Electronic Supplementary Information

Chiral spherical aromatic amides: one-step synthesis and their stereochemical/chiroptical properties

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Abbreviation: THF = tetrahydrofuran, IPA = isopropanol

1. Details of four structural isomers of spherical amides.

Spherical amides are composed of four meta-trisubstituted benzenes with six amide bonds. Thus, the number of carboxy and amino groups is only six in total. Based on this premise, we inspected how many structural isomers can exist by combining four monomers (**a**-**d**) (Figure S1). Each monomer has three substituents (carboxy group or amino group), with up to three being carboxy groups, and the number of carboxy groups is shown in superscript. The other substituents are amino groups, with the number of amino groups shown in subscript. Because an amide bond is formed by a carboxy group and an amino group, combinations containing two **a**'s or two **d**'s are eliminated in spherical amides where all monomers are adjacent. As a result, possible combinations with six carboxy and amino groups in total are only **abbb**, **bbcc**, **abcd** and **cccd**, which are corresponding to structural isomers **1**, **2**, **3** and **4**, respectively.

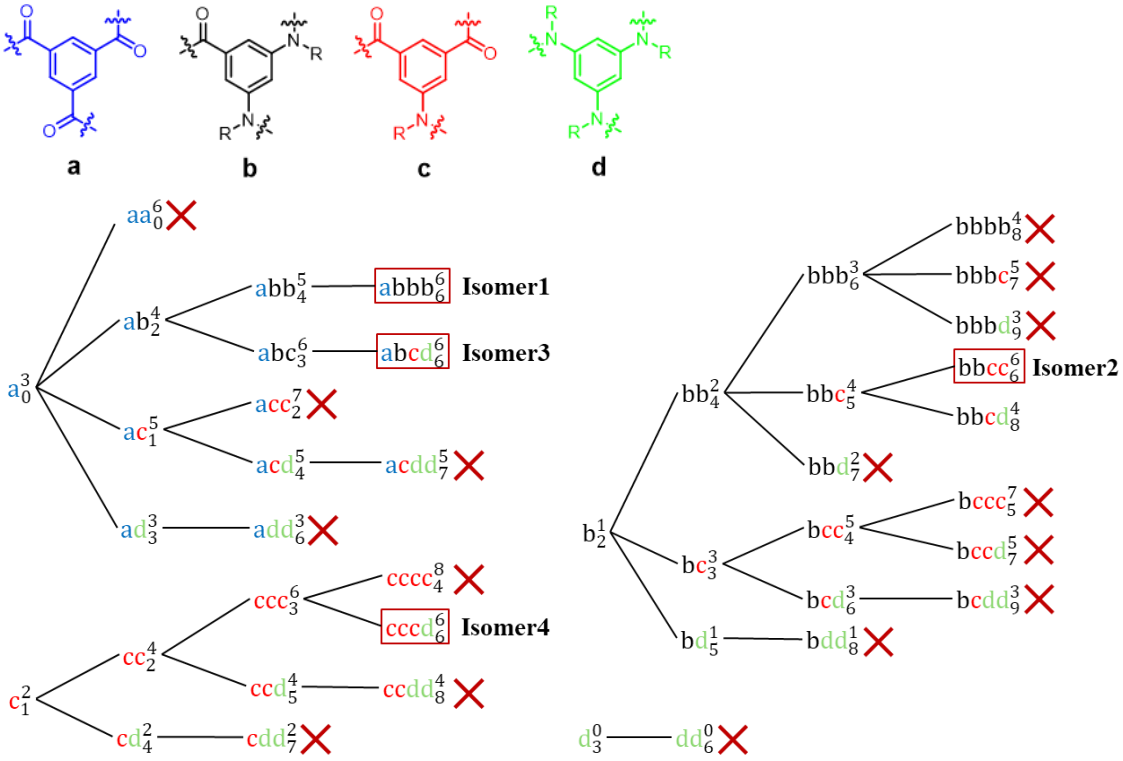


Fig. S1 Possible structural isomers of the spherical amide derived from combinations of four monomers **a**-**d**. A superscription and subscription showed a number of carboxy and amino groups respectively included in the partial structure in total.

2. General experimental

All of starting materials and solvents were purchased from KANTO CHEMICAL CO., INC., TCI, FUJIFILM Wako, JUNSEI CHEMICAL CO., LTD., Sigma-Aldrich Co. LLC, NACALAI TESQUE, INC. Ethyl 3,5-diaminobenzoate was synthesized following to the known procedure.[S1] ^{1}H and ^{13}C NMR spectra were recorded on JEOL JNM-ECS400 spectrometer (400 MHz for ^{1}H, 100 MHz for

^{13}C), and the internal standards of ^{1}H and ^{13}C NMR spectra were tetramethylsilane (0.00ppm) and solvent residual peaks. The following abbreviations are used: s = singlet, d = doublet, t = triplet, q = quartet, quin = quintet, dd = double doublet, m = multiplet, brs = broad singlet. Infrared (IR) spectra were recorded on a JASCO FT/IR-4100 spectrophotometer. Fast atom bombardment mass spectra (FAB-MS) were performed on a JEOL JMS700 MStation mass system. Column chromatography was performed on silica gel (Silica gel PSQ 100B, spherical, 3–100 nm, Fuji Silysia) with a specified solvent. Purifications with preparative gel permeation chromatography (GPC) were carried out on a Japan analytical industry LC-9210II NEXT system using tandem JAIGEL 2HH columns ($CHCl_3$ as an eluent, flow rate = 5.0 mL/min) equipped with an ultraviolet (UV) detector monitored at 254 nm. The chiral high performance liquid chromatography (HPLC) analysis was performed on a JASCO PU-2080 liquid chromatograph equipped with a UV detector (JASCO UV-2075) using a CHIRALPAK IC column (Daicel Chemical Industries, Ltd) (1.0 cm (i.d.) × 25 cm). The electronic circular dichroism (ECD) spectra of ~1.0×10^{-5} M solutions in acetonitrile were measured in 10 mm quartz cells on a JASCO J-1500 spectrophotometer. The UV spectra of ~1.0×10^{-5} M solutions in acetonitrile were measured in 10 mm quartz cells on a JASCO V730 spectrophotometer.

3. Synthesis

Synthesis of monomer compounds (7, 11)

General procedure 1 (GP1) -reductive amination-

To dimethyl 5-aminoisophthalate (**5**) and aldehyde (1.0 eq.) in THF or MeOH was added 2-picolineborane (0.5 eq.), and the reaction mixture was stirred at room temperature. After the reaction was completed, the solvent was evaporated in vacuo and 10% HCl was added to the residue. The mixture was stirred for 30 min at room temperature, and Na_2CO_3 (20% aq.) was added under cooling to make the solution alkaline. The aqueous mixture was extracted with ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography and trituration to give dimethyl 5-(alkylamino)isophthalate (**6**).

General procedure 2 (GP2) -reductive amination-

To ethyl 3,5-diaminobenzoate (**9**) and aldehyde (2 eq.) in THF or MeOH was added 2-picolineborane (1.0 eq.), and the reaction mixture was stirred at room temperature. After the reaction was completed, the solvent was evaporated in vacuo and 10% HCl was added to the residue. The mixture was stirred for 30 min at room temperature, and Na_2CO_3 (20% aq.) was added under cooling to make the solution alkaline. The aqueous mixture was extracted with ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography and trituration to give ethyl 3,5-bis(alkylamino)benzoate (**10**).

General procedure 3 (GP3) -hydrolysis-

To dimethyl 5-(alkylamino)isophthalate (**6**) or ethyl 3,5-bis(alkylamino)benzoate (**10**) in EtOH was added 4 M NaOH and the solution was stirred at 90 ℃ under argon atmosphere. After the reaction was completed, 2 M HCl was added under cooling to make the solution acidic. The mixture was extracted with ethyl acetate, and the organic layer was washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by trituration to obtain 5-(alkylamino)isophthalic acid (**7**) or 3,5-bis(alkylamino)benzoic acid (**11**).

Dimethyl 5-(methylamino)isophthalate (6a)

A sealed tube (40 mL of internal volume) was charged with a solution of dimethyl 5-aminoisophathalate (**5**) (5.5 mmol, 1.1 g) in dimethyl carbonate (20 mL) and ethylene glycol dimethyl ether (10 mL) and NaY, zeolite (1.1 g). The reaction tube was then heated by an oil bath at 150 ℃

while the mixture was kept under magnetic stirring for 24 h. After the reaction was completed, the mixture was filtered, and the solid catalyst was thoroughly washed with MeOH. After evaporation, the residue was purified by silica gel column chromatography (ethyl acetate : *n*-hexane = 1 : 3), and compound **6a** was obtained as a yellow solid (0.59 g, 48%).; M.p.: 157 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 8.00 (dd, *J* = 1.60, 1.37 Hz, 1H), 7.43 (d, *J* = 1.37 Hz, 2H), 4.04 (brs, 1H), 3.92 (s, 6H), 2.91 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.8, 149.4, 131.3, 119.2, 117.1, 52.3, 30.7; IR (KBr): 3404, 3007, 2957, 2807, 1722, 1608, 1444, 1264, 1003, 754, 722 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{11}H_{13}NO_4$: 224.0923, found: 224.0923.

Dimethyl 5-(ethylamino)isophthalate (6b)

According to **GP1**, to a solution of compound **5** (10 mmol, 2.1 g) and acetaldehyde (10 mmol, 0.44 g, 1.0 eq.) in THF (50 mL) was added 2-picolineborane (5 mmol, 0.5 g, 0.5 eq.), and the mixture was stirred for 20 h. The crude product was purified by trituration (*n*-hexane). Compound **6a** was obtained as a white-yellow powder (2.0 g, 84%).; M.p.: 123 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 7.97 (dd, *J* = 1.60, 1.37 Hz, 1H), 7.41 (d, *J* = 1.37 Hz, 2H), 3.90 (s, 6H), 3.23 (q, *J* = 7.10 Hz, 2H), 1.27 (t, *J* = 7.10 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.8, 148.5, 131.3, 119.2, 117.4, 52.3, 38.4, 14.6; IR (KBr): 3390, 3009, 2966, 2876, 1726, 1706, 1614, 1370, 1310, 1275, 1238, 1161, 754 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{12}H_{15}NO_4$: 238.1079, found: 238.1079.

Dimethyl 5-(propylamino)isophthalate (6c)

According to **GP1**, to a solution of compound **5** (10 mmol, 2.1 g) and propionaldehyde (10 mmol, 0.6 g, 1.0 eq.) in MeOH (50 mL) was added 2-picolineborane (5 mmol, 0.5 g, 0.5 eq.), and the mixture was stirred for 18 h. The crude product was purified by trituration (*n*-hexane : chloroform = 1 : 2). Compound **6c** was obtained as a white powder (1.5 g, 57%).; M.p.: 100 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 7.97 (dd, *J* = 1.60, 1.37 Hz, 1H), 7.42 (d, *J* = 1.37 Hz, 2H), 3.92 (s, 7H), 3.18–3.16 (m, 2H), 1.67 (sextet, *J* = 7.33 Hz, 2H), 1.02 (t, *J* = 7.33 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.9, 148.6, 131.4, 119.2, 117.5, 52.3, 38.5, 14.7; IR (KBr): 3397, 3081, 3029, 2982, 2953, 2879, 2844, 1704, 1437, 1240, 998, 880, 756 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{17}NO_4$: 252.1236; found: 252.1235.

Dimethyl 5-(isobutylamino)isophthalate (6d)

According to **GP1**, to a solution of compound **5** (10 mmol, 2.1 g) and isobutyraldehyde (10 mmol, 0.7 g, 1.0 eq.) in MeOH (45 mL) and acetic acid (5 mL) was added 2-picolineborane (5 mmol, 0.5 g, 0.5 eq.), and the mixture was stirred for 15 h. The crude product was purified by silica gel column chromatography (*n*-hexane : ethyl acetate = 2 : 1). Compound **6d** was obtained as a yellow oil (1.4 g, 51%).; M.p.: 108 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 7.97 (dd, *J* = 1.60, 1.37 Hz, 1H),

7.42 (d, J = 1.37 Hz, 2H), 3.98 (brs, 1H), 3.92 (s, 1H), 3.01 (d, J = 6.64 Hz, 2H), 1.91 (nonet, J = 6.64 Hz, 2H), 1.00 (d, J = 6.64 Hz, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 166.9, 148.7, 131.3, 118.9, 117.3, 52.2, 51.6, 28.0, 20.4; IR (KBr): 3413, 3399, 2954, 1712, 1608, 1523, 1436, 1236, 1120, 1094, 1002, 869 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{17}NO_4$: 266.1392; found: 266.1392.

5-(Methylamino)isophthalic acid (7a)

According to **GP3**, compound **7a** was prepared by using compound **6a**. The crude product was purified by trituration (*n*-hexane), and compound **7a** was obtained as a yellow solid (0.42 g, 82%).; M.p.: 275–290 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ (ppm): 7.68 (dd, J = 1.60, 1.37 Hz, 1H), 7.30 (d, J = 1.60 Hz, 2H), 6.23 (m, 1H), 2.73 (d, J = 4.12 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 167.4, 148.1, 132.5, 120.6, 119.0, 31.6; IR (KBr): 2885, 2670, 2426, 2365, 1699, 1393, 1243,1200, 915, 887, 727, 675 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_9H_9NO_4$: 196.0610, found: 196.0610.

5-(Ethylamino)isophthalic acid (7b)

According to **GP3**, compound **7b** was prepared by using compound **6b**. The crude product was purified by trituration (toluene : *n*-hexane = 1 : 1), and compound **7b** was obtained as an orange solid (1.0 g, 98%).; M.p.: 267.9–270.5 °C; ^{1}H NMR (400 MHz, DMSO-d_6) δ (ppm): 7.68 (dd, J = 1.60, 1.37 Hz, 1H), 7.33 (d, J = 1.60 Hz, 2H), 6.15 (s, 1H), 3.09 (q, J = 7.10 Hz, 2H), 1.18 (t, J = 7.10 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 168.3, 150.2, 132.7, 118.1, 117.1, 38.3, 15.1; IR (KBr): 1695, 2635, 2833, 2965, 3430 cm^{-1}; LRMS (FAB): *m/z* = 210 $[M+H]^+$; Anal. Calcd. for $C_{10}H_{11}NO_4$: C, 57.41; H, 5.30; N, 6.70; Found: C, 57.13; H, 5.17; N, 6.68.

5-(Propylamino)isophthalic acid (7c)

According to **GP3**, compound **7c** was prepared by using compound **6c**. The crude product was purified by trituration (*n*-hexane), and compound **7c** was obtained as a white-yellow powder (1.5 g, 99%).; M.p.: 237 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ (ppm): 7.65 (dd, J = 1.60, 1.37 Hz, 1H), 7.31 (d, J = 1.60 Hz, 2H), 6.18 (brs, 1H), 3.00 (t, J = 7.10 Hz, 2H), 1.56 (sextet, J = 7.10 Hz, 2H), 0.94 (t, J = 7.33 Hz, 3H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 167.2, 149.2, 131.6, 116.9, 115.9, 44.5, 21.6, 11.5; IR (KBr): 3439, 2972, 2878, 2646, 1700, 1602, 1433, 1346, 1265, 695 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{11}H_{13}NO_4$: 224.0923, found: 224.0923.

5-(Isobutylamino)isophthalic acid (7d)

According to **GP3**, compound **7d** was prepared by using compound **6d**. The crude product was purified by trituration (toluene : *n*-hexane = 1 : 1), and compound **7d** was obtained as a white powder (0.78 g, 88%).; M.p.: 255 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ (ppm): 7.65 (t, J = 1.37 Hz,

1H), 7.34 (d, J = 1.49 Hz, 2H), 6.23 (t, J = 5.27 Hz, 1H), 2.87 (t, J = 5.72 Hz, 2H), 1.84 (nonet, J = 6.64 Hz, 1H), 0.95 (d, J = 6.64 Hz, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 167.3, 149.3, 131.7, 117.1, 115.2, 50.8, 22.2, 20.4; IR (KBr): 3395, 2959, 2874, 2642, 1730, 1690, 1605, 1461, 1403, 1349, 1316, 1278, 693 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{11}H_{13}NO_4$: 238.1079, found: 238.1079.

Ethyl 3,5-bis(methylamino)benzoate (10a)

A sealed tube (40 mL of internal volume) was charged with a solution of ethyl 3,5-diaminobenzoate (**9**) (4.8 mmol, 0.85 g) in dimethyl carbonate (30 mL) and NaY, zeolite (2.0 g). The reaction tube was then heated by an oil bath at 150 °C while the mixture was kept under magnetic stirring for 24 h. After the reaction was completed, the mixture was filtered, and the solid catalyst was thoroughly washed with MeOH. After evaporation, the residue was purified by silica gel column chromatography (ethyl acetate : *n*-hexane = 1 : 3), and compound **10a** was obtained as a brown oil (0.68 g, 68%).; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.69 (d, J = 2.06 Hz, 2H), 6.01 (t, J = 2.06 Hz, 1H), 4.33 (q, J = 7.10 Hz, 2H), 3.74 (brs, 2H), 2.84 (s, 6H), 1.37 (t, J = 7.10 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): 167.5, 150.4, 132.2, 103.4, 100.2, 60.8, 30.9, 14.5; IR (KBr): 3406, 2980, 2935, 2899, 2809, 1705, 1610, 1376, 1240, 1106, 1025, 768 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{11}H_{16}N_2O_2$: 209.1290, found: 209.1290.

Ethyl 3,5-bis(ethylamino)benzoate (10b)

According to **GP2**, to a solution of compound **9** (10 mmol, 1.8 g) and acetaldehyde (20 mmol, 0.88 g, 2.0 eq.) in THF (50 mL) was added 2-picolineborane (10 mmol, 1.1 g, 1.0 eq.), and the mixture was stirred at room temperature for 2 h. The crude product was purified by silica gel column chromatography (ethyl acetate : toluene = 1 : 10), and compound **10b** was obtained as a yellow oil (1.8 g, 75%).; M.p.: 36.5–37.0 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.66 (d, J = 2.29 Hz, 2H), 6.00 (t, J = 2.29 Hz, 1H), 4.31 (q, J = 7.10 Hz, 2H), 3.55 (brs, 2H), 3.15 (q, J = 7.10 Hz, 4H), 1.35 (t, J = 7.10 Hz, 3H), 1.23 (t, J = 7.10 Hz, 6H);^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): 167.5, 149.5, 132.1, 103.8, 100.8, 60.7, 38.6, 15.0, 14.4; IR (KBr): 3357, 2944, 1693, 1473, 1377, 1352, 1246, 1192, 1095, 1028, 955, 845, 764, 437 cm^{-1}; LRMS (FAB): *m/z* = 237 $[M+H]^+$; Anal. Calcd. for $C_{13}H_{20}N_2O_2$: C, 66.07; H, 8.53; N, 11.85; Found: C, 65.99; H, 8.52; N, 11.86.

Ethyl 3,5-bis(propylamino)benzoate (10c)

According to **GP2**, to a solution of compound **9** (10 mmol, 1.8 g) and propionaldehyde (20 mmol, 1.2 g, 2.0 eq.) in MeOH (50 mL) was added 2-picolineborane (10 mmol, 1.1 g, 1.0 eq.), and the mixture was stirred at room temperature for 2 h. The crude product was purified by silica gel column chromatography (ethyl acetate : *n*-hexane = 1 : 4), and compound **10c** was obtained as a brown oil (1.4 g, 52%).; M.p.: 43 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.66 (d, J = 2.29 Hz, 2H),

6.01–6.00 (m, 1H), 4.32 (q, J = 7.10 Hz, 2H), 3.64 (brs, 2H), 3.09 (t, J = 7.10 Hz, 4H), 1.68–1.59 (m, 4H), 1.36 (t, J = 7.10 Hz, 3H), 0.99 (t, J = 7.33 Hz, 6H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): 167.5, 149.6, 132.1, 103.7, 100.7, 77.4, 77.1, 76.8, 60.7, 45.9, 22.8, 14.4, 11.7; IR (KBr): 3395.07, 3302.5, 2964.05, 1716.34, 1524.45, 1236.15 cm^{-1} ; LRMS (FAB): m/z = 265 $[M+H]^+$; Anal. Calcd. for $C_{15}H_{24}N_2O_2$: C, 68.15; H, 9.15; N, 10.60; Found: C, 68.09; H, 9.21; N, 10.05.

Ethyl 3,5-bis(isobutylamino)benzoate (10d)

According to **GP2**, to a solution of compound **9** (10 mmol, 1.8 g) and isobutyraldehyde (20 mmol, 1.4 g, 2.0 eq.) in MeOH (50 mL) was added 2-picolineborane (10 mmol, 1.1 g, 1.0 eq.), and the mixture was stirred at room temperature for 1 h. The crude product was purified by silica gel column chromatography (ethyl acetate : *n*-hexane = 1 : 5), and compound **10d** was obtained as a brown oil (2.5 g, 84%).; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.65 (d, J = 2.06 Hz, 2H), 6.00 (dd, J = 2.29, 2.06 Hz, 1H), 4.32 (q, J = 7.10 Hz, 2H), 2.93 (d, J = 6.64 Hz, 4H), 1.87 (nonet, J = 6.64 Hz, 2H), 1.36 (t, J = 7.10 Hz, 3H), 0.98 (t, J = 6.64 Hz, 12H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): 167.5, 149.6, 132.0, 103.4, 100.5, 60.7, 51.8, 28.1, 20.5, 14.4; IR (KBr): 3405, 2956, 2870, 1704, 1608, 1519, 1466, 1235, 1214, 1093, 1029, 768 cm^{-1}; HRMS (FAB) m/z $[M+H]^+$ calcd. for $C_9H_{12}N_2O_2$: 293.2229, found: 293.2229.

3,5-Bis(methylamino)benzoic acid (11a)

According to **GP3**, compound **11a** was prepared by using compound **10a**. The crude product was purified by trituration (*n*-hexane), and compound **11a** was obtained as a brown solid (0.53 g, 92%).; M.p.: 215 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ (ppm): 7.19 (d, J = 2.14 Hz, 2H), 6.89 (t, J = 2.14 Hz, 1H), 2.79 (s, 6H); ^{13}C NMR (100 MHz, DMSO-d_6) δ (ppm): 169.0, 151.1, 132.1, 102.1, 99.2, 30.3; IR (KBr): 3375, 2902, 2578, 2447, 1699, 1609, 1477, 1291 cm^{-1}; HRMS (FAB) m/z $[M+H]^+$ calcd. for $C_9H_{12}N_2O_2$: 181.0977, found: 181.0976.

3,5-Bis(ethylamino)benzoic acid (11b)

According to **GP3**, compound **11b** was prepared by using compound **10b**. The crude product was azeotrope with toluene, and purified by trituration (ethyl acetate : *n*-hexane = 1 : 6), and compound **11b** was obtained as a brown solid (0.63 g, 75%).; M.p.: 142.5 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.73 (d, J = 2.06 Hz, 2H), 6.06 (dd, J = 2.06, 2.06 Hz, 1H), 1.83 (s, 3H), 3.17 (q, J = 7.10 Hz, 4H), 3.17 (t, J = 7.10 Hz, 6H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): 172.8, 149.6, 131.0, 104.4, 101.9, 38.7, 15.0; IR (KBr): 3371, 2972, 2873, 1693 cm^{-1}; HRMS (FAB) m/z $[M+H]^+$ calcd. for $C_{11}H_{16}N_2O_2$: 209.1290, found: 209.1290.

3,5-Bis(propylamino)benzoic acid (11c)

According to **GP3**, compound **11c** was prepared by using compound **10c**. The crude product was purified by trituration (toluene: *n*-hexane = 1 : 1), and compound **11c** was obtained as a green-brown solid (0.54 g, 91%).; M.p.: 130 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-d_6) δ (ppm): 6.73 (d, *J* = 2.06 Hz, 2H), 6.06 (t, *J* = 2.06 Hz, 1H), 5.70 (brs,2H), 3.09 (t, *J* = 7.10 Hz, 4H), 1.64 (sextet, *J* = 7.10 Hz, 4H), 1.00 (t, *J* = 7.33 Hz, 6H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): 172.5, 149.5, 130.9, 104.3, 101.8, 77.4, 77.1, 76.8, 46.0, 22.7, 11.7; IR (KBr): 3383.5, 2363.34, 1685.48, 1541.81, 1213.01 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{20}N_2O_2$: 237.1603, found: 237.1603.

3,5-Bis(isobutylamino)benzoic acid (11d)

According to **GP3**, compound **11d** was prepared by using compound **10d**. The crude product was purified by trituration (toluene: *n*-hexane = 1 : 1), and compound **11d** was obtained as white solid (1.9 g, 85%).; M.p.: 135 °C; ^{1}H NMR (400 MHz, 298 K, DMSO-*d*6) δ (ppm): 6.41 (d, *J* = 2.06 Hz, 2H), 5.99 (t, *J* = 2.06 Hz, 1H), 5.53 (brs, 2H), 2.77 (d, *J* = 6.64 Hz, 4H), 1.81 (nonet, *J* = 6.64 Hz, 2H), 0.92 (d, *J* = 6.64 Hz, 12H); ^{13}C NMR (100 MHz, 298 K, DMSO-d_6) δ (ppm): 169.0, 150.2, 132.1, 102.4, 99.9, 51.6, 27.8, 21.0; IR (KBr): 3380, 2957, 2867, 2604, 2525, 1687, 1618, 1433, 1331, 1293, 847, 764 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{13}H_{20}N_2O_2$: 265.1916, found: 265.1915.

Synthesis of macrocycle (2)

General procedure 4 (GP4)

To a solution of the compound **7** and **11** in 1,1,2,2-tetrachloroethane was added triphenylphosphine and hexachloroethane (each 7.2 eq.) and stirred at 120 °C with argon bubbling for 2 h. The reaction mixture was poured into water, extracted with dichloromethane, washed with brine, dried over Na_2SO_4, and concentrated in vacuo. The residue was purified by silica gel column chromatography and gel permeation chromatography (GPC).

***N*-Methyl macrocycle (2a)**

According to **GP4**, compound **2a** was prepared by using compound **7a** (0.5 mmol, 0.098 g) and **11a** (0.5 mmol, 0.090 g) as monomers. The crude product was purified by silica gel column chromatography (chloroform, 10% MeOH) and GPC (chloroform). Compound **2a** was obtained as a white solid (0.014 g, 8.6%). Optical resolution was performed by chiral high-performance liquid chromatography using CHIRALPAK IC (acetonitrile : *n*-hexane : dichloromethane : IPA = 9 : 6 : 6 : 1). ; M.p.: ≥300 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.95 (dd, *J* = 1.72, 1.60 Hz, 1H), 6.94 (dd, *J* = 1.83, 1.60 Hz, 1H), 6.89–6.93 (m, 4H), 6.86 (dd, *J* = 1.72, 1.60 Hz, 1H), 6.85 (dd, *J* = 1.72, 1.37 Hz, 1H), 6.80 (dd, *J* = 1.60, 1.37 Hz, 1H), 6.79 (dd, *J* = 1.72, 1.60 Hz, 1H), 6.75 (dd, *J* =

2.06, 2.06 Hz, 1H), 6.74 (dd, *J* = 2.18, 2.16 Hz), 3.31 (s, 3H), 3.30 (s, 6H), 3.29 (s, 3H), 3.27 (s, 6H); ^{13}C NMR (100 MHz, $CDCl_3$) δ (ppm): (169.2, 169.1, 169.0, 168.9: 6C for signals of the carbonyl carbon in the region of 169.2-168.9 ppm), 145.6, 145.3, 143.9, 140.6, 139.22, 139.20, 129.3, 127.9, 127.6, 126.7, 126.6, 126.4, 126.3, 125.2, 125.1, 53.4, 38.3, 37.9, 37.7, 29.7; IR (KBr): 3406, 3060, 2927, 1652, 1594, 1378, 1119, 708 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{36}H_{30}N_6O_6$: 643.2305, found: 643.2305; $[\alpha]_D^{20}$($CHCl_3$: MeOH = 1 : 1): +1.7500 ((+)-**2a**, 1st eluent of chiral HPLC), -2.1800 ((-)-**2a**, 2nd eluent of chiral HPLC.

***N*-Ethyl macrocycle (2b)**

According to **GP4**, compound **2b** was prepared by using compound **7b** (0.5 mmol, 0.10 g) and **11b** (0.5 mmol, 0.10 g) as monomers. The crude product was purified by silica gel column chromatography (chloroform, 3% MeOH) and GPC (chloroform). The compound **2b** was obtained as a white solid (0.022 g, 12%). Optical resolution was performed by chiral high-performance liquid chromatography using CHIRALPAK IC (*n*-hexane : dichloromethane : acetonitrile : 2-propanol = 12 : 4 : 1 : 1).; M.p.: 270–278 °C; ^{1}H NMR (400 MHz, $CDCl_3$) δ (ppm): 6.95 (dd, *J* = 1.72, 1.49 Hz, 1H), 6.94–6.91 (m, 2H), 6.91-6.88 (m, 2H), 6.87 (dd, *J* = 1.43, 1.37 Hz, 1H), 6.78 (dd, *J* = 2.00, 1.49 Hz, 1H), 6.77 (dd, *J* = 2.06, 1.49 Hz, 1H), 6.73-6.75 (m, 2H), 6.63 (dd, *J* = 2.06, 1.83 Hz, 1H), 6.62 (dd, *J* = 1.83, 1.83 Hz, 1H), 3.99–3.59 (m, 12H), 1.09–1.22(m, 18H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): (168.74, 168.67, 168.59, 168.52: 6C for signals of the carbonyl carbon in the region of 168.74-168.52 ppm), 143.8, 143.5, 143.3, 142.7, 142.2, 141.1, 140.7, 140.0, 139.38, 139.35, 131.4, 131.2, 129.1, 128.7, 128.1, 127.22, 127.16, 126.9, 126.8, 125.2, 125.0, 45.5, 45.1, 45.0, 44.8, 12.90, 12.86, 12.80, 12.7; IR (KBr): 3565, 3059, 2977, 2937, 2877, 1635, 1593, 1327, 1128, 792 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{42}H_{42}N_6O_6$: 727.3244; found: 727.3244.

***N*-Propyl macrocycle (2c)**

According to **GP4**, compound **2c** was prepared by using compound **7c** (0.5 mmol, 0.11 g) and **11c** (0.5 mmol, 0.12 g) as monomers. The crude product was purified by silica gel column chromatography (chloroform, 3% MeOH) and GPC (chloroform). The compound **2c** was obtained as a white solid (0.031g, 14%). Optical resolution was performed by chiral high-performance liquid chromatography using CHIRALPAK IC (*n*-hexane : dichloromethane : acetonitrile : IPA = 15 : 5 : 1 : 1).; M.p.: 217 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.92 (dd, *J* = 1.72, 1.60 Hz, 1H), 6.90 (dd, *J* = 1.72, 1.60 Hz, 1H), 6.89 (dd, *J* = 1.60, 1.60 Hz, 1H), 6.87 (dd, *J* = 1.60, 1.60 Hz, 1H), 6.85 (dd, *J* = 1.37, 1.37 Hz, 1H), 6.84 (dd, *J* = 1.49, 1.37 Hz, 1H), 3.82–3.48 (m, 12H), 1.68–1.45 (m, 12H), 1.00–0.88 (m, 18H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): (168.86, 168.82, 168.78, 168.71, 168.6: 6C for signals of the carbonyl carbon in the region of 168.68-168.6 ppm), 144.2, 144.0, 143.7, 143.1, 142.6, 141.2, 140.7, 139.9, 139.5, 139.4, 131.1, 130.8, 128.8, 128.5, 127.9, 127.1, 127.0, 126.64, 126.58,

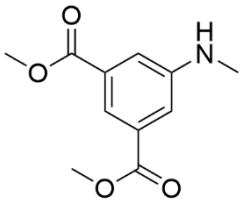
125.0, 124.8, 52.1, 51.7, 51.6, 51.5, 51.4, 20.91, 20.85, 20.82, 20.78, 11.3, 11.23, 11.21; IR (KBr): 2965, 1671, 1458, 1130 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{48}H_{54}N_6O_6$: 811.4183; found: 811.4184.

***N*-Isobutyl macrocycle (2d)**

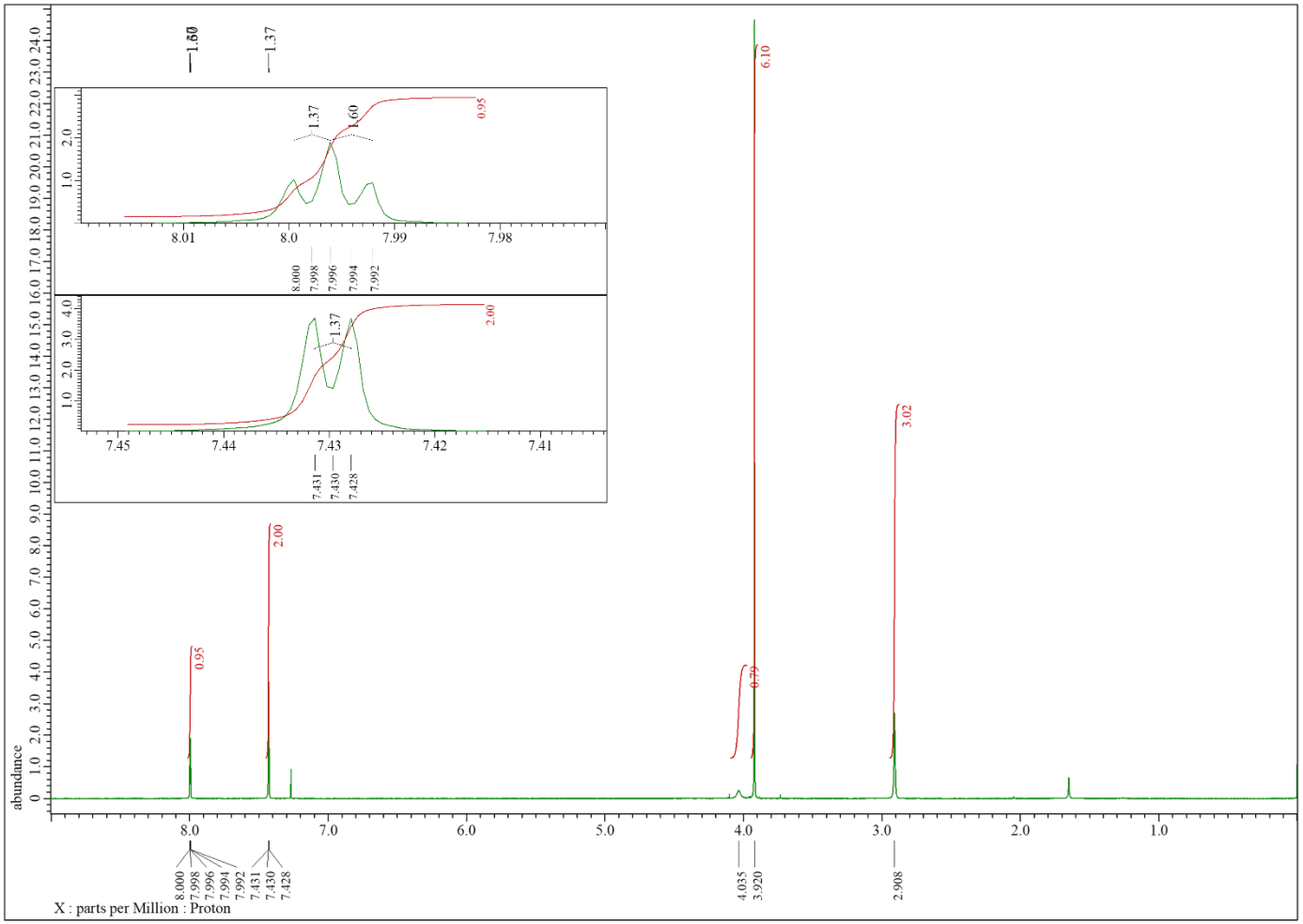
According to **GP4**, compound **2d** was prepared by using compound **7d** (0.5 mmol, 0.12 g) and **11d** (0.5 mmol, 0.13 g) as monomers. The crude product was purified by silica gel column chromatography (ethyl acetate : chloroform = 1 : 1). The compound **2d** was obtained as a white solid (0.025g, 12%). Optical resolution was performed by chiral high-performance liquid chromatography using CHIRALPAK IC (*n*-hexane : dichloromethane : IPA = 20 : 10 : 1).; M.p.: ≥300 °C; ^{1}H NMR (400 MHz, 298 K, $CDCl_3$) δ (ppm): 6.91 (dd, *J* = 1.72, 1.60 Hz, 1H), 6.88 (dd, *J* = 1.72, 1.37 Hz, 1H), 6.87 (dd, *J* = 1.77, 1.72 Hz, 1H), 6.85 (dd, *J* = 1.60, 1.37 Hz, 1H), 6.83 (dd, *J* = 1.49, 1.37 Hz, 1H), 6.82 (dd, *J* = 1.60, 1.37 Hz, 1H), 6.75 (dd, *J* = 1.72, 1.37 Hz, 1H), 6.74 (dd, *J* = 1.95, 1.37 Hz, 1H), 6.70 (dd, *J* = 1.60, 1.60 Hz, 1H), 6.69 (dd, *J* = 1.60, 1.60 Hz, 1H), 6.23 (dd, *J* = 1.72, 1.37 Hz, 1H), 6.62 (dd, *J* = 1.83, 1.83 Hz, 1H), 3.76–3.61 (m, 4H), 3.58 (s, 2H), 3.56 (s, 2H), 3.47–3.39 (m, 2H) , 3.38–3.29 (m, 2H) , 1.93–1.67 (m, 6H) , 1.10–0.92 (m, 36H); ^{13}C NMR (100 MHz, 298 K, $CDCl_3$) δ (ppm): (169.12, 169.08, 168.97, 168.92: 6C for signals of the carbonyl carbon in the region of 169.12-168.92 ppm), 144.5, 144.3, 144.3, 144.0, 143.4, 140.9, 130.5, 128.5, 128.2, 127.5, 126.7, 126.6, 126.2, 124.7, 124.6, 57.3, 56.9, 56.8, 56.6, 56.5, 26.98, 26.96, 26.91, 26.7, 20.2, 20.1, 20.1, 20.0; IR (KBr): 2961, 2872, 1660, 1651, 1402, 1135, 887, 710 cm^{-1}; HRMS (FAB) *m/z* $[M+H]^+$ calcd. for $C_{54}H_{66}N_6O_6$: 895.5122; found: 895.5122.

4. ^{1}H and ^{13}C NMR spectra

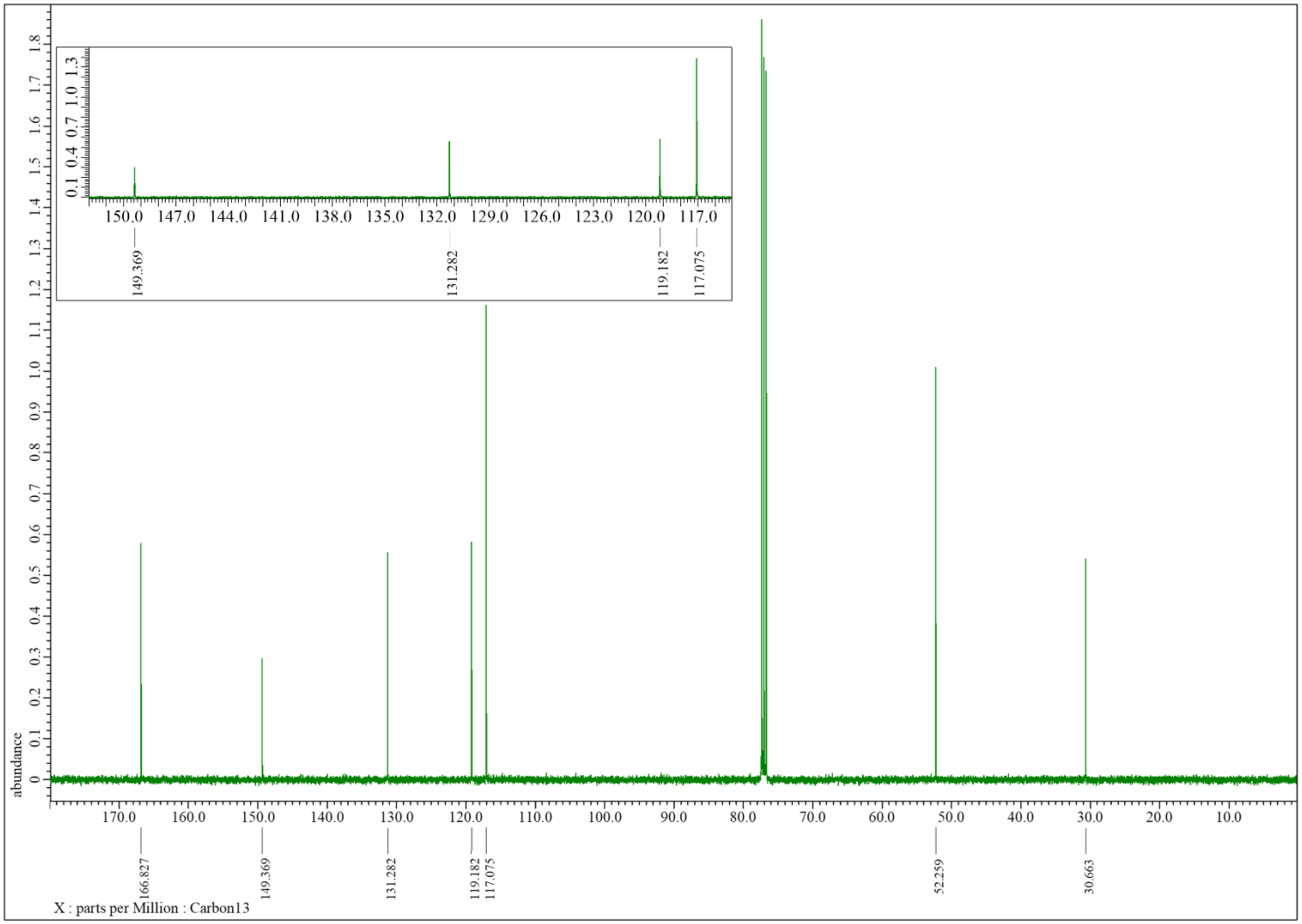
Dimethyl 5-(methylamino)isophthalate (6a)



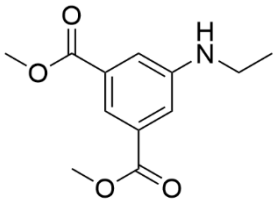
^{1}H NMR (400 MHz, $CDCl_3$)



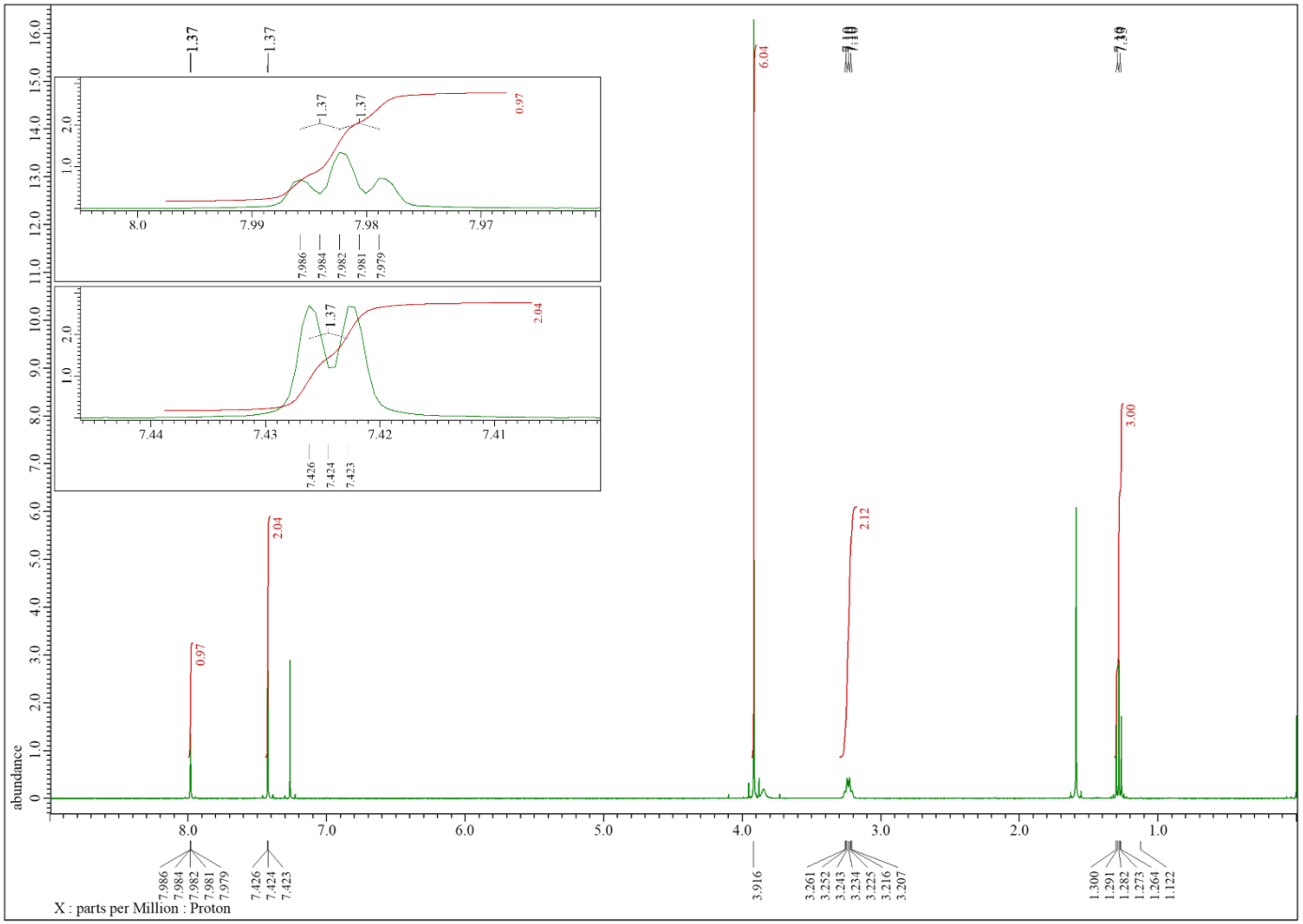
^{13}C NMR (100 MHz, $CDCl_3$)



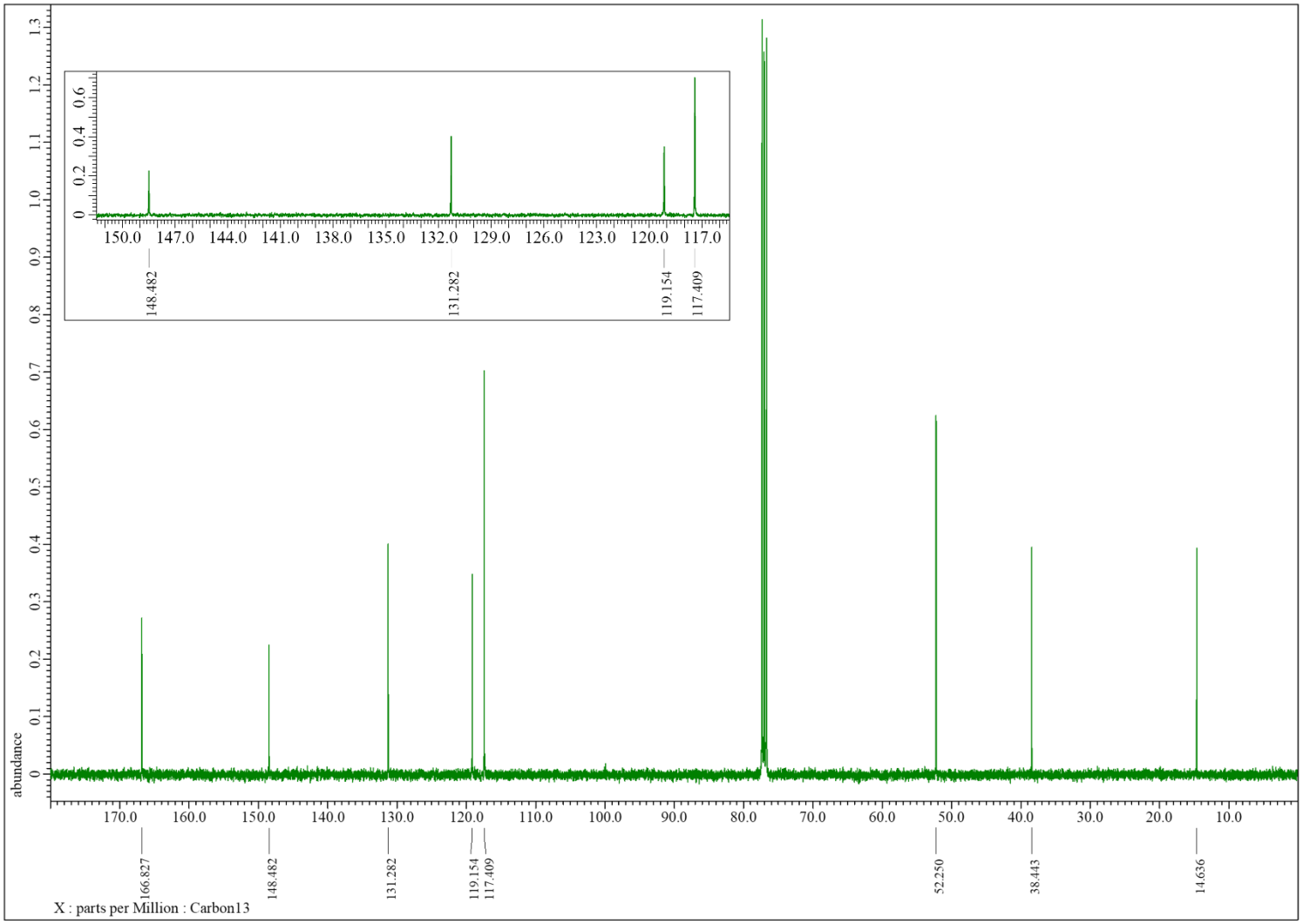
Dimethyl 5-(ethylamino)isophthalate (6b)



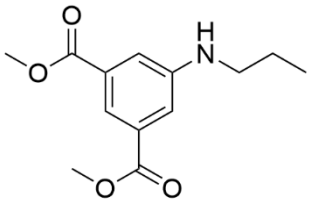
^{1}H NMR (400 MHz, $CDCl_3$)



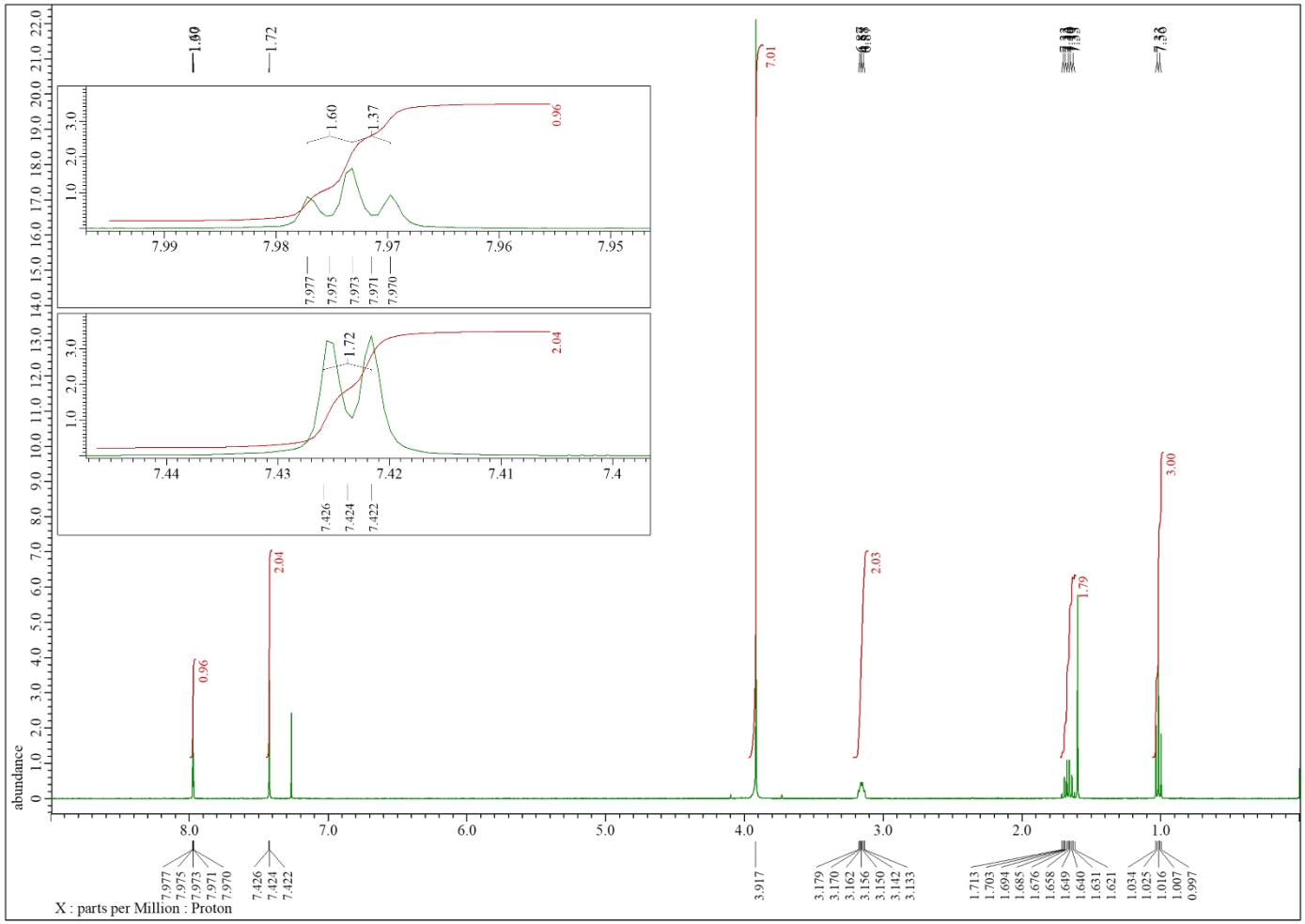
^{13}C NMR (100 MHz, $CDCl_3$)



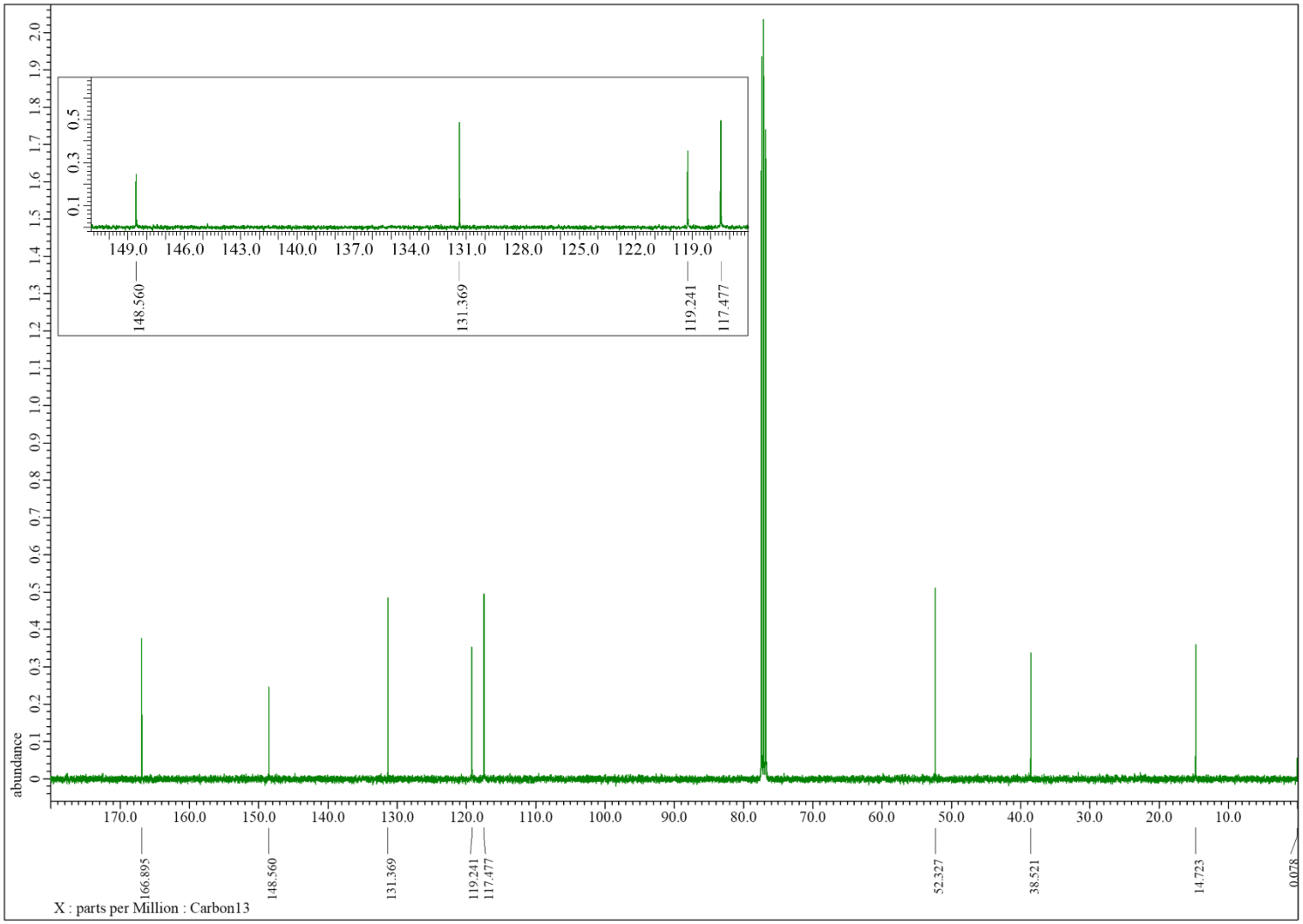
Dimethyl 5-(propylamino)isophthalate (6c)



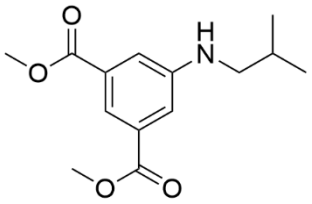
^{1}H NMR (400 MHz, $CDCl_3$)



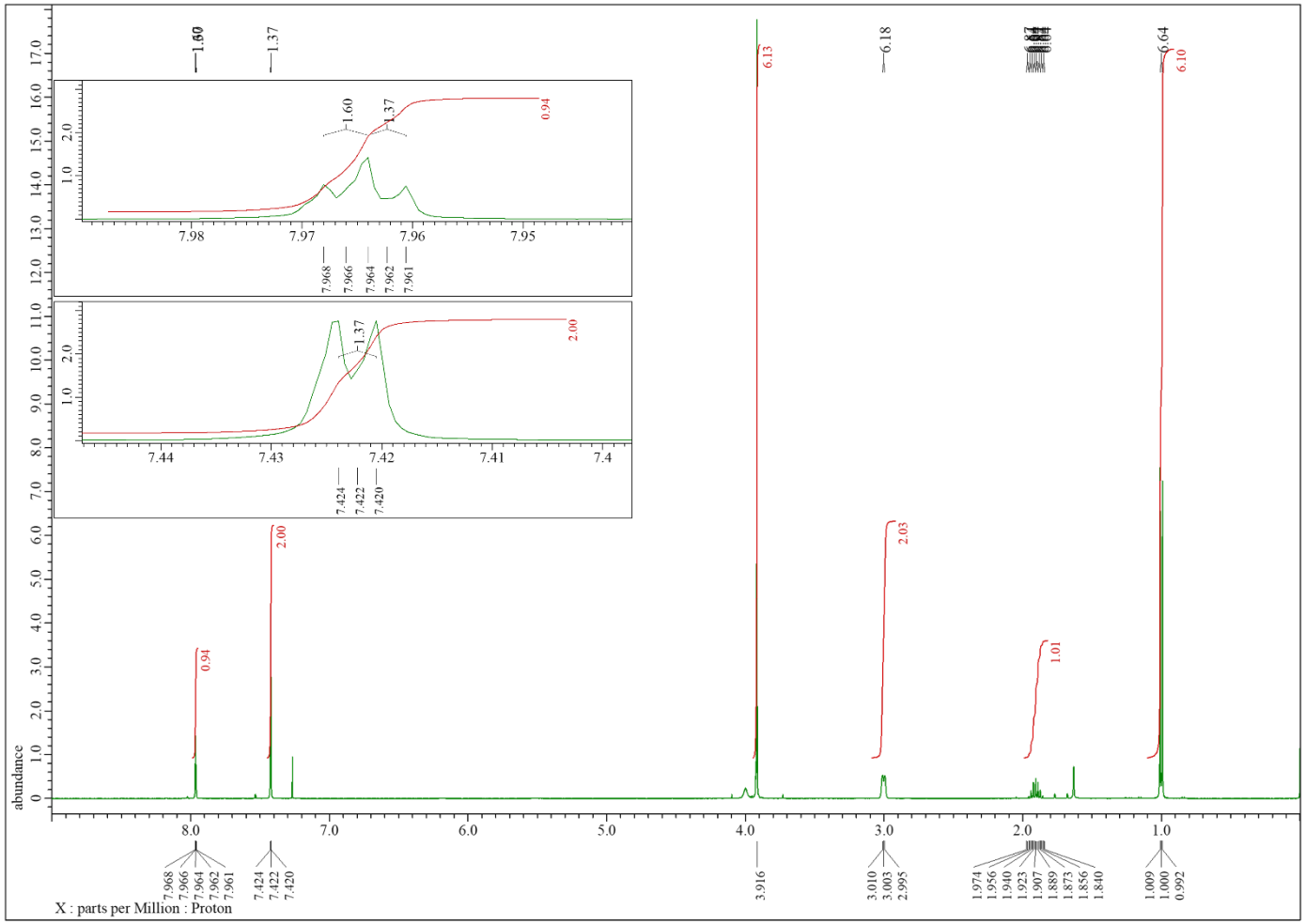
^{13}C NMR (100 MHz, $CDCl_3$)



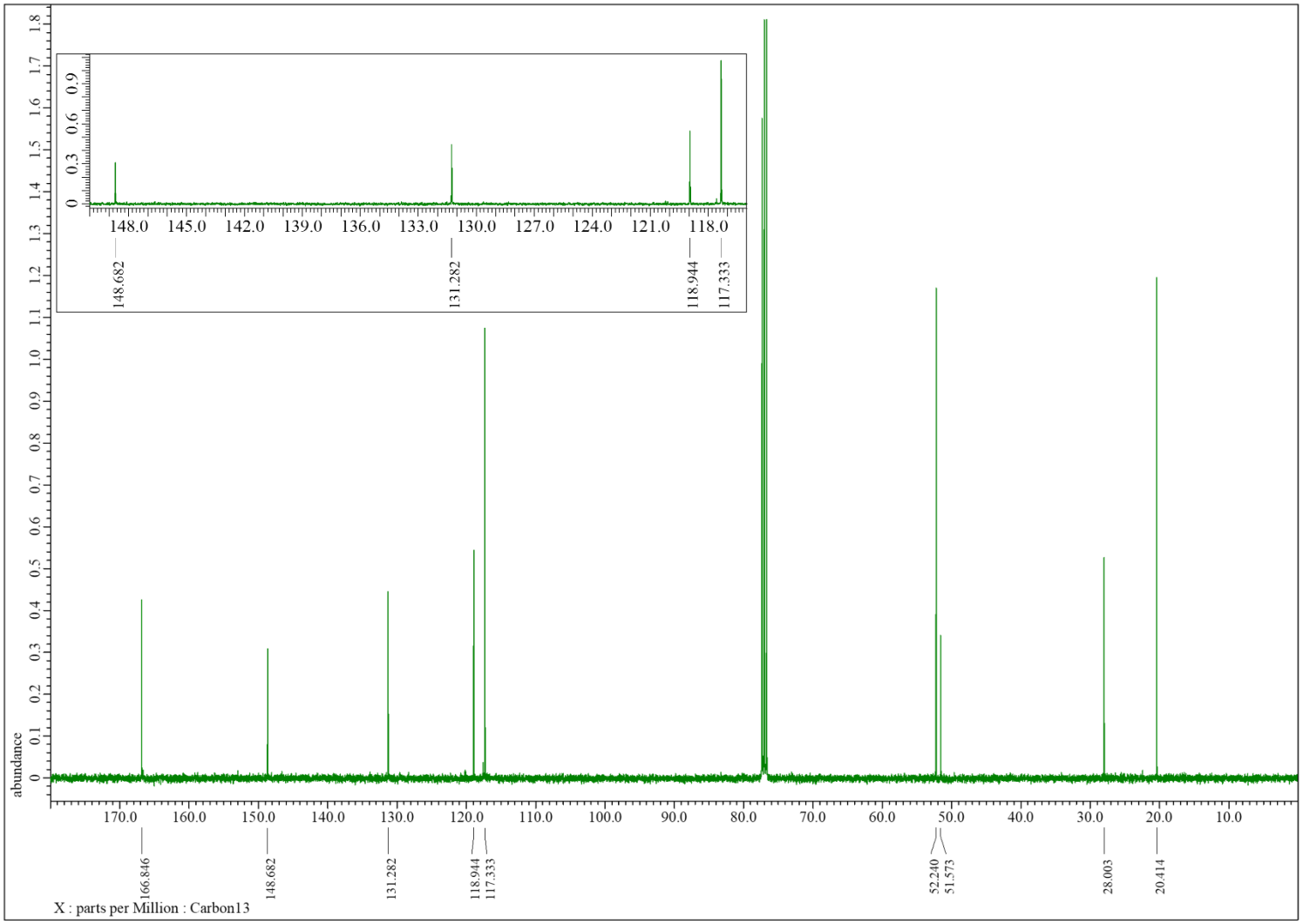
Dimethyl 5-(isobutylamino)isophthalate (6d)



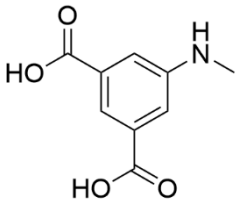
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

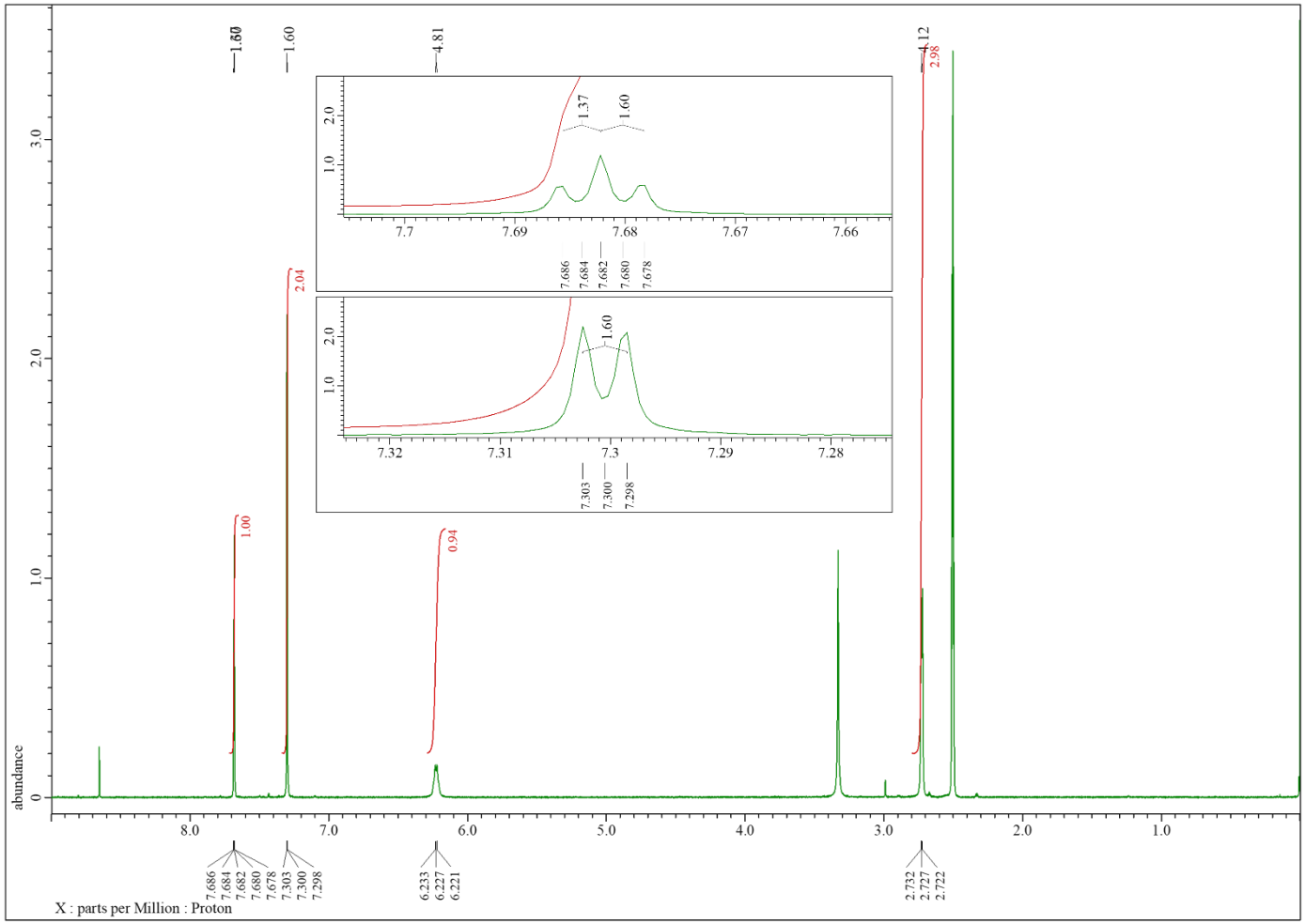


5-(Methylamino)isophthalic acid (7a)

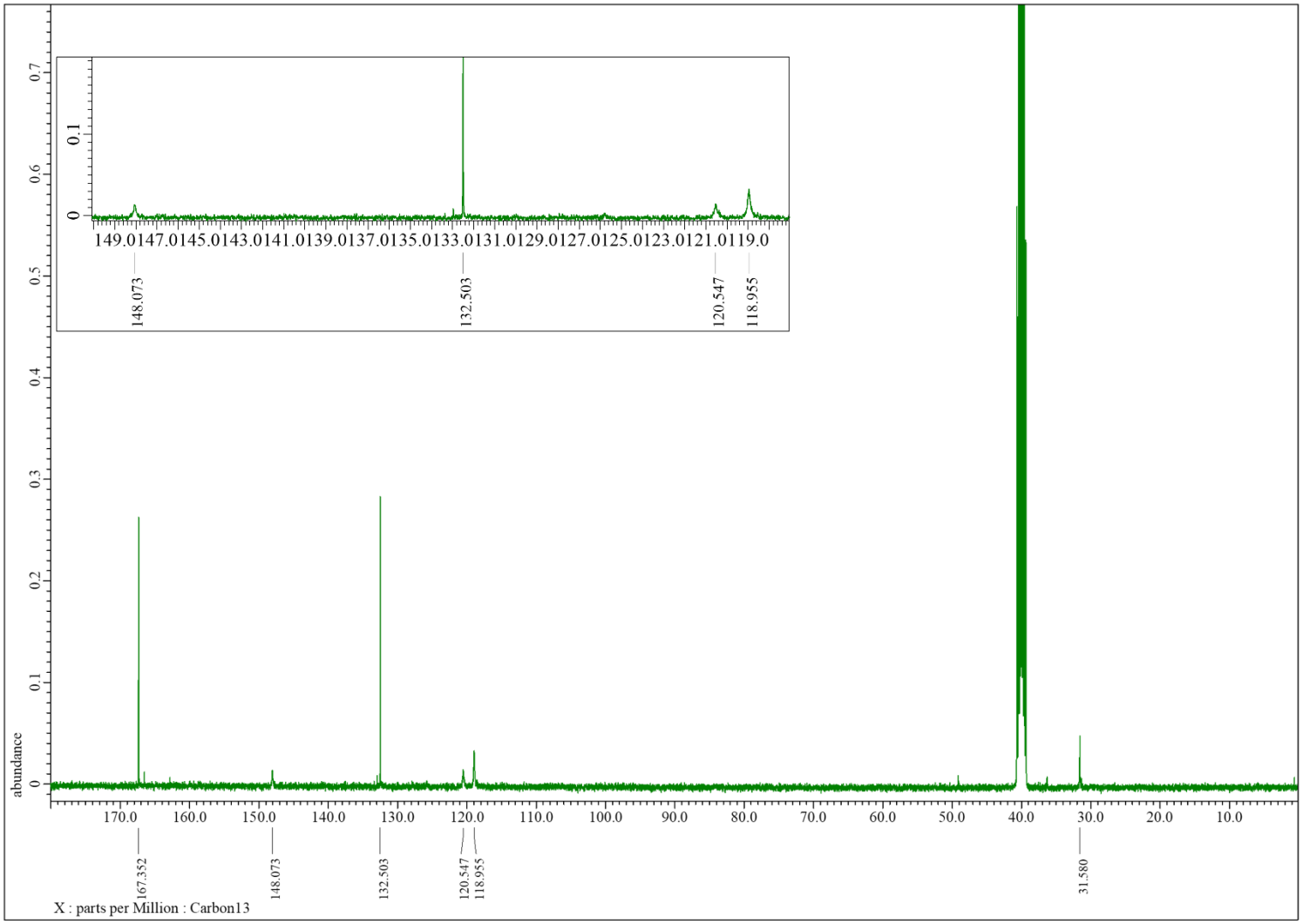


^{1}H NMR

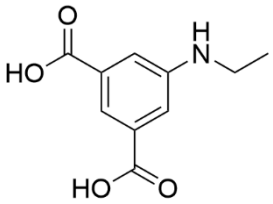
(400 MHz, DMSO-d_6)



^{13}C NMR (100 MHz, DMSO-d_6)

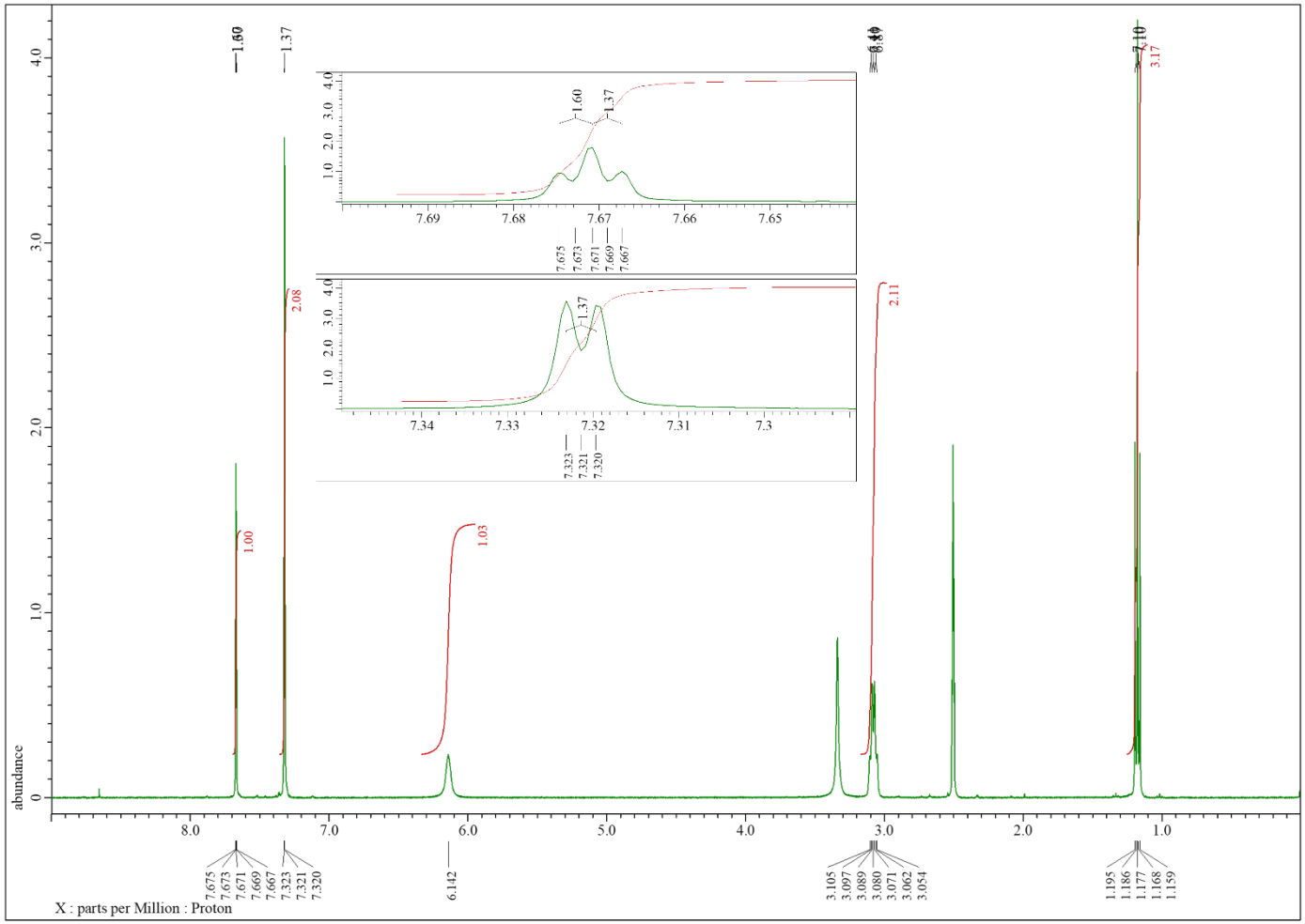


5-(Ethylamino)isophthalic acid (7b)

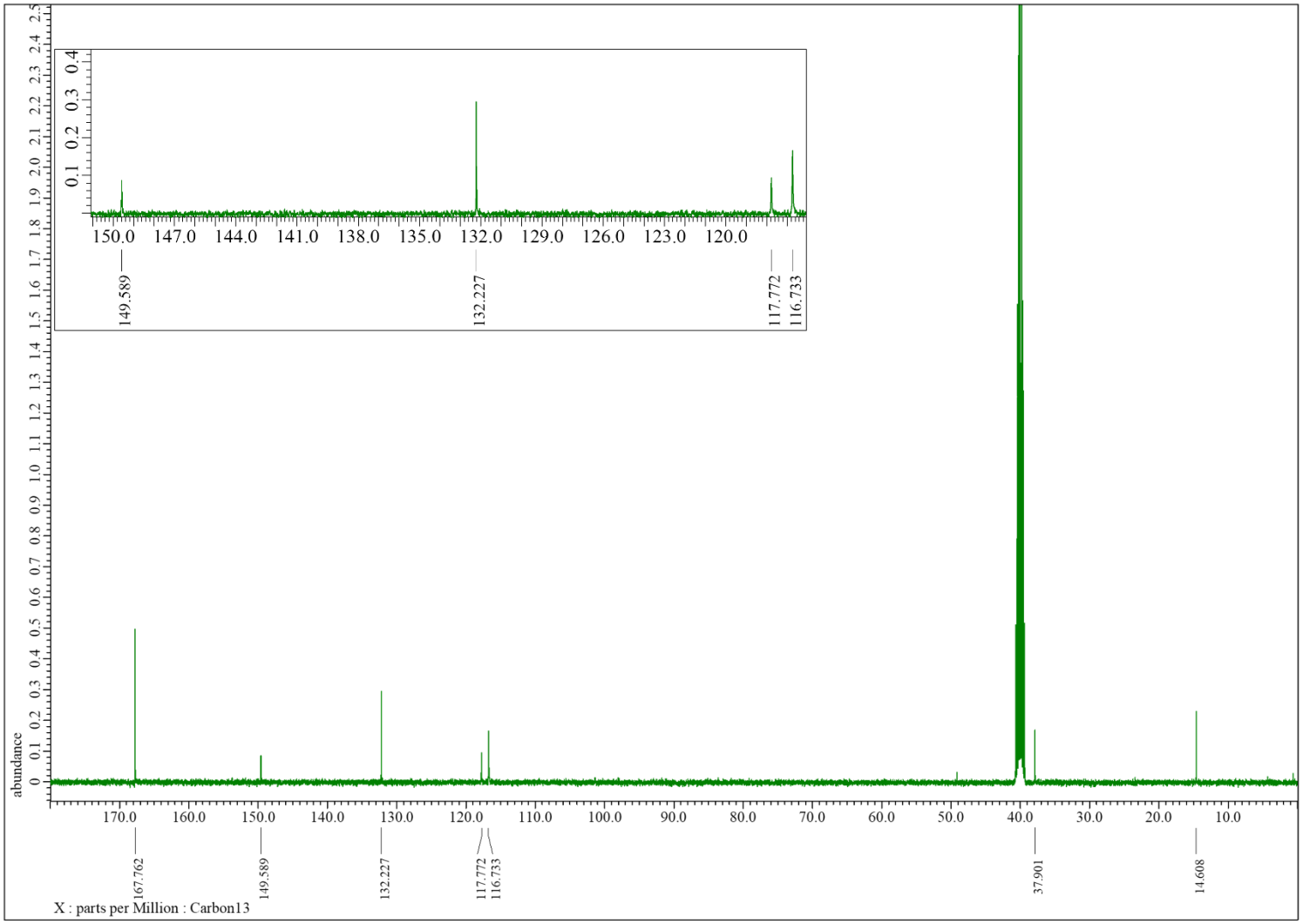


^{1}H NMR

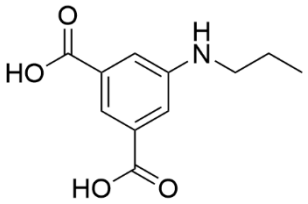
(400 MHz, DMSO-d_6)



^{13}C NMR (100 MHz, DMSO-d_6)

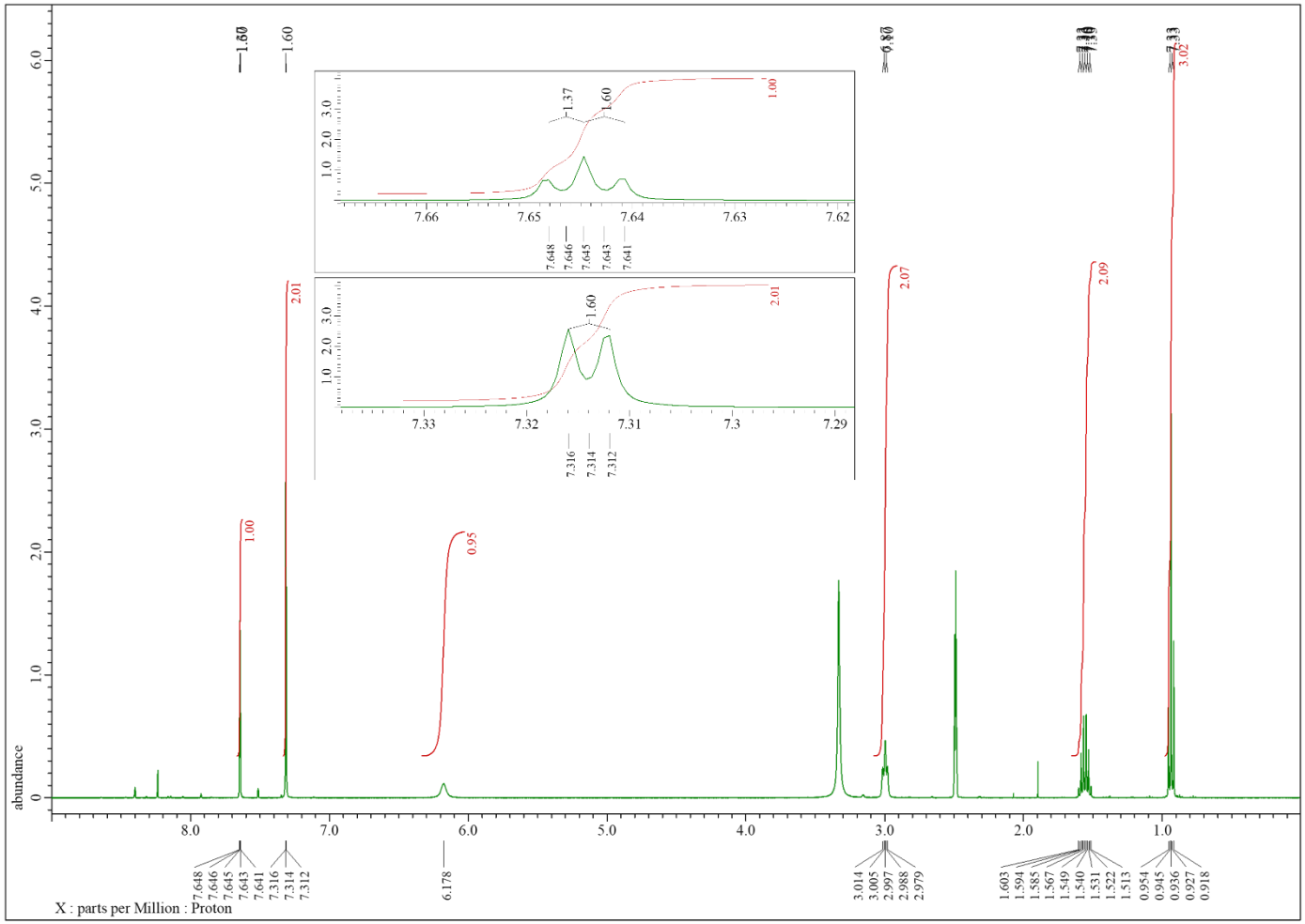


5-(Propylamino)isophthalic acid (7c)

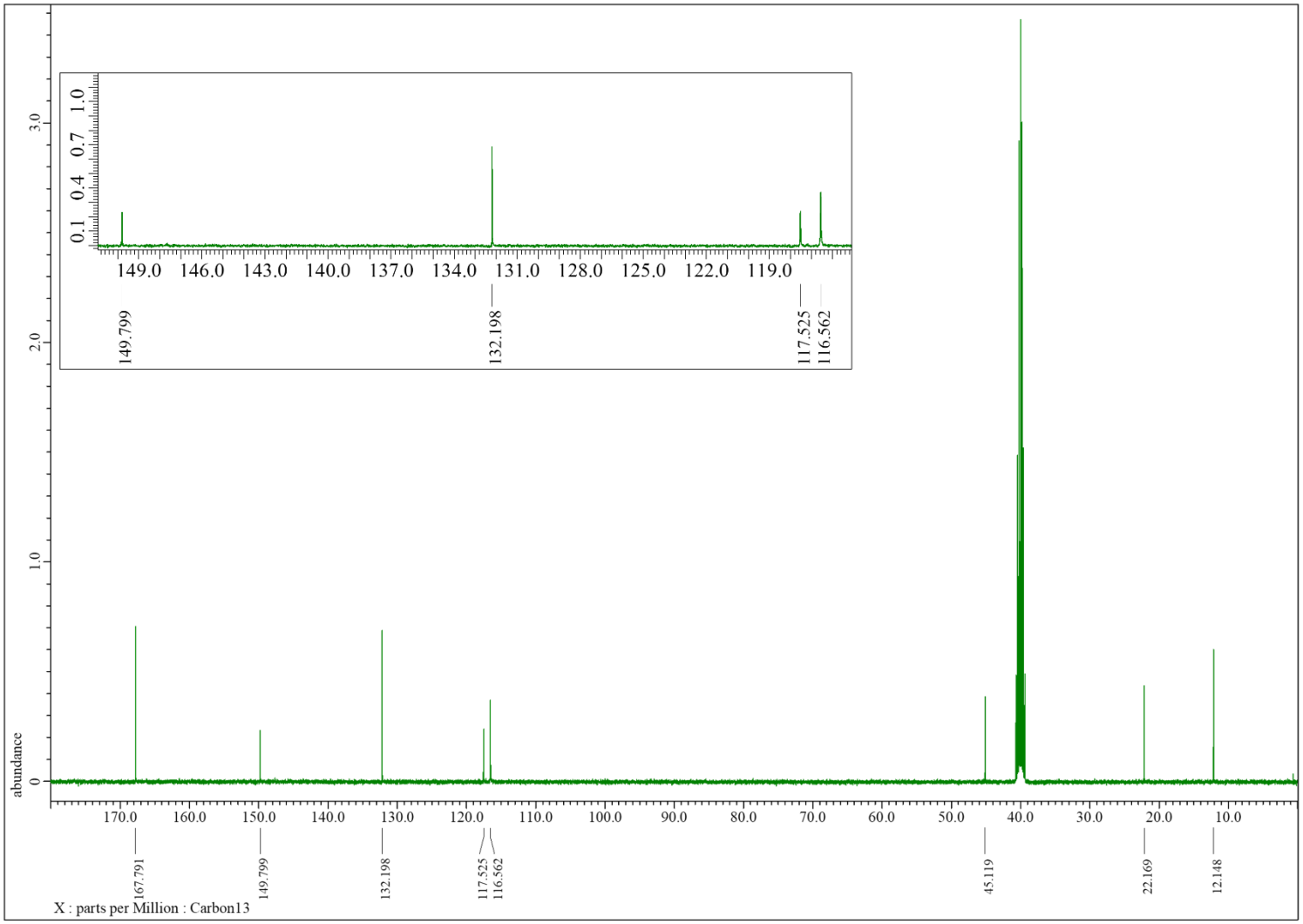


^{1}H NMR

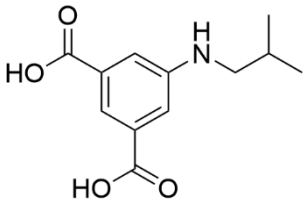
(400 MHz, DMSO-d_6)



^{13}C NMR (100 MHz, DMSO-d_6)

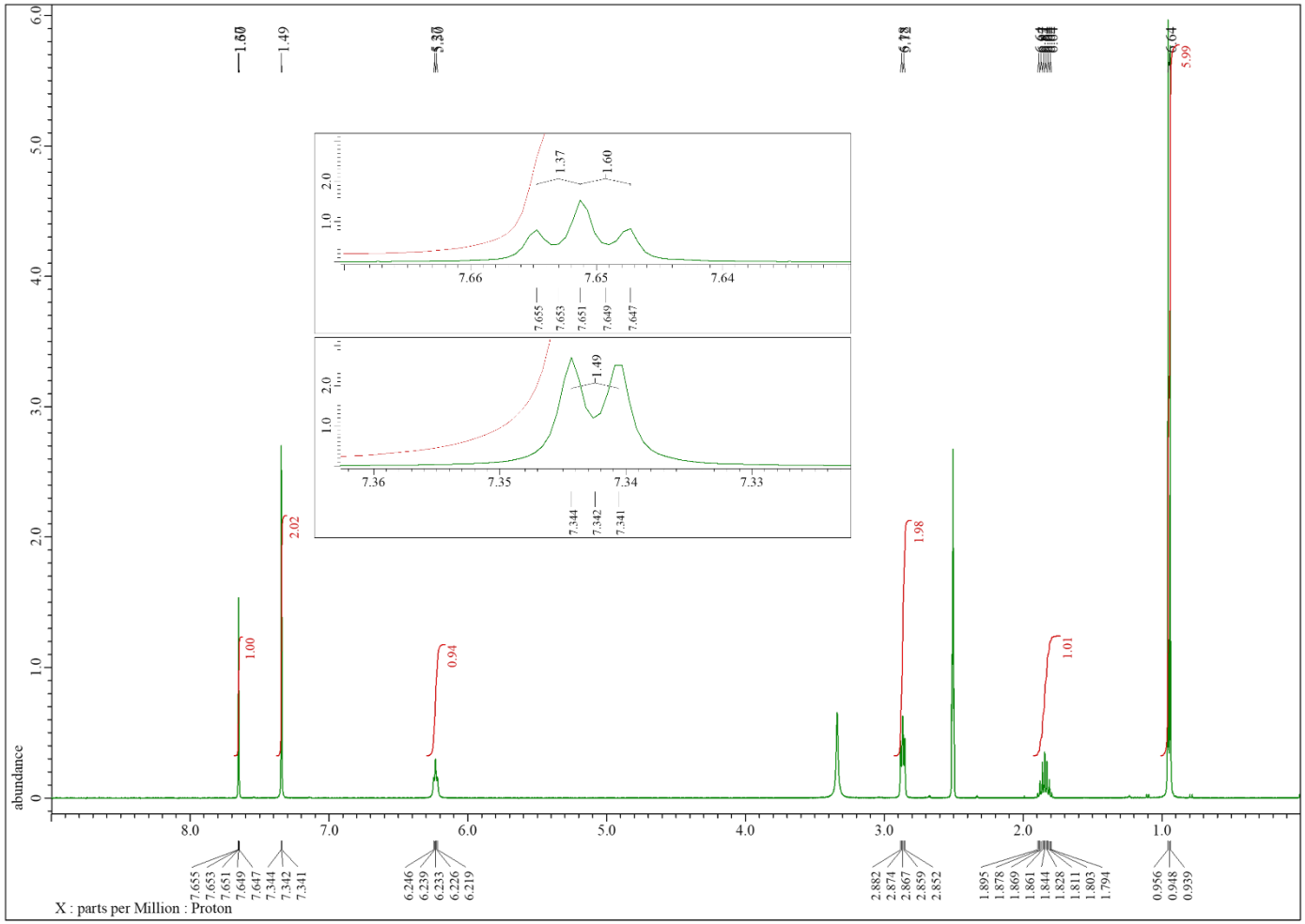


5-(Isobutylamino)isophthalic acid (7d)

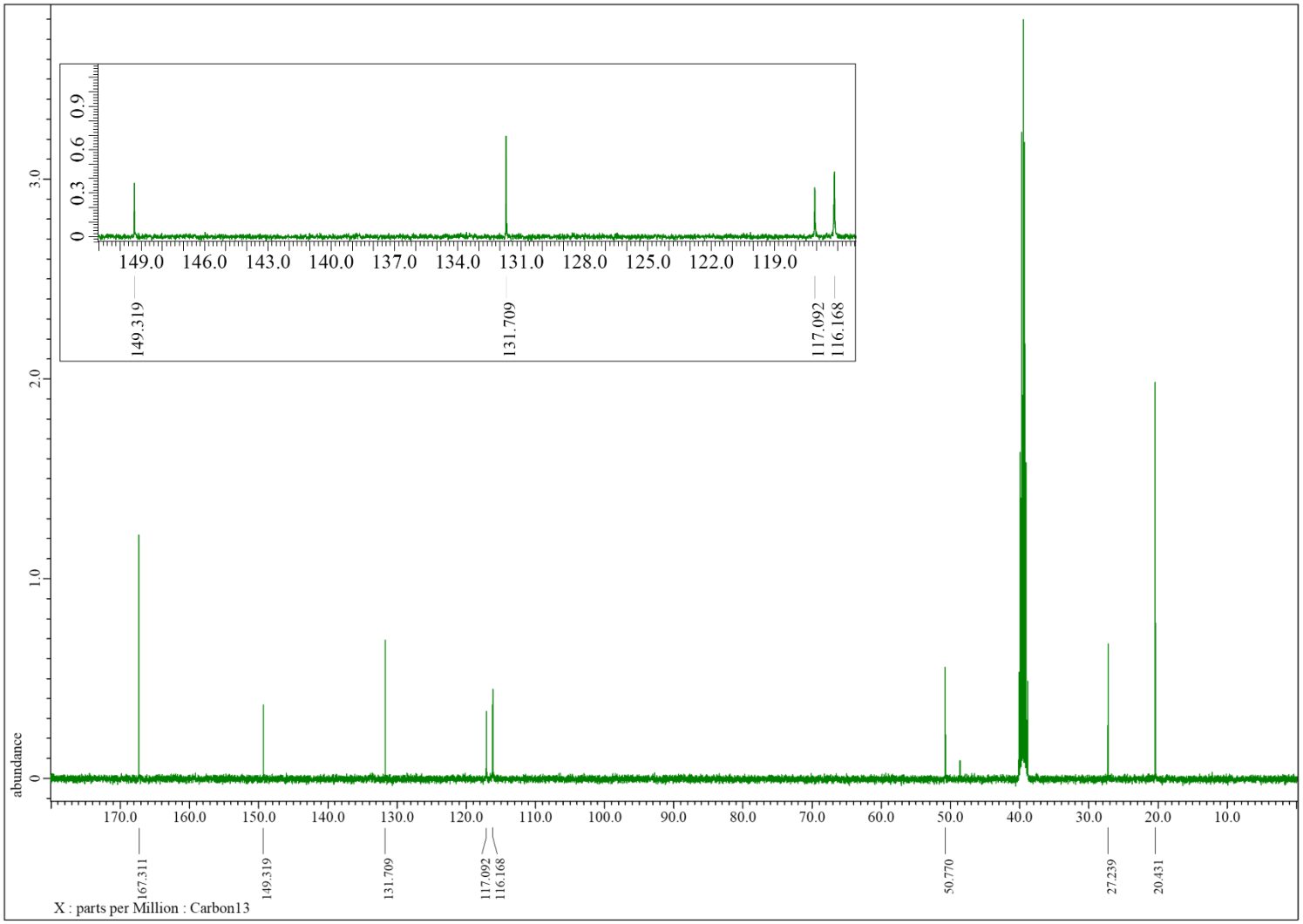


^{1}H NMR

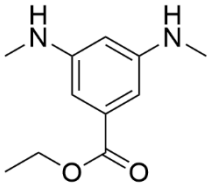
(400 MHz, DMSO-d_6)



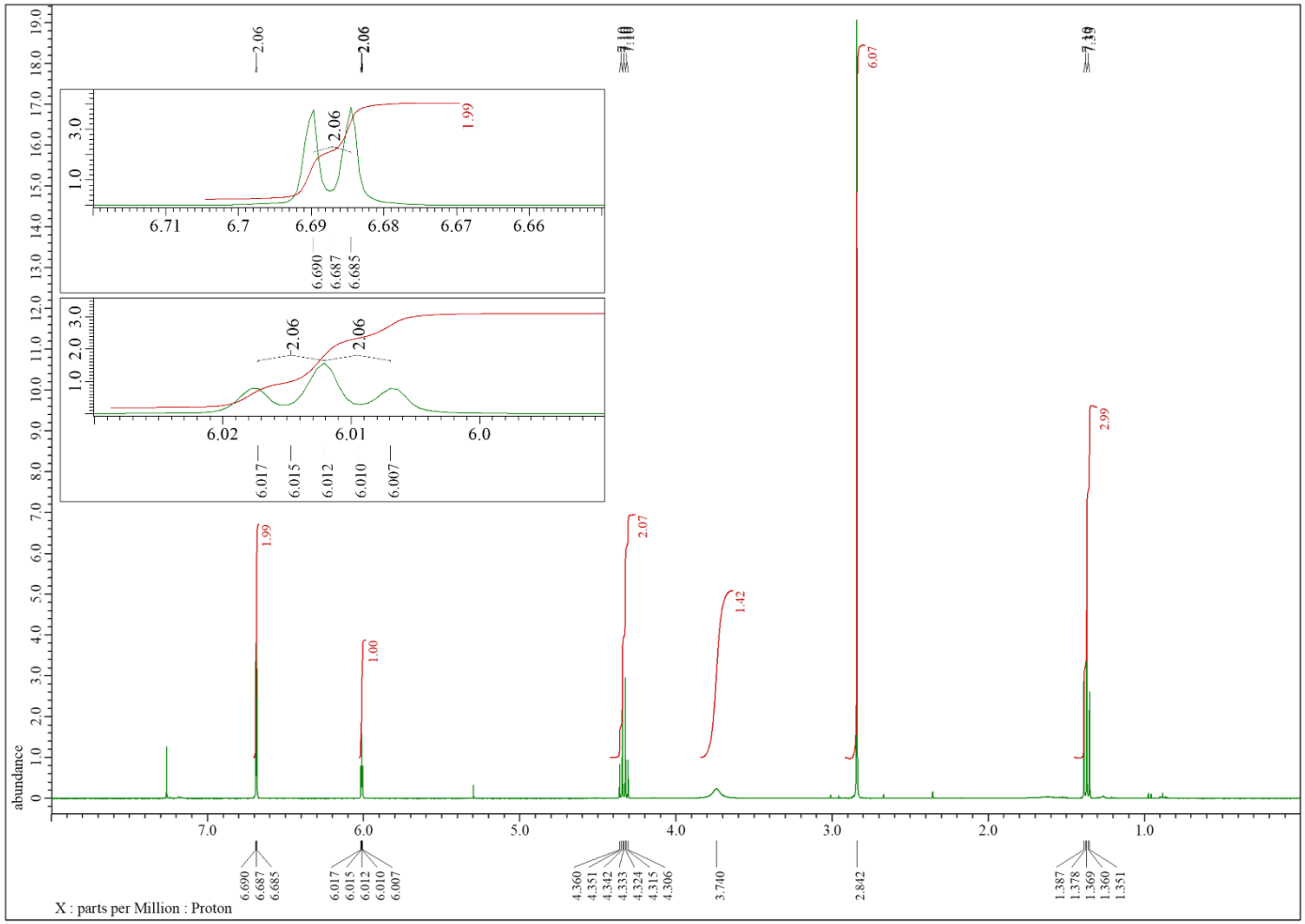
^{13}C NMR (100 MHz, DMSO-d_6)



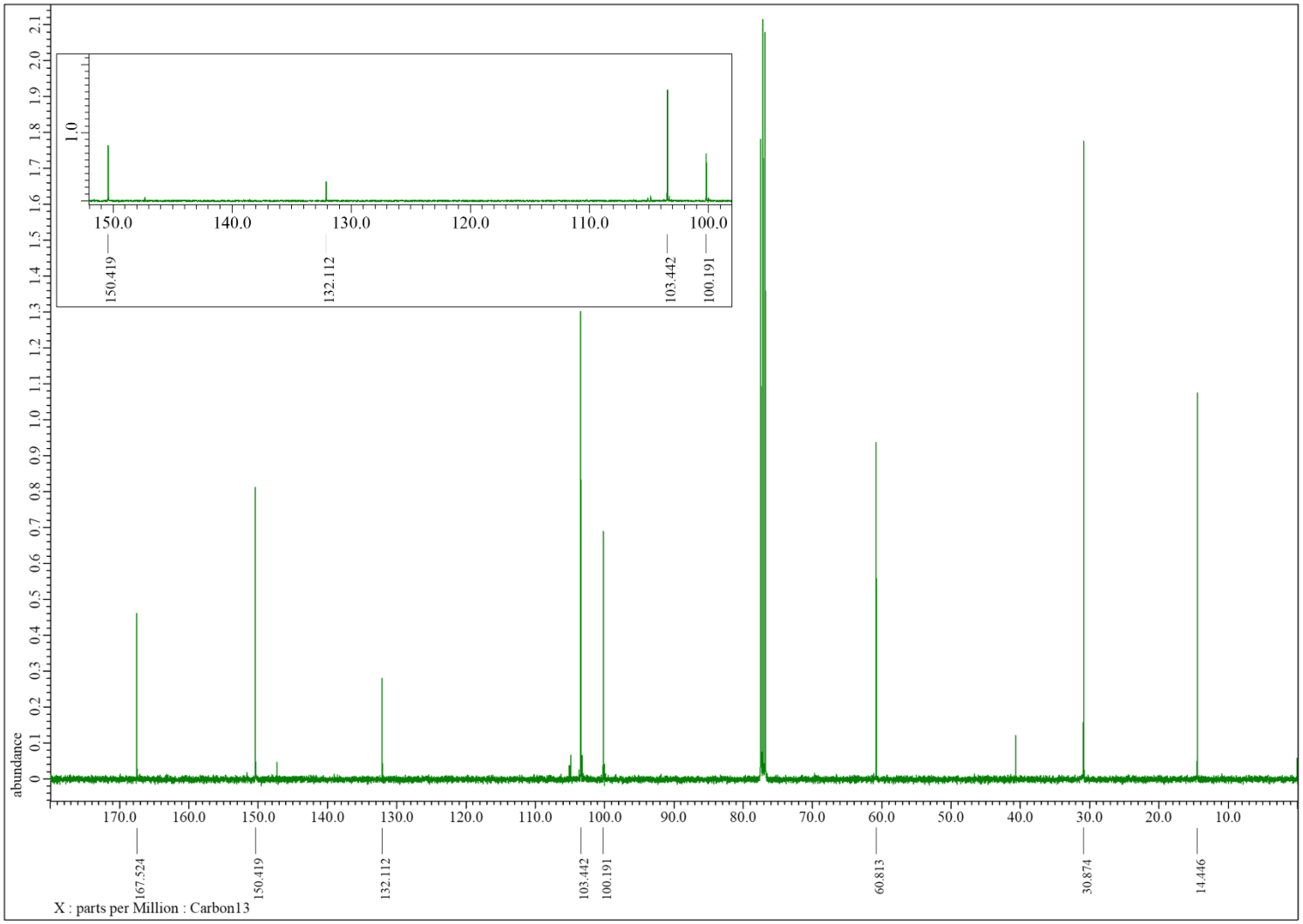
Ethyl 3,5-bis(methylamino)benzoate (10a)



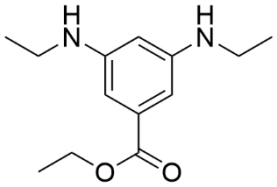
^{1}H NMR (400 MHz, $CDCl_3$)



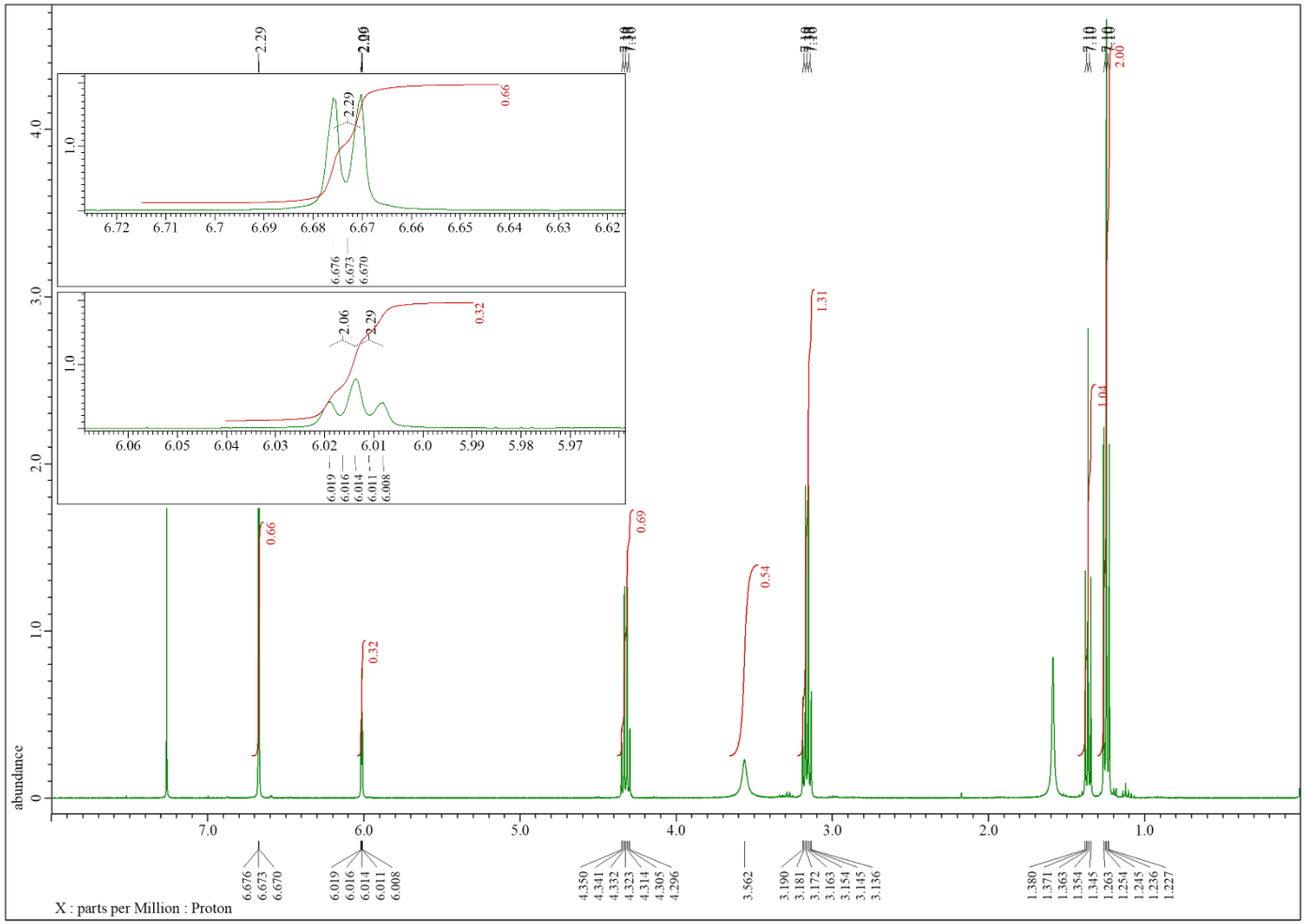
^{13}C NMR (100 MHz, $CDCl_3$)



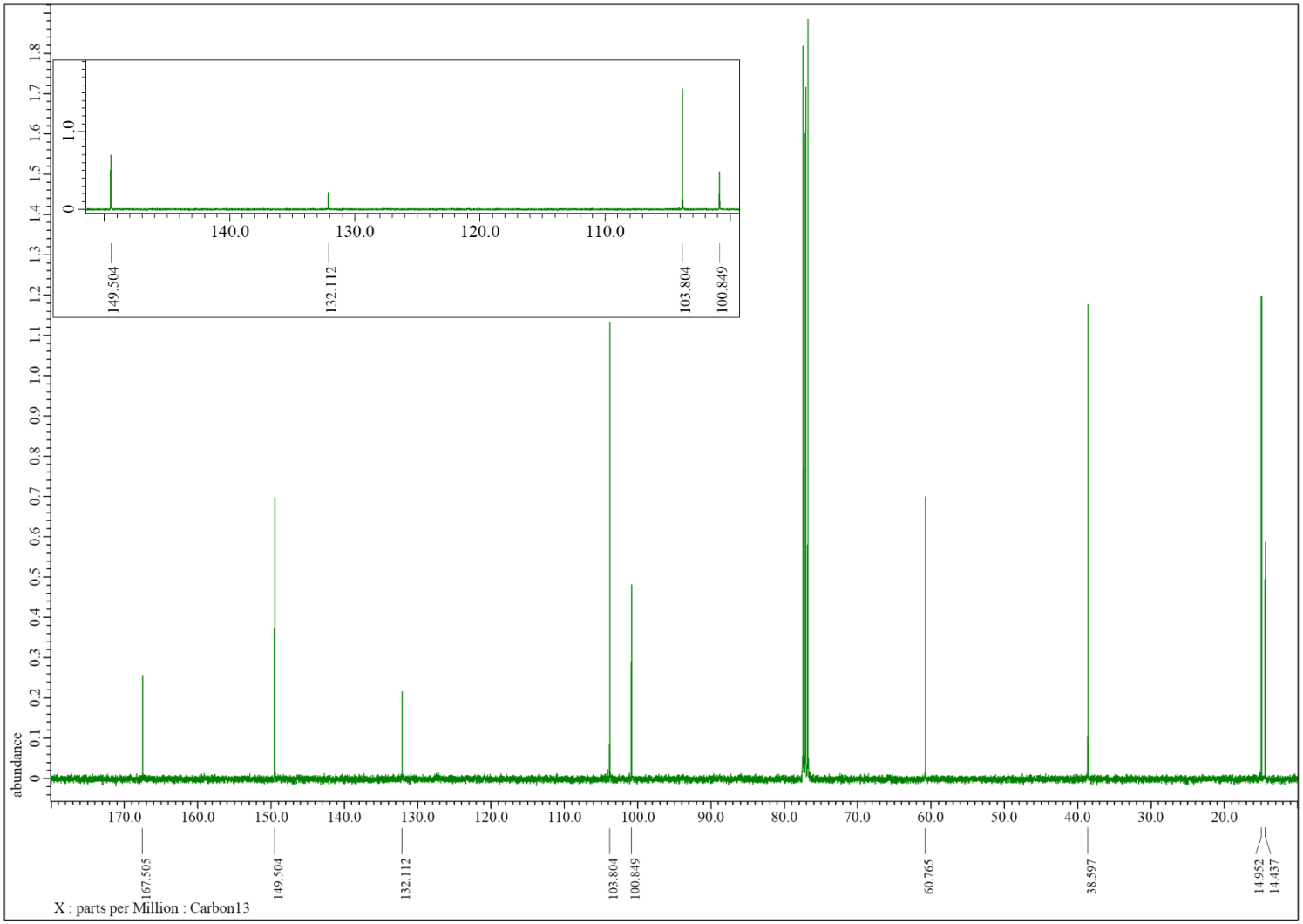
Ethyl 3,5-bis(ethylamino)benzoate (10b)



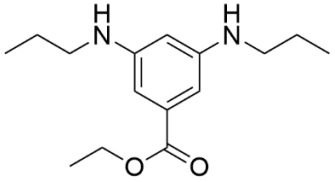
^{1}H NMR (400 MHz, $CDCl_3$)



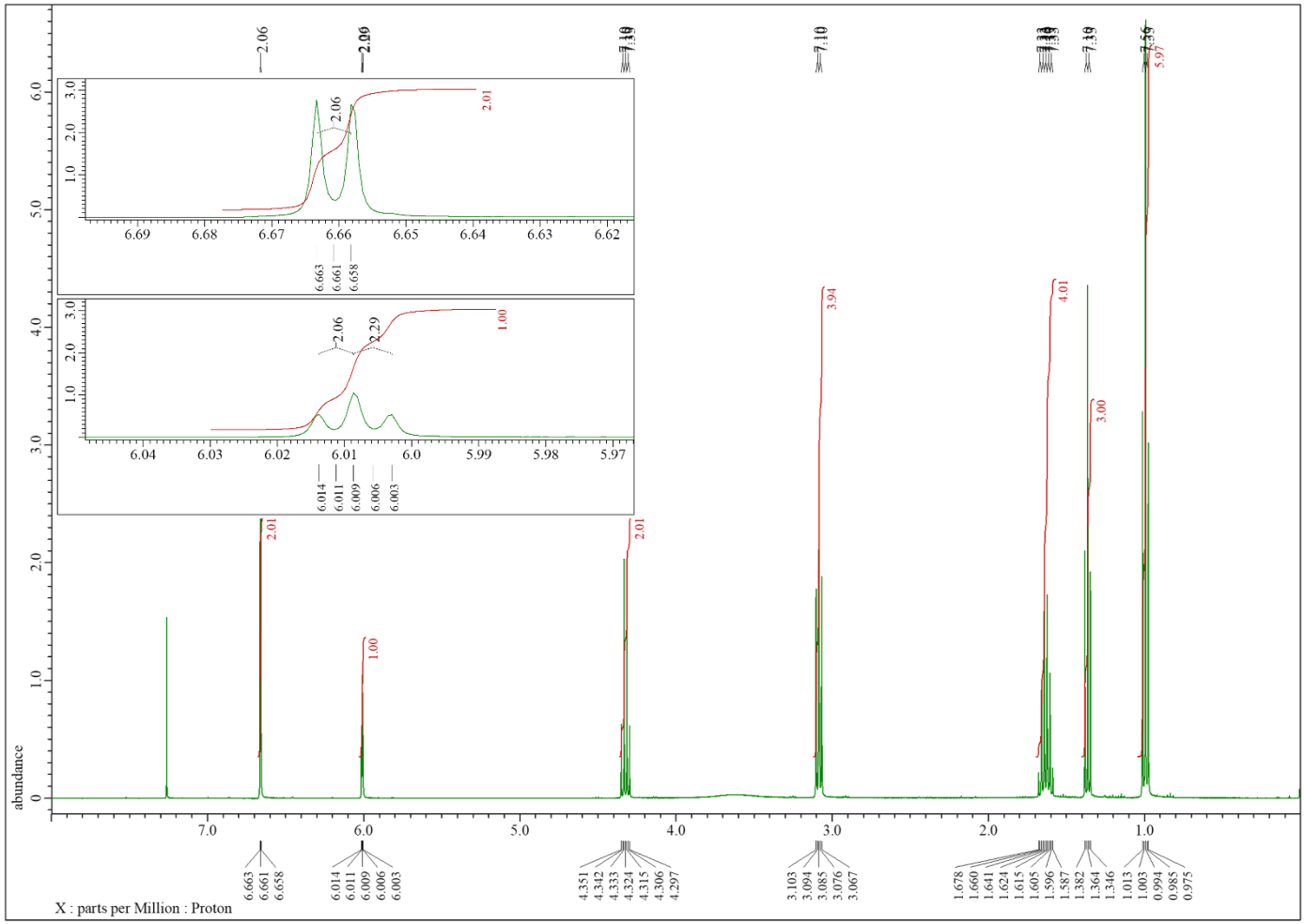
^{13}C NMR (100 MHz, $CDCl_3$)



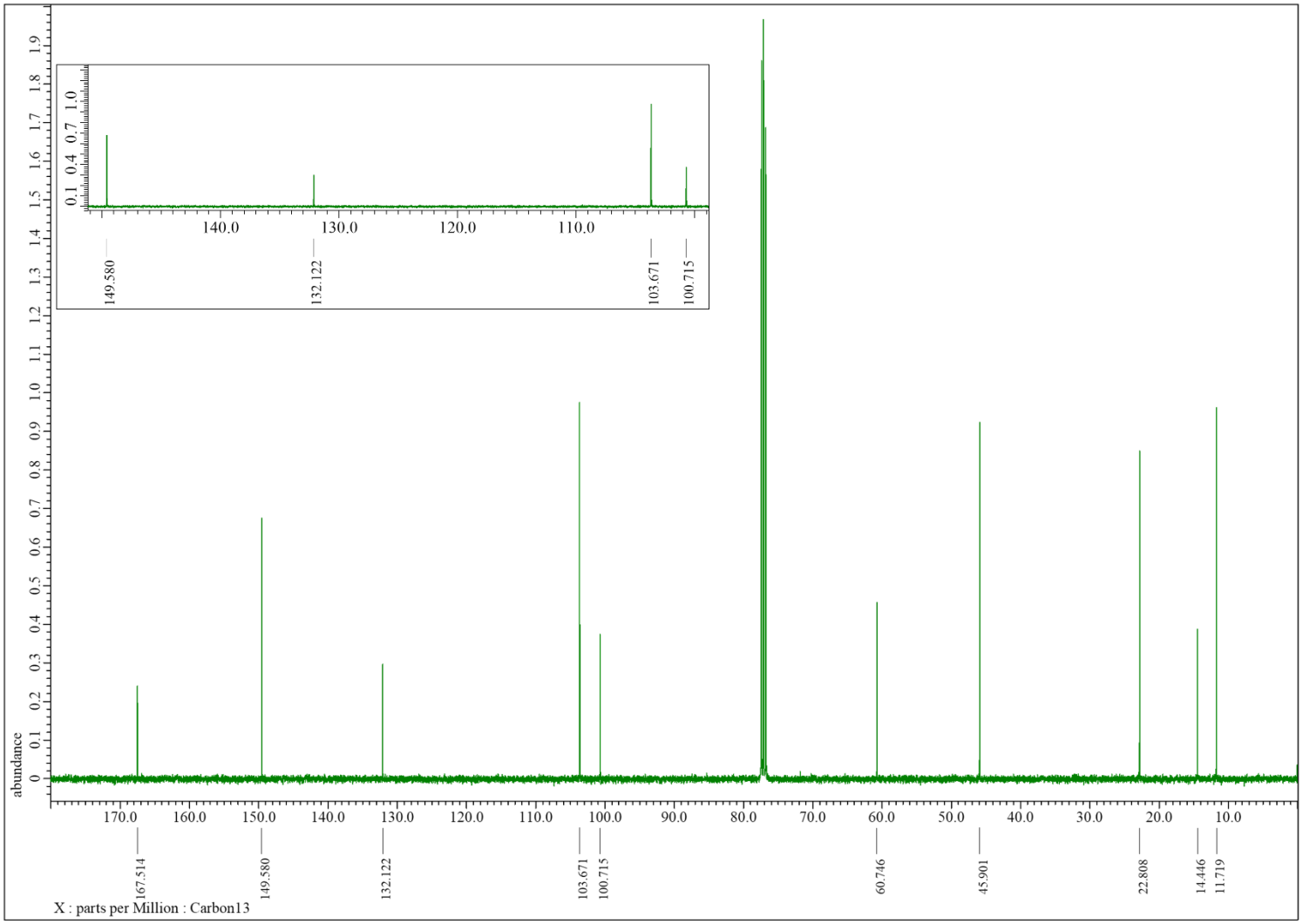
Ethyl 3,5-bis(propylamino)benzoate (10c)



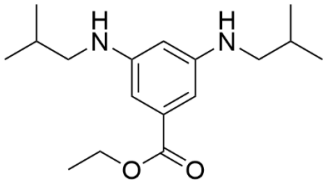
^{1}H NMR (400 MHz, $CDCl_3$)



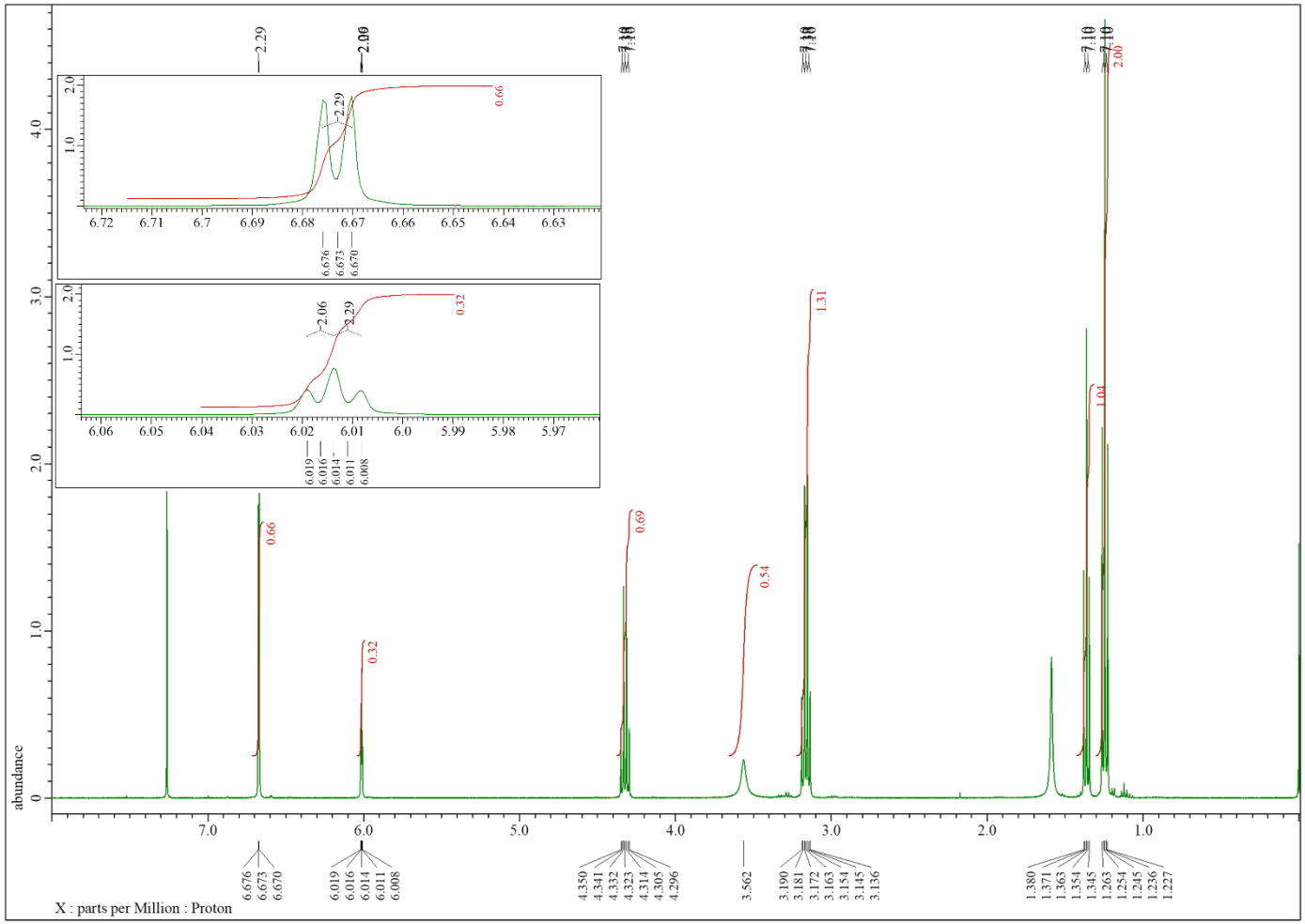
^{13}C NMR (100 MHz, $CDCl_3$)



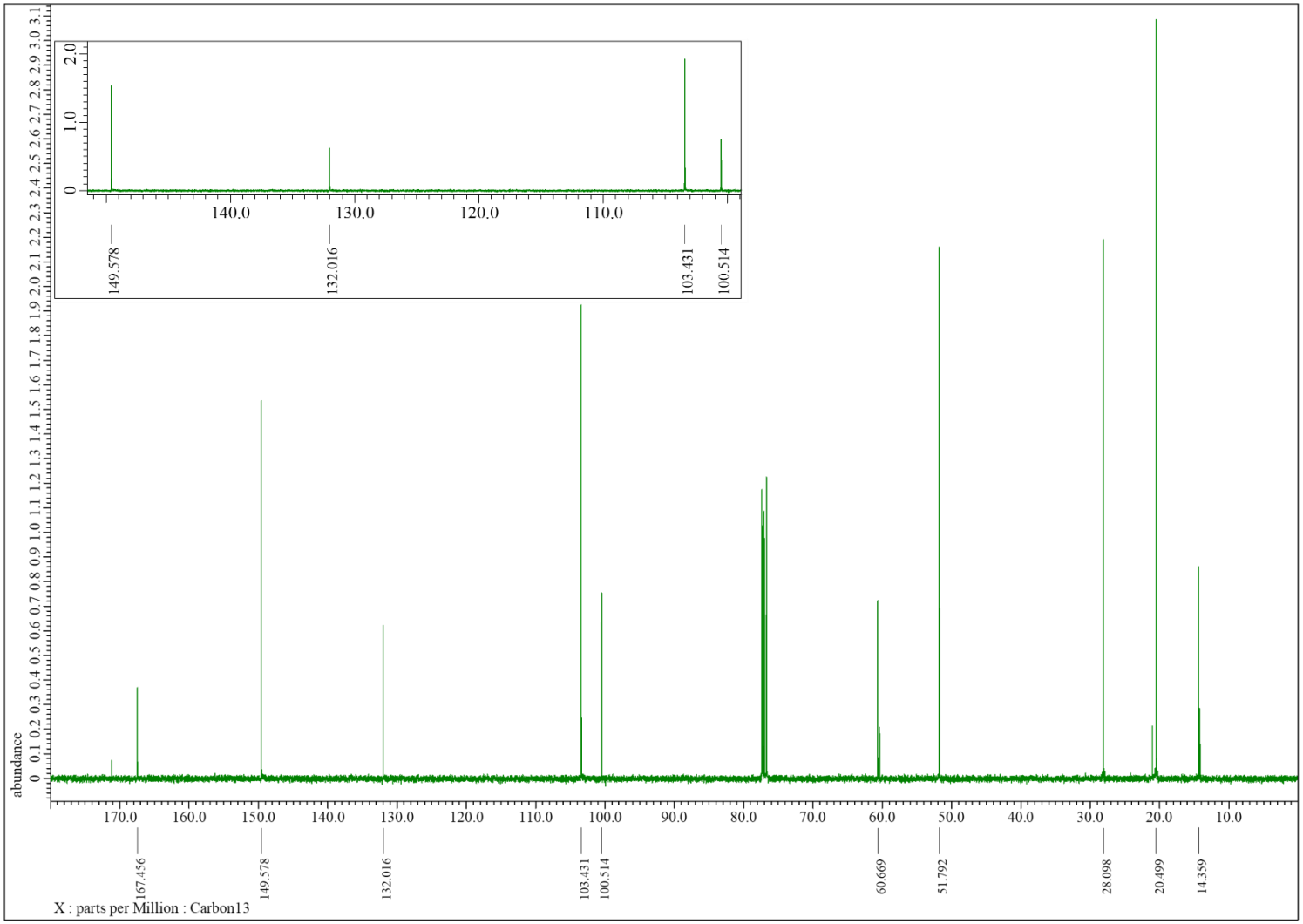
Ethyl 3,5-bis(isobutylamino)benzoate (10d)



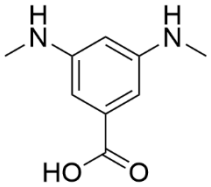
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

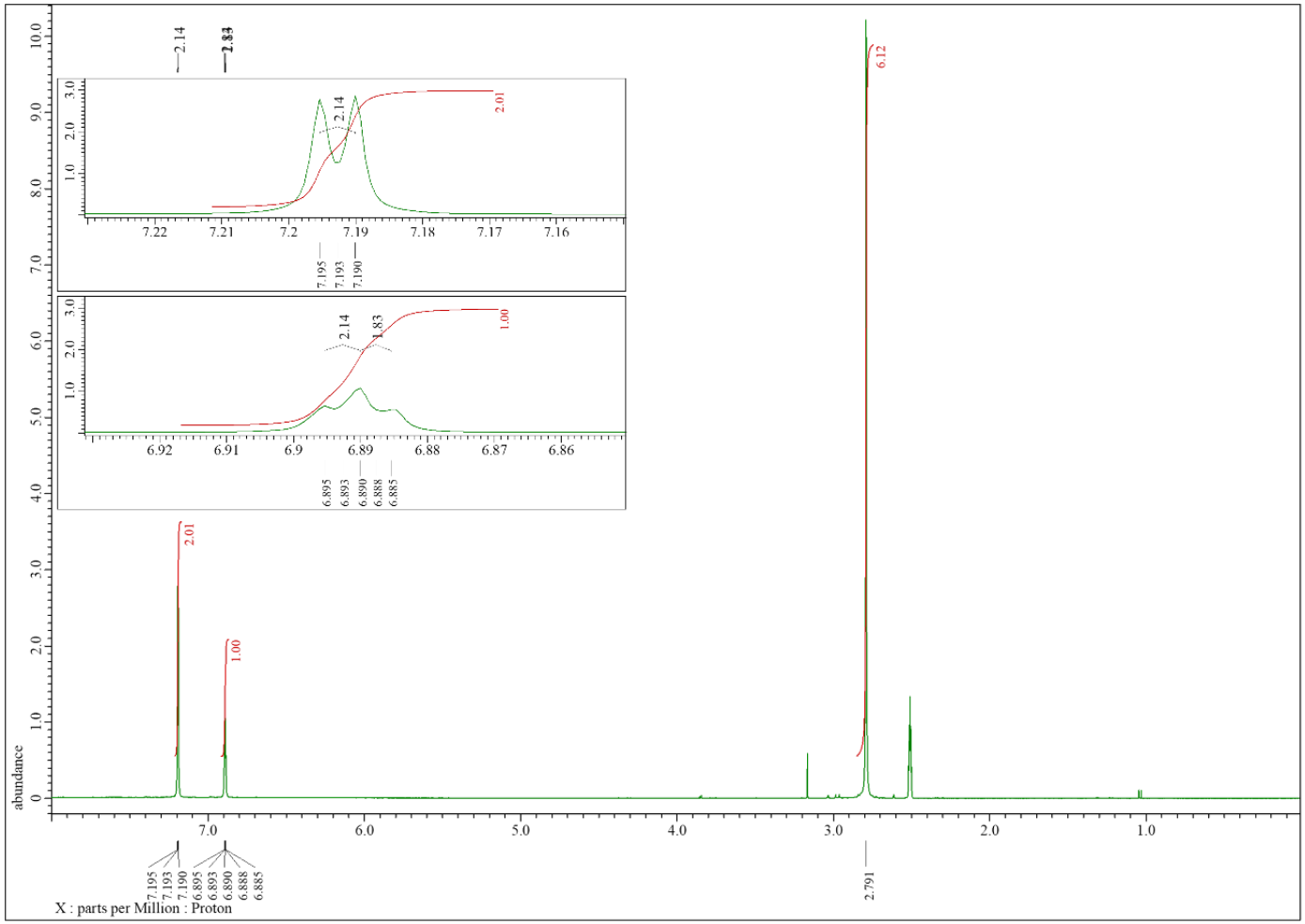


3,5-Bis(methylamino)benzoic acid (11a)

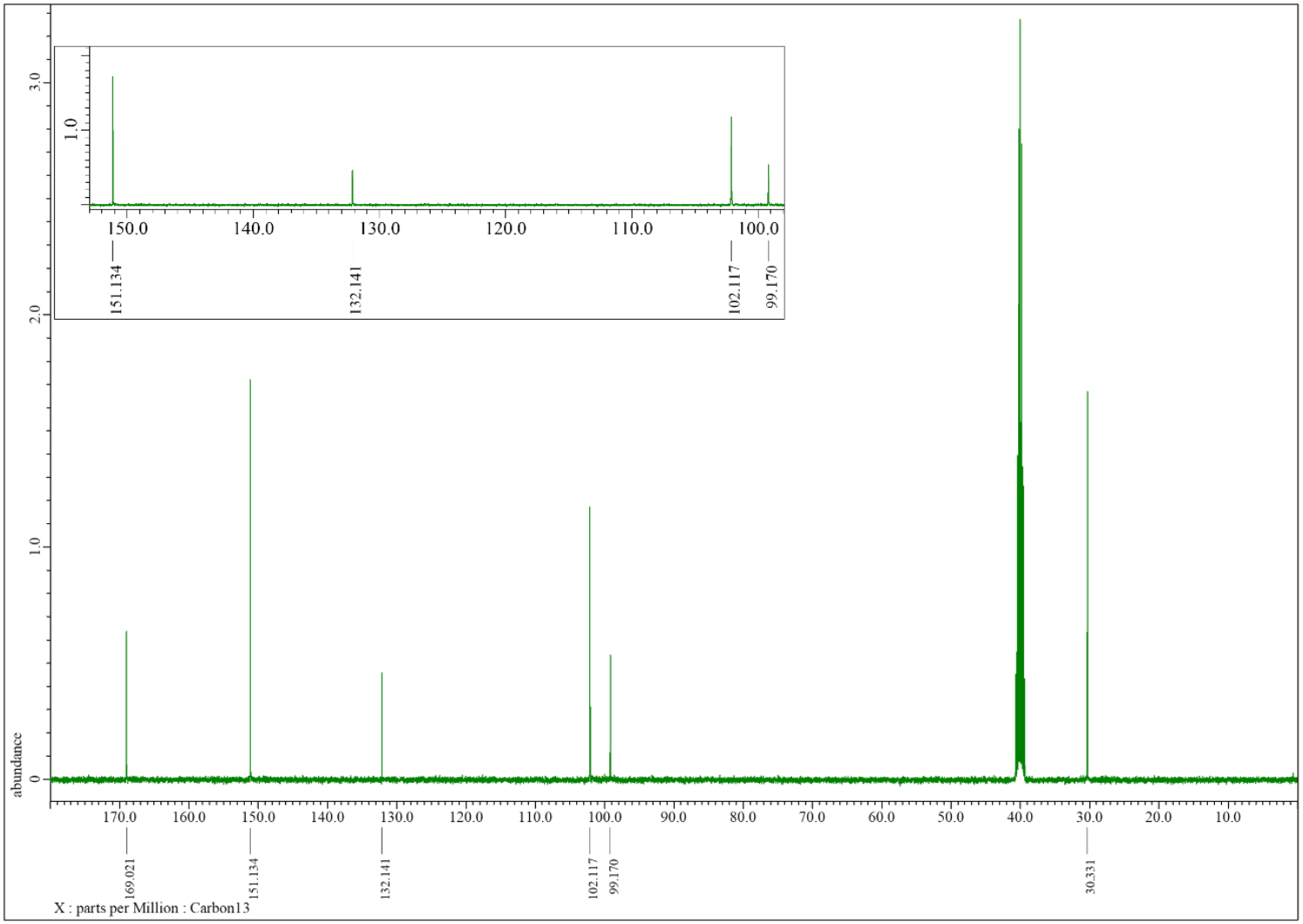


^{1}H NMR

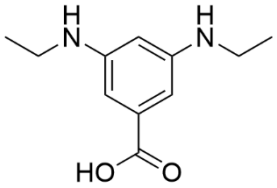
(400 MHz, DMSO-d_6)



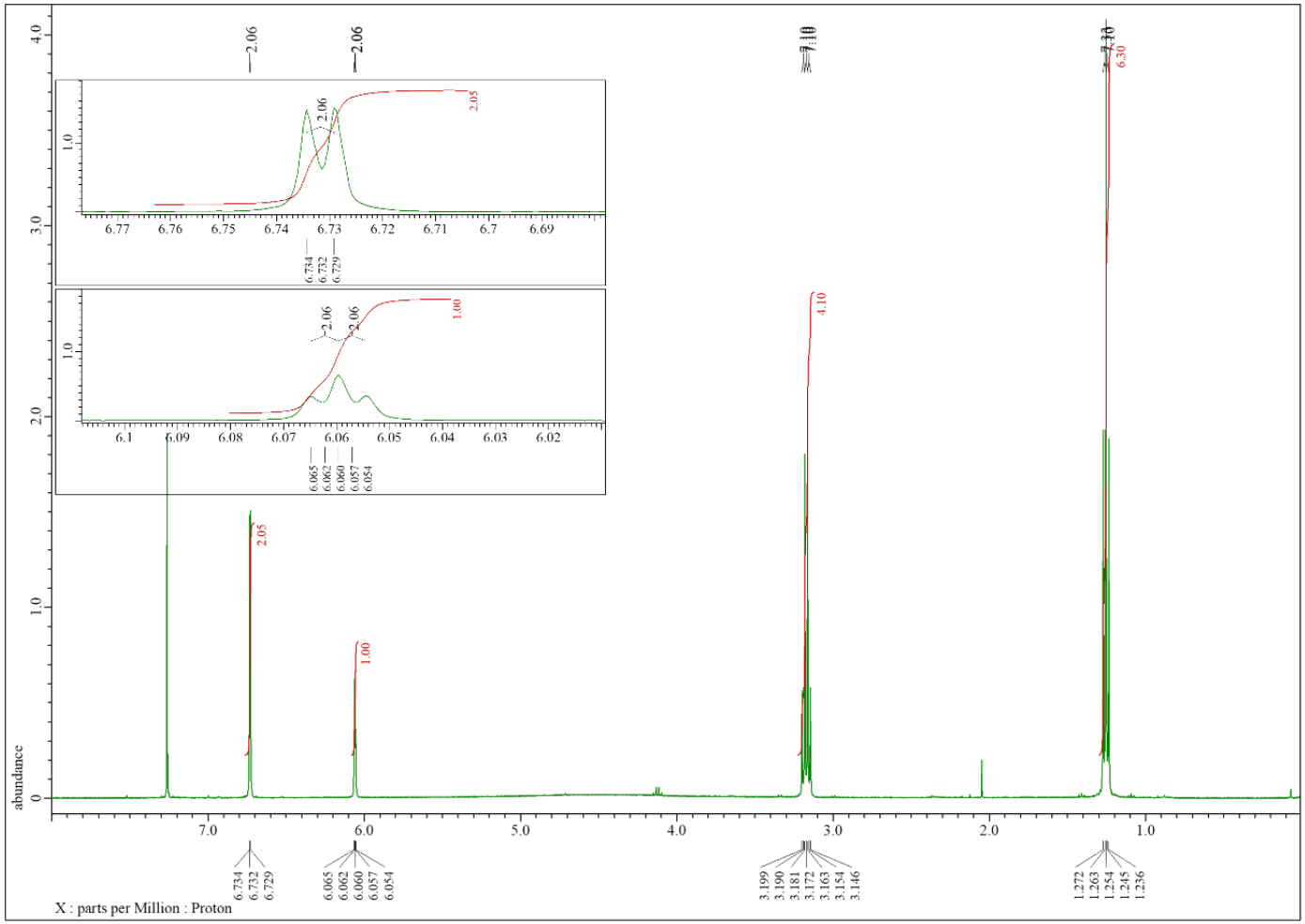
^{13}C NMR (100 MHz, DMSO-d_6)



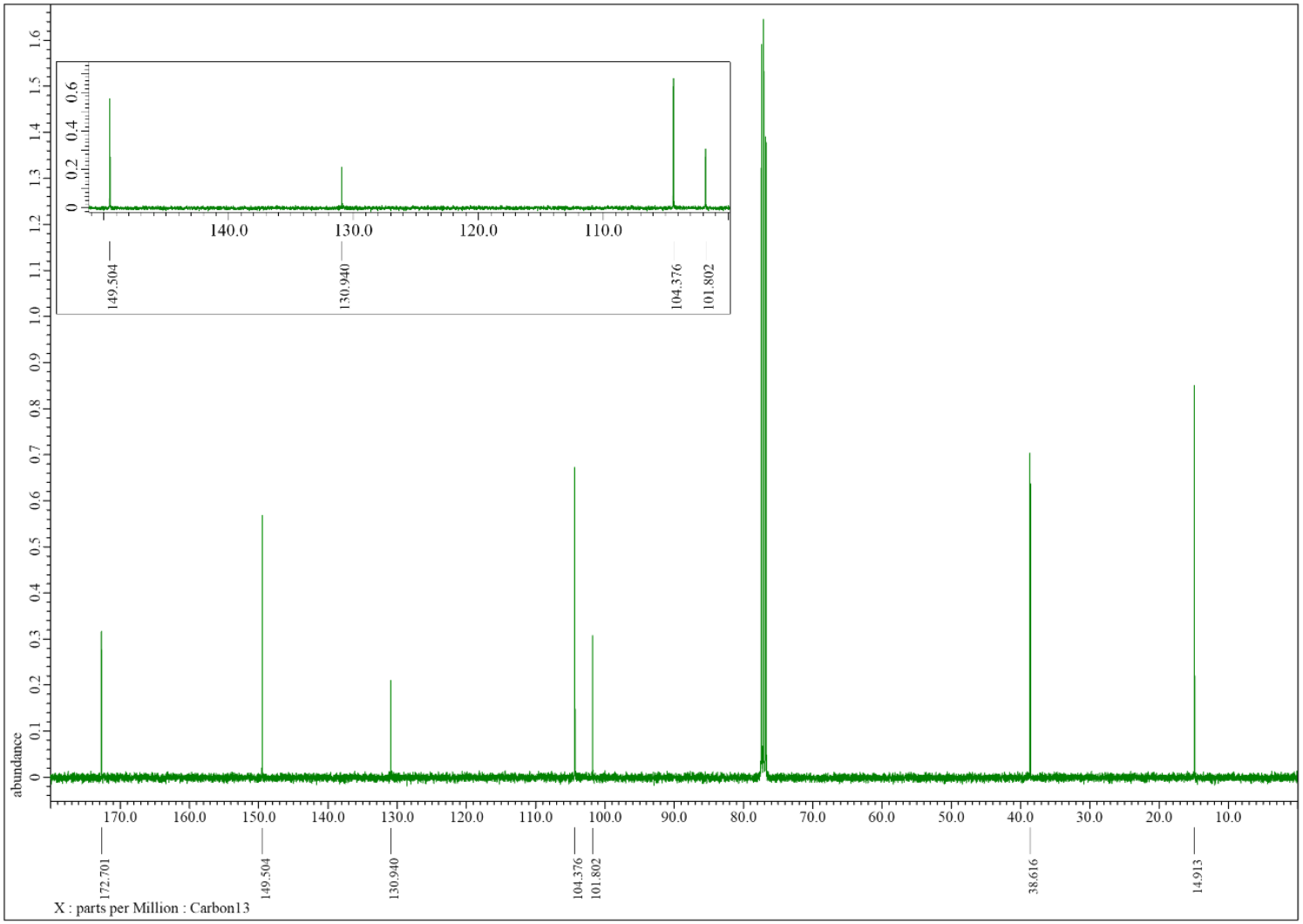
3,5-Bis(ethylamino)benzoic acid (11b)



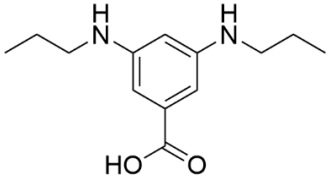
^{1}H NMR (400 MHz, $CDCl_3$)



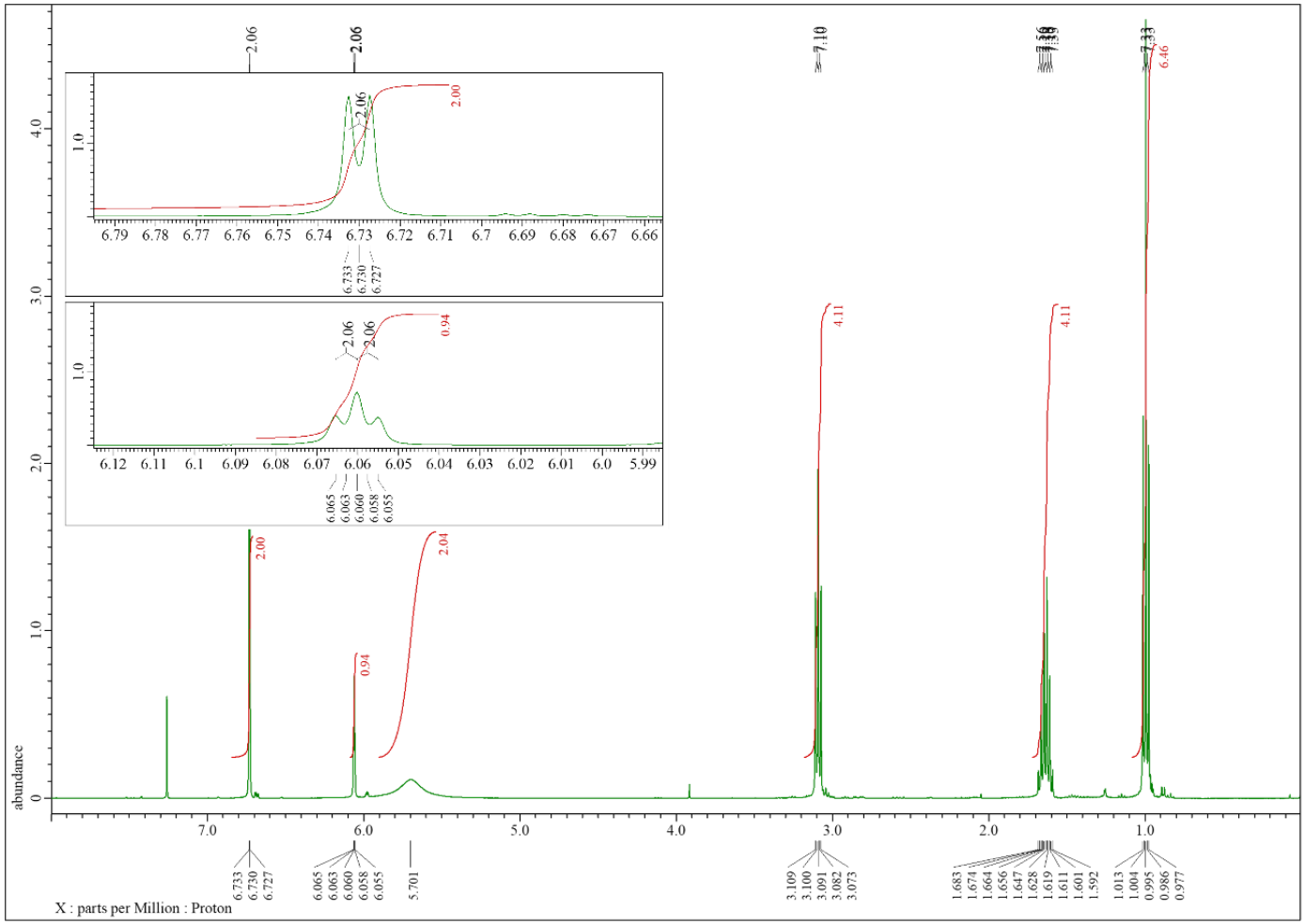
^{13}C NMR (100 MHz, $CDCl_3$)



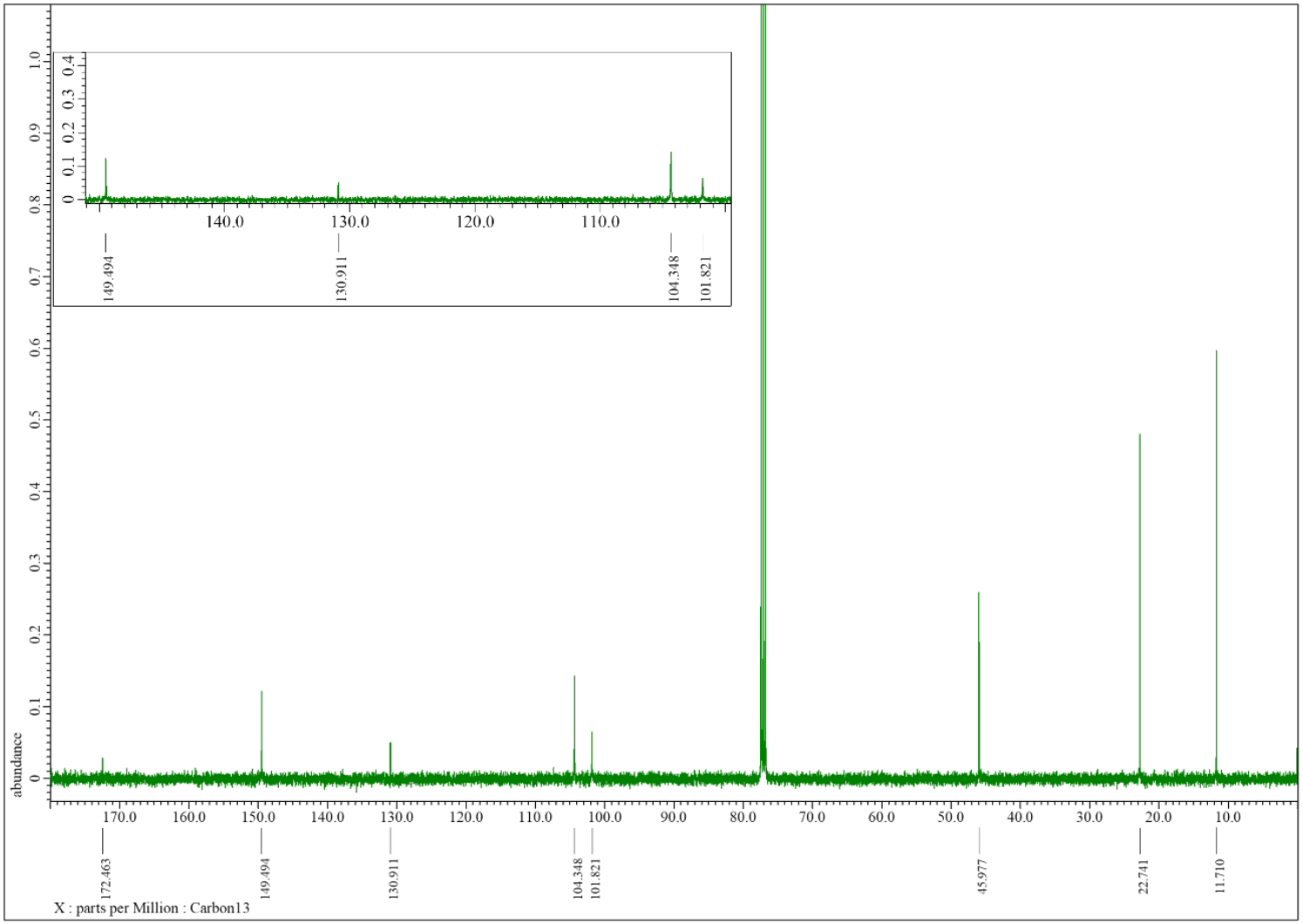
3,5-Bis(propylamino)benzoic acid (11c)



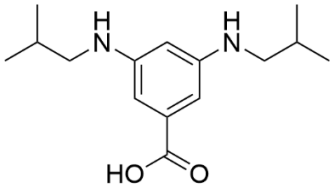
^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)

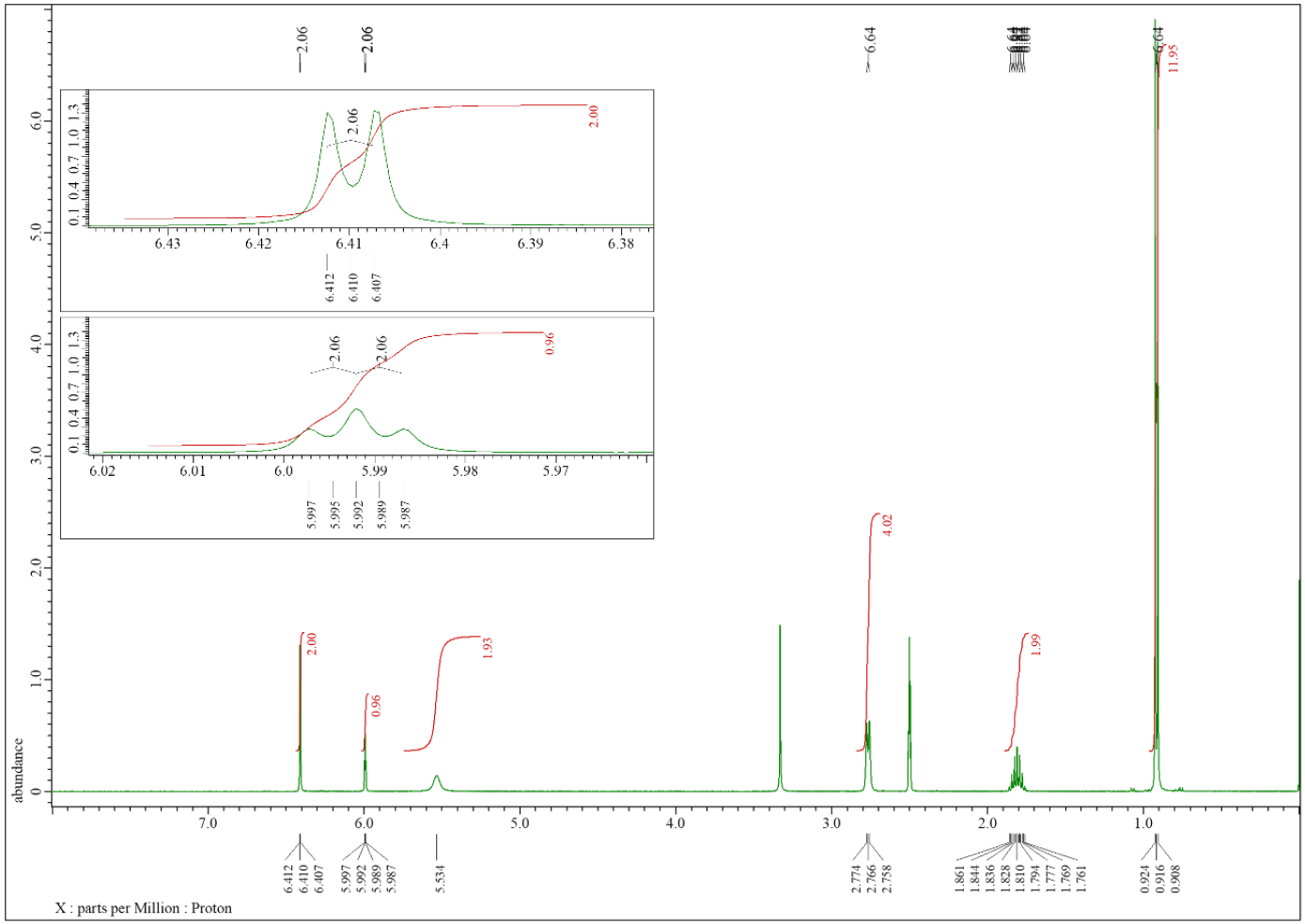


3,5-Bis(isobutylamino)benzoic acid (11d)

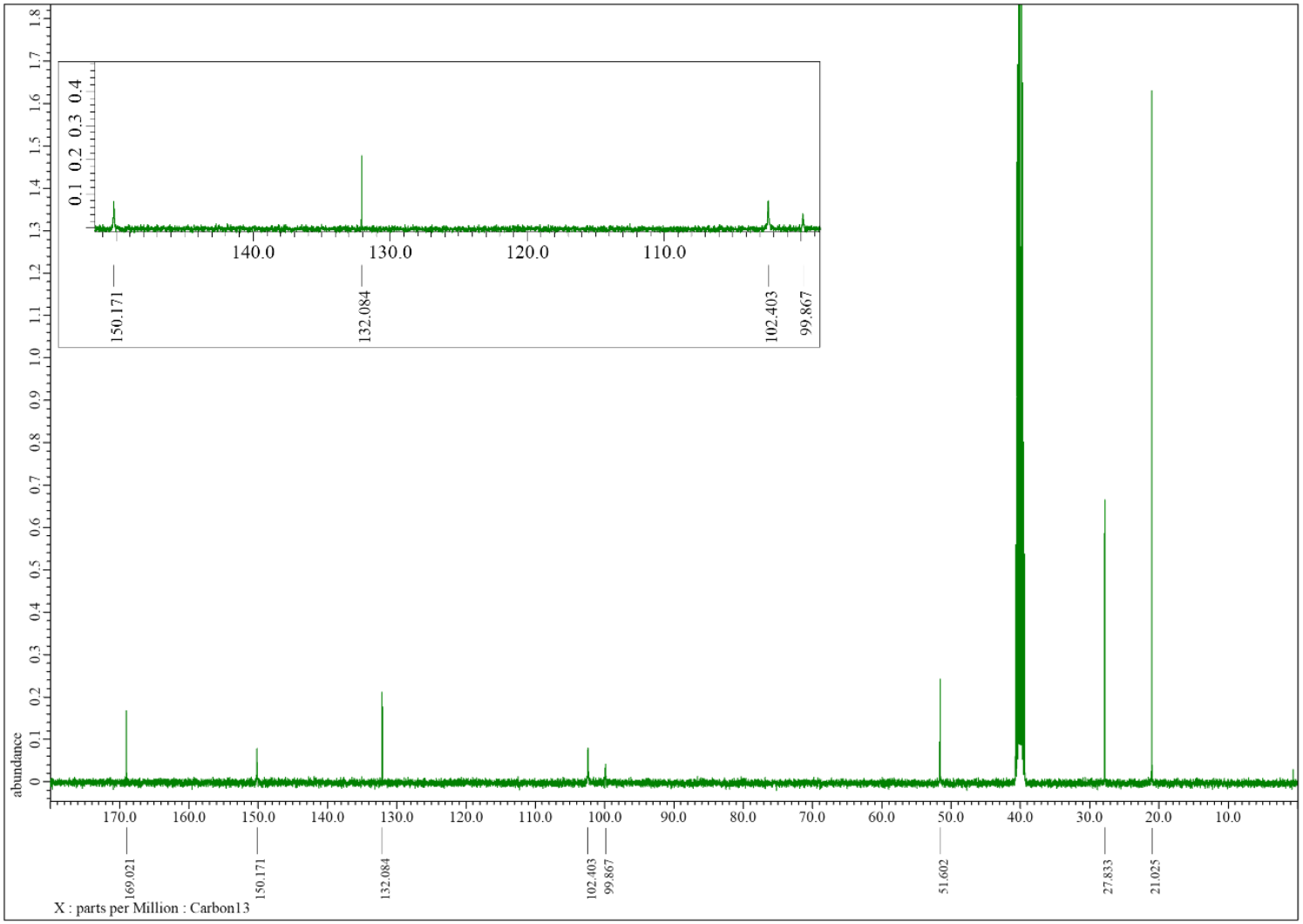


^{1}H NMR

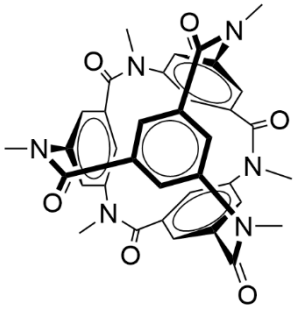
(400 MHz, DMSO-d_6)



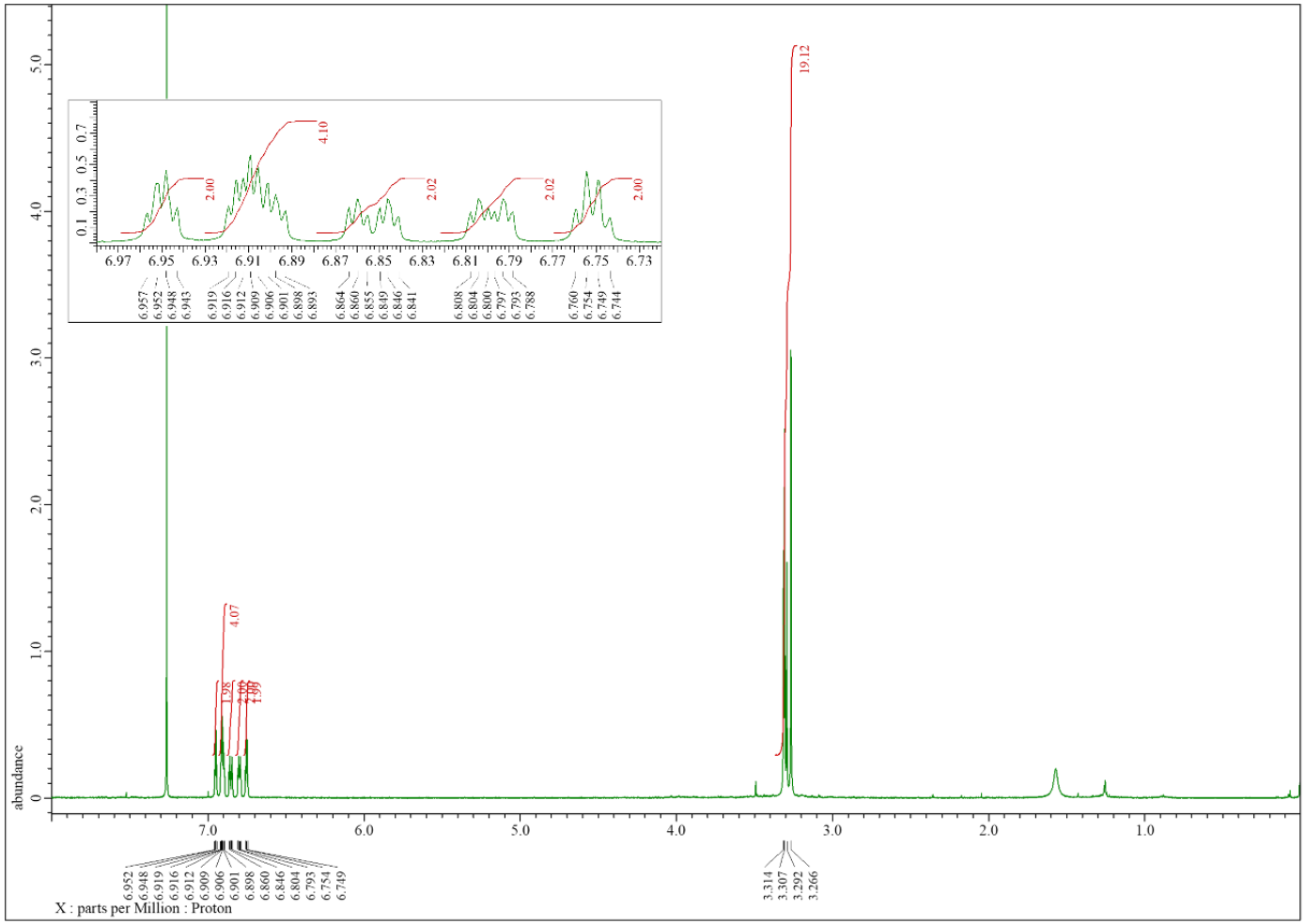
^{13}C NMR (100 MHz, DMSO-d_6)



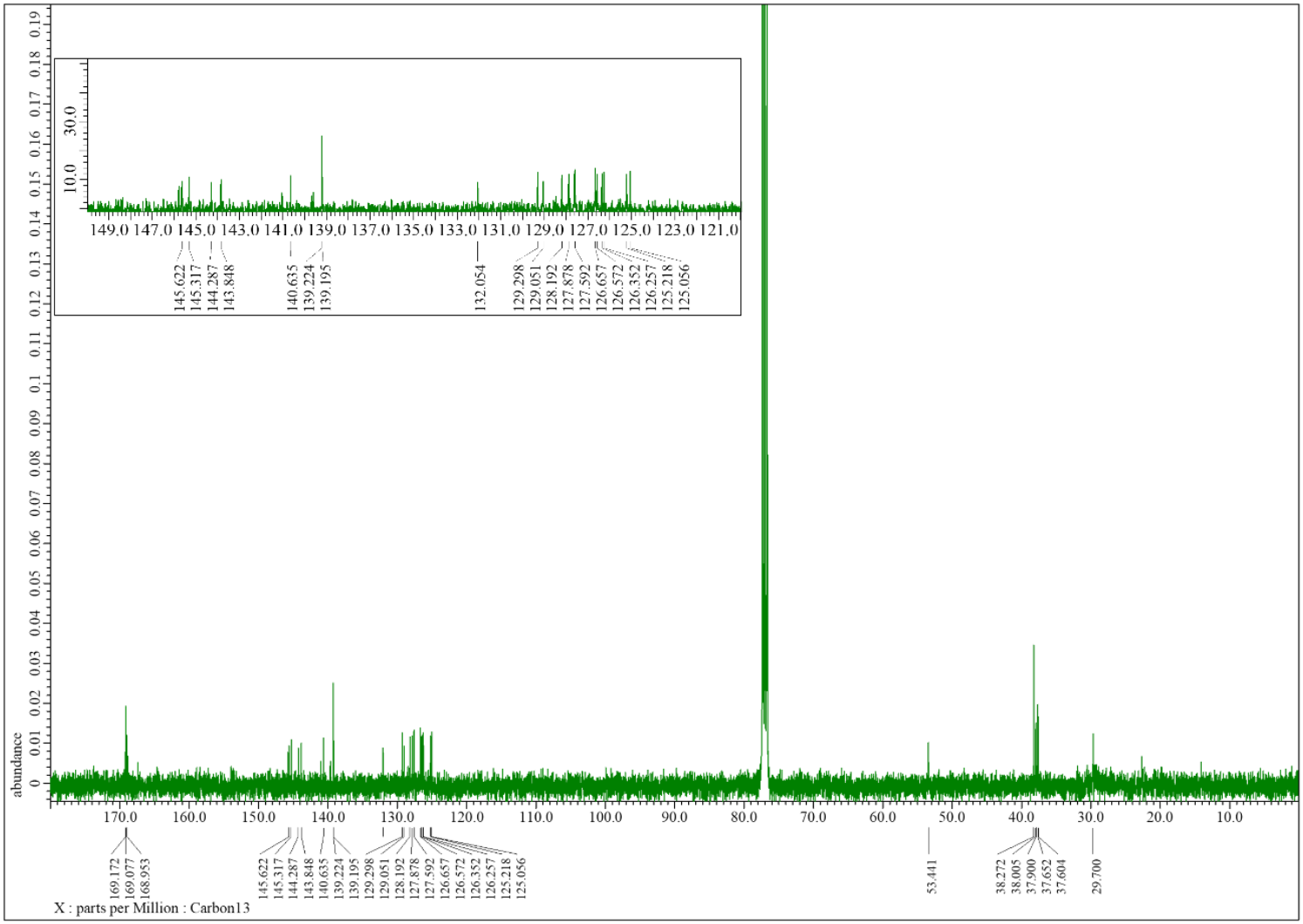
***N*-methyl macrocycle (2a)**



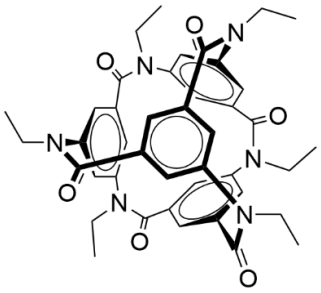
^{1}H NMR (400 MHz, $CDCl_3$)



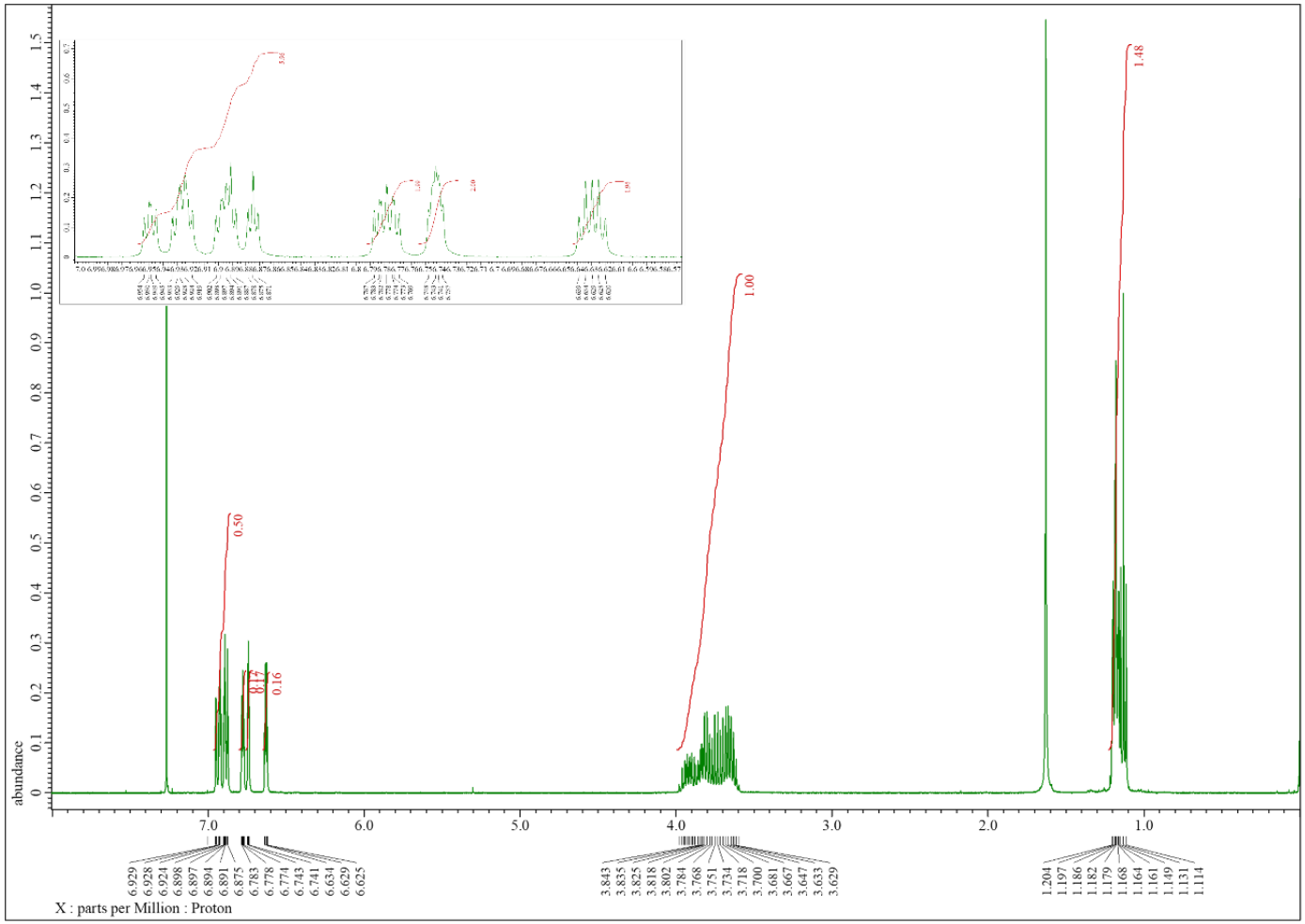
^{13}C NMR (100 MHz, $CDCl_3$)



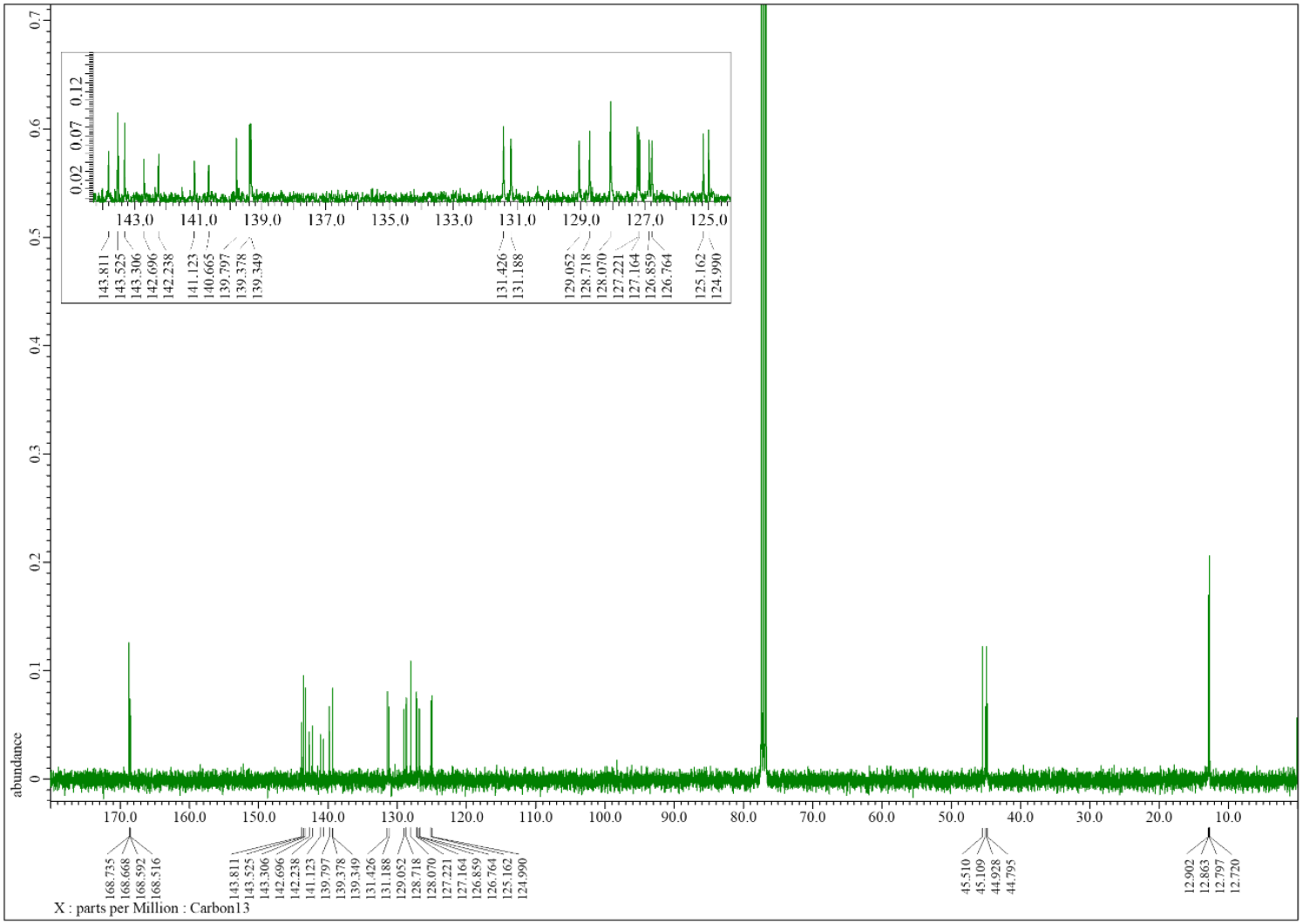
***N*-ethyl macrocycle (2b)**



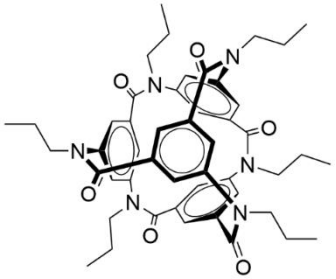
^{1}H NMR (400 MHz, $CDCl_3$)



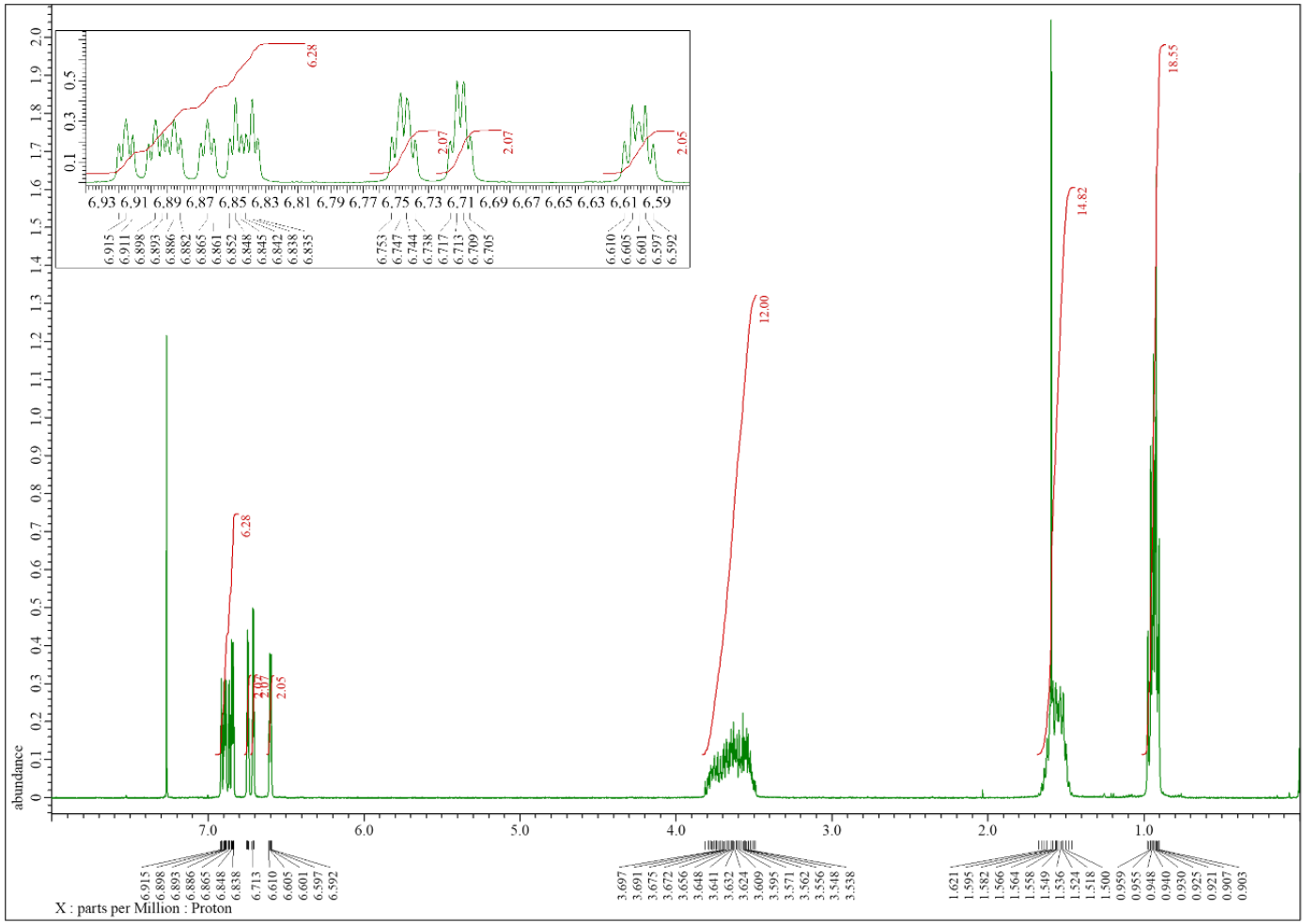
^{13}C NMR (100 MHz, $CDCl_3$)



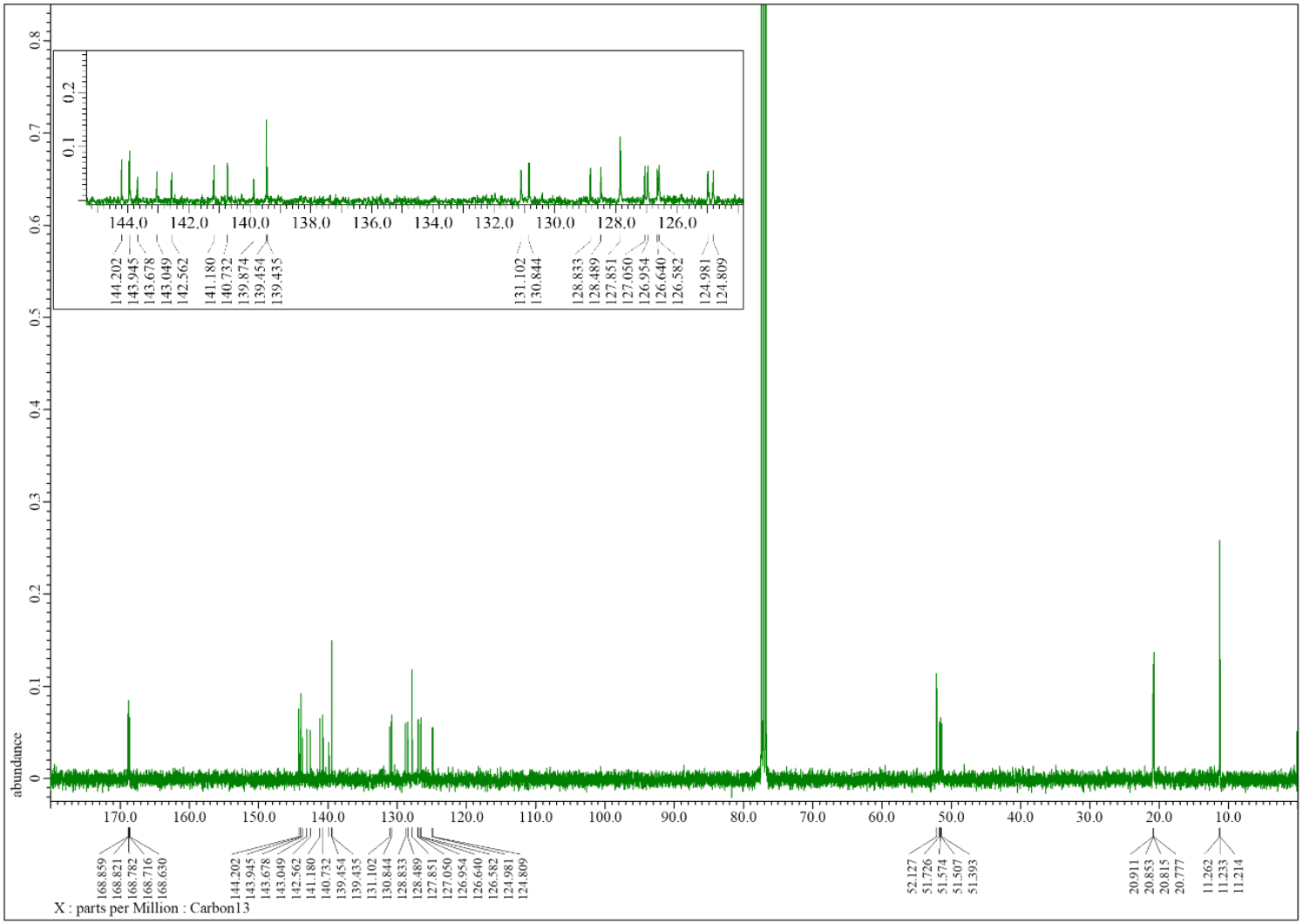
***N*-propyl macrocycle (2c)**



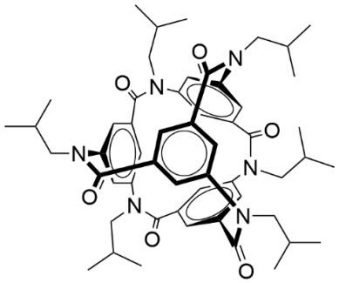
^{1}H NMR (400 MHz, $CDCl_3$)



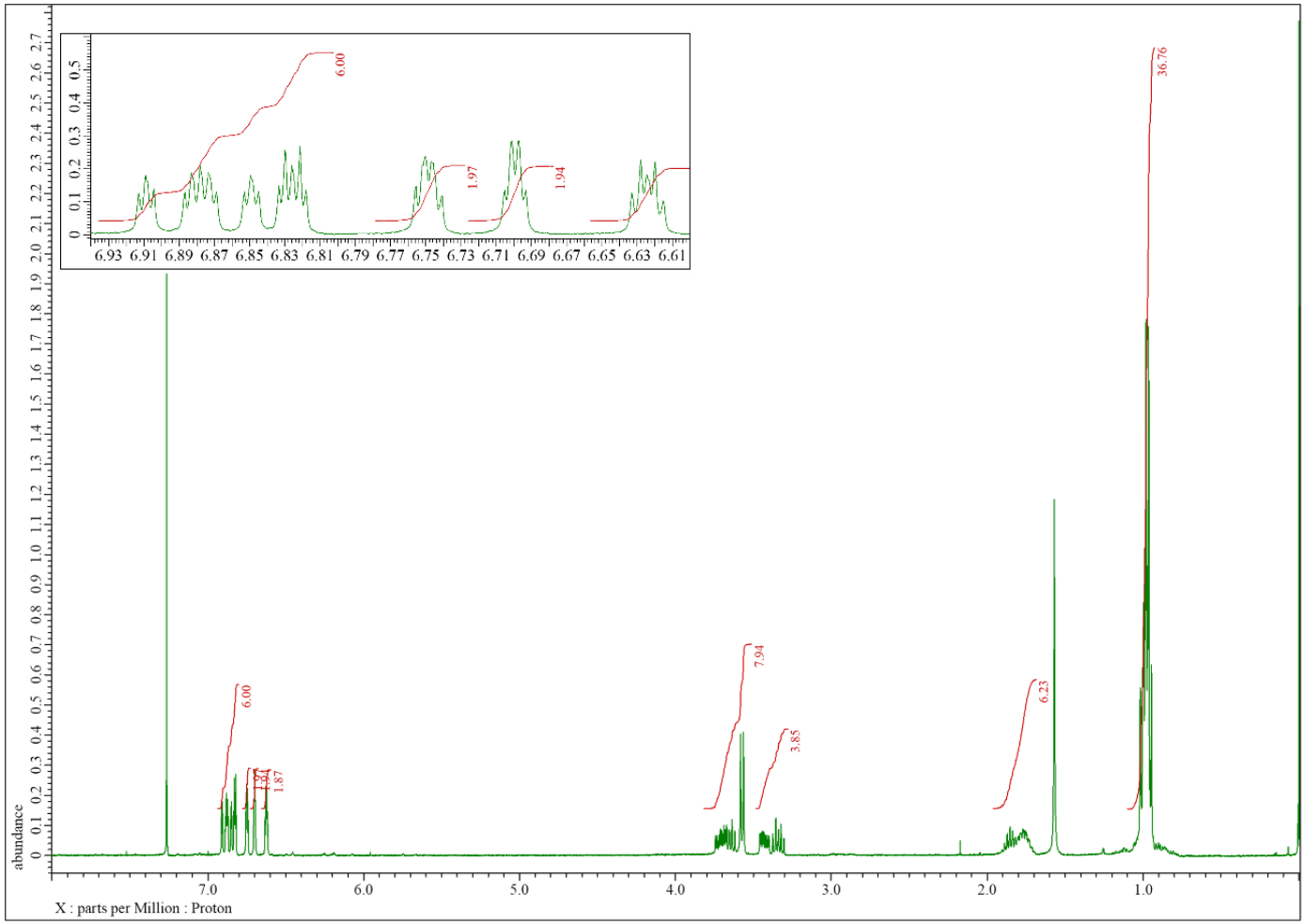
^{13}C NMR (100 MHz, $CDCl_3$)



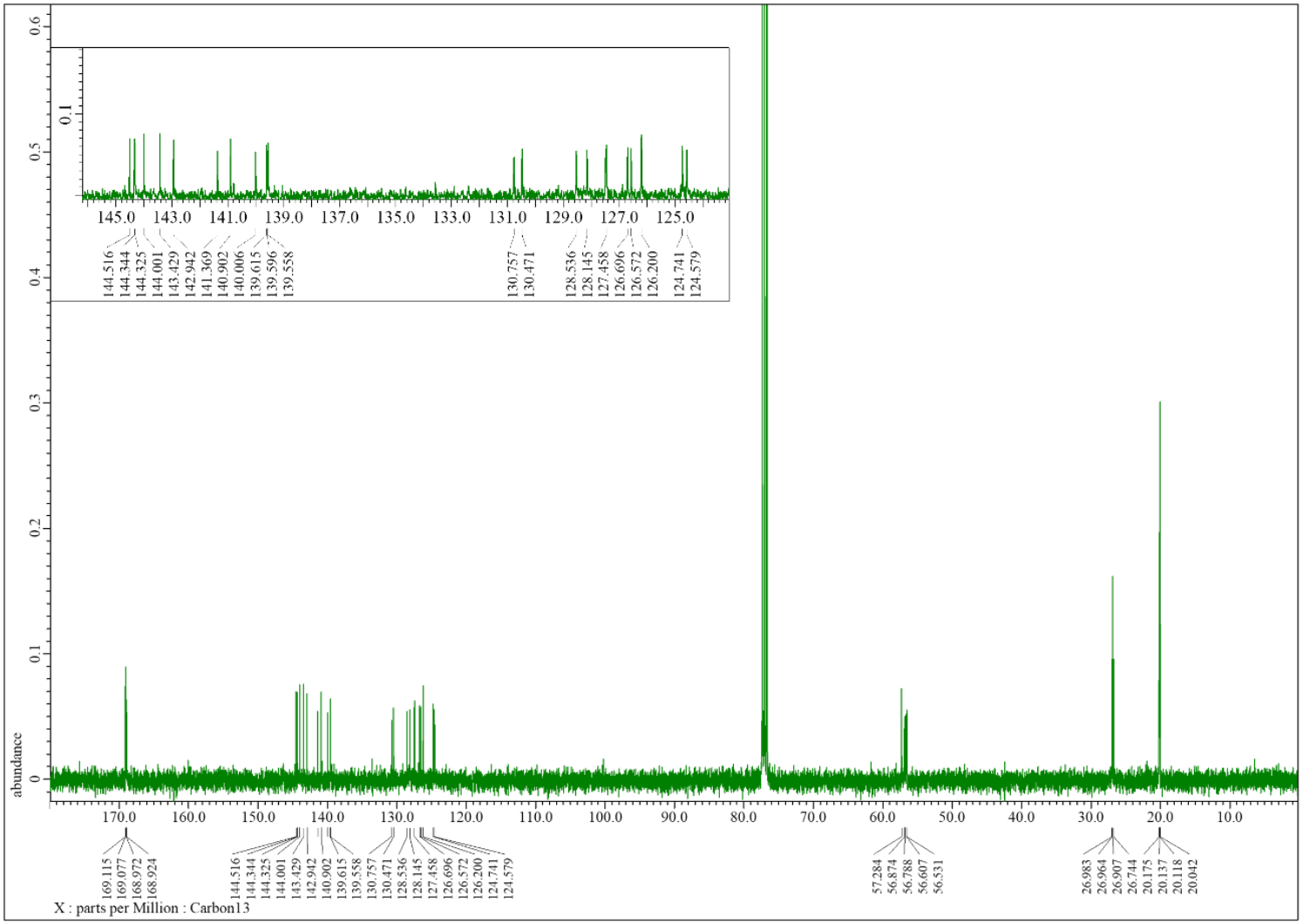
***N*-isobutyl macrocycle (2d)**



^{1}H NMR (400 MHz, $CDCl_3$)



^{13}C NMR (100 MHz, $CDCl_3$)



5. UV spectra

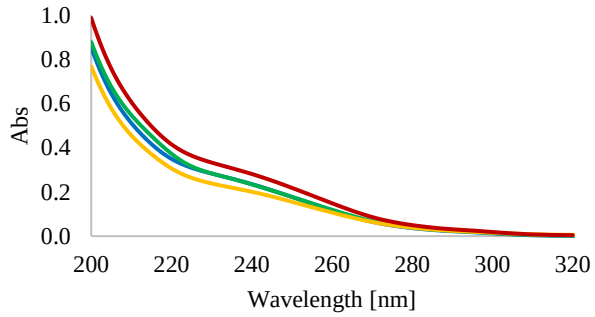
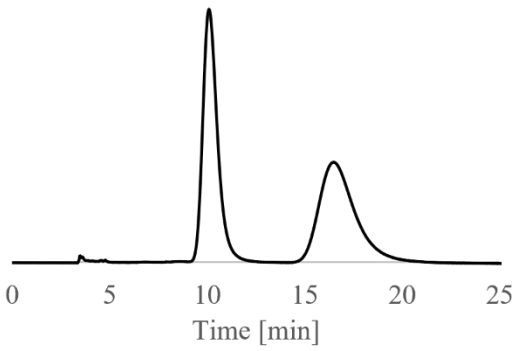


Figure S4 UV spectra of **2a-d** in acetonitrile. Blue: **2a** (*N*-methyl), Red: **2b** (*N*-ethyl), Green: **2c** (*N*-propyl), Yellow: **2d** (*N*-isobutyl).

6. Chiral separation and ECD spectra

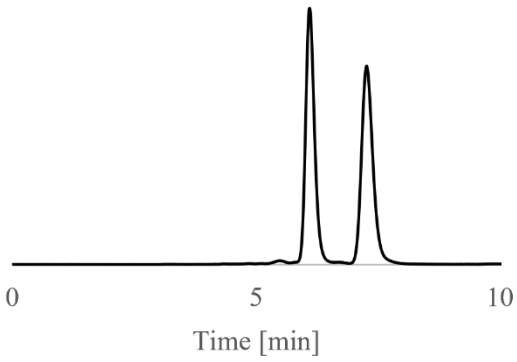
The chiral separations of **2a-d** were carried out by chiral HPLC with DAICEL CHIRALPAK IC column. Other details are described in Figure S5.1. In the HPLC chart of **2d**, two peaks are not completely separated, but enantio-pure molecules are obtained by fractionation. The enantiomeric purity of each compounds was 100% e.e, and for the each enantio-pure compounds, ECD spectra was measured on 200–320 nm (Figure S5.2).



2a (*N*-methyl)

Solvent : MeCN/*n*-Hexane/CH_2Cl_2/2-propanol
= 9 : 6 : 6 : 1
Flowrate : 1.0 mL/min

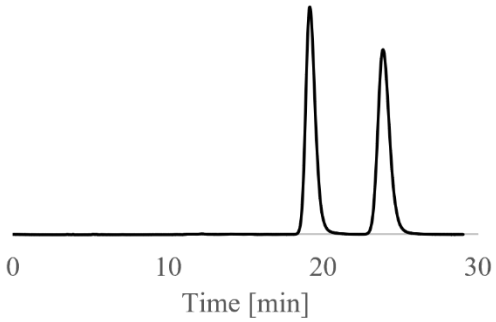
Retention time : 10.117, 13.008 min



2b (*N*-ethyl)

Solvent : *n*-Hexane/CH_2Cl_2/MeCN/2-propanol
= 12 : 4 : 4 : 1
Flowrate : 1.0 mL/min

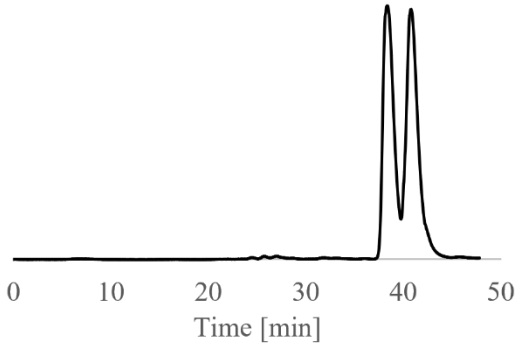
Retention time : 6.100, 7.267 min



2c (*N*-propyl)

Solvent : *n*-Hexane/CH_2Cl_2/MeCN/2-propanol
= 15 : 5 : 1 : 1
Flowrate : 1.0 mL/min

Retention time : 19.150, 23.867 min



2d (*N*-isobutyl)

Solvent : *n*-Hexane/CH_2Cl_2/2-propanol
= 20 : 10 : 1
Flowrate : 0.25 mL/min

Retention time : 38.308, 40.725 min

Figure S5.1 Charts of chiral HPLC and conditions of chiral separation.

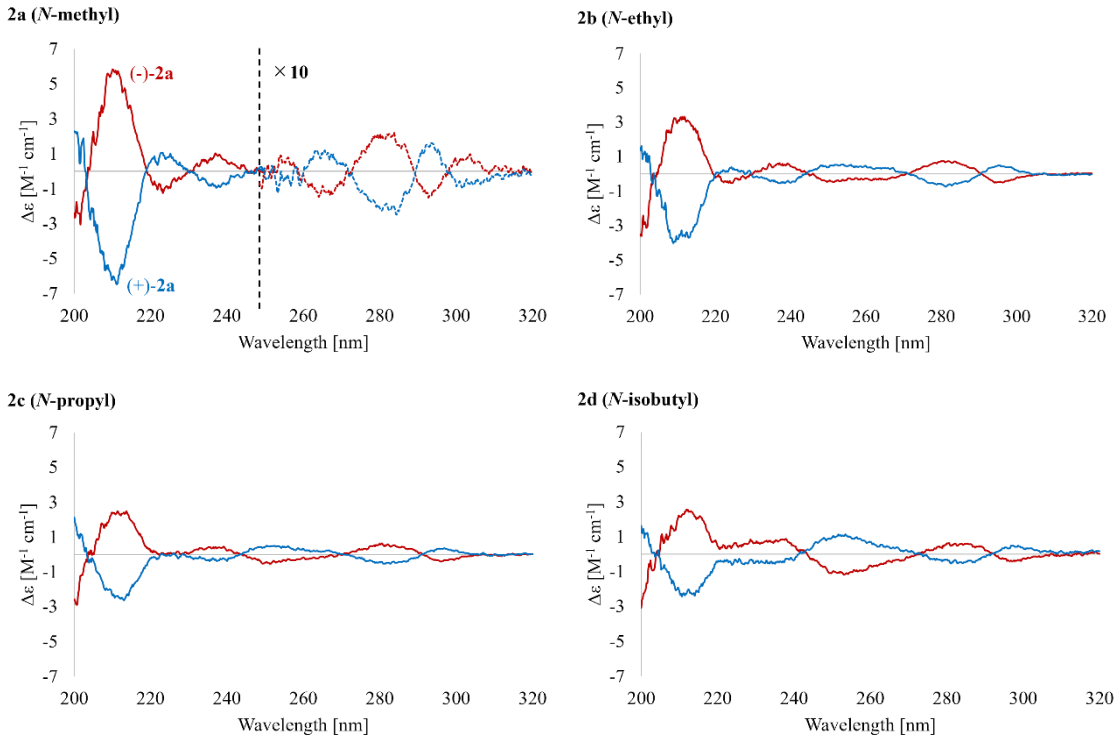


Figure S5.2 CD spectrum of **2a-d**. Red line: 1st eluent. Blue line: 2nd eluent. Dashed line on **2a** (250–320 nm): displayed at 10x for each eluents.

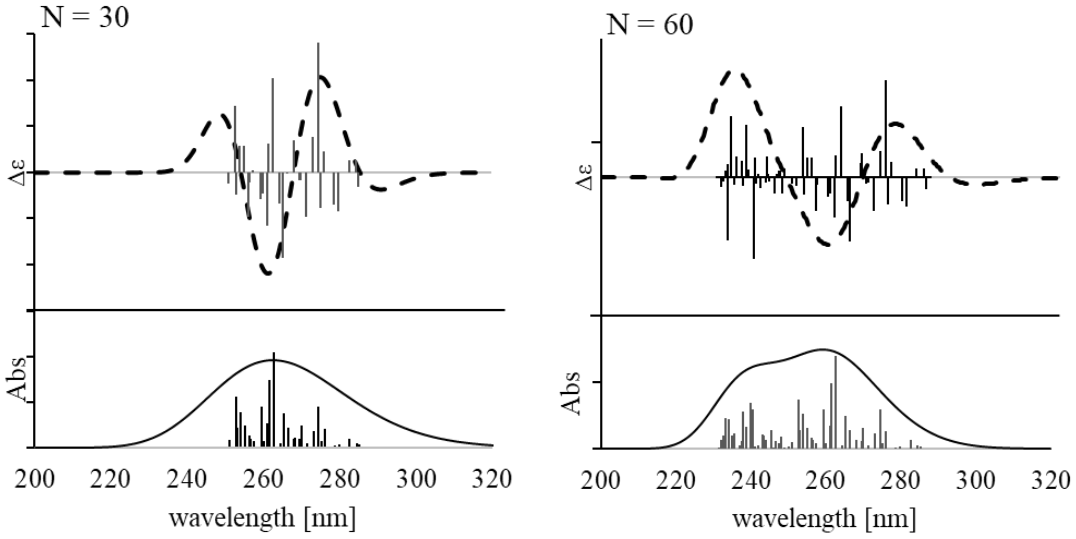
7. Calculation

7-1. MD calculation

First, for the molecular structure of (–)-**2a**, energy minimization with PRCG method, followed conformational search with low-mode sampling method were performed by using Macromodel (worked on Maestro 13.9, Schrödinger, Inc.) on the OPLS force field and 5 kcal/mol energy window. As a result, only one conformation of (−)-**2a** accounted for 95% of the free energy Boltzmann distribution, were used for the next DFT calculation.

7-2. DFT calculation

For the optimized structures obtained by conformational search using MD calculation, DFT and TD-DFT calculations were performed at the B3LYP/6-31+G(d) level with the addition of the acetonitrile solvent effect utilizing the polarizable continuum model (PCM) using Gaussian 16 package of programs[S2]. TD-DFT calculations were performed for 30, 60, 120 excited state (Figure S6), in consequence, to simulate UV/ECD spectra in the region 200–320 nm, especially intensely peak around 210 nm, 120 excited state were needed.



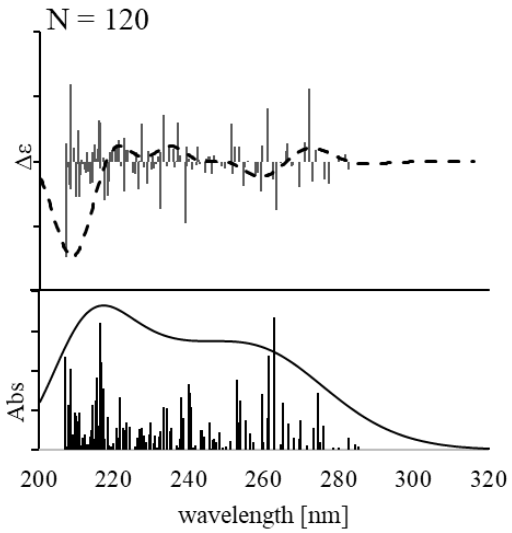


Figure S6. Simulated UV/ECD spectra of (−)-**2a** at 30, 60, 120 excited state.

(–)-2a optimized

Sum of electronic and zero-point Energies = -2169.262787 (Hartree/particle)

Sum of electronic and thermal Free Energies = -2169.335446 (Hartree/particle)

No imaginary frequencies

Cartesian coordinate:

O	0.88900000	0.17500000	-4.77600000
C	0.32500000	0.15700000	-3.68600000
N	-0.94600000	-0.36500000	-3.53200000
C	-1.61300000	-0.85600000	-4.74800000
O	0.07300000	1.42000000	4.66600000
C	0.05200000	0.75100000	3.63800000
N	0.59800000	-0.51700000	3.58300000
C	1.17100000	-1.04700000	4.83100000
O	1.05700000	-5.21000000	0.16800000
O	-5.25500000	-1.03000000	0.32400000
O	-1.10500000	5.25800000	-0.00400000
O	5.21100000	1.10500000	-0.50100000
N	-0.86000000	-4.04600000	-0.28600000
N	-4.02300000	0.83900000	0.80200000
N	0.73900000	4.06700000	-0.65400000
N	4.08800000	-0.78300000	0.14400000
C	0.43900000	-4.14900000	0.16900000

C	-1.53000000	-5.27200000	-0.74400000
C	-1.40900000	-2.79300000	-0.72900000
C	-2.50200000	-2.23200000	-0.06600000
C	-3.01400000	-0.99900000	-0.47900000
C	-2.47000000	-0.35600000	-1.59800000
C	-1.41200000	-0.94100000	-2.29700000
C	-0.87600000	-2.15600000	-1.85500000
C	-4.19400000	-0.41500000	0.25900000
C	-5.17500000	1.47700000	1.45400000
C	-2.71900000	1.36200000	1.11100000
C	-1.93400000	0.74700000	2.09300000
C	-0.68000000	1.27400000	2.42500000
C	-0.20200000	2.39600000	1.74200000
C	-0.97400000	2.99500000	0.73900000
C	-2.25000000	2.50100000	0.45500000
C	-0.47500000	4.20400000	-0.01000000
C	1.30700000	5.25100000	-1.31200000
C	1.22000000	2.78300000	-1.08700000
C	0.49800000	2.05100000	-2.03800000
C	0.98000000	0.82000000	-2.49800000
C	2.16800000	0.30700000	-1.97100000
C	2.87700000	1.02100000	-0.99800000
C	2.42300000	2.27900000	-0.58800000
C	4.15900000	0.47700000	-0.42300000
C	5.33900000	-1.39500000	0.61400000
C	2.86500000	-1.28100000	0.71000000
C	2.28900000	-0.63000000	1.80700000
C	1.10100000	-1.11000000	2.37100000
C	0.47900000	-2.23300000	1.82100000
C	1.06100000	-2.89600000	0.73300000
C	2.26900000	-2.43700000	0.20000000
H	-2.68700000	-0.90800000	-4.55900000
H	-1.41000000	-0.16600000	-5.56800000
H	-1.24800000	-1.85200000	-5.03400000
H	1.23400000	-2.13500000	4.75000000
H	2.17300000	-0.64100000	5.01800000

H	0.52500000	-0.77000000	5.66500000
H	-2.61000000	-5.13700000	-0.65600000
H	-1.20500000	-6.10600000	-0.12100000
H	-1.27900000	-5.49600000	-1.78900000
H	-2.94000000	-2.74400000	0.78600000
H	-2.87400000	0.59200000	-1.93900000
H	-0.05700000	-2.61600000	-2.40100000
H	-5.05000000	2.56200000	1.40900000
H	-5.25700000	1.16900000	2.50400000
H	-6.08500000	1.18200000	0.93100000
H	-2.31900000	-0.12200000	2.62000000
H	0.76400000	2.81500000	2.00300000
H	-2.86700000	2.99000000	-0.29400000
H	2.38900000	5.12500000	-1.39300000
H	1.07700000	6.13300000	-0.71400000
H	0.88700000	5.38800000	-2.31700000
H	-0.42200000	2.46300000	-2.44200000
H	2.55300000	-0.64100000	-2.33400000
H	2.99300000	2.85300000	0.13700000
H	5.21100000	-2.48000000	0.64400000
H	5.60900000	-1.03600000	1.61600000
H	6.14100000	-1.13300000	-0.07700000
H	2.77700000	0.24100000	2.23600000
H	-0.44700000	-2.59600000	2.25700000
H	2.73400000	-2.96600000	-0.62700000

8. X-ray crystallographic analysis

X-ray data were collected on and on a Rigaku XtaLAB P200 diffractometer with multi-layer mirror monochromated Mo*K*α (λ = 0.71075Å, for **2a**) and Cu*K*α (λ = 1.54187Å, for **2b**) and a hybrid photon counting detector (PILATUS 200K). The crystal structure was solved by direct methods (SHELXT Version 2014/5)[S3] and refined by full-matrix least-squares SHELXL-2014/7.[S4]

Crystallographic data for **2a** : $C_{36}H_{30}N_6O_6$, M_r = 642.66, 0.20 × 0.35 × 0.35 mm, trigonal, *R*3*c* (no. 161), $a = b$ = 29.5567(6), c = 18.0997(5) Å, V = 13693.5(7) Å^3, Z = 18, $D_{calcd.}$ = 1.403 gcm^{-3}, $2\theta_{max}$ = 29.564, T = 93(2) *K*, 49036 reflections measured, 7759 unique (R_{int} = 0.1068), μ = 0.098 mm^{-1}. The

final R_1 and wR_2 were 0.0931 and 0.2615 (all data) for 438 parameters and 11 restraints. The residual electron densities (peak and hole) were 0.740 and -0.386 eÅ^{-3}. CCDC 2377216. All non-H-atoms were refined anisotropically, and H-atoms were fixed in geometrically estimated positions and refined using the riding model. In an asymmetric unit of the crystal, two molecules having a different direction each other occupied same position. It is shown as a disorder of two amide parts (C33-O5-N5-C34 and C35-O6-N6-C36). The disorders cause pseudo symmetry in this molecule. A space group including the pseudo symmetry is *I*-43*d*. However, I think that a more appropriate space group based on true symmetry of the molecule is *R*3*c*.

Crystallographic data for **2b** : $C_{42}H_{42}N_6O_6$, M_r = 726.83, 0.078 × 0.043 × 0.010 mm, monoclinic, $P2_1/c$ (no. 14), a = 18.4033(5), b = 9.78786(18), c = 21.6095(7) Å, β = 113.206(3) °, V = 3577.57(18) Å^3, Z = 4, $D_{calcd.}$ = 1.349 gcm^{-3}, θ_{max} = 68.244, T = 93 *K*, 55003 reflections measured, 6489 unique (R_{int} = 0.0646), μ = 0.746 mm^{-1}, T_{min} = 0.890, T_{max} = 0.993.The final R_1 and wR_2 were 0.0645 and 0.2131 (all data) for 493 parameters and 0 restraints. The residual electron densities (peak and hole) were 0.41 and -0.53 eÅ^{-3}. All non-H-atoms were refined anisotropically, and H-atoms were fixed in geometrically estimated positions and refined using the riding model.

CCDC 2377216 (**2a**) and 2382135 (**2b**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre via www.ccdc.cam.ac.uk/data_request/cif.

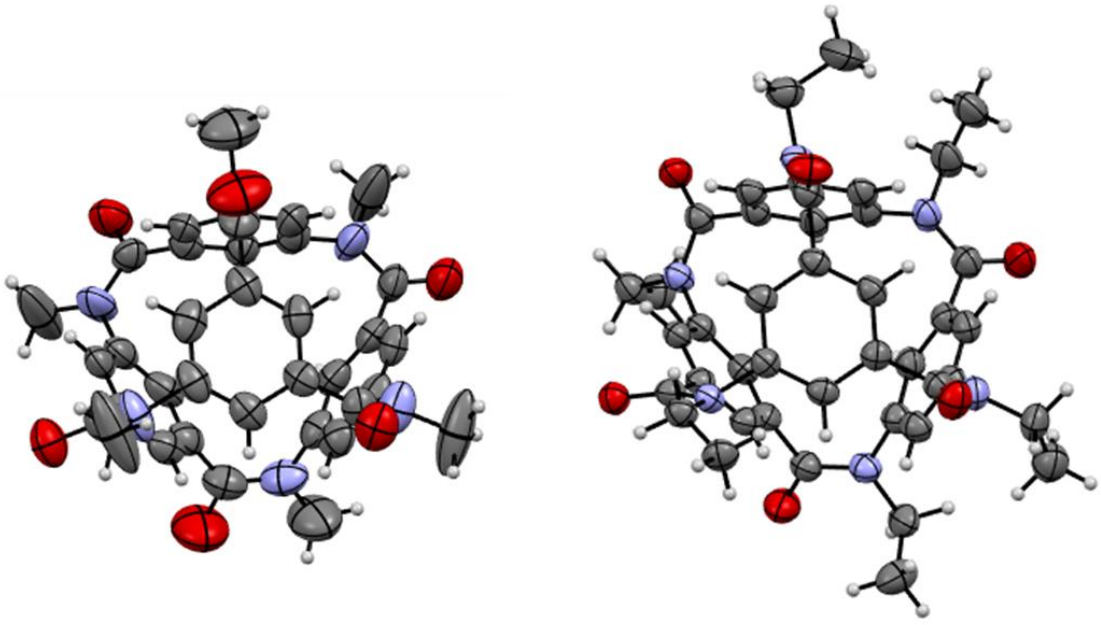


Figure S7.1 ORTEP diagram of asymmetric unit in a crystal of racemic **2a** (left) and **2b** (right). The ellipsoids of non-hydrogen atoms at the 50% probability level. Disordered atoms in **2a** are omitted for clarity.

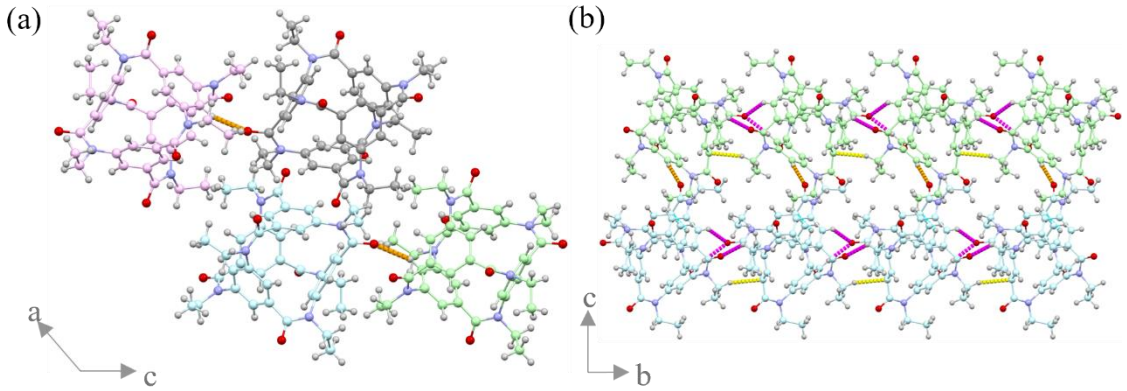


Figure S7.2 (a) Molecular interactions in unit cell, heterochiral chains are formed by CH/O interactions (orange). (b) Molecular interactions between blue/green-colored molecules (homochiral chain); magenta: CH/O interactions, yellow: CH/π interaction.

9. References

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