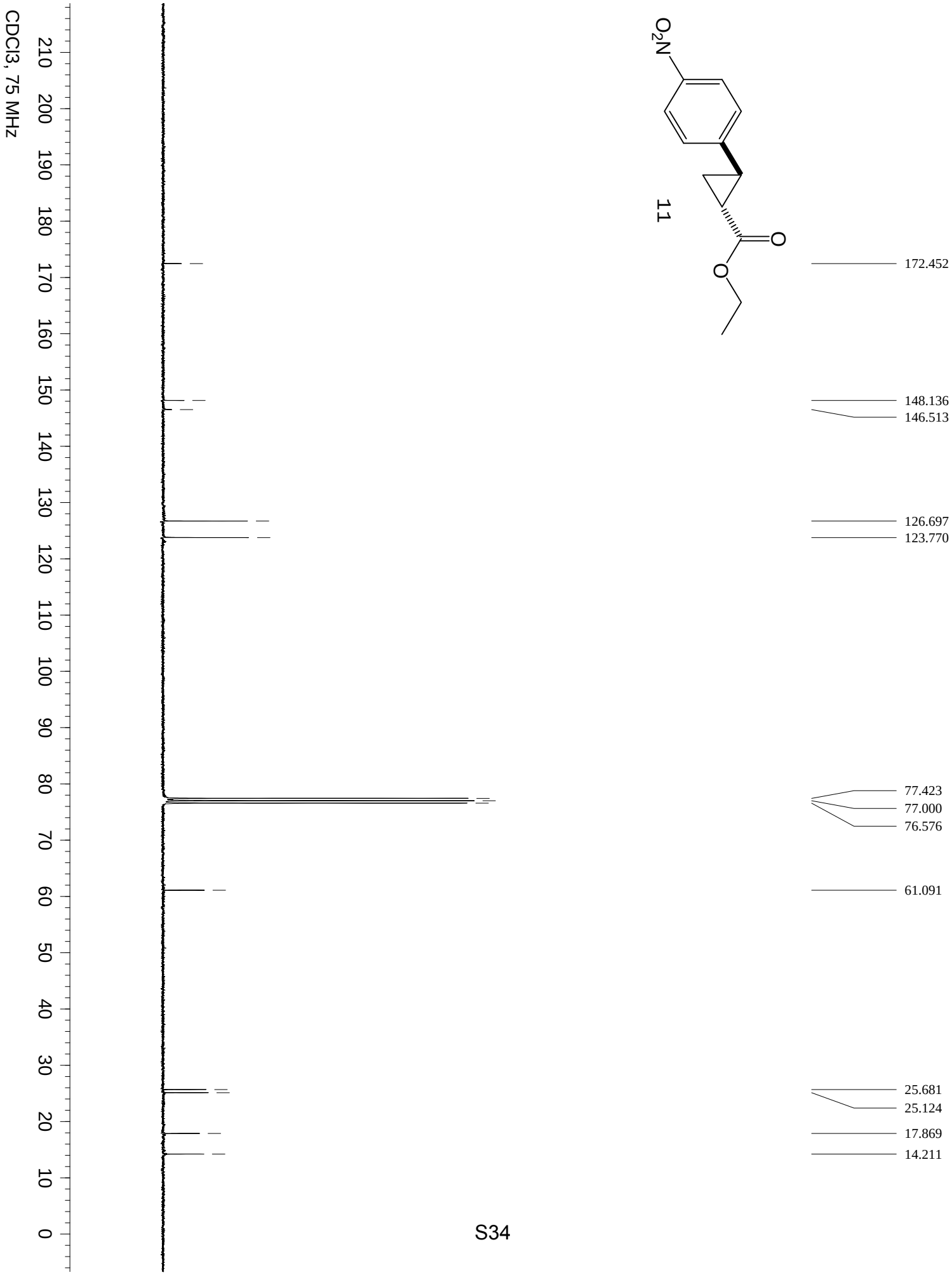
4.222 4.198 4.175 4.151 2.624 2.619 2.613 2.605 2.591 2.582 2.575 2.561 2.029 2.015 2.011 2.001 1.997 1.987 1.982 1.968 1.755 1.739 1.725 1.721 1.708 1.690 1.414 1.398 1.393 1.385 1.377 1.369 1.364

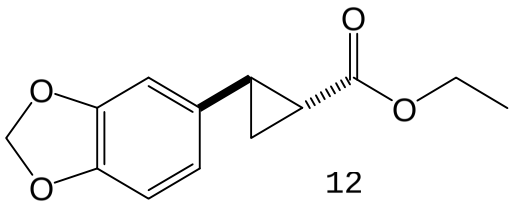


CDCl3, 300 MHz



CDCl3, 300 MHz

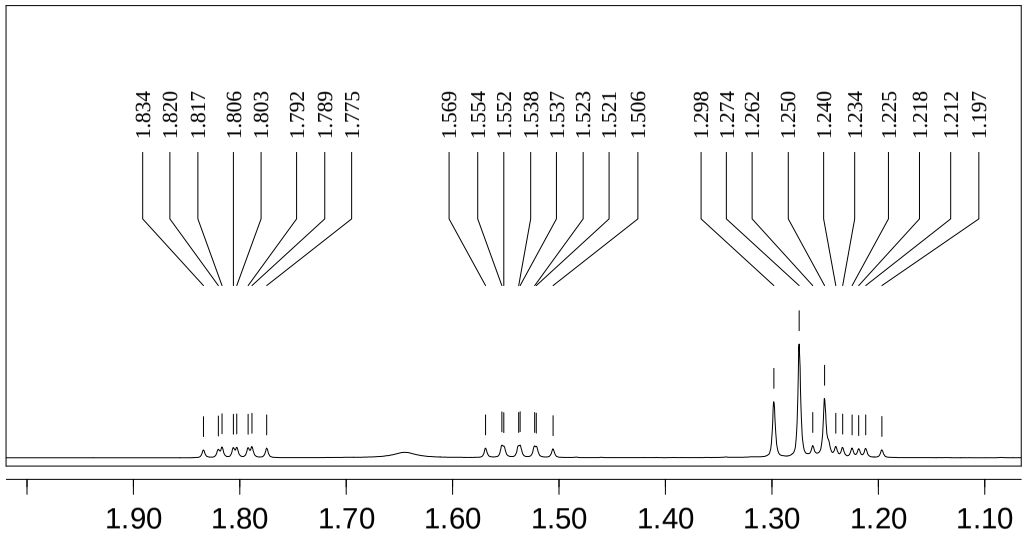

CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
O2N
11
O
O
172.452
148.136
146.513
126.697
123.770
77.423
77.000
76.576
61.091
25.681
25.124
17.869
14.211



12

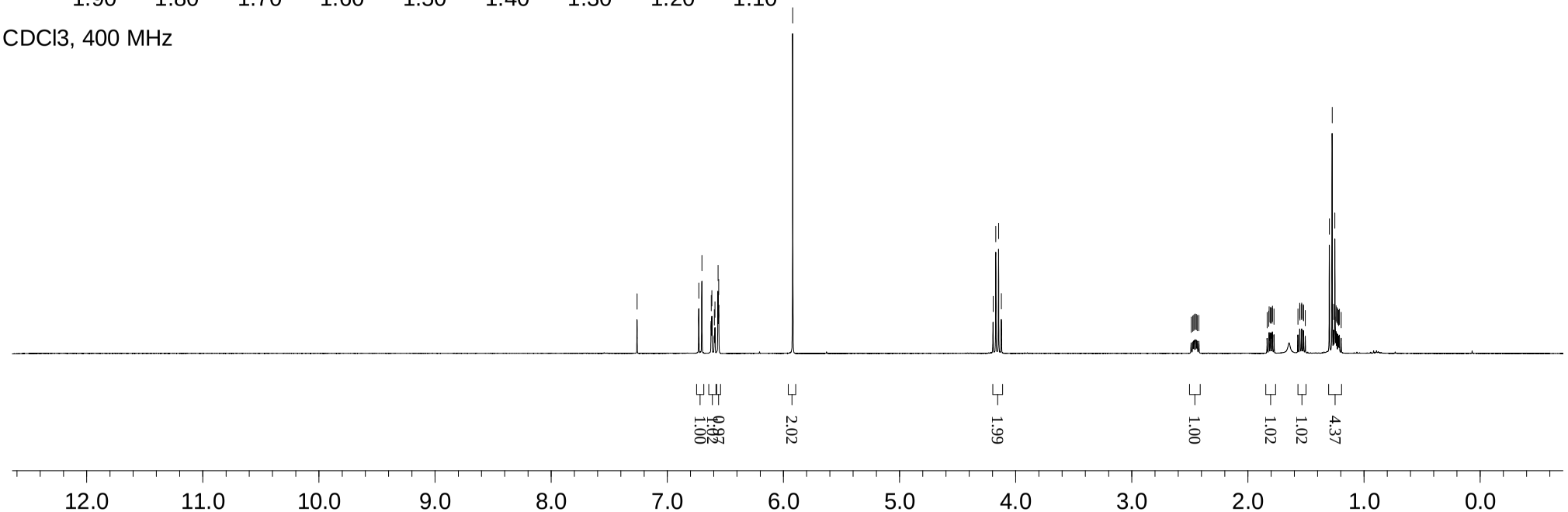
7.260 6.728 6.702 6.621 6.615 6.594 6.589 6.563 6.557 5.919

4.194 4.170 4.147 4.123 2.488 2.474 2.467 2.457 2.453 2.444 2.436 2.422 1.834 1.820 1.817 1.806 1.803 1.792 1.789 1.775 1.569 1.554 1.552 1.538 1.537 1.523 1.521 1.506 1.298 1.274 1.262 1.250 1.240

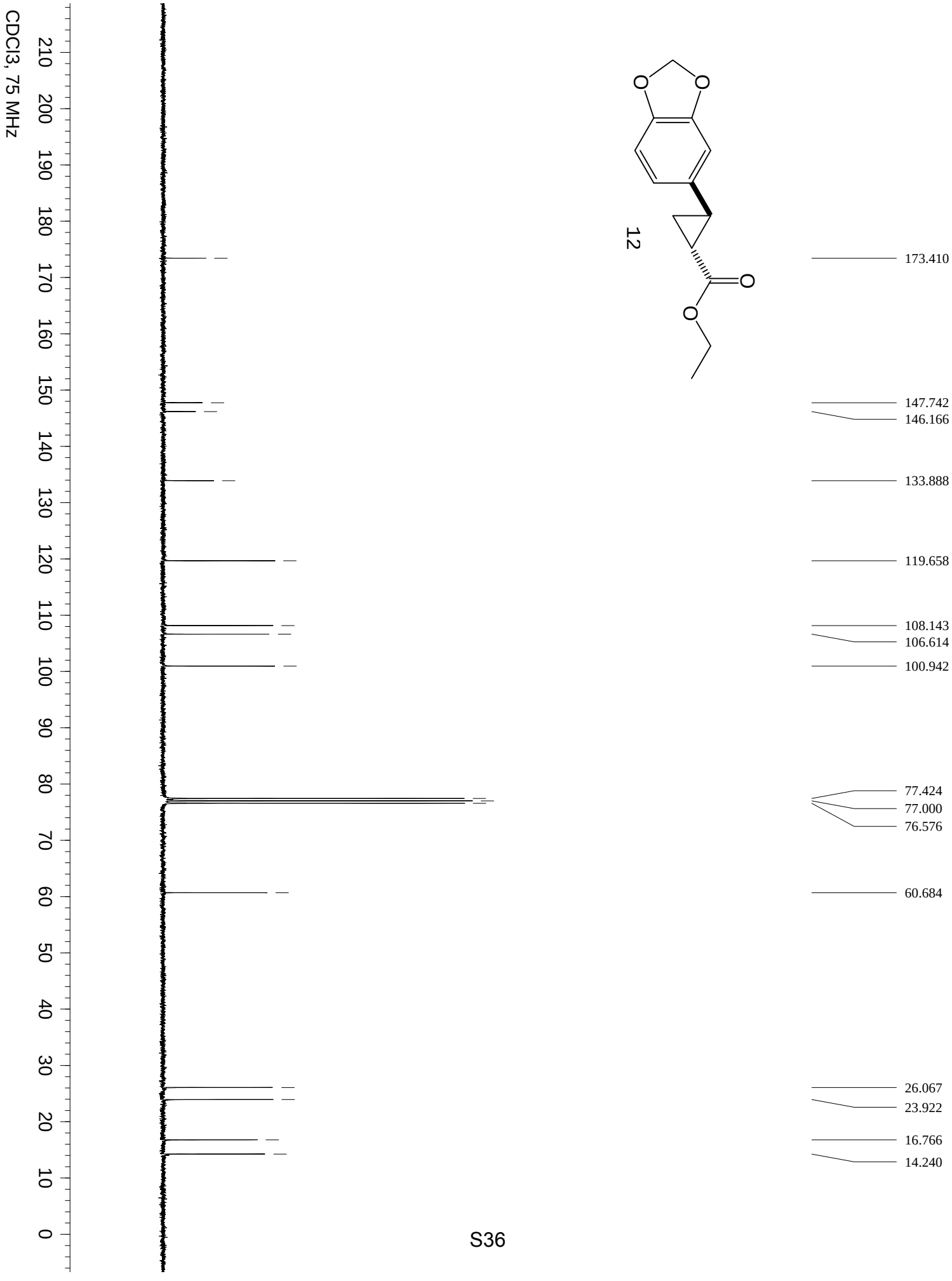


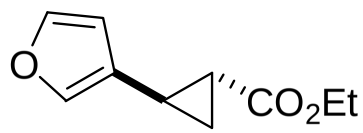
CDCl3, 400 MHz

S35



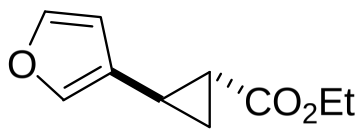
CDCl3, 400 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
O
O
O
O
12
173.410
147.742
146.166
133.888
119.658
108.143
106.614
100.942
77.424
77.000
76.576
60.684
26.067
23.922
16.766
14.240


O
CO2Et

13

7.324
7.289
7.260
6.155
4.184
4.166
4.148
4.130
2.353
2.342
2.337
2.328
2.320
2.314
2.304
1.777
1.765
1.755
1.745
1.733
1.582
1.517
1.505
1.494
1.482
1.471
1.294
1.276
1.258
1.145
1.134
1.129
1.124
1.118
1.114
1.108
1.097
2.40
2.30
2.20
2.10
2.00
1.90
1.80
1.70
1.60
1.50
1.40
1.30
1.20
1.10
1.00
0.90
CDCl3, 400 MHz
0.97
1.98
1.01
0.99
0.98
3.03
1.00
13.0
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
CDCl3, 400 MHz

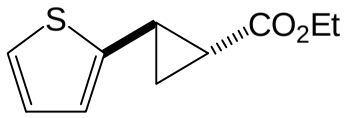


13

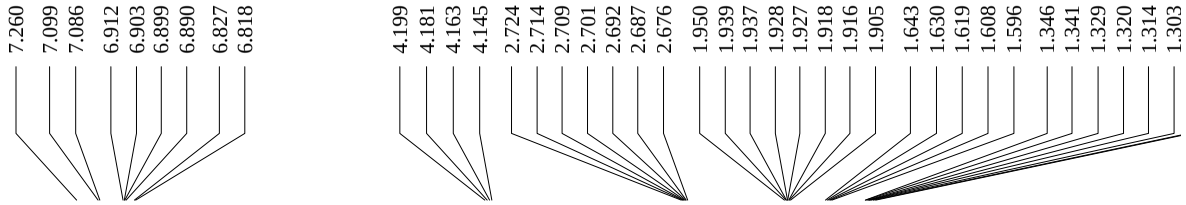
173.413
143.118
139.167
124.719
108.916
77.317
77.000
76.682
60.680
22.677
17.186
16.109
14.250

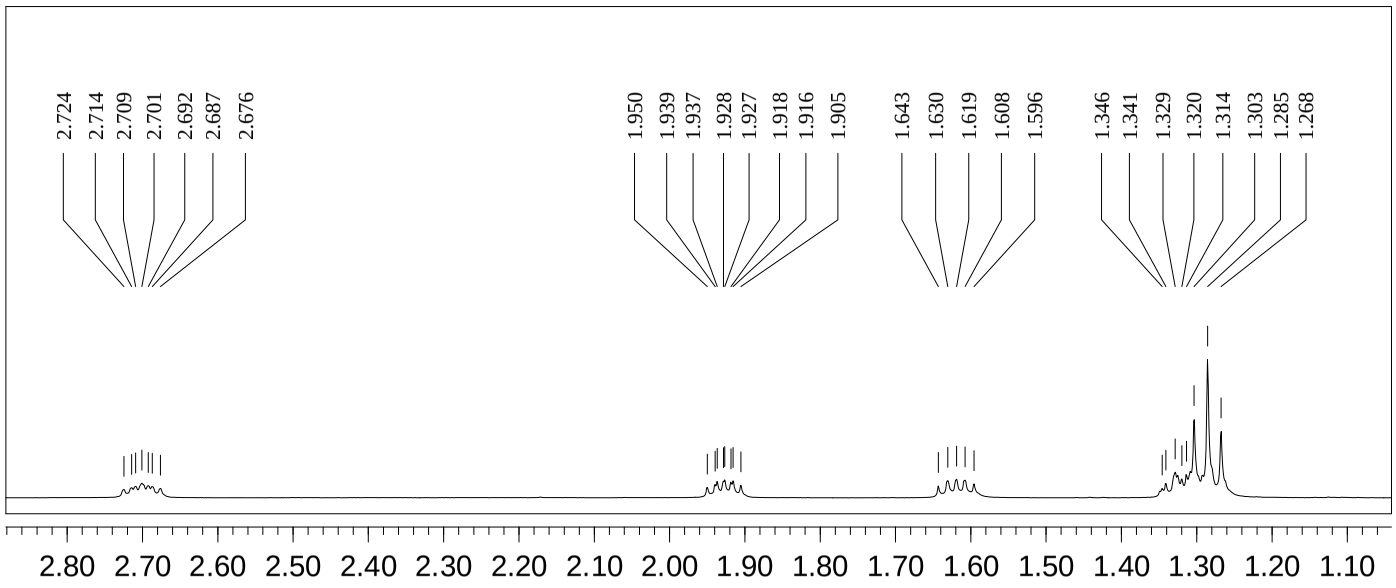
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

CDCl3, 100 MHz

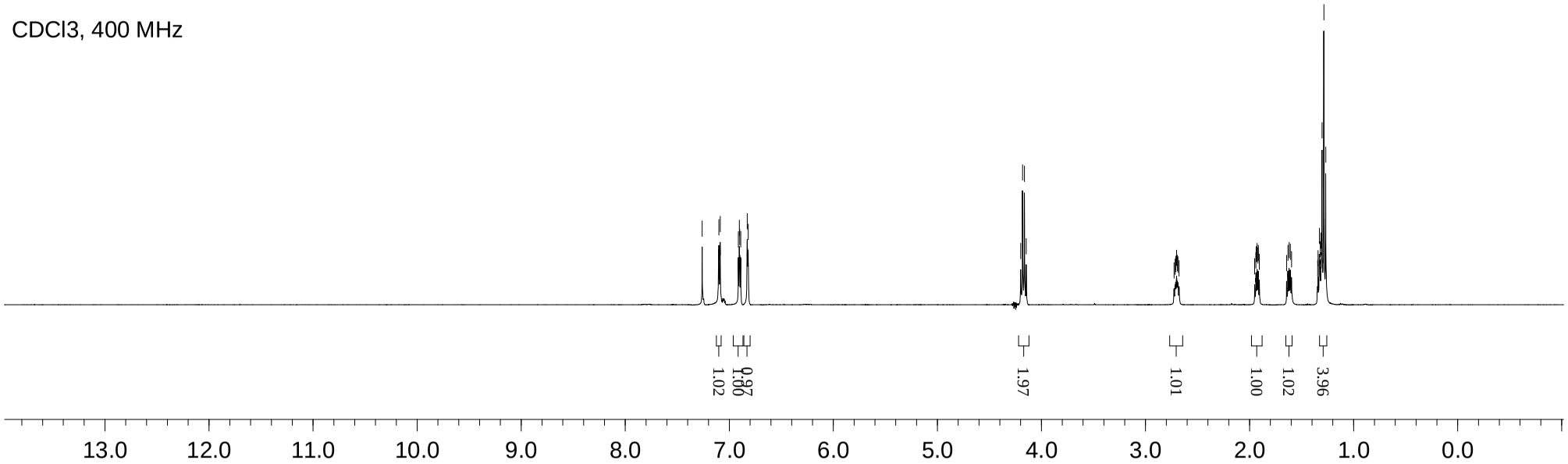


14

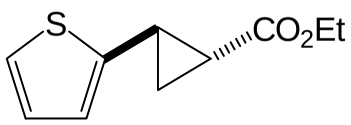




CDCl3, 400 MHz



CDCl3, 400 MHz

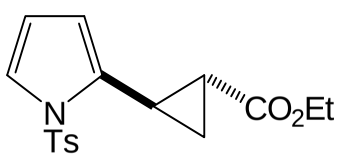


14

172.843
144.182
126.833
123.868
123.062
77.318
77.000
76.682
60.795
24.944
21.447
17.904
14.232

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

CDCl3, 100 MHz



15

7.662 7.642 7.260 7.239 7.216 6.110 6.102 6.094 5.837

4.176 4.158 4.141 4.123 2.573 2.556 2.548 2.539 2.524 2.368 1.589 1.577 1.566 1.556 1.544 1.397 1.385 1.374 1.363 1.351 1.332 1.280 1.262 1.245 1.068 1.057 1.051 1.047 1.040

1.589 1.577 1.566 1.556 1.544 1.397 1.385 1.374 1.363 1.351 1.332 1.280 1.262 1.245 1.068 1.057 1.051 1.047 1.040 1.036 1.031 1.019

1.06 1.00 3.05 1.00

1.70 1.60 1.50 1.40 1.30 1.20 1.10 1.00

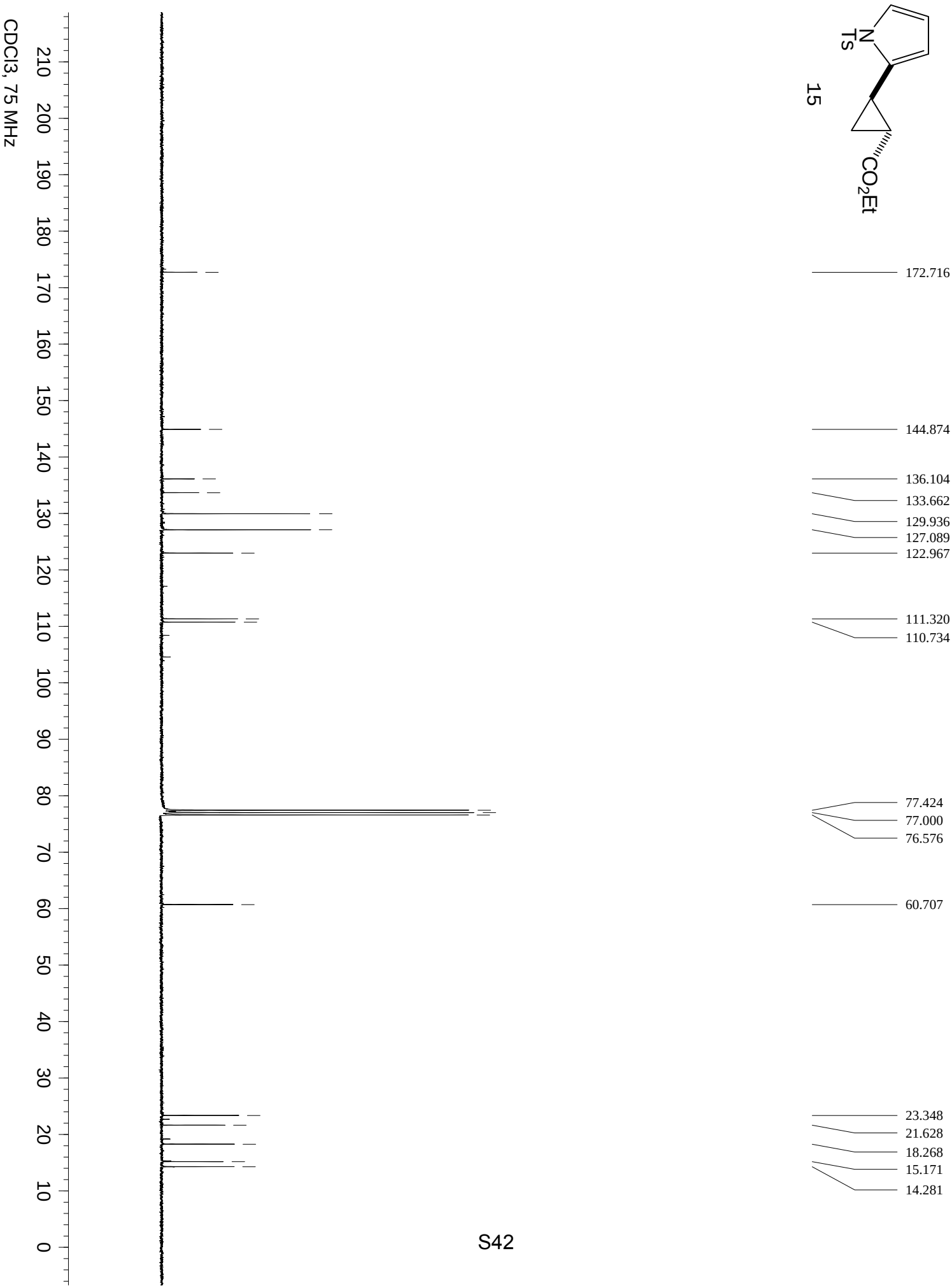
CDCl3, 400 MHz

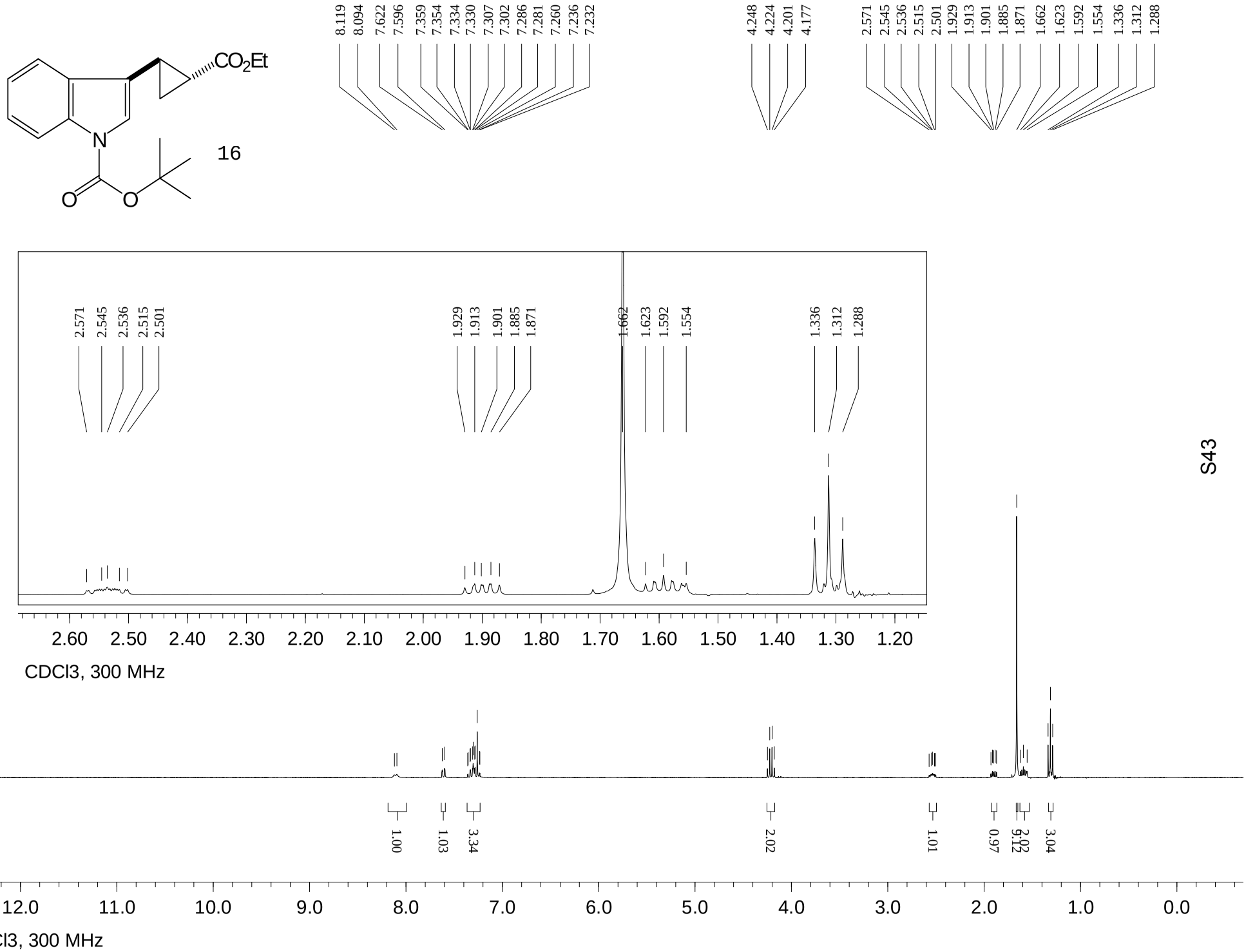
S41

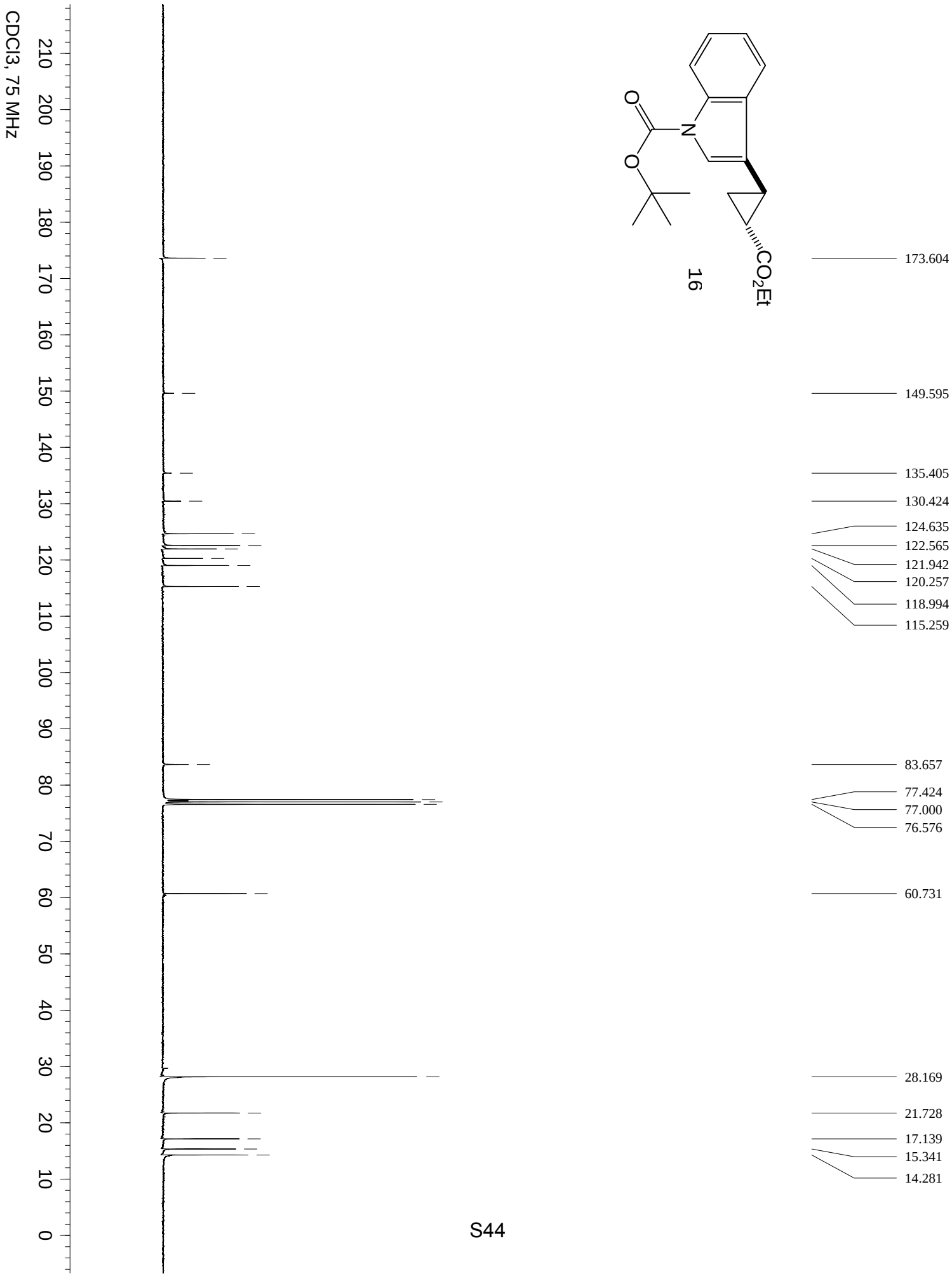
1.97 3.21 0.98 1.04 1.99 0.98 3.03 1.06 1.00 3.05 1.00

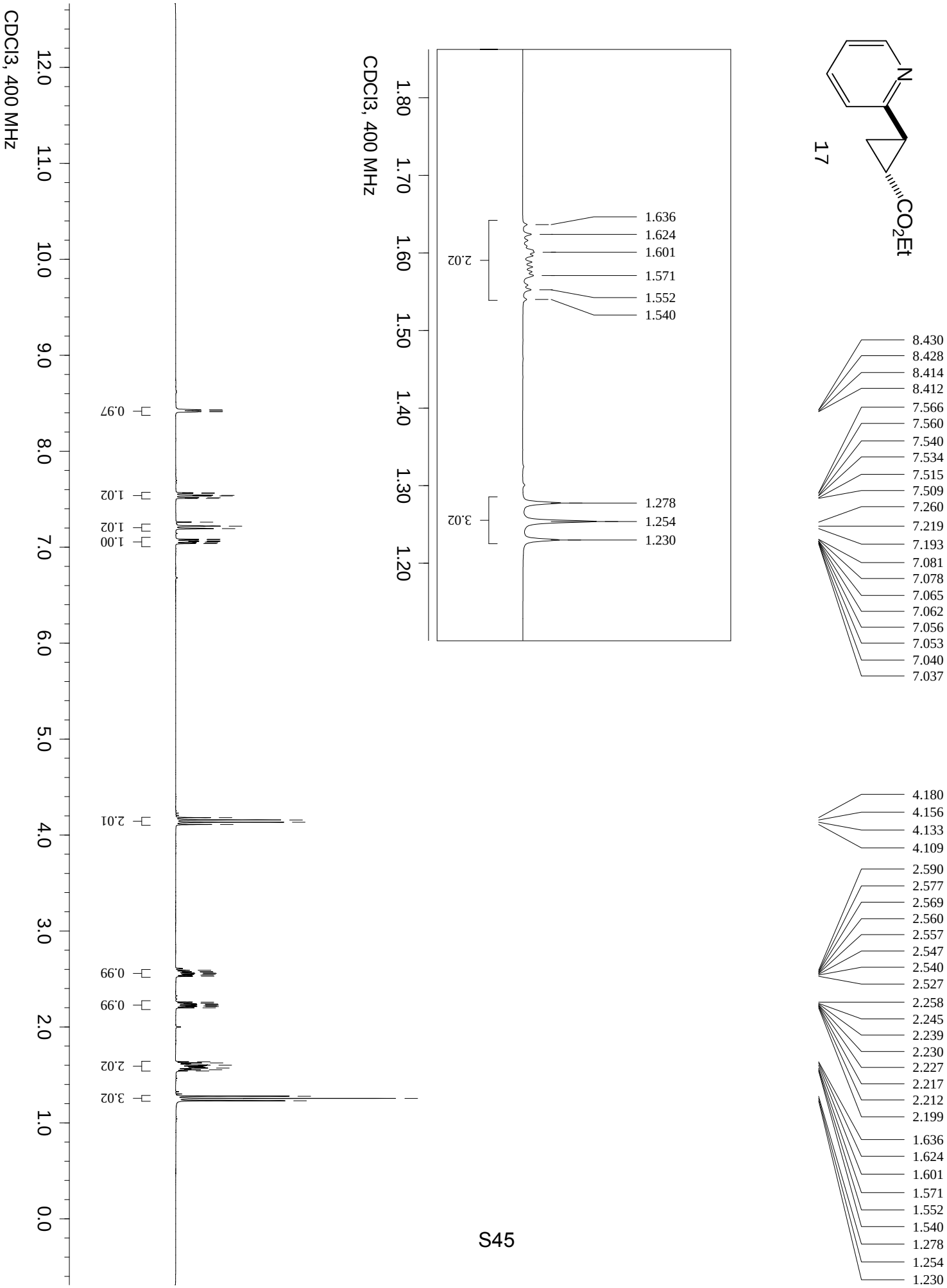
13.0 12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0

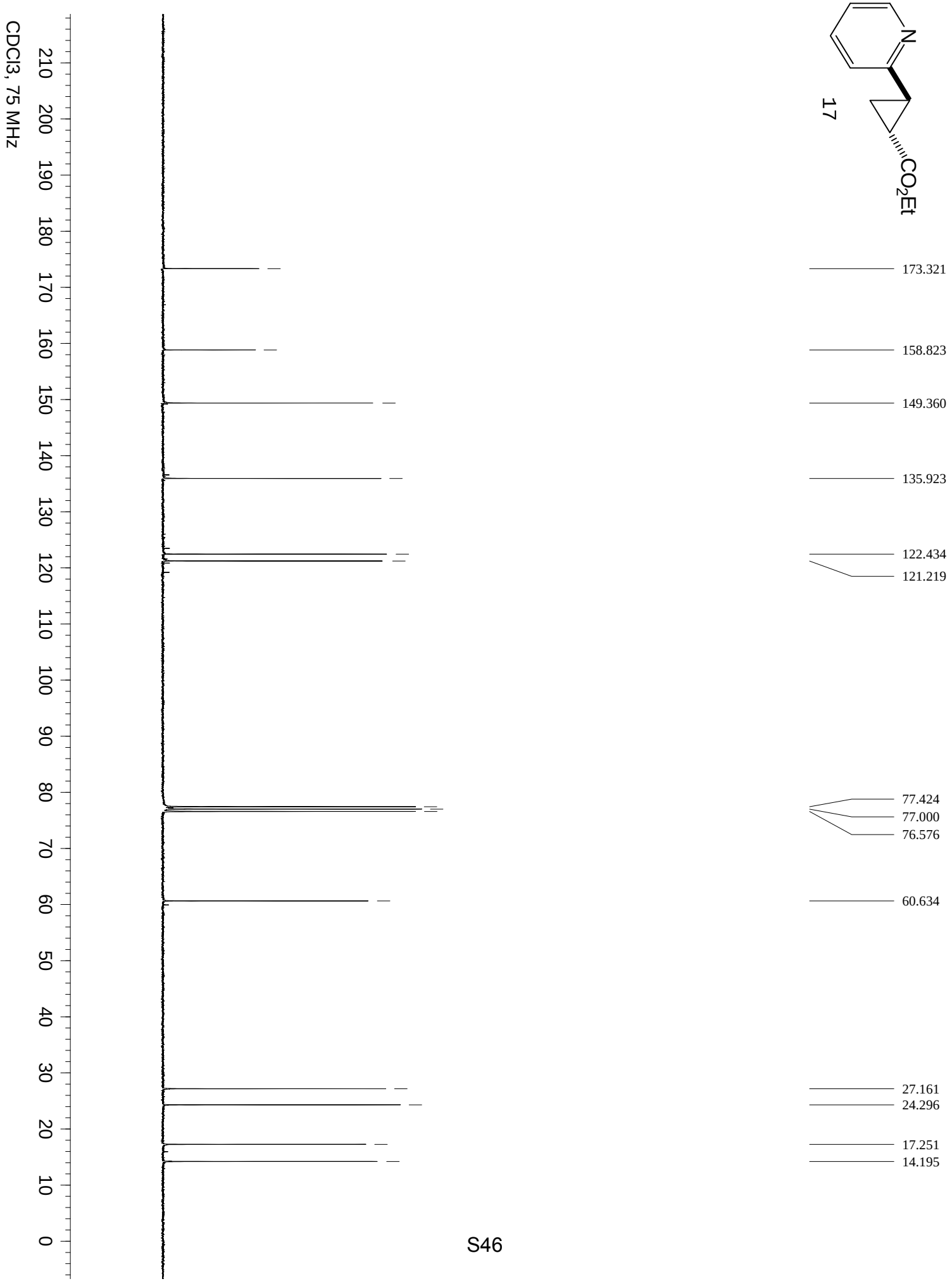
CDCl3, 400 MHz

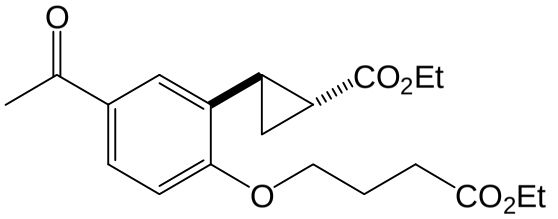

CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
N
Ts
CO2Et
15
172.716
144.874
136.104
133.662
129.936
127.089
122.967
111.320
110.734
77.424
77.000
76.576
60.707
23.348
21.628
18.268
15.171
14.281


CO2Et
N
O
O
16
8.119
8.094
7.622
7.596
7.359
7.354
7.334
7.330
7.307
7.302
7.286
7.281
7.260
7.236
7.232
4.248
4.224
4.201
4.177
2.571
2.545
2.536
2.515
2.501
1.929
1.913
1.901
1.885
1.871
1.662
1.623
1.592
1.554
1.336
1.312
1.288
2.60 2.50 2.40 2.30 2.20 2.10 2.00 1.90 1.80 1.70 1.60 1.50 1.40 1.30 1.20
CDCl3, 300 MHz
1.00
1.03
3.34
2.02
1.01
0.97
2.12
2.02
3.04
12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
CDCl3, 300 MHz

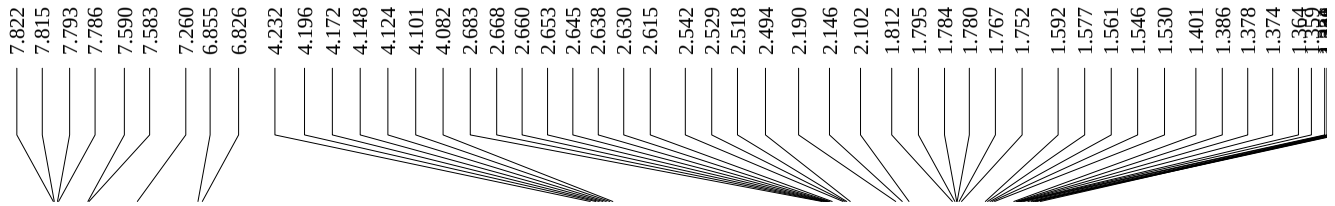

CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
O
O
N
CO2Et
16
173.604
149.595
135.405
130.424
124.635
122.565
121.942
120.257
118.994
115.259
83.657
77.424
77.000
76.576
60.731
28.169
21.728
17.139
15.341
14.281

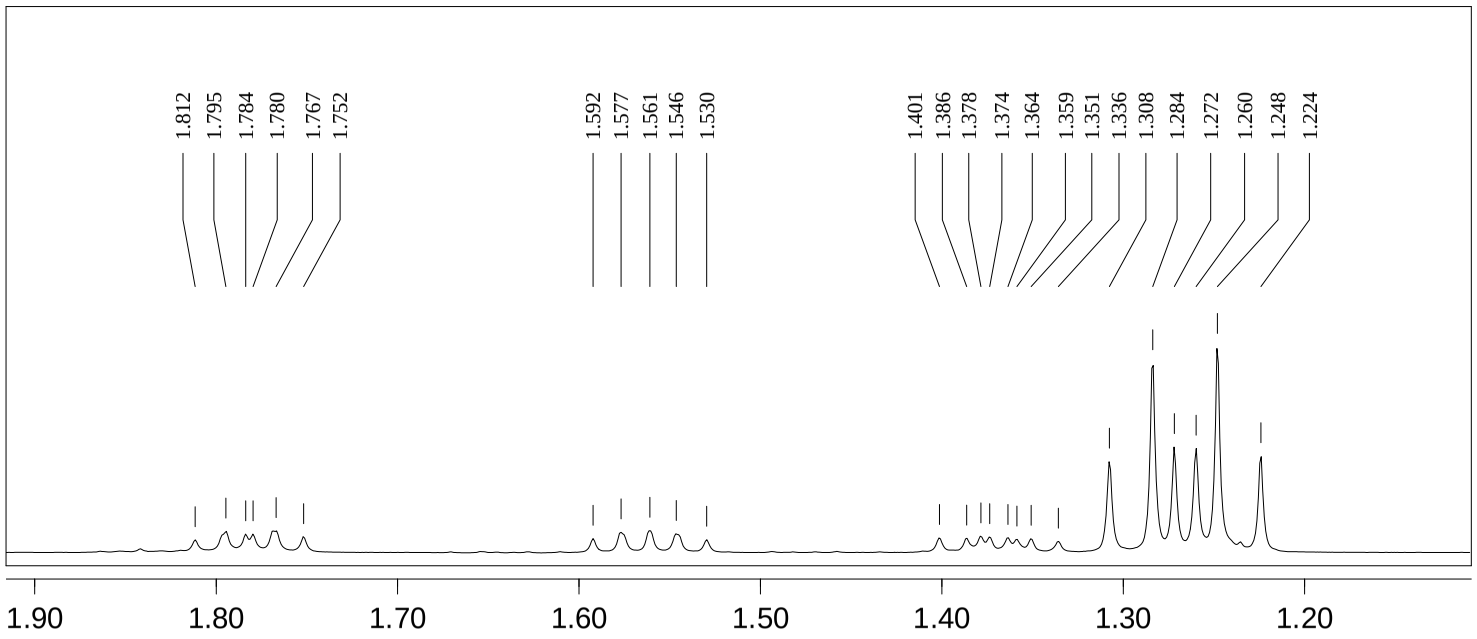

CDCl3, 400 MHz
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
0.97
1.02
1.02
1.00
2.01
0.99
0.99
2.02
3.02
CDCl3, 400 MHz
1.80
1.70
1.60
1.50
1.40
1.30
1.20
2.02
3.02
1.636
1.624
1.601
1.571
1.552
1.540
1.278
1.254
1.230
N
17
CO2Et
8.430
8.428
8.414
8.412
7.566
7.560
7.540
7.534
7.515
7.509
7.260
7.219
7.193
7.081
7.078
7.065
7.062
7.056
7.053
7.040
7.037
4.180
4.156
4.133
4.109
2.590
2.577
2.569
2.560
2.557
2.547
2.540
2.527
2.258
2.245
2.239
2.230
2.227
2.217
2.212
2.199
1.636
1.624
1.601
1.571
1.552
1.540
1.278
1.254
1.230


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
N
17
CO2Et
173.321
158.823
149.360
135.923
122.434
121.219
77.424
77.000
76.576
60.634
27.161
24.296
17.251
14.195

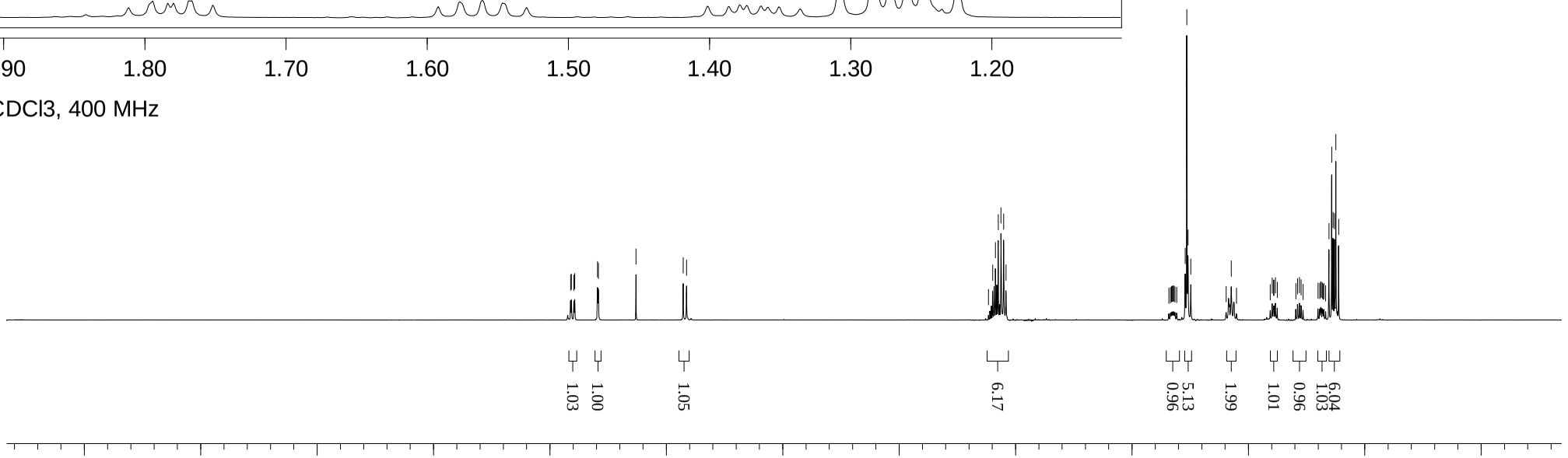


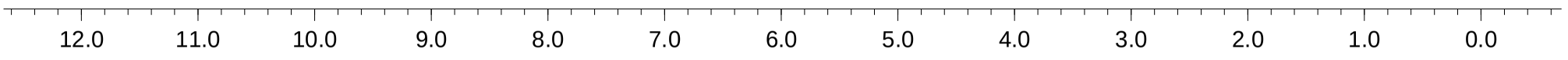
19



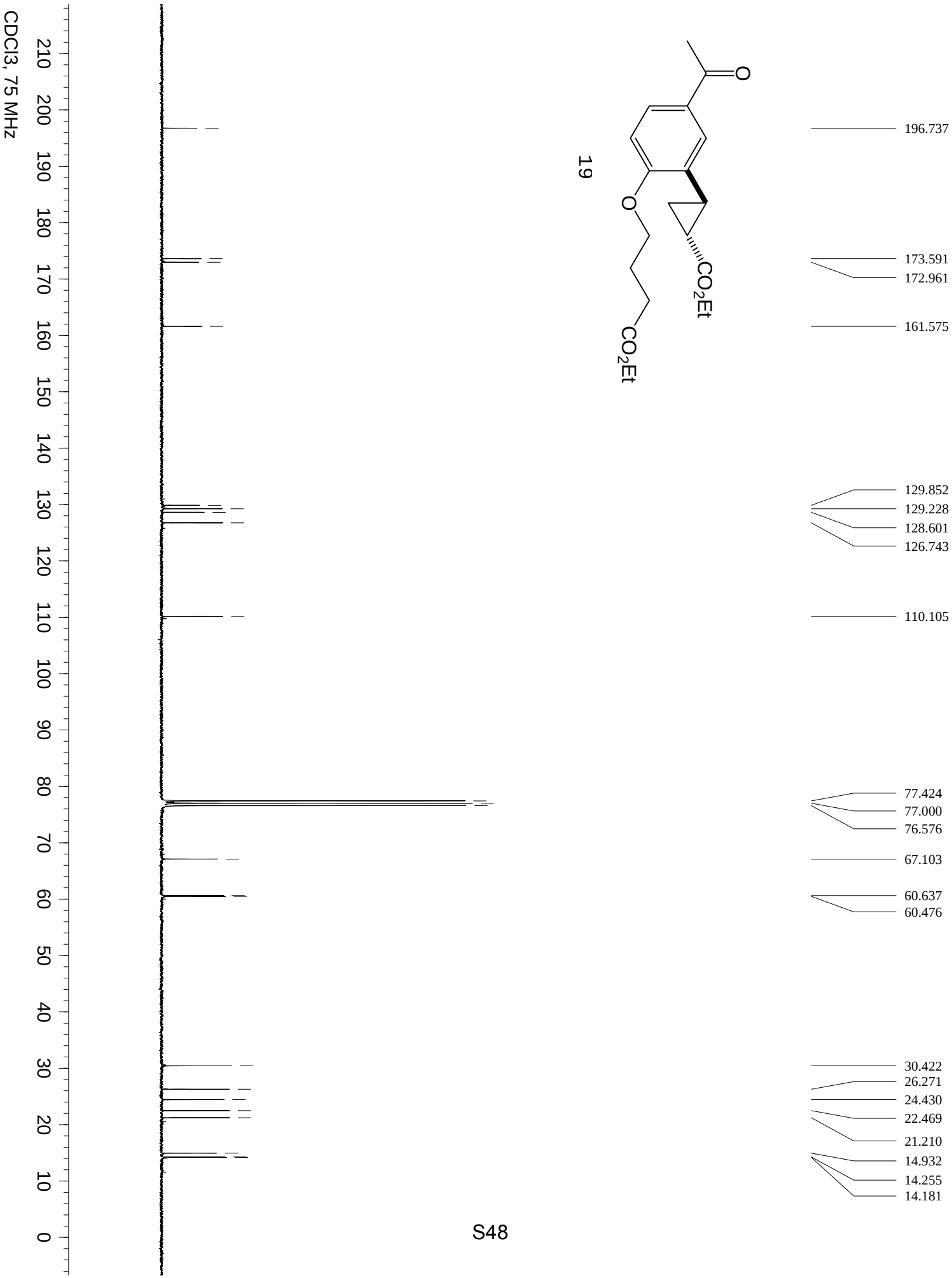


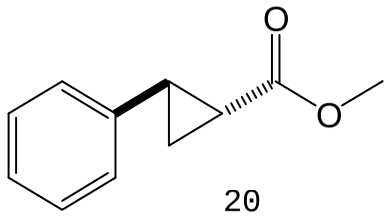
CDCl3, 400 MHz

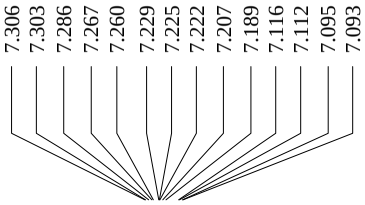


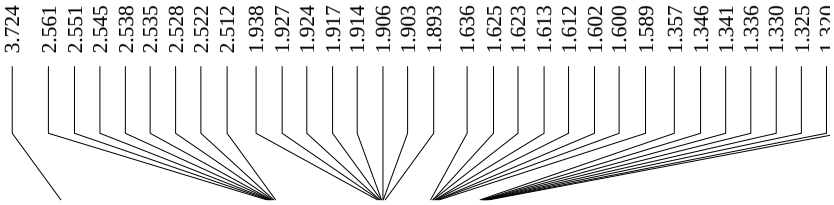


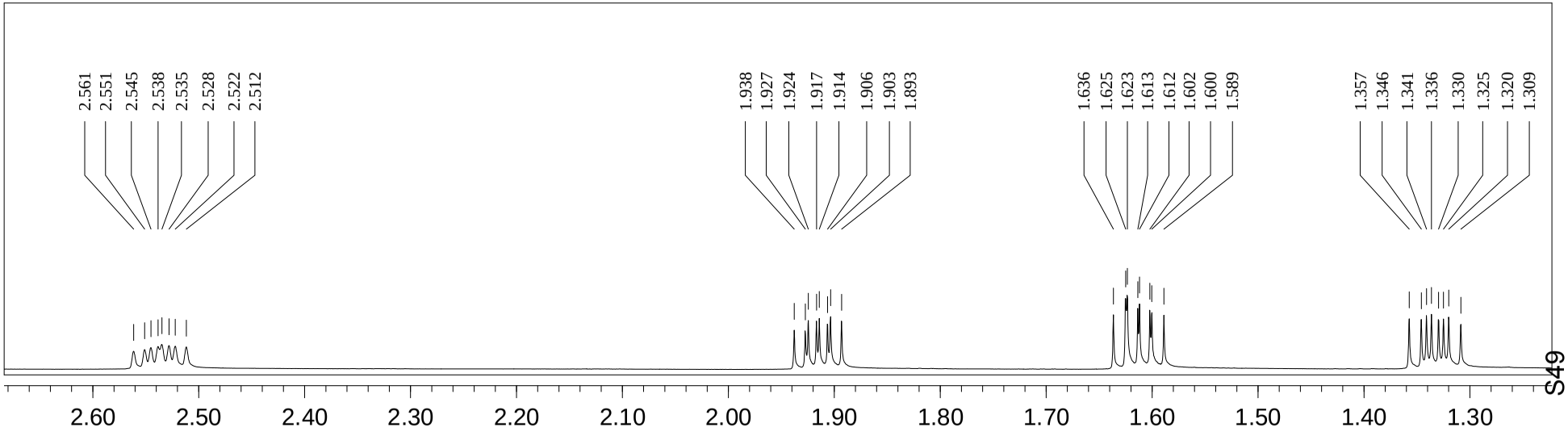
CDCl3, 400 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
O
O
CO2Et
CO2Et
19
196.737
173.591
172.961
161.575
129.852
129.228
128.601
126.743
110.105
77.424
77.000
76.576
67.103
60.637
60.476
30.422
26.271
24.430
22.469
21.210
14.932
14.255
14.181

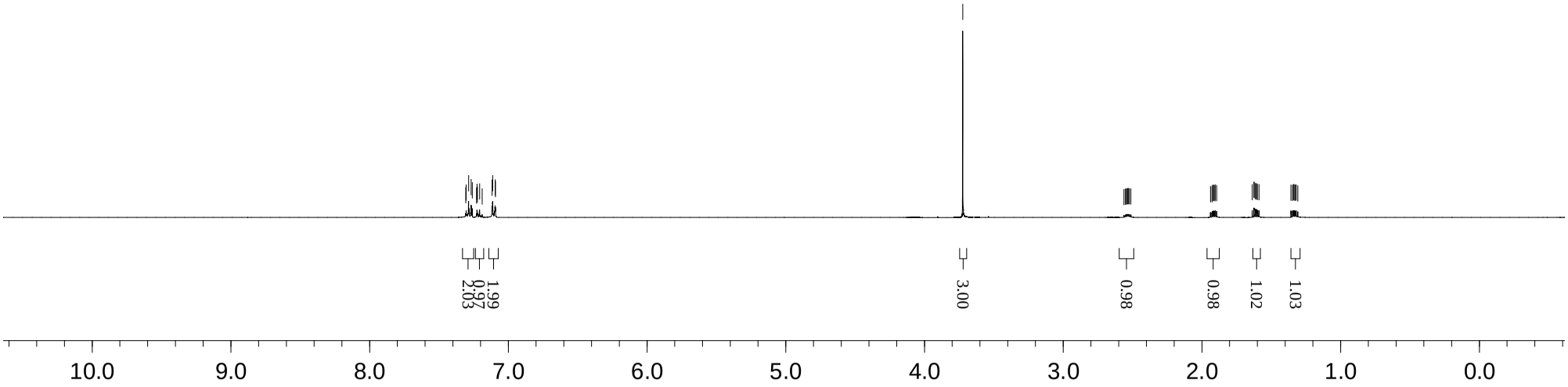




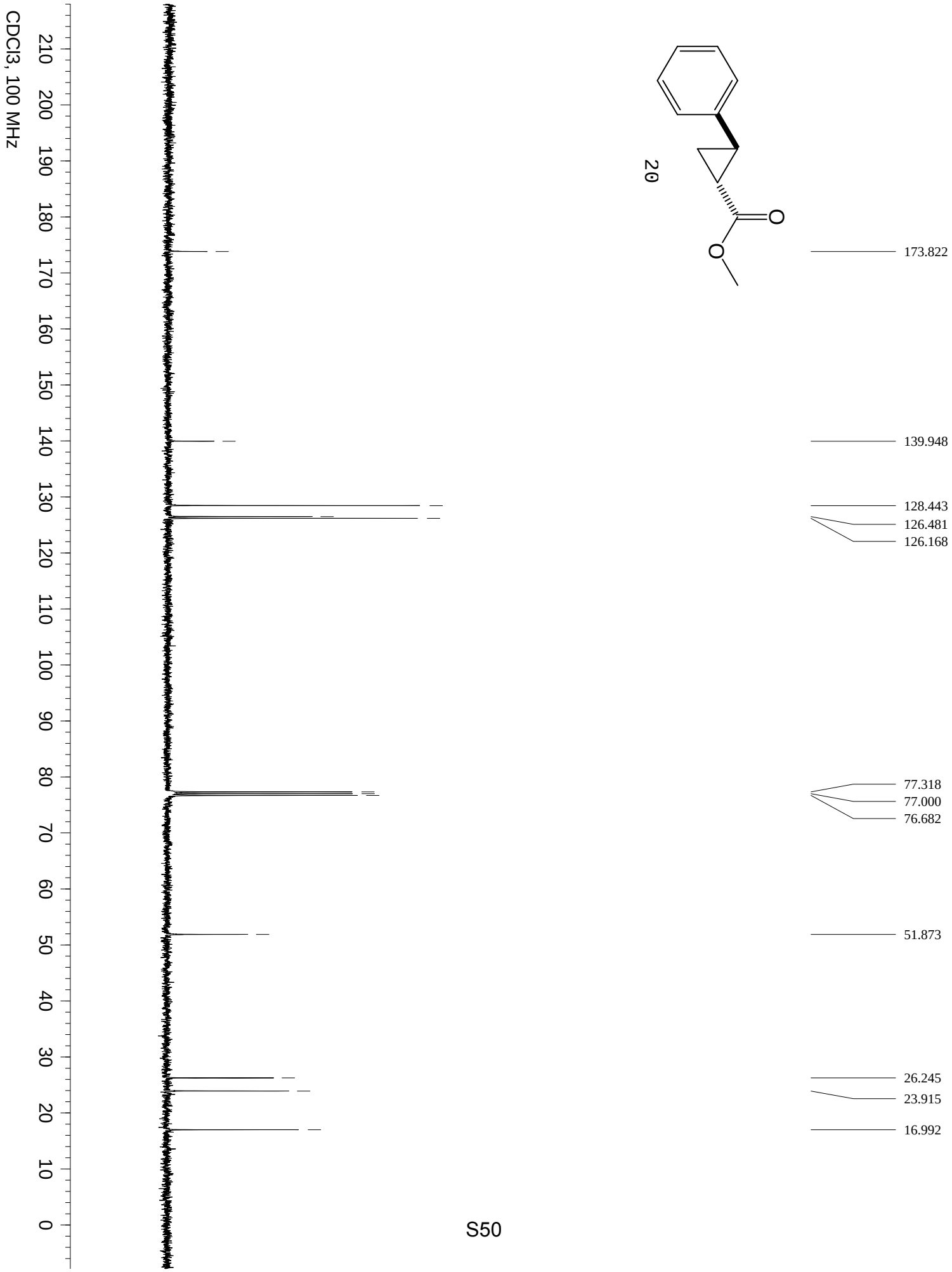


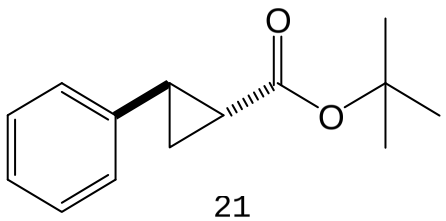


CDCl3, 400 MHz

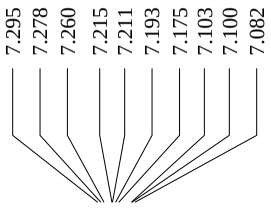


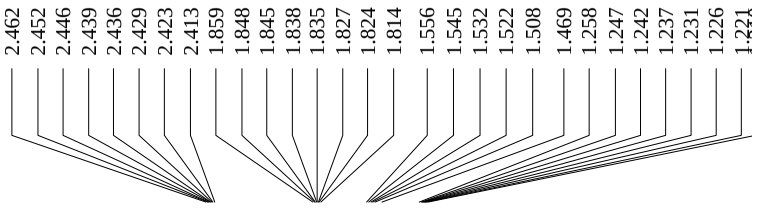
CDCl3, 400 MHz

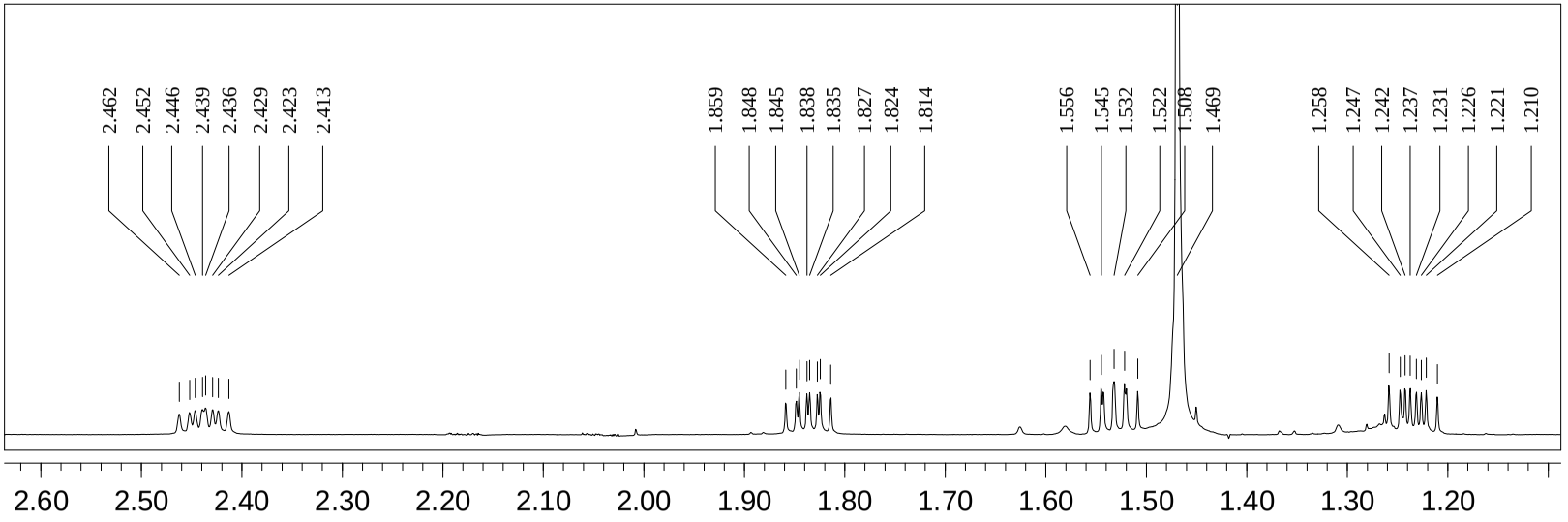

CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
20
O
O
173.822
139.948
128.443
126.481
126.168
77.318
77.000
76.682
51.873
26.245
23.915
16.992



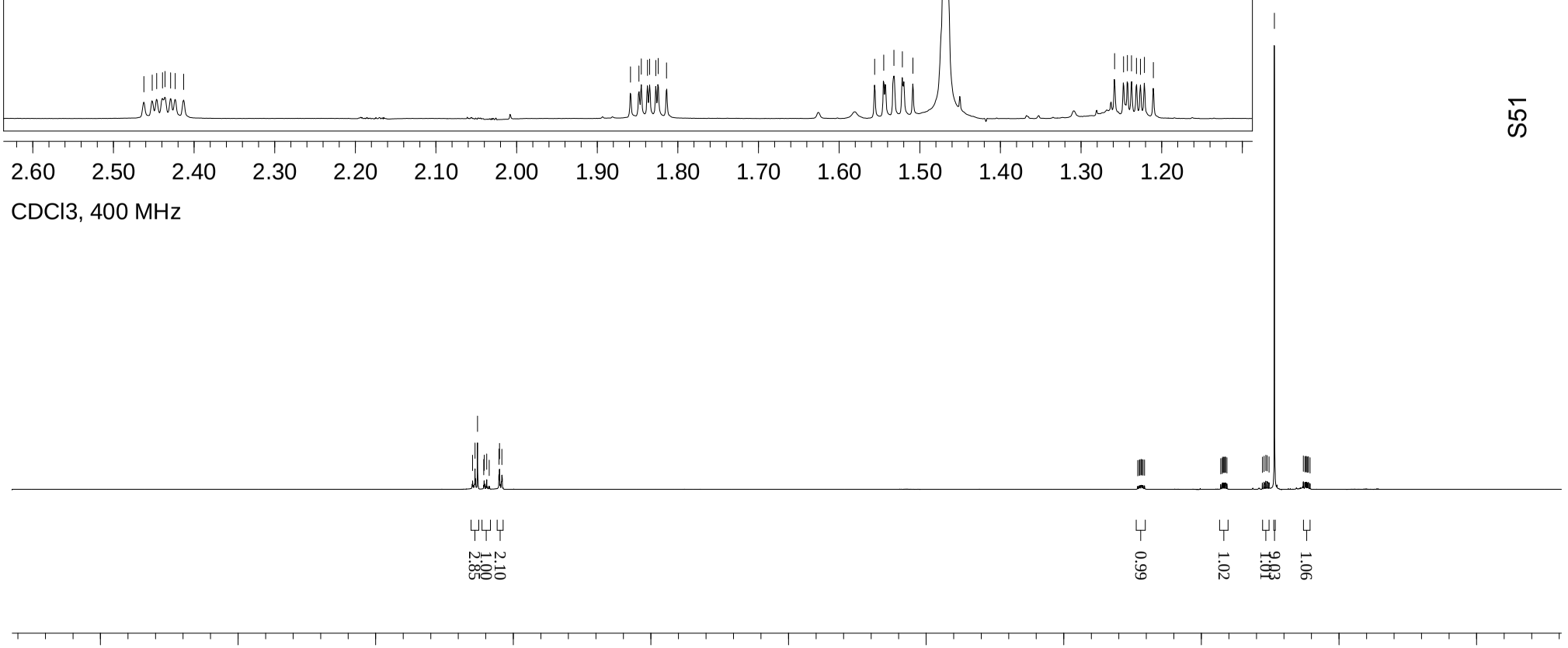
21



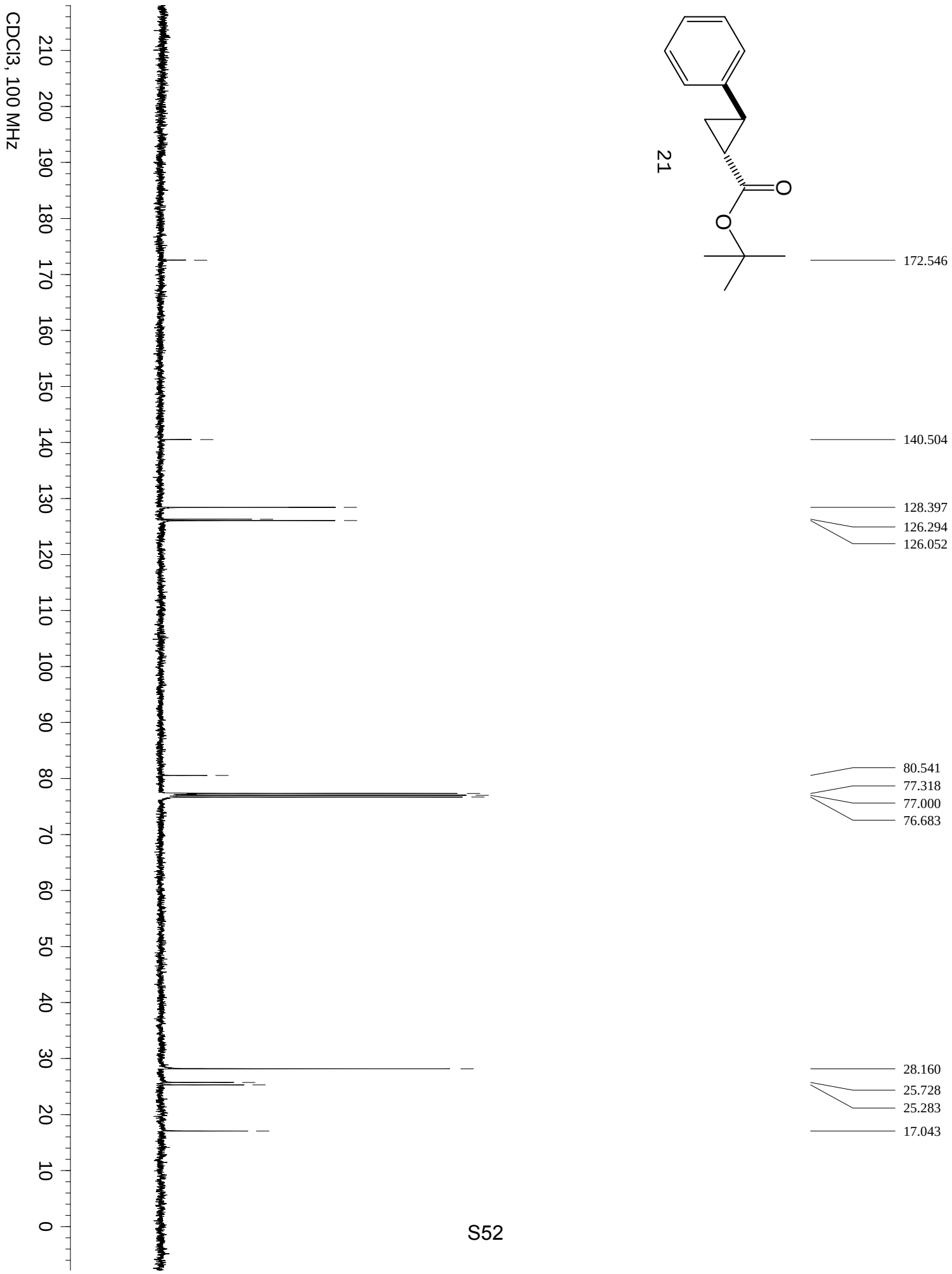


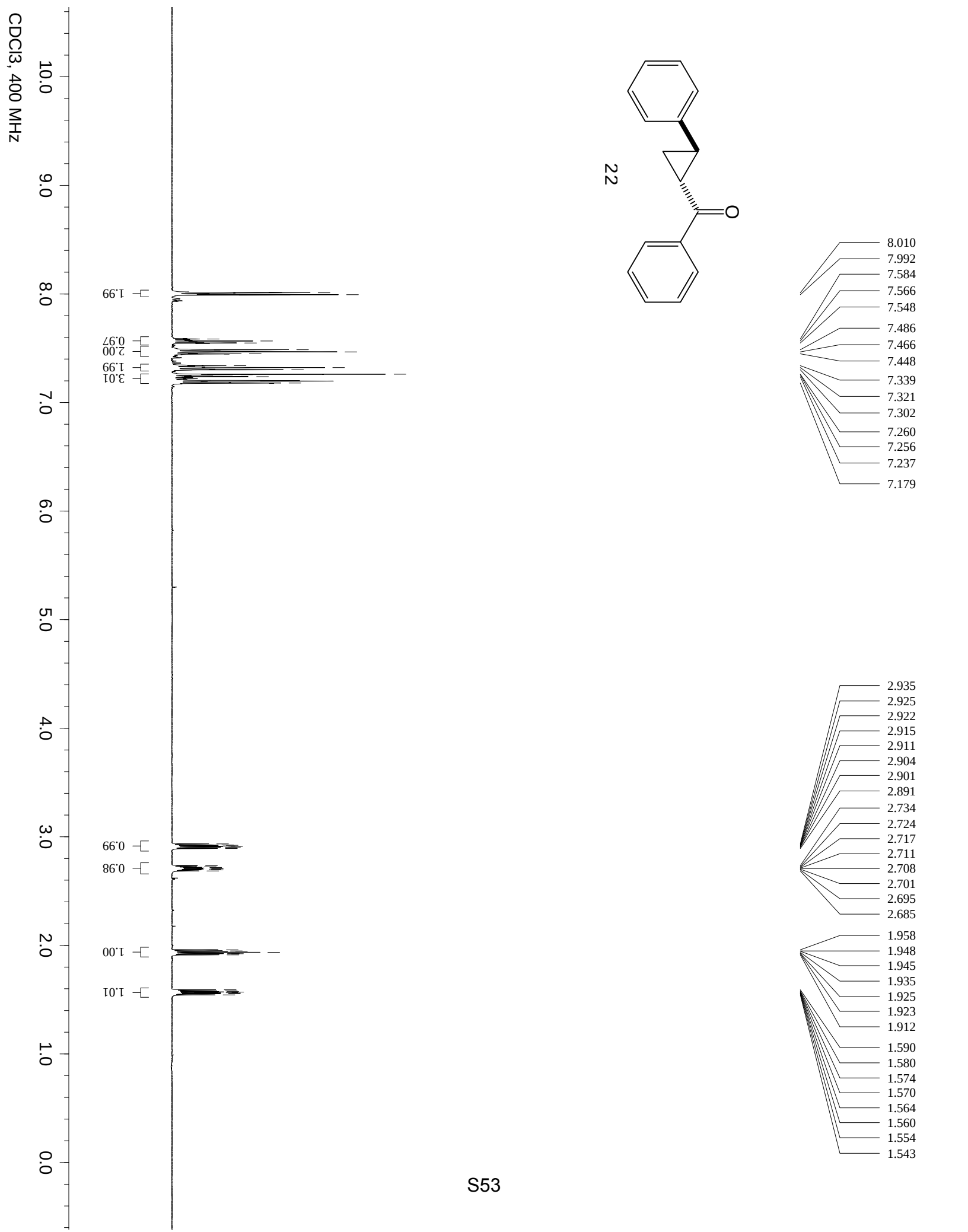


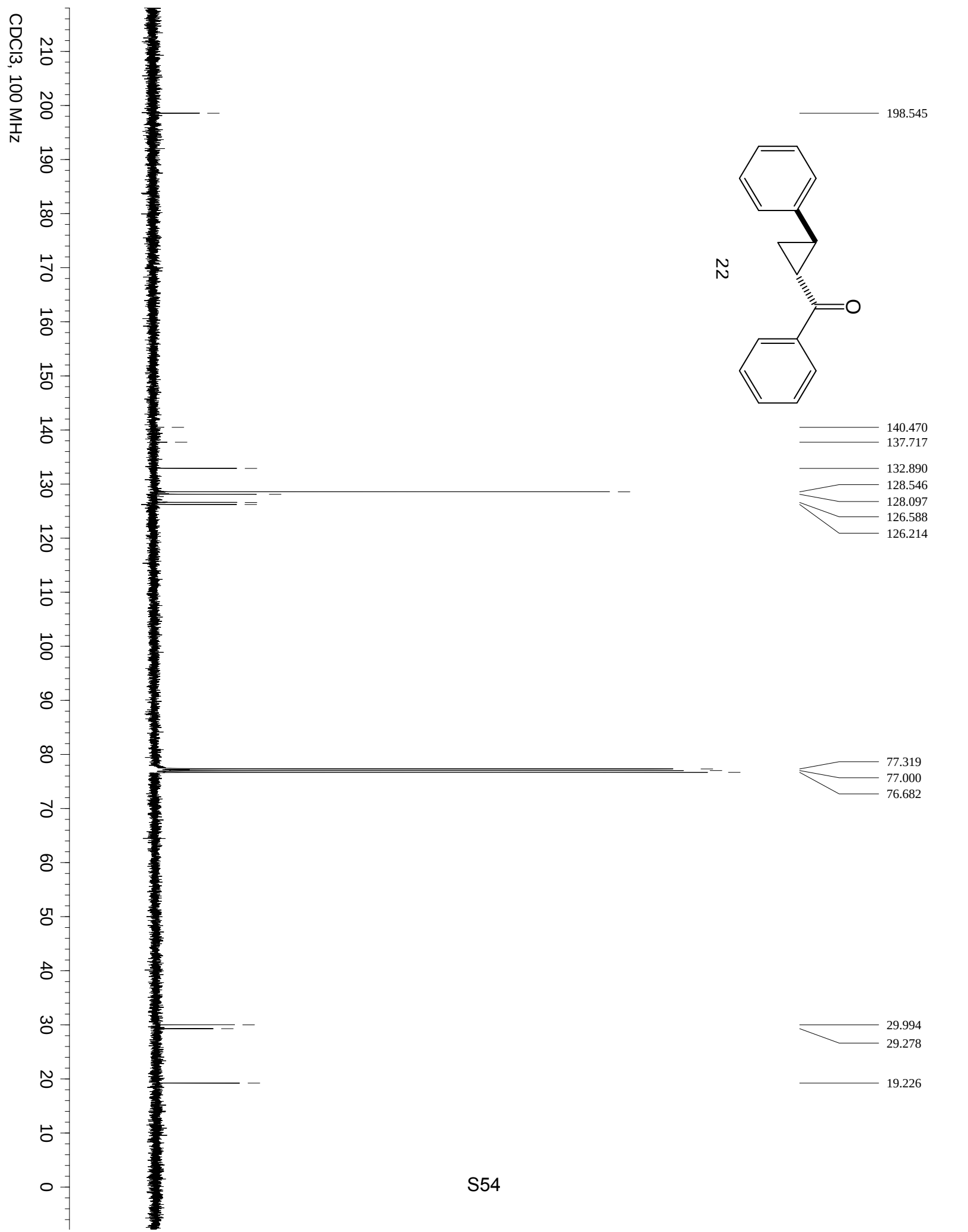
CDCl3, 400 MHz

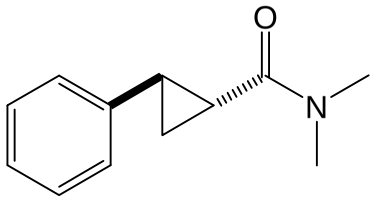


CDCl3, 400 MHz

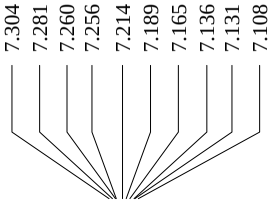

CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
21
O
O
172.546
140.504
128.397
126.294
126.052
80.541
77.318
77.000
76.683
28.160
25.728
25.283
17.043

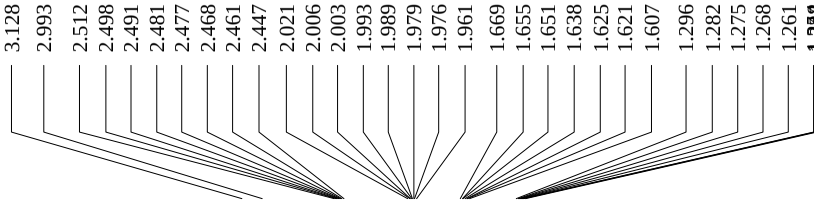

CDCl3, 400 MHz
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
1.99
0.97
2.00
1.99
3.01
0.99
0.98
1.00
1.01
22
O
8.010
7.992
7.584
7.566
7.548
7.486
7.466
7.448
7.339
7.321
7.302
7.260
7.256
7.237
7.179
2.935
2.925
2.922
2.915
2.911
2.904
2.901
2.891
2.734
2.724
2.717
2.711
2.708
2.701
2.695
2.685
1.958
1.948
1.945
1.935
1.925
1.923
1.912
1.590
1.580
1.574
1.570
1.564
1.560
1.554
1.543

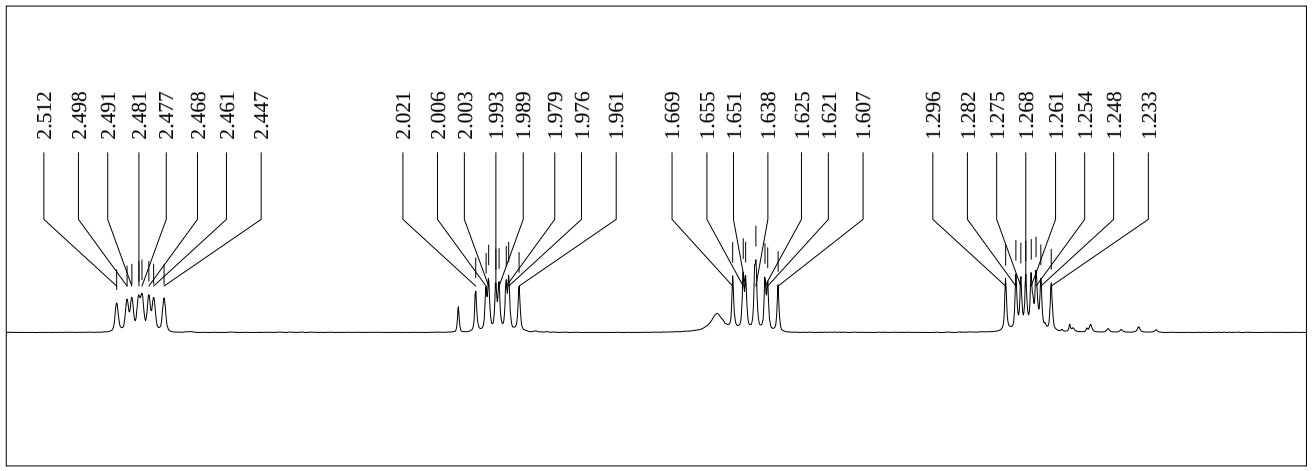

CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
198.545
140.470
137.717
132.890
128.546
128.097
126.588
126.214
77.319
77.000
76.682
29.994
29.278
19.226
22
O

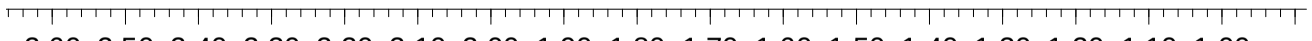


23



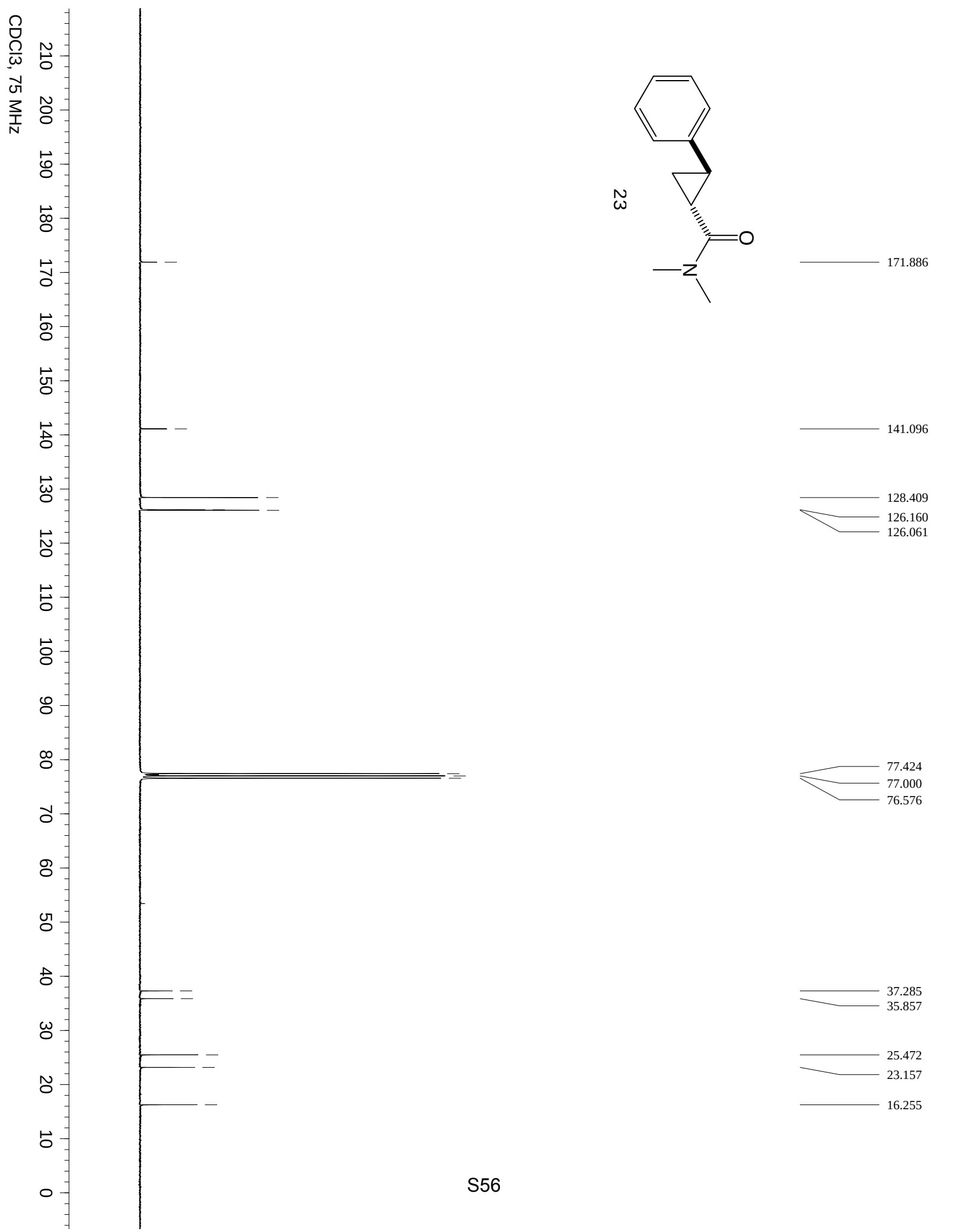


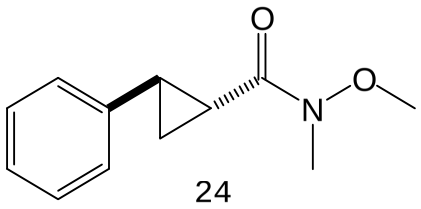




CDCl3, 300 MHz

CDCl3, 300 MHz

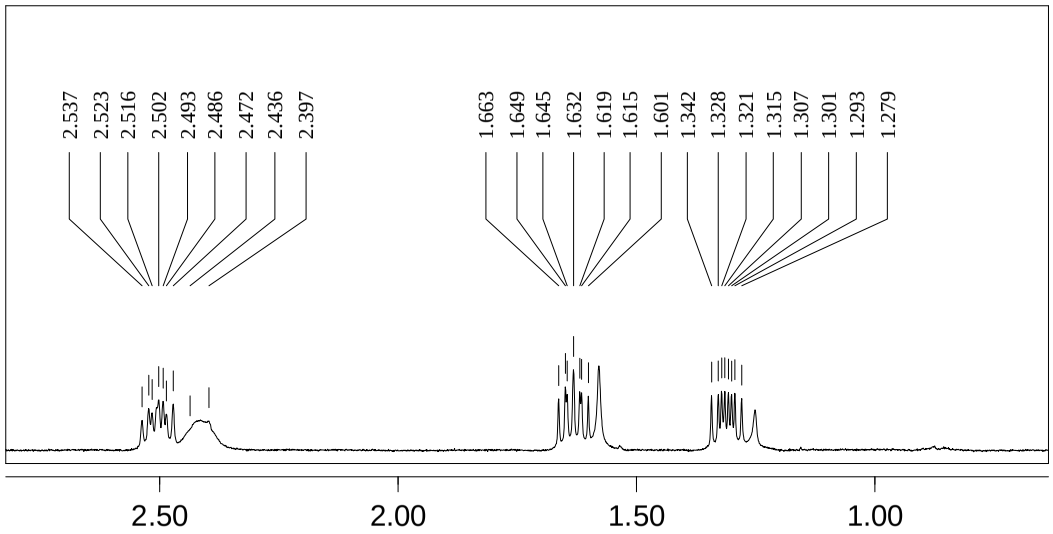

CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
23
O
N
171.886
141.096
128.409
126.160
126.061
77.424
77.000
76.576
37.285
35.857
25.472
23.157
16.255



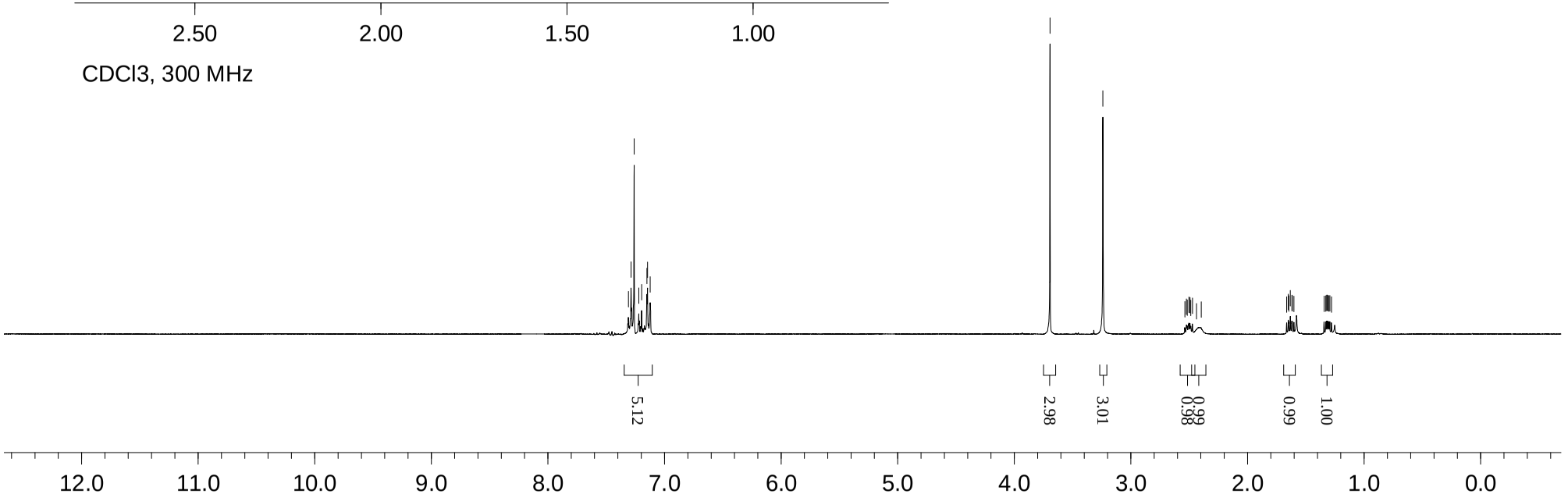
24

7.309 7.286 7.260 7.220 7.196 7.150 7.145 7.122

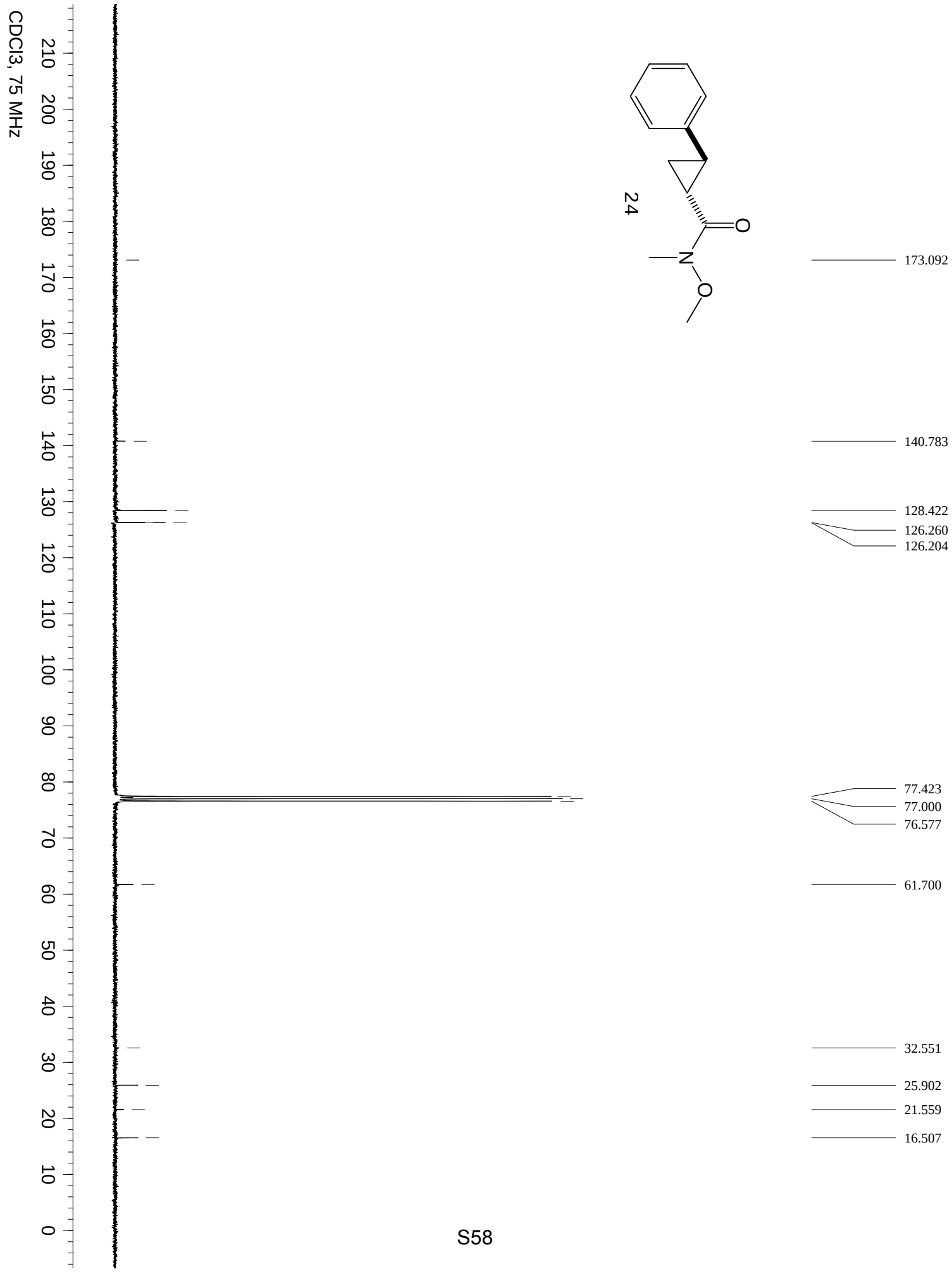
3.693 3.239 2.537 2.523 2.516 2.502 2.493 2.486 2.472 2.436 2.397 1.663 1.649 1.645 1.632 1.619 1.615 1.601 1.342 1.328 1.321 1.315 1.307 1.301 1.293 1.279



CDCl3, 300 MHz



CDCl3, 300 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
24
O
N
O
173.092
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128.422
126.260
126.204
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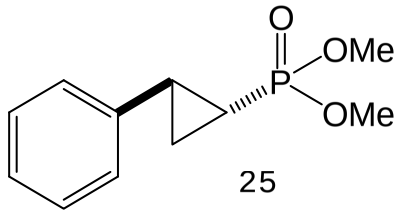
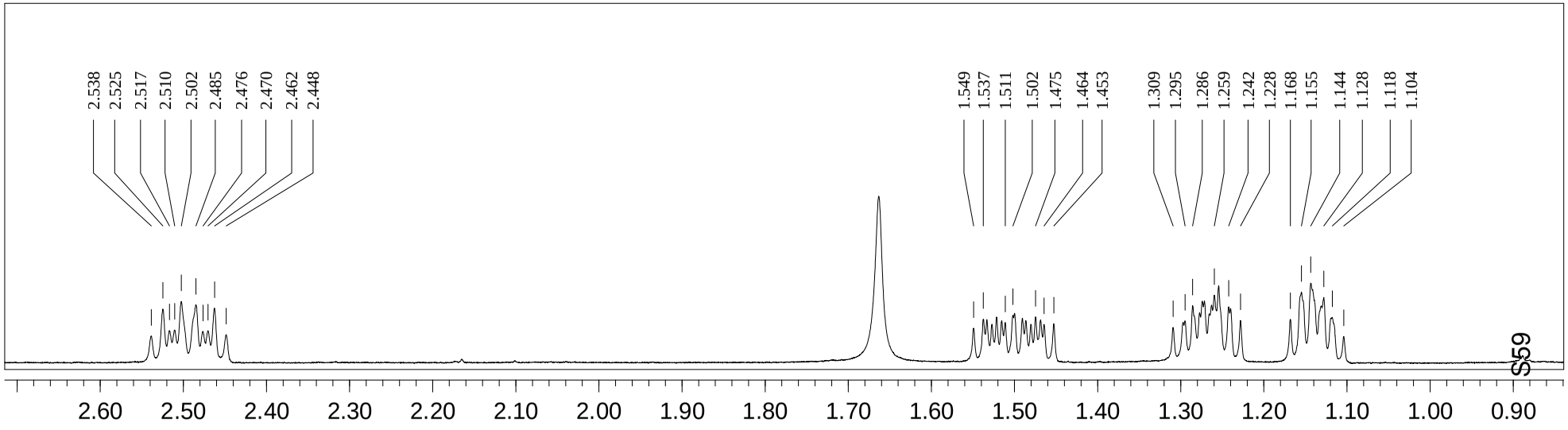
77.000
76.577
61.700
32.551
25.902
21.559
16.507



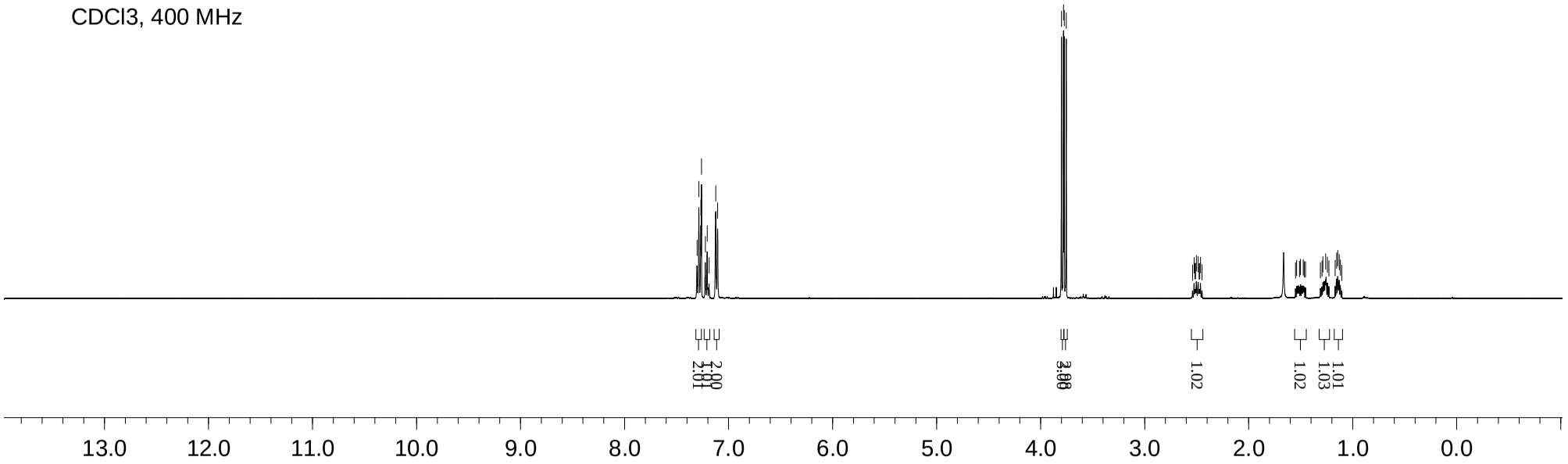
25

7.303 7.285 7.266 7.260 7.224 7.205 7.187 7.123 7.105

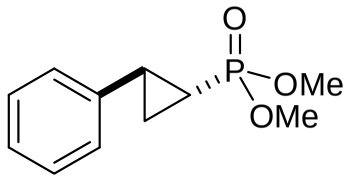
3.799 3.780 3.772 3.753 2.538 2.525 2.517 2.510 2.502 2.485 2.476 2.470 2.462 2.448 1.549 1.537 1.511 1.502 1.475 1.464 1.453 1.309 1.295 1.286 1.259 1.242 1.228 1.168 1.155 1.144



CDCl3, 400 MHz



CDCl3, 400 MHz

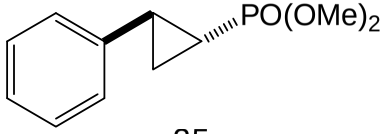


25

139.834
139.804
128.568
126.606
126.181
77.316
76.997
76.679
52.700
52.640
20.985
20.940
14.721
12.806
12.456
12.395

230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

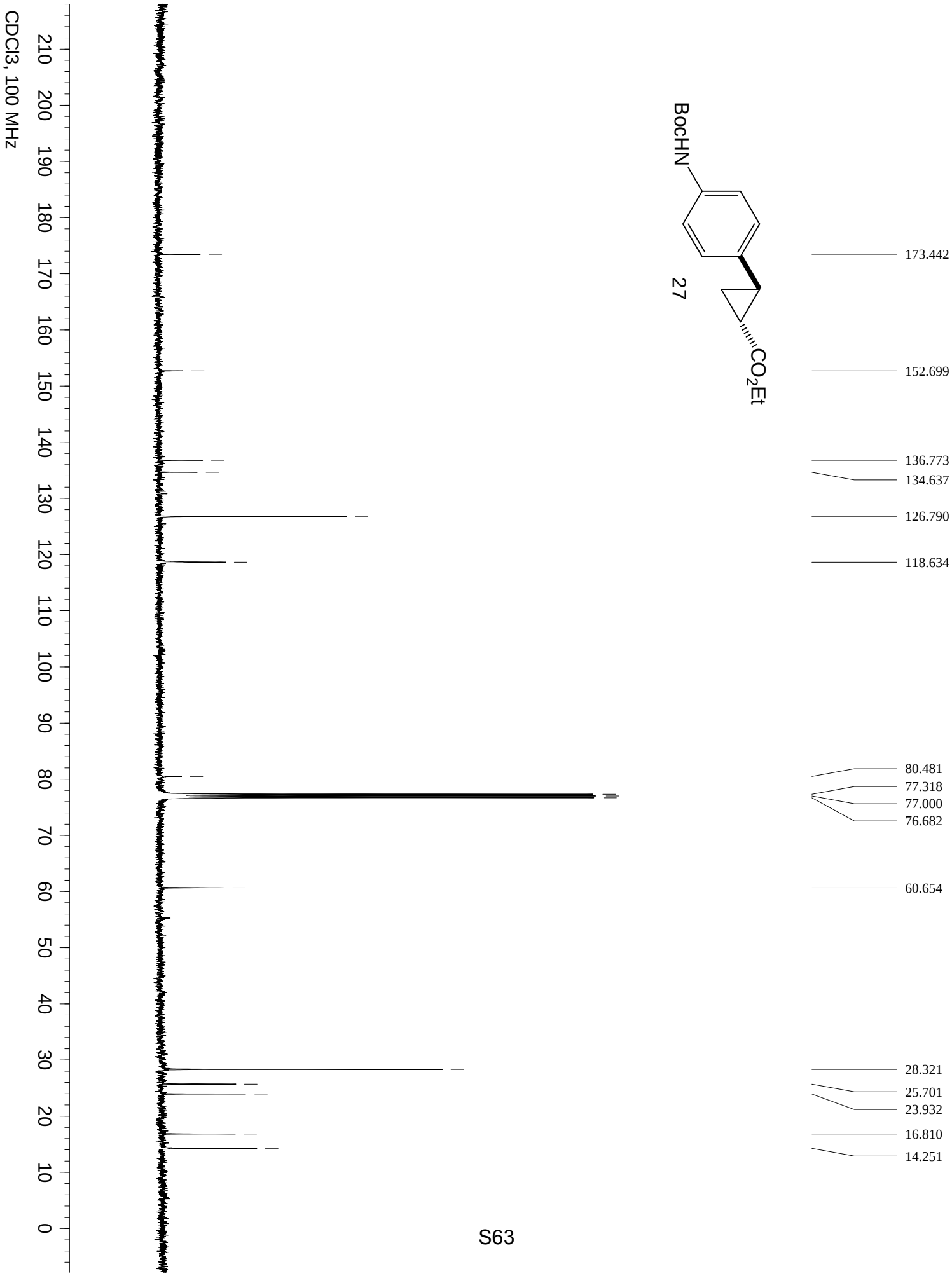
CDCl3, 100 MHz

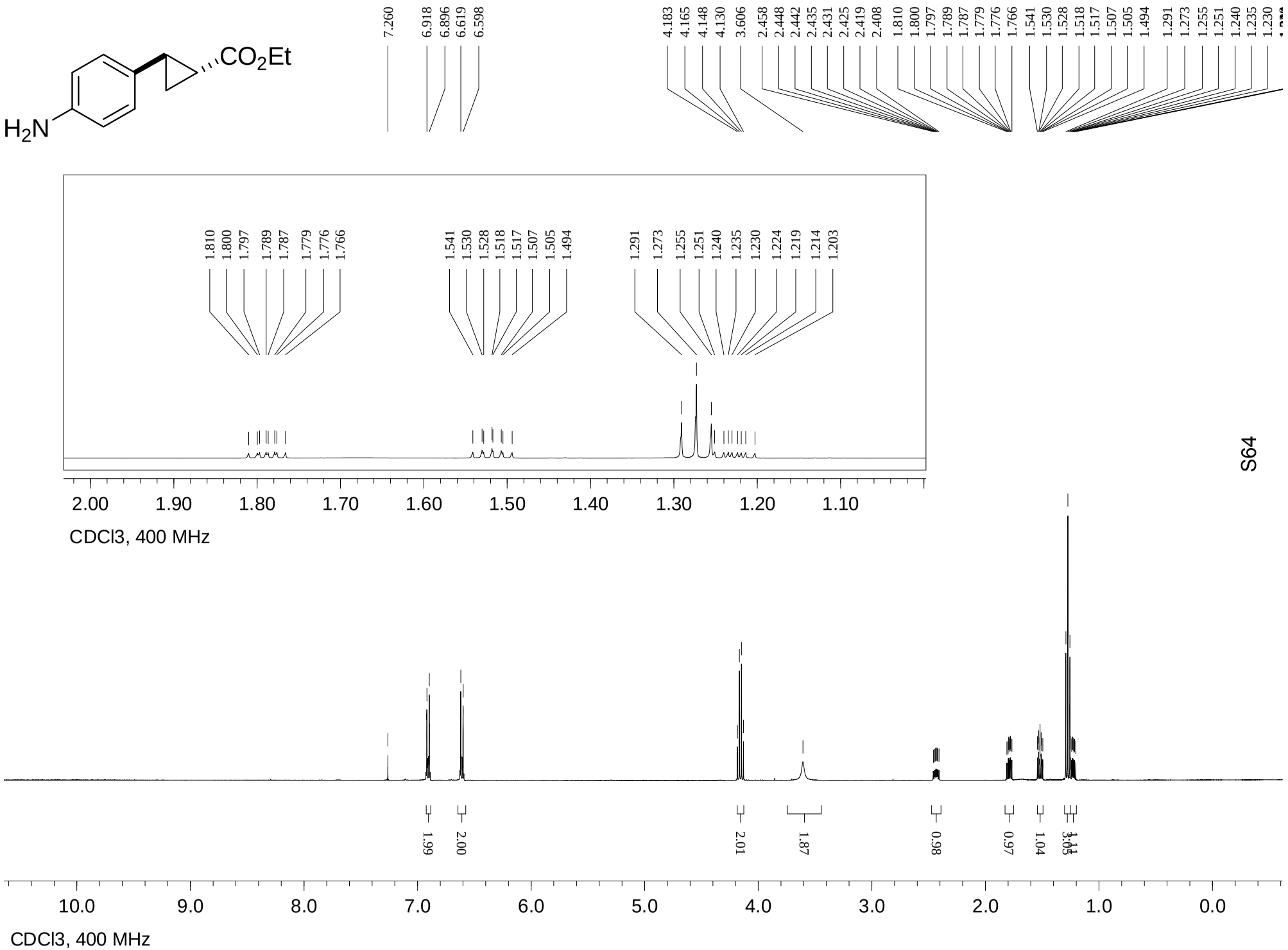

PO(OMe)2

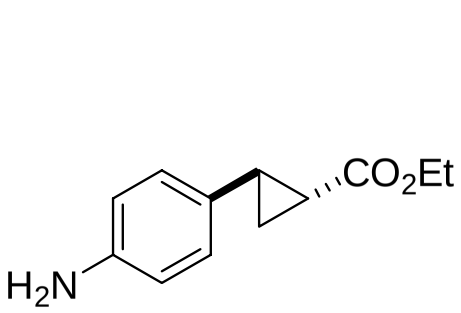
25

23.188
140 130 120 110 100 90 80 70 60 50 40 30 20 10 0 -10 -20 -30 -40 -50 -60 -70 -80 -90 -100 -110 -120 -130 -140
CDCl3, 121 MHz

CDCl3, 400 MHz


CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
BocHN
27
CO2Et
173.442
152.699
136.773
134.637
126.790
118.634
80.481
77.318
77.000
76.682
60.654
28.321
25.701
23.932
16.810
14.251

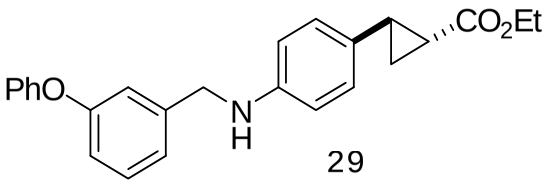

H_2N
CO_2Et
7.260
6.918
6.896
6.619
6.598
4.183
4.165
4.148
4.130
3.606
2.458
2.448
2.442
2.435
2.431
2.425
2.419
2.408
1.810
1.800
1.797
1.789
1.787
1.779
1.776
1.766
1.541
1.530
1.528
1.518
1.517
1.507
1.505
1.494
1.291
1.273
1.255
1.251
1.240
1.235
1.230
1.224
1.219
1.214
1.203
2.00
1.90
1.80
1.70
1.60
1.50
1.40
1.30
1.20
1.10
CDCl3, 400 MHz
1.99
2.00
2.01
1.87
0.98
0.97
1.04
3.05
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
CDCl3, 400 MHz



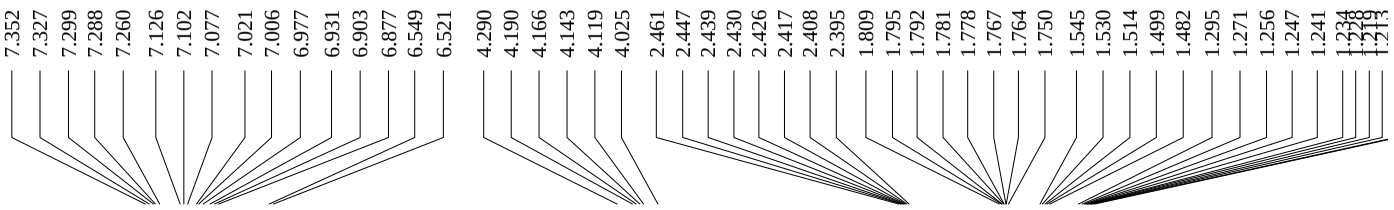
173.698
144.902
129.836
127.223
115.122
77.318
77.000
76.682
60.537
25.807
23.719
16.580
14.247

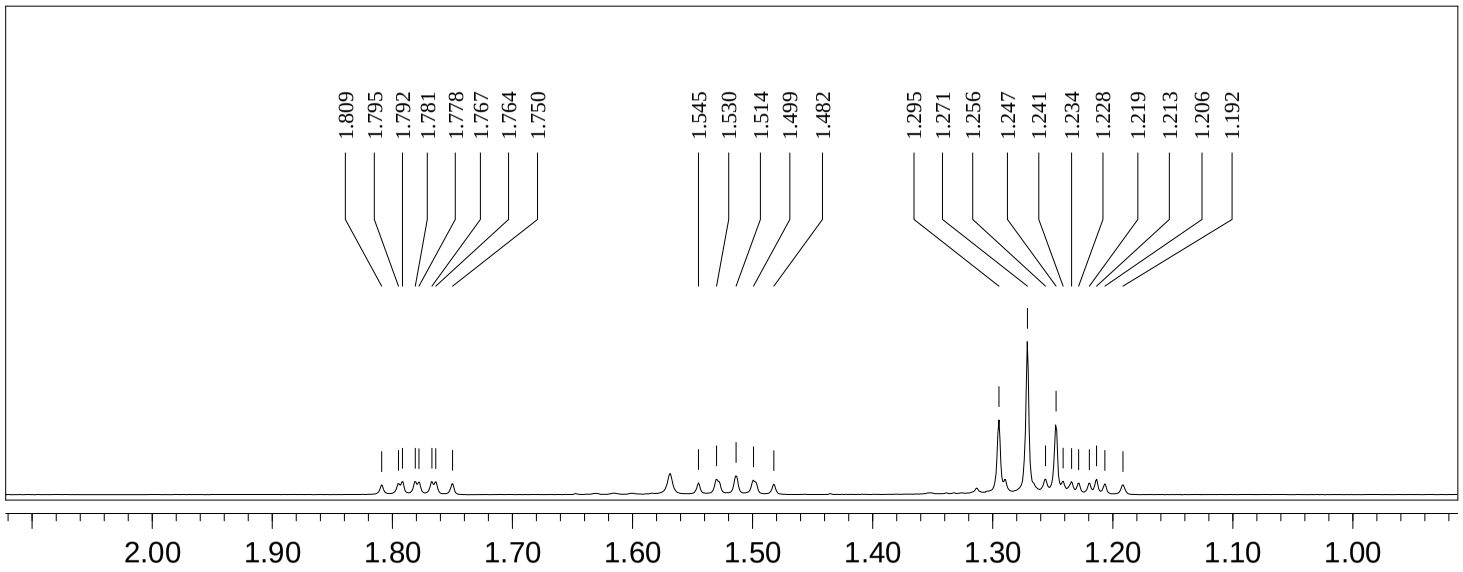
230 220 210 200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0

CDCl3, 100 MHz

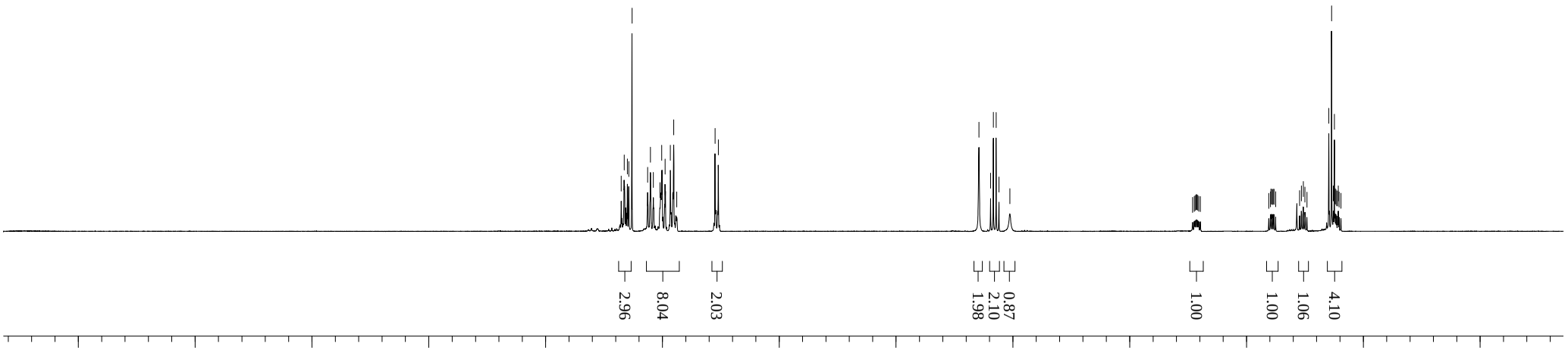


29

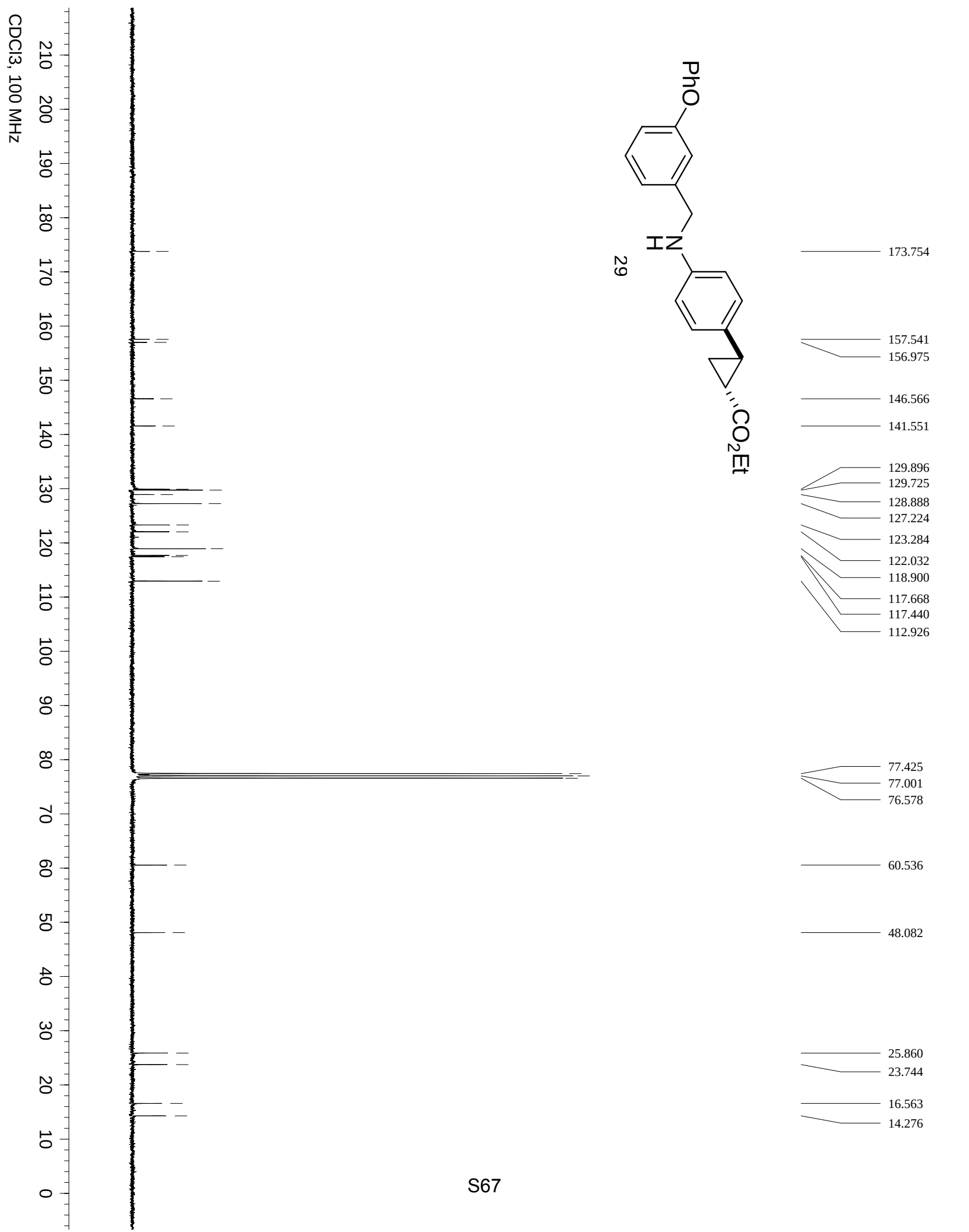


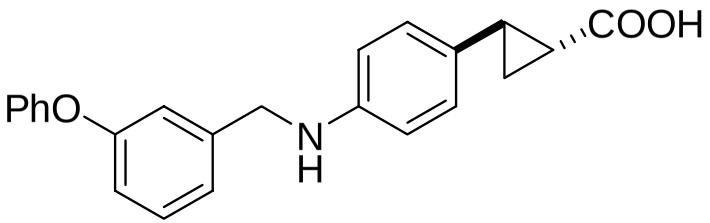


CDCl3, 300 MHz

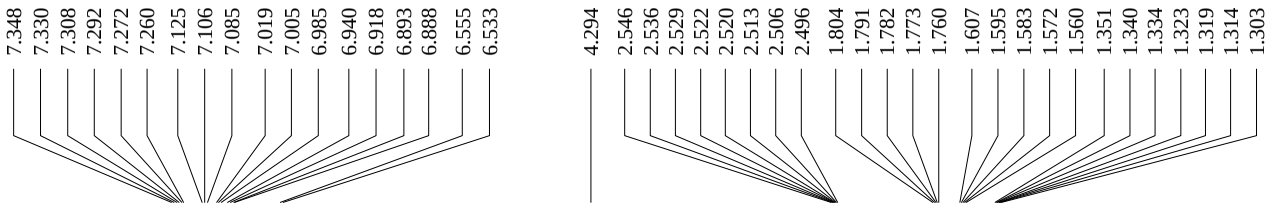


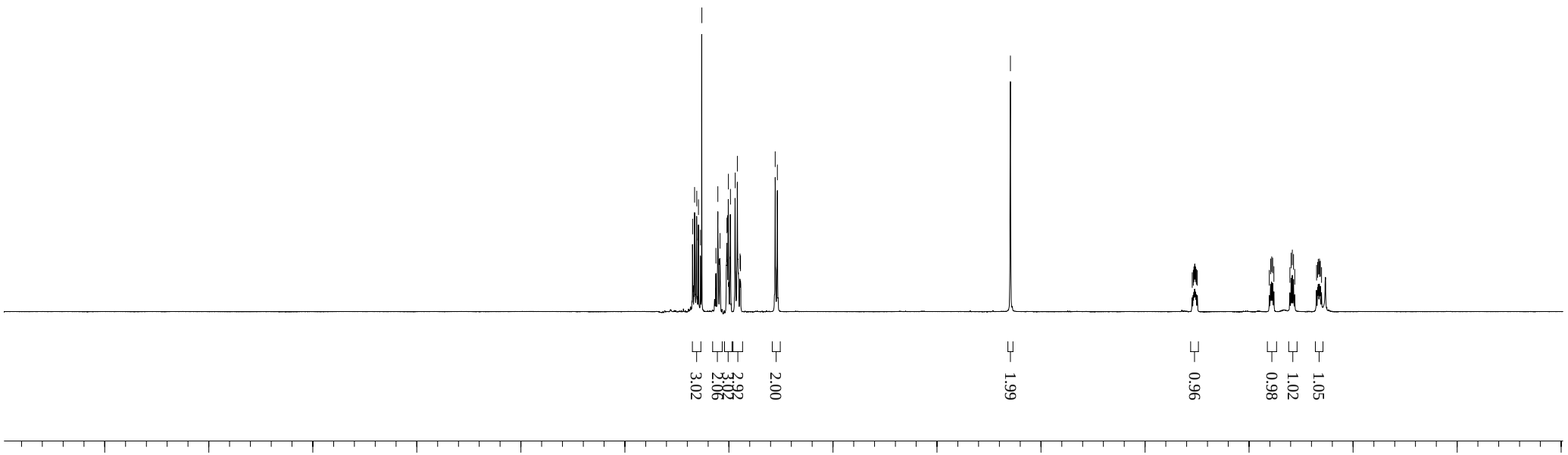
CDCl3, 300 MHz

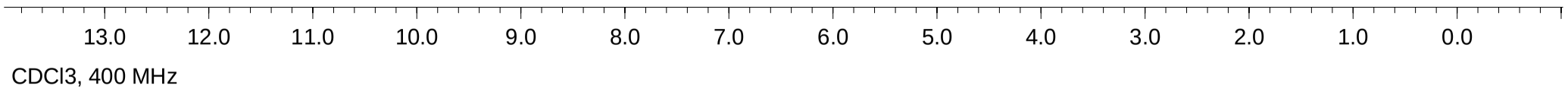

CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PhO
N
H
CO2Et
29
173.754
157.541
156.975
146.566
141.551
129.896
129.725
128.888
127.224
123.284
122.032
118.900
117.668
117.440
112.926
77.425
77.001
76.578
60.536
48.082
25.860
23.744
16.563
14.276



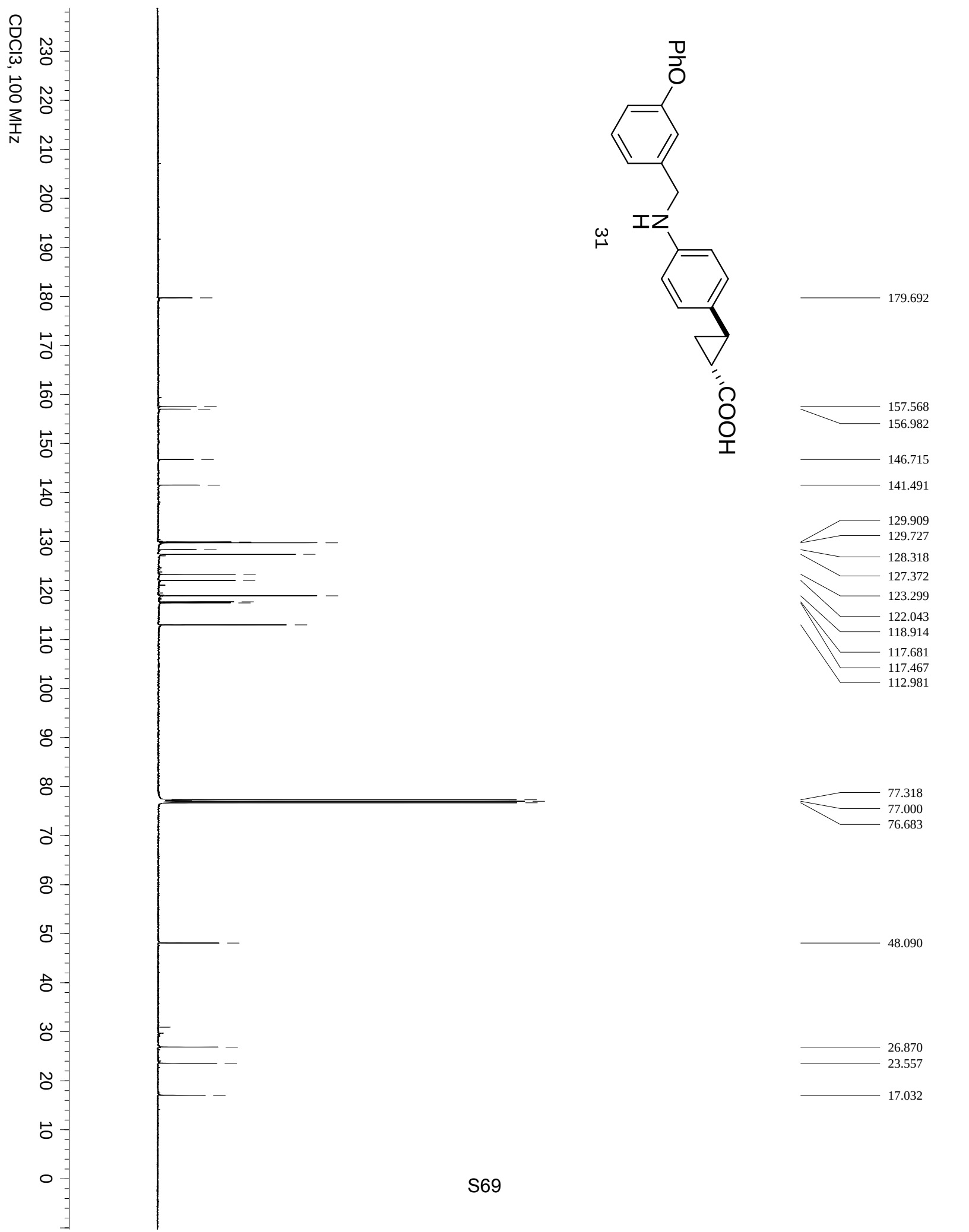
31

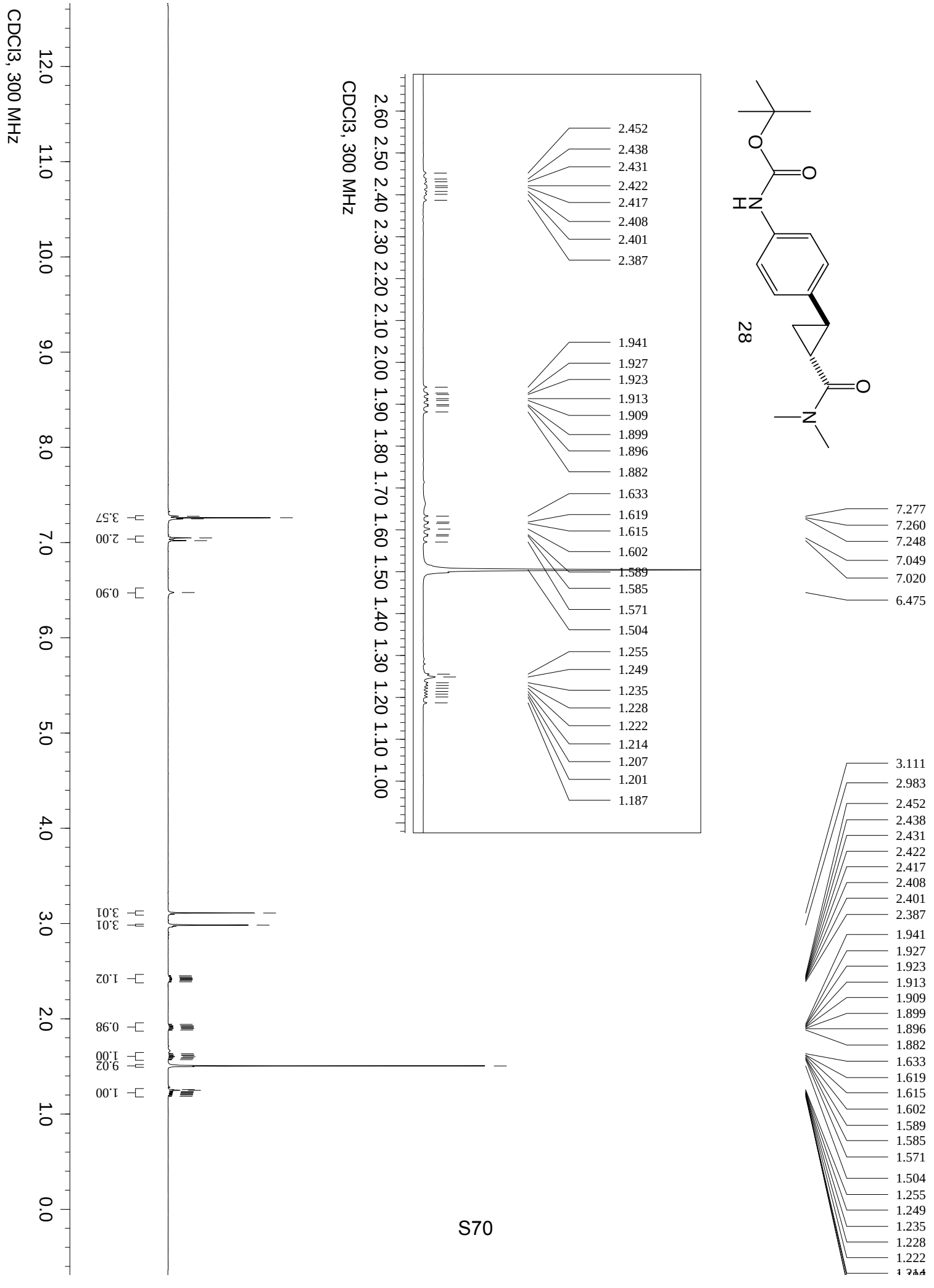


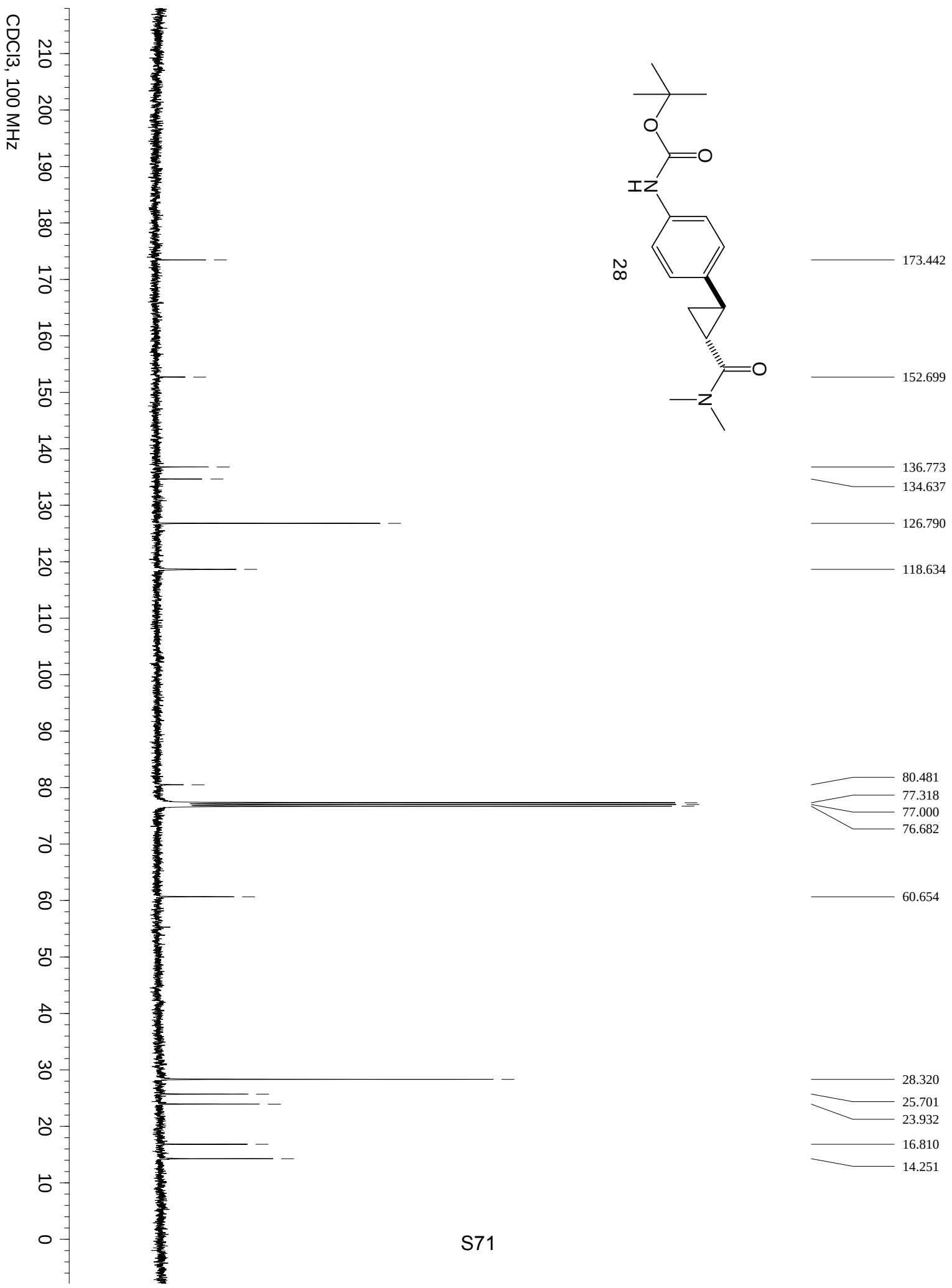


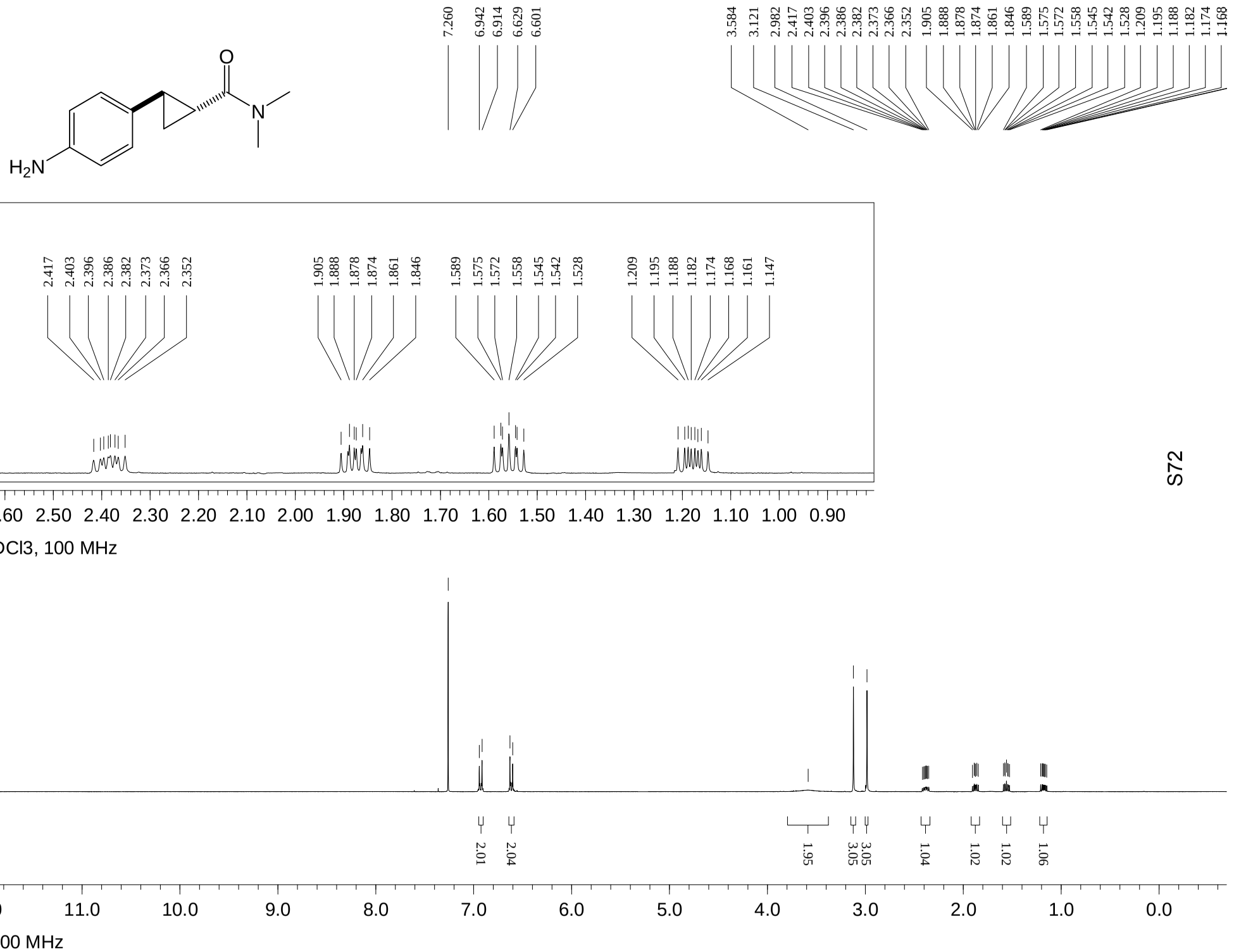


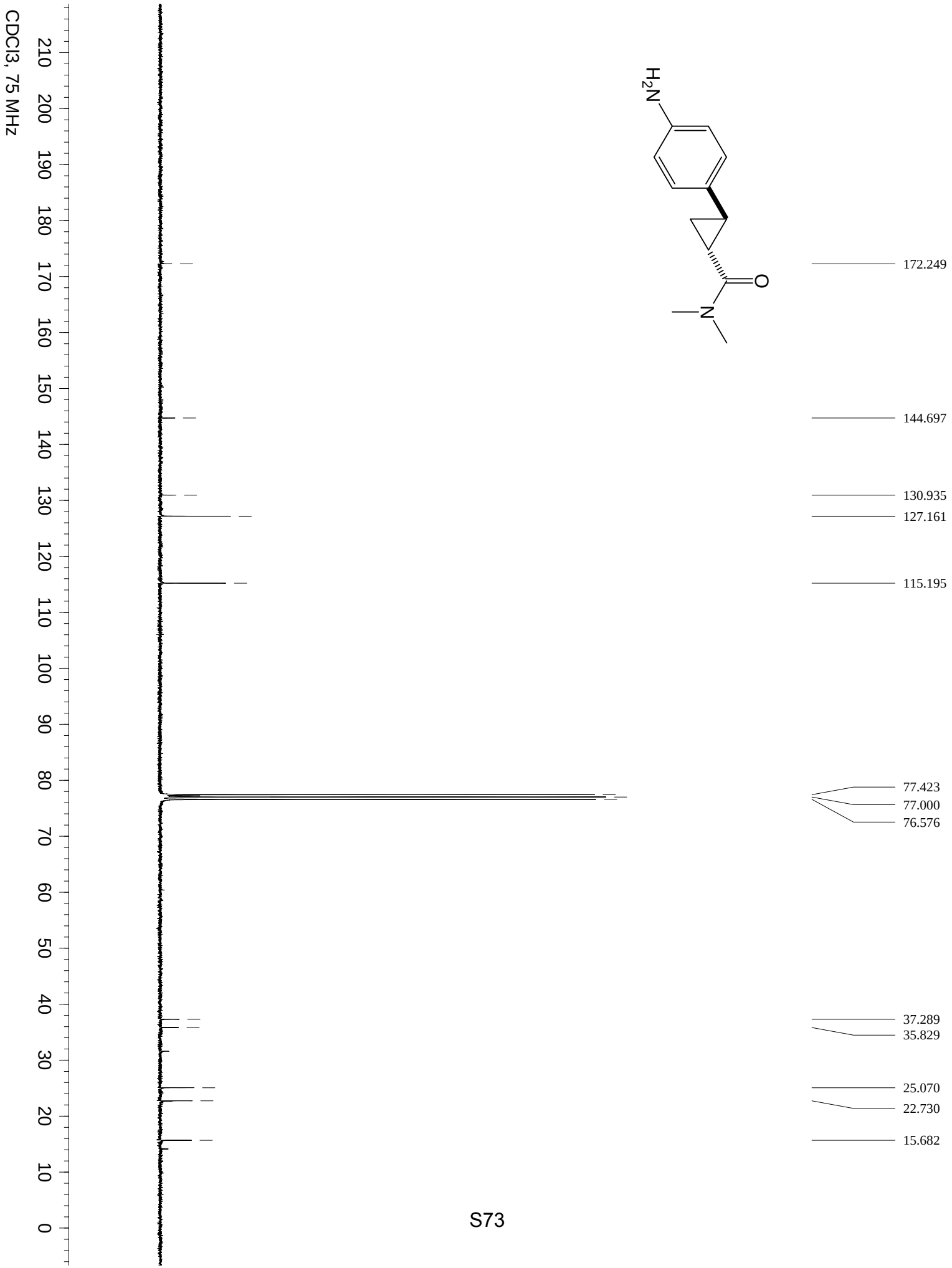
CDCl3, 400 MHz

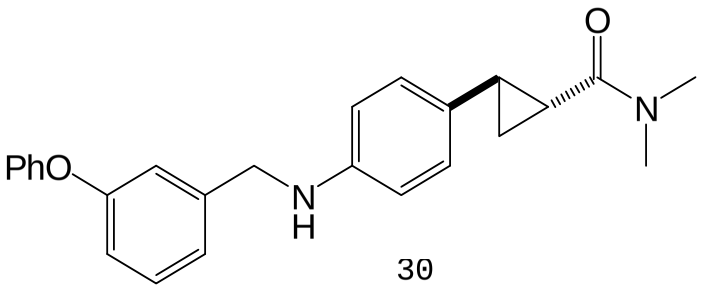

CDCl3, 100 MHz
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PhO
N
H
COOH
31
179.692
157.568
156.982
146.715
141.491
129.909
129.727
128.318
127.372
123.299
122.043
118.914
117.681
117.467
112.981
77.318
77.000
76.683
48.090
26.870
23.557
17.032


CDCl3, 300 MHz
12.0
11.0
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
3.57
2.00
0.90
3.01
3.01
1.02
0.98
1.00
9.02
1.00
CDCl3, 300 MHz
2.60 2.50 2.40 2.30 2.20 2.10 2.00 1.90 1.80 1.70 1.60 1.50 1.40 1.30 1.20 1.10 1.00
2.452
2.438
2.431
2.422
2.417
2.408
2.401
2.387
1.941
1.927
1.923
1.913
1.909
1.899
1.896
1.882
1.633
1.619
1.615
1.602
1.589
1.585
1.571
1.504
1.255
1.249
1.235
1.228
1.222
1.214
1.207
1.201
1.187
28
7.277
7.260
7.248
7.049
7.020
6.475
3.111
2.983
2.452
2.438
2.431
2.422
2.417
2.408
2.401
2.387
1.941
1.927
1.923
1.913
1.909
1.899
1.896
1.882
1.633
1.619
1.615
1.602
1.589
1.585
1.571
1.504
1.255
1.249
1.235
1.228
1.222


CDCl3, 100 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
28
O
O
H
N
O
N
173.442
152.699
136.773
134.637
126.790
118.634
80.481
77.318
77.000
76.682
60.654
28.320
25.701
23.932
16.810
14.251

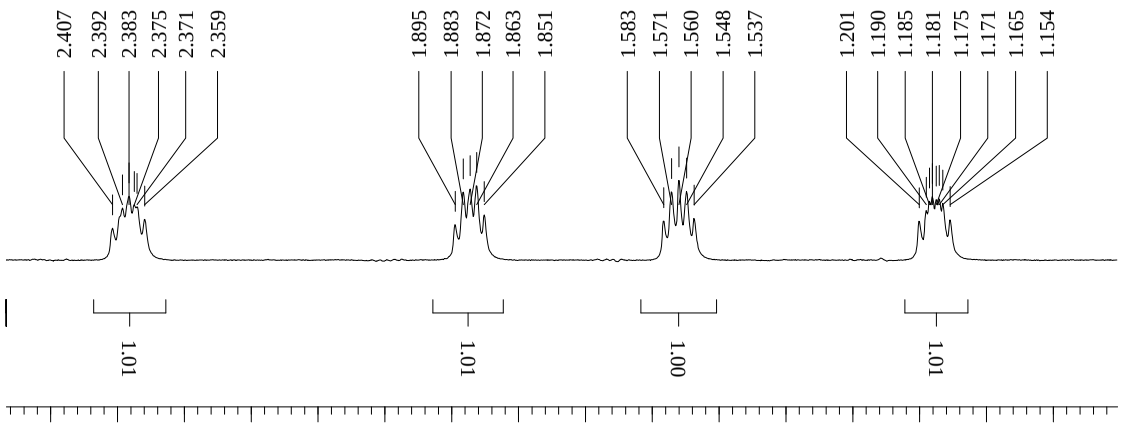

O
N
H_2N
7.260
6.942
6.914
6.629
6.601
3.584
3.121
2.982
2.417
2.403
2.396
2.386
2.382
2.373
2.366
2.352
1.905
1.888
1.878
1.874
1.861
1.846
1.589
1.575
1.572
1.558
1.545
1.542
1.528
1.209
1.195
1.188
1.182
1.174
1.168
1.161
1.147
2.60 2.50 2.40 2.30 2.20 2.10 2.00 1.90 1.80 1.70 1.60 1.50 1.40 1.30 1.20 1.10 1.00 0.90
CDCl3, 100 MHz
2.01
2.04
1.95
3.05
3.05
1.04
1.02
1.02
1.06
12.0 11.0 10.0 9.0 8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0 0.0
CDCl3, 300 MHz


CDCl3, 75 MHz
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
H2N
O
N
172.249
144.697
130.935
127.161
115.195
77.423
77.000
76.576
37.289
35.829
25.070
22.730
15.682

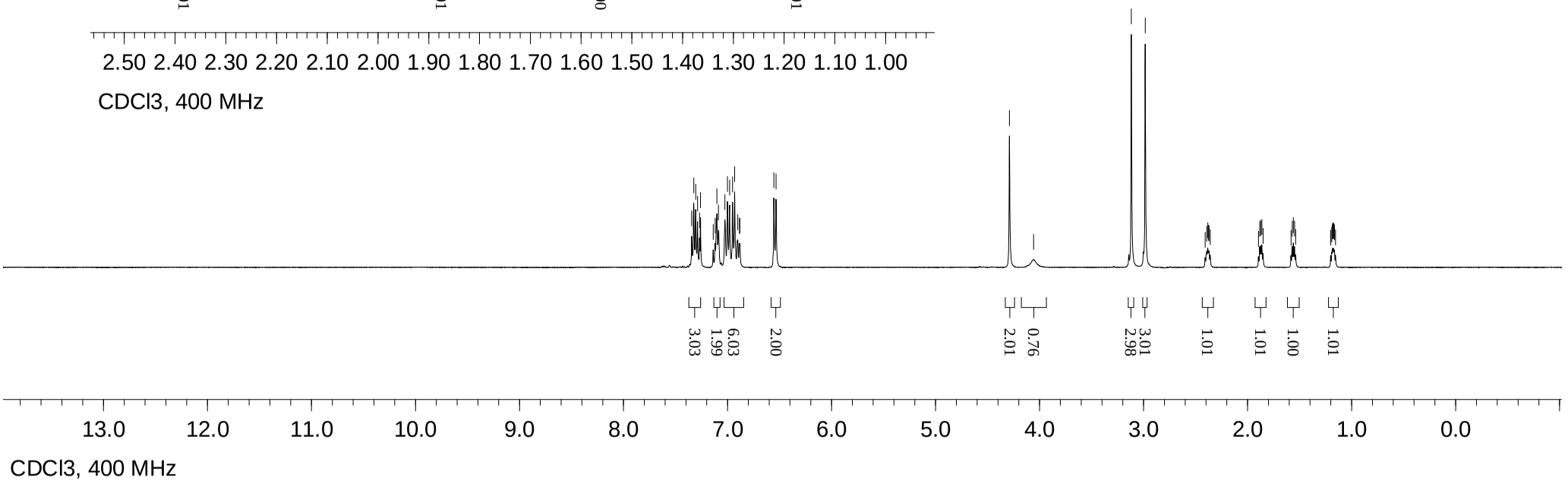


30

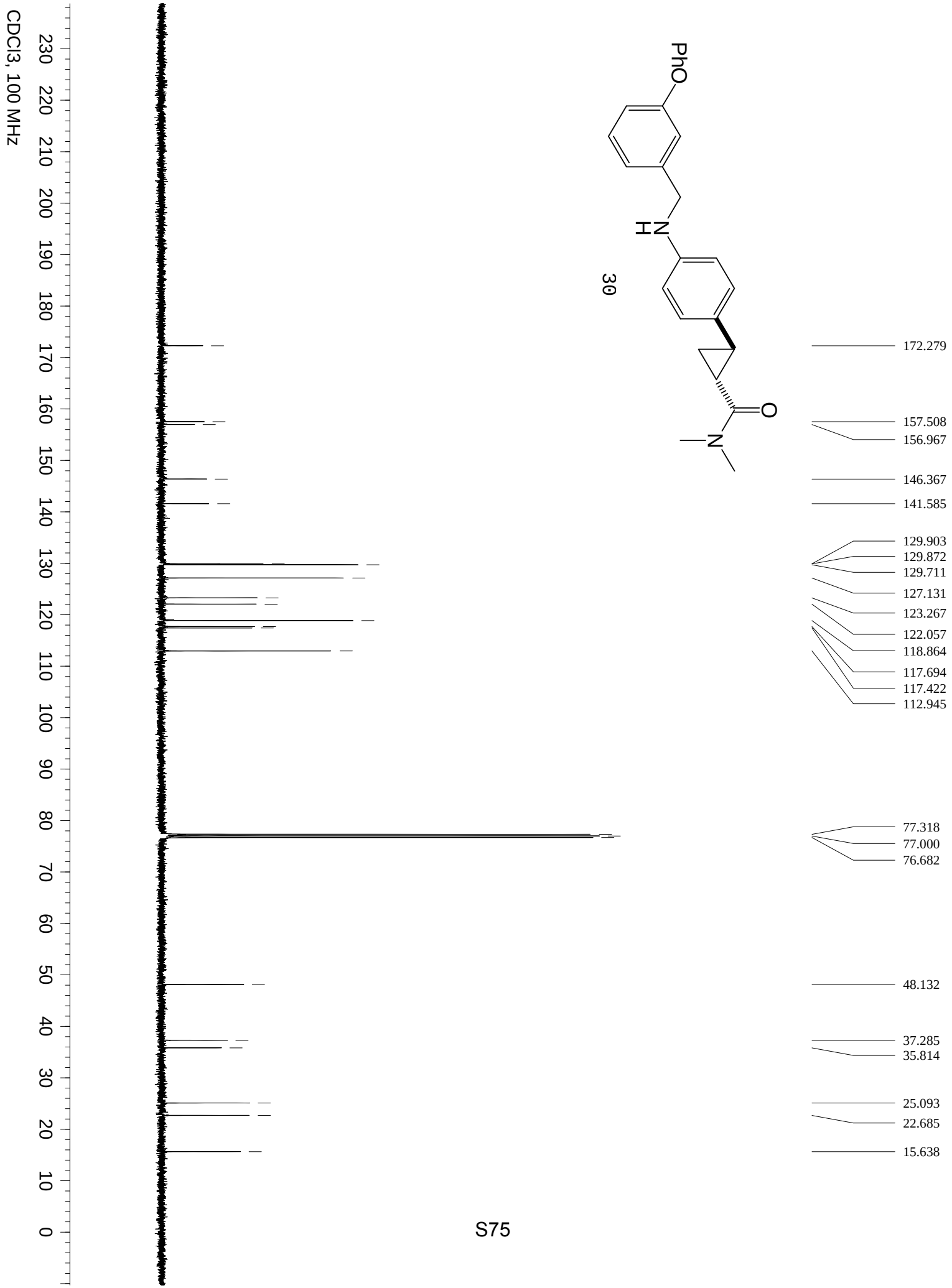
7.344 7.324 7.306 7.288 7.269 7.260 7.137 7.118 7.102 7.086 7.024 7.000 6.980 6.952 6.931 6.901 6.886 6.881 6.554 6.533 4.289 4.057 3.118 2.984 2.407 2.392 2.383 2.375 2.371 2.359 1.895 1.883 1.872 1.863 1.851 1.583 1.571 1.560 1.548 1.537 1.201 1.190 1.185 1.181 1.175 1.171 1.165 1.154



CDCl3, 400 MHz



CDCl3, 400 MHz


CDCl3, 100 MHz
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
PhO
HN
O
N
30
172.279
157.508
156.967
146.367
141.585
129.903
129.872
129.711
127.131
123.267
122.057
118.864
117.694
117.422
112.945
77.318
77.000
76.682
48.132
37.285
35.814
25.093
22.685
15.638