Supporting Information

Synthesis of 6/6/6-Tricyclic Ether System via Achmatowicz and Intramolecular Oxa-Michael Reactions

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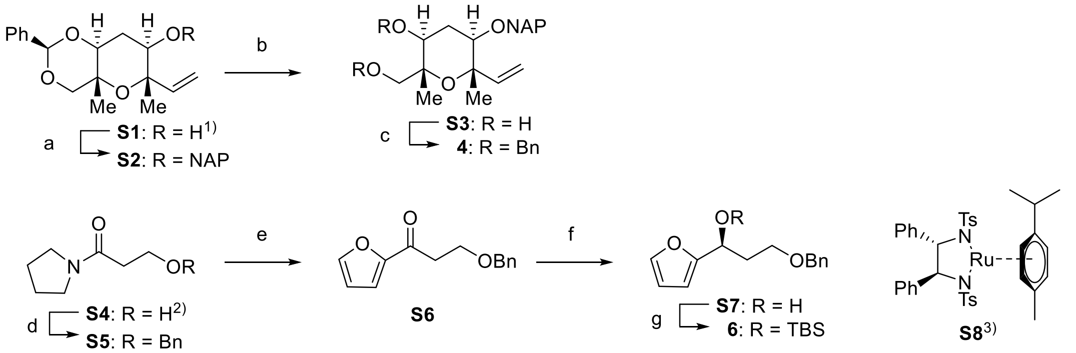
Abbreviations

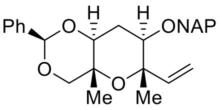
Ac: acetyl, AIBN: azobisisobutyronitrile, acac: acetylacetone, Bn: benzyl, Bu: butyl, COSY: correlation spectroscopy, DDQ: 2,3-dichloro-5,6-dicyano-1,4-benzoquinone, DMF: *N*, *N*-dimethylformamide, ESI: electrospray ionization, Et: ethyl, HMBC: heteronuclear multiple bond coherence, HMQC: heteronuclear multiple quantum coherence, HRMS: high resolution mass spectrometry, Im: imidazole, IR: infrared spectroscopy, *i*: iso, Me: methyl, MS: molecular sieves, *n*: normal, NAP: 2-naphtylmethyl, NIS: *N*-iodosuccinimide, NMR: nuclear magnetic resonance, NOE: nuclear Overhauser effect, NOESY: nuclear overhauser effect spectroscopy, *p*: para, Ph: phenyl, Pr: propyl, RSM: recovery of starting material, rt: room temperature, *s*: secondary, *t*: tertiary, TBAC: tetrabuthylammonium chloride, TBAF: tetrabutylammonium fluoride, TBAI: tetrabutylammonium iodide, TBS: *t*-butyldimethylsilyl, Tf: trifluoromethanesulfonyl, THF: tertrahydrofuran, TLC: thin layer chromatography, TOF: time-of flight, TsOH: *p*-toluenesulfonic acid.

General methods for organic syntheses. All reactions sensitive to air or moisture were performed under an argon atmosphere with dry glassware unless otherwise noted in particular. The dehydrated solvents, CH_2Cl_2, THF, toluene, MeOH, DMF and Et_2O were purchased from Kanto Chemical Co. Inc. or Wako Pure Chemical Industries Ltd., and was used without further dehydration. Benzyl bromide, $BF_3{\cdot}OEt_2$, Bu_3SnH, CS_2, Et_3SiH and furan were distilled before using. MS3A was preactivated by microwave irradiation. $ZnBr_2$, $MgBr_2{\cdot}OEt_2$, $Zn(OTf)_2$ and $Ag(OTf)_2$ were preactivated by heating in vacuo. All other chemicals were obtained from local venders, and used as supplied unless otherwise stated. Thin-layer chromatography (TLC) was performed using pre-coated TLC glass plates (E. Merck silica gel 60 F254, 0.25-mm thickness) for the reaction analyses. For column chromatography and flash column chromatography, Kanto silica gel 60N (spherical, neutral, 100–210 μm) and Kanto silica gel 60N (spherical, neutral, 40–50 μm) were used, respectively. Optical rotations were recorded on a JASCO P-1010 polarimeter. IR spectra were recorded on a JASCO FT/IR-4000. ^1H and ^{13}C NMR spectra were recorded on a JEOL JNM-ECA600 spectrometer. Chemical shifts are reported in ppm from tetramethylsilane (TMS) with reference to internal residual solvent [^1H NMR, $CHCl_3$ (7.26), C_6HD_5 (7.16), C_5HD_4N (7.21); ^{13}C NMR, $CDCl_3$ (77.16), C_5D_5N (125.8)]. The following abbreviations are used to designate the multiplicities: s = singlet, d = doublet, t = triplet, q = quartet, quint = quinted, m = multiplet, br = broad. High resolution mass spectrometry (HRMS) were recorded on Bruker microTOF II mass spectrometer under ESI-TOF conditions.



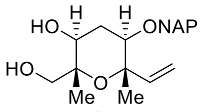
Scheme S1. Reagents and conditions: (a) NAPBr, NaH, DMF, 0 °C to rt, 2 h; (b) TsOH·H_2O, MeOH, THF, H_2O, rt, 20 h, 94% (2 steps); (c) BnBr, NaH, DMF, 0 °C to rt, 3 h, 98%; (d) BnBr, NaH, DMF, 0 °C to rt, 1 h, 90%; (e) furan, *n*-BuLi, THF, 0 °C, 1.5 h; then **S5**, THF, -78 °C, 1 h, 76%; (f) Ru[(*S*,*S*)-Tsdpen](*p*-cymene) **S8**, TBAC, HCO_2Na, CH_2Cl_2, H_2O, rt, 27 h, 98%, (g) TBSCl, Im, DMF, 0 °C to rt, 1.5 h, 97%.

1. K. C. Nicolaou, D. A. Nugiel, E. Couladouros, C.-K. Hwang, *Tetrahedron* 1990, **46**, 4517.
2. W. D. Jones, N. J. Summit, U.S. Patent, 1956, 2’749’355.
3. K. Matsumura, S. Hashiguchi, T. Ikariya, R. Noyori, *J. Am. Chem. Soc.* **1997**, *119*, 8738.



S2

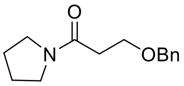
Olefin S2. 2-Napthylmethyl bromide (916.0 mg, 4.14 mmol) and NaH (60% in mineral oil, 177.4 mg, 4.44 mmol) were added to a solution of alcohol **S1** (859.1 g, 2.96 mmol) in DMF (10.0 mL) at 0 °C under an argon atmosphere. After stirring at room temperature for 2 h, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford olefin **S2** as a colorless oil, which was used for the next reaction without further purification.



S3

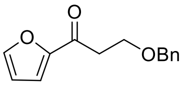
Diol S3. TsOH·H_2O (563.0 mg, 2.96 mmol) was added to a stirred solution of the crude **S2** in a mixture of solution of THF (4.7 mL), MeOH (4.7 mL) and H_2O (0.47 mL) at 0 °C. After stirring at room temperature for 20 h, the reaction mixture was quenched with saturated aqueous NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give diol **S3** (949.6 mg, 2.77 mmol, 94%) as a colorless solid: $[\alpha]_D^{20}$ −37.3 (*c* 1.01,

$CHCl_3$); IR (film) 3327, 2921, 1509, 1470, 1441, 1411, 1380, 1365, 1334, 1271, 1176, 1113, 1085, 1067, 999, 945, 930, 859, 821, 750 cm^{-1}; R_f = 0.24 (hexane/EtOAc = 1/2); ^1H NMR (600 MHz, $CDCl_3$) δ 7.83–7.82 (m, 3H), 7.75 (s, 1H), 7.50–7.44 (m, 3H), 6.00 (dd, *J* = 18.0, 10.8 Hz, 1H), 5.21 (d, *J* = 18.0 Hz, 1H), 5.07 (d, *J* = 10.8 Hz, 1H), 4.79 (d, *J* = 12.0 Hz, 1H), 4.65 (d, *J* = 12.0 Hz, 1H), 3.82 (ddd, *J* = 10.2, 4.8, 4.8 Hz, 1H), 3.53 (dd, *J* = 10.8, 10.8 Hz, 1H), 3.44–3.41 (m, 2H), 2.51 (brs, 1H), 2.19 (ddd, *J* = 10.2, 4.8, 4.8 Hz, 1H), 2.10 (brs, 1H), 1.93 (ddd, *J* = 10.2, 10.2, 10.2 Hz, 1H), 1.40 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 144.4, 136.0, 133.3, 133.1, 128.3, 127.9, 127.8, 126.5, 126.3, 126.1, 125.8, 112.8, 79.2, 77.3, 77.1, 72.0, 68.0, 67.8, 29.5, 21.5, 18.8; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{21}H_{26}O_4Na$ 365.1723, found 365.1710.



S5

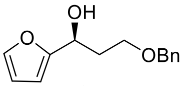
Amide S5. Benzyl bromide (11.4 mL, 95.4 mmol) and NaH (60% in mineral oil, 4.45 g, 111.3 mmol) were added to a solution of alcohol **S4** (0.68 g, 2.41 mmol) in DMF (30.0 mL) at 0 °C under an argon atmosphere. After stirring at room temperature for 1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to give amide **S5** (16.85 g, 72.2 mmol, 90%) as a colorless oil: IR (film) 3466, 2969, 2871, 1073 cm^{-1}; R_f = 0.41 (hexane/EtOAc = 1/2) ; ^1H NMR (600 MHz, $CDCl_3$) δ 7.28–7.19 (m, 5H), 4.47 (s, 2H), 3.76 (t, *J* = 6.9 Hz, 2H), 3.40 (t, *J* = 6.9Hz, 2H), 3.37 (t, *J* = 6.9 Hz, 2H), 2.53 (t, *J* = 6.9 Hz, 2H), 1.86 (quint, *J* = 6.9 Hz, 2H), 1.78 (quint, *J* = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 169.6, 138.5, 128.5 (2C), 127.8 (2C), 127.7, 73.4, 66.6, 46.9, 45.7, 35.5, 26.3, 24.6; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{14}H_{19}NO_2Na$ 256.1308, found 256.1311.



S6

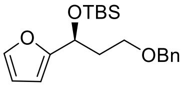
Ketone S6. *n*-BuLi (1.6 M in hexane, 20.0 mL, 32.1 mmol) was added dropwise to a stirred solution of furan (3.0 mL, 41.2 mmol) in THF (130.7 mL) under an argon atmosphere at 0 °C. After stirring at 0 °C for 1.5 h, a solution of amide **S5** (5.02 g, 21.5 mmol) in THF (72.0 mL) was added via cannula to the reaction mixture at –78 °C. After stirring at –78 °C for 1 h, the reaction mixture was quenched with saturated aqueous

NH_4Cl and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to afford ketone **S6** (3.86 g, 16.8 mmol, 76%) as a colorless oil: IR (film) 2873, 2367, 1672, 1569, 1467, 1095 cm^{-1}; R_f = 0.82 (hexane/EtOAc = 1/2) ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.58 (d, *J* = 1.4 Hz, 1H), 7.34–7.26 (m, 5H), 7.21 (d, *J* = 4.1 Hz, 1H), 6.53 (dd, *J* = 4.1, 1.4 Hz, 1H), 4.54 (s, 2H), 3.89 (t, *J* = 6.9 Hz, 2H), 3.14 (t, *J* = 6.9 Hz, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 187.4, 152.9, 146.6, 138.3, 128.5 (2C), 127.8 (3C), 117.6, 112.4, 73.4, 65.4, 39.0 ; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{14}O_3Na$ 253.0835, found 253.0832.



S7

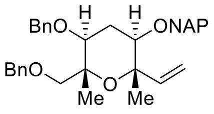
Alcohol S7. TBAC (0.240 g, 0.847 mmol), a solution of sodium formate (3.84 g, 56.5 mmol) in H_2O (10 mL), and **S8** (51.0 mg, 0.085 mmol) were added to a stirred solution of ketone **S6** (0.63 g, 2.82 mmol) in CH_2Cl_2 (10.0 mL) at room temperature. After stirring vigorously at room temperature for 7 h, **S8** (25.2 mg, 0.042 mmol) was added to the reaction mixture again. After stirring at room temperature for 20 h, the reaction mixture was diluted with H_2O and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel column chromatography to furnish alcohol **S7** (0.64 g, 2.77 mmol, 98%) as a colorless oil: $[\alpha]_D^{18}$ −15.8 (*c* 1.25, $CHCl_3$); IR (film) 3412, 2865, 1454, 1073, 1009, 697 cm^{-1}; R_f = 0.51 (hexane/EtOAc = 2/1) ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36 (d, *J* = 2.1 Hz, 1H), 7.35–7.28 (m, 5H), 6.32 (dd, *J* = 3.4, 2.1 Hz, 1H), 6.24 (d, *J* = 3.4 Hz, 1H), 4.94 (dt, *J* = 8.9, 4.1 Hz, 1H), 4.53 (s, 2H), 3.73–3.63 (m, 1H), 3.67–3.63 (m, 1H), 3.11 (d, *J* = 4.1 Hz, 1H), 2.17–2.14 (m, 2H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 156.6, 141.9, 138.0, 128.6 (2C), 127.9 (2C), 127.8, 110.3, 105.9, 73.5, 68.2, 67.1, 35.3; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{14}H_{16}O_3Na$ 255.2682, found 255.2630.



6

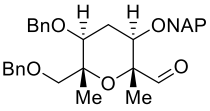
TBS ether 6. Imidazole (0.38 g, 5.17 mmol) was added to a solution of alcohol **S7** (0.33 g, 1.42 mmol) in DMF (4.3 mL) at room temperature under an argon atmosphere. TBSCl (0.42 g, 2.78 mmol) was added to the reaction mixture at 0 °C. After stirring at room temperature for 1.5 h, the reaction mixture was quenched with saturated aqueous NH_4Cl

and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give compound **6** (0.47 g, 1.36 mmol, 97%) as a colorless oil: $[\alpha]_D^{21}$ −30.6 (*c* 1.06, $CHCl_3$); IR (film) 3839, 2860, 2360, 2338, 1746, 1648, 1541, 1508, 1240, 1040, 814, 742, 669 cm^{-1}; R_f = 0.51 (hexane/EtOAc = 2/1) ; ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.36-7.26 (m, 6H), 6.29 (dd, *J* = 3.4, 1.4 Hz, 1H), 6.15 (d, *J* = 3.4 Hz, 1H), 4.90 (dd, *J* = 8.3, 4.5 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.76 (d, *J* = 11.7 Hz, 1H), 3.65-3.62 (m, 1H), 3.50-3.47 (m, 1H), 2.12-2.06 (m, 2H), 0.86 (s, 9H), 0.04 (s, 3H), -0.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 157.2, 141.5, 138.7, 128.5 (2C), 127.8 (2C), 127.6, 110.1, 106.0, 73.1, 66.8, 65.5, 37.2, 25.9 (3C), 18.3, −4.8, −5.0; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{20}H_{30}O_3SiNa$ 369.1856, found 369.1852.



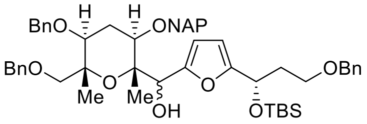
4

Olefin 4. BnBr (0.25 mL, 2.07 mmol) and NaH (100.2 mg, 2.45 mmol) were added to a solution of diol **S3** (295.3 mg, 0.862 mmol) in DMF (6.0 mL) at 0 °C. After stirring at room temperature for 3 h, saturated aqueous NH_4Cl was added to the suspension, and resultant mixture was extracted with Et_2O. The organic layer was dried over Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish olefin **4** (440.5 mg, 0.842 mmol, 98%) as a colorless oil: $[\alpha]_D^{19}$ +9.38 (*c* 1.50, $CHCl_3$); IR (film) 3027, 2941, 1454, 1361, 1092, 1028, 737, 697 cm^{-1}; R_f = 0.64 (hexane/EtOAc = 5/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79–7.76 (m, 3H), 7.69 (s, 1H), 7.45–7.36 (m, 3H), 7.27–7.14 (m, 10H), 5.98 (dd, *J* = 17.4, 10.8 Hz, 1H), 5.33 (dd, *J* = 17.4, 1.8 Hz, 1H), 5.02 (dd, *J* = 10.8, 1.8 Hz, 1H), 4.68 (d, *J* = 11.4 Hz, 1H), 4.58 (d, *J* = 12.6 Hz, 2H), 4.52 (d, *J* = 11.4 Hz, 1H), 4.47 (d, *J* = 12.6 Hz, 1H), 4.36 (d, *J* = 11.4 Hz, 1H), 3.68 (dd, *J* = 12.0, 4.2 Hz, 1H), 3.41 (d, *J* = 10.8 Hz, 1H), 3.35 (d, *J* = 10.8 Hz, 1H), 3.30 (dd, *J* = 12.0, 4.2 Hz, 1H), 2.24 (ddd, *J* = 12.0, 4.2, 4.2 Hz, 1H), 1.74 (ddd, *J* = 12.0, 12.0, 12.0 Hz, 1H), 1.37 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 145.0, 139.1, 138.7, 136.1, 133.3, 133.1, 128.4 (2C), 128.3 (2C), 128.2, 128.0, 127.8, 127.6 (5C), 127.4, 126.2 (2C), 126.0, 125.8, 112.9, 80.6, 77.5, 76.3, 75.9, 75.0, 73.6, 71.9, 71.4, 27.0, 20.6, 19.0; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{35}H_{38}O_4Na$ 545.2662, found 545.2673.



5

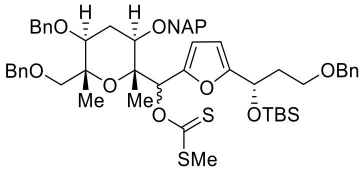
Aldehyde 5. Ozone was bubbled through a solution of olefin **4** (440.5 mg, 0.843 mmol) in a mixed solvent of CH_2Cl_2 (4.2 mL) and MeOH (4.2 mL) at −78 °C for 20 min. Oxygen was then passed through the reaction mixture for 5 min, and then PPh_3 (0.271 g, 1.01 mmol) was added. The reaction mixture was warmed to room temperature slowly over a period of 6 h, and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to afford aldehyde **5** (378.6 mg, 0.721 mmol, 86%) as a colorless solid: $[\alpha]_D^{17}$ +28.3 (*c* 1.03, $CHCl_3$); IR (film) 2942, 2862, 1741, 1332, 1170, 1029, 680 cm^{-1}; R_f = 0.30 (hexane/EtOAc = 5/1); ^1H NMR (600 MHz, $CDCl_3$) δ 9.40 (s, 1H), 7.85–7.82 (m, 3H), 7.71 (s, 1H), 7.50–7.48 (m, 2H), 7.42–7.40 (m, 1H), 7.32–7.28 (m, 8H), 7.23–7.21 (m, 2H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.61 (d, *J* = 11.7 Hz, 1H), 4.59 (d, *J* = 9.6 Hz, 1H), 4.56 (d, *J* = 9.6 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 11.7 Hz, 1H), 3.70–3.65 (m, 2H), 3.47 (d, *J* = 10.3 Hz, 1H), 3.38 (d, *J* = 10.3 Hz, 1H), 2.33 (ddd, *J* = 11.7, 4.8, 4.8 Hz, 1H), 1.84 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.42 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 201.0, 138.5, 138.4, 135.4, 133.3, 133.1, 128.4 (4C), 128.3, 128.0, 127.8, 127.7, 127.6 (5C), 126.5, 126.2, 126.1, 125.8, 80.3, 78.1, 75.1, 73.9, 73.6, 73.3, 71.6, 71.5, 26.4, 18.7, 17.0; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{34}H_{36}O_5Na$ 547.2455, found 545.2473.



7

Alcohol 7. *s*-BuLi (0.80 M in hexane, 3.43 mL, 2.74 mmol) was added to a stirred solution of compound **6** (1.18 g, 3.201 mmol) in THF (32 mL) at –78 °C. After stirring at –78 °C for 10 min, a solution of aldehyde **5** (479.8 mg, 0.91 mmol) in THF (9.0 mL) was added via cannula at –78 °C. After stirring at –78 °C for 30 min, the reaction mixture was quenched with saturated aqueous NH_4Cl, and the resulting biphasic mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dired over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give alcohol **7** (552.2 mg, as a mixture of small amount of **5**) as a colorless oil: IR (film) 2950, 2927, 2856, 1454, 1361, 1252, 1091, 1028, 1009, 837, 778, 735, 697 cm^{-1}; R_f = 0.30 (hexane/EtOAc = 5/1); ^1H

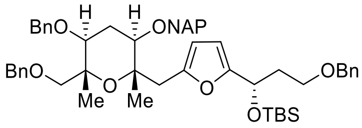
NMR (600 MHz, $CDCl_3$) δ 7.78–7.75 (m, 2H), 7.73 (d, *J* = 8.4 Hz, 1H), 7.56 (s, 1H), 7.45–7.41 (m, 2H), 7.35–7.25 (m, 13H), 7.23–7.19 (m, 3H), 6.38 (d, *J* = 3.6 Hz, 1H), 5.99 (d, *J* = 3.6 Hz, 1H), 4.72 (dd, *J* = 6.0, 6.0 Hz, 1H), 4.58 (d, *J* = 2.4 Hz, 1H), 4.53 (d, *J* = 11.0 Hz, 2H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.34 (d, *J* = 11.7 Hz, 1H), 4.33 (d, *J* = 11.7 Hz, 1H), 4.31 (d, *J* = 11.0 Hz, 1H), 4.27 (d, *J* = 11.0 Hz, 1H), 3.90 (d, *J* = 2.4 Hz, 1H), 3.76 (dd, *J* = 2.4 Hz, 1H), 3.67 (d, *J* = 2.4 Hz, 1H), 3.45 (d, *J* = 9.6 Hz, 1H), 3.42–3.37 (m, 1H), 3.35 (d, *J* = 9.6 Hz, 1H), 3.32–3.29 (m, 1H), 2.29 (ddd, *J* = 12.4, 4.1, 4.1 Hz, 1H), 1.81 (dd, *J* = 13.0, 6.1 Hz, 2H), 1.72 (ddd, *J* = 12.4, 12.4, 12.4 Hz, 1H), 1.50 (s, 3H), 1.21(s, 3H), 0.84 (s, 9H), 0.00 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ156.2, 152.9, 138.7, 138.6, 138.2, 136.3, 133.3, 133.0, 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.0 (4C), 127.8 (6C), 127.6 (3C), 126.1, 126.0, 125.8 (2C), 107.0, 106.3, 79.7, 77.3, 74.8 (2C), 74.7, 73.8, 73.4, 73.0, 71.4, 70.5, 66.7, 65.4, 36.7, 26.0 (3C), 19.6, 18.5, 18.3, −4.5, −5.0; HRMS (ESI-TOF) *m*/*z* $[M+Na]^+$ calcd for $C_{54}H_{66}O_8SiNa$ 893.4419, found 893.4379.



S9

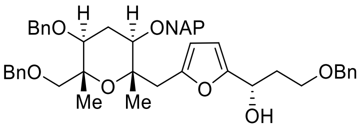
Xanthate S9. A solution of impure alcohol **7** (552.2 mg, 0.634 mmol) in THF (9.0 mL) was added to a suspensuon of NaH (200.3 mg, 5.00 mmol) in THF (11.0 mL) via cannula at 0 °C. After stirring for 20 min at room temperature, carbon disulfide (0.28 mL, 4.73 mmol) was added to the reaction mixture at 0 °C. After stirring for 40 min at room temperature, methyl iodide (0.33 mL, 5.30 mmol) was added to the reaction mixture at 0 °C, and the mixture was allowed to warm to room temperature. After stirring at room temperature for 20 min, the reaction mixture was quenched with saturated aqueous NH_4Cl at 0 °C, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to afford xanthate **S9** (569.5 mg, 0.529 mol, 65% for two steps) as a pale yellow oil: IR (film) 2952, 2927, 2855, 1645, 1361, 1093, 864, 778, 697 cm^{-1}; R_f = 0.50 (hexane/EtOAc = 5/1); ^1H NMR (600 MHz, $CDCl_3$) δ 7.85–7.82 (m, 3H), 7.73 (s, 1H), 7.49–7.44 (m, 3H), 7.34–7.32 (m, 5H), 7.31–7.23 (m, 7H), 7.22–7.21 (m, 3H), 6.53 (d, *J* = 3.4 Hz, 1H), 5.82 (d, *J* = 3.4 Hz, 1H), 5.25 (s, 1H), 4.78 (dd, *J* = 7.6, 6.9 Hz, 1H), 4.57–4.53 (m, 4H), 4.42 (d, *J* = 12.4 Hz, 1H), 4.38 (d, *J* = 6.2 Hz, 1H), 4.36 (d, *J* = 6.2 Hz, 1H), 3.62 (dd, *J* = 12.4, 4.2 Hz, 1H), 3.58–

3.54 (m, 1H), 3.56 (d, *J* = 9.6 Hz, 1H), 3.46–3.42 (m, 2H), 3.40 (d, *J* = 12.4, 4.2 Hz, 1H), 2.42 (s, 3H), 2.27 (ddd, *J* = 12.4, 4.1, 4.1 Hz, 1H), 2.02 (dd, *J* = 13.0, 6.9 Hz, 2H), 1.75 (ddd, *J* = 12.4, 12.4, 12.4 Hz, 1H), 1.50 (s, 3H), 1.23 (s, 3H), 0.83 (s, 9H), 0.03 (s, 3H), −0.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 189.4, 155.5, 151.9, 138.7 (3C), 136.1, 133.4, 133.1, 128.4 (7C), 128.2, 128.1, 127.8 (5C), 127.7, 127.6, 127.5 (3C), 126.3, 126.1, 125.9 (2C), 110.7, 107.6, 79.7, 77.9, 75.9, 74.8, 73.5, 73.1, 71.8, 71.4, 66.8, 65.3, 52.7, 36.7, 27.0, 25.9 (3C), 21.2, 18.5, 18.3, 13.3, −4.5, −5.0; HRMS (ESI-TOF) *m/z* $[M+Na]^+$ calcd for $C_{56}H_{68}O_8S_2SiNa$ 983.4017, found 983.4038.



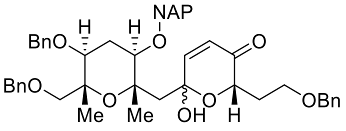
8

Compound 8. Bu_3SnH (0.78 mL, 2.91 mmol) and AIBN (76.5 mg, 0.47 mmol) were added to a solution of xanthate **S9** (560.1 mg, 0.583 mmol) in toluene (6.0 mL) at room temperature. After stirring at 110 °C for 3 h, the reaction mixture was concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnished compound **8** (436.3 mg, 0.51 mmol, 88%) as a colorless oil: $[\alpha]_D^{16}$ −1.87 (*c* 0.94, $CHCl_3$); IR (film) 2855, 2360, 1454, 1361, 1251, 1091, 836, 734, 696 cm^{-1}; R_f = 0.56 (hexane/EtOAc = 5/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.78–7.76 (m, 3H), 7.70 (s, 1H), 7.43–7.40 (m, 3H), 7.27–7.18 (m, 15H), 6.10 (d, *J* =3.8 Hz, 1H), 5.87 (d, *J* = 3.8 Hz, 1H), 4.75 (dd, *J* = 8.2, 4.8 Hz, 1H), 4.68 (d, *J* = 11.7 Hz, 1H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.57 (d, *J* = 11.7 Hz, 1H), 4.51 (d, *J* = 11.7 Hz, 1H), 4.48 (d, *J* = 11.7 Hz, 1H), 4.40 (d, *J* = 11.7 Hz, 1H), 4.35 (d, *J* = 11.7Hz, 1H), 4.33 (d, *J* = 11.7Hz, 1H), 3.55–3.50 (m, 2H), 3.40–3.36 (m, 3H), 3.33 (dd, *J* = 11.7, 4.1 Hz, 1H), 2.88 (d, *J* = 15.1 Hz, 1H), 2.82 (d, *J* = 15.1 Hz, 1H), 2.26 (ddd, *J* = 11.7, 4.1, 4.1 Hz, 1H), 2.05–1.93 (m, 2H), 1.70 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.28 (s, 3H), 1.17 (s, 3H), 0.80 (s, 9H), −0.02 (s, 3H), −0.15 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.8, 151.8, 139.1, 138.8, 138.7, 136.4, 133.4, 133.1, 128.5 (2C), 128.4 (4C), 128.2, 128.0, 127.8 (3C), 127.7 (2C), 127.6 (2C), 127.5 (2C), 127.4, 126.2 (2C), 125.9 (2C), 109.0, 107.3, 78.3, 77.5, 76.8, 76.3, 75.4, 73.7, 73.1, 71.6, 71.4, 66.9, 65.4, 40.2, 36.9, 26.4, 26.0 (3C), 21.9, 18.7, 18.3, −4.4, −5.0; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{54}H_{66}O_7SiNa$ 877.4470, found 877.4497.



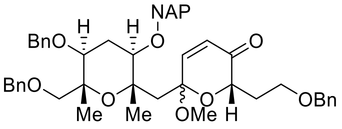
9

Furfuryl alcohol 9. A solution of TBAF (1 M in THF, 2.80 mL, 2.80 mmol) was added to a solution of compound **8** (402.9 mg, 0.47 mmol) in THF (4.7 mL) at 0 °C. After stirring at room temperature for 7 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to give alcohol **9** (307.0 mg, 0.41 mol, 88%) as a colorless solid: $[\alpha]_D^{19}$ −1.63 (*c* 0.99, $CHCl_3$); IR (film) 2928, 2857, 1454, 1362, 1251, 1090, 835, 735, 697 cm^{-1}; R_f = 0.49 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.79–7.77 (m, 3H), 7.70 (s, 1H), 7.43–7.40 (m, 3H), 7.28–7.16 (m, 15H), 6.09 (d, *J* = 3.4 Hz, 1H), 5.96 (d, *J* = 3.4 Hz, 1H), 4.73 (dd, *J* = 7.6, 4.8 Hz, 1H), 4.70 (d, *J* = 11.7 Hz, 1H), 4.54 (d, *J* = 11.7 Hz, 1H), 4.53 (d, *J* = 11.7 Hz, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.42 (s, 2H), 4.33 (d, *J* = 11.7 Hz, 1H), 3.60–3.54 (m, 2H), 3.52–3.49 (m, 1H), 3.37 (s, 2H), 3.32 (dd, *J* = 11.7, 4.1 Hz, 1H), 2.80 (d, *J* = 15.1 Hz, 1H), 2.82 (d, *J* = 15.1 Hz, 1H), 2.26 (ddd, *J* = 11.7, 4.1, 4.1 Hz, 1H), 2.02–1.95 (m, 2H), 1.69 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.30 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 154.6, 152.2, 138.9, 138.8, 138.1, 136.3, 133.4, 133.1, 128.6 (2C), 128.4 (4C), 128.2, 128.0, 127.8 (2C), 127.7 (4C), 127.6, 127.5 (2C), 126.2 (2C), 126.0, 125.8, 108.9, 106.7, 78.2, 77.5, 76.8, 76.2, 75.3, 73.6, 73.3, 71.4 (2C), 68.1, 66.6, 40.2, 35.1, 31.1, 26.3, 22.0, 18.7; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{48}H_{52}O_7Na$ 763.3605, found 763.3625.



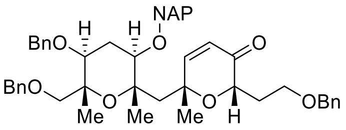
10

Pyranone 10. $CO(NH)_2 \cdot H_2O_2$ (30.6 mg, 0.33 mmol) was added to a solution of $MeReO_3$ (8.7 mg, 35.0 μmol) in CH_2Cl_2 (0.50 mL) at 0 °C. After stirring at 0 °C for 5 min, a solution of alcohol **3** (116.8 mg, 0.16 mmol) in CH_2Cl_2 (1.60 mL) was added to the reaction mixture at 0 °C via cannula. After stirring at 0 °C for 1 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$, and extracted with Et_2O. The organic layer was washed with saturated aqueous NaCl, and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford pyranone **10** as a colorless amorphous solid, which was used for the next reaction without further purification.



11

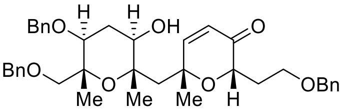
Methylacetal 11. A solution of the above crude **10** in a mixed solvent of Et_2O (1.6 mL) and MeOH (1.6 mL) was transferred to a flask containing MS3A (119.6 mg, 100w/w%) via cannula. $(MeO)_3CH$ (0.21 mL, 1.89 mmol) and $BF_3 \cdot OEt_2$ (34.0 μL, 0.24 mmol) were added to the mixture at 0 °C. After stirring at 0 °C for 25 min, the reaction mixture was quenched with Et_3N and saturated aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish methylacetal **11** (101.7 mg, 0.13 mmol, 84% for two steps) as a pale yellow oil: IR (film) 2860, 1689, 1454, 1362, 1029, 816, 669 cm^{-1}; R_f = 0.55 (hexane/EtOAc = 2/1); HRMS (ESI-TOF) m/z $[M + Na]^+$ calcd for $C_{49}H_{54}O_8Na$ 793.3711, found 793.3742.



12a

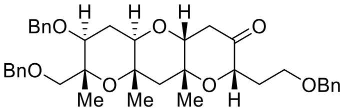
Enone 12a. Me_2Zn (1.0 M in hexane, 0.65 mL, 0.65 mmol) and $BF_3 \cdot OEt_2$ (0.16 mL, 1.30 mmol) were added to a solution of methylacetal **11** (100.2 mg, 0.13 mmol) in CH_2Cl_2 (1.3 mL) at 0 °C. After stirring at room temperature for 2.0 h, the reaction mixture was quenched with Et_3N, and the resulting mixture was extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, saturated aqueous $NaHCO_3$ and saturated aqueous NH_4Cl, and dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish enone **12a** (60.6 mg, 0.08 mmol, 62%) as a colorless oil: $[\alpha]_D^{29}$ −18.5 (c 0.49, $CHCl_3$); IR (film) 2856, 2360, 1683, 1454, 1362, 1205, 815 cm^{-1}; R_f = 0.57 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.85–7.83 (m, 3H), 7.76 (s, 1H), 7.51–7.45 (m, 3H), 7.32–7.22 (m, 15H), 7.17 (d, J = 10.3 Hz, 1H), 7.71 (d, J = 10.3 Hz, 1H), 4.79 (d, J = 11.7 Hz, 1H), 4.60 (d, J = 11.7 Hz, 1H), 4.57 (d, J = 11.7 Hz, 1H), 4.52 (d, J = 11.7 Hz, 1H), 4.49 (d, J = 11.7 Hz, 1H), 4.46 (d, J = 11.7 Hz, 1H), 4.44 (d, J =

11.7 Hz, 1H), 4.41 (d, *J* = 11.7 Hz, 1H), 4.36 (dd, *J* = 7.6, 4.1 Hz, 1H), 3.70–3.60 (m, 3H), 3.33 (d, *J* = 10.3 Hz, 1H), 3.25 (dd, *J* = 12.4, 3.5 Hz, 2H), 2.36–2.31 (m, 1H), 2.27 (ddd, *J* = 11.7, 4.1, 4.1 Hz, 1H), 2.20 (d, *J* = 14.4 Hz, 1H), 1.94–1.88 (m, 1H), 1.70 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.67 (d, *J* = 14.4 Hz, 1H), 1.33 (s, 3H), 1.30 (s, 3H), 1.09 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 197.1, 158.2, 138.8 (2C), 138.7, 136.2, 133.4, 133.1, 128.5 (2C), 128.4 (4C), 128.3, 128.0, 127.9, 127.8 (3C), 127.7 (5C), 127.5, 126.4, 126.3, 126.1, 125.9, 121.8, 81.5, 77.1, 76.9, 75.8, 75.0, 74.7, 73.4, 72.9, 72.2, 71.3, 71.2, 66.4, 53.2, 30.7, 25.8, 23.8, 21.0, 18.8; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{49}H_{54}O_7Na$ 777.3762, found 777.3796.



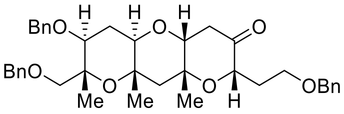
1a

Alcohol 1a. DDQ (34.4 mg, 0.15 mmol) was added to a solution of enone **12a** (57.3 mg, 76.0 μmol) in CH_2Cl_2 (1.0 mL) containing pH 7.0 phosphate buffer (0.5 mL) at 0 °C. After stirring at 0 °C for 1.5 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$. The resulting mixture was extracted with EtOAc, and the organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish alcohol **1a** (39.6 mg, 64.0 μmol, 84%) as a colorless amorphous solid: $[\alpha]_D^{29}$ +12.2 (*c* 0.51, $CHCl_3$); IR (film) 3417, 2856, 2361, 1685, 1453, 1363, 1205, 1098, 734, 697 cm^{-1}; R_f = 0.35 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.33–7.24 (m, 15H), 6.94 (d, *J* = 10.3 Hz, 1H), 5.86 (d, *J* = 10.3 Hz, 1H), 4.59 (d, *J* = 11.7 Hz, 1H), 4.53 (d, *J* = 11.7 Hz, 1H), 4.50 (d, *J* = 12.4 Hz, 1H), 4.47 (d, *J* = 12.4 Hz, 1H), 4.47 (d, *J* = 12.4 Hz, 1H), 4.44 (dd, *J* = 8.3, 3.4 Hz, 1H), 4.39 (d, *J* = 12.4 Hz, 1H), 3.78–3.74 (m, 1H), 3.73 (dd, *J* = 12.4, 4.1 Hz, 1H), 3.60 (dd, *J* = 6.9, 4.8 Hz, 1H), 3.37 (d, *J* = 10.3 Hz, 1H), 3.32 (d, *J* = 10.3 Hz, 1H), 3.06 (brs, 1H), 2.40–2.34 (m, 1H), 2.13 (ddd, *J* = 11.7, 4.1, 4.1 Hz, 1H), 2.01 (d, *J* = 15.1 Hz, 1H), 1.96–1.85 (m, 1H), 1.89 (d, *J* = 15.1 Hz, 1H), 1.75 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.45 (s, 3H), 1.26 (s, 3H), 1.16 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.1, 157.0, 138.8, 138.7, 138.5, 128.5 (2C), 128.4 (4C), 127.8 (4C), 127.7 (4C), 127.6 (2C), 123.5, 78.3, 76.2, 75.5, 75.4, 73.5, 73.0, 72.5, 71.8, 71.2, 66.2, 52.7, 30.6, 29.1, 22.1, 21.2, 19.4; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{38}H_{46}O_7Na$ 637.3136, found 637.3200.



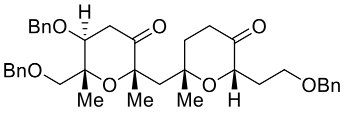
3a

Ketone 3a (acidic conditions). TsOH·H_2O (31.2 mg, 0.16 mmol) was added to a solution of alcohol **1a** (9.9 mg, 16.0 µmol) in CH_2Cl_2 (0.16 mL) at 0 °C. After stirring at room temperature for 1.5 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish ketone **3a** (5.6 mg, 9.1 µmol, 57%) as a colorless amorphous solid: $[\alpha]_D^{30}$ −3.28 (*c* 0.28, $CHCl_3$); IR (film) 3750, 2922, 2362, 1731, 1454, 1375, 1073, 734 cm^{-1}; R_f = 0.50 (hexane/EtOAc = 2/1); ^1H NMR (600 MHz, $CDCl_3$) δ 7.34–7.22 (m, 15H), 4.63 (d, *J* = 12.4 Hz, 1H), 4.60 (d, *J* = 11.7 Hz, 1H), 4.52 (d, *J* = 12.4 Hz, 1H), 4.47 (d, *J* = 11.7 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.38 (d, *J* = 11.7 Hz, 1H), 4.03 (dd, *J* = 11.7, 4.1 Hz, 1H), 3.96 (dd, *J* = 9.6, 3.4 Hz, 1H), 3.78 (dd, *J* = 11.7, 4.1 Hz, 1H), 3.61–3.52 (m, 2H), 3.51 (dd, *J* = 12.4, 3.4 Hz, 1H), 3.41 (d, *J* = 10.3 Hz, 1H), 3.34 (d, *J* = 10.3 Hz, 1H), 2.99 (dd, *J* = 15.1, 9.6 Hz, 1H), 2.45 (dd, *J* = 15.1, 3.4 Hz, 1H), 2.21–2.14 (m, 1H), 2.13 (ddd, *J* = 11.7, 4.1, 4.1 Hz, 1H), 2.03 (d, *J* = 13.8 Hz, 1H), 1.94 (d, *J* = 13.8 Hz, 1H), 1.86–1.80 (m, 1H), 1.68 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.43 (s, 3H), 1.36 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 210.2, 139.0, 138.6 (2C), 128.5 (2C), 128.4 (4C), 127.8 (2C), 127.7 (4C), 127.5 (3C), 78.3, 76.3, 76.2, 75.6, 74.1, 73.7, 73.0, 72.7, 72.0, 71.3, 71.2, 65.8, 51.2, 41.2, 30.2, 26.8, 25.4, 21.5, 20.3; HRMS (ESI-TOF) *m/z* $[M + Na]^+$ calcd for $C_{38}H_{46}O_7Na$ 637.3136, found 637.3131.



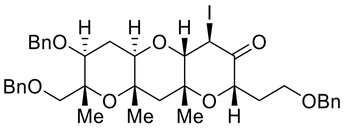
3a

Ketone 3a (basic conditions). NaH (2.2 mg, 56.0 µmol) was added to a solution of alcohol **1a** (8.6 mg, 14.0 µmol) in THF (0.4 mL) at 0 °C. After stirring at room temperature for 2.1 h, the reaction mixture was quenched with saturated aqueous NH_4Cl, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish ketone **3a** (3.2 mg, 5.2 µmol, 37%) as a colorless amorphous solid.



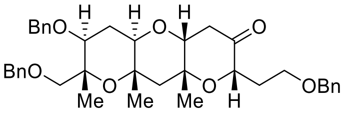
13

Diketone 13. $BF_3 \cdot OEt_2$ (9.3 μL, 75.0 μmol) was added to a solution of alcohol **1a** (9.3 mg, 15.0 μmol) in CH_2Cl_2 (1.51 mL) at 0 °C. After stirring at room temperature for 40 min, the reaction mixture was quenched with Et_3N, and diluted with EtOAc. The organic layer was washed with saturated aqueous NaCl, saturated aqueous NH_4Cl and saturated aqueous $NaHCO_3$, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish diketone **13** (5.9 mg, 9.6 μmol, 63%) as a colorless oil: $[\alpha]_D^{28}$ −28.3 (*c* 0.30, $CHCl_3$); IR (film) 3751, 2924, 2369, 1729, 1454, 1363, 1096, 739 cm^{-1}; R_f = 0.50 (hexane/EtOAc = 2/1); ^1H NMR (600 MHz, $CDCl_3$) δ 7.33–7.23 (m ,15H), 4.58 (d, *J* = 11.7Hz, 1H), 4.52 (d, *J* = 11.7 Hz, 1H), 4.49 (d, *J* = 12.4 Hz, 1H), 4.46 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 12.4 Hz, 1H), 4.38 (d, *J* = 11.7 Hz, 1H), 4.13 (dd, *J* = 4.8, 3.4 Hz, 1H), 3.96 (dd, *J* = 6.2, 4.8 Hz, 1H), 3.55–3.48 (m, 2H), 3.47 (d, *J* = 9.6 Hz, 1H), 3.43 (d, *J* = 9.6 Hz, 1H), 3.02 (dd, *J* = 15.1, 3.4 Hz, 1H), 2.54 (dd, *J* = 15.1, 6.2 Hz, 1H), 2.47 (ddd, *J* = 17.2, 11.7, 4.8 Hz, 1H), 2.34 (d, *J* = 14.4 Hz, 1H), 2.20 (ddd, *J* = 17.2, 4.8, 4.8 Hz, 1H), 2.01–1.95 (m, 1H), 1.85 (ddd, *J* = 13.8, 4.8,4.8 Hz, 1H), 1.82–1.77 (m ,1H), 1.73 (d, *J* = 14.4 Hz, 1H), 1.65–1.60 (m, 1H), 1.42 (s, 3H), 1.39 (s, 3H), 1.38 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 212.6, 212.5, 138.6, 138.3, 128.5 (6C), 127.8, 127.7 (3C), 127.6 (4C), 82.4, 77.9, 76.5, 75.8, 73.9, 73.6, 73.3, 72.9, 71.4, 66.3, 52.0, 39.6, 35.1, 33.9, 30.4, 29.8, 27.9; HRMS (ESI-TOF) *m*/*z* $[M + Na]^+$ calcd for $C_{38}H_{46}O_7Na$ 637.3136, found 637.3145.



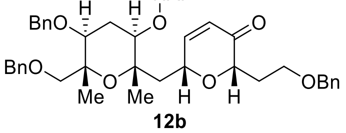
14

Iodide 14. NIS (7.0 mg, 31.2 μmol) was added to a solution of $Fe(acac)_3$ (1.0 mg, 31.2 μmol) in CH_2Cl_2 (0.5 mL) at 0 °C in the dark. After stirring at room temperature for 10 min, a solution of alcohol **1a** (9.6 mg, 15.6 μmol) in CH_2Cl_2 (1.0 mL) was added to this reaction mixture at 0 °C via cannula. After stirring at room temperature for 27 h, the reaction mixture was quenched with saturated aqueous $Na_2S_2O_3$ and saturated aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish iodide **14** (7.7 mg, 10.0 μmol, 67%, d.r. = 13:1) as a yellow oil: IR (film) 2924, 1739, 1454, 1379, 1077, 1027, 737, 696 cm^{-1}; R_f = 0.70 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.34–7.19 (m, 15H), 5.44 (d, *J* = 13.1 Hz, 1H), 4.64 (d, *J* = 11.7 Hz, 1H), 4.60 (d, *J* = 12.4 Hz, 1H), 4.56 (d, *J* = 12.4 Hz, 1H), 4.44 (d, *J* = 11.7 Hz, 1H), 4.43 (d, *J* = 11.7 Hz, 1H), 4.38 (d, *J* = 11.7 Hz, 1H), 4.09 (dd, *J* = 6.9, 4.1 Hz, 1H), 3.82 (dd, *J* = 11.7, 4.8 Hz, 1H), 3.66–3.62 (m, 1H), 3.58 (d, *J* = 13.1 Hz, 1H), 3.55–3.51 (m, 1H), 3.40 (d, *J* = 10.3 Hz, 1H), 3.34 (d, *J* = 10.3 Hz, 1H), 2.98 (d, *J* = 11.7, 3.4 Hz, 1H), 2.23 (ddd, *J* = 11.7, 3.4, 3.4 Hz, 1H), 2.18–2.12 (m, 1H), 2.07 (d, *J* = 13.1 Hz, 1H), 2.02–1.97 (m, 1H), 1.84 (d, *J* = 13.1 Hz, 1H), 1.74 (ddd, *J* = 11.7, 11.7, 11.7 Hz, 1H), 1.46 (s, 3H), 1.37 (s, 3H), 1.26 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 204.7, 139.0, 138.3, 138.1, 128.6 (2C), 128.5 (2C), 128.4 (2C), 128.0 (2C), 127.8 (2C), 127.7 (2C), 127.6 (2C), 127.5, 80.8, 78.4, 76.2 (2C), 75.6, 73.7, 73.1, 71.7, 71.5, 71.3 (2C), 65.1, 51.0, 39.0, 31.3, 26.6 (2C), 20.7, 20.1; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $C_{38}H_{45}IO_7Na$ 763.6647, found 763.2102.



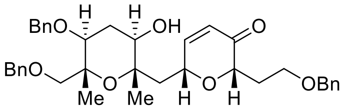
3a

Ketone 3a (from 14). Bu_3SnH (27.0 μL, 0.10 mmol) and AIBN (16.6 mg, 10 μmol) were added to a solution of iodide **14** (7.5 mg, 10.0 μmol) in benzene (0.2 mL) at room temperature. After stirring under reflux (80 °C) for 25 min, H_2O was added and the resulting mixture was extracted with EtOAc. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish ketone **3a** (3.5 mg, 5.7 μmol, 56%) as a colorless amorphous solid.



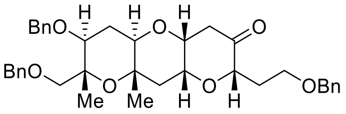
12b

Enone 12b. $CO(NH_2)_2{\cdot}H_2O_2$ (19.6 mg, 0.50 mmol) was added to a solution of $MeReO_3$ (5.4 mg, 22.0 μmol) in CH_2Cl_2 (0.7 mL) at 0 °C. After stirring at 0 °C for 5 min, a solution of alcohol **9** (73.6 mg, 0.10 mmol) in CH_2Cl_2 (1.30 mL) was added to the reaction mixture at 0 °C via cannula. After stirring at 0 °C for 1 h, the reaction mixture was quenched with saturated aqueous $NaHCO_3$ and saturated aqueous $Na_2S_2O_3$, and extracted with Et_2O. The organic layer was dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure to afford pyranone **10** as a colorless amorphous solid, which was used for the next reaction without further purification. MS4A (75.6 mg, 100w/w%), $\mathrm{BF_3{\cdot}OEt_2}$ (61.2 μL, 0.50 mmol) and $\mathrm{Et_3SiH}$ (32.0 μL, 0.20 mmol) were added to a solution of crude pyranone **10** in $\mathrm{CH_2Cl_2}$ (2.0 mL) at −78 °C. After stirring at −78 °C for 30 min, the reaction mixture was quenched with saturated aqueous $\mathrm{NaHCO_3}$, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous $\mathrm{Na_2SO_4}$, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish enone **12b** (31.1 mg, 42.0 μmol, 42% for two steps) as a colorless oil: $[\alpha]_D^{25}$ +16.2 (*c* 1.32, $\mathrm{CHCl_3}$); IR (film) 2863, 1688, 1454, 1362, 1202, 1094, 1028, 733, 698 cm^{-1}; R_f = 0.50 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, $\mathrm{C_6D_6}$) δ 7.77 (s, 1H), 7.70–7.62 (m, 5H), 7.51 (dd, *J* = 8.3, 1.4 Hz, 1H), 7.29–7.03 (m, 15H), 6.61 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.95 (dd, *J* = 10.3, 2.1 Hz, 1H), 4.79 (brs, 1H), 4.67 (d, *J* = 11.7 Hz, 1H), 4.61 (d, *J* = 11.7 Hz, 1H), 4.50 (d, *J* = 11.7 Hz, 1H), 4.32 (s, 2H), 4.31 (d, *J* = 11.7 Hz, 1H), 4.24 (d, *J* = 11.7 Hz, 1H), 4.20 (d, *J* = 11.7 Hz, 1H), 3.94 (dd, *J* = 12.4, 4.1 Hz, 1H), 3.89–3.87 (m, 2H), 3.66–3.63 (m, 1H), 3.61–3.57 (m, 1H), 3.42 (d, *J* = 9.6 Hz, 1H), 3.26 (d, *J* = 9.6 Hz, 1H), 2.60–2.55 (m, 1H), 2.33 (ddd, *J* = 12.4, 4.1, 4.1 Hz, 1H), 2.23 (dd, *J* = 14.4, 6.9 Hz, 1H), 2.09–2.03 (m, 1H), 1.80 (ddd, *J* = 12.4, 12.4, 12.4 Hz, 1H), 1.68 (dd, *J* = 14.4, 4.1 Hz, 1H), 1.35 (s, 3H), 1.24 (s, 3H); ^{13}C NMR (150 MHz, $\mathrm{CDCl_3}$) δ 196.6, 154.5, 138.7, 138.6, 138.5, 136.3, 133.4, 133.1, 128.5 (4C), 128.4 (2C), 128.2, 128.0, 127.8 (4C), 127.7, 127.6 (3C), 127.5 (2C), 126.2, 126.1, 126.0 (2C), 125.7, 77.6, 77.0, 76.8, 75.8, 75.6, 74.8, 73.4, 72.8, 71.5, 71.4, 71.3, 66.7, 44.9, 30.1, 26.2, 23.5, 18.8; HRMS (ESI-TOF) *m/z* [M + Na]$^+$ calcd for $\mathrm{C_{48}H_{52}O_7Na}$ 763.3605, found 763.3632.



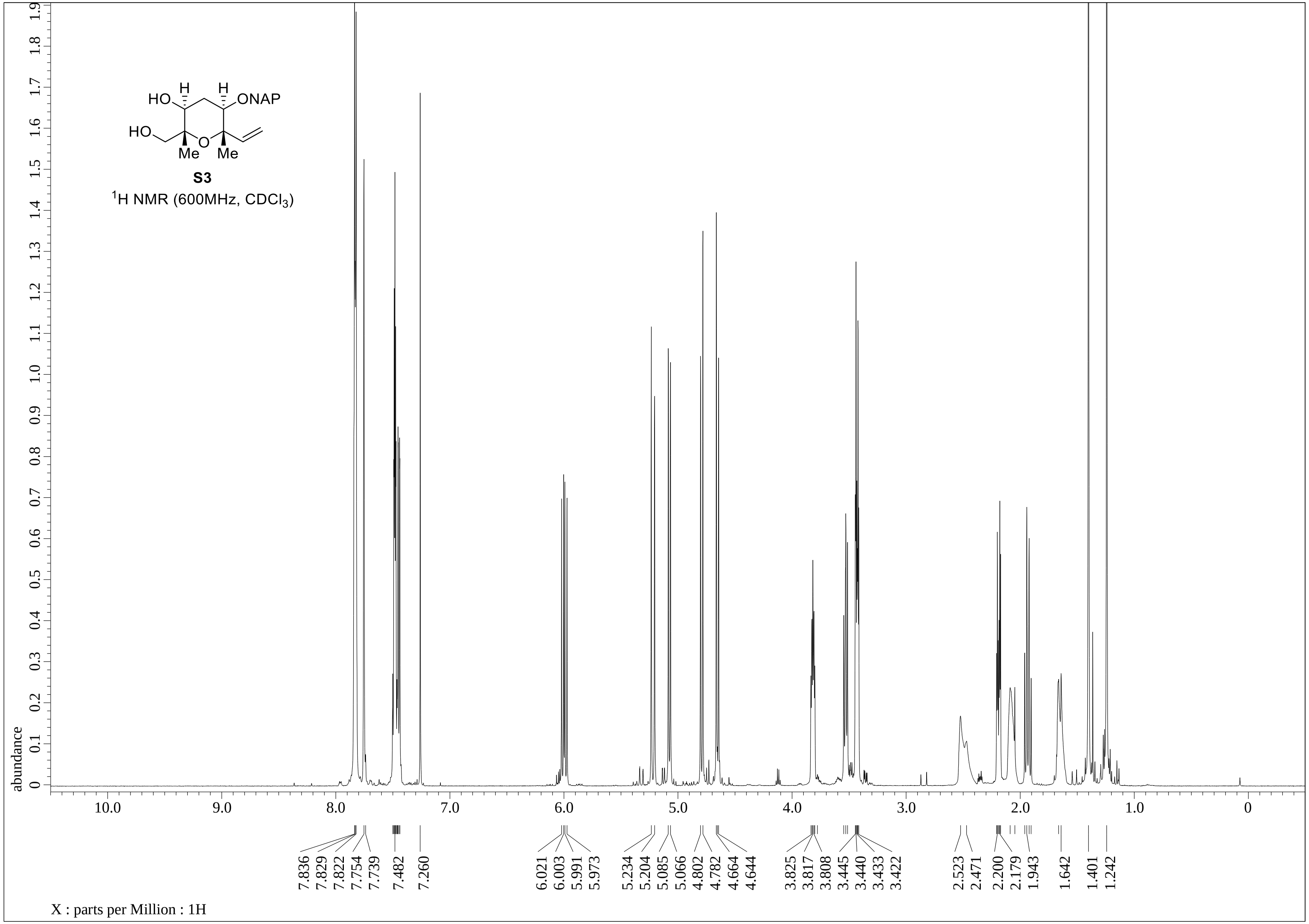
1b

Alcohol 1b. DDQ (19.1 mg, 84.2 μmol) was added to a solution of enone **12b** (29.5 mg, 40.0 μmol) in $\mathrm{CH_2Cl_2}$ (2.8 mL) containing pH 7.0 phosphate buffer (1.4 mL) at 0 °C. After stirring at 0 °C for 1.5 h, the reaction mixture was quenched with saturated aqueous $\mathrm{NaHCO_3}$ and saturated aqueous $\mathrm{Na_2S_2O_3}$, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous $\mathrm{Na_2SO_4}$, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish alcohol **1b** (19.2 mg, 32.0 μmol, 80%) as a colorless amorphous solid: $[\alpha]_D^{23}$ +70.3 (*c* 0.96, $\mathrm{CHCl_3}$); IR (film) 3459, 2860, 1688, 1454, 1363, 1206, 1100, 1063, 737, 698 cm^{-1}; R_f = 0.30 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, $CDCl_3$) δ 7.28 (d, *J* = 7.6 Hz, 2H), 7.24 (d, *J* = 7.6 Hz, 4H), 7.19–7.14 (m, 6H), 7.10–7.03 (m, 3H), 6.35 (dd, *J* = 10.3, 1.4 Hz, 1H), 5.88 (dd, *J* = 10.3, 2.8 Hz, 1H), 4.66–4.64 (m, 1H), 4.40 (d, *J* = 11.7 Hz, 2H), 4.31 (d, *J* = 12.4 Hz, 1H), 4.30 (d, *J* = 12.4 Hz, 1H), 4.26 (d, *J* = 12.4 Hz, 1H), 4.18 (d, *J* = 12.4 Hz, 1H), 3.96–3.91 (m, 2H), 3.90 (dd, *J* = 11.7, 4.1 Hz, 1H), 3.54–3.50 (m, 1H), 3.45–3.41 (m, 2H), 3.25 (d, *J* = 9.6 Hz, 1H), 2.54–2.48 (m, 1H), 2.16–2.13 (m, 2H), 1.88–1.82 (m, 3H), 1.62 (dd, *J* = 15.1, 2.8 Hz, 1H), 1.26 (s, 3H), 1.21 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 196.2, 153.3, 138.8, 138.7, 138.5, 128.5 (2C), 128.4 (4C), 127.7, 127.6 (5C), 127.5 (2C), 127.4 (2C), 126.8, 77.8, 76.6, 75.7, 75.5, 73.3, 72.9, 71.2, 71.0, 68.9, 66.5, 45.5, 29.9, 28.9, 22.0, 19.4; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{44}O_7Na$ 623.2979, found 623.3010.



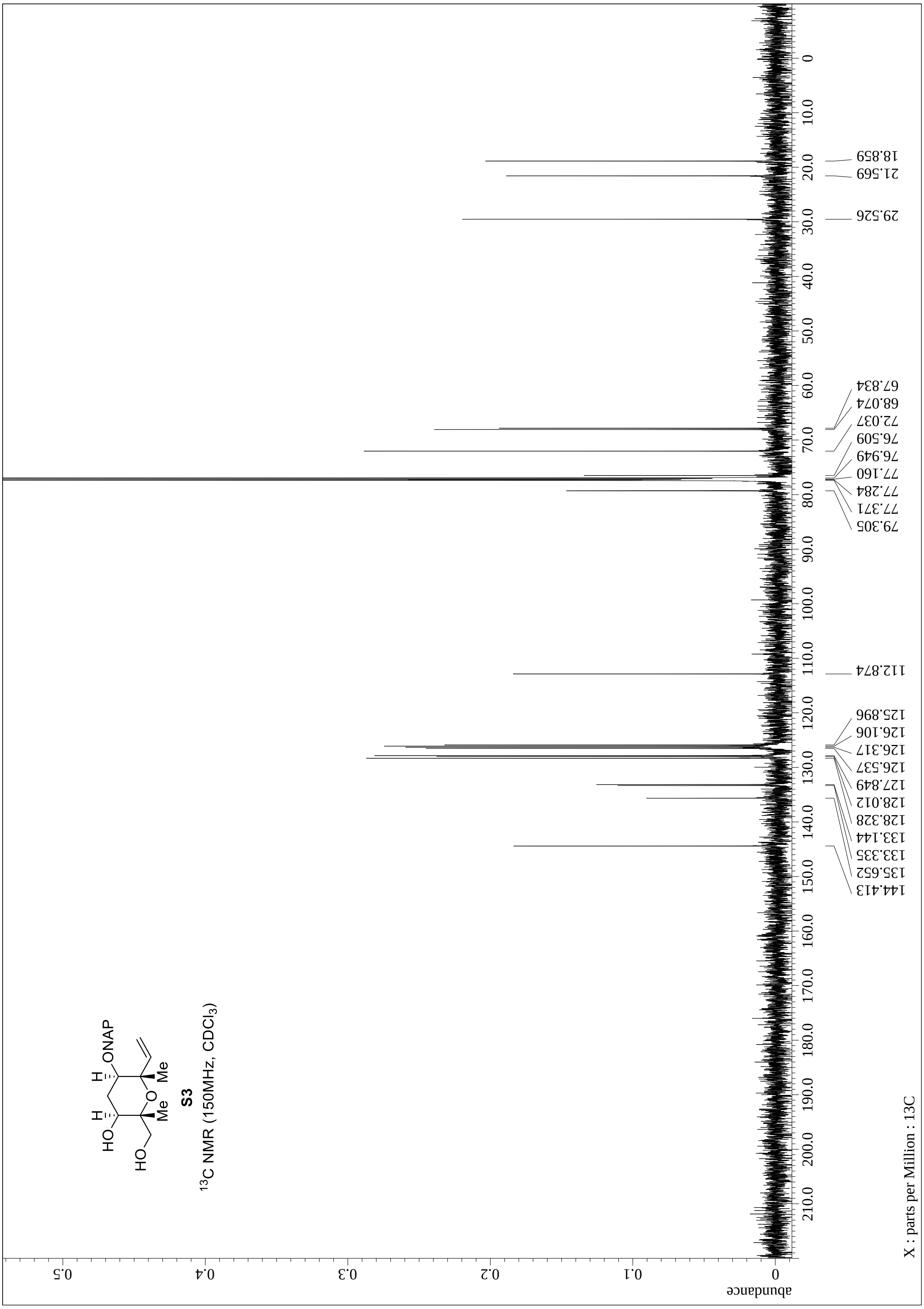
3b

Ketone 3b. $TsOH{\cdot}H_2O$ (40.3 mg, 0.21 mmol) was added to a solution of alcohol **1b** (12.8 mg, 21.3 μmol) in CH_2Cl_2 (0.45 mL) at 0 °C. After stirring at room temperature for 24 h, the reaction mixuture was quenched with saturated aqueous $NaHCO_3$, and extracted with EtOAc. The organic layer was washed with saturated aqueous NaCl, dried over anhydrous Na_2SO_4, filtered and concentrated under reduced pressure. The residue was purified by silica gel flash column chromatography to furnish ketone **3b** (6.4 mg, 10.6 μmol, 50%) as a colorless amorphous solid: $[\alpha]_D^{18}$ −1.15 (*c* 0.32, $CHCl_3$); IR (film) 3733, 2868, 2366, 2341, 1730, 1093, 736, 701 cm^{-1}; R_f = 0.45 (hexane/EtOAc = 2/1); ^{1}H NMR (600 MHz, C_6D_6) δ 7.33 (d, *J* = 7.6 Hz, 2H), 7.27 (d, *J* = 7.6 Hz, 2H), 7.20–7.14 (m, 8H), 7.11–7.06 (m, 3H), 4.57 (d, *J* = 12.4 Hz, 1H), 4.43 (d, *J* = 12.4 Hz, 1H), 4.35 (d, *J* = 11.7 Hz, 1H), 4.32 (d, *J* = 12.4 Hz, 1H), 4.27 (d, *J* = 12.4 Hz, 1H), 4.16 (d, *J* = 11.7 Hz, 1H), 3.88 (dd, *J* = 12.4, 4.1 Hz, 1H), 3.78–3.74 (m, 1H), 3.67 (dd, *J* = 7.6, 4.1 Hz, 1H), 3.63 (dd, *J* = 12.4, 6.9 Hz, 1H), 3.57–3.52 (m, 2H), 3.49–3.45 (m, 2H), 3.37 (d, *J* = 10.3 Hz, 1H), 2.74 (dd, *J* = 14.4, 9.6 Hz, 1H), 2.38–2.33 (m, 1H), 2.17 (dd, *J* = 13.1, 6.9 Hz, 1H), 2.13 (ddd, *J* = 12.4, 4.1, 4.1 Hz, 1H), 2.07 (dd, *J* = 14.4, 4.1 Hz, 1H), 1.89–1.83 (m, 2H), 1.72 (ddd, *J* = 12.4, 12.4, 12.4 Hz, 1H), 1.26 (s, 3H), 1.17 (s, 3H); ^{13}C NMR (150 MHz, $CDCl_3$) δ 209.7, 138.9, 138.5 (2C), 128.5 (2C), 128.4 (4C), 127.8 (2C), 127.7 (4C), 127.5 (3C), 78.3, 76.8, 75.9 (2C), 73.7, 72.8, 72.3, 72.0, 71.3 (2C), 69.7, 65.6, 43.2, 40.5, 30.0, 26.7, 20.9, 19.9; HRMS (ESI-TOF) *m*/*z* [M + Na]$^+$ calcd for $C_{37}H_{44}O_7Na$ 623.2979, found 623.2993.



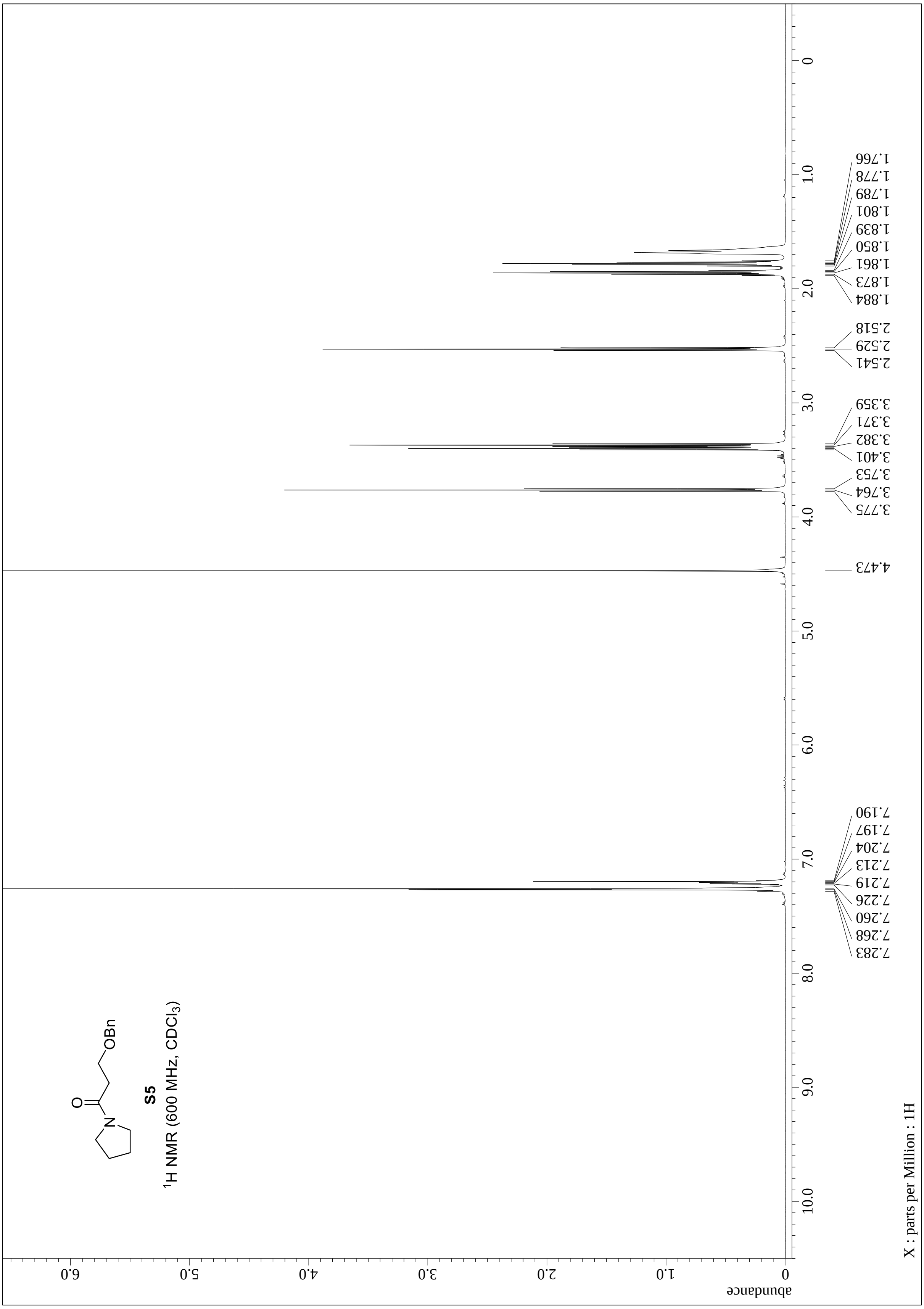
S3

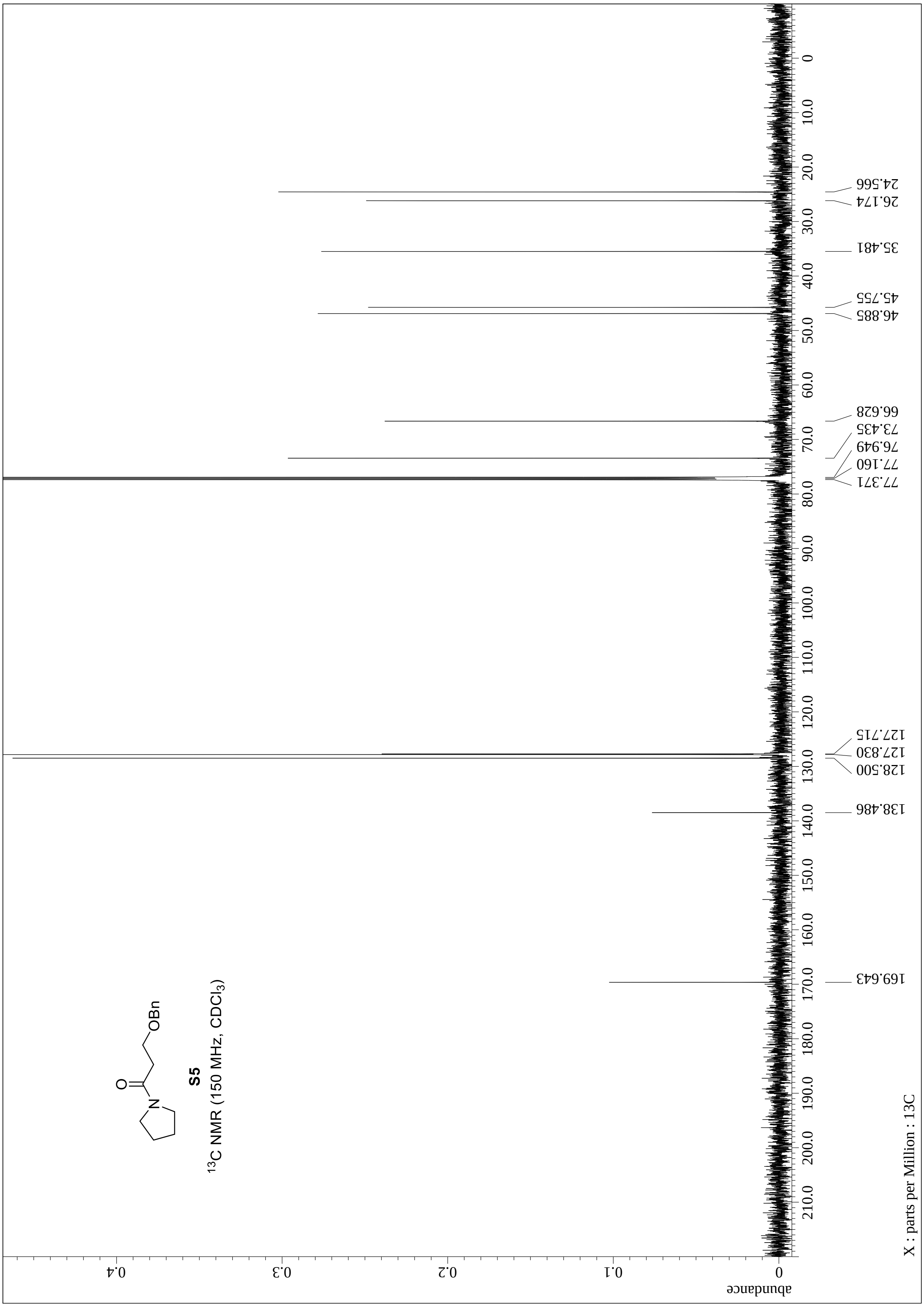
^{1}H NMR (600MHz, CDCl$_3$)



S3

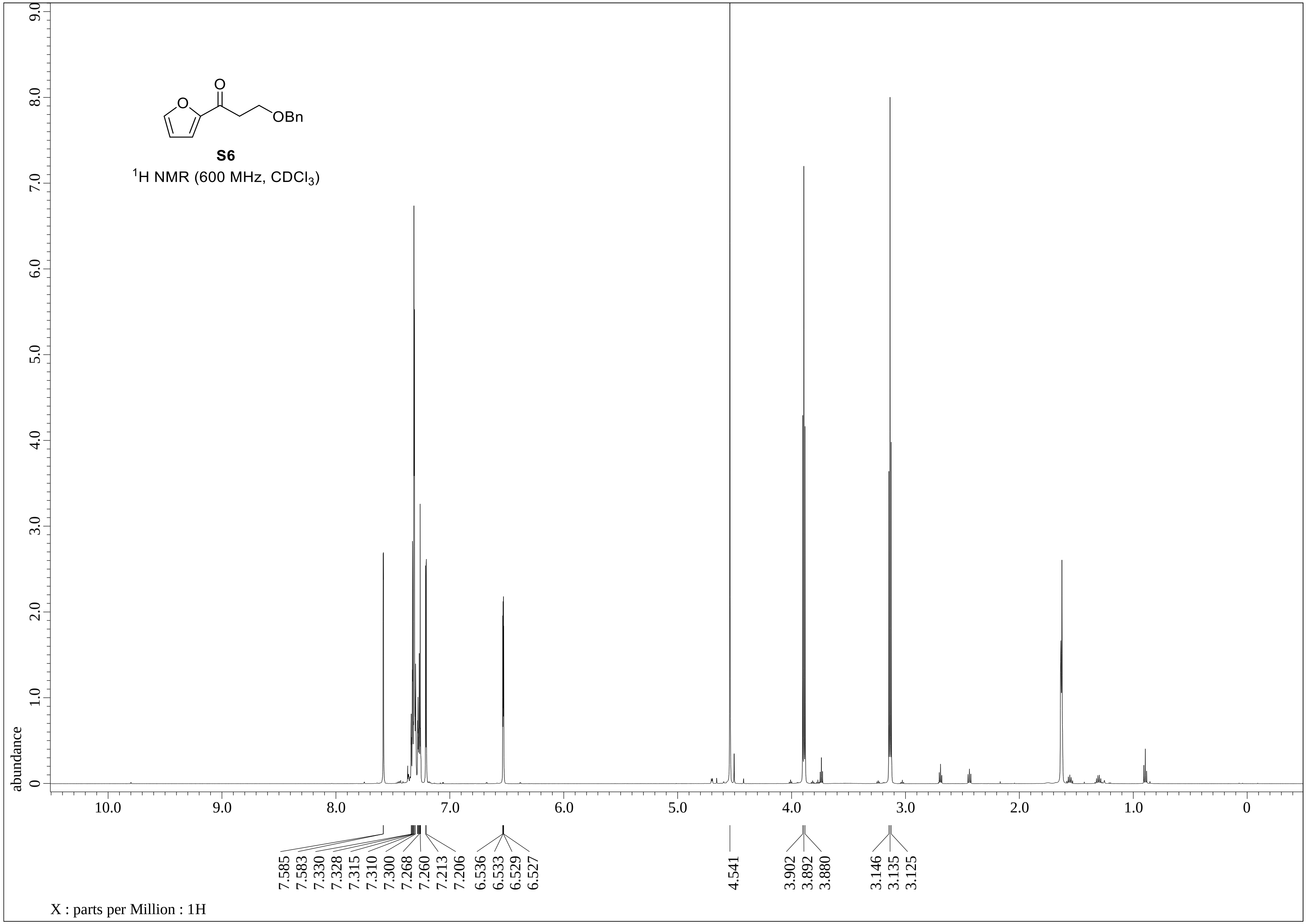
^{13}C NMR (150MHz, CDCl$_3$)


S5
^{1}H NMR (600 MHz, CDCl$_3$)
OBn
O
N
7.283
7.268
7.260
7.226
7.219
7.213
7.204
7.197
7.190
4.473
3.775
3.764
3.753
3.401
3.382
3.371
3.359
2.541
2.529
2.518
1.884
1.873
1.861
1.850
1.839
1.801
1.789
1.778
1.766
10.0
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
X : parts per Million : 1H
abundance
0
1.0
2.0
3.0
4.0
5.0
6.0



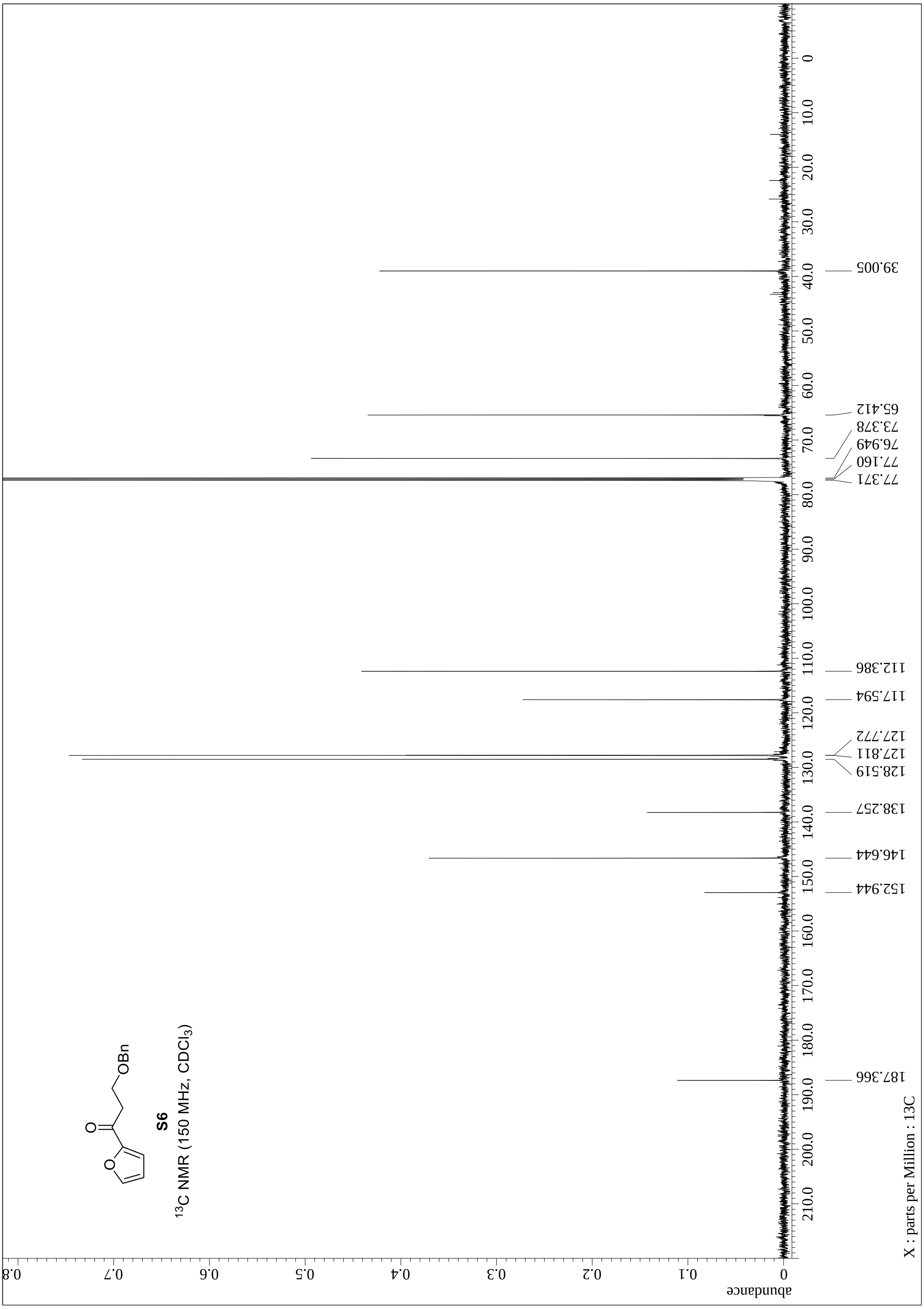
S5

^{13}C NMR (150 MHz, CDCl$_3$)



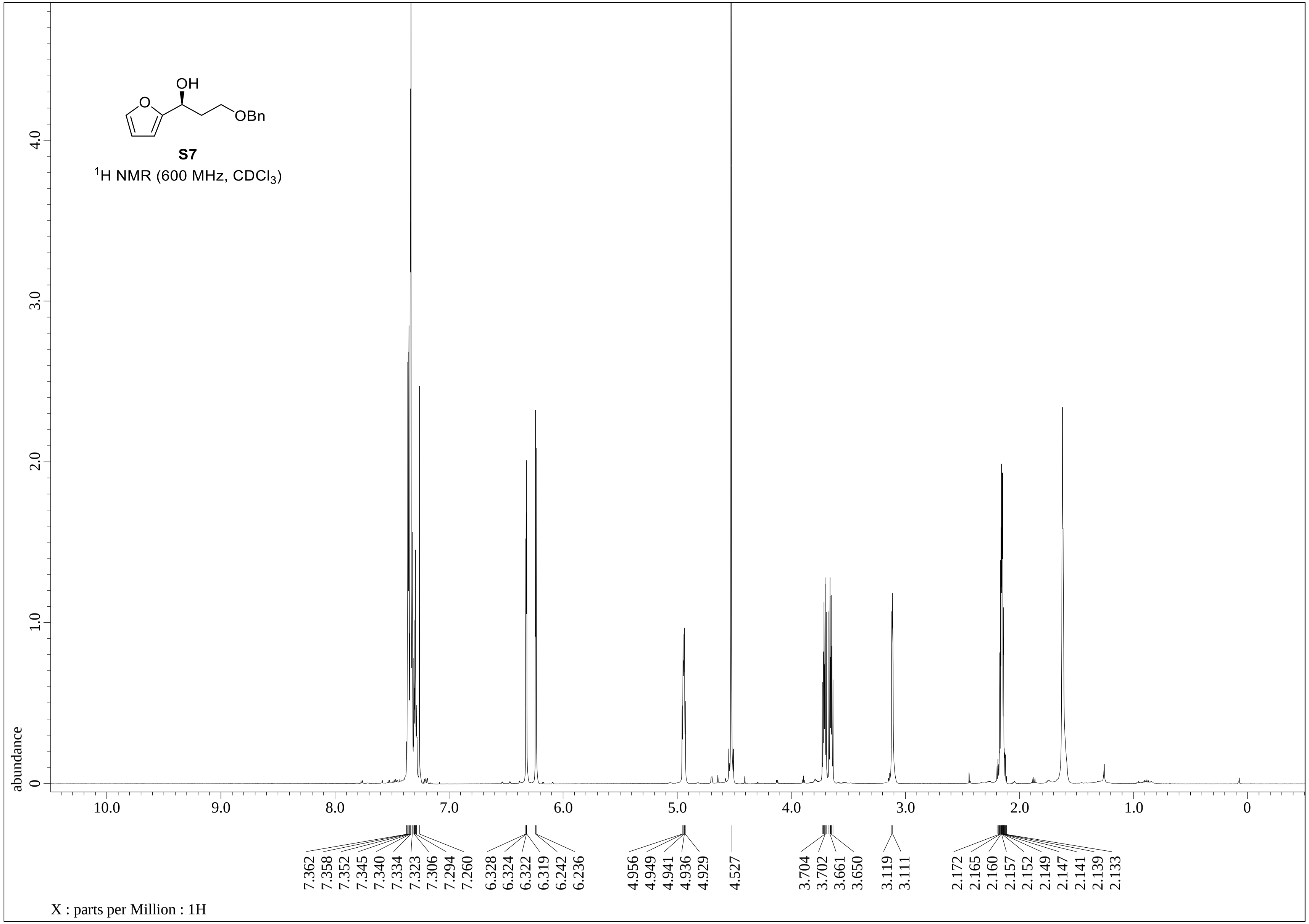
S6

^{1}H NMR (600 MHz, CDCl$_3$)



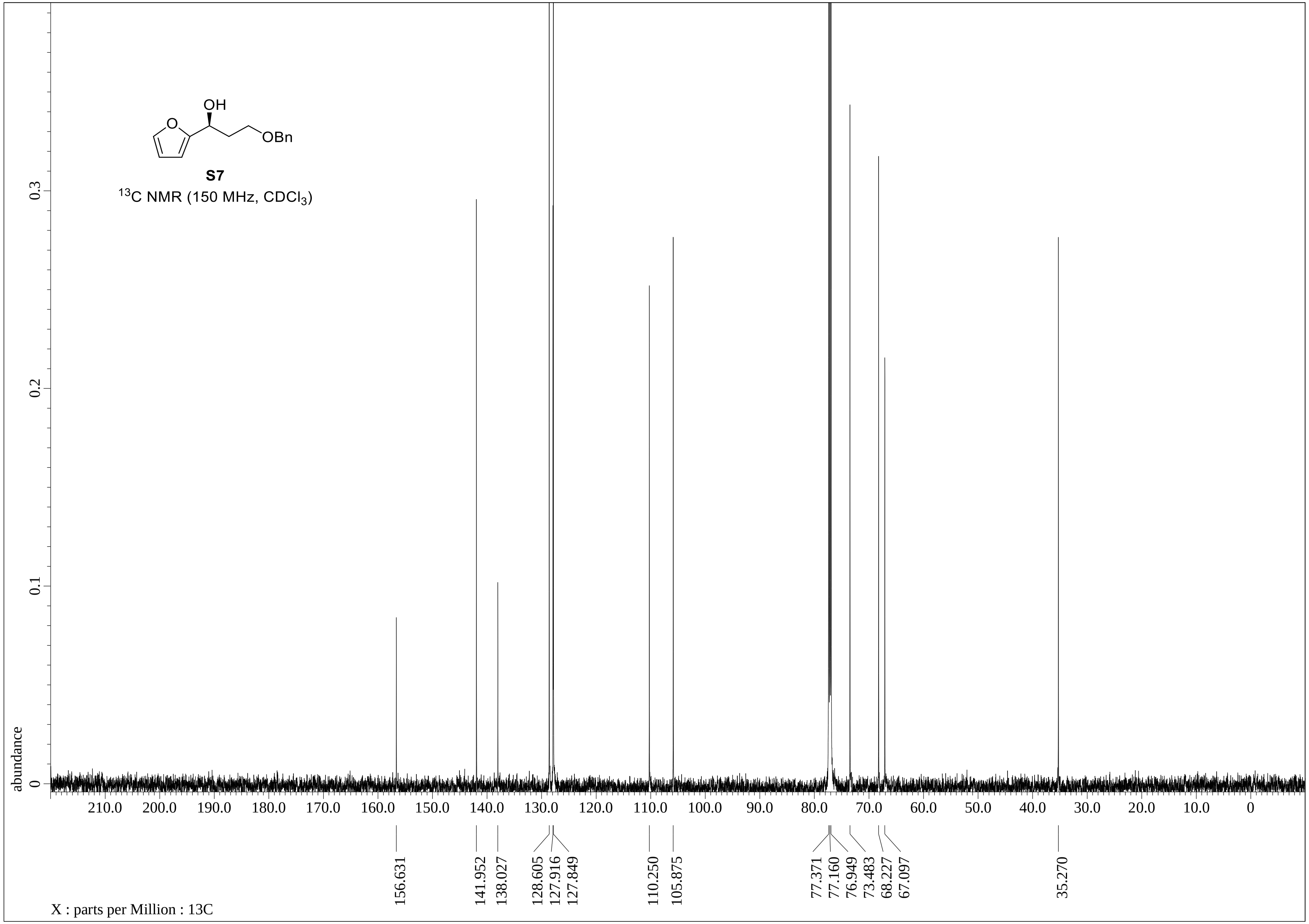
S6

^{13}C NMR (150 MHz, $CDCl_3$)



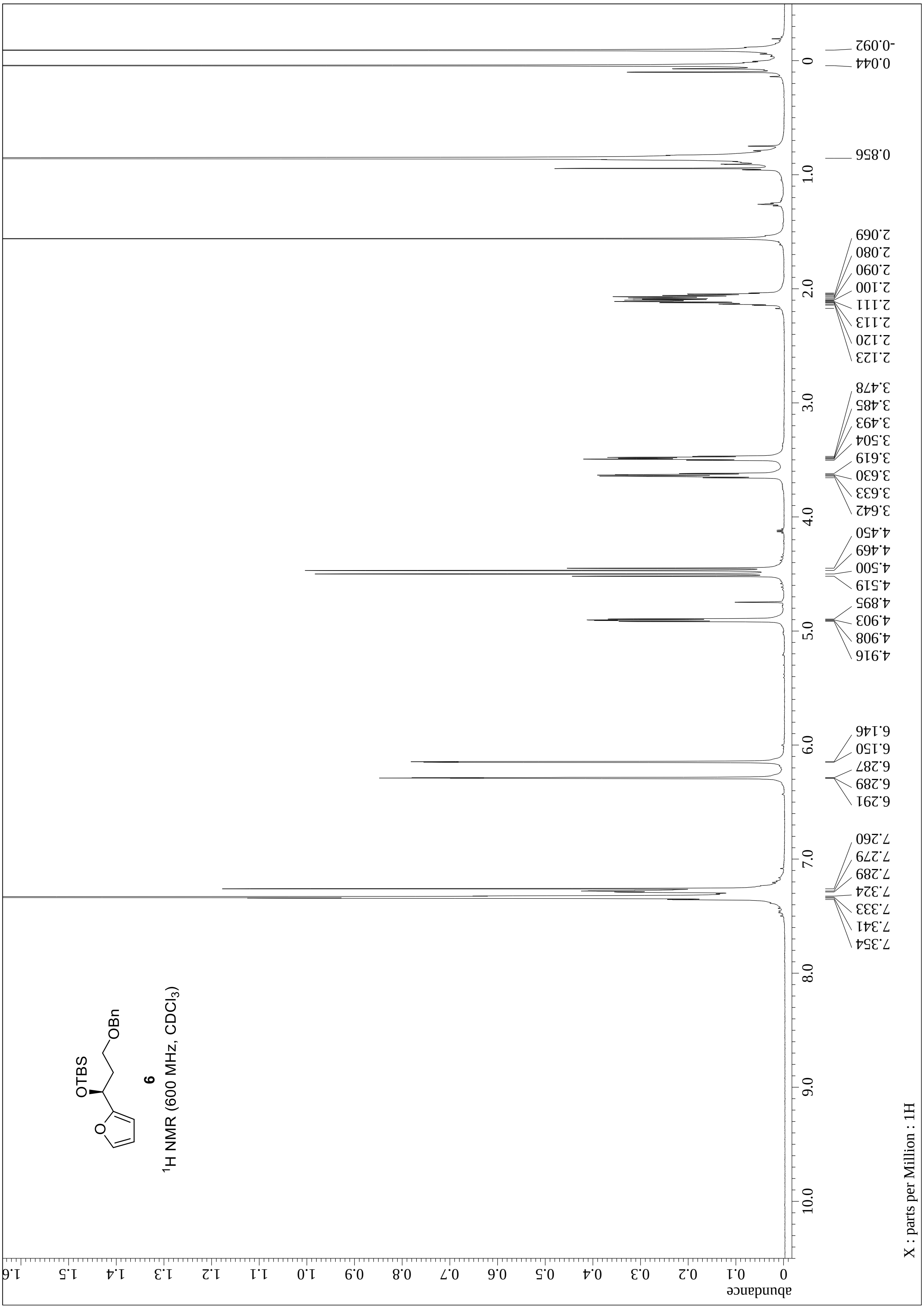
S7

^{1}H NMR (600 MHz, $CDCl_3$)

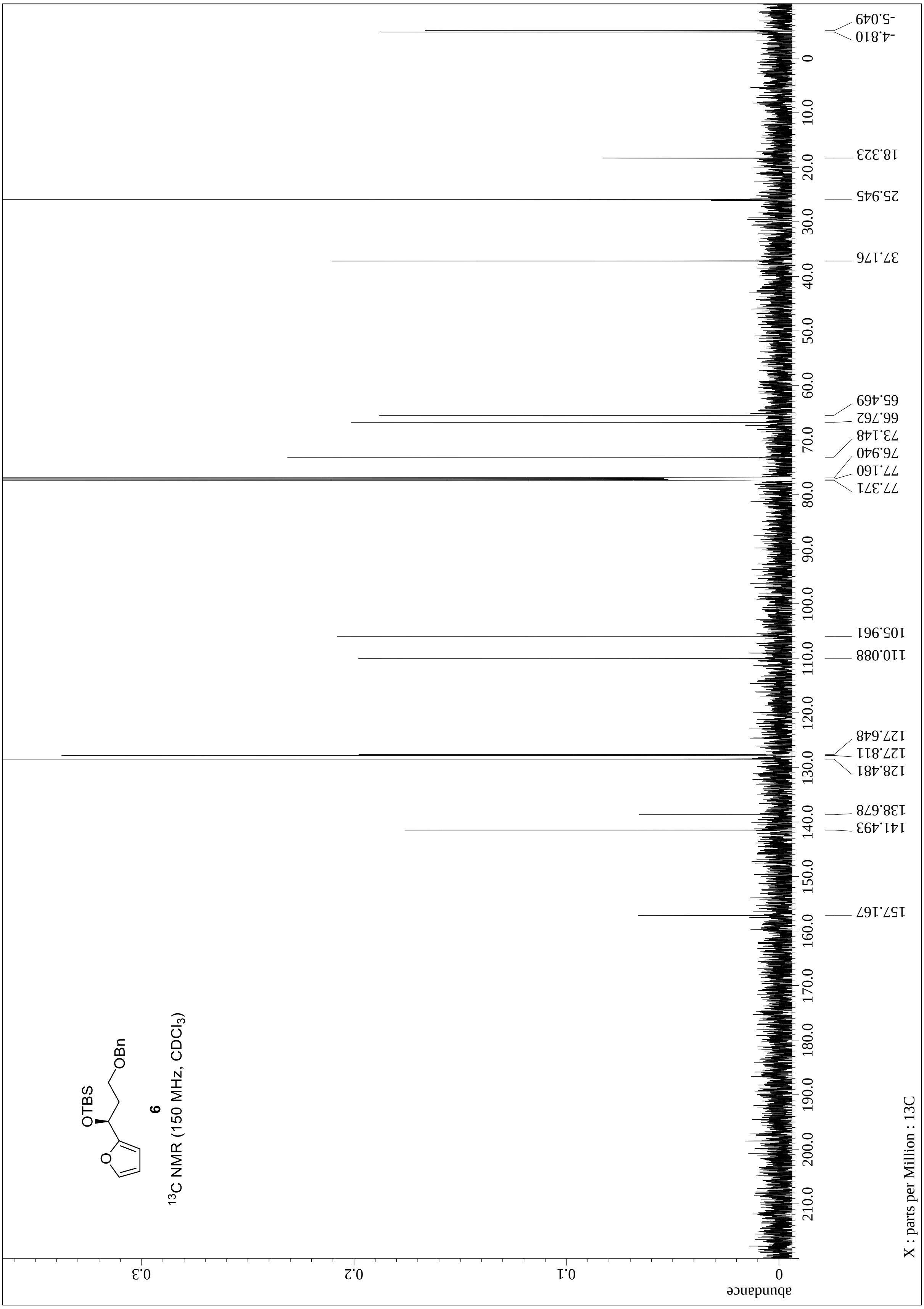


S7

^{13}C NMR (150 MHz, CDCl$_3$)

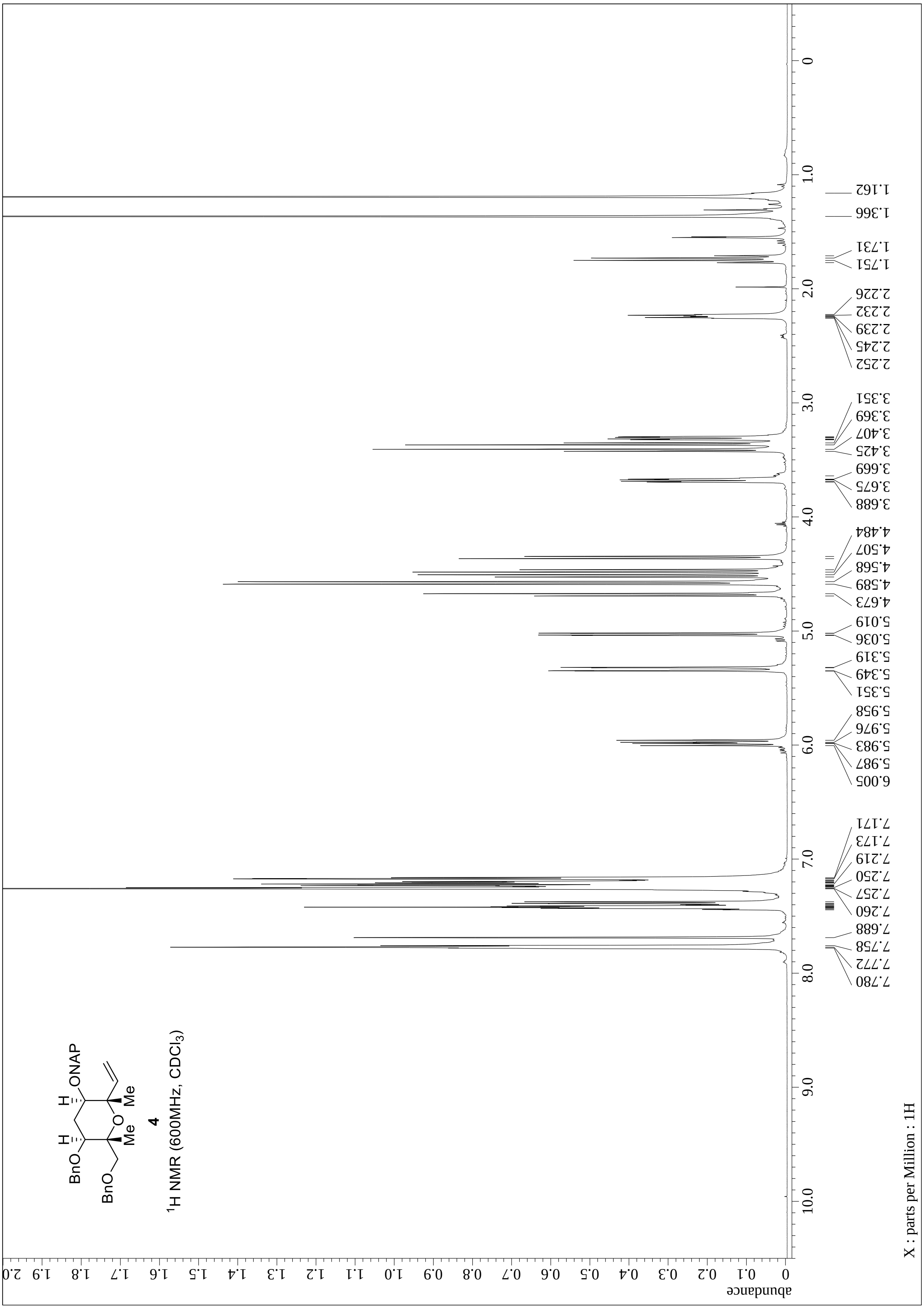

6

^{1}H NMR (600 MHz, $CDCl_3$)



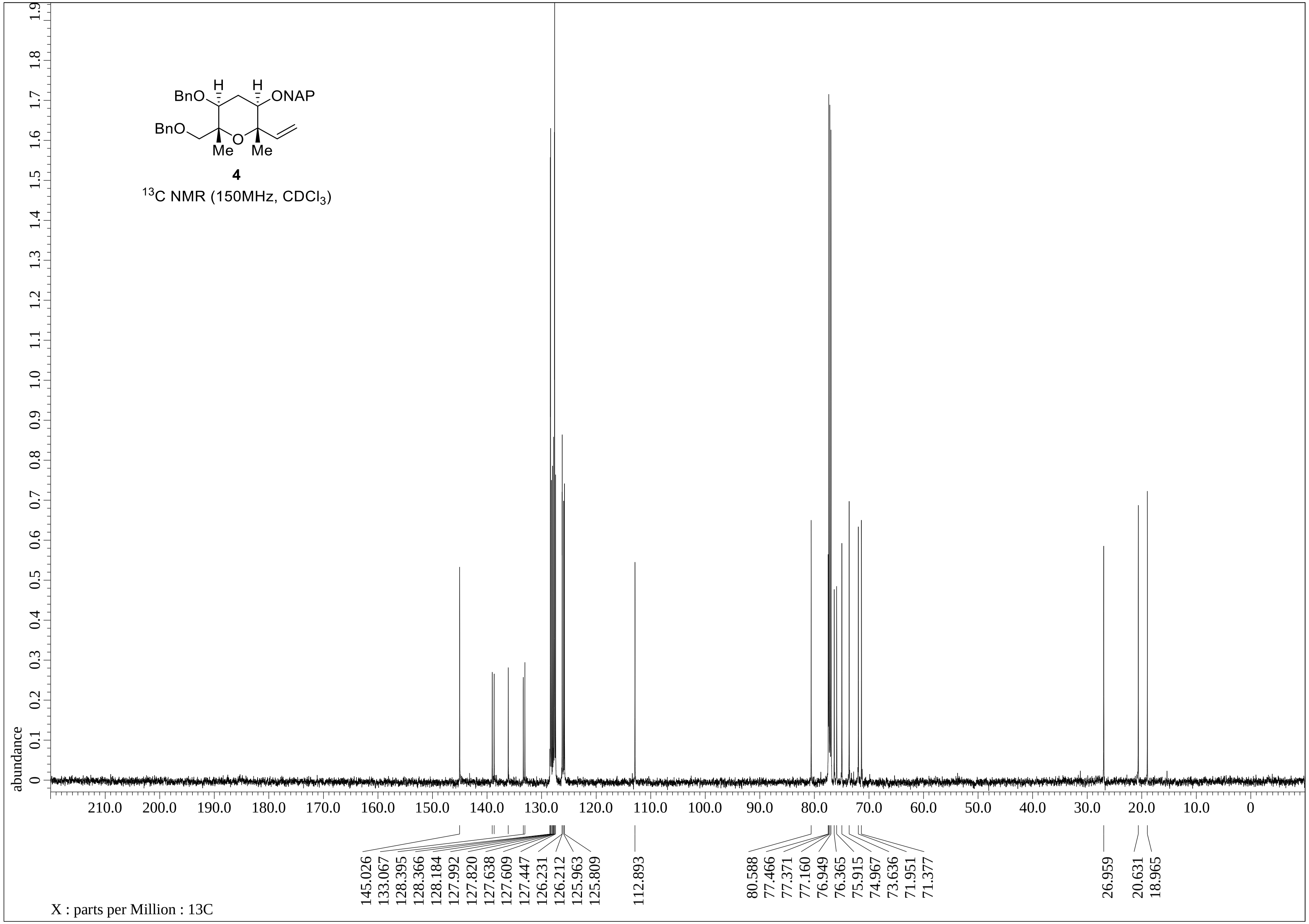
6

^{13}C NMR (150 MHz, $CDCl_3$)



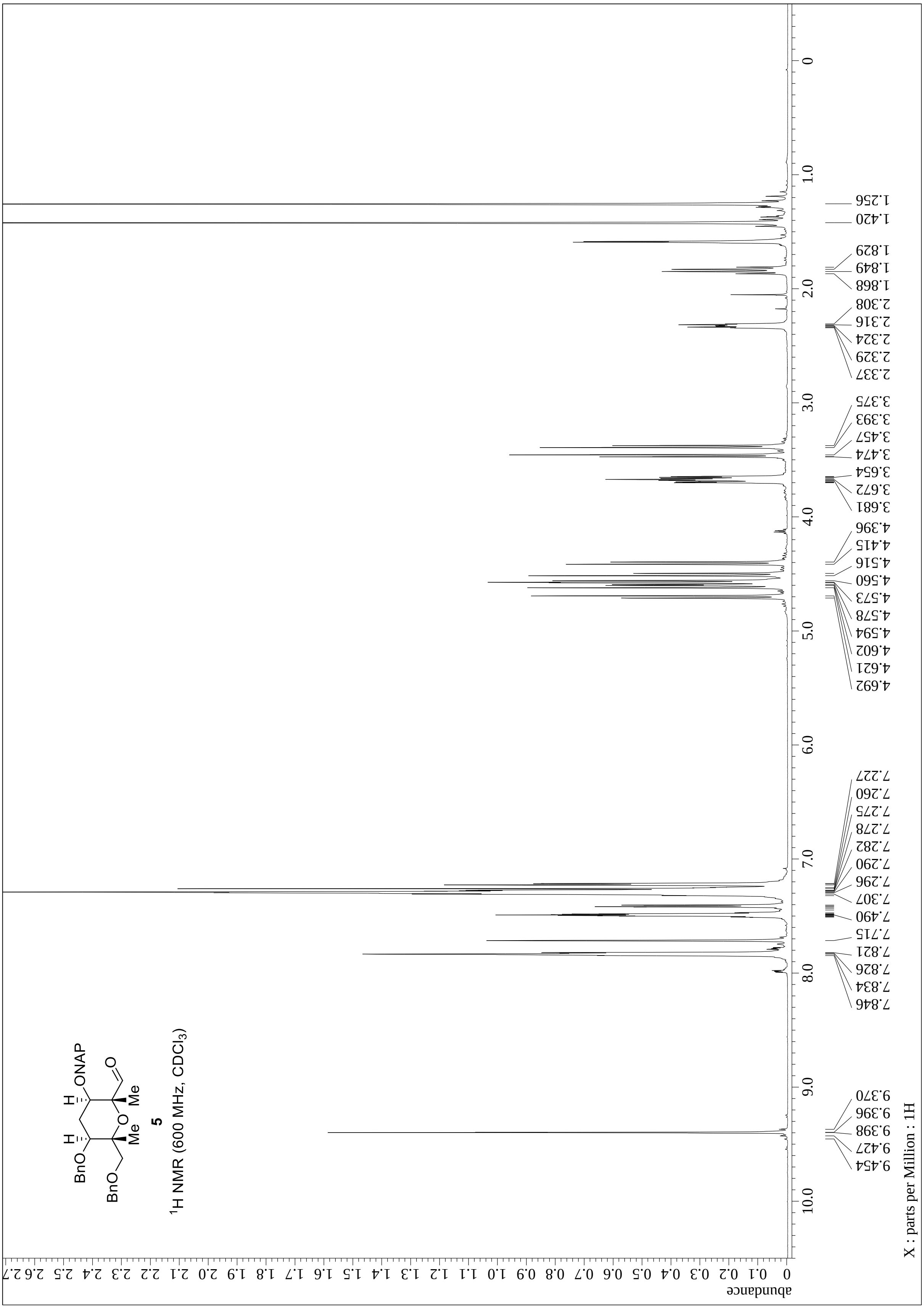
4

^{1}H NMR (600MHz, CDCl$_3$)



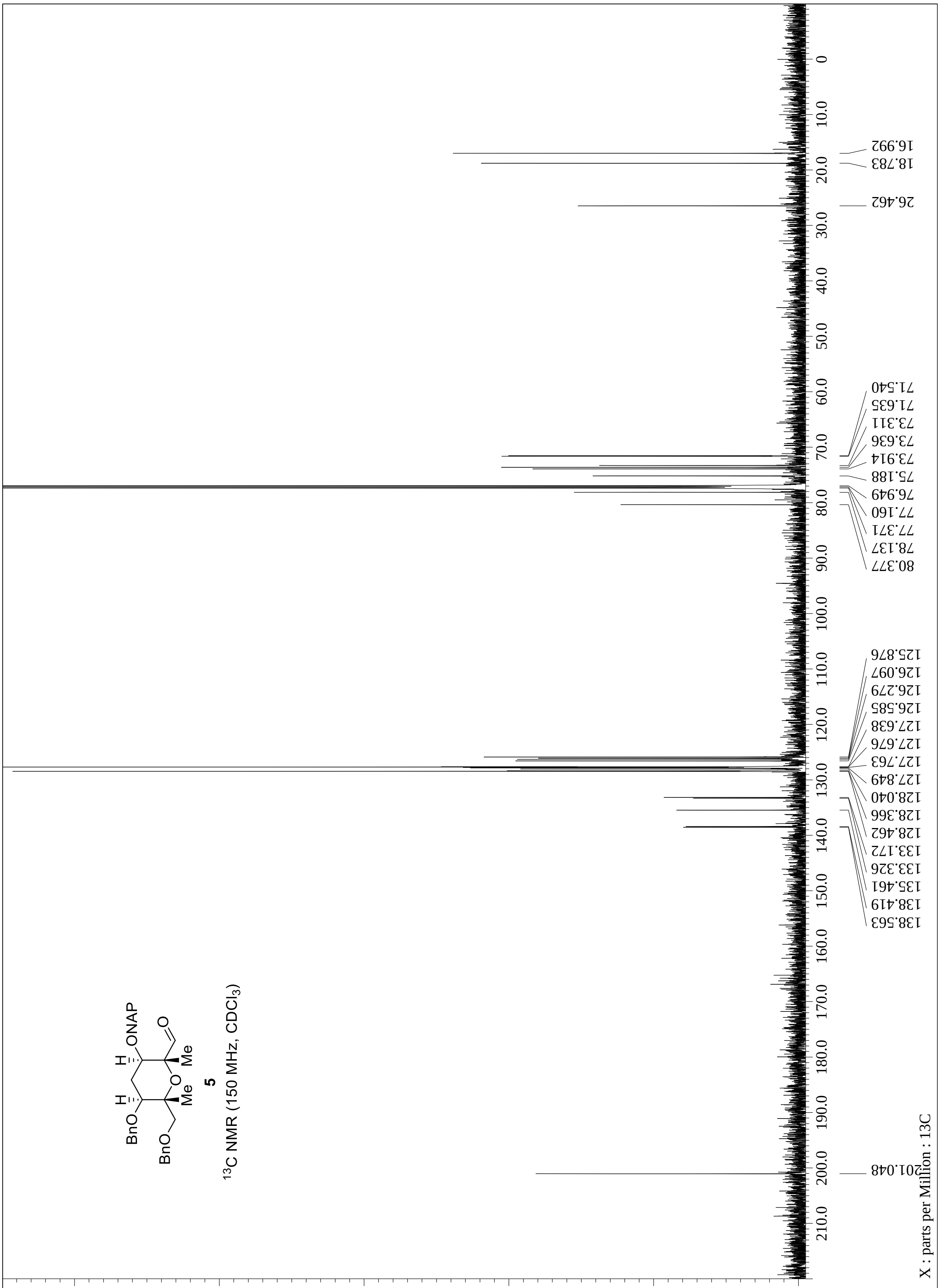
4

^{13}C NMR (150MHz, CDCl$_3$)



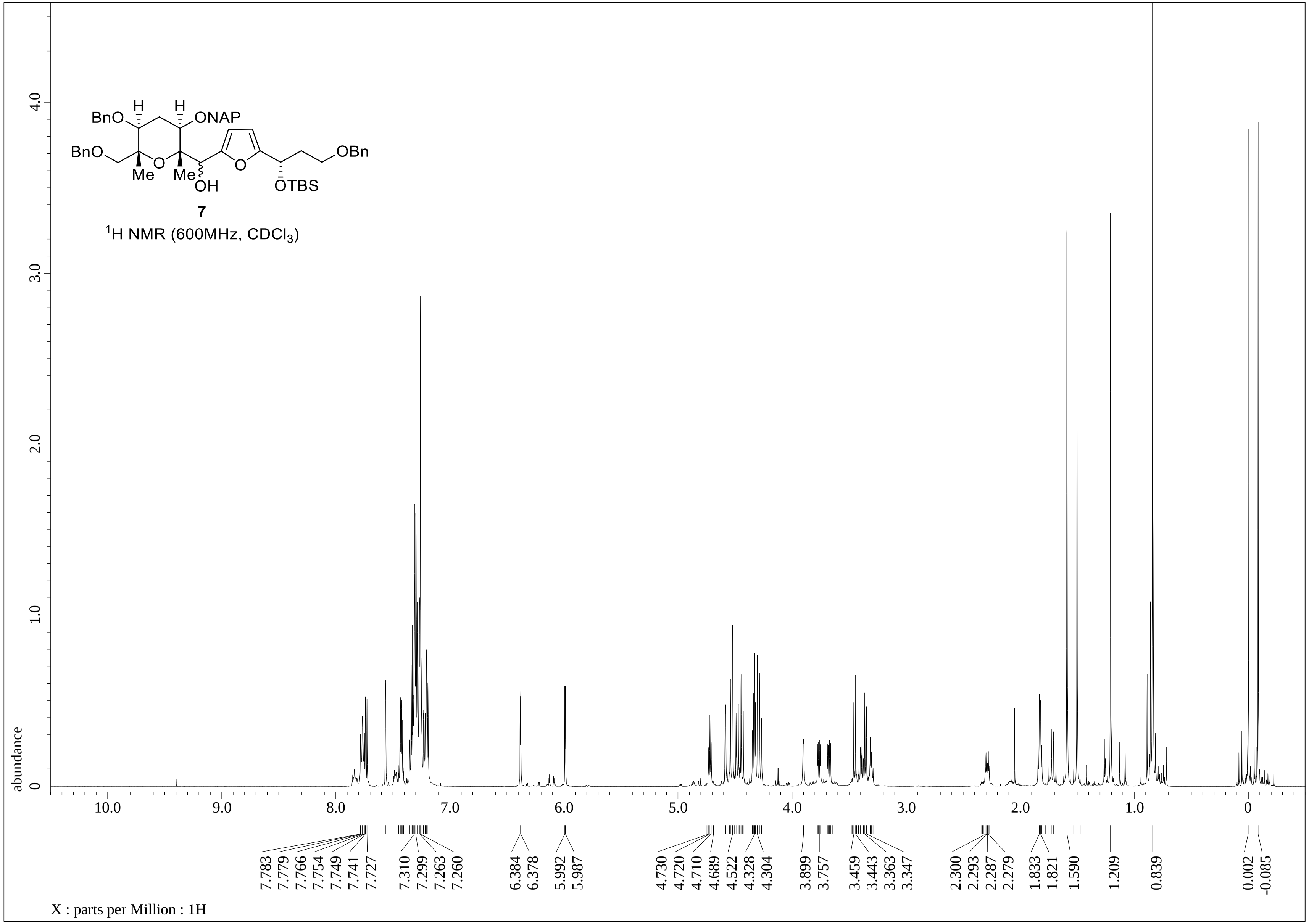
5

^{1}H NMR (600 MHz, CDCl$_3$)



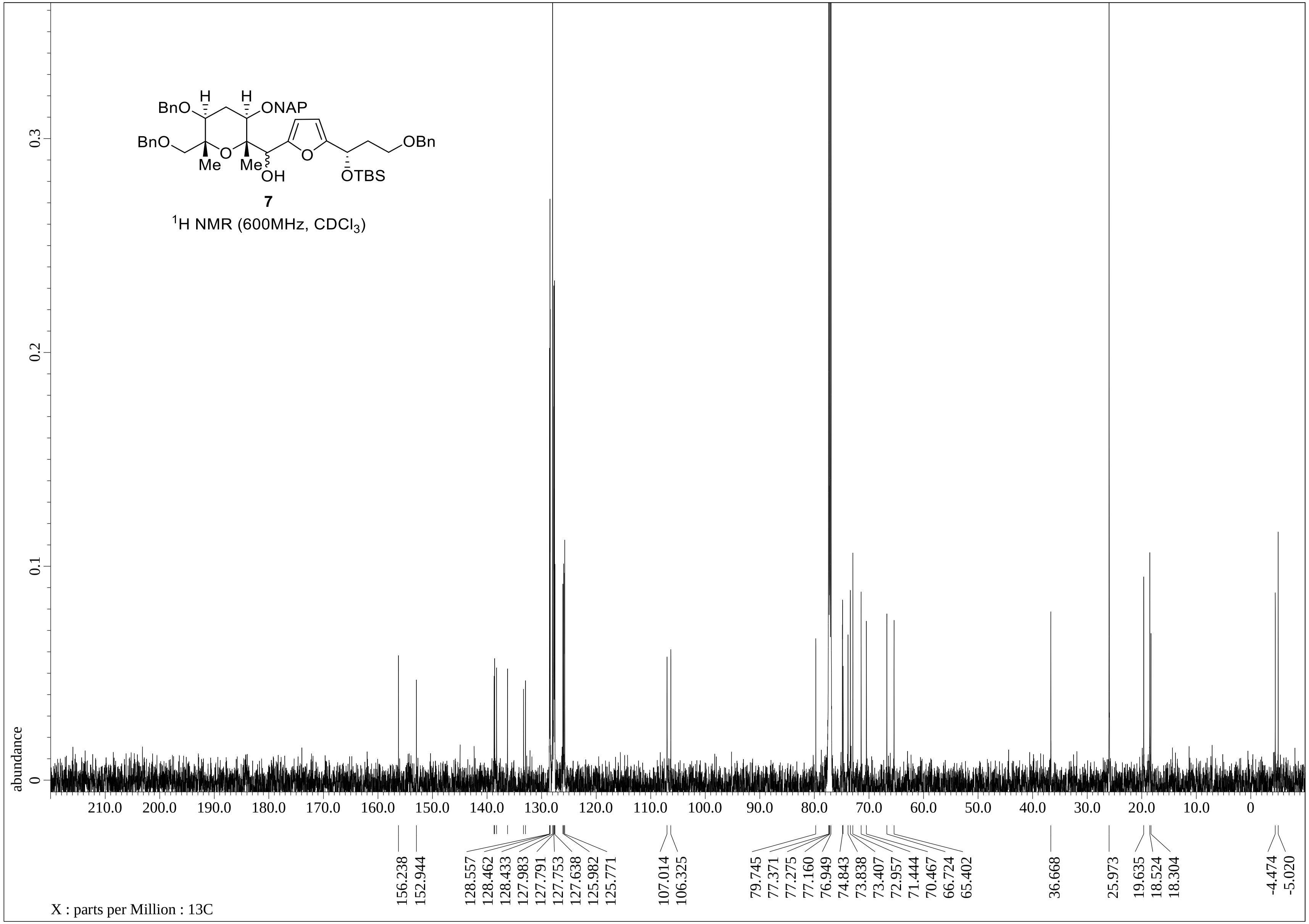
5

^{13}C NMR (150 MHz, $CDCl_3$)



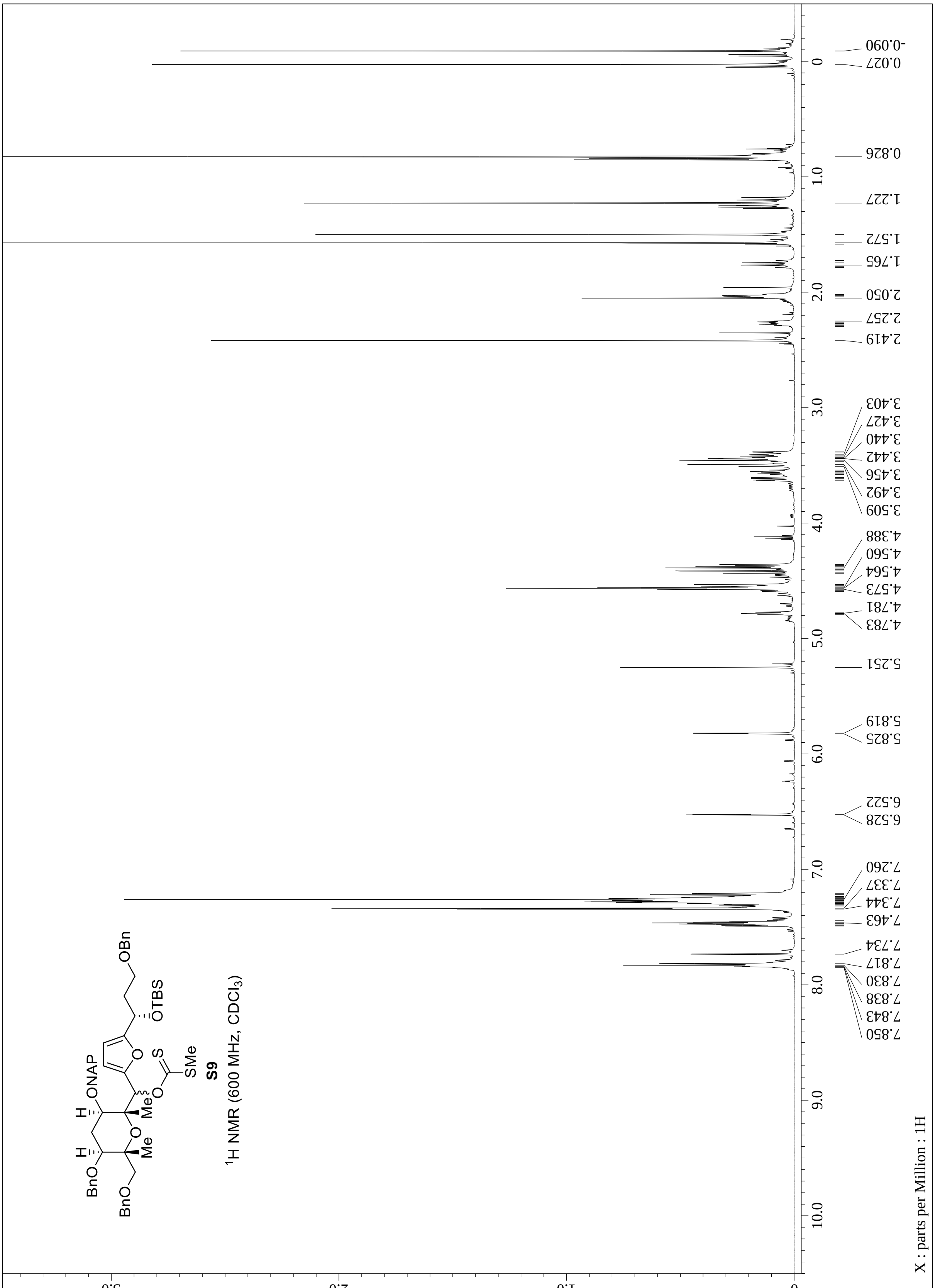
7

^{1}H NMR (600MHz, CDCl$_3$)



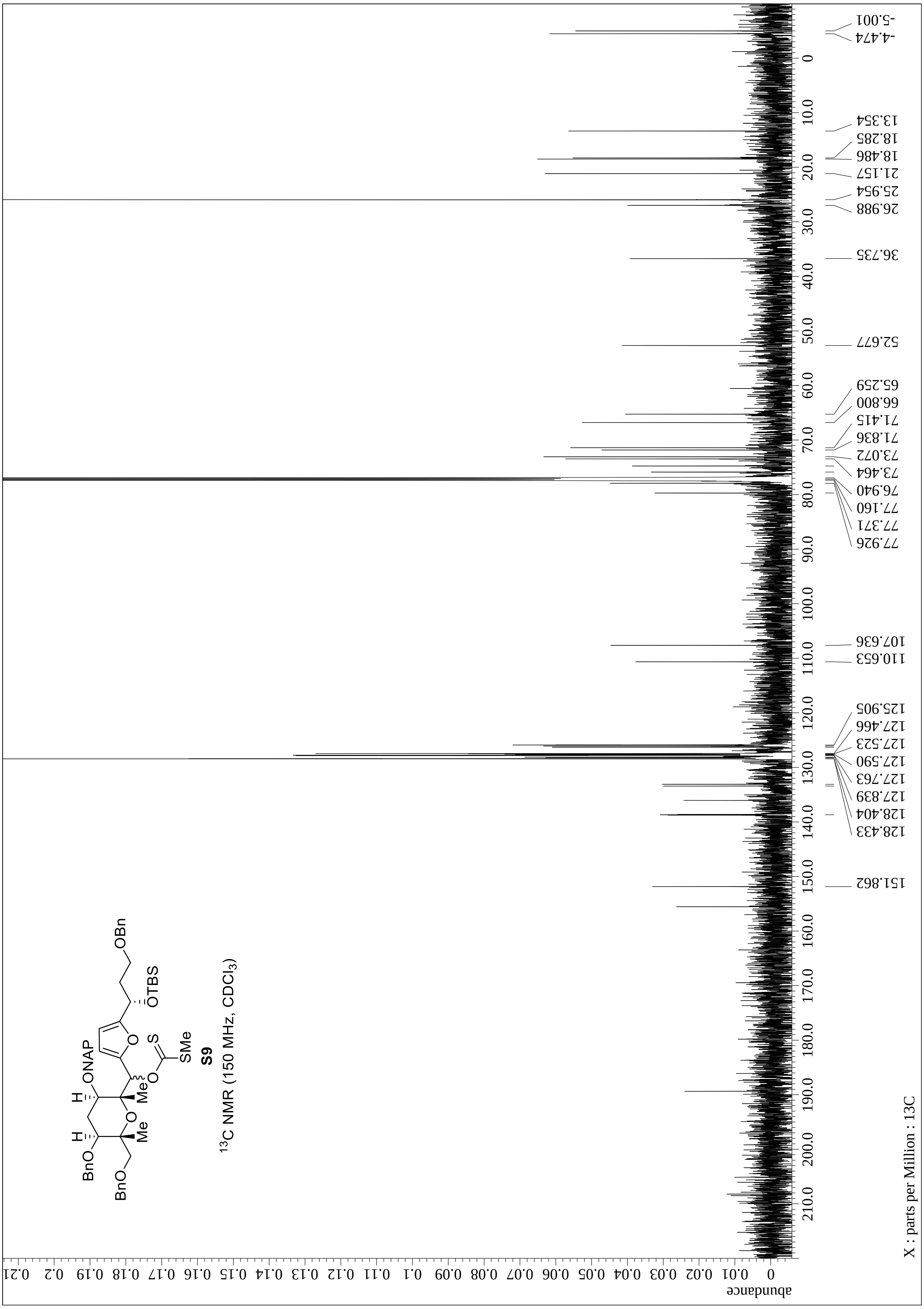
7

^1H NMR (600MHz, $CDCl_3$)

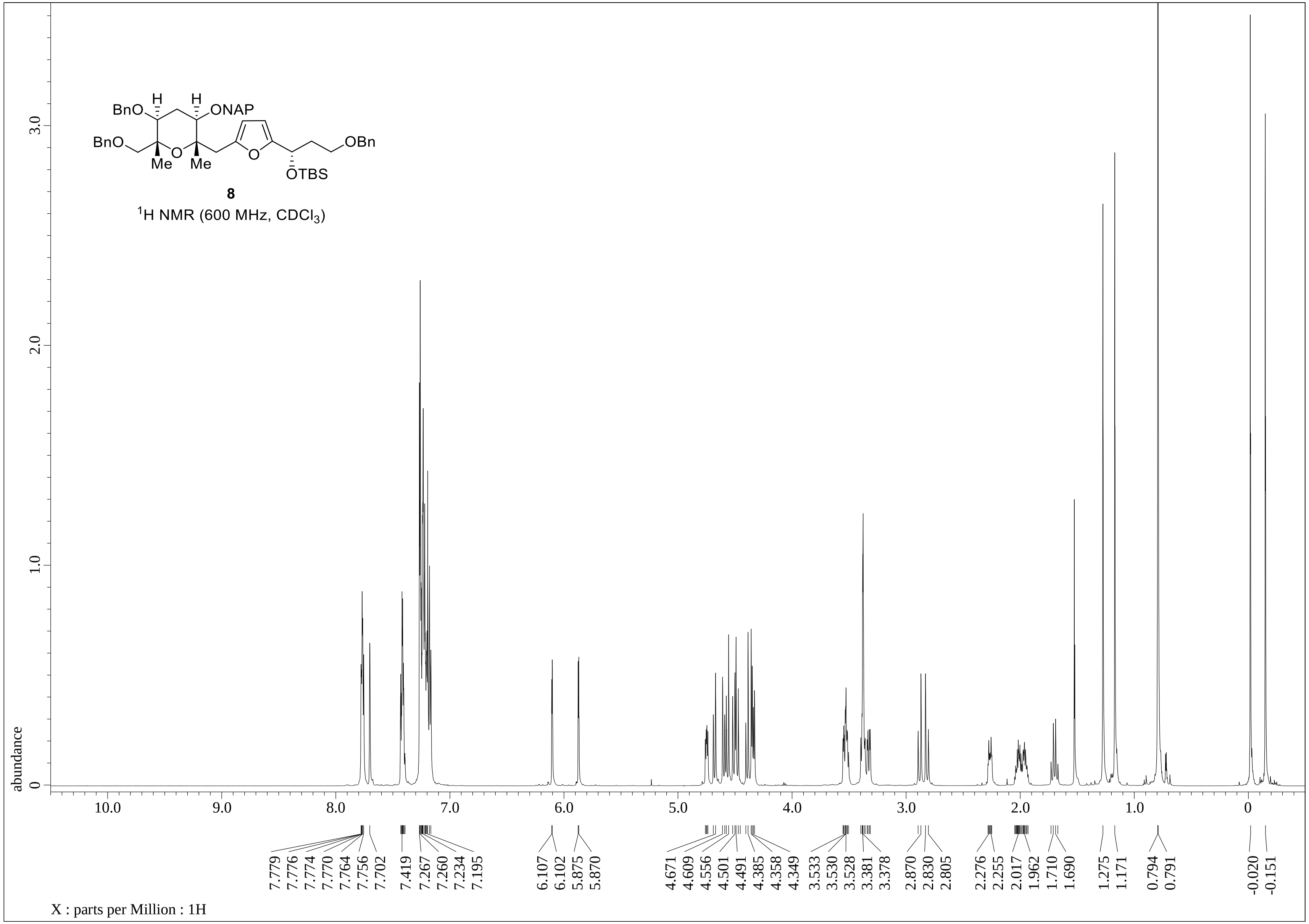


S9

^{1}H NMR (600 MHz, CDCl$_3$)

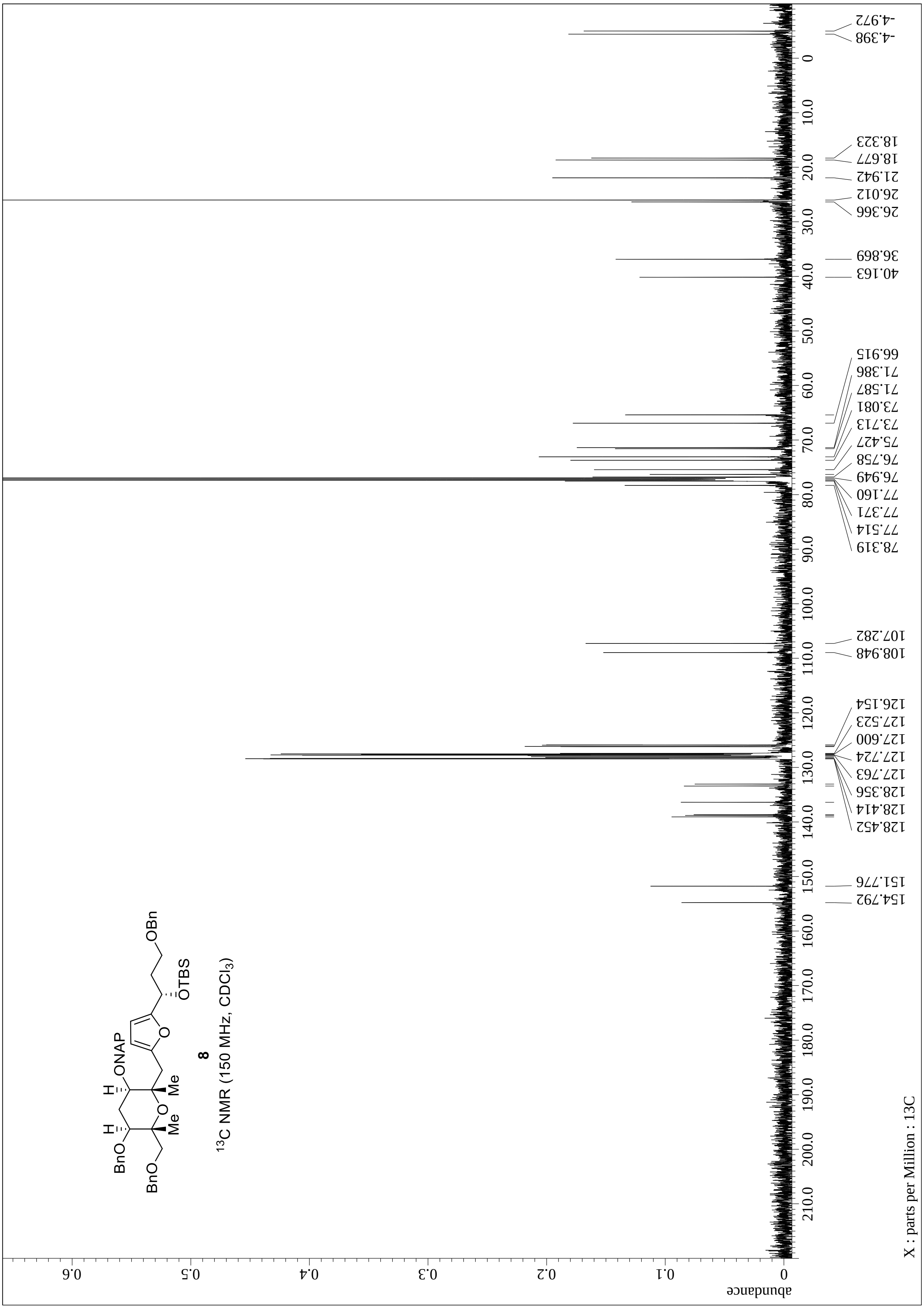

S9

^{13}C NMR (150 MHz, CDCl$_3$)



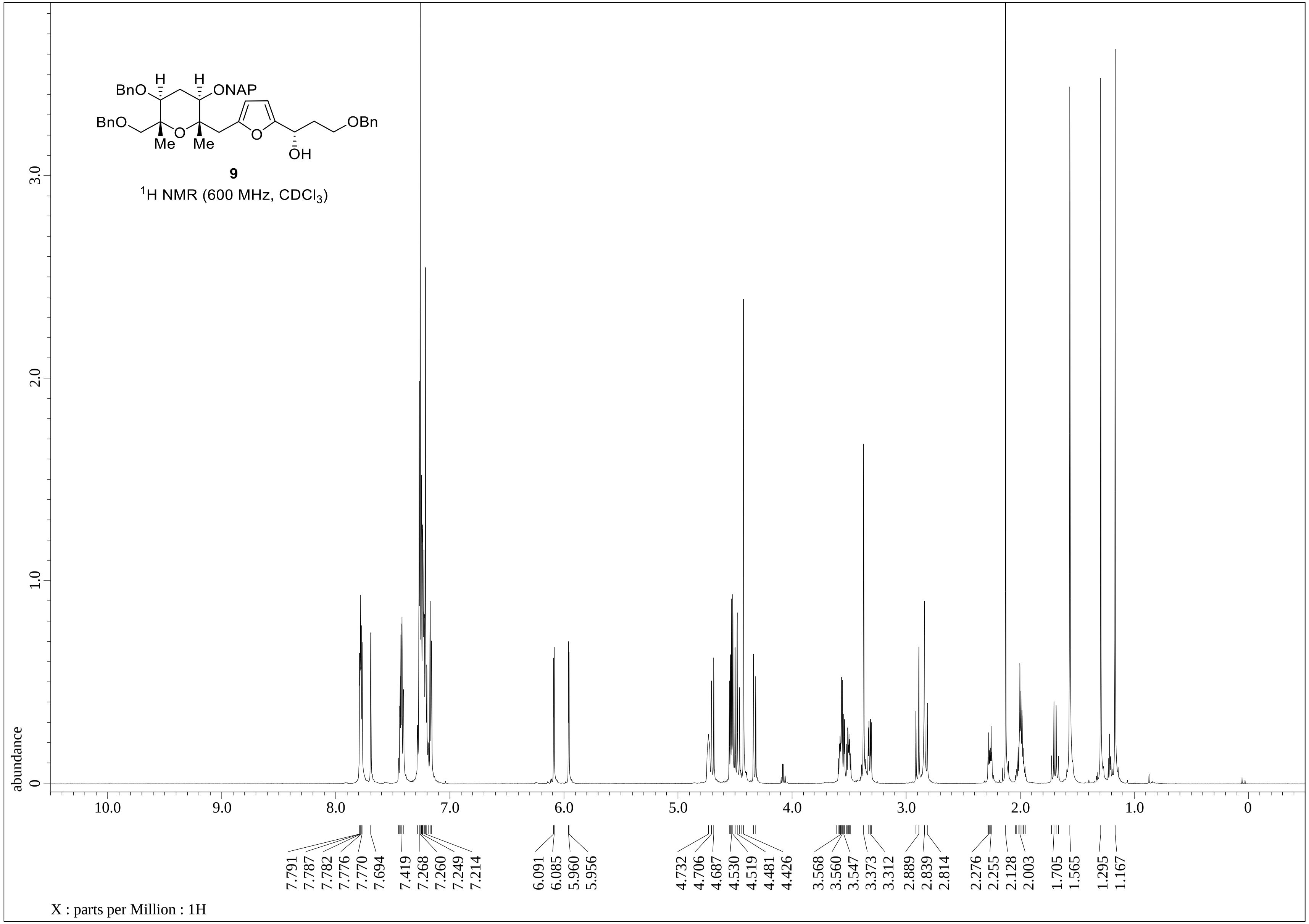
8

^{1}H NMR (600 MHz, $CDCl_3$)



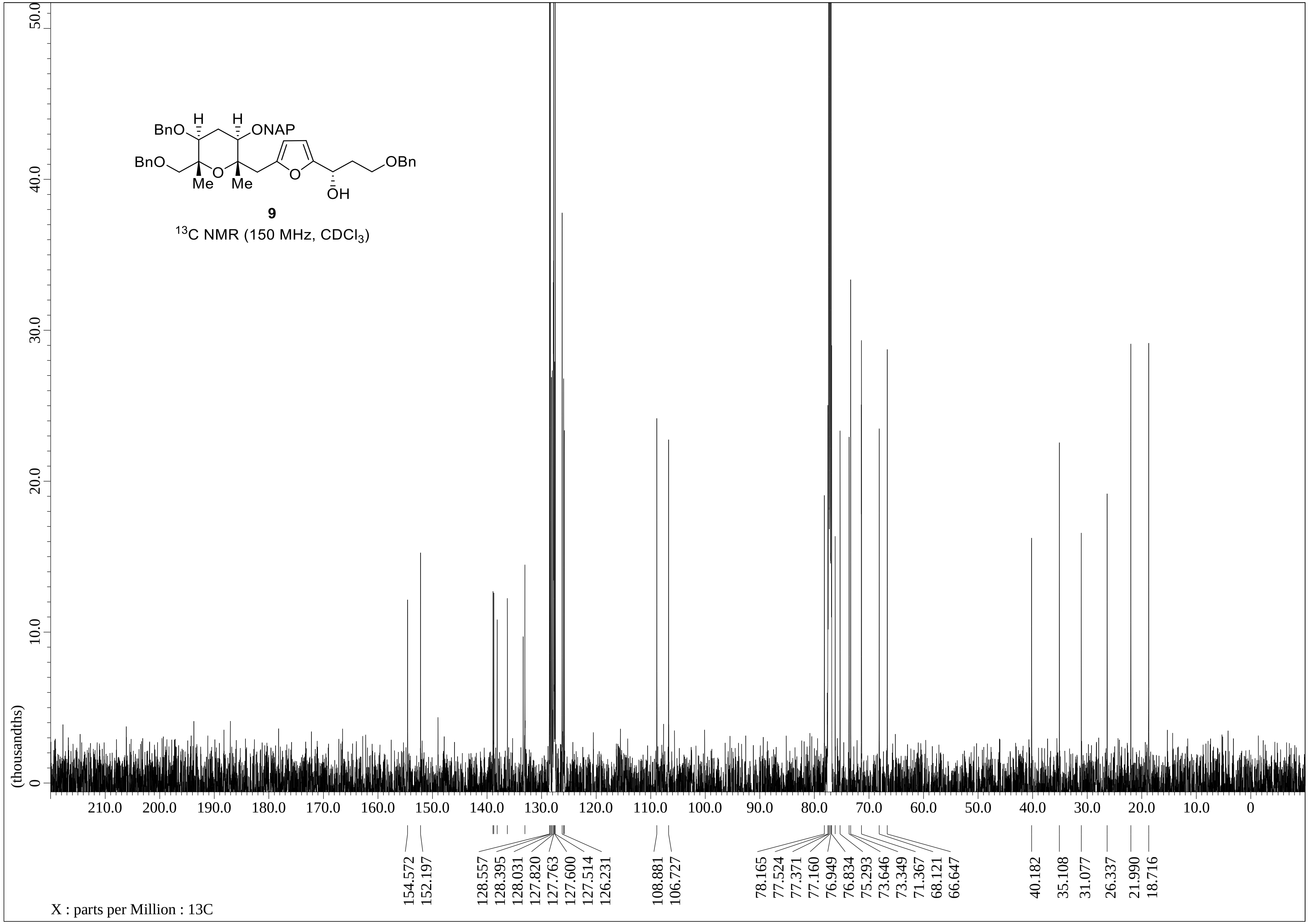
8

^{13}C NMR (150 MHz, CDCl$_3$)



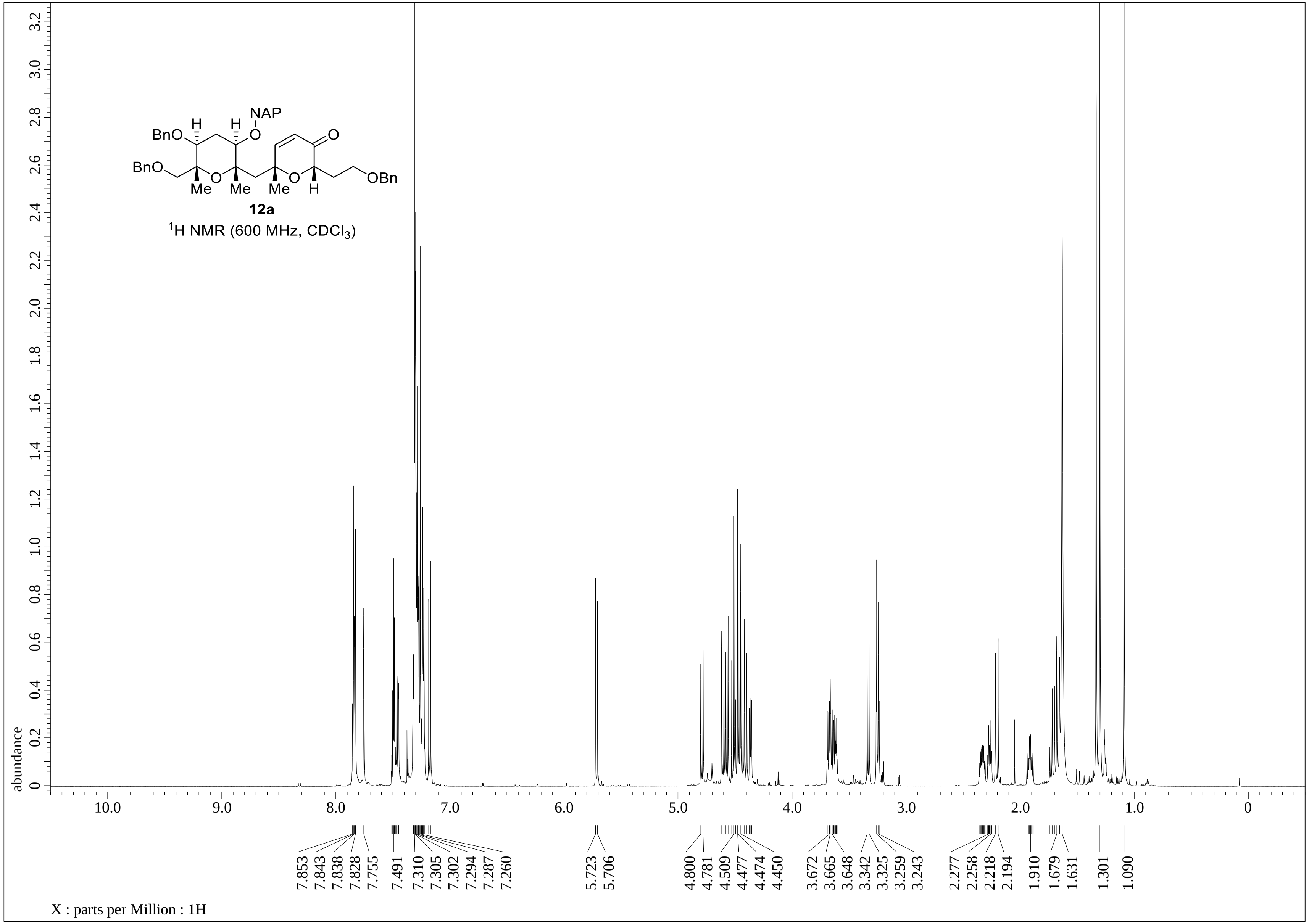
9

^{1}H NMR (600 MHz, CDCl$_3$)



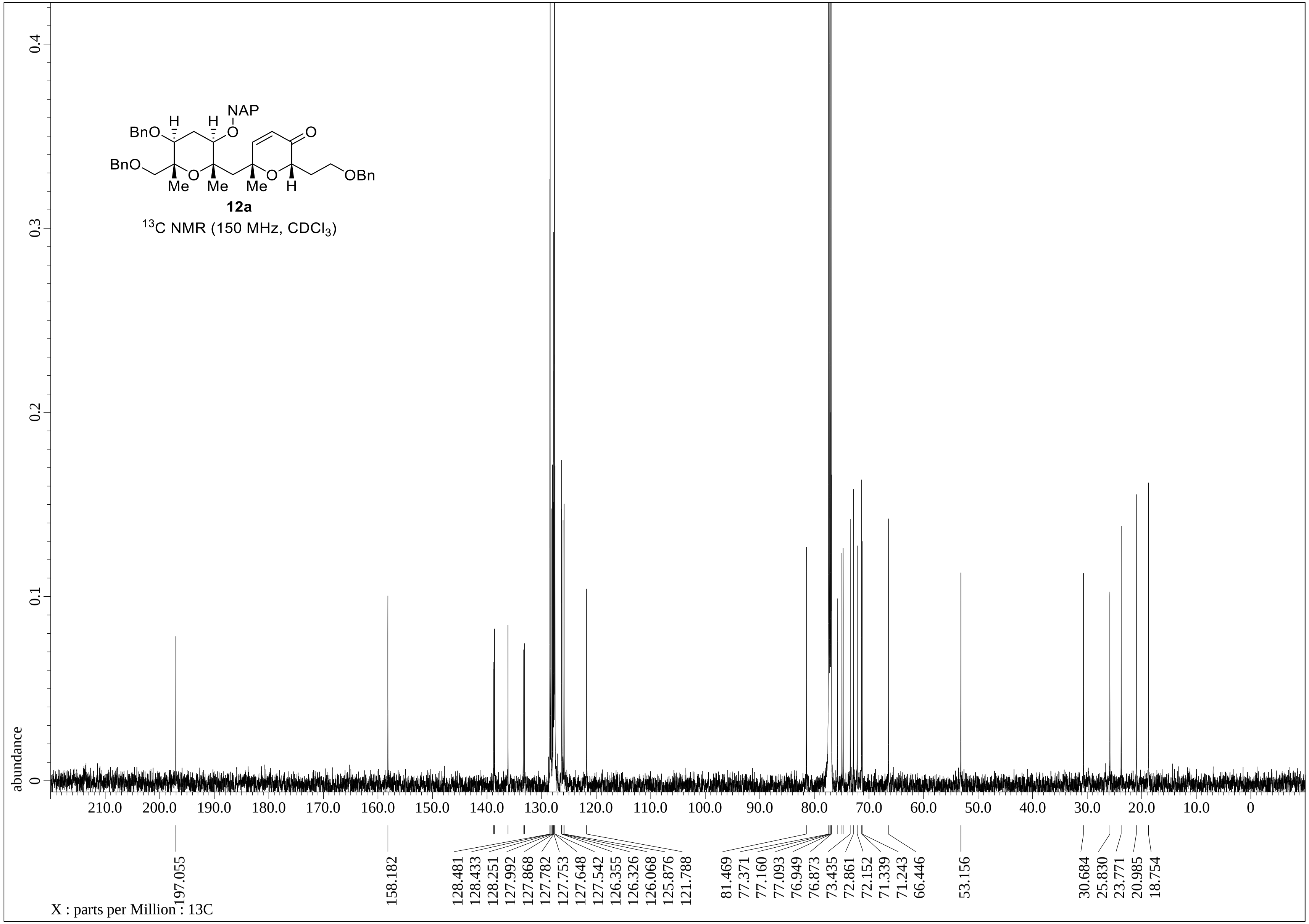
9

^{13}C NMR (150 MHz, CDCl$_3$)



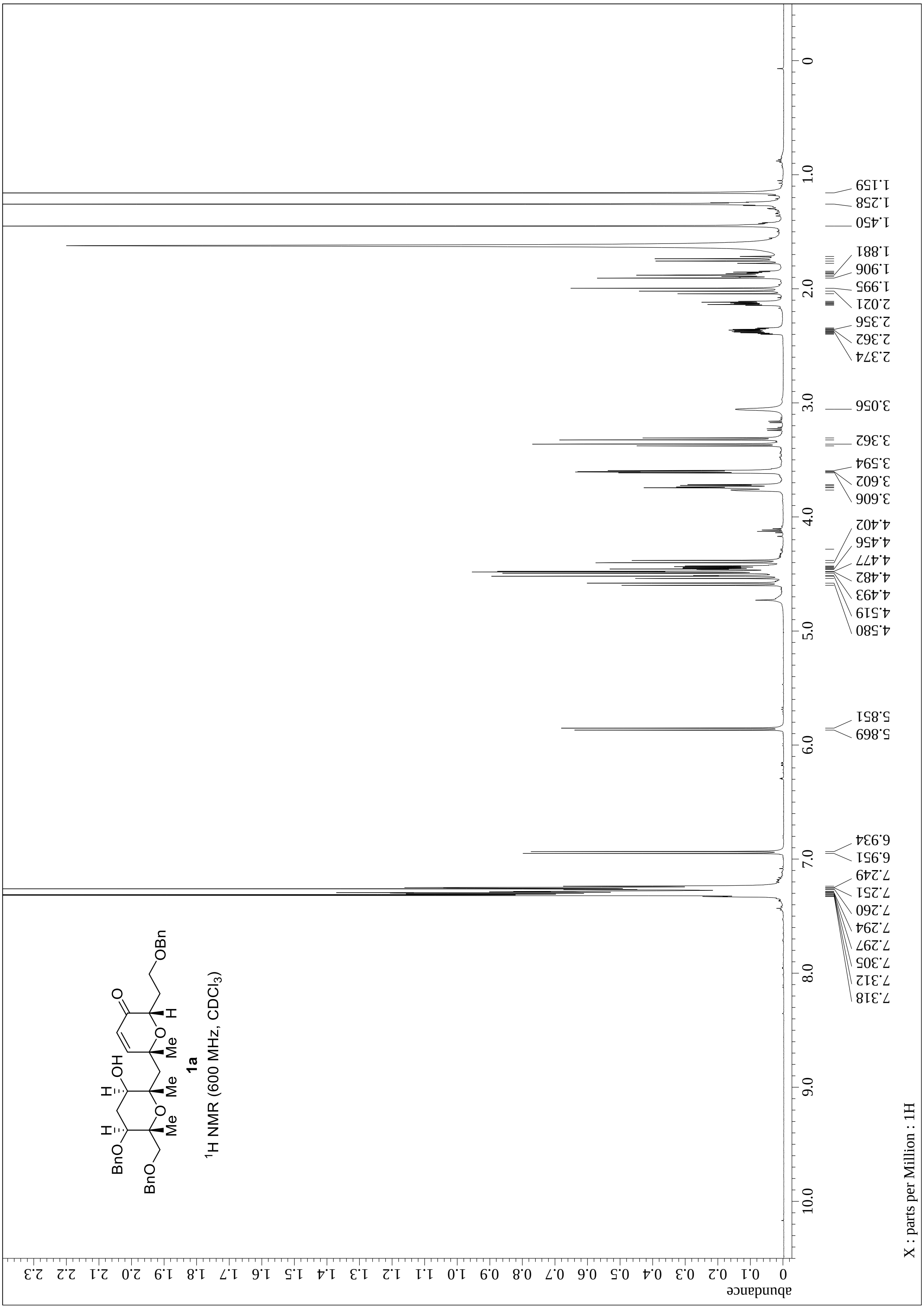
12a

^{1}H NMR (600 MHz, CDCl$_3$)



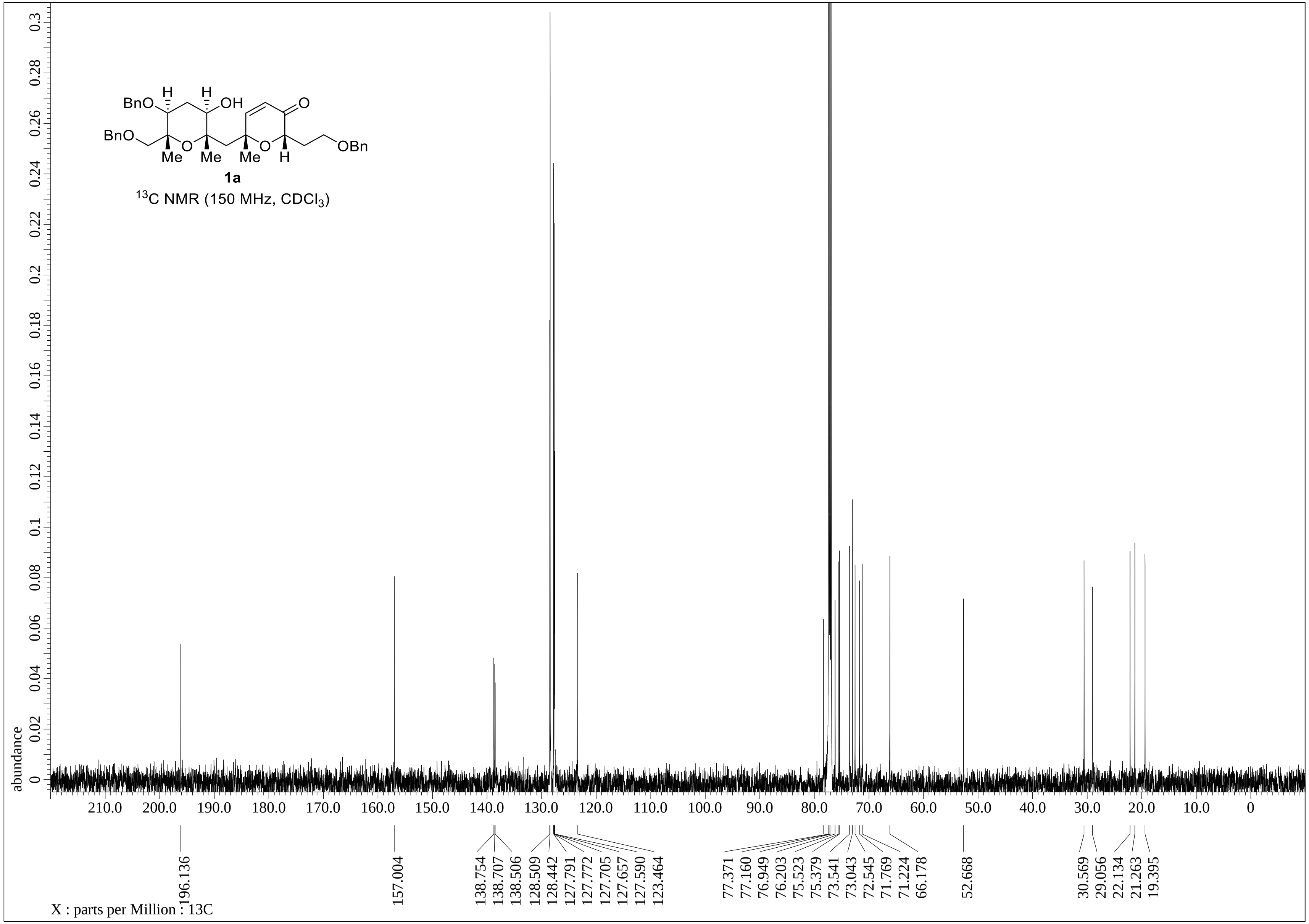
12a

^{13}C NMR (150 MHz, $CDCl_3$)



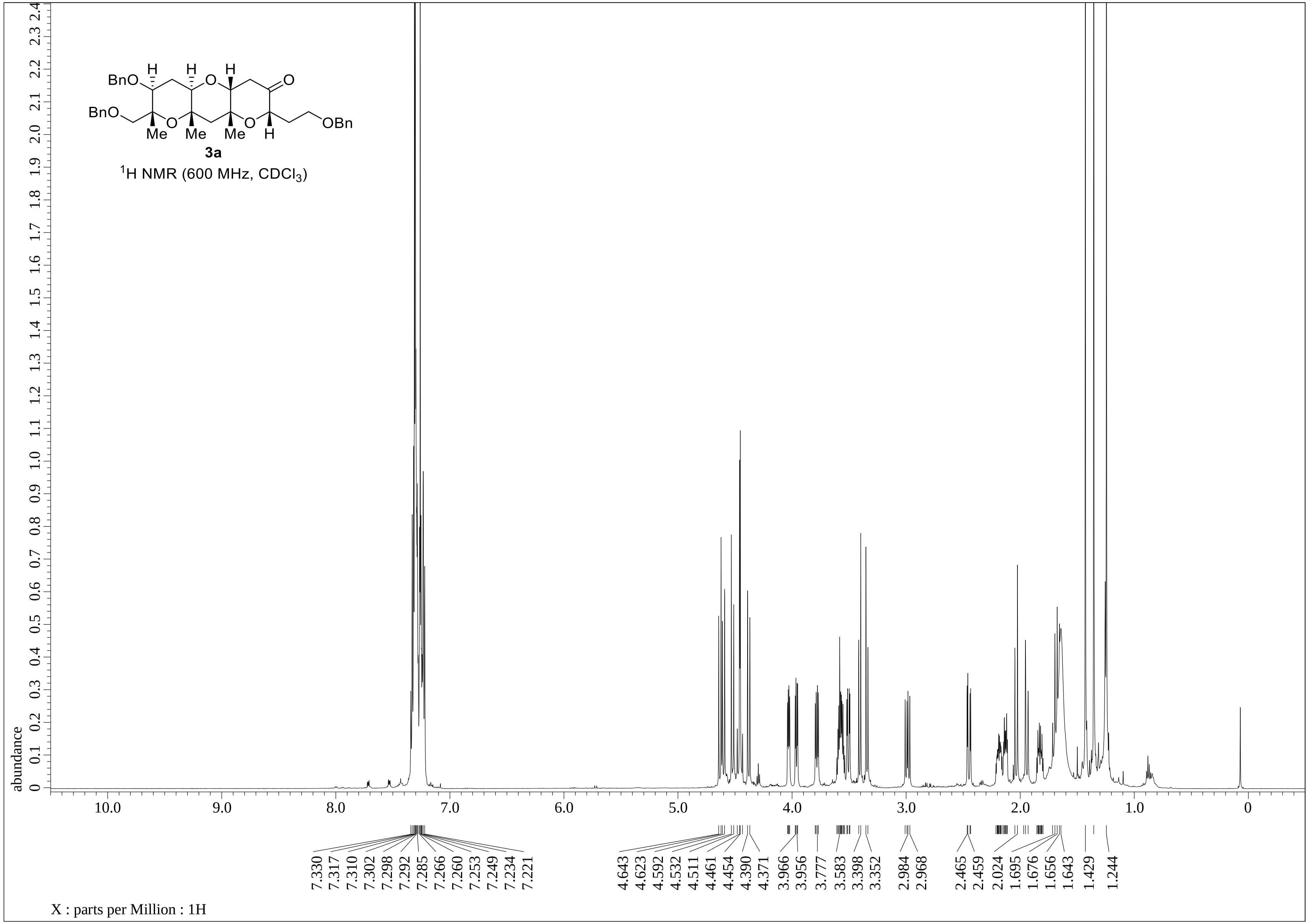
1a

^{1}H NMR (600 MHz, CDCl$_3$)



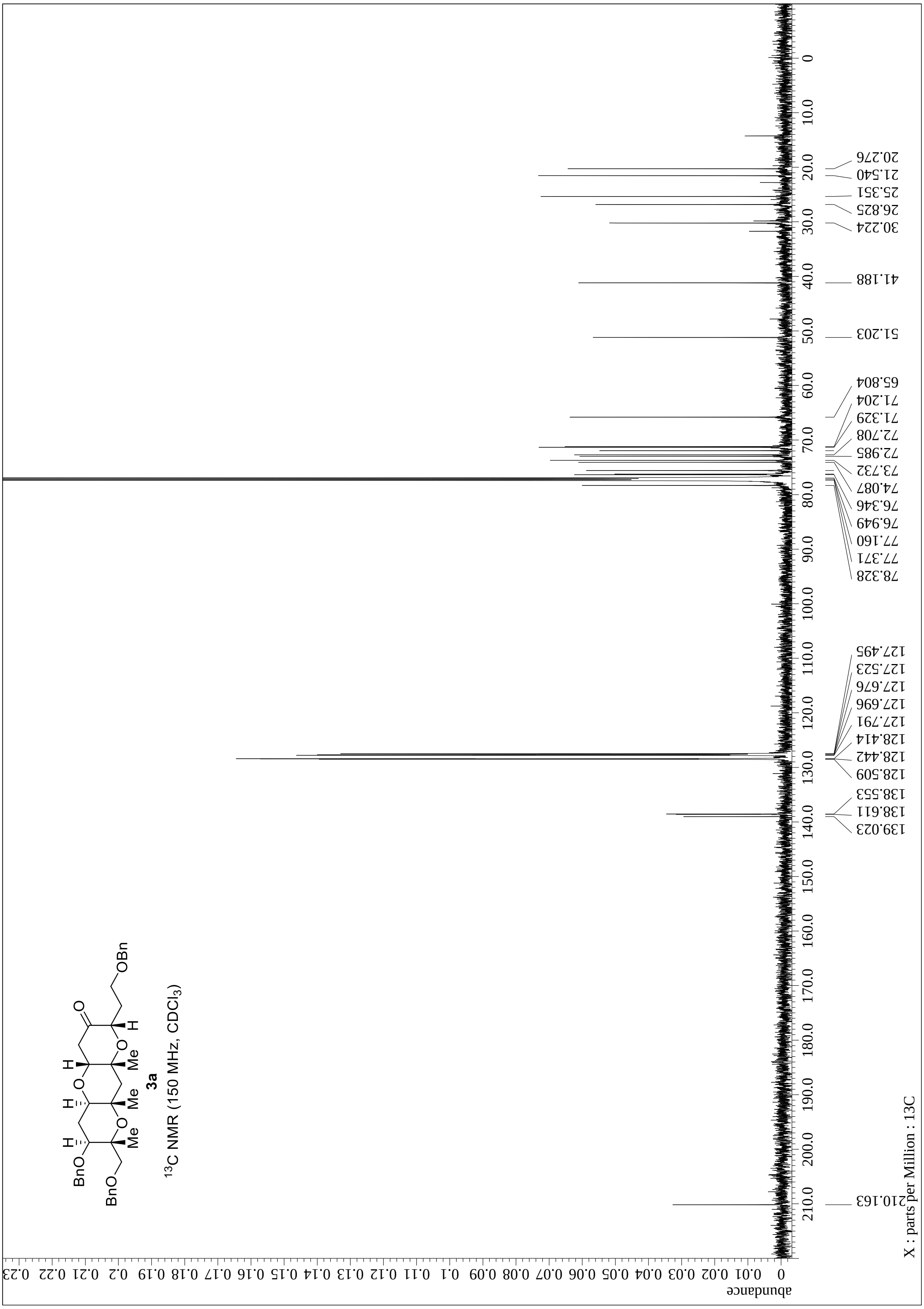
1a

^{13}C NMR (150 MHz, $CDCl_3$)

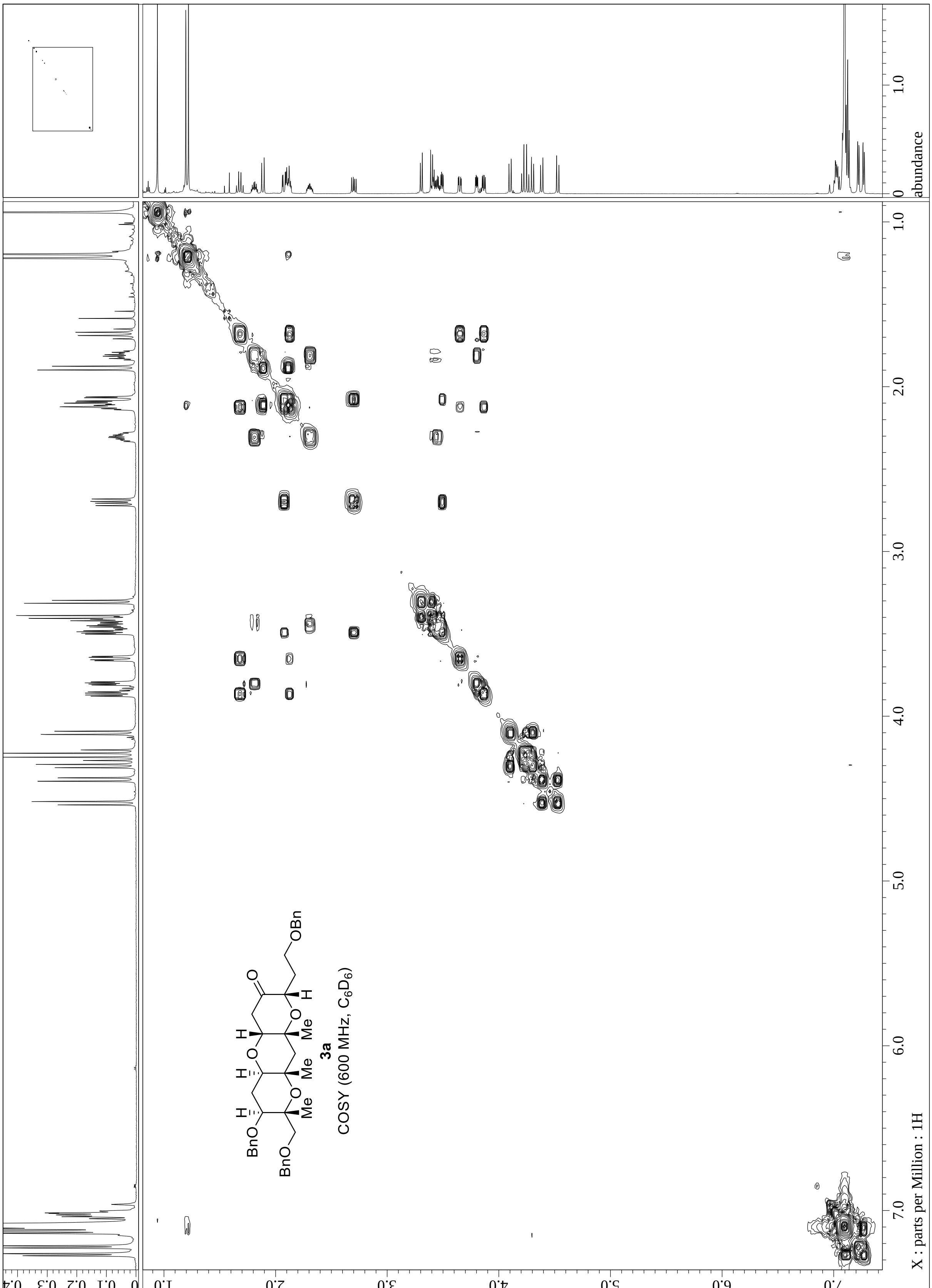


3a

^{1}H NMR (600 MHz, $CDCl_3$)

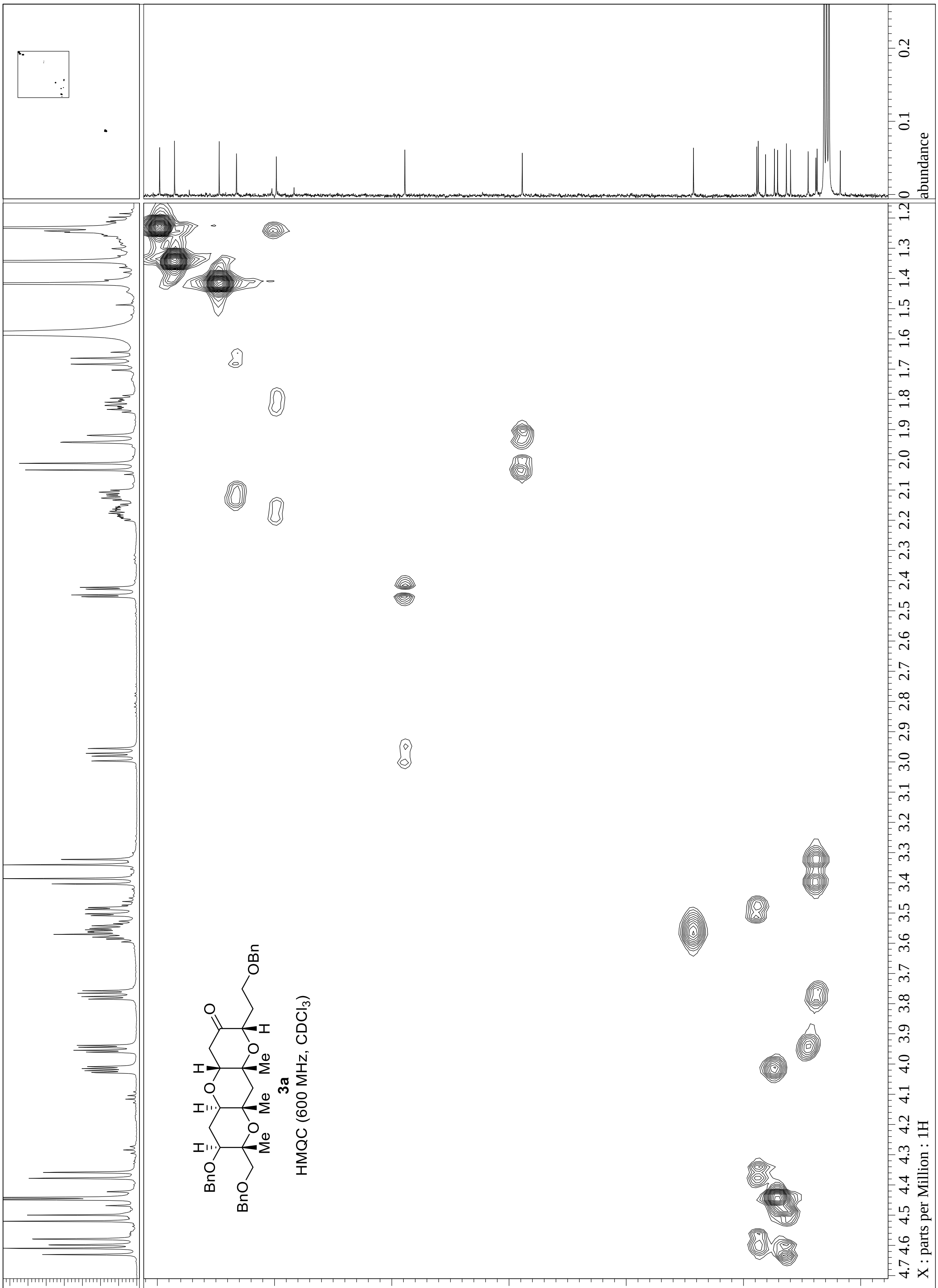

3a

^{13}C NMR (150 MHz, CDCl$_3$)



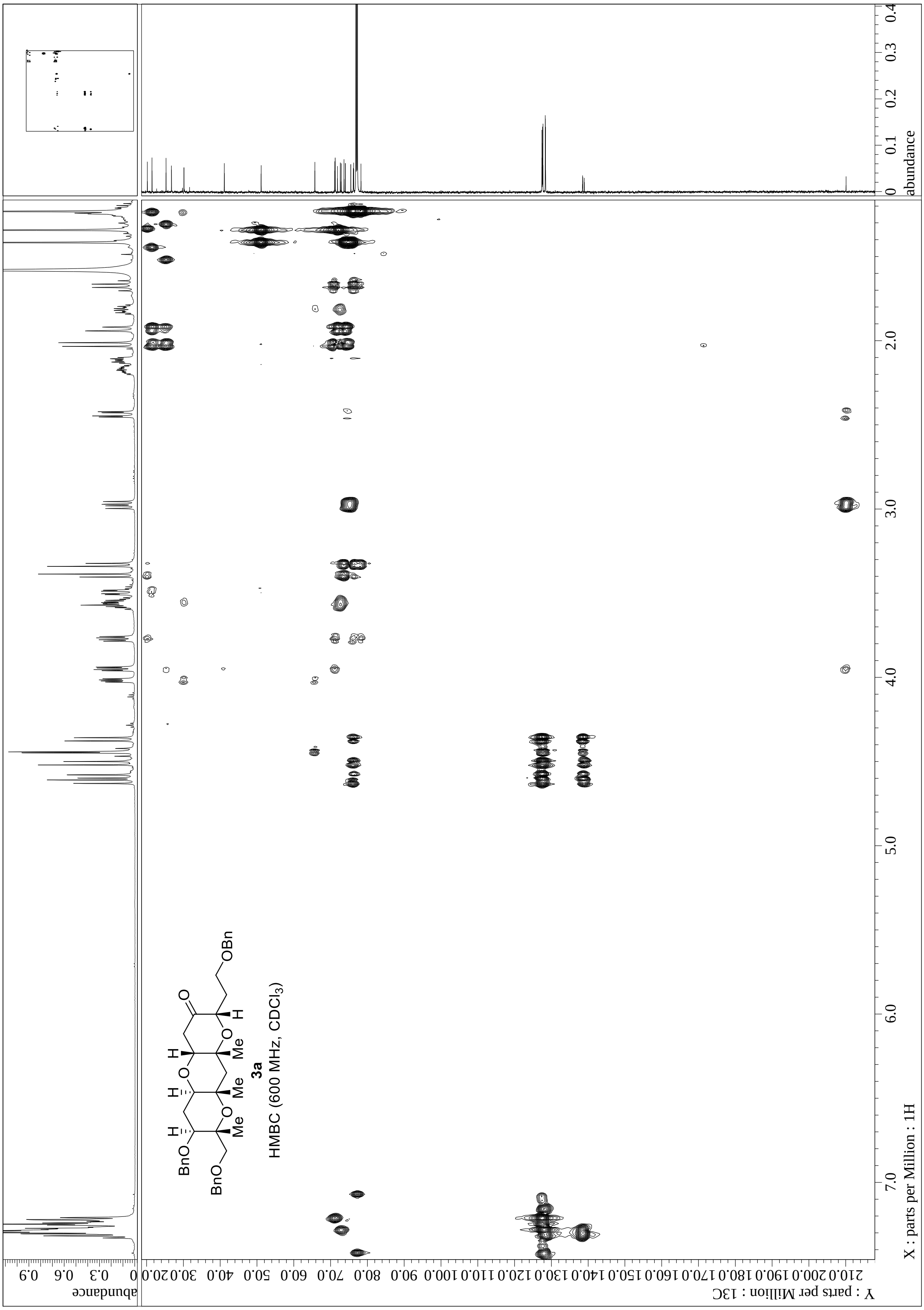
3a

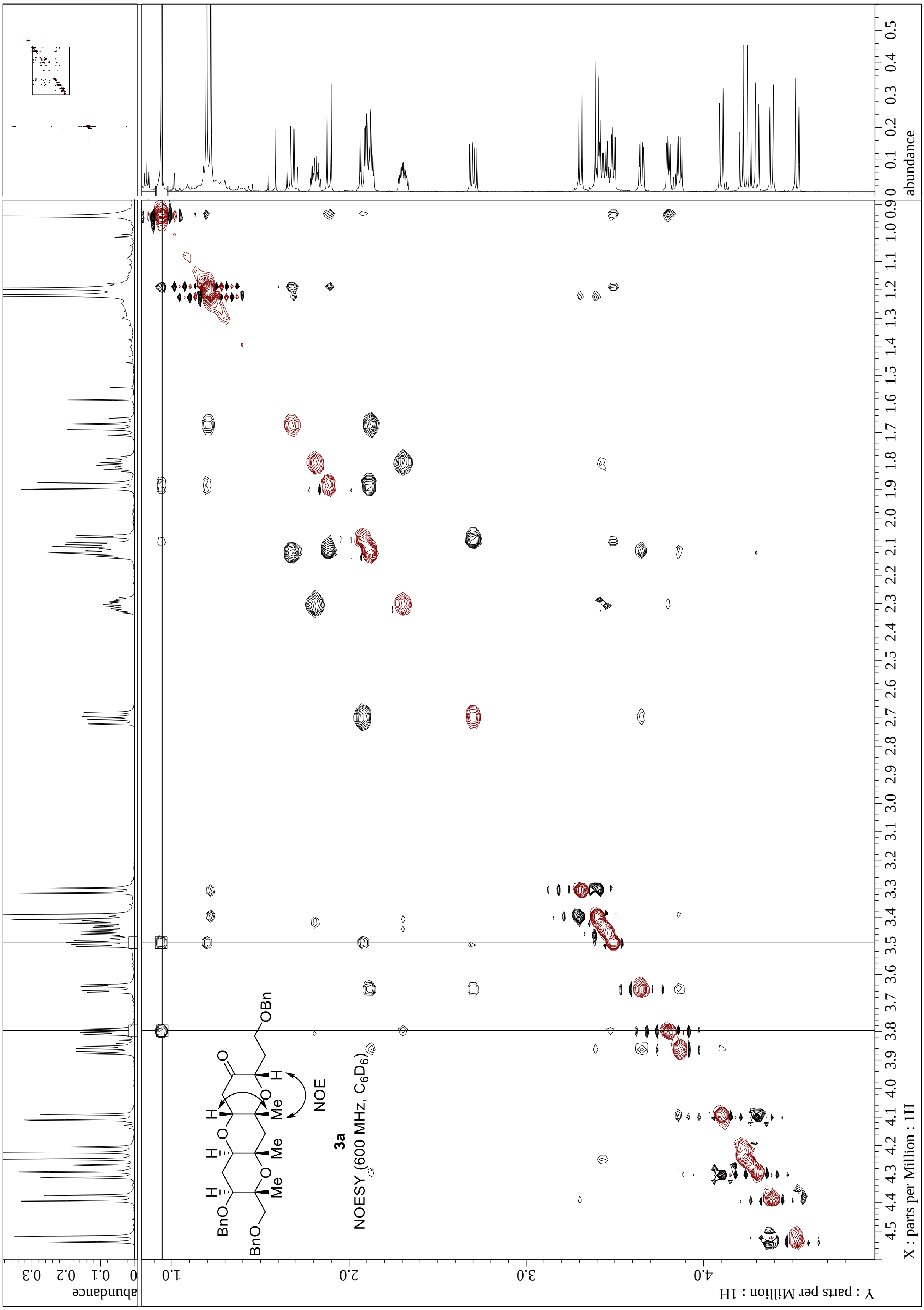
COSY (600 MHz, C_6D_6)



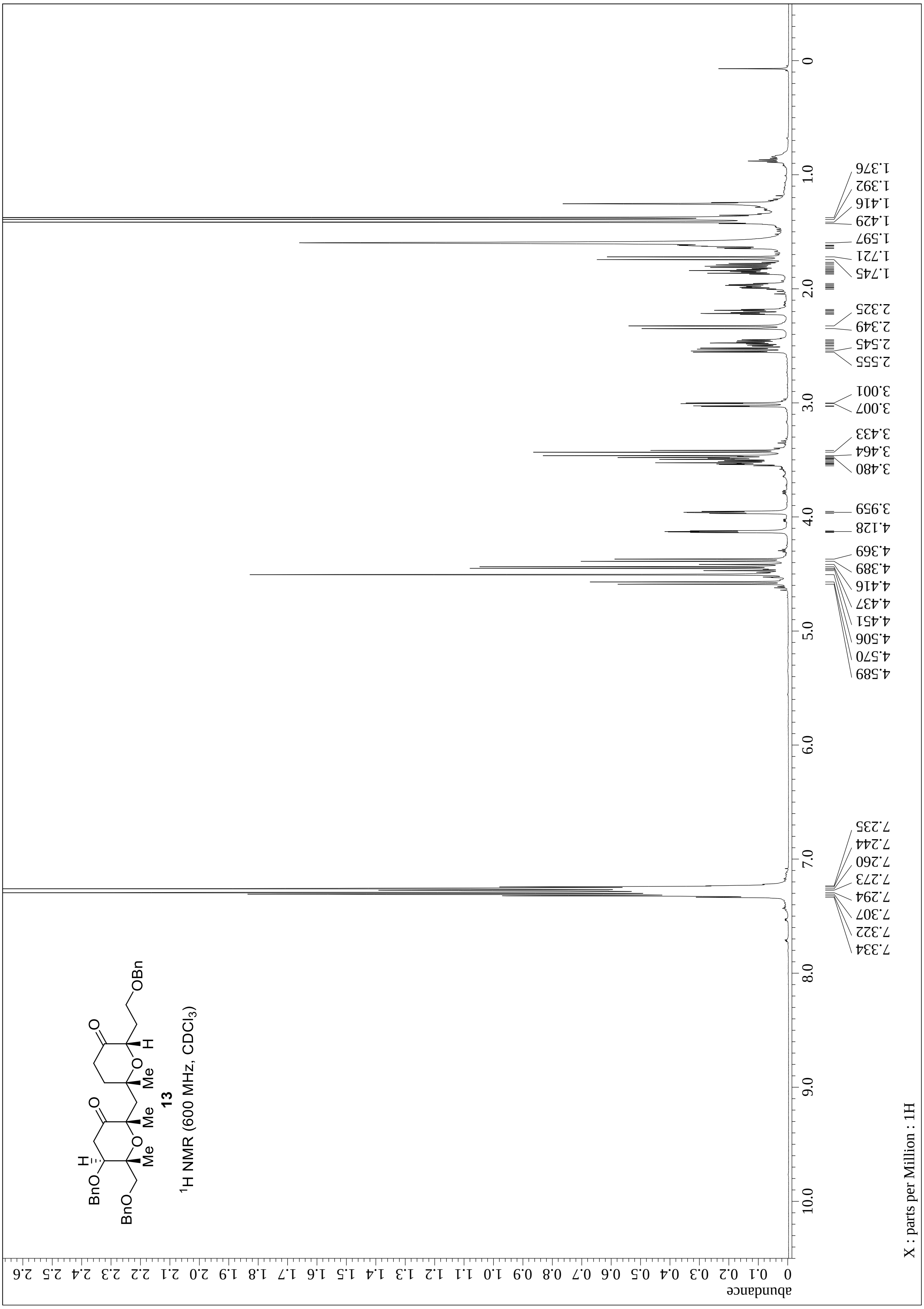
3a

HMQC (600 MHz, $CDCl_3$)

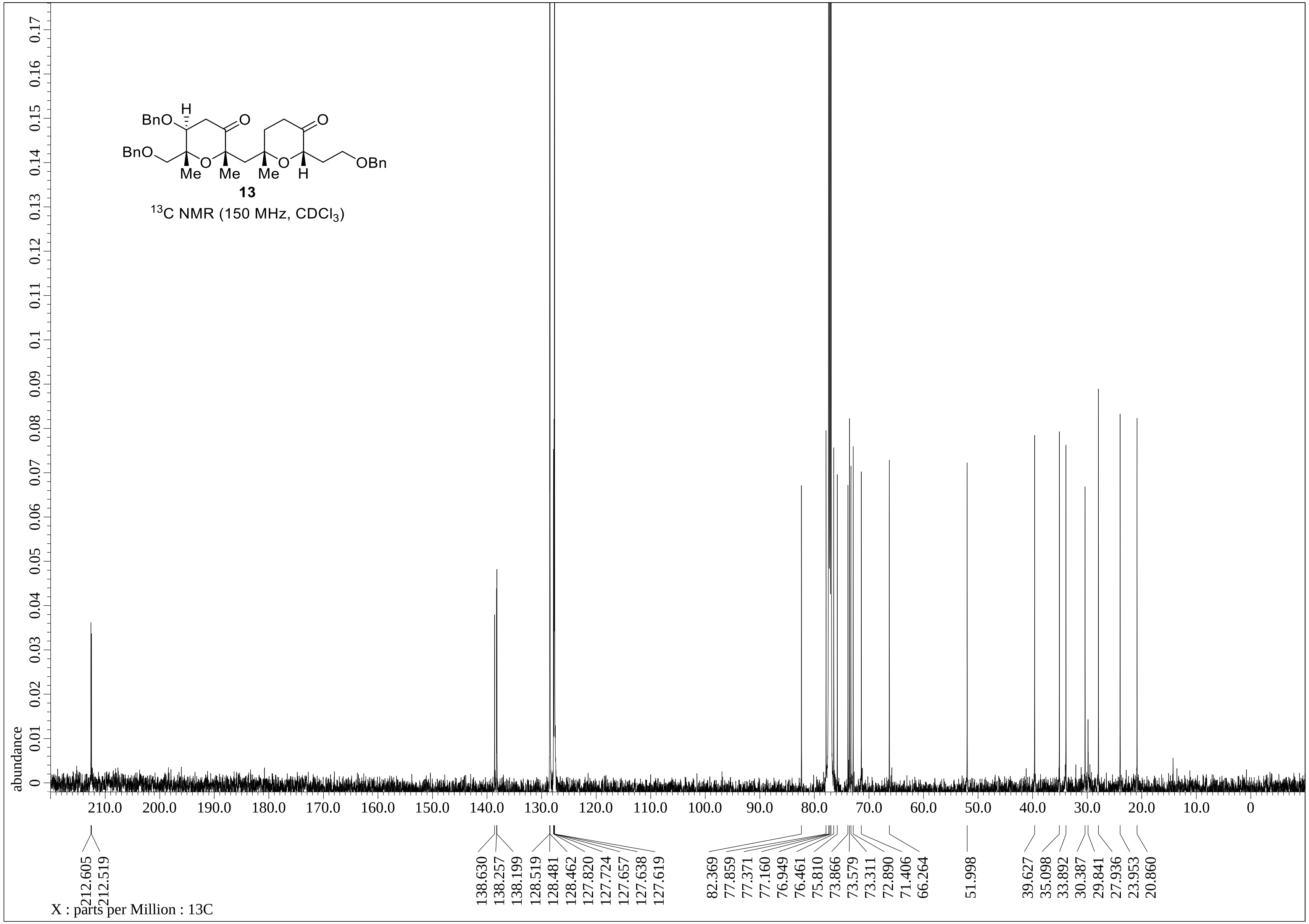

BnO
BnO
OBn
O
H
Me
Me
Me
3a
HMBC (600 MHz, CDCl3)
X : parts per Million : 1H
Y : parts per Million : 13C
abundance
abundance
0 0.1 0.2 0.3 0.4
0 0.3 0.6 0.9
2.0 3.0 4.0 5.0 6.0 7.0
20.0 30.0 40.0 50.0 60.0 70.0 80.0 90.0 100.0 110.0 120.0 130.0 140.0 150.0 160.0 170.0 180.0 190.0 200.0 210.0


3a

NOESY (600 MHz, C_6D_6)

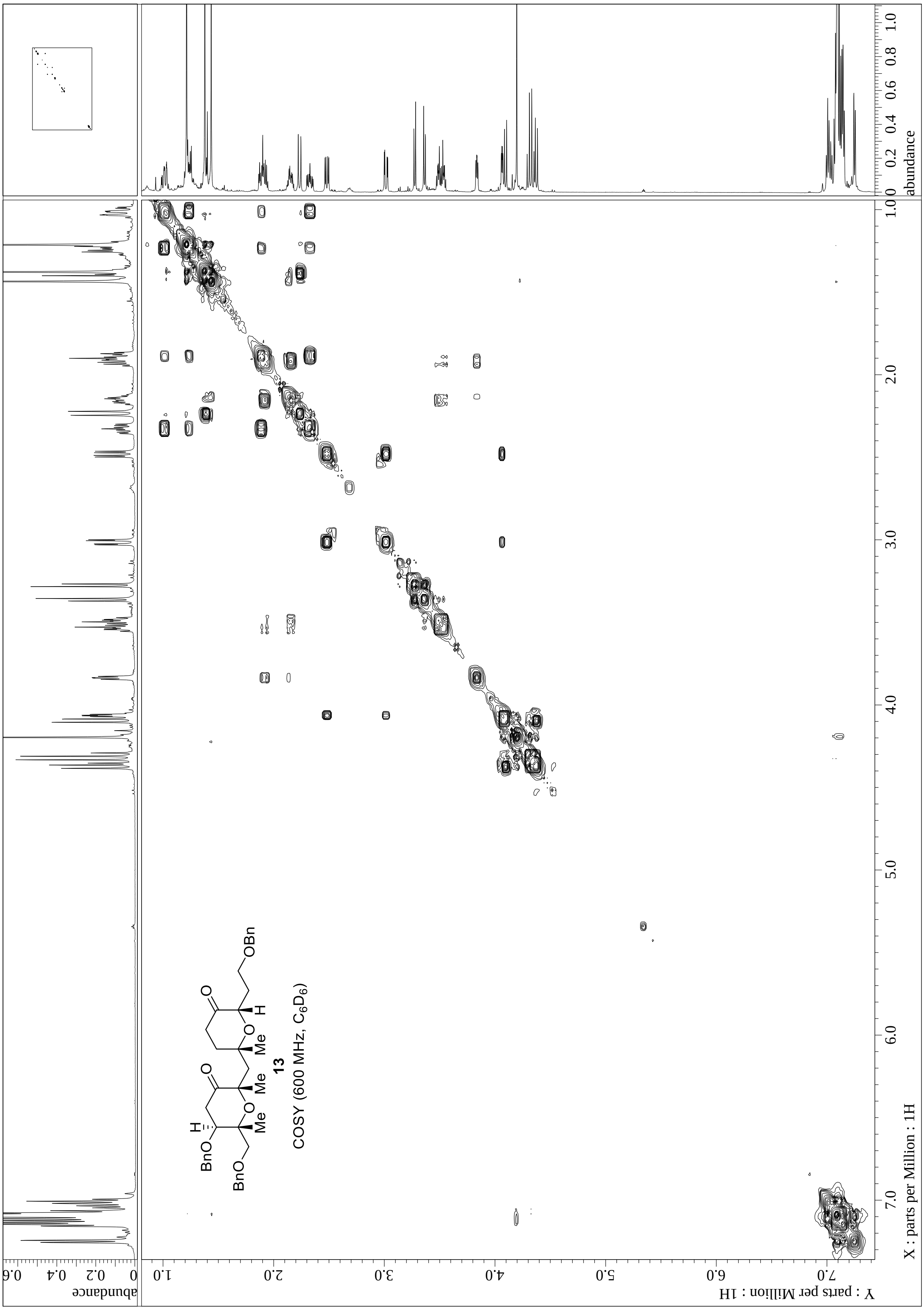

13

^{1}H NMR (600 MHz, CDCl$_3$)

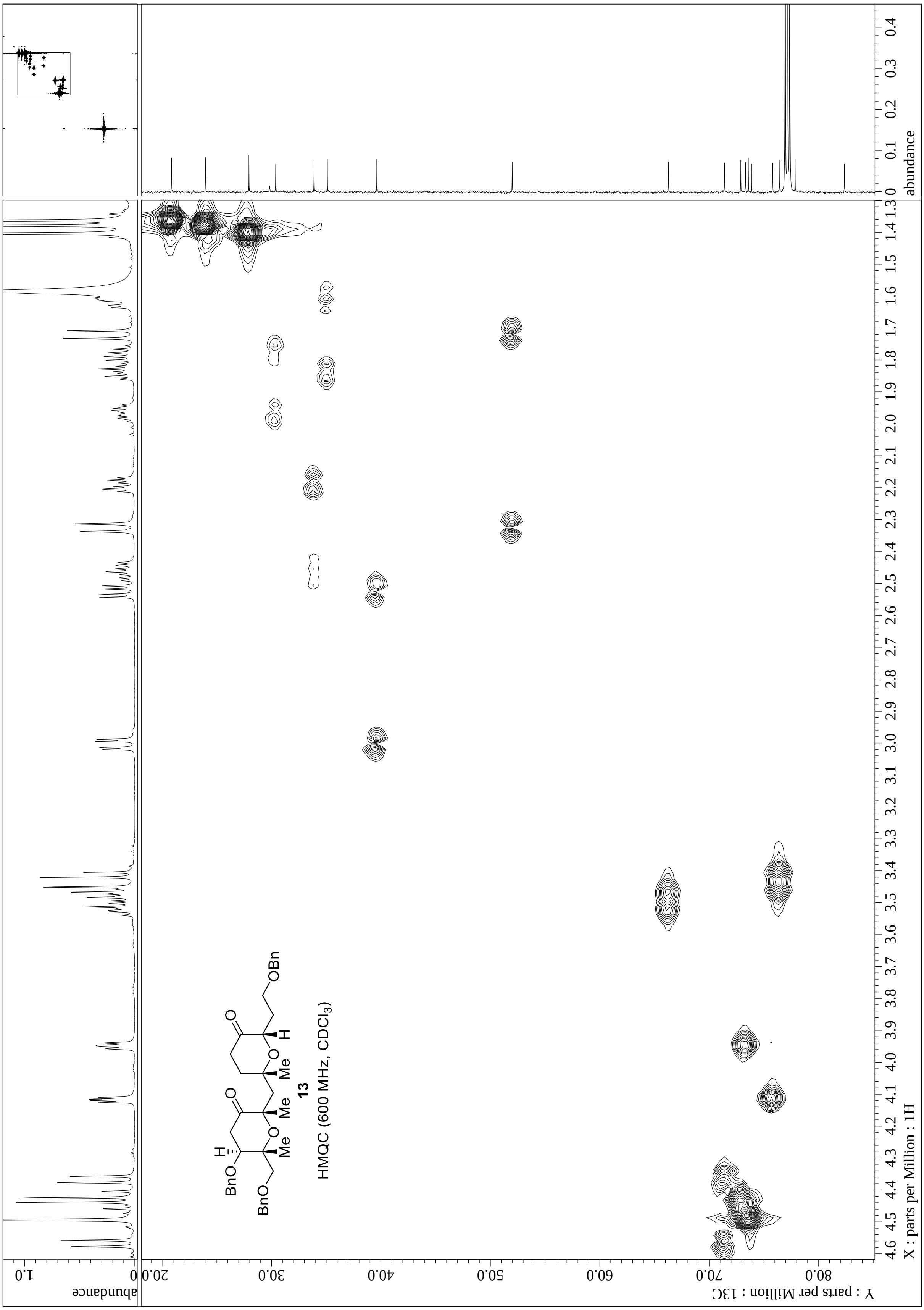


13

^{13}C NMR (150 MHz, CDCl$_3$)

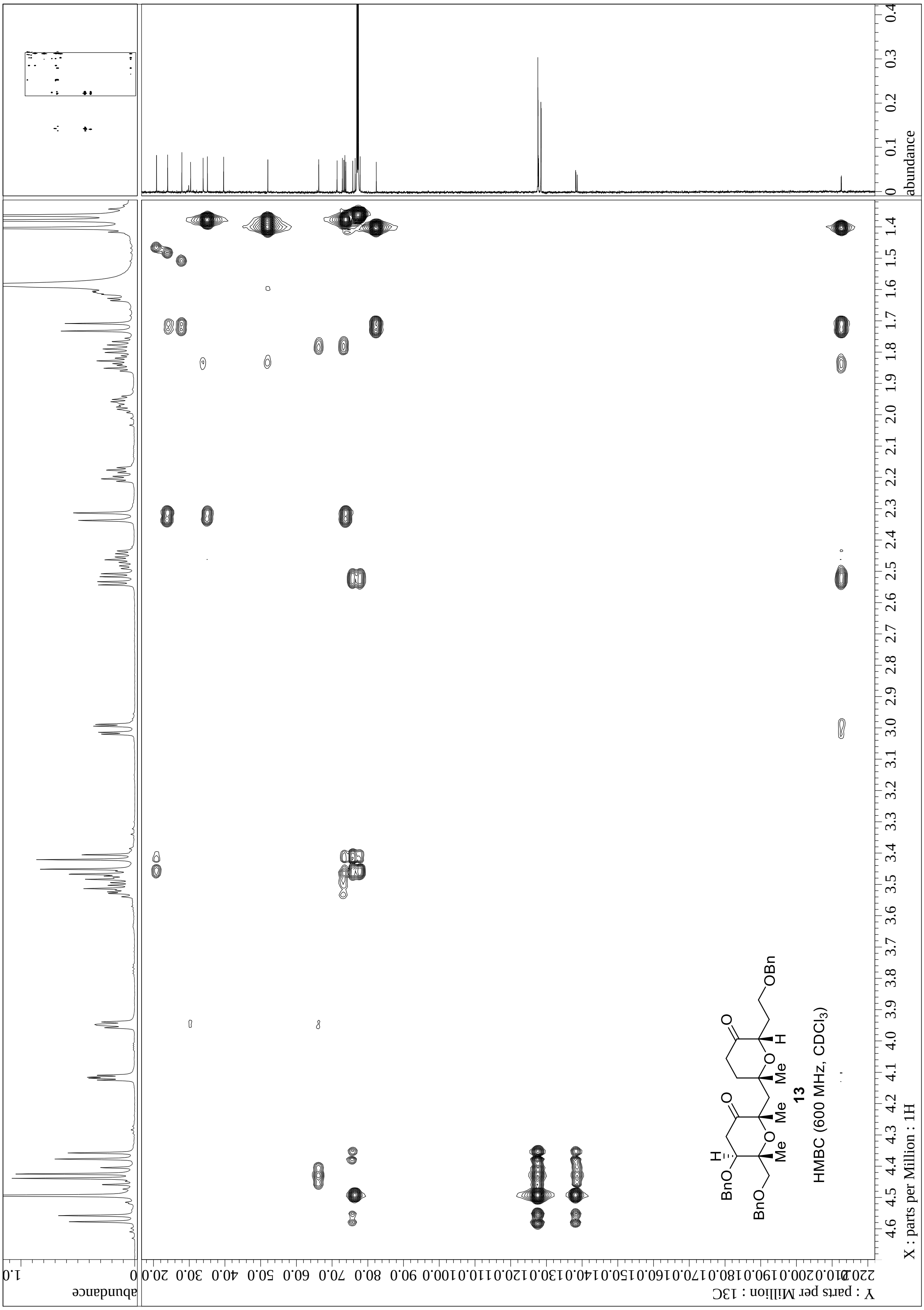

13

COSY (600 MHz, C_6D_6)



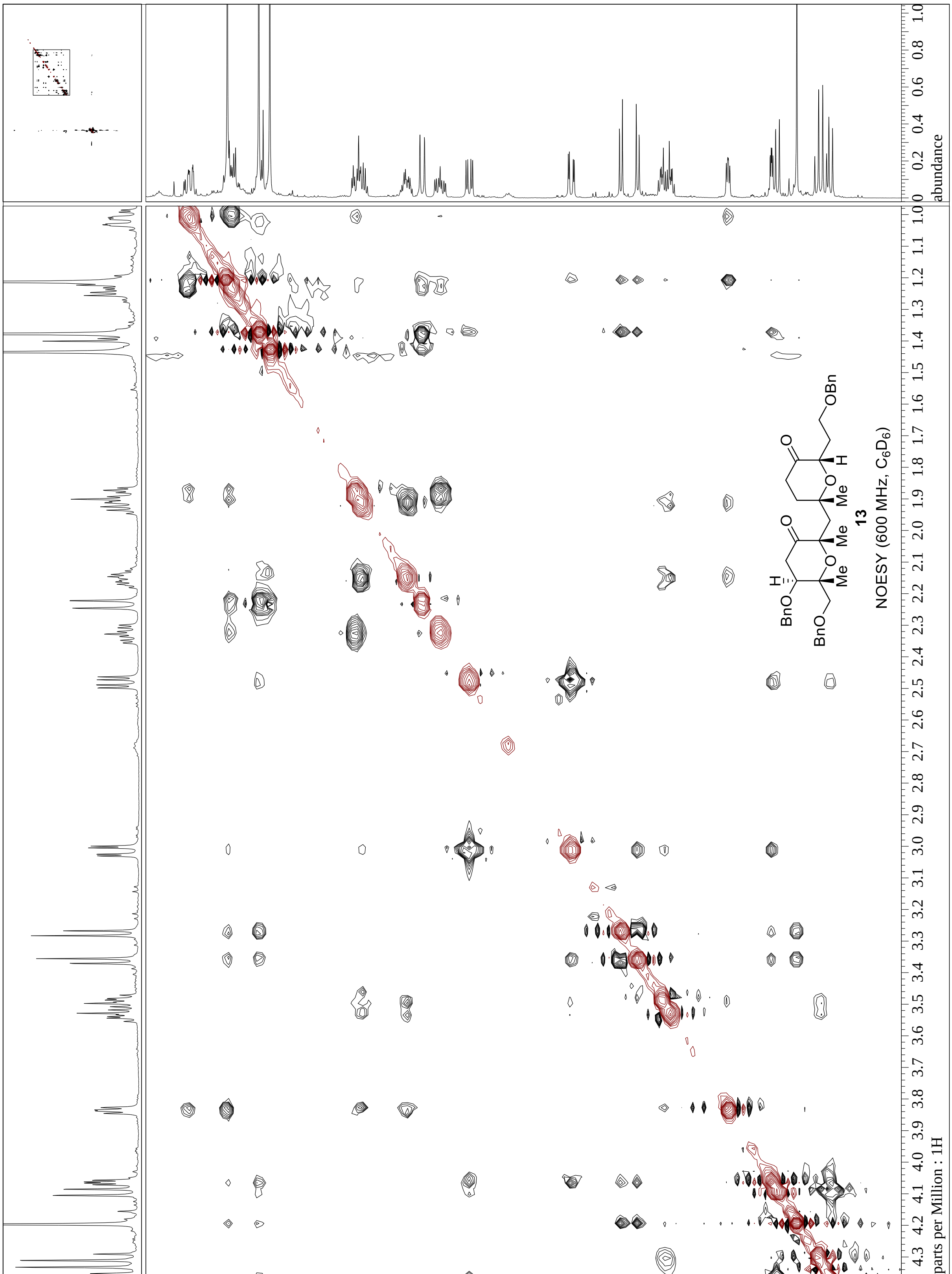
13

HMQC (600 MHz, $CDCl_3$)



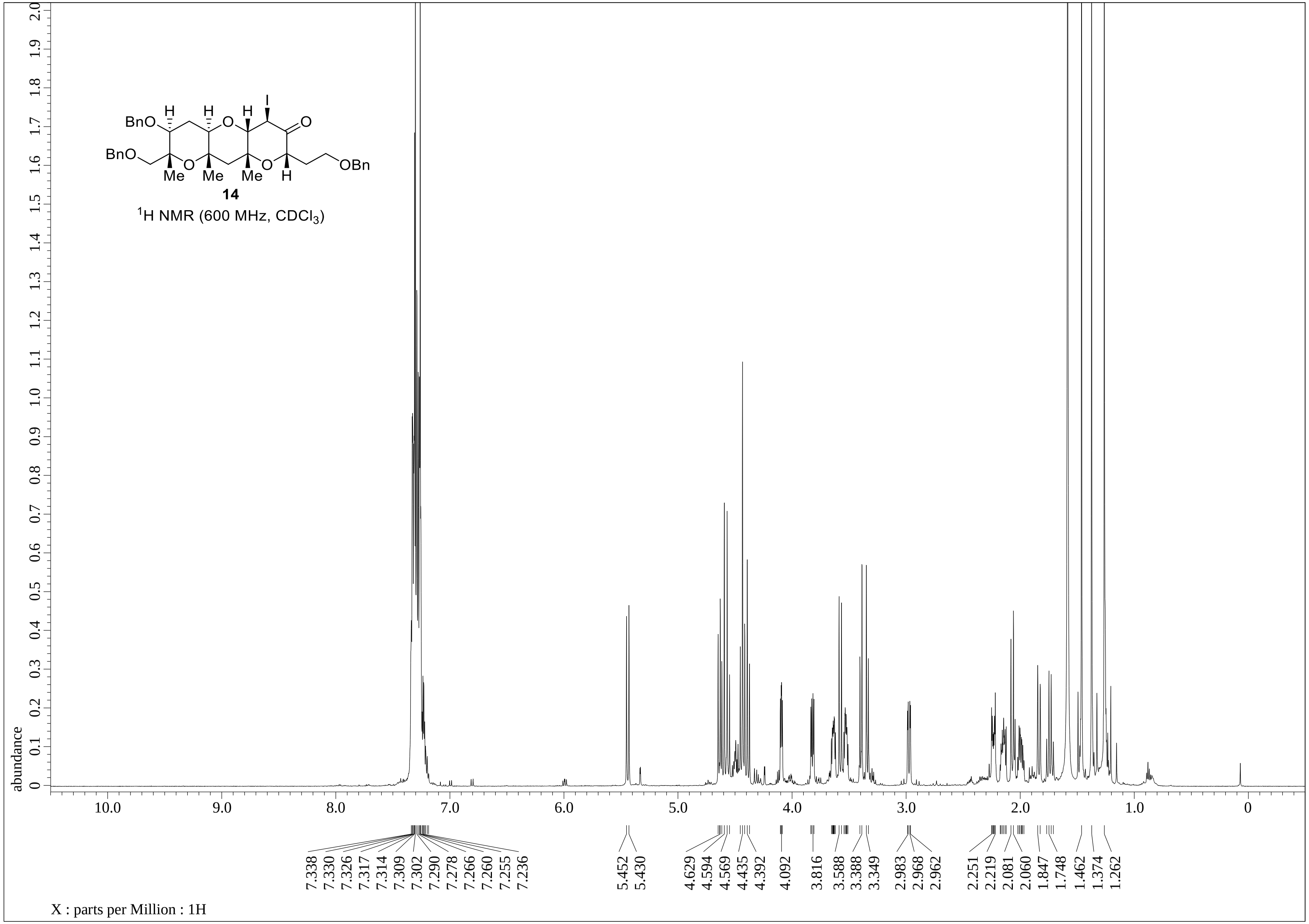
13

HMBC (600 MHz, $CDCl_3$)



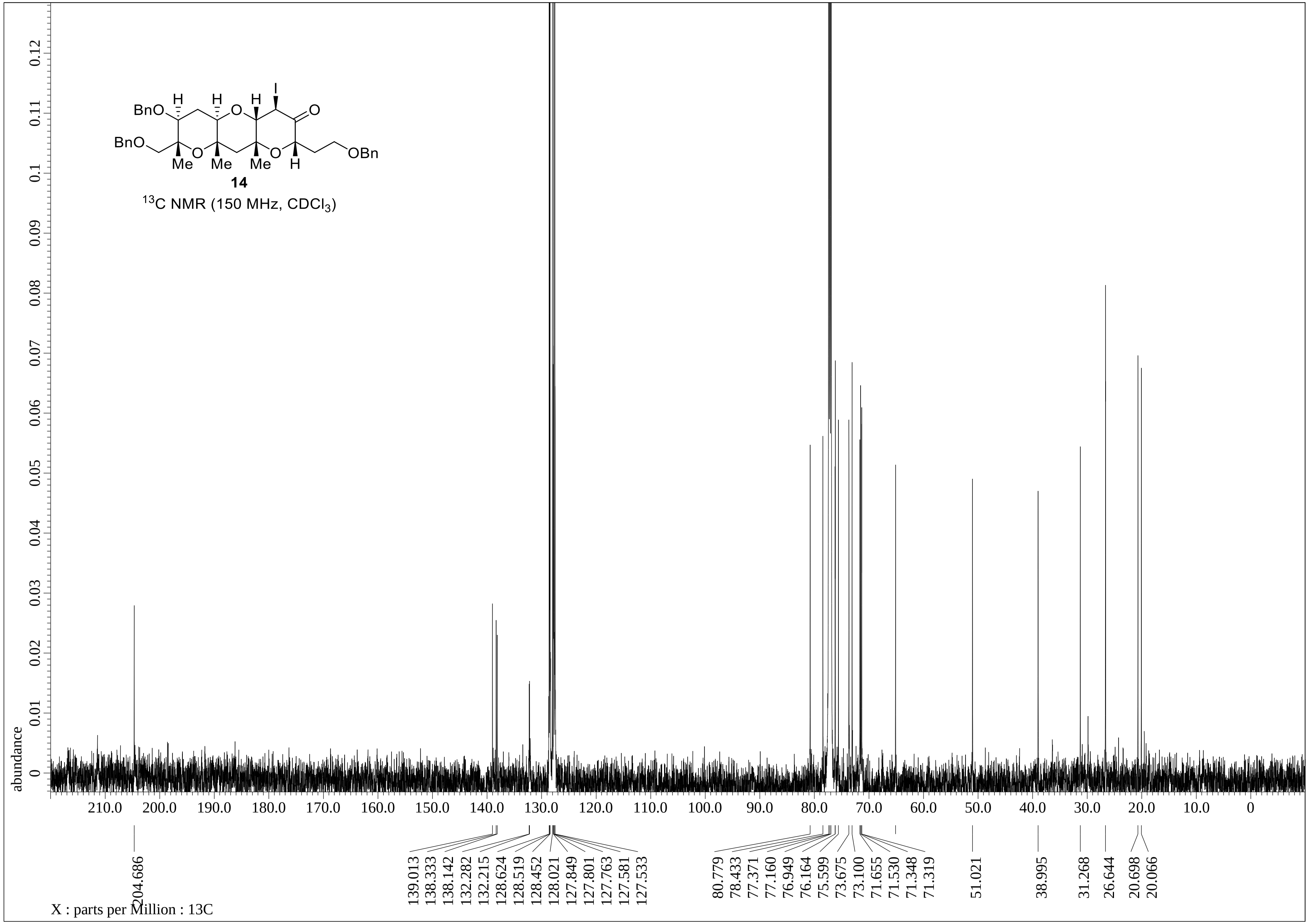
13

NOESY (600 MHz, C_6D_6)



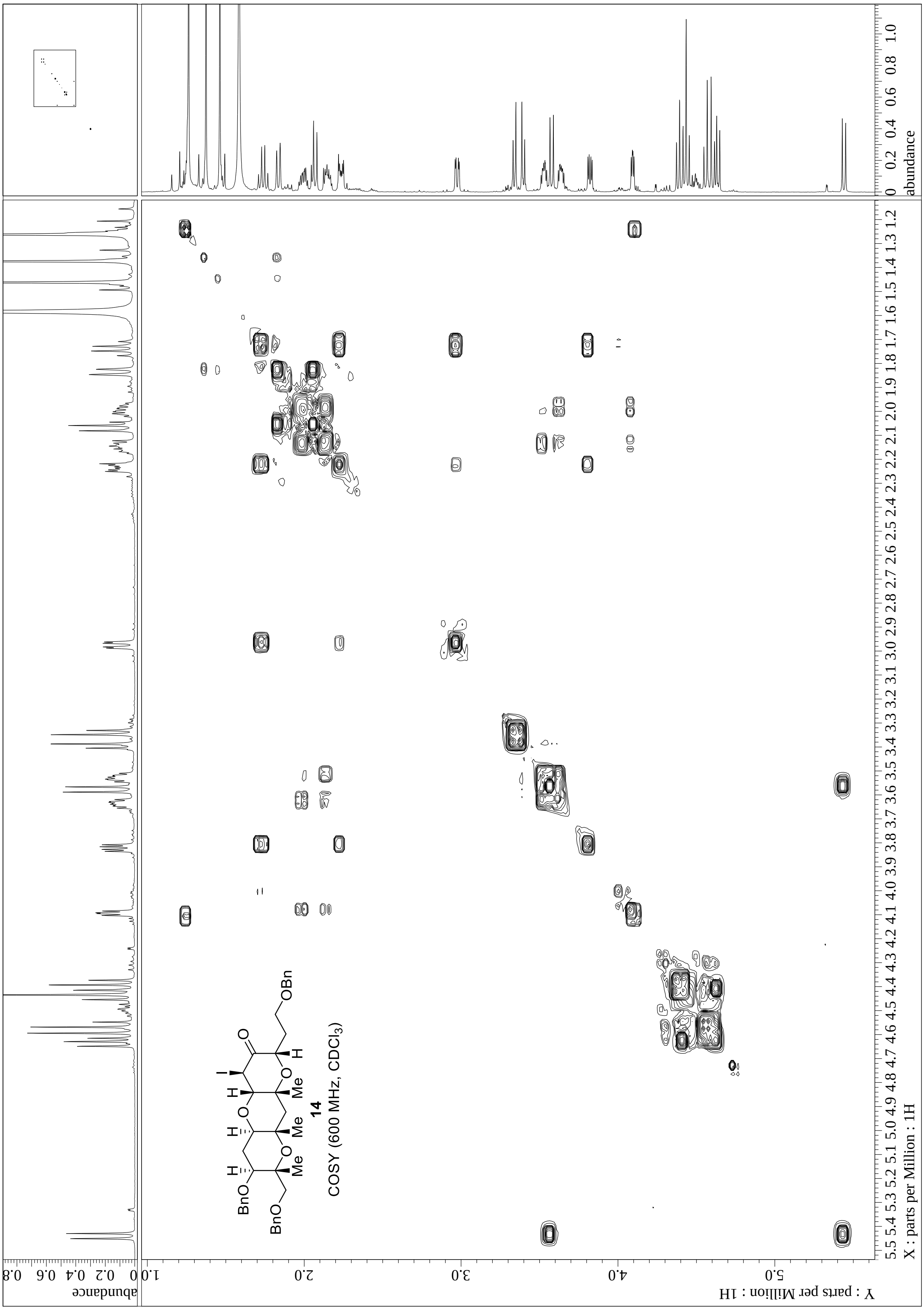
14

^{1}H NMR (600 MHz, $CDCl_3$)

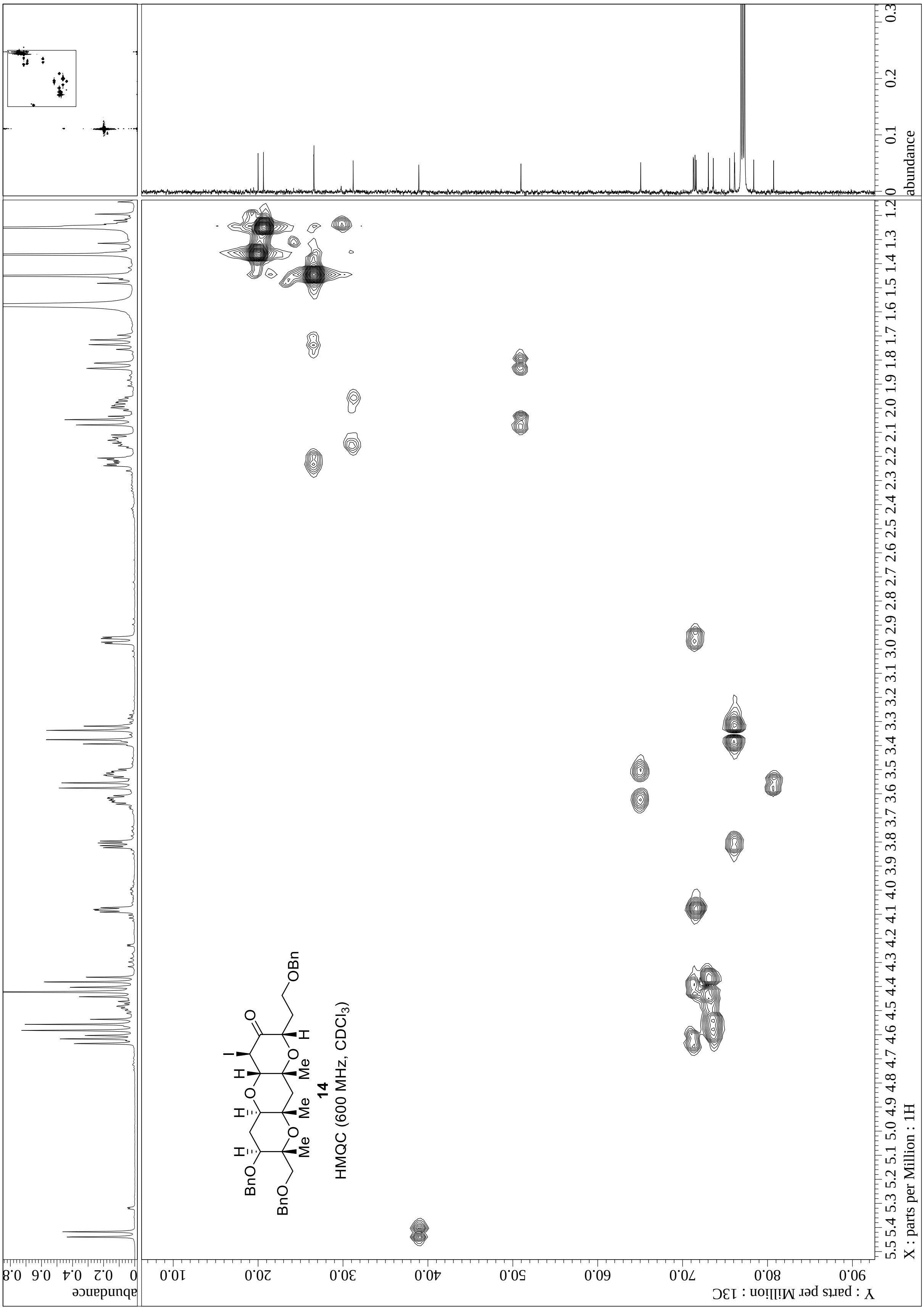


14

^{13}C NMR (150 MHz, $CDCl_3$)

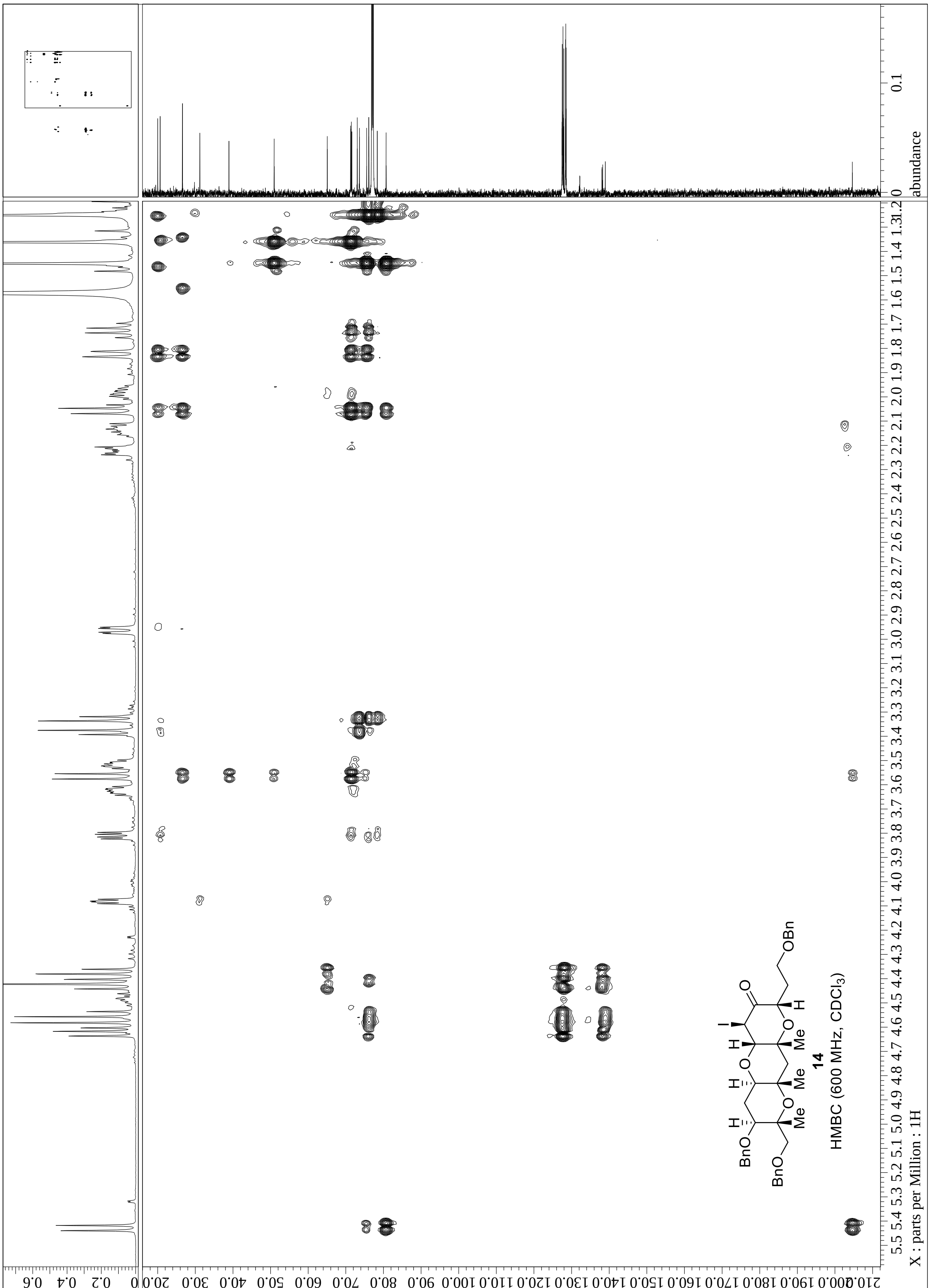

14

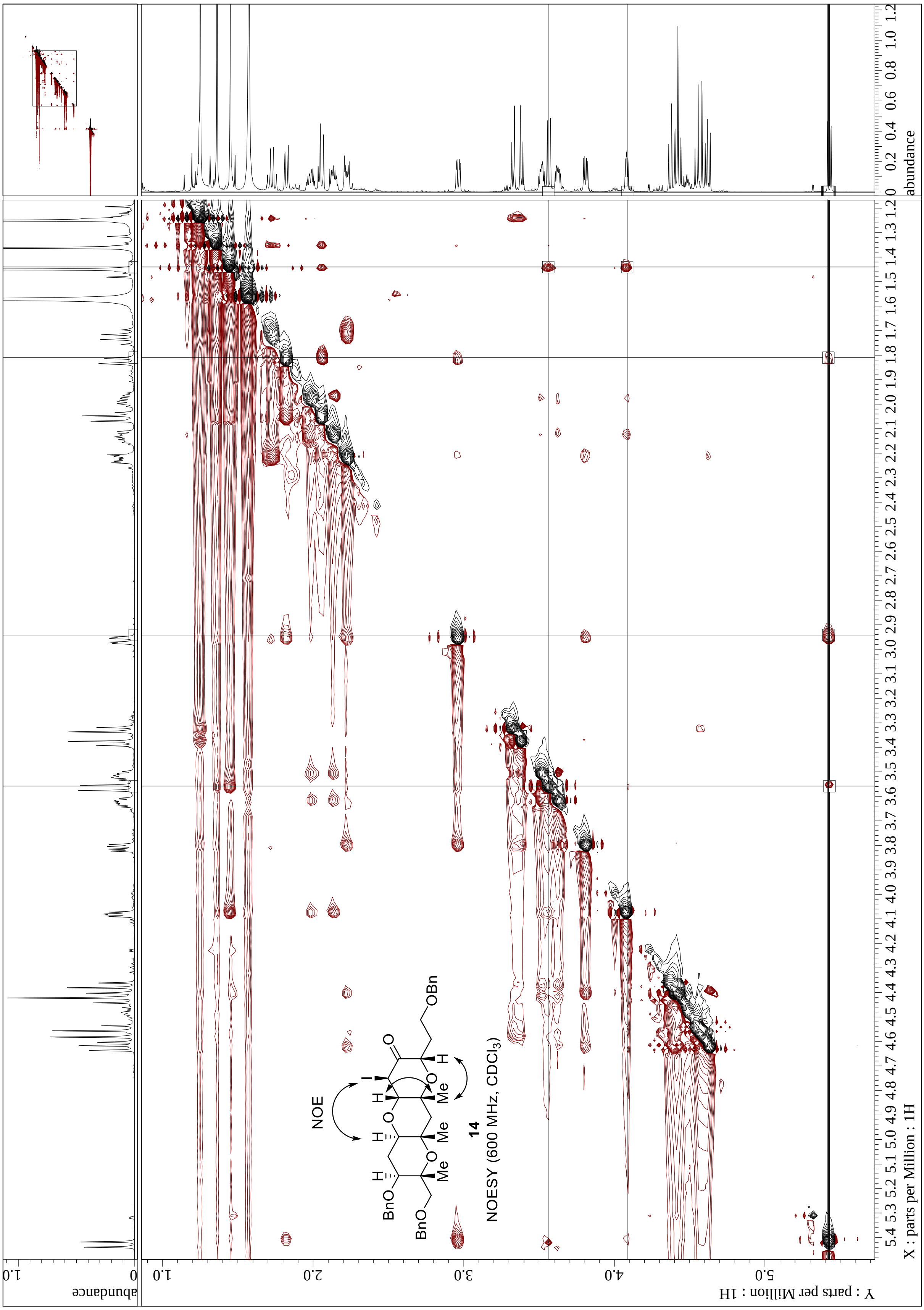
COSY (600 MHz, CDCl$_3$)



14

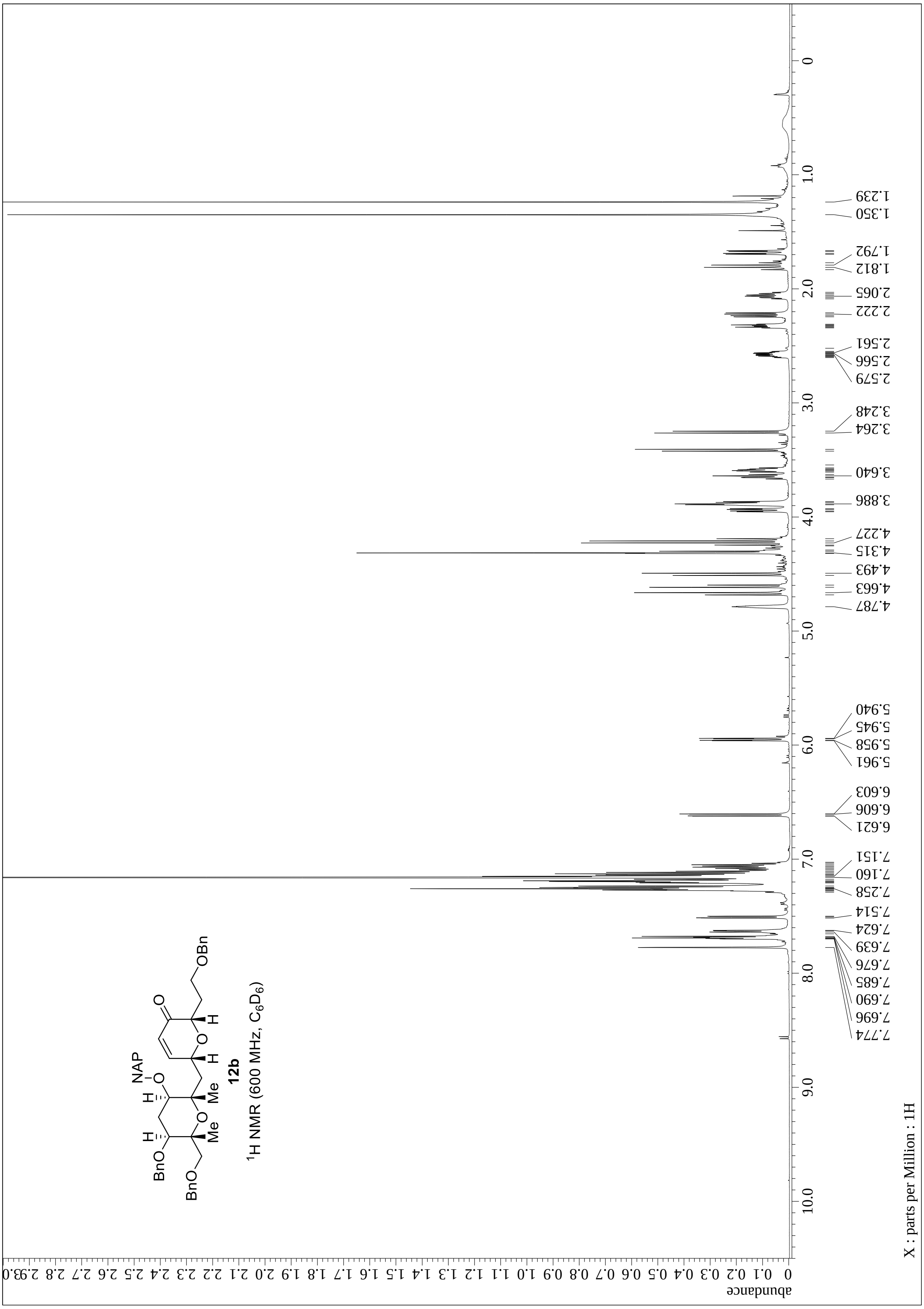
HMQC (600 MHz, $CDCl_3$)


14
HMBC (600 MHz, CDCl$_3$)
X : parts per Million : 1H
Y : parts per Million : 13C
abundance
BnO
OBn
Me
H
I
O



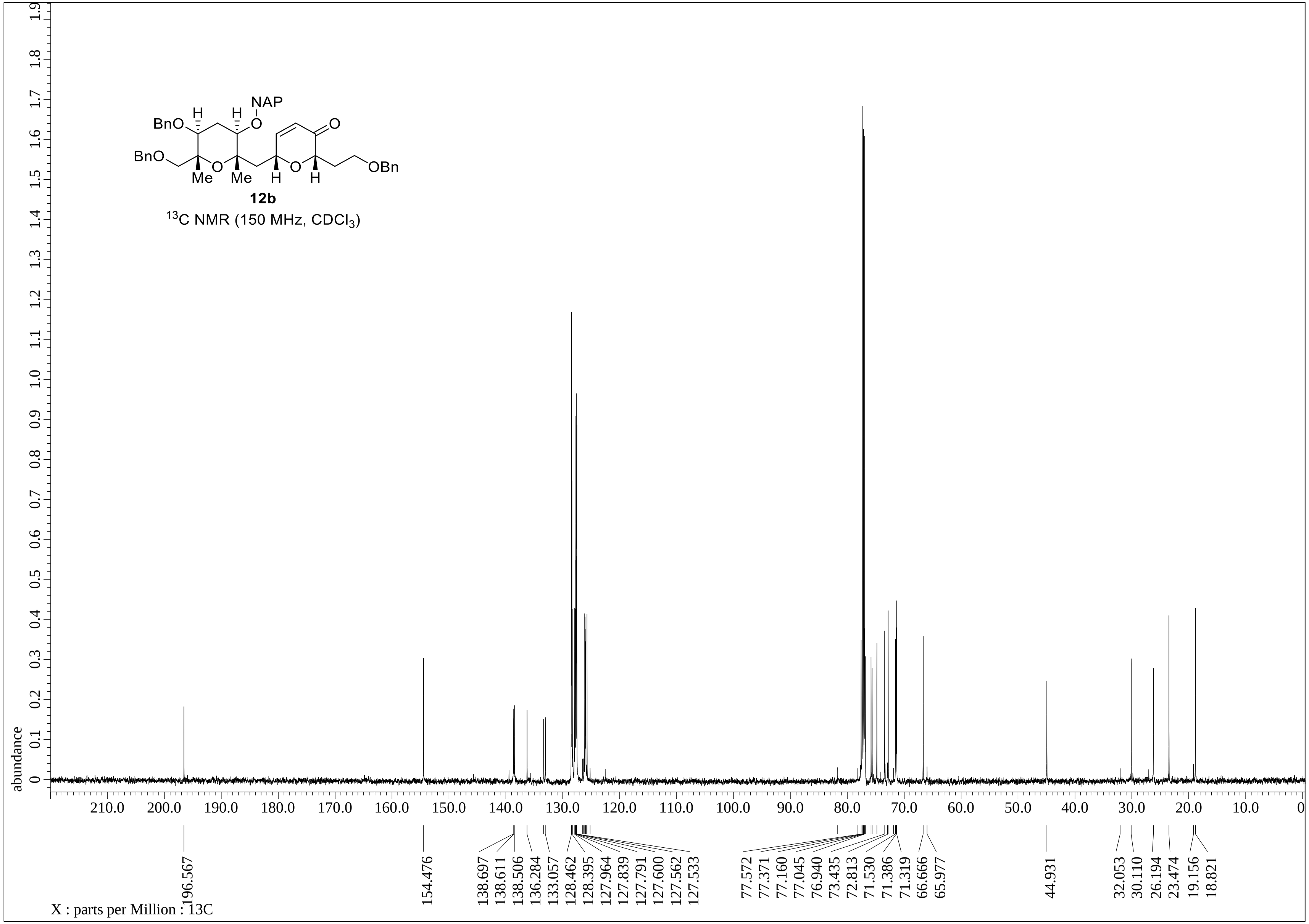
14

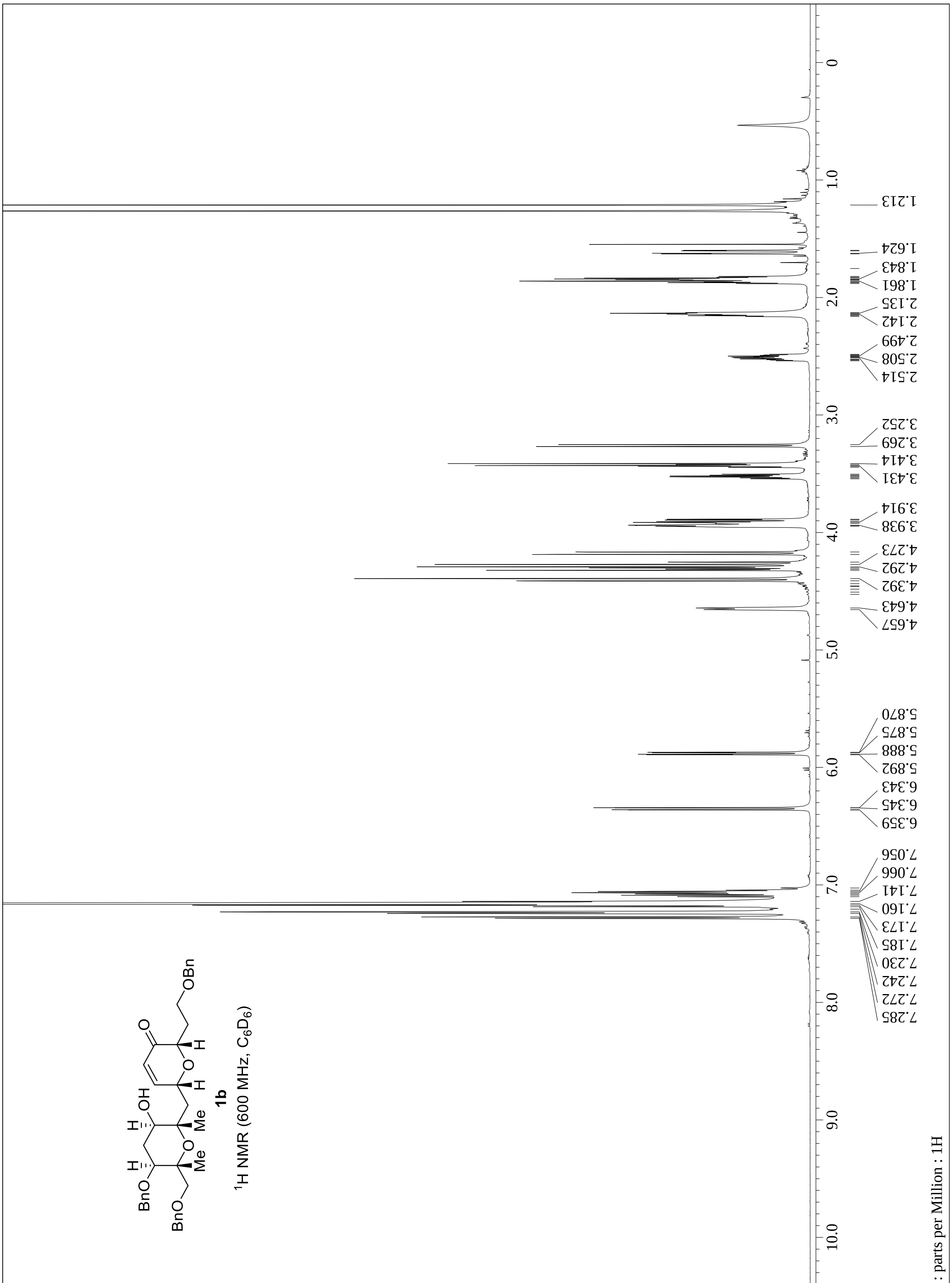
NOESY (600 MHz, CDCl$_3$)



12b

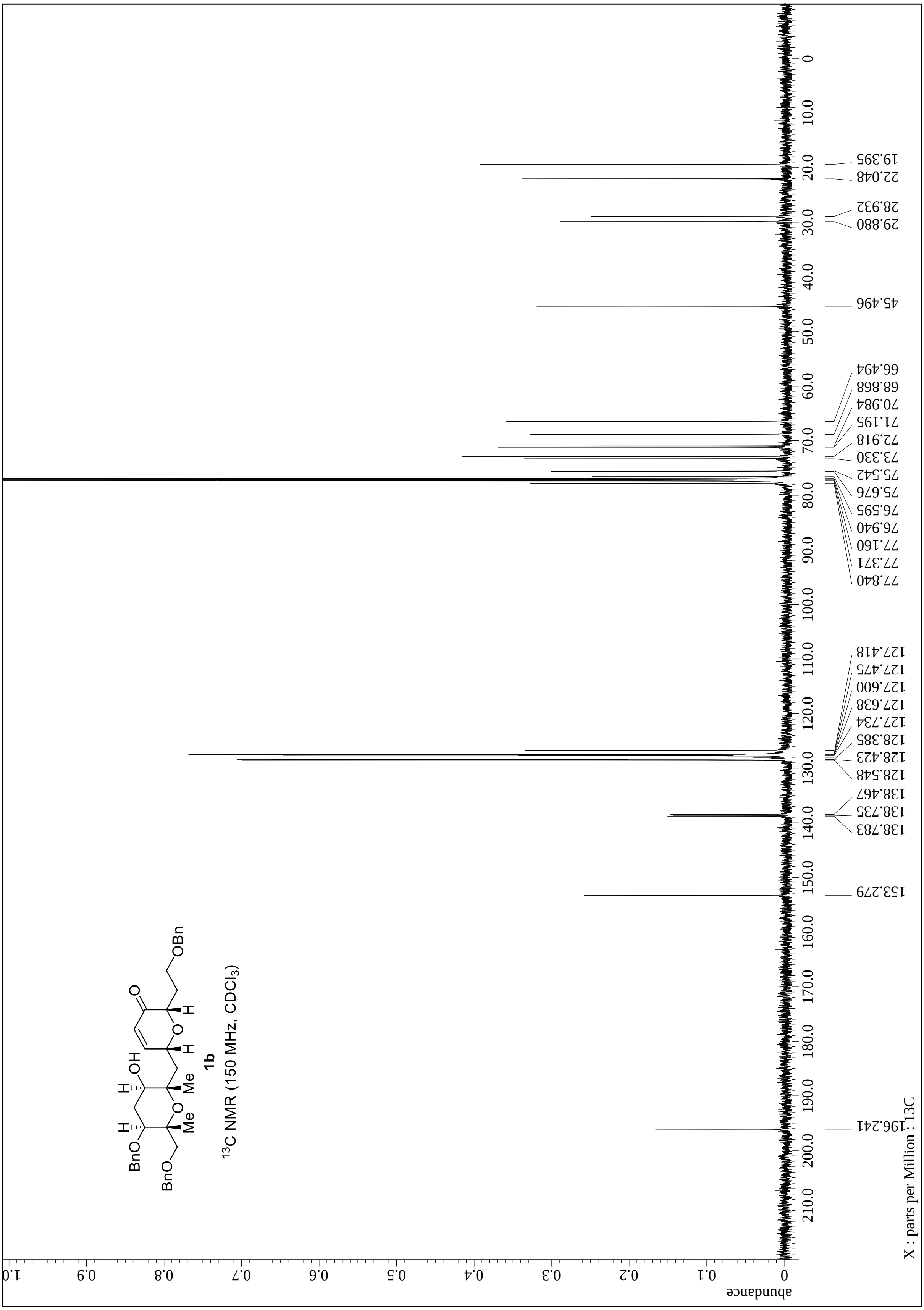
^{1}H NMR (600 MHz, C_6D_6)


12b
^{13}C NMR (150 MHz, CDCl$_3$)
BnO
BnO
H
H
NAP
O
O
O
O
OBn
Me
Me
H
H
abundance
0
0.1
0.2
0.3
0.4
0.5
0.6
0.7
0.8
0.9
1.0
1.1
1.2
1.3
1.4
1.5
1.6
1.7
1.8
1.9
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
196.567
154.476
138.697
138.611
138.506
136.284
133.057
128.462
128.395
127.964
127.839
127.791
127.600
127.562
127.533
77.572
77.371
77.160
77.045
76.940
73.435
72.813
71.530
71.386
71.319
66.666
65.977
44.931
32.053
30.110
26.194
23.474
19.156
18.821
X : parts per Million : 13C

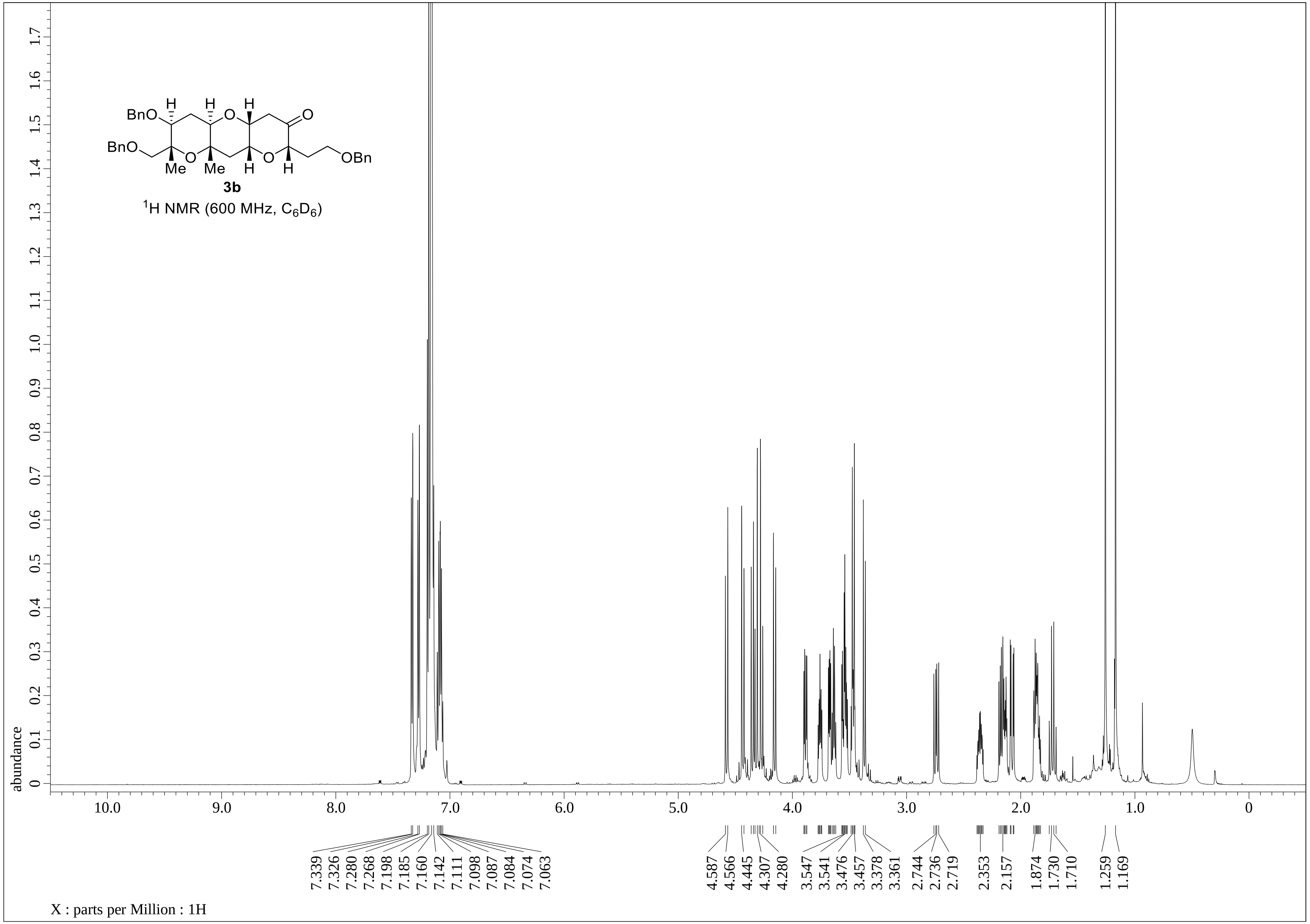


1b

^{1}H NMR (600 MHz, C_6D_6)

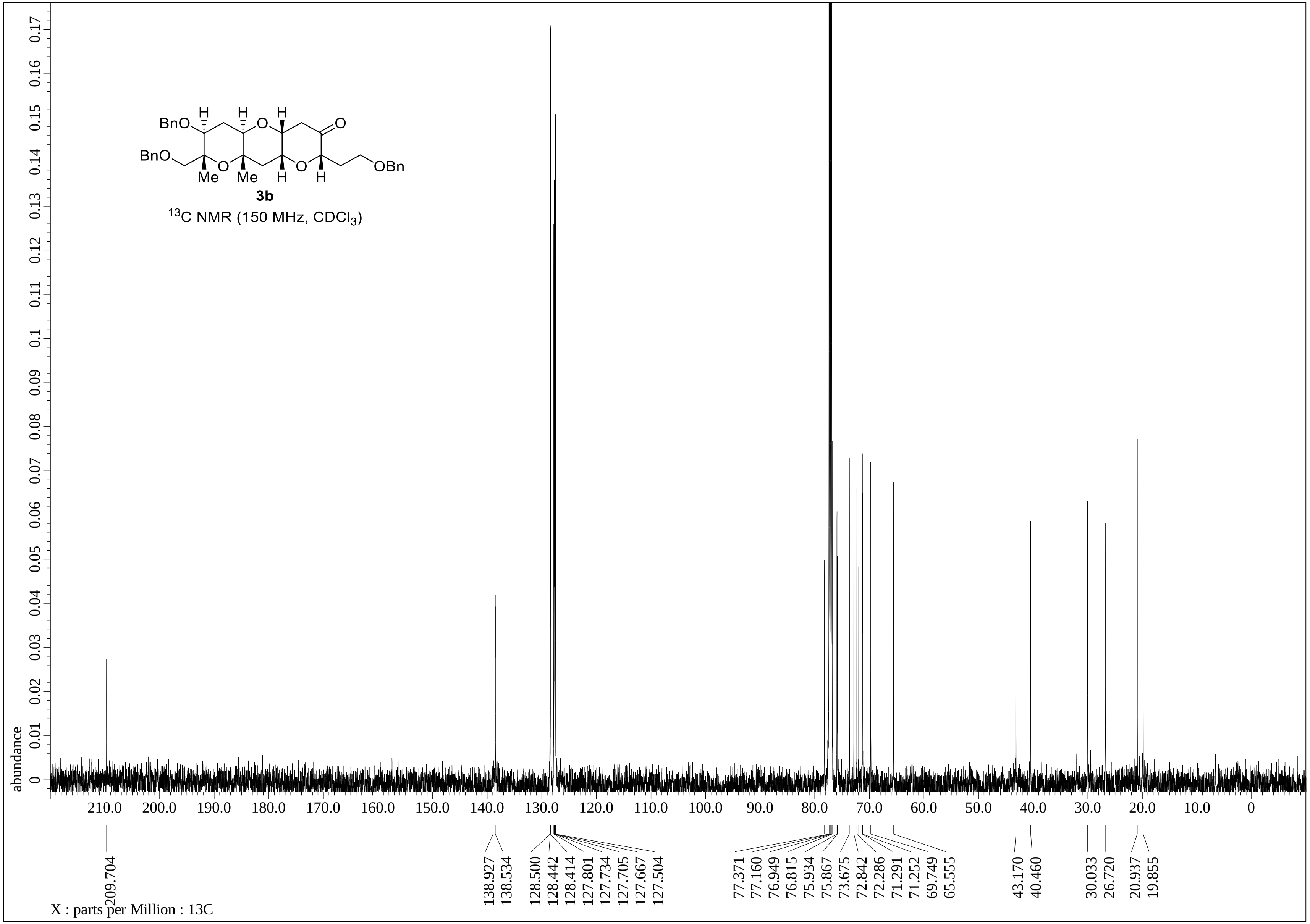


1b
^{13}C NMR (150 MHz, CDCl$_3$)
BnO
BnO
OH
OBn
Me
Me
O
H
196.241
153.279
138.783
138.735
138.467
128.548
128.423
128.385
127.734
127.638
127.600
127.475
127.418
77.840
77.371
77.160
76.940
76.595
75.676
75.542
73.330
72.918
71.195
70.984
68.868
66.494
45.496
29.880
28.932
22.048
19.395
X : parts per Million : 13C
210.0
200.0
190.0
180.0
170.0
160.0
150.0
140.0
130.0
120.0
110.0
100.0
90.0
80.0
70.0
60.0
50.0
40.0
30.0
20.0
10.0
0
abundance
1.0
0.9
0.8
0.7
0.6
0.5
0.4
0.3
0.2
0.1
0



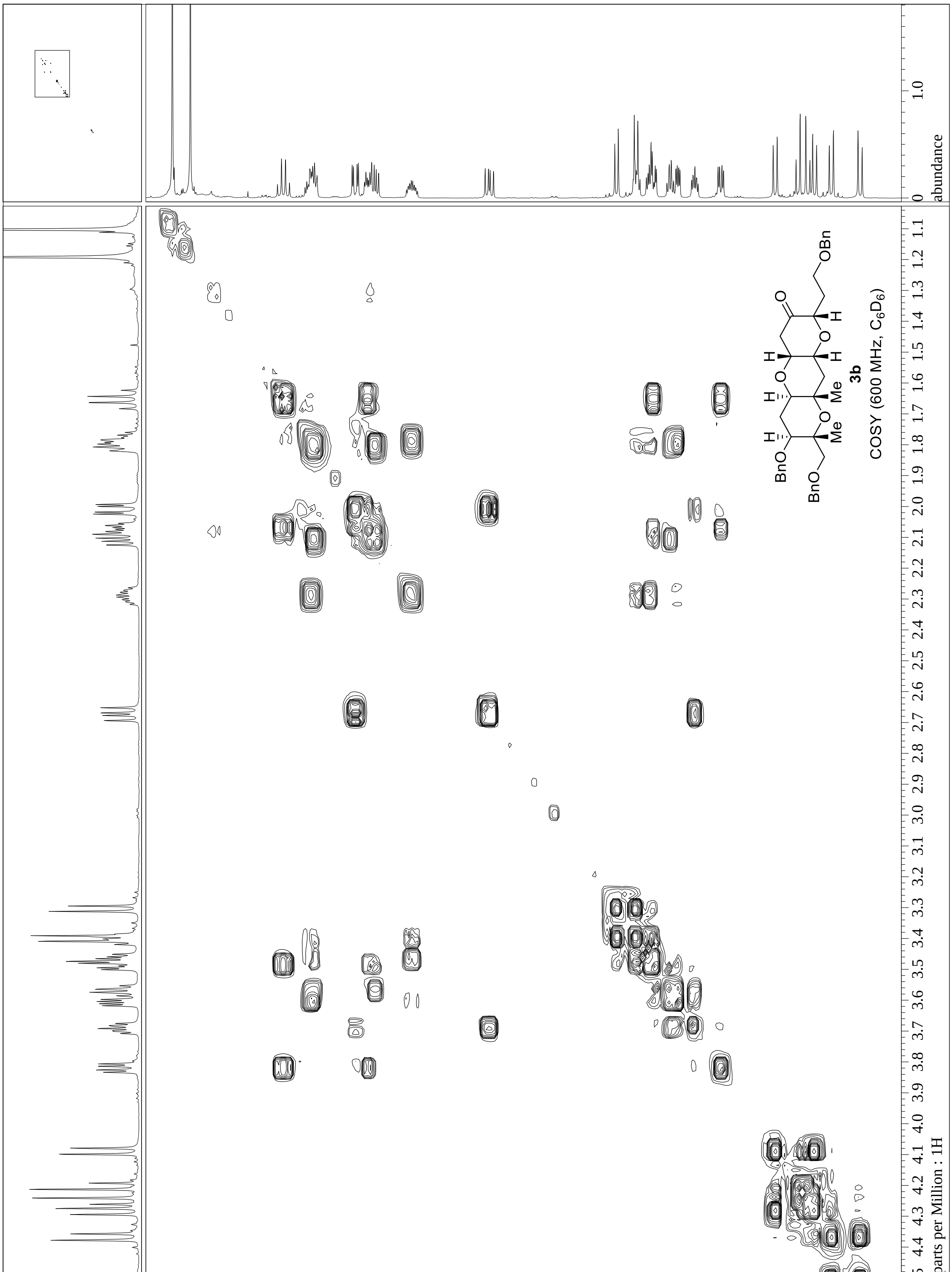
3b

^{1}H NMR (600 MHz, C_6D_6)



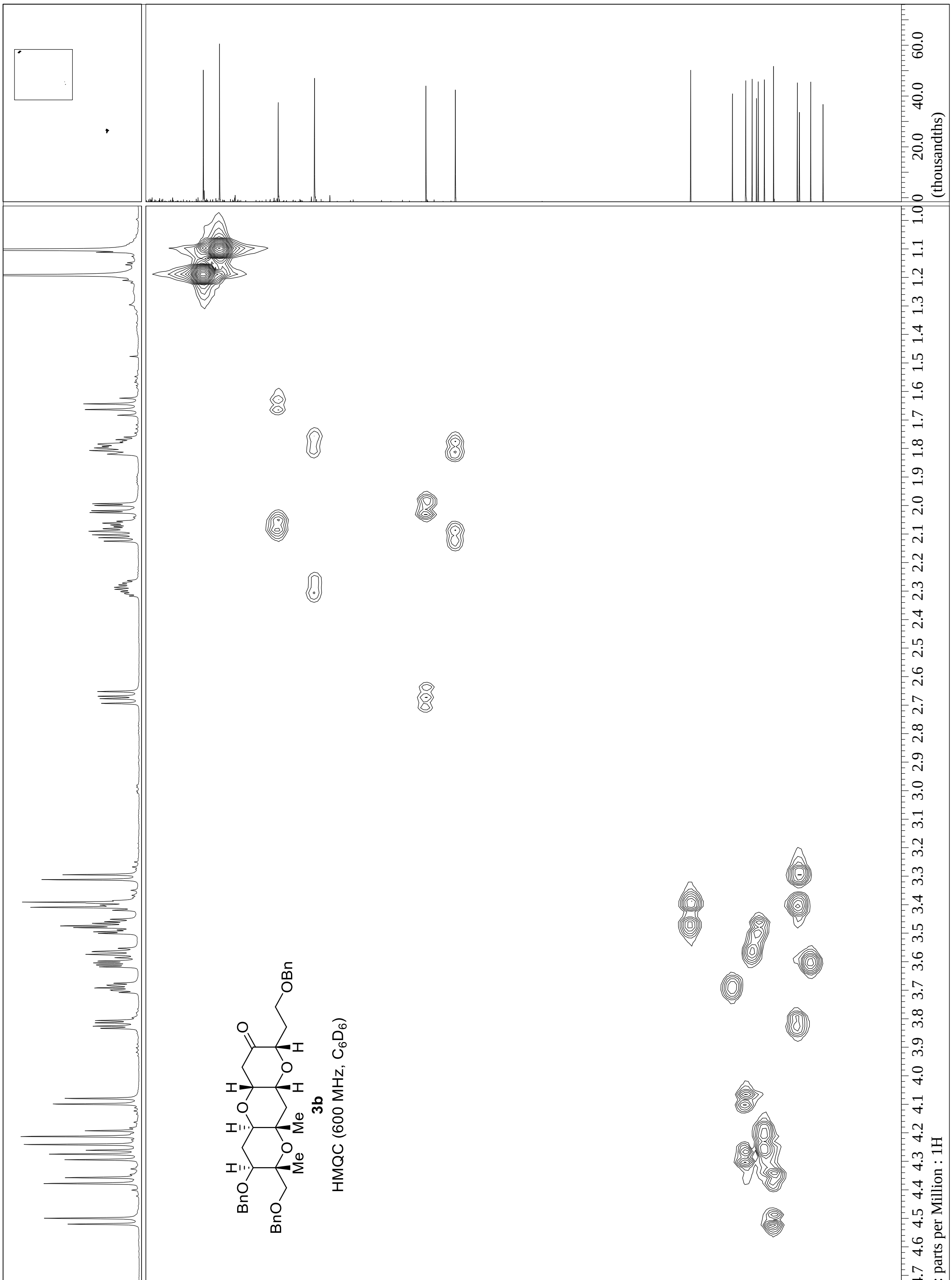
3b

^{13}C NMR (150 MHz, CDCl$_3$)



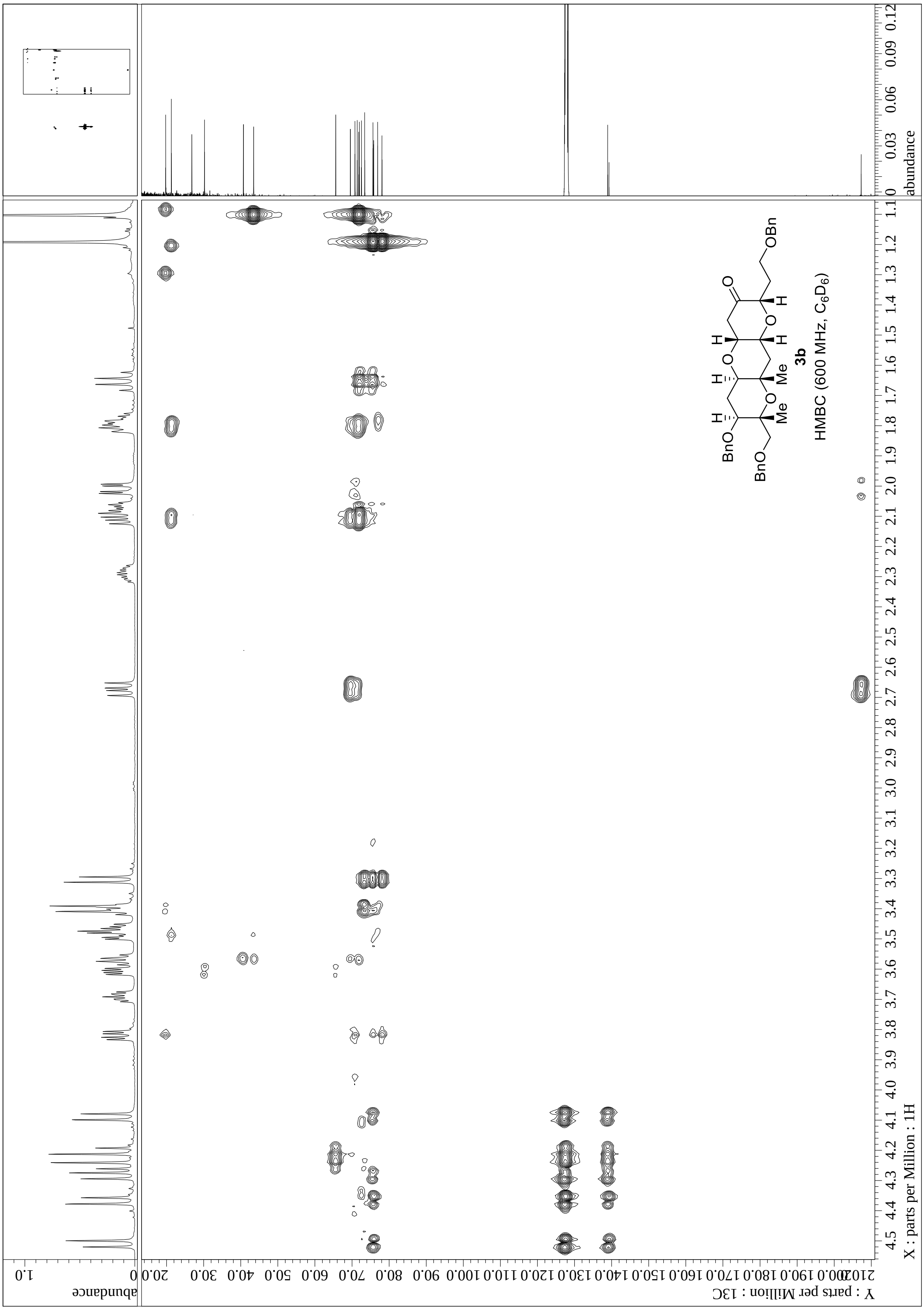
3b

COSY (600 MHz, C_6D_6)



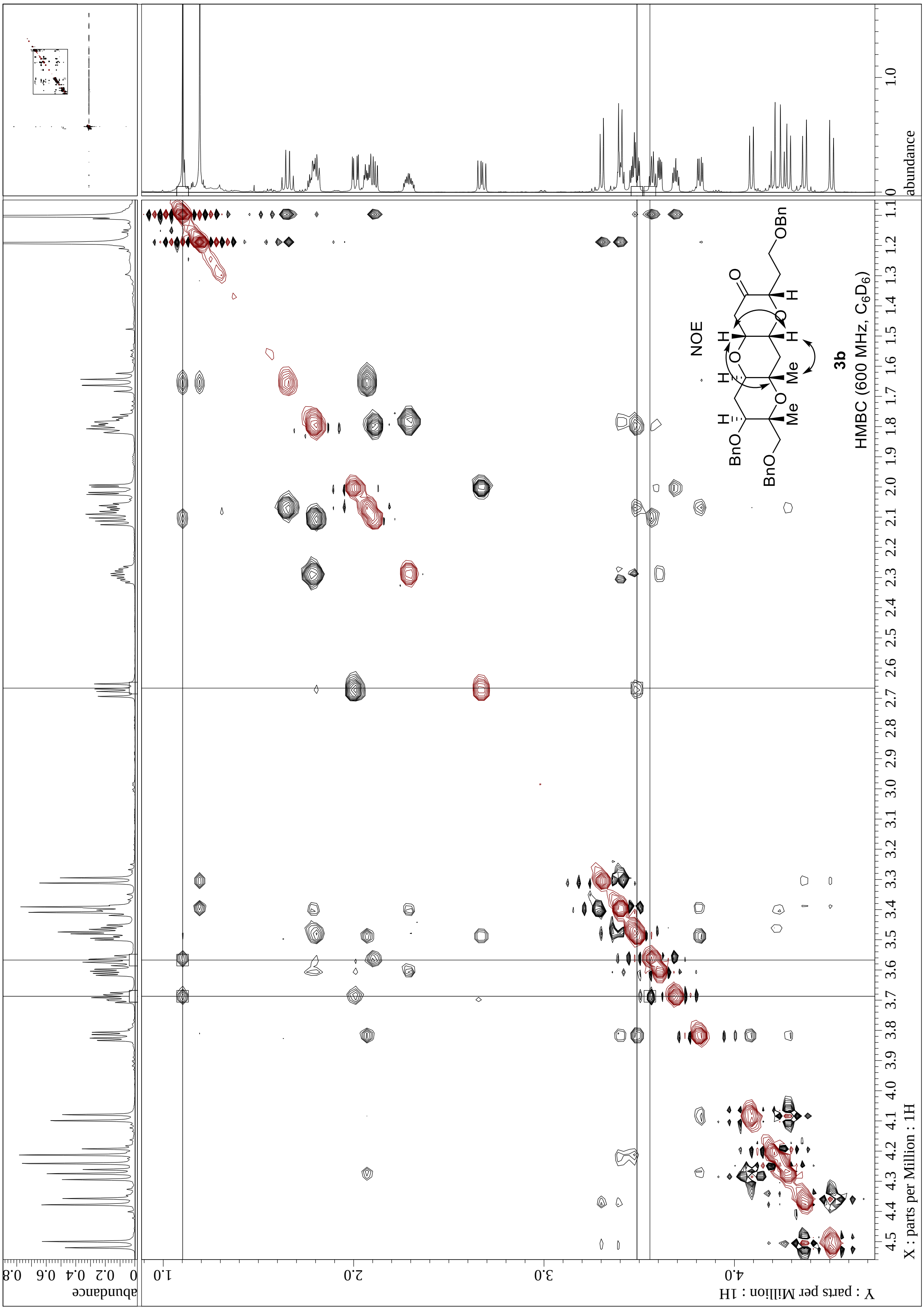
3b

HMQC (600 MHz, C_6D_6)



3b

HMBC (600 MHz, C_6D_6)



3b

HMBC (600 MHz, C_6D_6)