Luminescent Crown Ether Amino Acids - Selective Binding to *N*-terminal Lysine in Peptides

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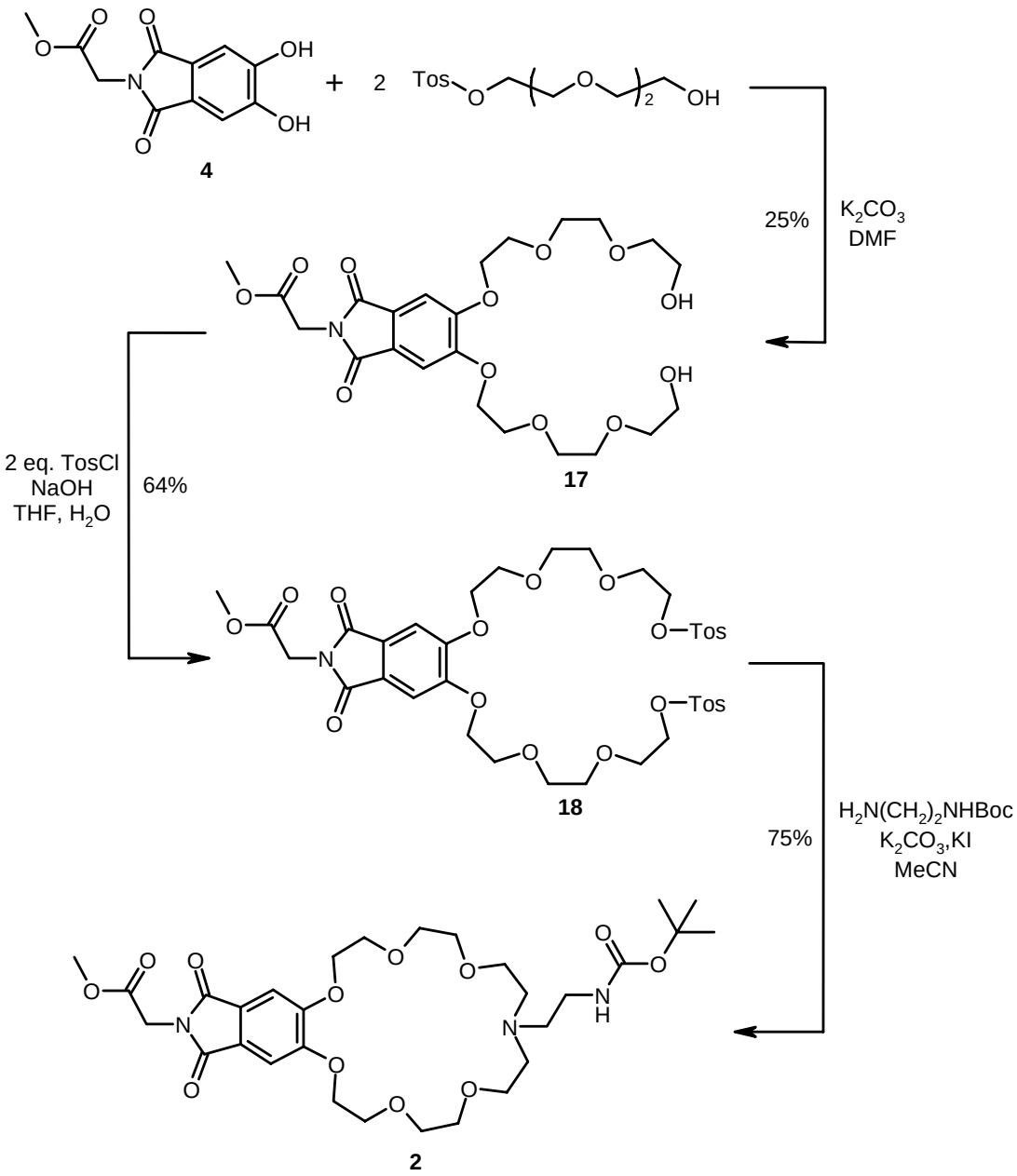
SUPPORTING INFORMATION

1) Experimental procedures

Tripeptides **10 – 12** were synthesized using standard peptide coupling procedures. Compounds **3**[1] and **13**[2] were synthesized according to published procedures.

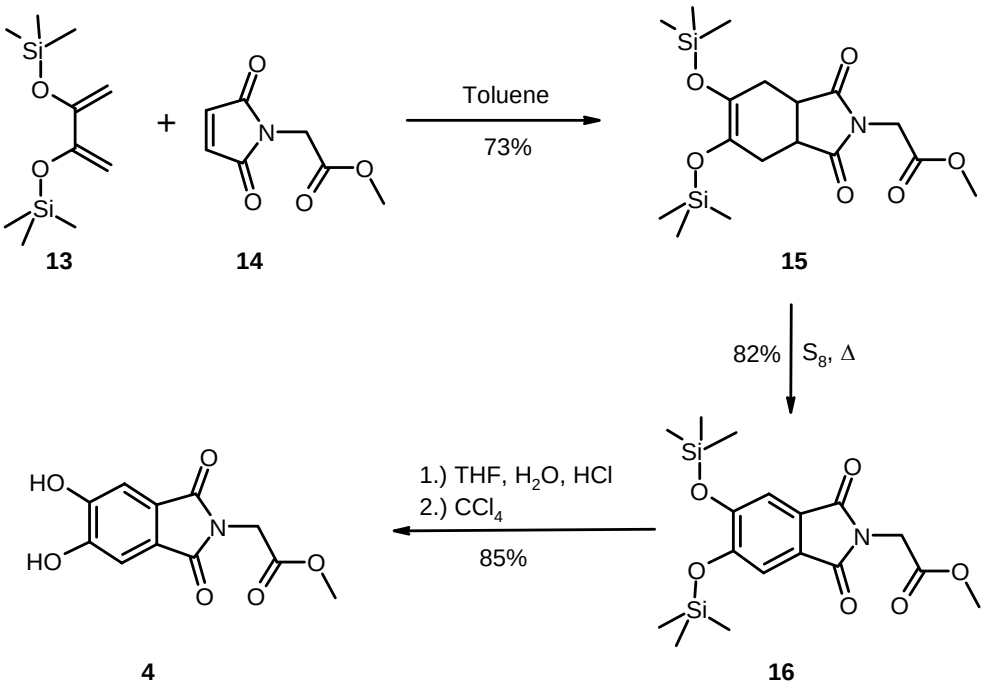
Synthesis of crown ether **2**:



[1] Drager, A. S.; O'Brien, D. F. *J. Org. Chem.* **2000**, *65*, 2257 - 2260.

[2] Murai, S.; Ryu, I.; Kadono, Y.; Katayama, H.; Kondo, K.; Sonoda, N. *Chem. Lett.* **1977**, 1219 - 1222.

Synthesis of phthalimide **4**:



14-(2-tert-Butoxycarbonylamino-ethyl)-6,7,9,10,13,14,15,16,18,19,21,22-dodecahydro-12H-5,8,11,17,20,23-hexaoxa-14-aza-benzocycloheneicosen-2,3-dicarbonic acid dimethyl ester (**1**): Compound **6** (1.49 g, 1.87 mmol) is dissolved in 30 ml of acetonitile and 0.2 ml of H_2O in ambient atmosphere. *N-Boc* ethylene diamine (300 mg, 1.87 mmol), 450 mg (2.70 mmol) KI and 2.50 g (18.0 mmol) K_2CO_3 are added successively and the mixture is refluxed overnight. After cooling to room temperature, the mixture is filtered over celite and the residue washed with acetonitrile and dichloromethane. The solvent is evaporated and the crude product purified by column chromatography (silica gel, ethyl acetate/ EtOH 3/1, R_f = 0.1). A yellowish solid is obtained (900 mg, 1.46 mmol, 79%).

Mp.: 52 – 54°C; **^{1}H- NMR** (400 MHz, $CDCl_3$): δ = 1.22 (s, 9 H, 17), 2.69 (bs, 2 H, 12), 2.75 (bs, 4 H, 11), 3.16 – 3.23 (m, 2 H, 13), 3.54 – 3.58 (m, 4 H, 10), 3.63 – 3.66 (m, 4 H, 9), 3.73 – 3.76 (m, 4 H, 9), 3.81 (s, 6 H, 1), 3.90 – 3.93 (m, 4 H, 8), 4.19 – 4.22 (m, 4 H, 7), 5.45 – 5.50 (bs, 1 H, 14), 7.19 (s, 2 H, 4); **^{13}C- NMR** (100 MHz, $CDCl_3$): δ = 28.4 (+, 3 C, 17), 39.2 (-, 1 C, 13), 52.6 (+, 2 C, 1), 54.6 (-, 1 C, 12), 54.6 (-, 2 C, 11), 68.1 (-, 2 C, 10), 69.1 (-, 2 C, 6), 69.3 (-, 2 C, 7), 70.1 (-, 4 C, 8, 9), 79.2 (C_{quat}, 1 C, 16), 114.5 (+, 2 C, 4), 126.1 (C_{quat}, 2 C, 3), 150.3 (C_{quat}, 2 C, 5), 156.5 (C_{quat}, 1 C, 15), 167.5 (C_{quat}, 2 C, 2); **IR** (KBr): $\bar{\nu}$ (cm^{-1}) = 3414 (bm), 2947 (m), 2878 (m), 1716 (s), 1600 (m), 1520 (m), 1436 (m), 1352 (m), 1291 (s), 1252 (m), 1181 (m), 1130 (m), 1055 (m), 977 (m), 945 (m), 781 (m); **MS** (ESI-MS,

CH_2Cl_2/MeOH + 10 mmol/l NH_4OAc): e/z (%) = 615 (100, MH^+), 559 (23, MH^+ - C_4H_8); **UV** (MeOH): λ (ε) = 268 (7600), 224 (29500); **HRMS** (PI-LSIMS, MeOH/Glycerin): calc. for $C_{29}H_{46}N_2O_{12}*H^+$: 615.3129, found: 615.3114

[11-(2-tert-Butoxycarbonylamino-ethyl)-24,26-dioxo-2,5,8,14,17,20-hexaoxa-11,25-diaza-tricyclo[19.7.0.0^{23,27}]octacosa-1(28),21,23(27)-trien-25-yl]-acetic acid methyl ester (**2**): Compound **18** (256 mg, 0.31 mg) and 50 mg (0.31 mmol) *N-Boc* ethylene diamine are dissolved in 6 ml of acetonitrile. The mixture is refluxed overnight after addition of 75 mg (0.45 mmol) KI and 430 mg (3.1 mmol) K_2CO_3. Filtration of the cooled mixture, washing with acetonitrile and dichloromethane and removal of the solvent through distillation results in the crude product, which is purified by column chromatography (silica gel, dichloromethane/EtOH 15/1). A yellowish solid is obtained (150 mg, 0.23 mmol, 75%).
Mp.: 90 – 92°C; **^{1}H- NMR** (300 MHz, $CDCl_3$): δ = 1.3 (s, 9 H), 2.63 – 2.93 (m, 6 H), 3.19 (bs, 2 H), 3.58 – 3.65 (m, 8 H), 3.69 (s, 3 H), 3.71 – 3.73 (m, 4 H), 3.88 – 3.90 (m, 4 H), 4.18 – 4.21 (m, 4 H), 4.33 (s, 2 H), 5.52 (bs, 1 H), 7.25 (s, 2 H); **^{13}C- NMR** (75 MHz, $CDCl_3$): δ = 27.4 (+, 3 C), 37.8 (-, 1 C), 51.6 (+, 1 C), 52.9 (-, 1 C), 53.5 (-, 2 C), 57.3 (-, 1 C), 67.6 (-, 2 C), 68.3 (-, 2 C), 68.5 (-, 2 C), 69.5 (-, 2 C), 70.1 (-, 2 C), 78.1 (C_{quat}, 1 C), 106.2 (+, 2 C), 124.5 (C_{quat}, 2 C), 152.6 (C_{quat}, 2 C), 155.2 (C_{quat}, 1 C), 166.5 (C_{quat}, 2 C), 167.0 (C_{quat}, 1 C); **IR** (KBr): (cm^{-1}) = 3379 (bm), 3111 (w), 3058 (w), 2932 (m), 2881 (m), 1749 (s), 1705 (s), 1597 (m), 1504 (m), 1412 (s), 1304 (s), 1219 (s), 1113 (s), 1045 (m), 943 (m), 750 (m); **MS** (ESI-MS, CH_2Cl_2/MeOH + 10 mmol/l NH_4OAc): e/z (%) = 640 (100, MH^+), 584 (23, MH^+ - C_4H_8); **UV** (MeOH): λ (ε) = 343 (1800), 297 (1800), 247 (41700)

(5,6-Dihydroxy-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-acetic acid methyl ester (**4**): Compound **16** (4.10 g, 10.4 mmol) is added to a mixture of 30 ml of H_2O, 10 ml of THF and 5 ml 1 N HCl. The resulting 2-phase system is stirred thoroughly overnight at room temperature. The precipitate is collected by filtration and the remaining solution is extracted three times with ethyl acetate. The organic phases are combined, dried over $MgSO_4$ and the solvent evaporated on a rotary evaporator. The remaining solid is combined with the product collected by filtration and suspended in 100 ml CCl_4. After subjecting the suspension to ultrasound for 30 min., traces of sulfur in the raw product are dissolved, allowing the pure product to be obtained by filtration. After drying the product, 2.2 g (8.76 mmol, 85%) are obtained.
Mp.: 223 – 225°C; **^{1}H- NMR** (300 MHz, DMSO-d_6): δ = 3.63 (s, 3H), 4.28 (s, 2H), 7.13 (s, 2H), 10.42 (bs, 2H); **^{13}C- NMR** (75 MHz, DMSO-d_6): δ = 38.4 (-, 1C), 52.2 (+, 1C), 109.8 (+,

2C), 123.4 (C_{quat}, 2C), 151.2 (C_{quat}, 2C), 167.1 (C_{quat}, 2C), 168.2 (C_{quat}, 1C); **IR** (KBr): $\bar{\nu}$ (cm^{-1}) = 3352 (bs), 3050 (w), 2963 (w), 1740 (s), 1699 (s), 1600 (m), 1476 (m), 1423 (s), 1320 (s), 1237 (s), 937 (m), 886 (m), 753 (m), 628 (m); **MS** (EI, 70eV) : e/z (%) = 251 (26, M^+), 192 (100); **$C_{11}H_9NO_6$** (251.2): calc.: C 52.60 H 3.61 N 5.58, found: C 52.28 H 3.41 N 5.52

4,5-Bis{2-[2-(2-hydroxy-ethoxy)-ethoxy]-ethoxy}-phthalic acid dimethyl ester (**5**): Dimethyl-4,5-dihydroxyphthalate (**3**, 6.79 g, 30.0 mmol) is dissolved in 50 ml of DMF and 9.12 g (66.0 mmol) K_2CO_3 is added. 20.1 g (66.0 mmol) Triethyleneglycol monotosylate in 50 ml of DMF is added and the resulting mixture is stirred for 18 h at 60°C. After cooling the mixture to room temperature, it is poured onto a solution of 100 ml of ice and saturated NH_4Cl. The mixture is extracted 4 times with 50 ml of dichloromethane, the combined organic phases dried over $MgSO_4$ and the solvent is evaporated. After purification by column chromatography (silica gel, Et_2O/EtOH 6/4 $\rightarrow$ 5/5, R_f (6/4) = 0.27) 11.6 g (23.6 mmol, 79%), a slightly brownish oil is obtained.

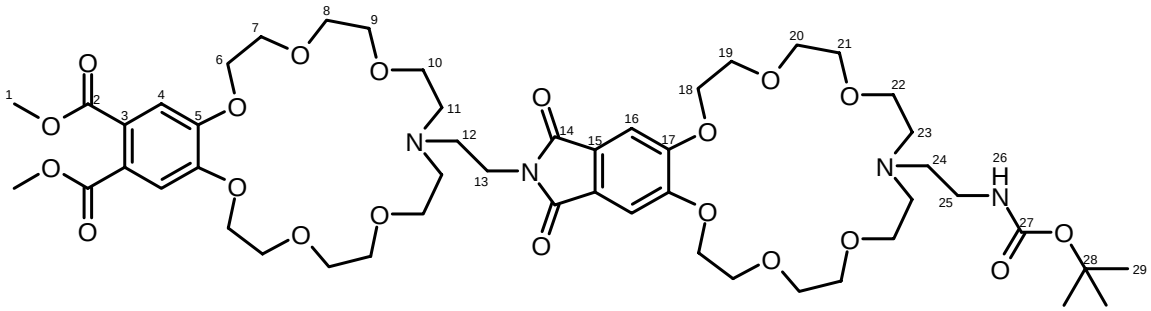
^{1}H- NMR (400 MHz, DMSO-d_6): δ = 3.39 – 3.42 (m, 4H), 3.45 – 3.49 (m, 4H), 3.51 – 3.54 (m, 4H), 3.58 – 3.61 (m, 4H), 3.73 –3.77 (m, 4H), 3.78 (s, 6H), 4.17 – 4.20 (m, 4H), 4.53 (bs, 2H), 7.28 (s, 2H); **^{13}C- NMR** (100 MHz, DMSO-d_6): δ = 52.4 (+, 2C), 60.2 (-, 2C), 68.7 (-, 2C), 68.8 (-, 2C), 69.8 (-, 2C), 70.0 (-, 2C), 72.3 (-, 2C), 113.2 (-, 2C), 124.7 (C_{quat}, 2C), 149.9 (C_{quat}, 2C), 167.0 (C_{quat}, 2C); **IR** (KBr): $\bar{\nu}$ (cm^{-1}) = 3422 (bs), 2923 (s), 2875 (s), 1720 (s), 1599 (m), 1520 (m), 1436 (m), 1351 (m), 1290 (s), 1200 (s), 1126 (s), 1063 (m), 977 (w), 945 (w), 887 (w), 782 (w); **MS** (CI-MS/ DCI, NH_3): e/z (%) = 508 (100, M^++NH_4^+), 491 (3, MH^+), 376 (13), 359 (16); **HR-MS** (CI-MS/ DCI, NH_3): calc. for $C_{22}H_{34}O_{12}$: 490.20503, found 490.20490

4,5-Bis{2-[2-(2-(toluol-4-sulfonyloxy)-ethoxy)-ethoxy]-ethoxy}-phthalic acid dimethyl ester (**6**): Compound **5** (1.47 g, 3.00 mmol) and *p*-toluylsulfonylchloride (1.72 g, 9.00 mmol) are dissolved in 20 ml of THF. A solution of 1.18 g (21.0 mmol) KOH in 3 ml of H_2O is slowly added over a period of 1 h at 0°C. The mixture continues to be stirred for 2 h at room temp. It is then is poured into 20 ml of H_2O/ 60 ml Et_2O and the aqueous phase is extracted three times with 20 ml Et_2O. The combined organic phases are washed with 20 ml of saturated NH_4Cl solution and water, dried over $MgSO_4$ and evaporated. The product (2.28 g, 2.85 mmol, 95%) is sufficiently pure for further reactions.

^{1}H- NMR (250 MHz, $CDCl_3$): δ = 2.43 (s, 6H), 3.57 – 3.61 (m, 4H), 3.65 – 3.70 (m, 8H), 3.83 – 3.87 (m, 10H), 4.13 – 4.21 (m, 8H), 7.22 (s, 2H), 7.57 (d, J = 8.12 Hz, 4H), 7.78 (d, J =

8.12 Hz, 4H); **^{13}C- NMR** (63 MHz, $CDCl_3$): δ = 21.6 (+, 2C), 52.5 (+, 2C), 68.7 (-, 2C), 68.8 (-, 2C), 69.2 (-, 2C), 69.5 (-, 2C), 70.7 (-, 2C), 70.8 (-, 2C), 113.8 (+, 2C), 125.4 (C_{quat}, 2C), 127.9 (+, 4C), 129.8 (+, 4C), 133.0 (C_{quat}, 2C), 144.8 (C_{quat}, 2C), 150.4 (C_{quat}, 2C), 167.9 (C_{quat}, 2C); **IR** (NaCl): $\bar{\nu}$ (cm^{-1}) = 2951 (m), 2877 (m), 1722 (s), 1598 (m), 1520 (s), 1436 (m), 1354 (s), 1290 (s), 1177 (s), 1128 (s), 1014 (m), 923 (m), 818 (m), 779 (m); **MS** (CI-MS/ DCI, NH_3): e/z (%) = 816 (75, $M^+ + NH_4^+$), 728 (36), 644 (26), 618 (22), 530 (26), 513 (26), 376 (37), 341 (21), 327 (29), 322 (24), 315 (28), 304 (97), 278 (57), 271 (29), 253 (100); **HR-MS** (CI-MS/ DCI, NH_3): calc. for $C_{36}H_{46}S_2O_{16}$: 798.22273, found 798.22280; **$C_{36}H_{46}O_{16}S_2$** (798.9): calc. C 54.13 H5.80 S 8.03, found C 54.04 H 5.70 S 7.99

Bis CEAA (**7**):



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Compounds **9** (355 mg, 0.59 mmol) and **8** (349 mg, 0.59 mmol) are dissolved in 10 ml of $CHCl_3$. 250 mg (1.2 mmol) of DCC and 160 mg (1.2 mmol) HOBt are added at room temp. The mixture is stirred for 2 h at room temp. and then refluxed overnight. After cooling to room temp., insoluble material is separated by filtration over celite and washing with $CHCl_3$. Evaporation of the solvent yields the raw product, which is purified by column chromatography (silica gel, $CHCl_3$/ MeOH 9/1 → 6/1, R_f ($CHCl_3$/ MeOH 6/1) = 0.21). A yellowish oil is obtained, which solidifies to glass over a period of time (440 mg, 0.41 mmol, 70%).

^{1}H- NMR (600 MHz, $CDCl_3$): δ = 1.42 (s, 9 H, 29), 2.60 (bs, 2 H, 24), 2.74 (bs, 4 H, 11), 2.74 – 2.77 (m, 2 H, 12), 2.80 – 2.82 (m, 4 H, 23), 3.16 (bs, 2 H, 25), 3.53 – 3.54 (m, 4 H, 22), 3.56 (bs, 4 H, 10), 3.58 – 3.60 (m, 4 H, 9), 3.67 –3.68 (m, 6 H, 21, 13), 3.69 – 3.71 (m, 4 H, 8), 3.78 – 3.79 (m, 4 H, 20), 3.85 (s, 6 H), 3.88 – 3.89 (m, 4 H, 7), 3.93 – 3.94 (m, 4 H, 19), 4.17 – 4.19 (m, 4 H, 6), 4.22 – 4.23 (m, 4 H, 18), 5.48 (bs, 1 H), 7.16 (s, 2 H, 4), 7.23 (s, 2 H, 16); **^{13}C- NMR** (150 MHz, $CDCl_3$): δ = 28.5 (+, 3 C, 29), 36.1 (-, 1 C, 13), 38.7 (-, 1 C, 25), 52.5 (+, 2 C, 1), 52.9 (-, 1 C, 12), 54.1 (-, 1 C, 24), 54.2 (-, 2 C, 23), 54.6 (-, 2 C, 11), 69.3 (-,

2 C, 6), 69.4 (-, 2 C, 19), 69.5 (-, 2 C, 7), 69.6 (-, 2 C, 18), 69.7 (-, 2 C, 10), 70.2 (-, 2 C, 22), 70.5 (-, 2 C, 9), 70.7 (-, 2 C, 21), 71.1 (-, 2 C, 8), 71.3 (-, 2 C, 20), 78.8 (C_{quat}, 1 C, 28), 106.9 (+, 2 C, 16), 113.7 (+, 2 C, 4), 125.3 & 125.6 (C_{quat}, 4 C, 3, 15), 150.5 (C_{quat}, 2 C, 5), 153.4 (C_{quat}, 2 C, 17), 156.2 (C_{quat}, 1 C, 27), 167.7 (C_{quat}, 2 C, 14), 168.4 (C_{quat}, 2 C, 2); **IR** (NaCl): $\bar{\nu}$ (cm^{-1}) = 3400 (bw), 2930 (m), 2880 (m), 1707 (s), 1599 (m), 1510 (m), 1436 (m), 1393 (m), 1352 (m), 1291 (s), 1196 (m), 1129 (s), 1056 (m), 980 (w), 945 (w); **MS** (ESI-MS, CH_2Cl_2/MeOH + 10 mmol/l NH_4OAc): e/z (%) = 1065 (100, MH^+), 965 (18, MH^+ - C_4H_8 - CO_2), 922 (15, MH^+ - C_4H_8 - CO_2 - C_2H_5N); **UV** (MeOH): λ (ε) = 340 (1400), 248 (40300), 227 (38200); **HRMS** (PI-LSIMS, MeOH/Glycerin): calc. for $C_{51}H_{76}N_4O_{30}*H^+$: 1065.5131, found: 1065.5136

14-(2-Amino-ethyl)-6,7,9,10,13,14,15,16,18,19,21,22-dodecahydro-12H-5,8,11,17,20,23-hexaoxa-14-aza-benzocycloheneicosen-2,3-dicarbonic acid dimethyl ester dihydrochloride (**8**): Compound **1** (730 mg, 1.18 mmol) is dissolved in 15 ml dichloromethane and treated with 10 ml of HCl-saturated diethyl ether. The mixture is stirred for 3 h and the solvent is then decanted from the generated precipitate. Diethyl ether is added and decanted. After drying the mixture in a high vacuum, a white solid is obtained (660 mg, 1.12 mmol, 95 %).

^{1}H- NMR (300 MHz, $CDCl_3$): δ = 3.35 (bs, 4 H), 3.50 – 3.68 (m, 12 H), 3.76 (bs, 4 H), 3.79 (s, 6 H), 3.84 (bs, 4 H), 4.20 (bs, 4 H), 7.15 (s, 2 H), 7.83 (bs, 3 H), 12.61 (bs, 1 H)

^{13}C- NMR (75 MHz, $CDCl_3$): δ = 36.1 (-, 1 C), 51.0 (-, 1 C), 52.7 (+, 2 C), 56.3 (-, 2 C), 65.2 (-, 2 C), 68.9 (-, 2 C), 69.0 (-, 2 C), 69.9 (-, 2 C), 70.3 (-, 2 C), 112.8 (+, 2 C), 125.0 (C_{quat}, 2 C), 147.9 (C_{quat}, 2 C), 166.4 (C_{quat}, 2 C); **MS** (ESI-MS, CH_2Cl_2/MeOH + 10 mmol/l NH_4OAc): e/z (%) = 515 (100, MH^+)

Dilithium-14-(2-tert-Butoxycarbonylamino-ethyl)-6,7,9,10,13,14,15,16,18,19,21,22-dodecahydro-12H-5,8,11,17,20,23-hexaoxa-14-aza-benzocycloheneicosen-2,3-dicarboxylate (**9**): Compound **1** (370 mg , 0.60 mmol) is dissolved in 6 ml of THF and treated with 0.6 ml (1.2 mmol) of an aqueous 2 N LiOH solution. After stirring for 2 d at room temp., the solvent is evaporated and the residue lyophilized. A white solid is obtained (360 mg, 0.60 mmol, 100%).

^{1}H- NMR (300 MHz, $CDCl_3$): δ = 1.28 (s, 9 H), 3.41 – 3.48 (m, 8 H), 3.60 (s, 8 H), 3.79 – 3.85 (m, 8 H), 4.17 – 4.24 (m, 4 H), 6.16 (bs, 1 H), 7.77 (s, 2 H); **MS** (ESI-MS, CH_2Cl_2/MeOH + 10 mmol/l NH_4OAc): e/z (%) = 587 (100, MH^+)

(2,5-Dioxo-2,5-dihydro-pyrrol-1-yl)-acetic acid methyl ester (**14**): Maleic acid anhydride (32.6 g, 0.33 mol) and glycine methyl ester hydrochloride (46 g, 0.37 mmol) are added to 400 ml of dichloromethane and cooled to 0°C. NEt_3 (55 ml, 40.5 g, 0.40 mol) is added dropwise over a period of 1 h. The mixture is stirred at room temp. overnight and afterwards treated with 200 ml of 1 M HCl. The organic phase is collected and the water phase extracted with dichloromethane (3 x 100 ml). The combined organic phases are evaporated using a rotary evaporator and the remaining white solid is suspended in 300 ml of xylene. The suspension is heated to reflux for 1 h while water is collected in a dean stark apparatus. After cooling the oily residue to room temperature, it is diluted with 100 ml of a saturated $NaHCO_3$ solution and 100 ml of ethyl acetate. The water phase is then extracted twice using 50 ml of ethyl acetate. The combined organic phases are washed with 50 ml of a saturated $NaHCO_3$ solution and 50 ml of brine. After drying over $MgSO_4$, the solvent is evaporated. The raw product (17.0 g, 0.10 mol, 30 %) is obtained as brownish oil which is sufficiently pure for the successive steps. It can be further purified through bulb-to-bulb distillation (bp 120°C @ $2*10^{-1}$ mbar).

^{1}H- NMR (300 MHz, $CDCl_3$): δ = 3.69 (s, 3 H), 4.22 (s, 2 H), 6.73 (s, 2 H); **^{13}C- NMR** (75 MHz, $CDCl_3$): δ = 38.5 (-, 1C), 52.7 (+, 1 C), 134.5 (+, 2 C), 167.6 (C_{quat}, 1 C), 169.8 (C_{quat}, 2 C)

(1,3-Dioxo-5,6-bis-trimethylsilanyloxy-1,3,3a,4,7,7a-hexahydro-isoindol-2-yl)- acetic acid methyl ester (**15**): Compound **14** (846 mg, 5 mmol) and 131 ml (1.15 g, 5 mmol) 2,3-bis-trimethylsilanyloxy-buta-1,3-dien (**11**) are dissolved in 5 ml of toluene and stirred for 24 h at 90°C. The solvent is evaporated and the remaining oil purified through bulb-to-bulb distillation (bp. 195°C @ $4 * 10^{-3}$ mbar). A yellowish oil (1.45 g, 3.63 mmol, 73%) is obtained, which slowly solidifies.

^{1}H- NMR (300 MHz, $CDCl_3$): δ = 0.09 (s, 18 H), 2.48-2.51 (m, 4H), 3.11 –3.14 (m, 2H), 3.70 (s, 3H), 4.19 (s, 2H); **^{13}C- NMR** (75 MHz, $CDCl_3$): δ = -0.0 (+, 6C), 28.3 (-, 2C), 39.0 (-, 1C), 39.3 (+, 2 C), 52.0 (+, 1C), 128.8 (C_{quat}, 2C), 166.4 (C_{quat}, 1C), 177.9 (C_{quat}, 2C); **MS** (PI-DCIMS, NH_3) : e/z (%) = 417 (100, $M+NH_4^+$).

(1,3-Dioxo-5,6-bis-trimethylsilanyloxy-1,3-dihydro-isoindol-2-yl)-acetic acid methyl ester (**16**): Compound **15** (5.5 g, 12.63 mmol) is combined with 829 mg (25.9 mmol) of sulfur and stirred for 20 min at 230°C. Hereby the oil darkens and the drop of molten sulfur vanishes almost completely. After cooling the solidified oil to room temp., it is dissolved in 80 ml of

CCl_4 and 5.05 g (77 mmol) of Cu powder are added. Beforehand the Cu powder was washed with 5 M HCl, H_2O, THF and finally CCl_4. After 30 min of stirring at room temp., the copper powder is collected through filtration and the solvent is evaporated. The oily residue is distilled using the bulb-to-bulb distillation apparatus (bp. 280°C @ 10^{-2} mmbar). However, the yellowish oil (4.1 g, 10.4 mmol, 82%) obtained still contains traces of sulfur.

^{1}H-NMR (300 MHz, $CDCl_3$): δ = 0.25 (s, 18 H), 3.71 (s, 3 H), 4.33 (s, 2 H), 7.23 (s, 2 H); **^{13}C-NMR** (75 MHz, $CDCl_3$): δ = 0.0 (+, 6 C), 38.5 (-, 1 C), 52.3 (+, 1 C), 115.5 (+, 2 C), 125.8 (C_{quat}, 2 C), 152.1 (C_{quat}, 2 C), 167.1 (C_{quat}, 2 C), 167.8 (C_{quat}, 1 C); **MS** (EI-MS, 70 eV): e/z (%) = 395 (77, M^+), 336 (82), 264 (21), 248 (100), 147 (11), 73 (86); **HR-MS** (EI-MS, 70 eV): calc. for $C_{17}H_{25}NO_6Si_2$: 395.1220, found : 395.1215.

(5,6-Bis-{2-[2-(2-hydroxy-ethoxy)-ethoxy]-ethoxy}-1,3-dioxo-1,3-dihydro-isoindol-2-yl)-acetic acid methyl ester (**17**): Compound **4** (803 mg, 3.2 mmol) and triethylenglycol mono tosylate (2.06 g, 6.77 mmol) are refluxed with 1.38 g (10 mmol) of K_2CO_3 for 16 h in 20 ml of acetonitrile. After cooling to room temp., the mixture is poured into 100 ml of ice and water and extracted 4 times with 50 ml of dichloromethane. The combined organic phases are dried over $MgSO_4$, the solvent is evaporated and the crude product purified by column chromatography (silica gel, ethyl acetate/ EtOH 8/2). A colourless oil is obtained (412 mg, 0.80 mmol, 25 %).

^{1}H- NMR (300 MHz, $CDCl_3$): δ = 3.04 (bs, 2 H, OH), 3.52 – 3.55 (m, 4 H), 3.60 – 3.70 (m, 12 H), 3.68 (s, 3 H), 3.84 – 3.87 (m, 4 H), 4.20 – 4.23 (m, 4 H), 4.32 (s, 2 H), 7.28 (s, 2 H); **^{13}C- NMR** (75 MHz, $CDCl_3$): δ = 38.7 (-, 1 C), 52.6 (+, 1 C), 61.6 (-, 2 C), 69.1 (-, 2 C), 69.2 (-, 2 C), 70.3 (-, 2 C), 70.6 (-, 2 C), 70.9 (-, 2 C), 72.7 (-, 2 C), 107.5 (+, 2 C), 125.5 (C_{quart}, 2 C), 153.6 (C_{quat}, 2 C), 167.5 (C_{quat}, 2 C), 168.0 (C_{quat}, 1 C); **IR** (KBr): $\bar{\nu}$ (cm^{-1}) = 3390 (bm), 3113 (w), 3075 (w), 3053 (w), 2875 (m), 1725 (s), 1702 (s), 1595 (s), 1494 (m), 1421 (s), 1308 (s), 1224 (s), 1115 (s), 940 (s), 895 (m), 750 (m); **MS** (PI-EIMS, 70 eV): e/z (%) = 515 (25, M^+), 277 (12), 262 (10), 218 (50), 191 (12), 133 (43), 89 (51), 45 (100); **$C_{23}H_{33}NO_{12}$*0.5H_2O**: calc.: C 52.67 H 6.53 N 2.67, found: C 52.60 H 6.27 N 2.84

(5,6-Bis-{2-[2-(2-(toluol-4-sulfonyloxy)-ethoxy)-ethoxy]-ethoxy}-1,3-dioxo-1,3-dihydro-isoindol-2-yl)- acetic acid methyl ester (**18**): Compound **17** (320 mg, 0.62 mmol) is dissolved in 5 ml of dichloromethane and 262 mg (1.37 mmol) of tosyl chloride are added at 0°C. Subsequently 20 mg of DMAP and 194 µl (142 mg, 1.4 mmol) of NEt_3 are added. The solution is stirred for 3 days, after which equal amounts of tosyl chloride and NEt_3 are again

added to complete reaction conversion. Stirring continues for another 24 h, after which the solution is poured into 20 ml of H_2O. The mixture is extracted three times with 20 ml of dichloromethane and the combined organic phases are washed with 10 ml of water and dried over $MgSO_4$. After evaporation of the solvent, the crude product is purified by column chromatography (silica gel, PE/ ethyl acetate 2/8). A yellowish wax is obtained (326 mg, 0.4 mmol, 64%).

^{1}H- NMR (300 MHz, $CDCl_3$): δ = 2.41 (s, 6 H), 3.57 – 3.60 (m, 4 H), 3.64 – 3. 69 (m, 8 H), 3.73 (s, 3 H), 3.84 – 3.87 (m, 4 H), 4.12 – 4.15 (m, 4 H), 4.21 – 4.24 (m, 4 H), 4.37 (s, 2 H), 7.31 (d, *J* = 8.4 Hz, 4 H), 7.32 (s, 2 H), 7.76 (d, *J* = 8.4 Hz, 4 H); **^{13}C- NMR** (75 MHz, $CDCl_3$): δ = 21.6 (+, 2 C), 38.7 (-, 1 C), 52.6 (+, 1 C), 68.7 (-, 2 C), 69.2 (-, 2 C), 69.3 (-, 2 C), 69.4 (-, 2 C), 70.8 (-, 2 C), 70.9 (-, 2 C), 107.5 (+, 2 C), 125.5 (C_{quat}, 2 C), 127.9 (+, 4 C), 129.8 (+, 4 C), 132.9 (C_{quat}, 2 C), 144.8 (C_{quat}, 2 C), 153.7 (C_{quat}, 2 C), 167.5 (C_{quat}, 2 C), 168.0 (C_{quat}, 1 C); **IR** (NaCl): $\bar{\nu}$ (cm^{-1}) = 2954 (w), 2925 (w), 2872 (w), 1751 (m), 1712 (s), 1598 (m), 1499 (w), 1416 (m), 1356 (m), 1308 (s), 1219 (m), 1176 (s), 1121 (m), 1096 (m), 1015 (w), 922 (m), 816 (w), 754 (m); **MS** (ESI-MS, CH_2Cl_2/MeOH + 10 mmol/l NH_4OAc): e/z (%) = 841 (100, $M+NH_4^+$), 824 (35, MH^+)

2) Comparison of Bu^4N^+ binding

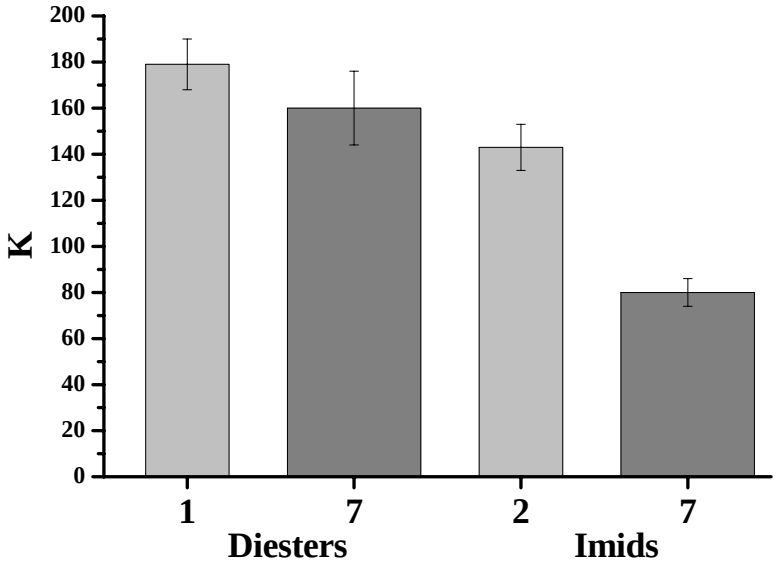
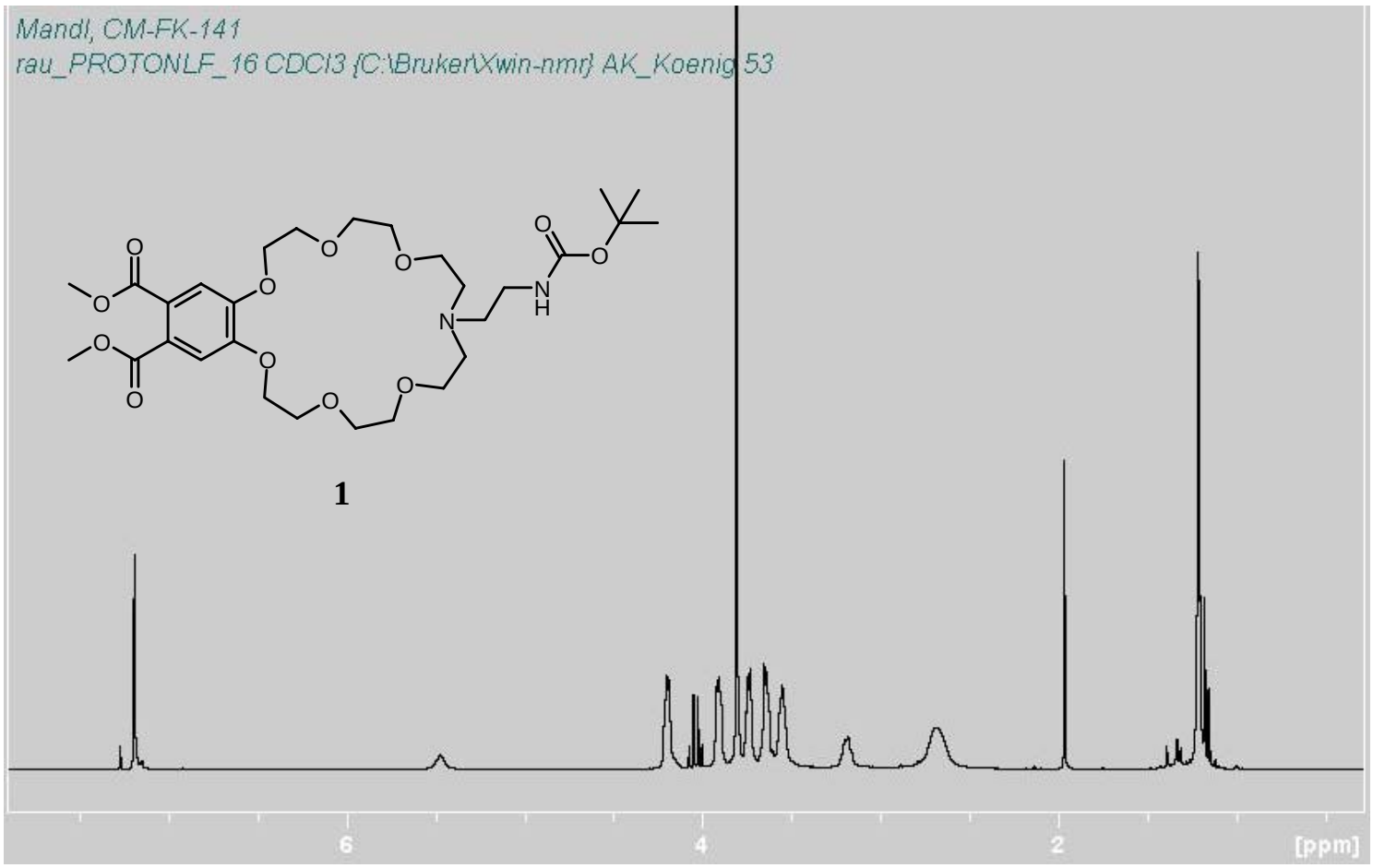


Figure S-1: A comparison of *n*-butylammonium binding constants of compounds **1** and **2**, and the two crown ether binding sites in compound **7**.

3) ^{1}H – and ^{13}C-NMR spectra of new compounds

For solvents and conditions of measurement, see experimental procedures.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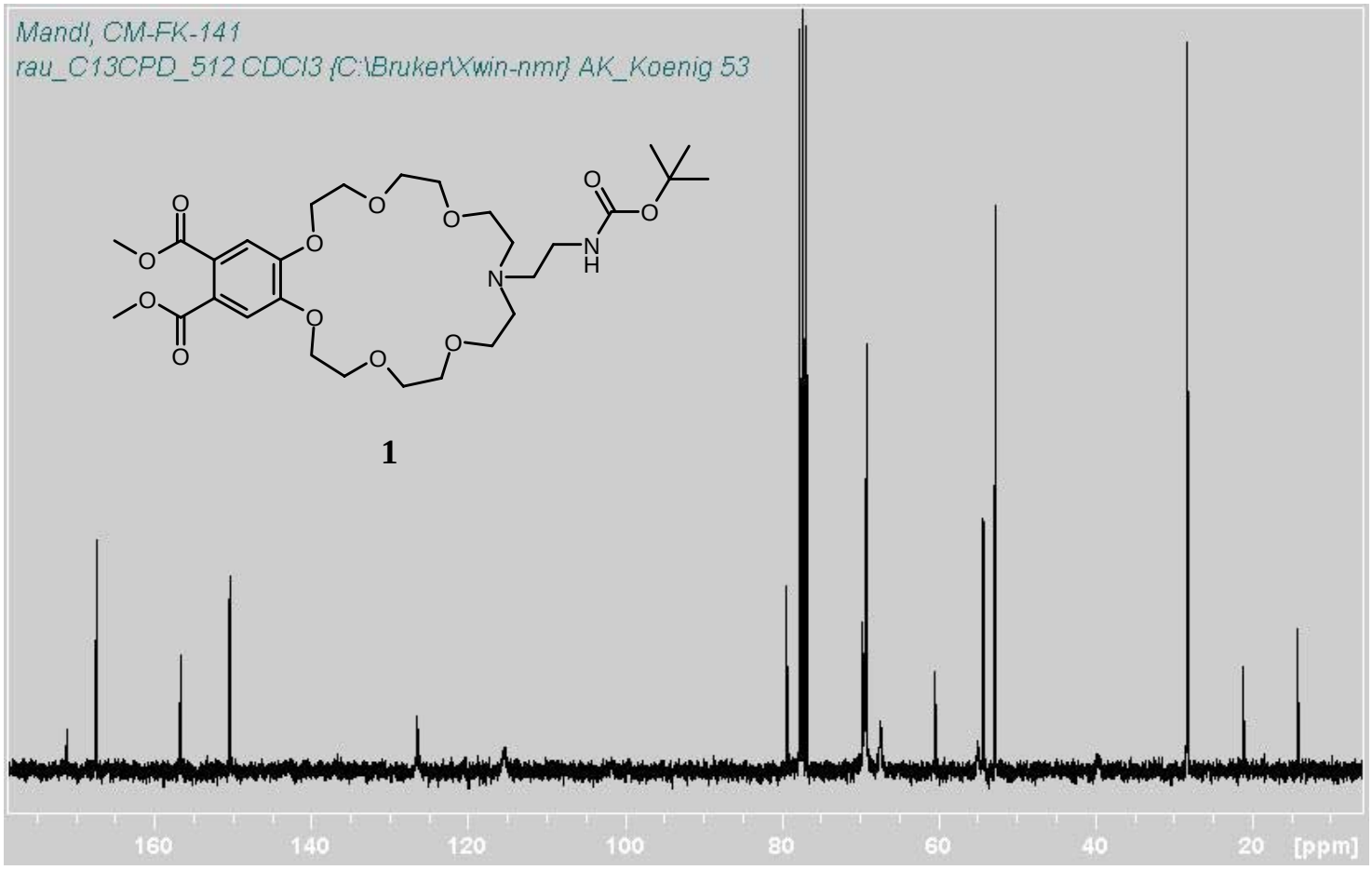
4
2
[ppm]

1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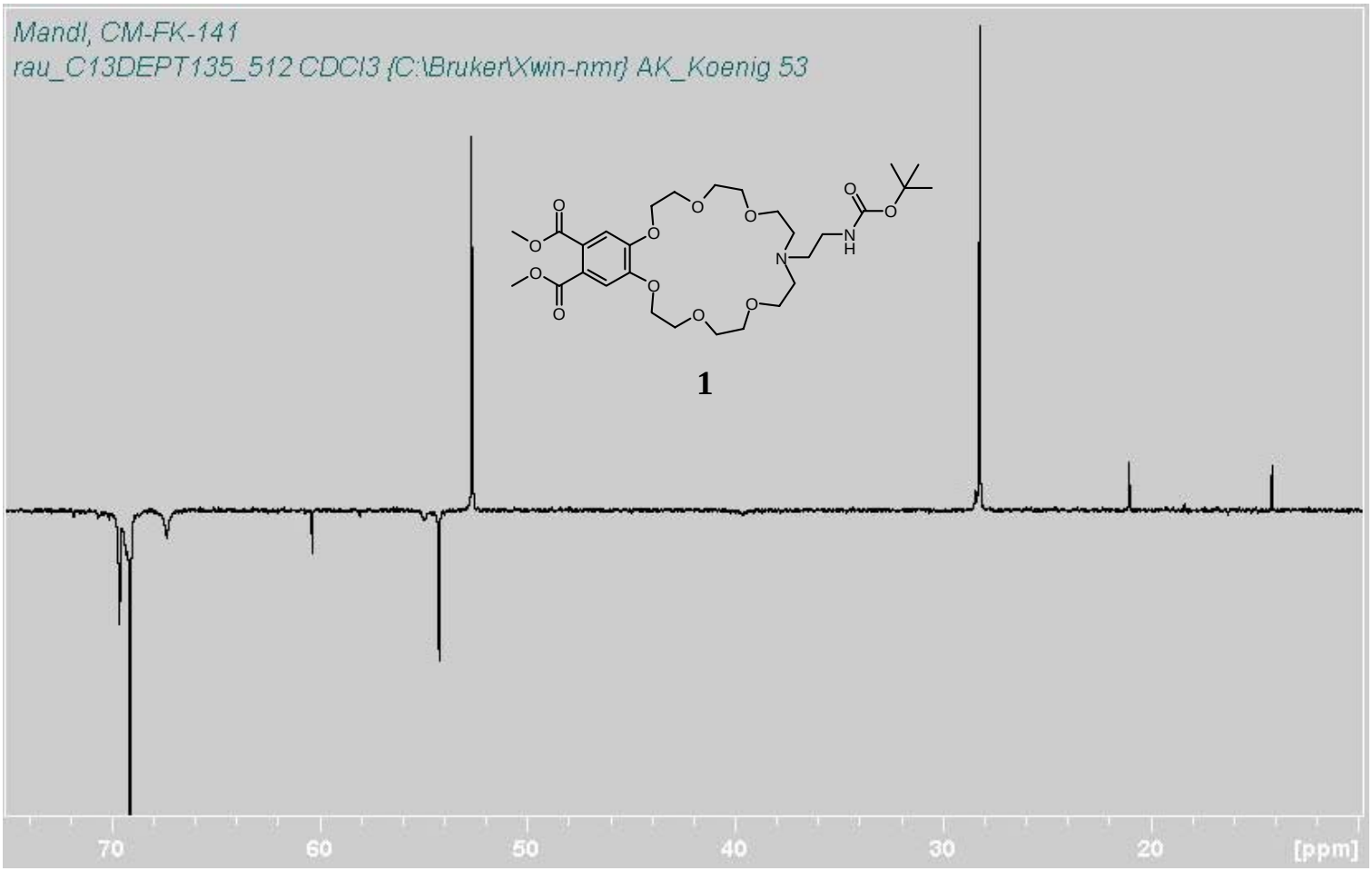
140
120
100
80
60
40
20
[ppm]

1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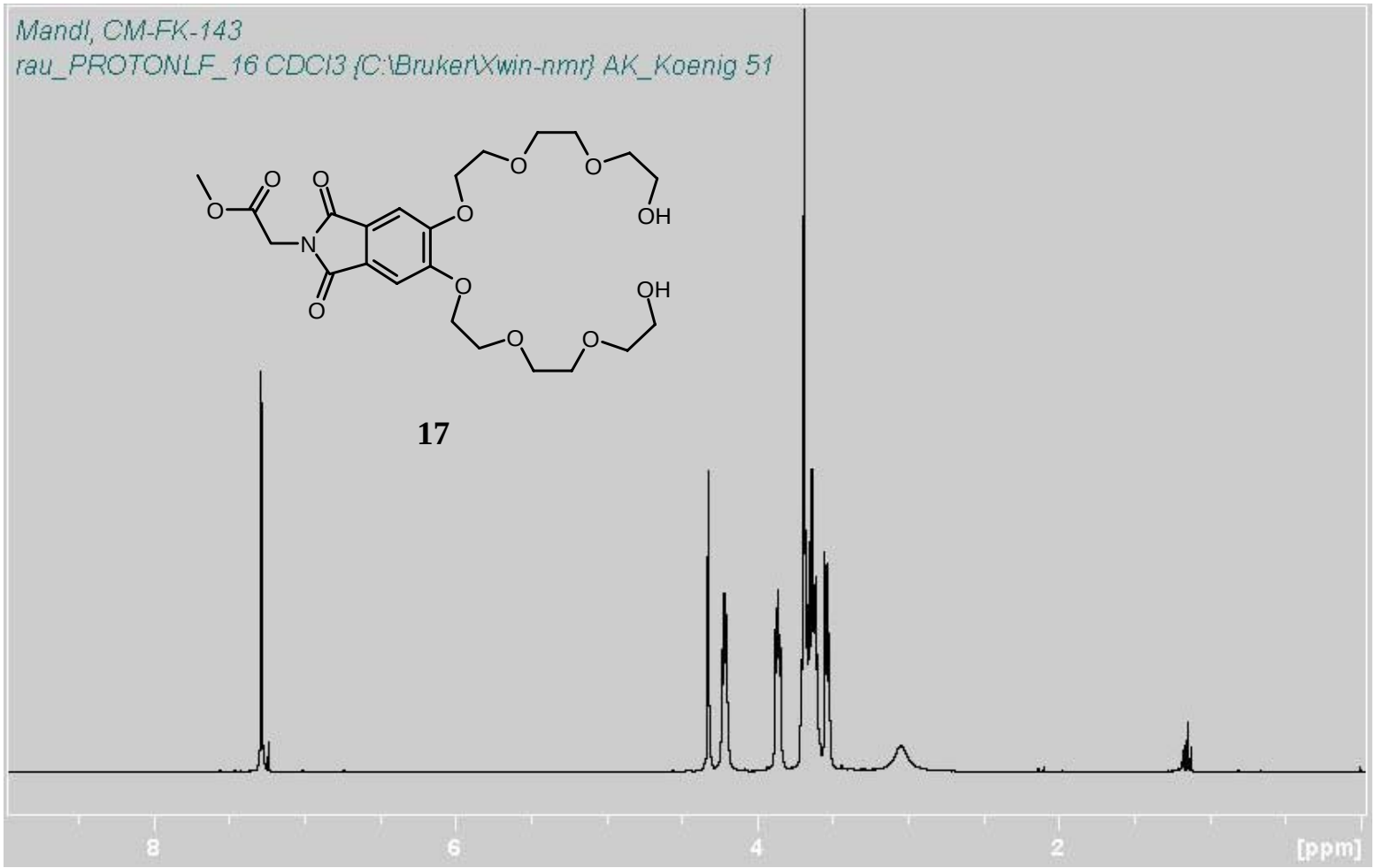
60
50
40
30
20
[ppm]

1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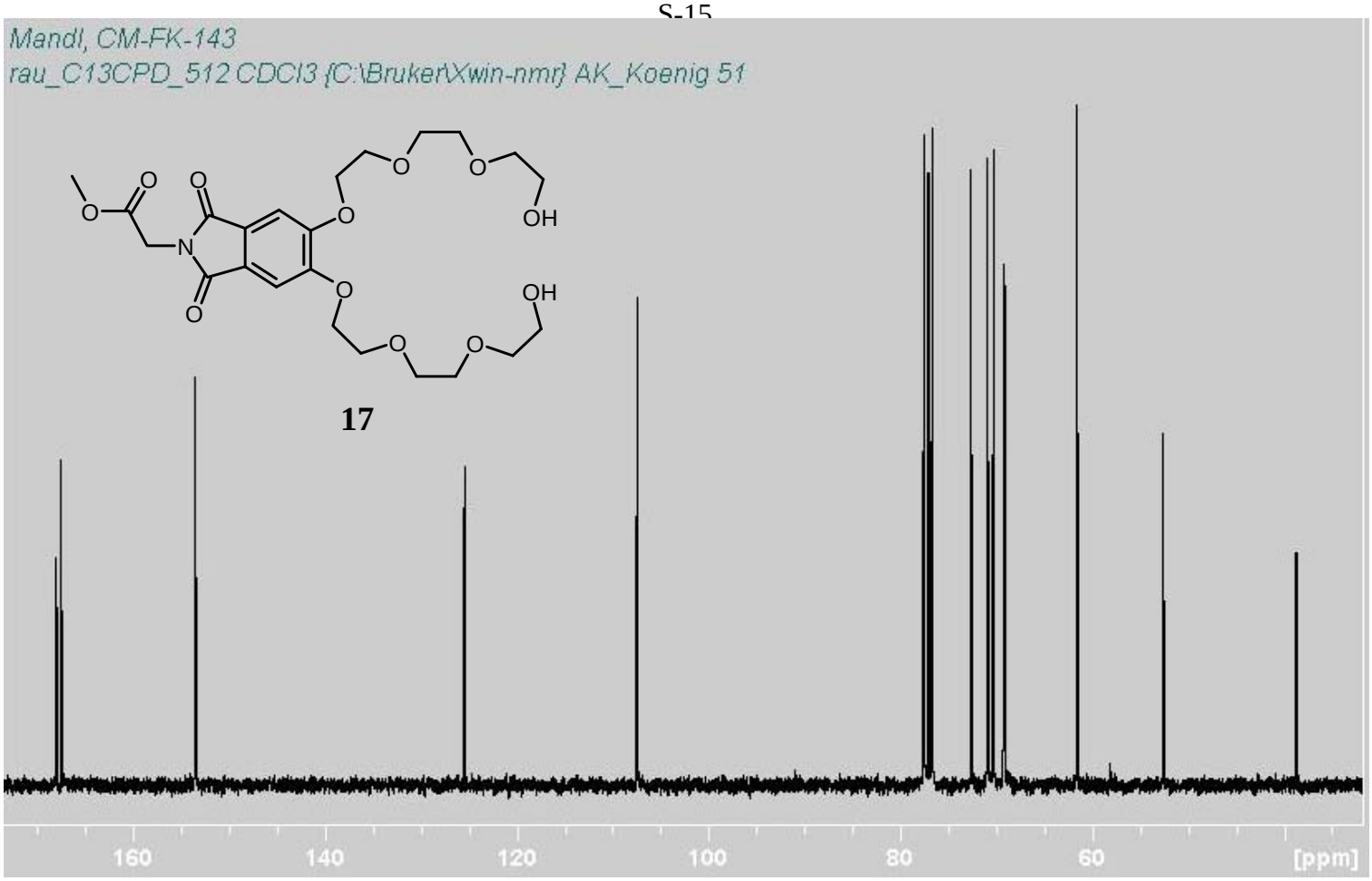
8
6
4
2
[ppm]

17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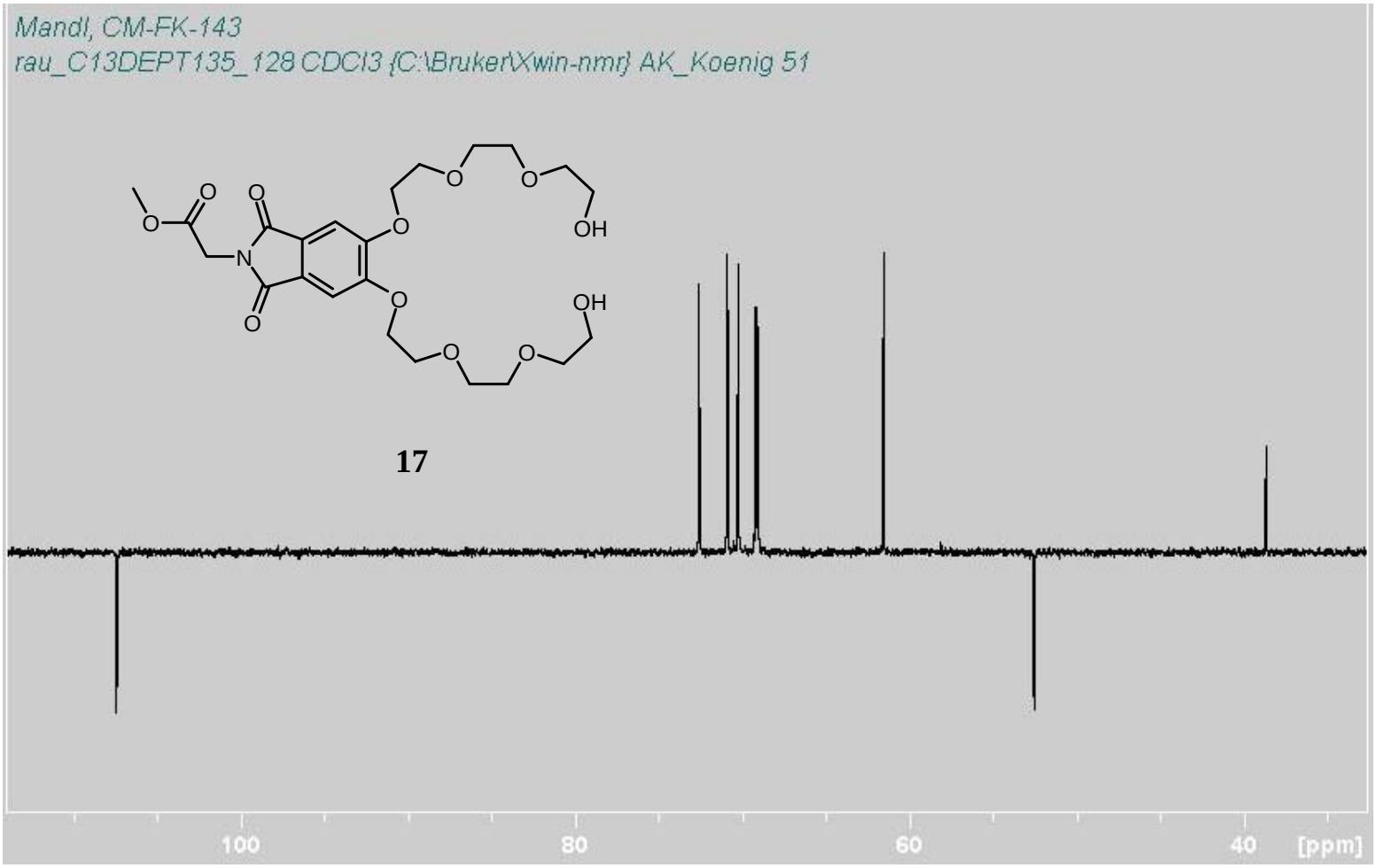
140
120
100
80
60
[ppm]

17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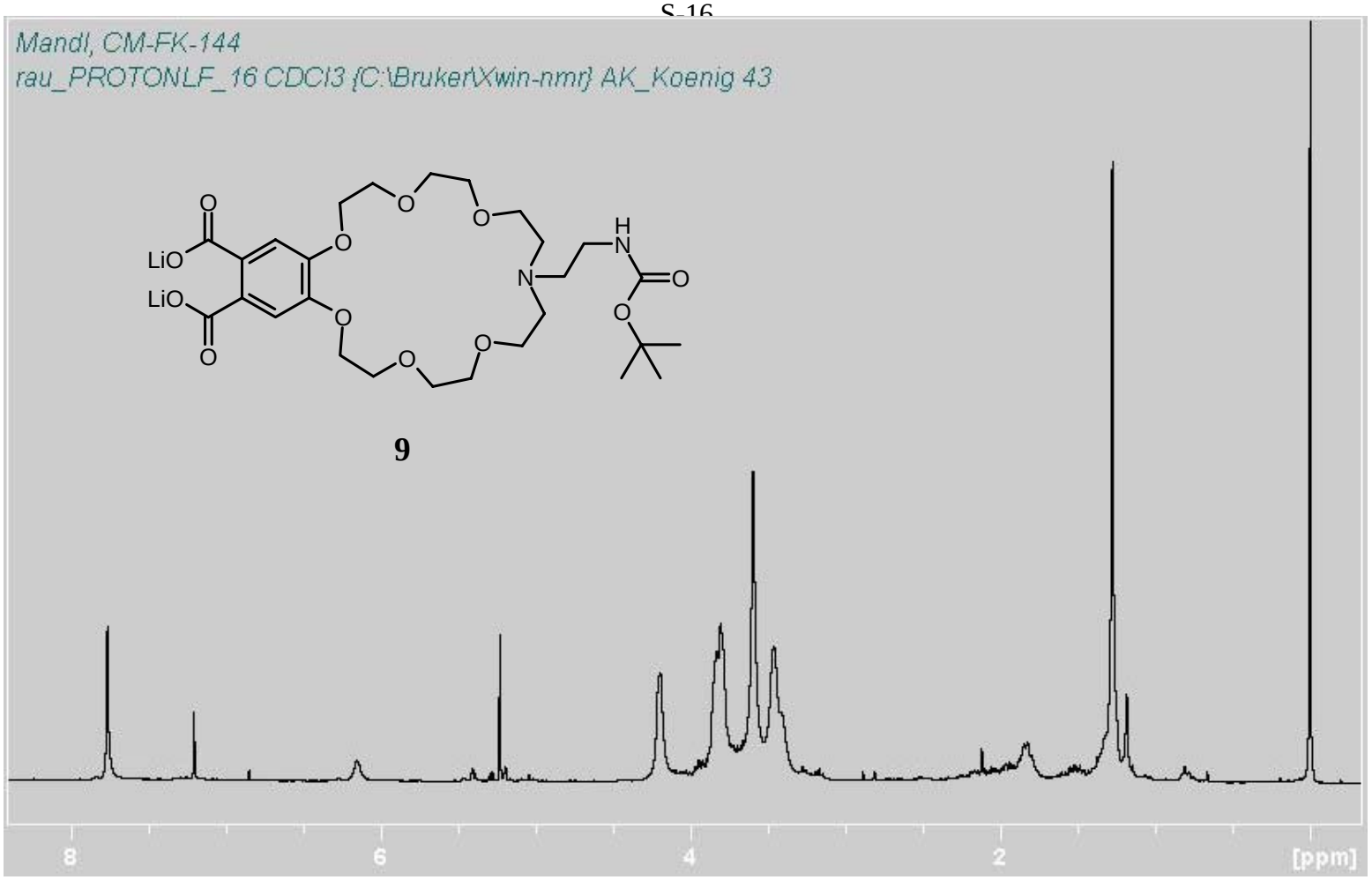
100
80
60
40
[ppm]

17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LiO
LiO
O
O
O
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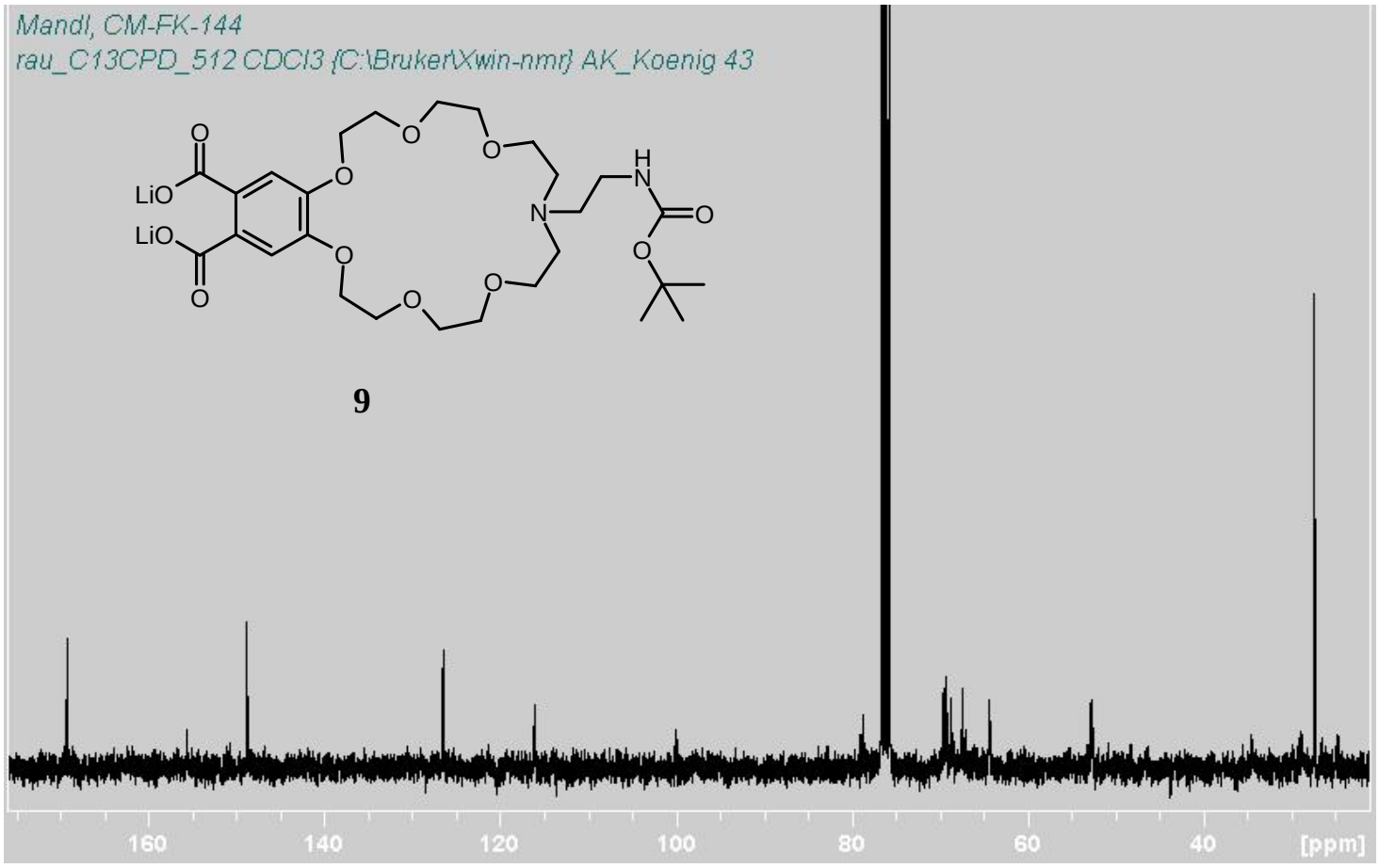
N
O
O
O
8
6
4
2
[ppm]

9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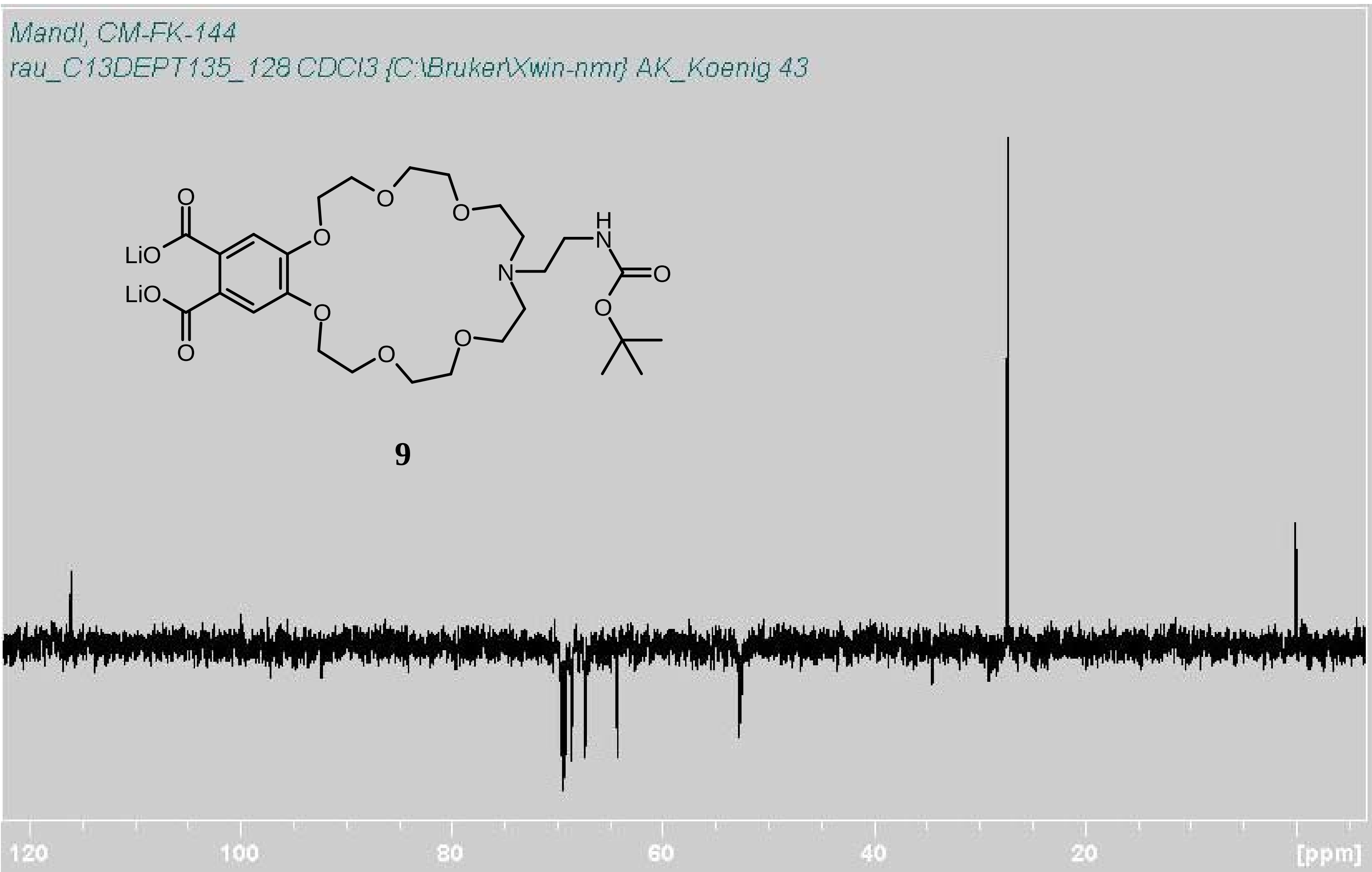
LiO
O
O
O
O
O
O
O
O
O
N
H
N
O
O
O
160
140
120
100
80
60
40
[ppm]

9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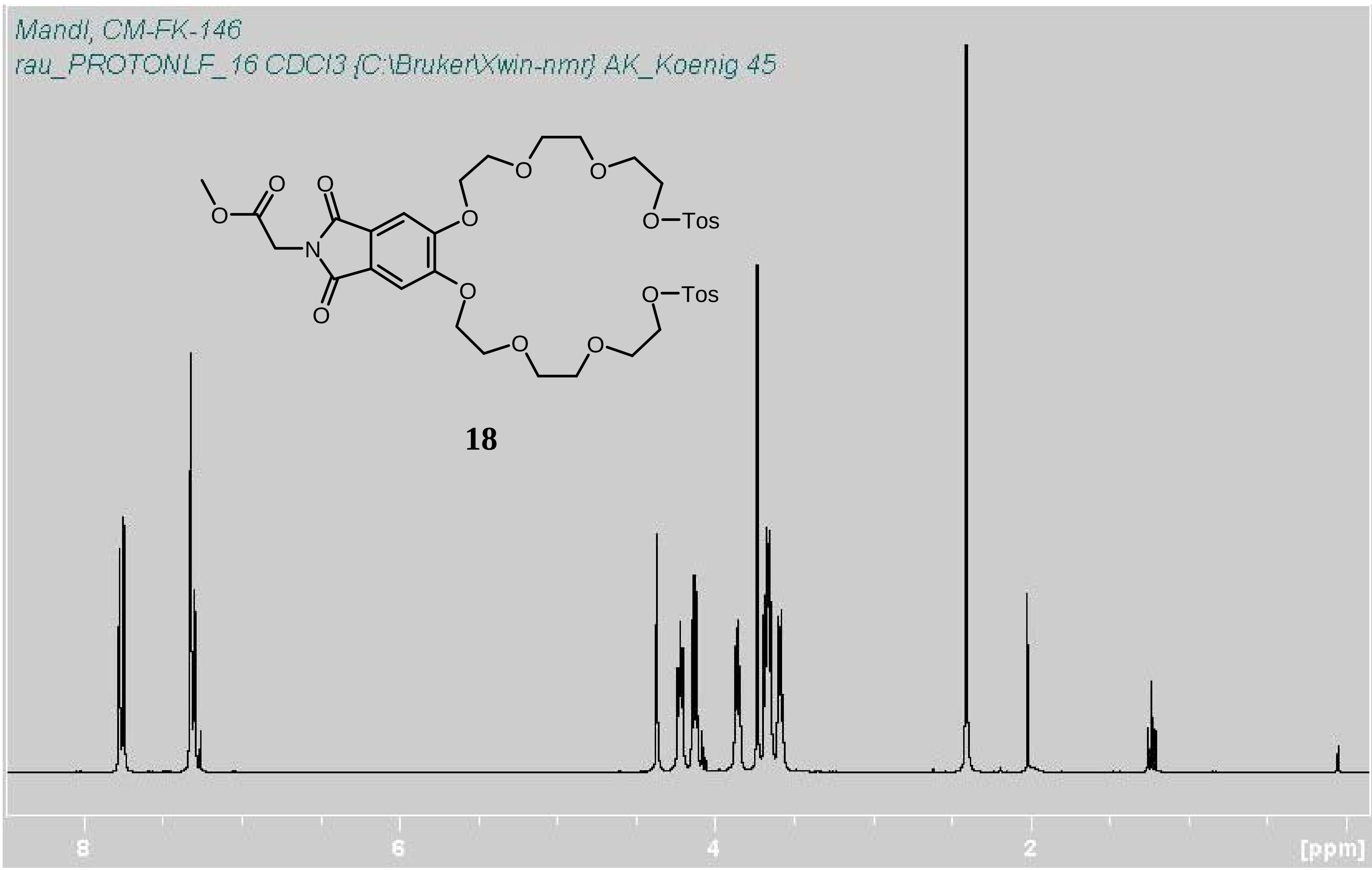
LiO
LiO
O
N
H
9
120
100
80
60
40
20
[ppm]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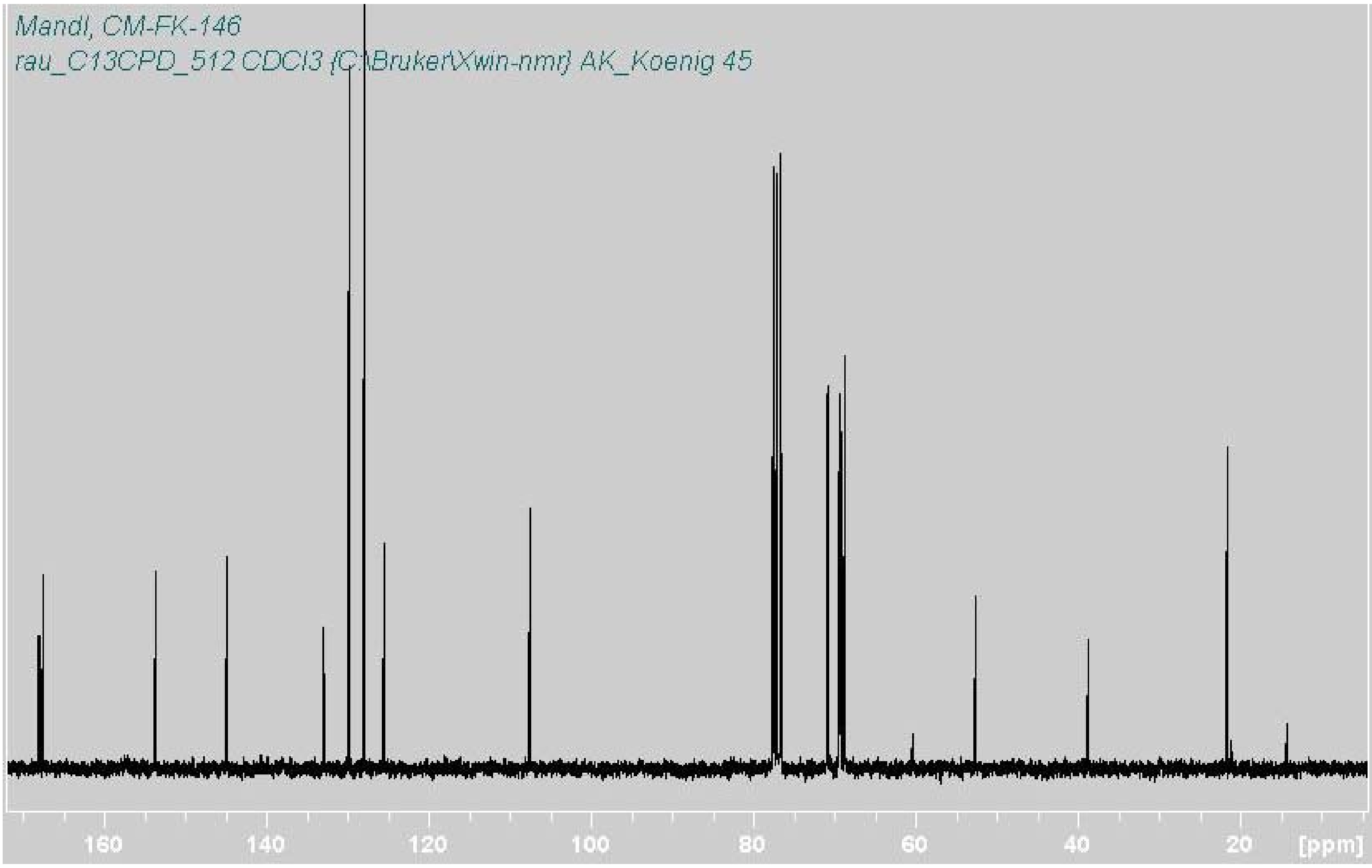
O
N
O–Tos
18
8
6
4
2
[ppm]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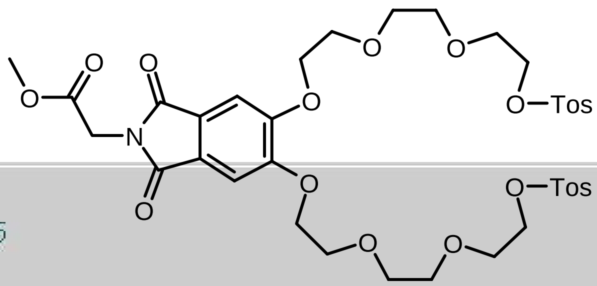
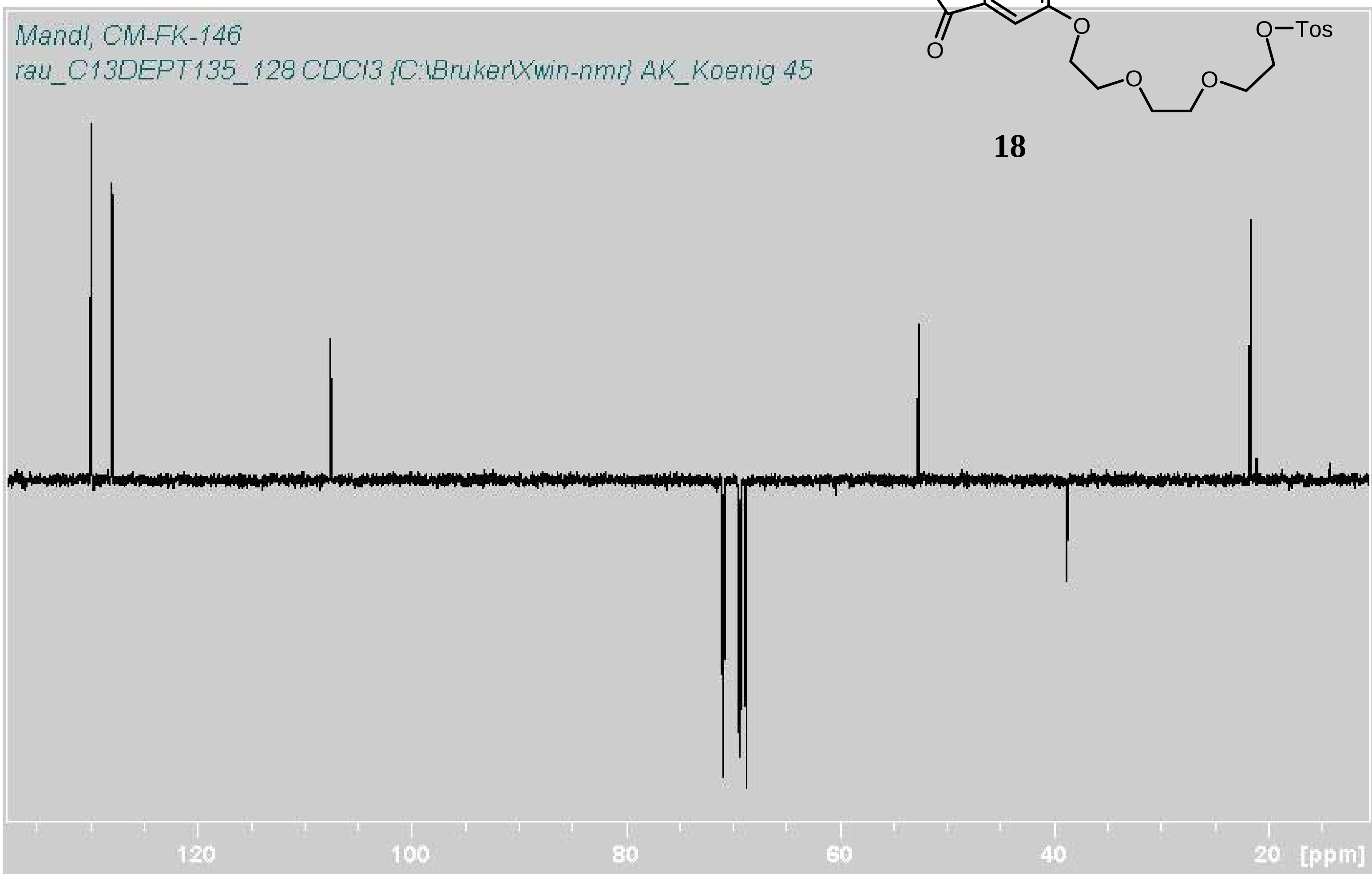
140
120
100
80
60
40
20
[ppm]


O
O
N
O
O
O
O
O
O-Tos
O
O
O
O-Tos

18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80
60
40
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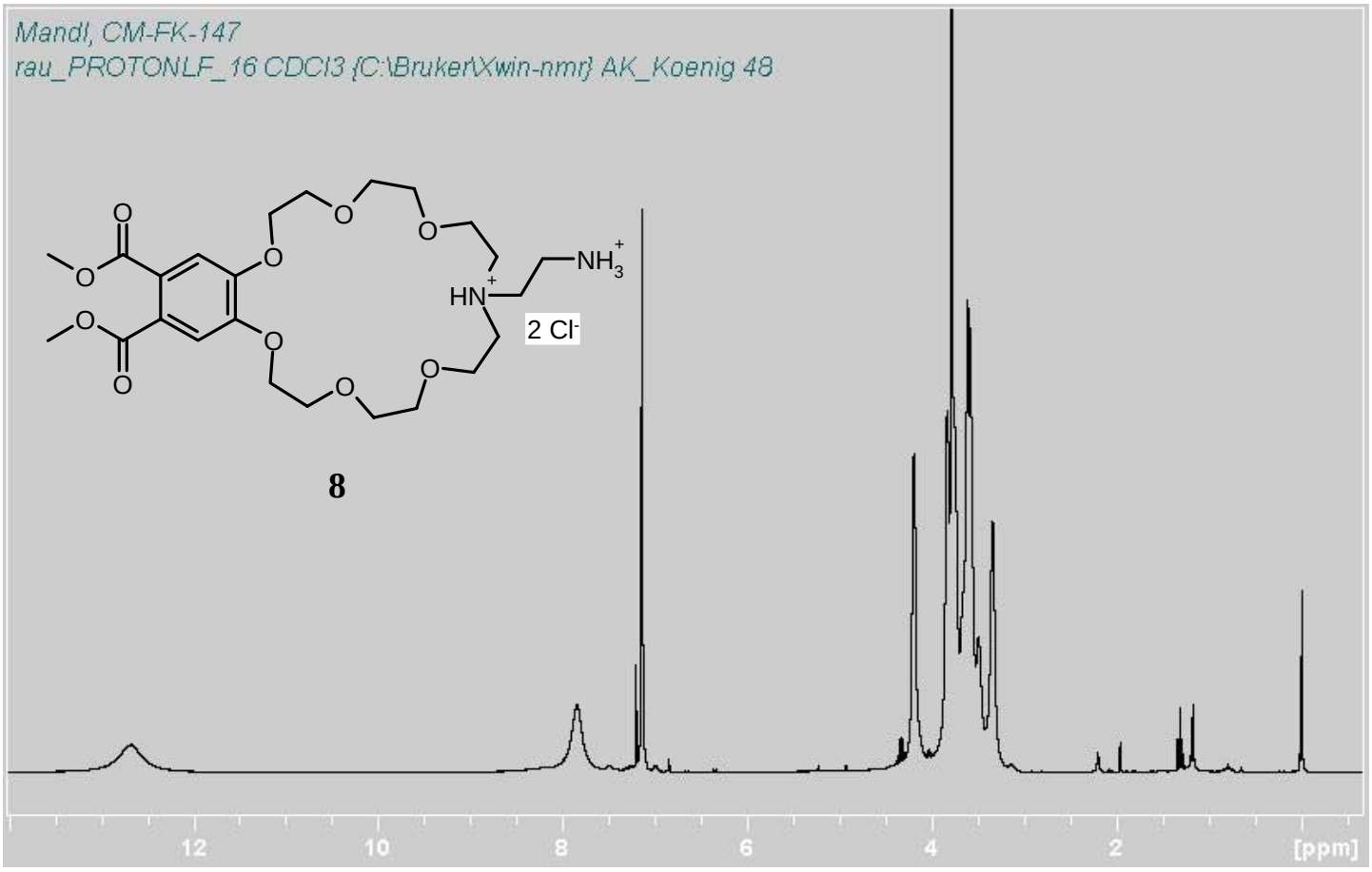
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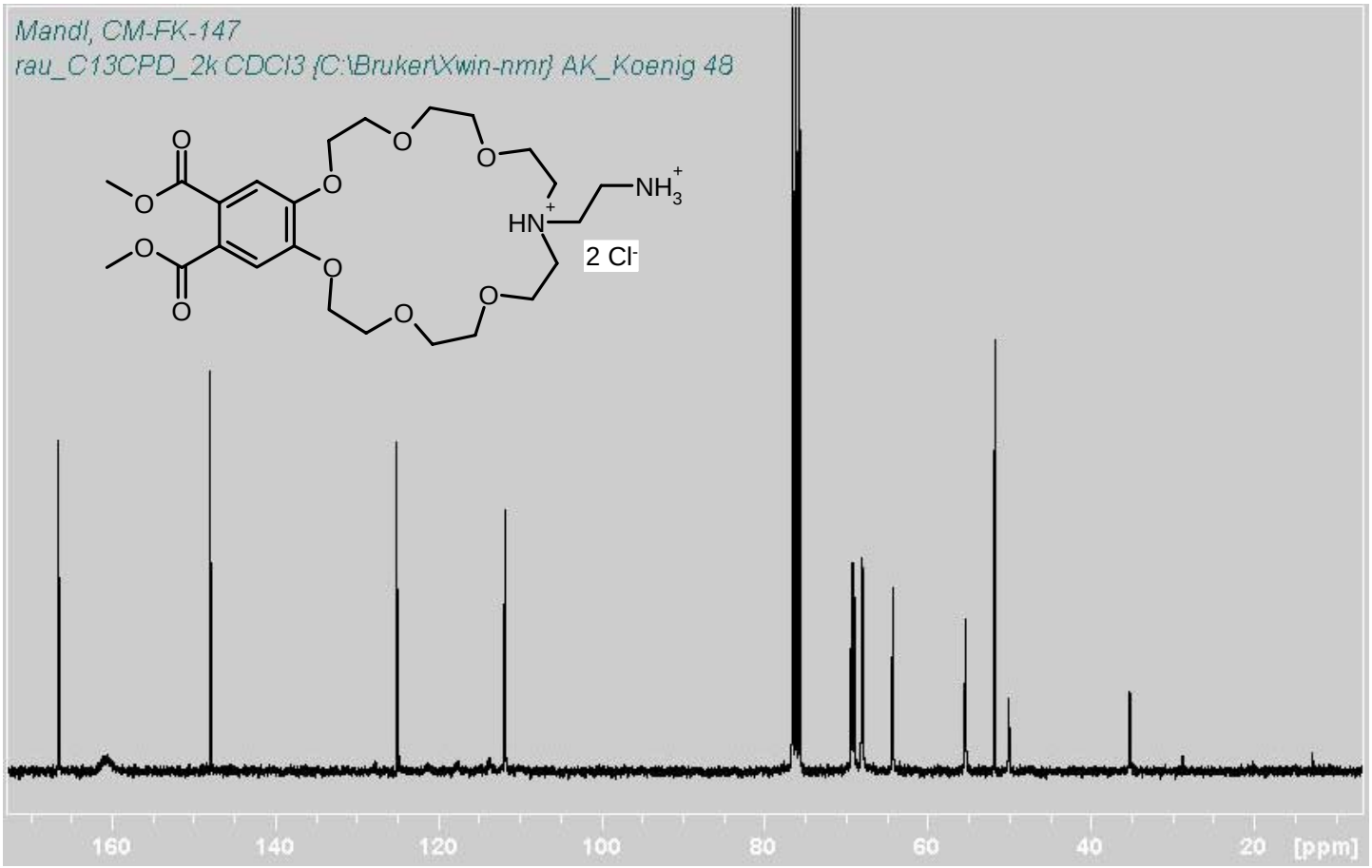
HN+
2 Cl-
12
10
8
6
4
2
[ppm]

8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HN+
2 Cl-
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60
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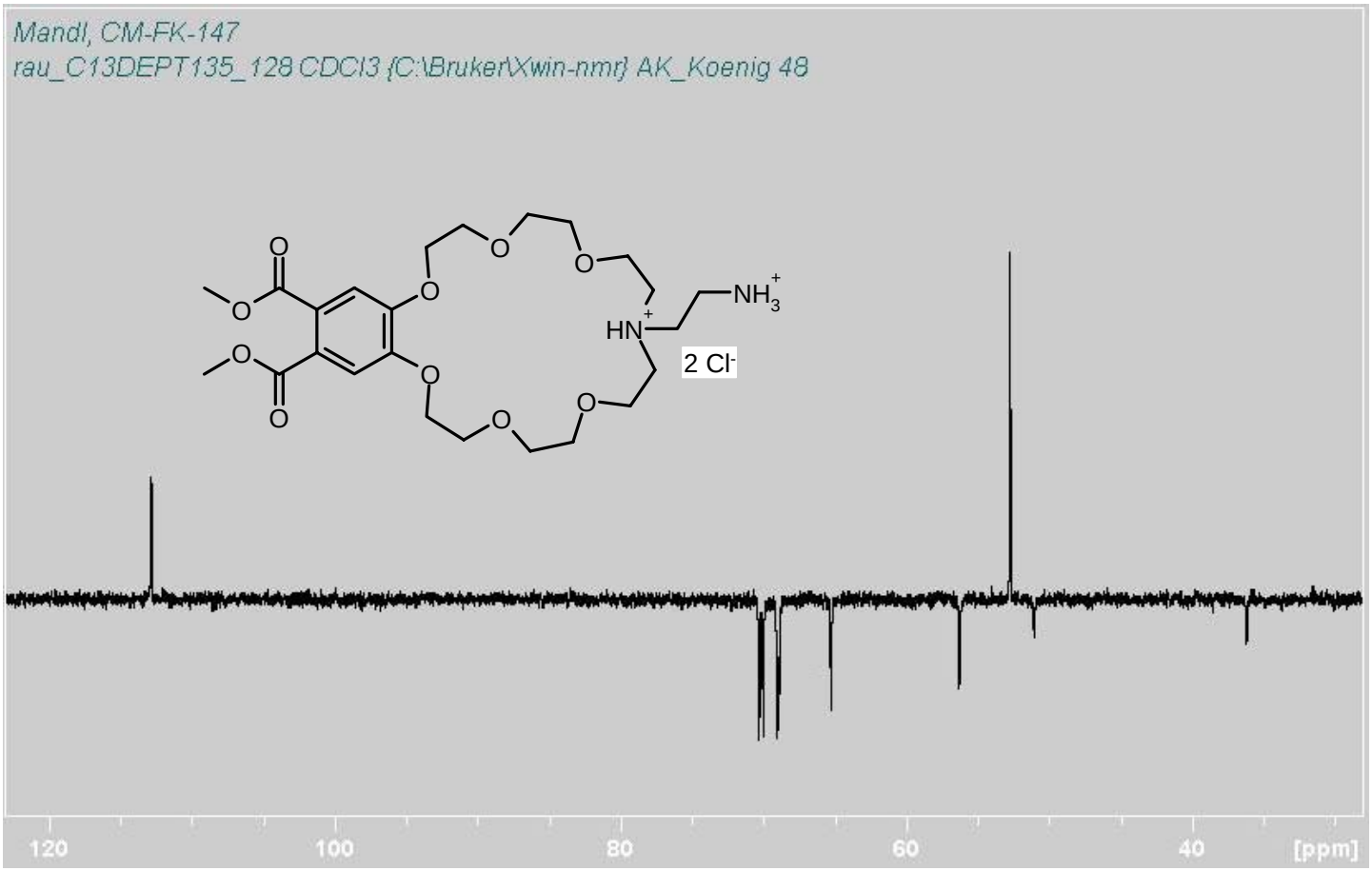
[ppm]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HN+
2 Cl-
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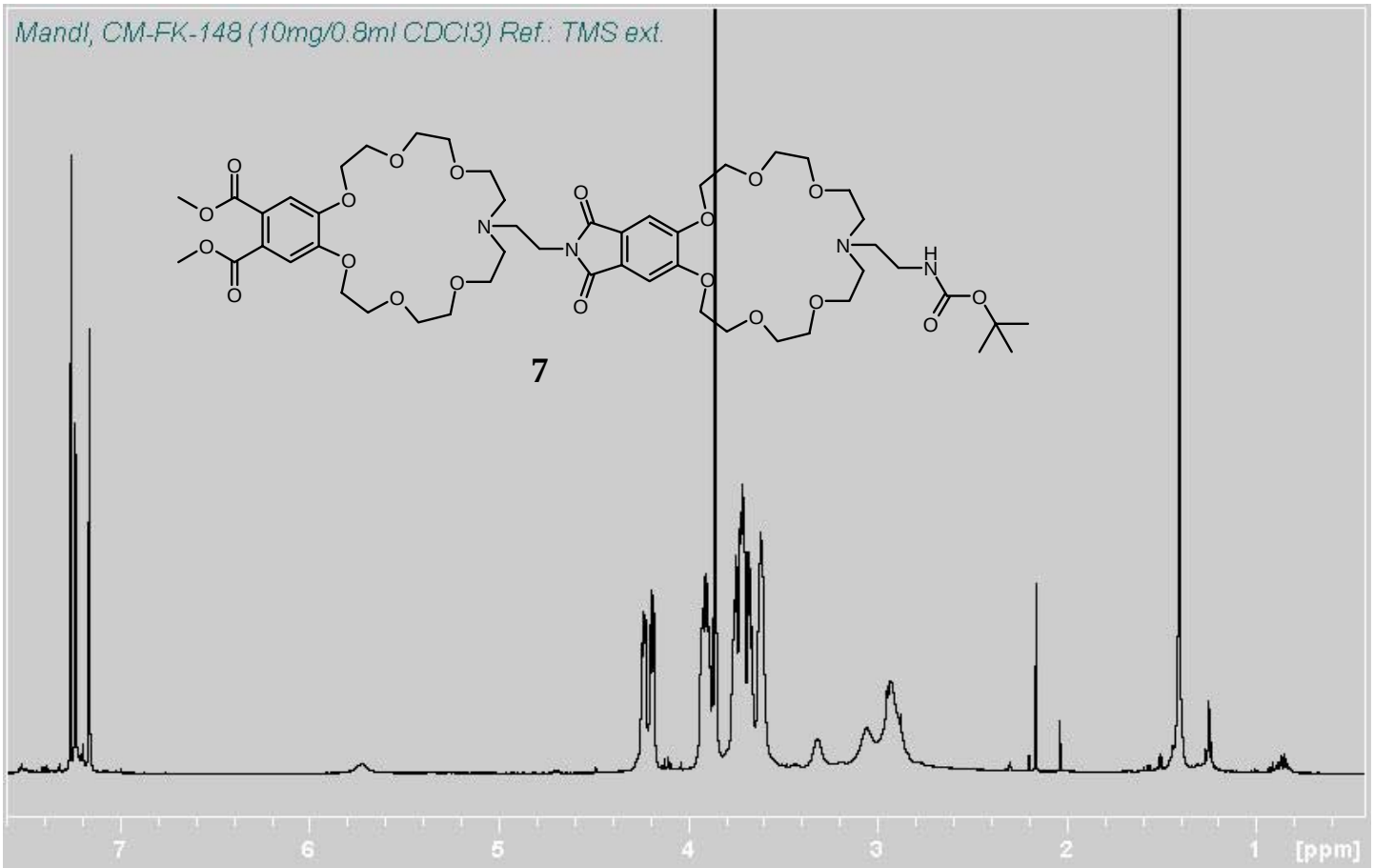
80
60
40
[ppm]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7
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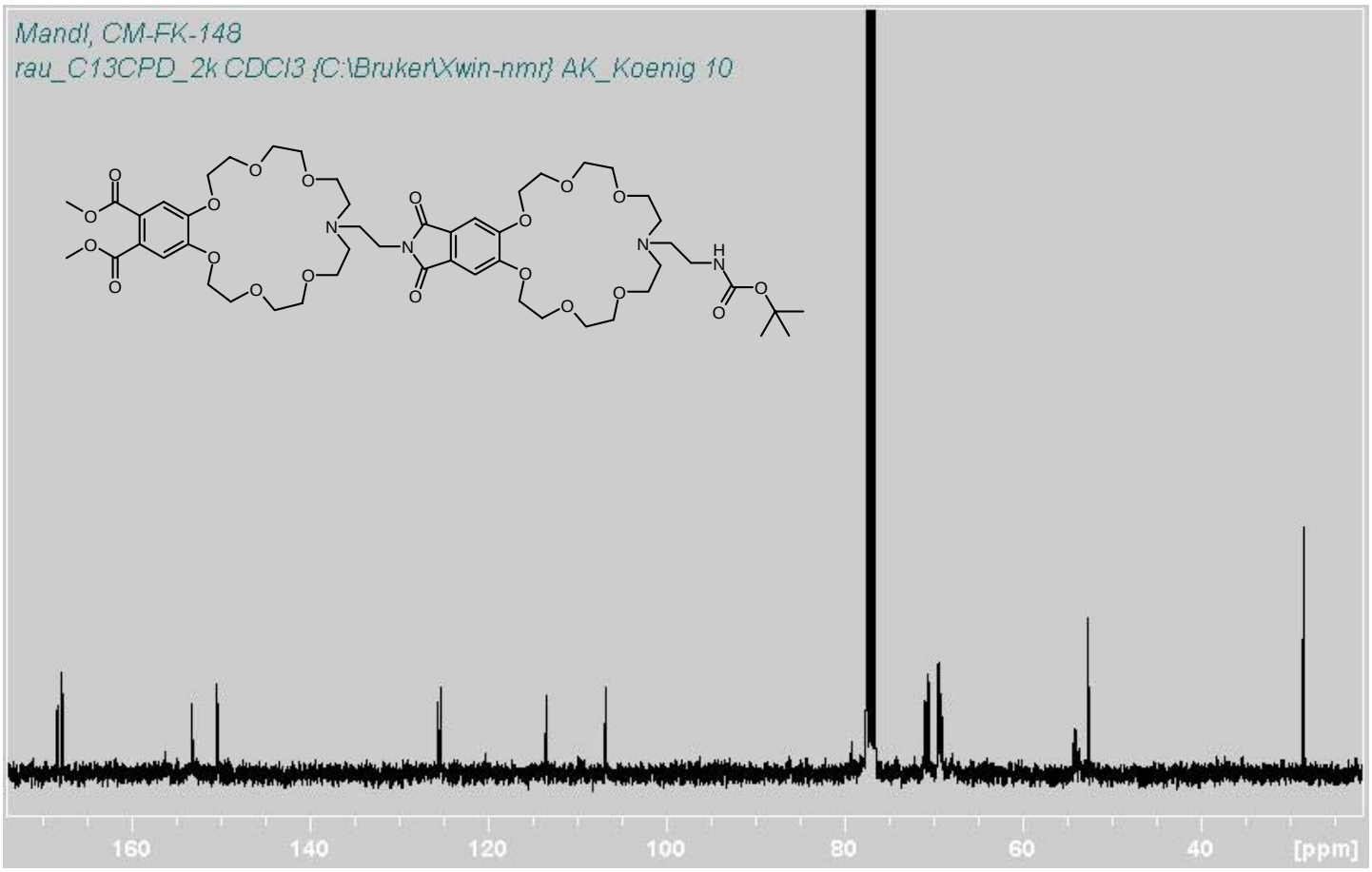
5
4
3
2
1
[ppm]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140
120
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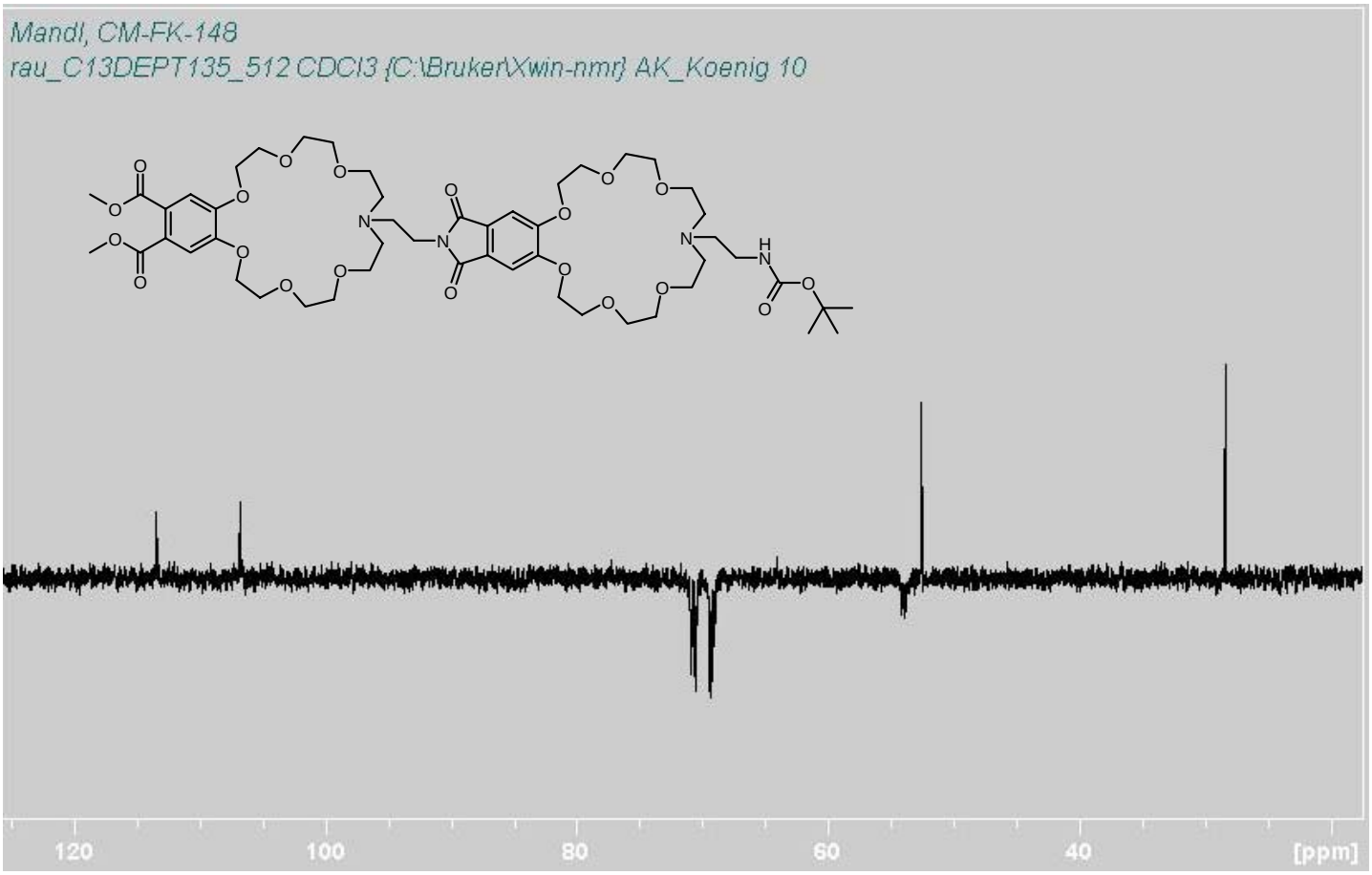
80
60
40
[ppm]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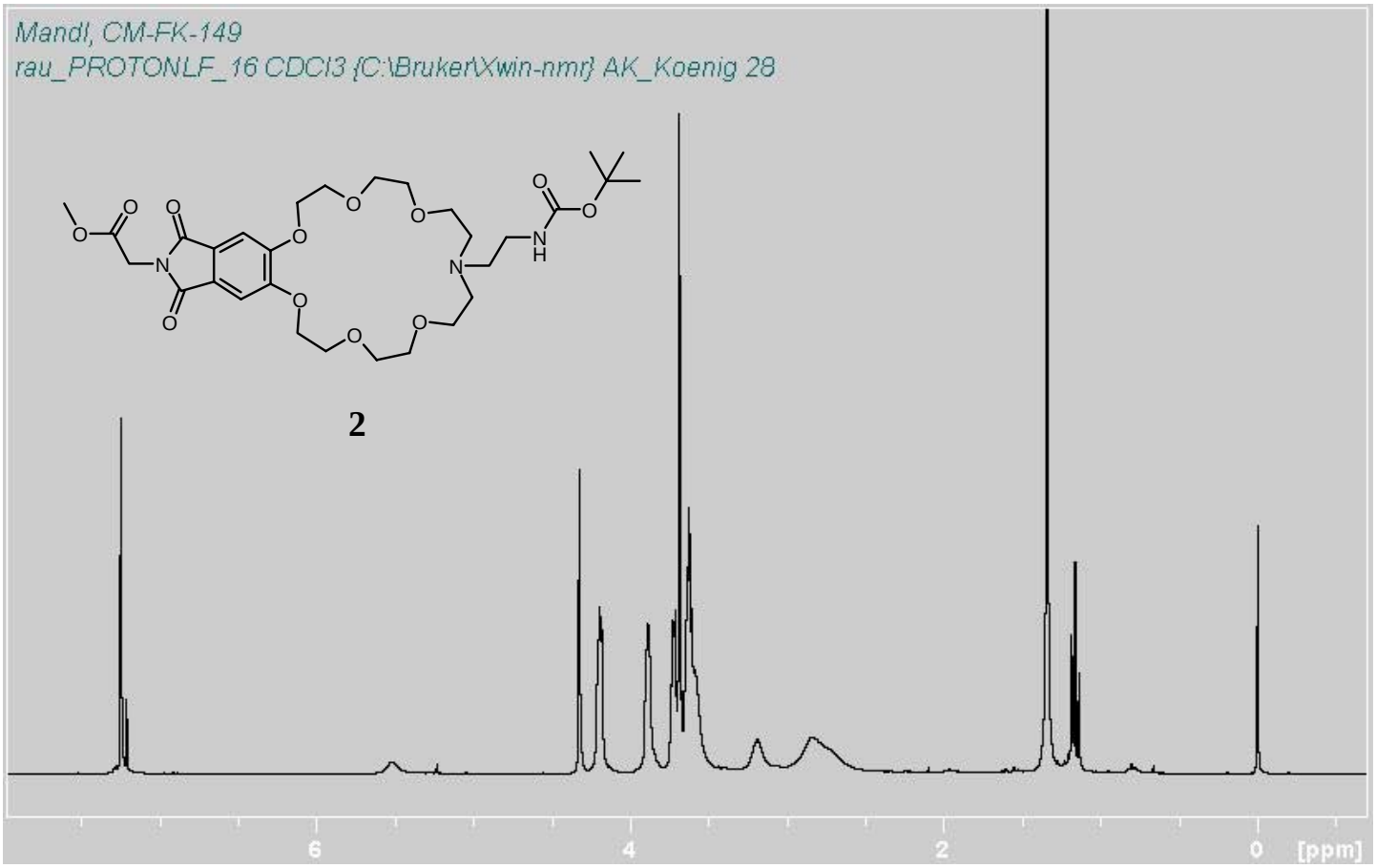
100
80
60
40
[ppm]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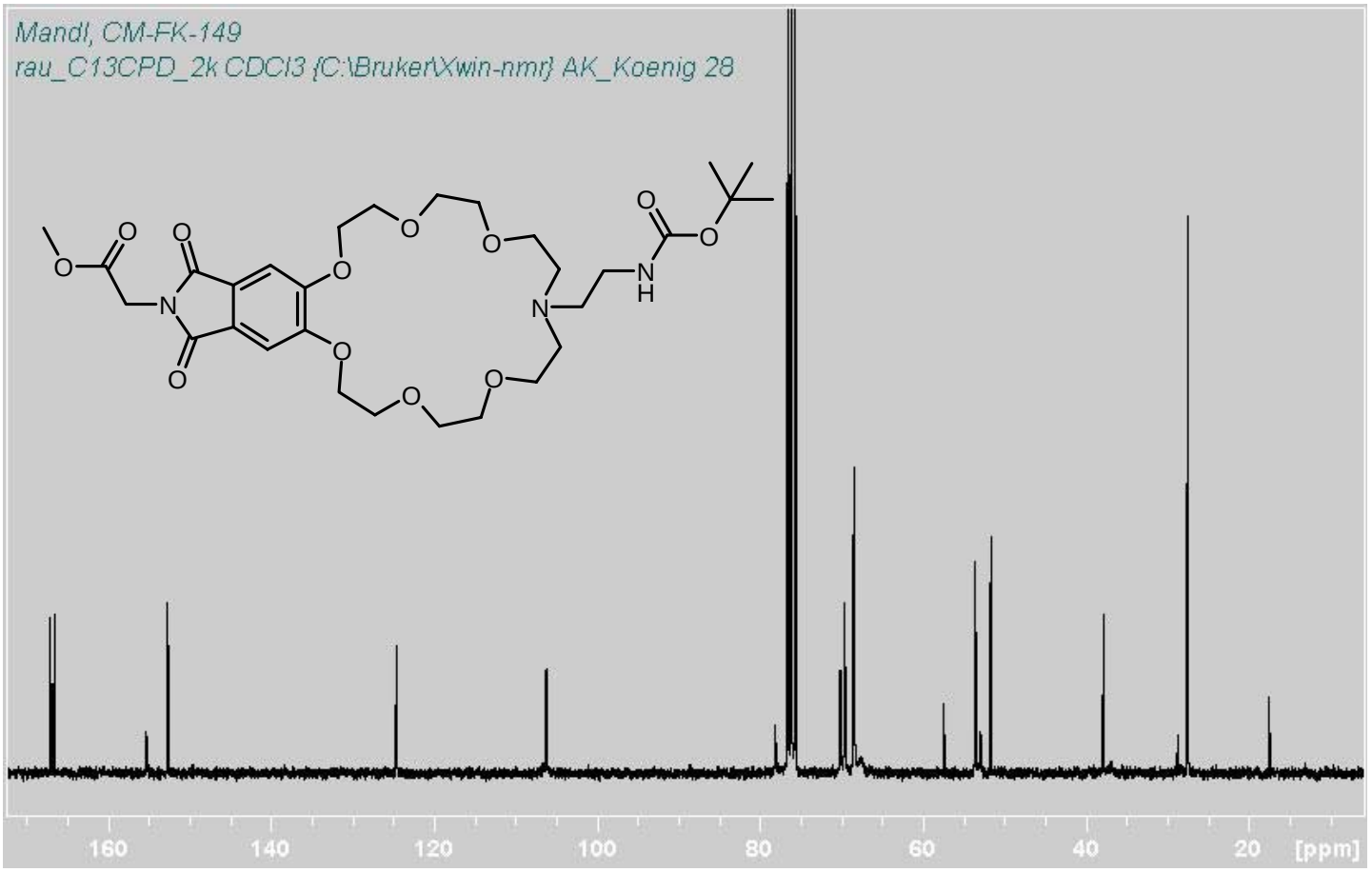
4
2
0
[ppm]

2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120
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80
60
40
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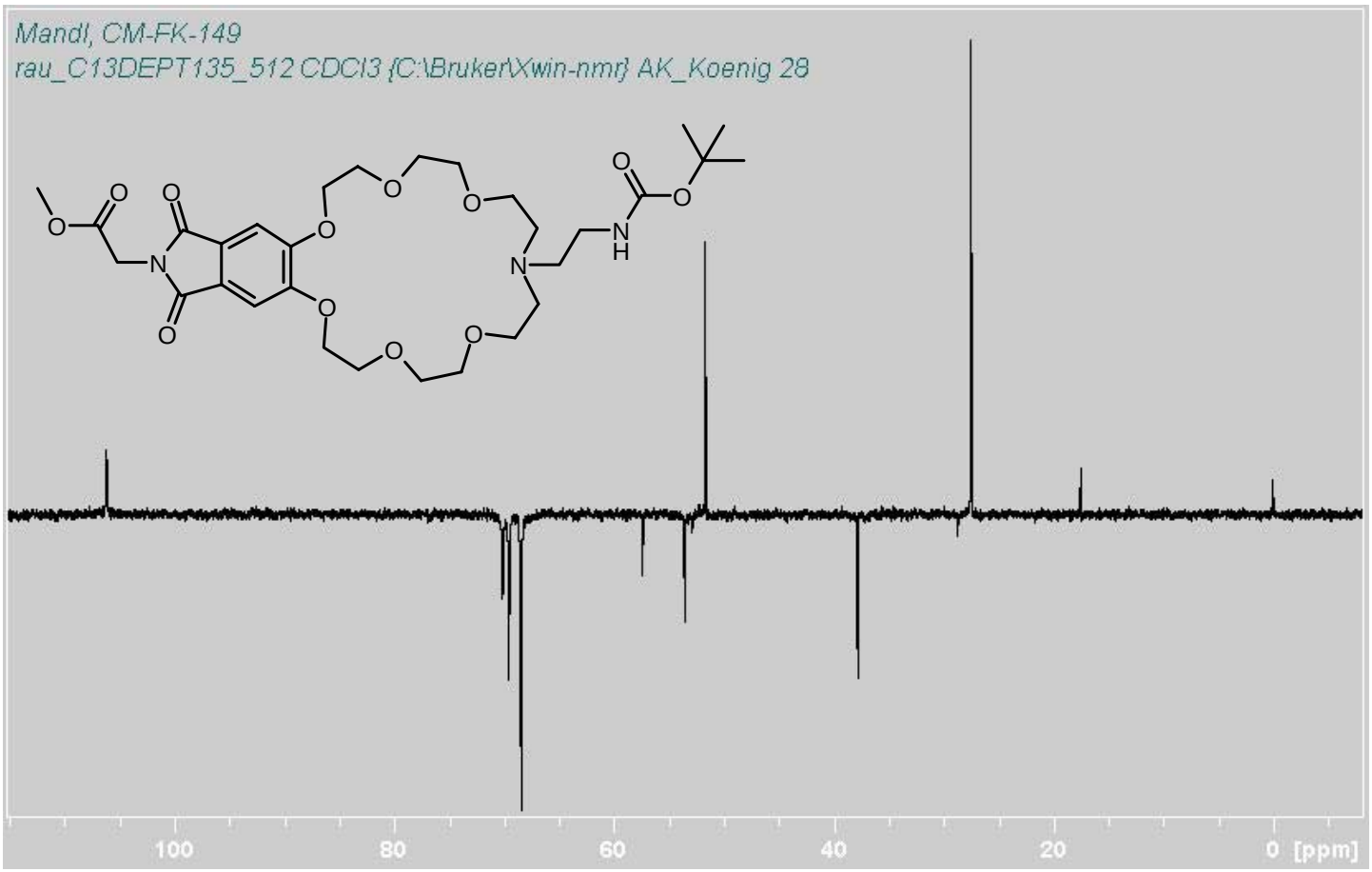
[ppm]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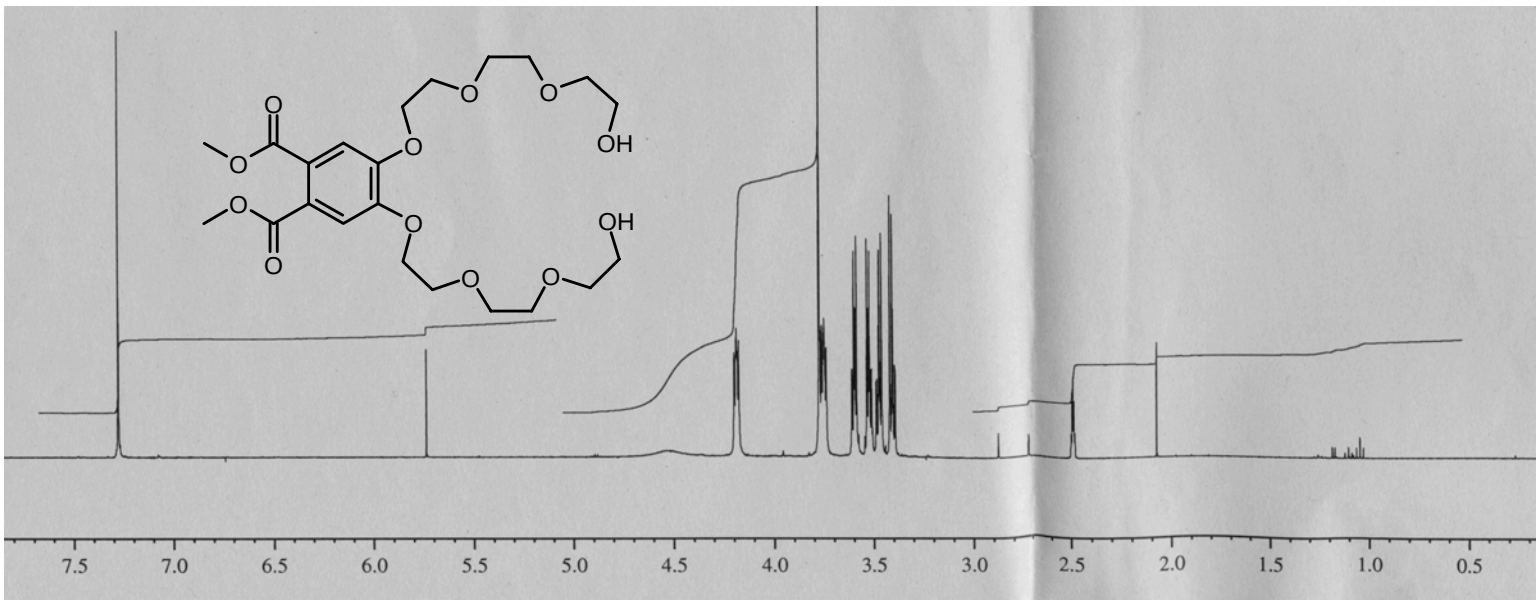
80
60
40
20
0 [ppm]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OH
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7.0
6.5
6.0
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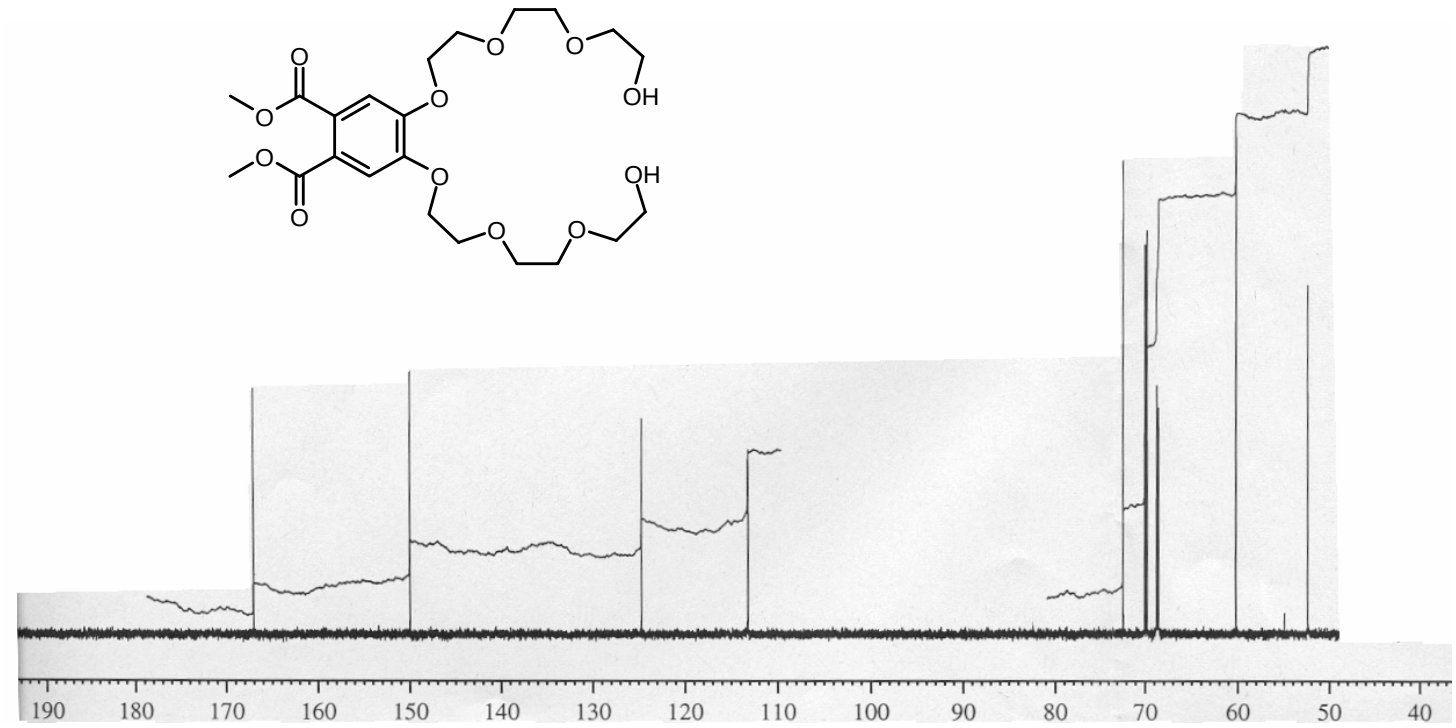
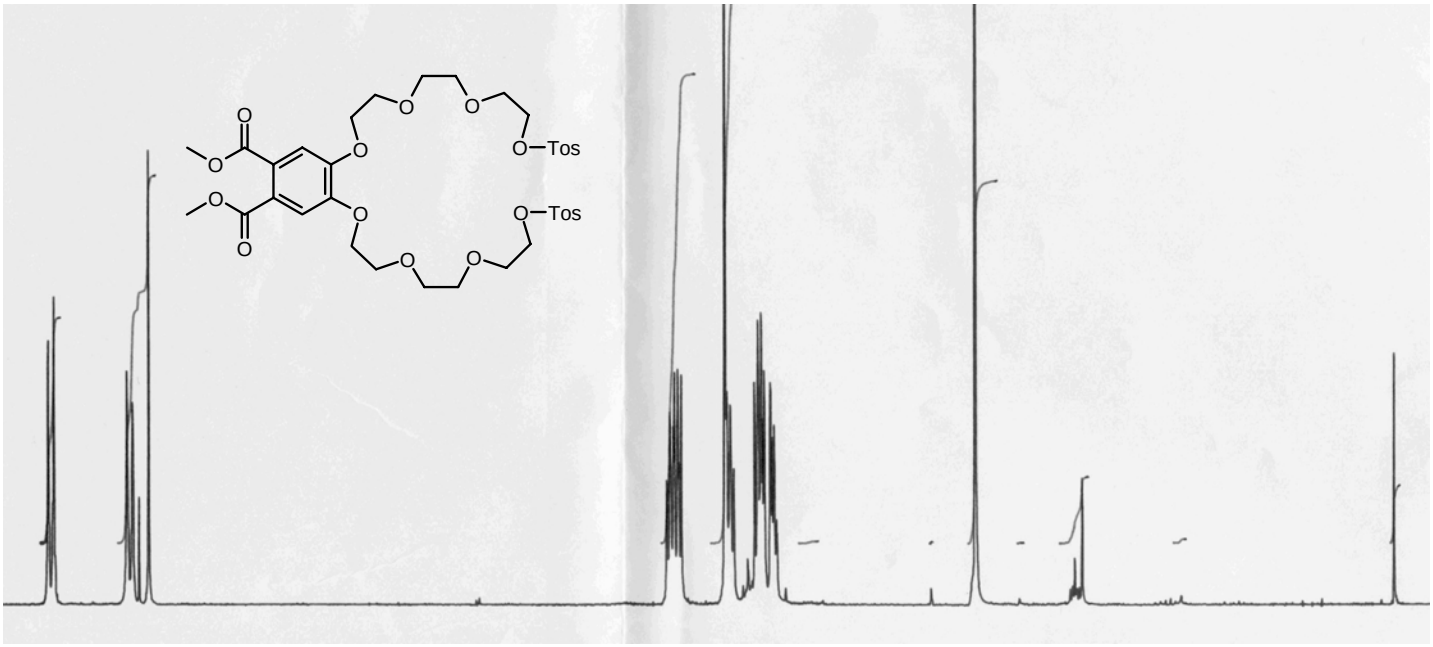
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5

Compound **5**



Compound **5**



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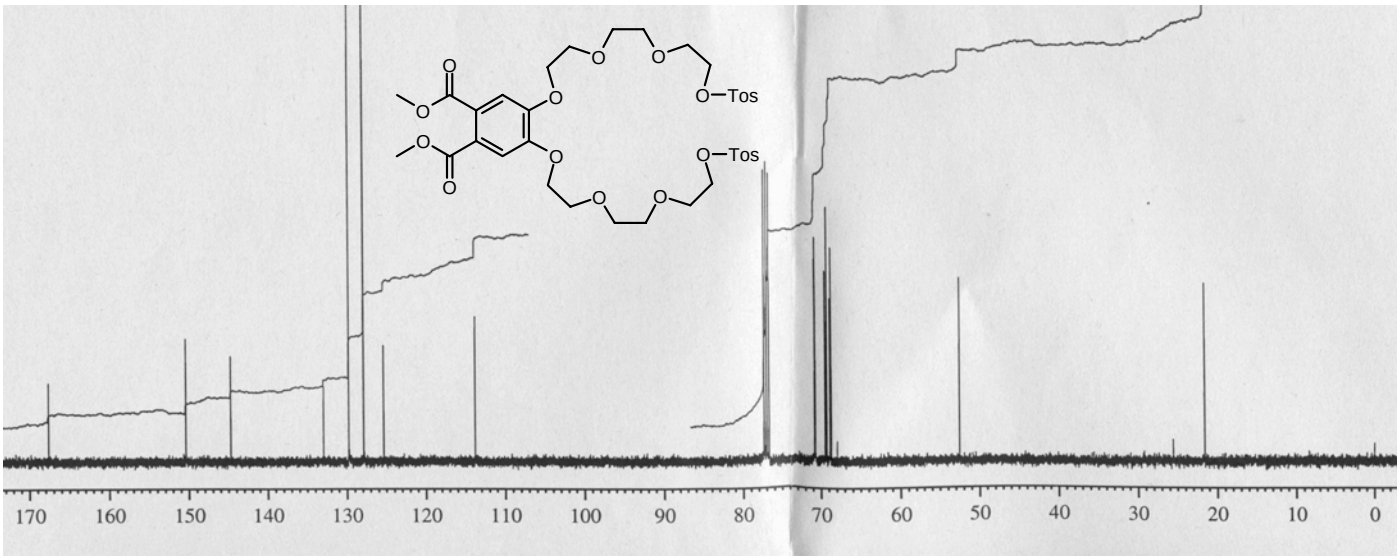
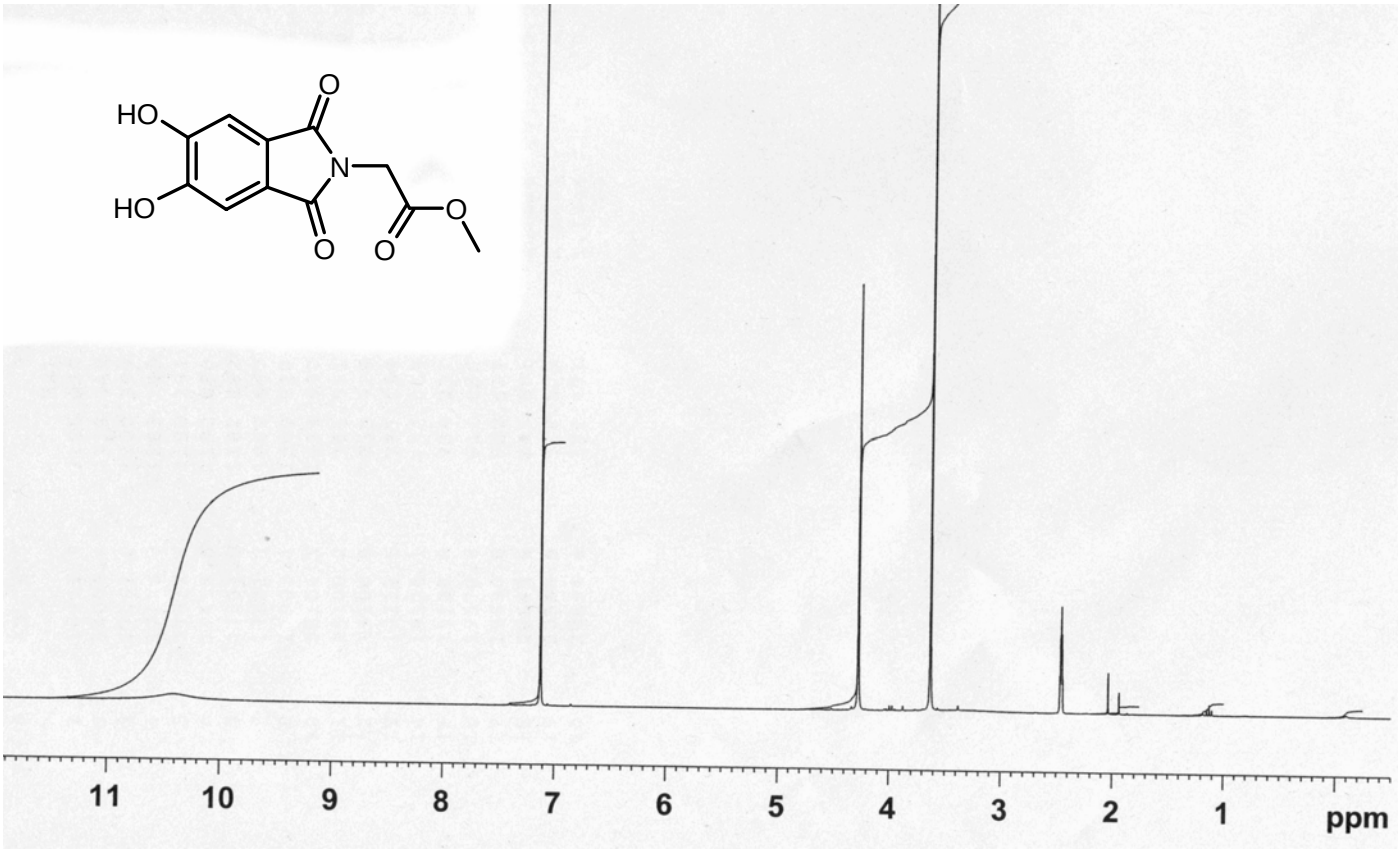


Compound **6**



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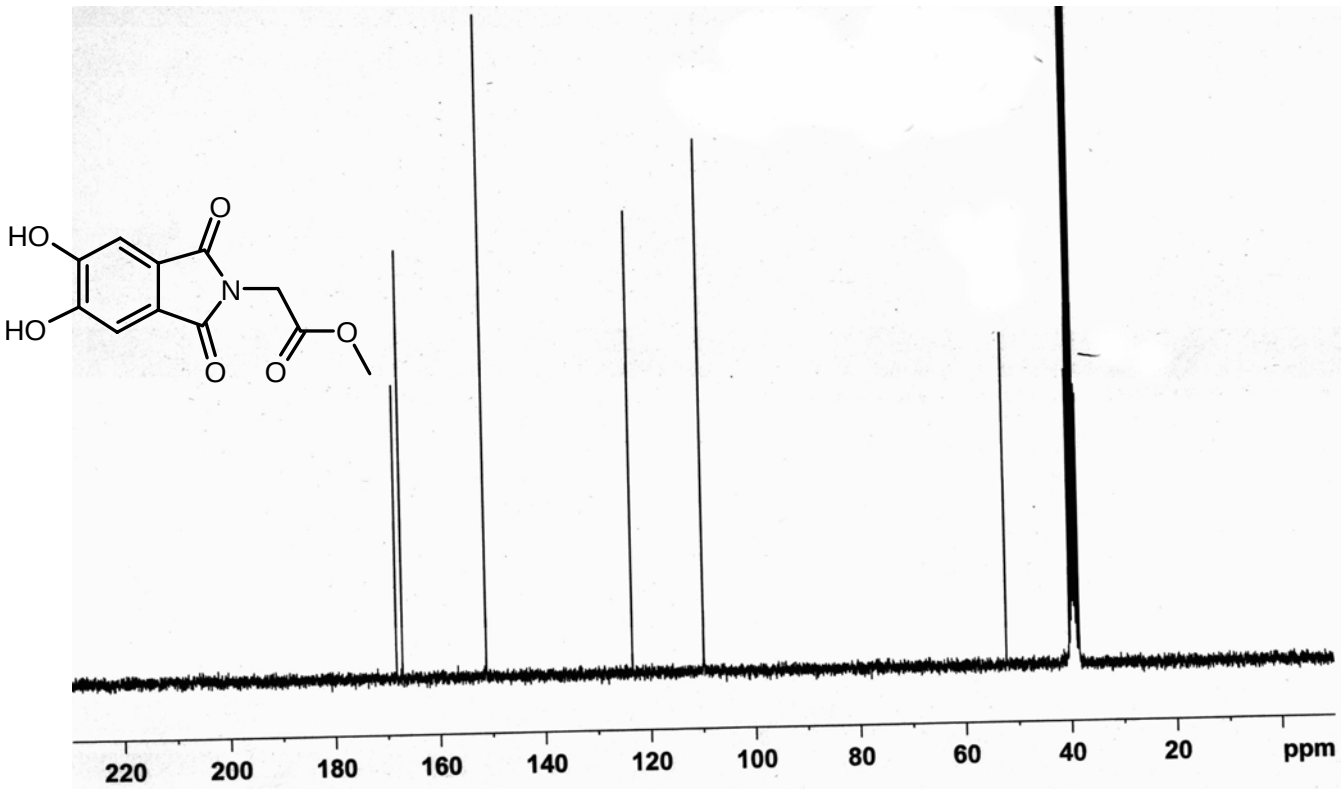

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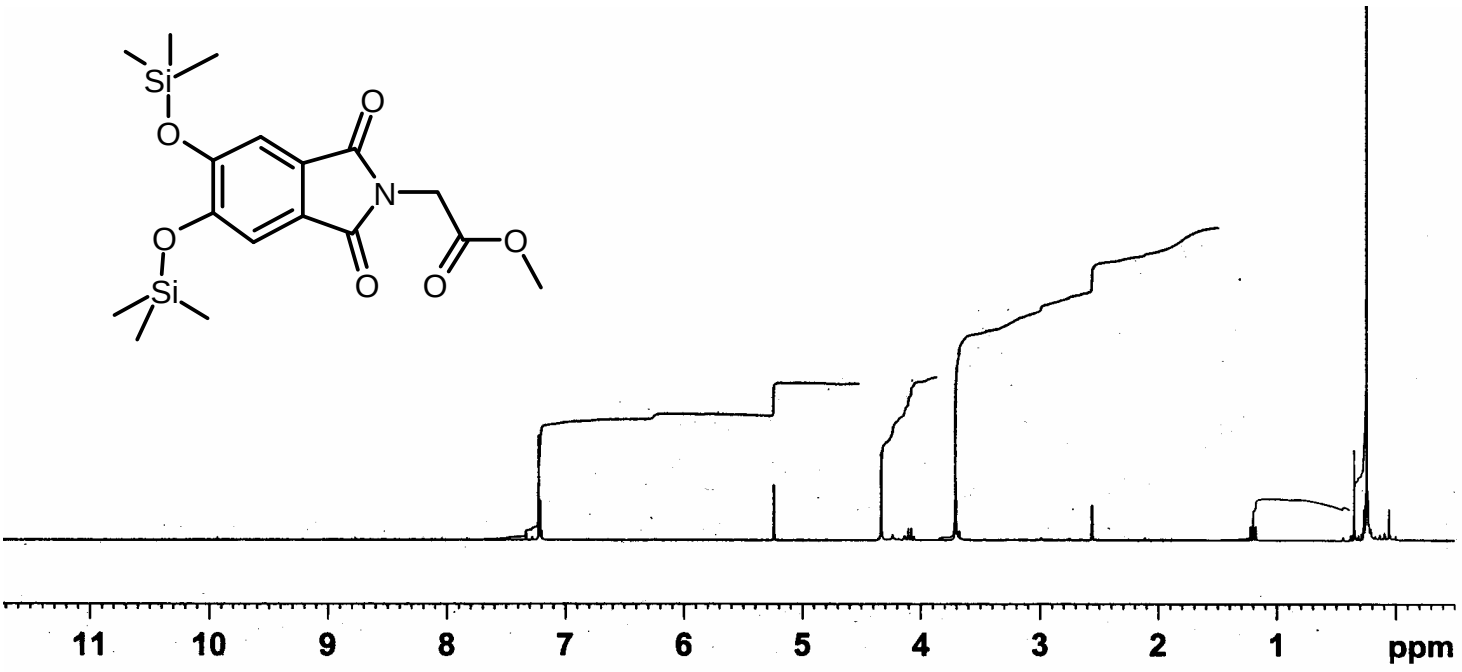
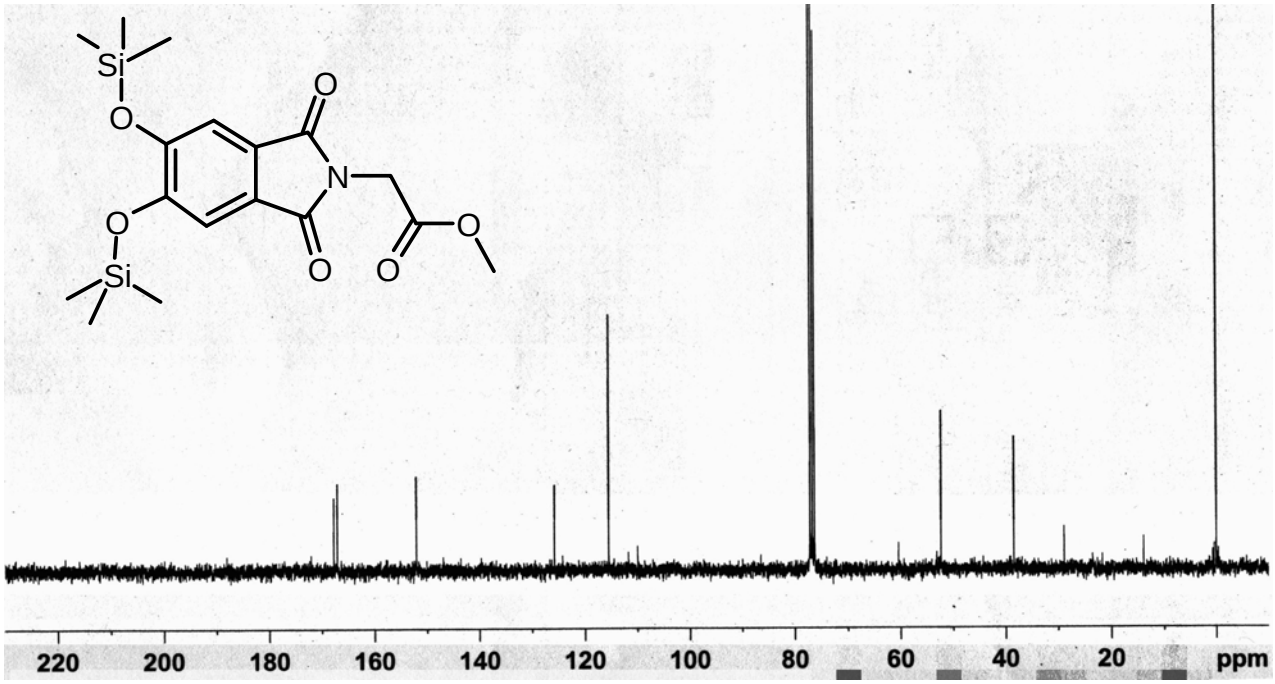
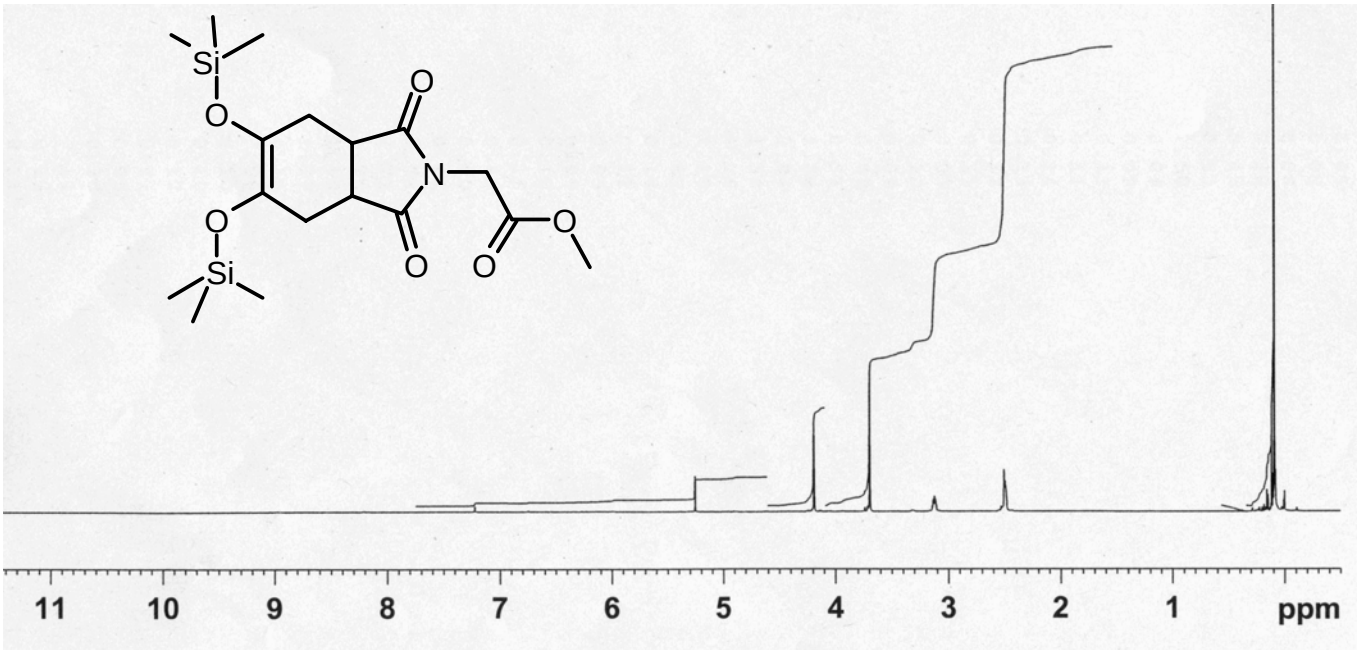


Compound **16**



Compound **16**



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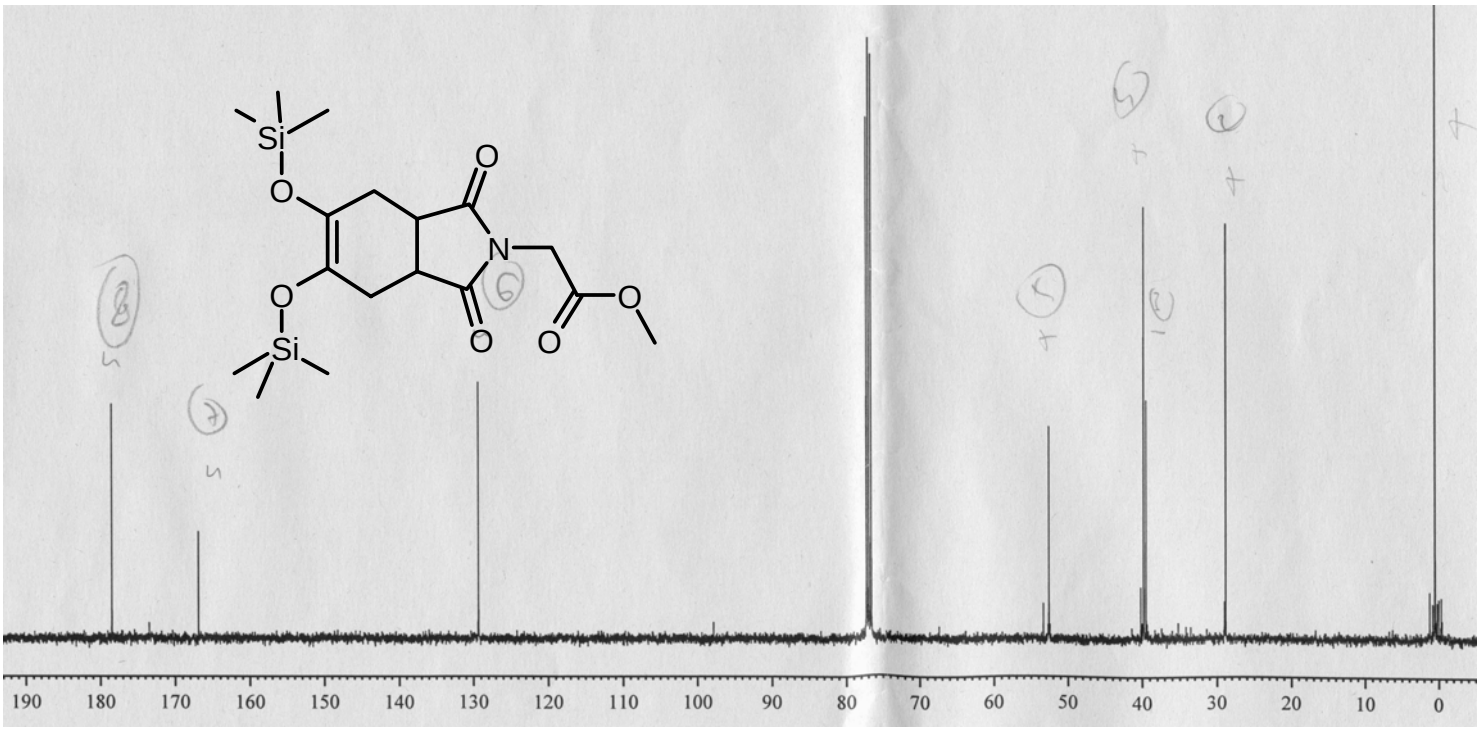
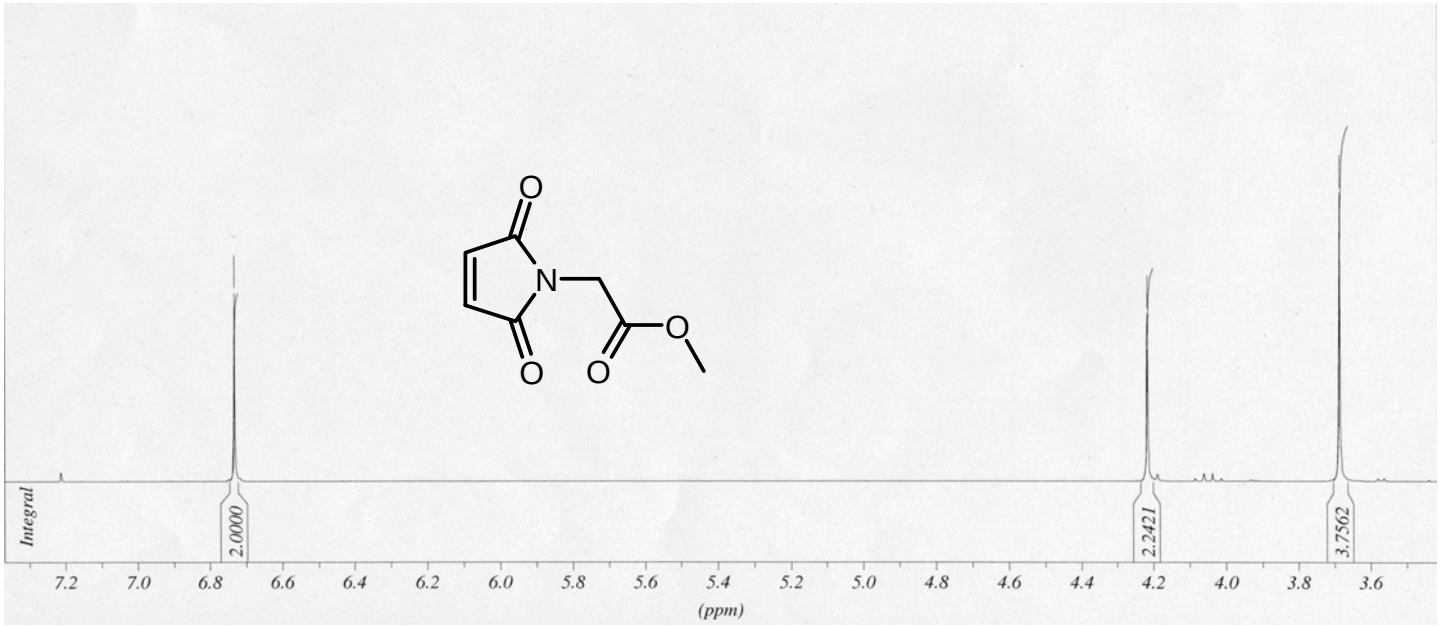
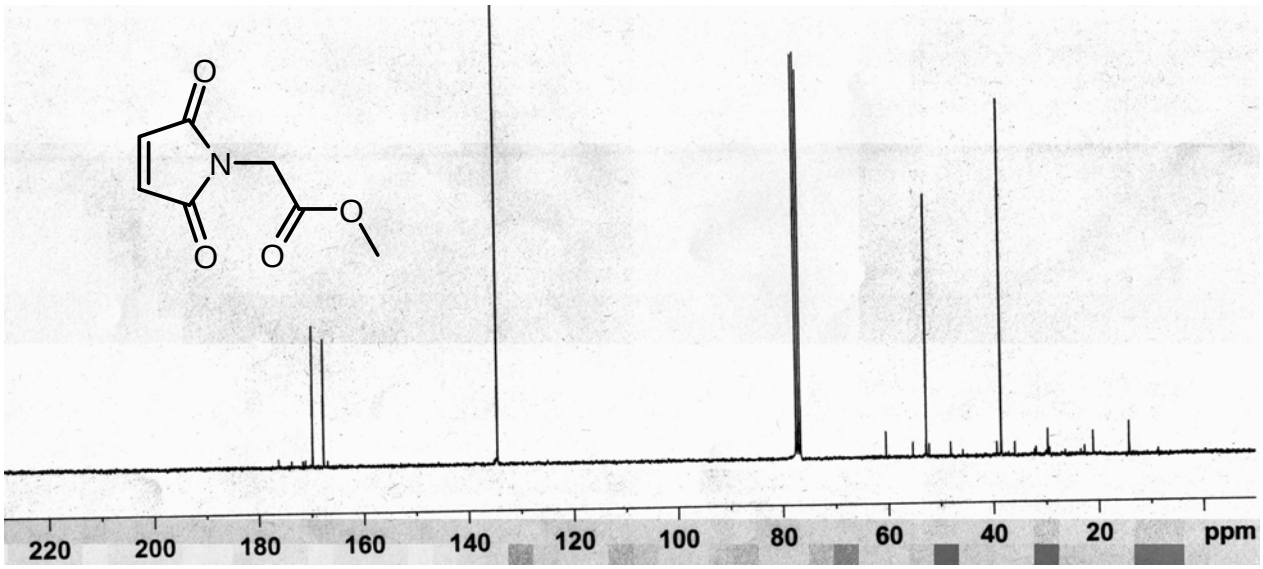


Compound **15**



Compound **14**



Compound **14**