Supporting Information To:

Synthesis of Conformationally Locked Versions of Puromycin Analogues

Hisao Saneyoshi,[1] Benoît Y. Michel,[2] Yongseok Choi,[1] Peter Strazewski,[2]* Victor E. Marquez[1]*

[1]*Laboratory of Medicinal Chemistry, Center for Cancer Research, National Cancer Institute, National Institutes of Health, Frederick, MD, 21702, USA,* [2] *Université de Lyon, F–69622, Lyon, France; Université Claude Bernard Lyon 1, Villeurbanne; UMR 5246, CNRS, Laboratoire de Synthèse de Biomolécules.*

*To whom correspondence should be addressed. Laboratory of Medicinal Chemistry, Center for Cancer Research, National Cancer Institute at Frederick, National Institutes of Health, 376 Boyles Street, Frederick, MD 21702. Phone: 301-846-5954. Fax: 301-846-6033. E-mails: marquezv@mail.nih.gov and strazewski@univ-lyon1.fr (for the compounds described on pages 37-123)

Table of contents

General synthetic methods

All chemical reagents were commercially available. Melting points are uncorrected. Flash column chromatography was performed on silica gel 60 (230-240 mesh) and analytical TLC was developed on silica gel GF. Unless otherwise indicated, NMR spectra were determined in $CDCl_3$ (99.8%) with residual $CHCl_3$ as the reference peak (7.26) in ^{1}H-NMR and the central peak of the $CDCl_3$ signal (77.0 ppm) in the ^{13}C-NMR spectra. The spectra were recorded at 400 MHz, 300 MHz, or 500 MHz as indicated. The coupling constants are reported in Hertz and the peak shifts are reported in the δ (ppm) scale; abbreviations s (singlet), d (doublet), dd (doublet-of-doublets), ddd (doublet-of-doublet-of doublets), t (triplet), q (quartet), and m (multiplet). Positive-ion fast atom bombardment mass spectra (FABMS) were obtained at an accelerating voltage of 6 kV and a resolution of 2000; glycerol was used as the sample matrix, and ionization was effected by a beam of xenon atoms. The electrospray MS were obtained in cationic and anionic mode. Infrared spectroscopy was performed neat and specific optical rotations were measured in the indicated solvents. All reaction glassware was oven-dried and cooled to room temperature in an argon or dry nitrogen atmosphere prior to use.

Procedures for the synthesis of compounds in Schemes 2 and 3

1*S*,3*S*,4*R*,5*S*)-1-[6-(Dimethylamino)purin-9-yl]-4-(hydroxymethyl)bicyclo[3.1.0]-hexan-3-ol (12). Compound **11**[9] (651 mg, 1.41 mmol) was dissolved in a mixture consisting of an aqueous solution of 40% dimethylamine and EtOH (30 mL, 2:1, v/v) and heated in a sealed tube to 90 ˚C for 4 h. After cooling to room temperature and concentrated *in vacuo*, the residue was dissolved in MeOH (15 mL) under argon atmosphere and treated with 10% Pd-C (500 mg). The argon was then replaced with H_2 and stirred at room temperature for 15 h. The mixture was filtered through a Celite® pad and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with $CHCl_3$-MeOH (90/10 → 85/15, v/v) to give **12** (354 mg, 87%) as a white solid: mp 176-178˚C; $[\alpha]^{20}_D$ = –42.0° (c, 0.50, MeOH); ^{1}H-NMR (CD_3OD, 400 MHz) δ 1.34 (1H, ddd, *J* = 9.6, 5.3, 2.3 Hz, H-6'a), 1.60 (1H, pseudo t, *J* ≈ 5.2 Hz, H-5'), 1.78 (1H, ddd, *J* = 9.6, 4.8, 1.2 Hz, H-6'b), 2.15 (1H, pseudo t, *J* ≈ 3.6 Hz, H-4'), 2.18 (1H, d, *J* = 13.5 Hz, H-2'a), 2.50 (1H, ddd, *J* = 13.5, 7.0, 2.4 Hz, H-2'b), 3.45 (6H, br s, N(CH_3)$_2$), 3.78 (1H, dd, *J* = 11.5, 4.3 Hz, C*H*HOH), 3.96 (1H, dd, *J* = 11.3, 2.9 Hz, CH*H*OH), 4.33 (1H, d, *J* = 6.8 Hz, H-3'), 8.02 (1H, s, H-8), 8.14 (1H, s, H-2); ^{13}C-NMR (CD_3OD, 100 MHz) δ 18.1, 28.2, 39.0, 43.6, 44.7, 53.5, 66.1, 76.3, 121.1, 141.4, 151.7, 152.6, 156.1; FAB-MS m/z (relative intensity) 290 (MH^+, 100%). Anal. Calcd for $C_{14}H_{19}N_5O_2$: C, 58.12; H, 6.62; N, 24.21. Found: C, 58.09; H, 6.71; N, 24.06.

(1*S*,3*S*,4*R*,5*S*)-1-[6-(Dimethylamino)purin-9-yl]-4-[2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]bicyclo[3.1.0]hexan-3-ol (14). Compound **12** (244 mg, 0.843 mmol) was dissolved in pyridine (10 mL) and treated with imidazole (126 mg, 1.85 mmol) and TBDPS-Cl (476 mL, 1.85 mmol) at 0˚C. The mixture was allowed to reach room temperature and stirred for 2 h. The reaction was quenched with MeOH (1 mL). Volatiles were removed *in vacuo*, and the residue extracted with EtOAc and brine. The organic solution was dried ($MgSO_4$) and filtered. The solution was evaporated *in vacuo* and the residue was purified by column chromatography on a silica gel eluted with $CHCl_3$/MeOH (95/5, v/v) to give **14** (434 mg, 98%) as a white foam: $[\alpha]^{20}_D = -43.4°$ (c, 0.45, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.08 (9H, s, *t*-Bu), 1.31 (1H, ddd, *J* = 9.5, 5.5, 2.0 Hz, H-6'a), 1.72 (1H, pseudo t, *J* ≈ 5.2 Hz, H-5'), 1.80 (1H, ddd, *J* = 9.2, 4.9, 0.8 Hz, H-6'b), 2.27-2.33 (2H, m, H-2'a, H-4'), 2.48 (1H, ddd, *J* = 13.8, 6.7, 2.0 Hz, H-2'b), 3.49 (6H, br, $N(CH_3)_2$), 3.92 (1H, dd, *J* = 10.2, 7.0, Hz, C*H*HOSi), 3.99 (1H, *J* = 10.2, 8.1 Hz, CH*H*OSi), 4.41 (1H, d, *J* = 6.6 Hz , H-3'), 7.36-7.42 (5H, m, Ph-H), 7.43-7.72 (6H, m, Ph-H, H-8), 8.22 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 17.8, 19.3, 26.1, 26.9, 38.5, 41.2, 42.5, 52.8, 65.3, 74.0, 120.5, 127.7, 129.7, 135.5, 135.6, 138.6, 151.4, 152.2, 154.9; FAB-MS m/z (relative intensity) 528.3 (MH^+, 100%); HRMS (FAB) calc for ($C_{30}H_{38}N_5O_2Si^+$) 528.2795 (MH^+), found 528.2820.

(1*S*,3*R*,4*R*,5*S*)-1-[6-(Dimethylamino)purin-9-yl]-4-[2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]bicyclo[3.1.0]hexan-3-ol (16). Compound **14** (230 mg, 0.436 mmol) was dissolved in CH_2Cl_2 (4 mL) and treated with the Dess-Martin periodinane reagent (277 mg, 0.653 mmol) at 0˚C under argon. The mixture was allowed to reach room temperature and stirred for 4.5 h. After diluting with Et_2O (20 mL) the entire reaction mixture was poured into cold aqueous $NaHCO_3$ (10 mL) containing $Na_2S_2O_3$ (700 mg) and washed with brine. The organic solution was dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue was dissolved in THF (4 mL) and treated with 1M L-selectride® in THF (567 μL) at –78˚C under argon. After stirring for 30 min, the reaction was quenched with acetone (1 mL) and diluted with $CHCl_3$ (30 mL). The solution was extracted with aqueous NH_4Cl and then with brine, dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with $CHCl_3$/MeOH (90/10, v/v) to give **16** (211 mg, 92%) as a white foam: $[\alpha]^{20}_D = -21.2°$ (c, 0.20, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.04-1.08 (1H, m, H-6'a), 1.08 (9H, s, *t*-Bu), 1.66-1.73 (2H, m, H-6'b, H-5'), 2.06 (1H, m, H-4'), 2.26 (1H, dd, *J* = 14.3, 4.6 Hz, H-2'a), 2.34 (1H, dd, *J* = 14.4, 4.4 Hz, H-2'b), 3.54 (6H, br, N(C*H*$_3$)$_2$), 4.05 (1H, dd, *J* = 10.2, 7.4, Hz, C*H*HOSi), 4.23 (1H, br s, H-3'), 4.29 (1H, dd, *J* = 10.4, 7.4 Hz, CH*H*OSi), 7.35-7.44 (5 H, m, Ph-H), 7.70-7.75 (6H, m, Ph-H, H-8), 8.27 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 19.2, 24.9, 26.8, 27.5, 38.4, 43.0, 44.4, 51.5, 63.9, 77.8, 120.4, 127.7, 129.6, 133.6, 133.7, 135.5, 135.6, 138.3, 150.5, 151.8, 154.8; FAB-MS m/z (relative intensity) 528.2 (MH^+, 100%); Anal. Calcd for $C_{30}H_{37}N_5O_2Si$: C, 68.28; H, 7.07; N, 13.27. Found: C, 68.11, H, 7.26, N, 12.97.

(9-{(1*S*,3*S*,4*S*,5*S*)-3-Azido-4-[(2,2-dimethyl-1,1-diphenyl-1-silapropoxy)methyl]-bicyclo[3.1.0]hexyl}purin-6-yl)dimethylamine (18). Compound **16** (200 mg, 0.379 mmol) was co-evaporated 3 times with pyridine and dissolved in anhydrous pyridine (4 mL). After cooling to 0˚C, the solution was treated with MsCl (59 μL, 0.759 mmol), allowed to reach room temperature, and stirred for 4 h. The reaction was quenched with H_2O (1 mL) and evaporated *in vacuo*. The residue was diluted with $CHCl_3$ (30 mL) and extracted with brine and aqueous $NaHCO_3$. The extract was dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue was dissolved in DMF (15 mL) and treated with NaN_3 (493 mg, 7.58 mmol). The reaction mixture was stirred at 120 ˚C for 2 h. After cooling to room temperature it was diluted with Et_2O (100 mL) and the resulting organic solution and washed with H_2O and brine. The extract was dried ($MgSO_4$) and evaporated *in vacuo*. The residue was purified by chromatography on silica gel eluted with hexane/EtOAc (70/30, v/v) to give **18** (148 mg, 71%) as a white foam: $[\alpha]^{20}_D = -34.2°$ (c, 1.45, $CHCl_3$); IR (neat) 2099 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.09 (9H, s, *t*-Bu), 1.32 (1H, ddd, *J* = 9.3, 6.1, 2.2 Hz, H-6'a), 1.51 (1H, pseudo t, *J* ≈ 5.4 Hz, H-5'), 1.66 (1H, dd, *J* = 9.5, 4.8 Hz, H-6'b), 2.19 (1H, d, *J* = 14.0 Hz, H-2'a), 2.39 (1H, dd, *J* = 9.2, 6.2 Hz, H-4'), 2.57 (1H, ddd, J = 13.9, 7.9, 1.9 Hz, H-2'b), 3.49 (6H, br, N(CH_3)$_2$), 3.96 (1H, dd, *J* = 10.4, 6.3 Hz, C*H*HOSi), 4.10 (1H, pseudo t, *J* ≈ 9.9, Hz, CH*H*OSi), 4.25 (1H, d, *J* = 7.8 Hz, H-3'), 7.38-7.44 (6H, m, Ph-H), 7.62 (1H, s, H-8), 7.70-7.73 (4H, m, Ph-H), 8.17 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 16.0, 19.3,

25.8, 26.9, 37.0, 38.5, 42.4, 50.2, 62.4, 64.6, 120.5, 127.8, 129.8, 133.4, 135.5, 135.6, 138.4, 151.4, 152.3, 154.8; FAB-MS m/z (relative intensity) 553.4 (MH^+, 47.8%); HRMS (FAB) calc for ($C_{30}H_{37}N_8OSi^+$) 553.2860 (MH^+), found: 553.2878.

{(1*S*,2*S*,3*S*,5*S*)-3-Azido-5-[6-(dimethylamino)purin-9-yl]bicyclo[3.1.0]hex-2-yl}methan-1-ol (6). Compound **18** (126 mg, 0.228 mmol) was dissolved in THF (2 mL) and treated with 1M TBAF-THF (251 μL). After stirring at room temperature for 30 min, the solution was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with hexane/EtOAc (1/1, v/v) to give **6** (64 mg, 89%) as white crystals: mp 109˚C-111˚C; $[\alpha]^{20}_D$ = +15.9° (c, 0.50,$CHCl_3$); IR (neat) 2102, 1595 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.32 (1H, ddd, *J* = 8.2, 5.8, 2.3 Hz, H-6'a), 1.51 (1H, pseudo t, *J* ≈ 5.3 Hz, H-1'), 1.66 (1H, dd, *J* = 9.5, 4.8 Hz, H-6'b), 2.19 (1H, d, *J* = 14.0 Hz, H-4a'), 2.30 (1H, d, *J* = 2.7 Hz, H-2'), 2.67 (1H, ddd, *J* = 14.0, 8.0, 1.9 Hz, H-4'b), 3.49 (6H, v br s, $N(CH_3)_2$), 3.96 (1H, br d, C*H*HOH), 4.10 (1H, d, *J* = 11.8 Hz, CH*H*OH), 4.25 (1H, d, *J* = 7.7 Hz, H-3'), 6.99 (1H, br s, 5'-OH), 7.80 (1H, s, H-8), 8.30 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 16.2, 27.3, 38.6, 40.0, 43.1, 49.5, 64.5, 65.7, 120.1, 139.0, 150.1, 151.7, 154.9; FAB-MS m/z (relative intensity) 315.2 (MH^+, 100%). HRMS (FAB) calc for ($C_{14}H_{19}N_8O^+$) 315.1682 (MH^+), found 315.1697.

(1*S*,3*S*,4*R*,5*S*)-1-(6-Aminopurin-9-yl)-4-[(2,2-dimethyl-1,1-diphenyl-1-silapro-propoxy)methyl]bicyclo[3.1.0]hexan-3-ol (15). The known compound **13**[9] (415 mg, 1.59 mmol) was co-evaporated 3 times with pyridine and dissolved in anhydrous pyridine (5 mL). The solution was treated with TBDPS-Cl (613 μL, 2.39 mmol) at 0 ˚C and further stirred at room temperature for 1 h and treated again with TBDPS-Cl (204 μL, 0.794 mmol). After 10 min, the reaction was quenched with MeOH (1 mL) and evaporated *in vacuo*. The residue was diluted with $CHCl_3$ and washed with brine and aqueous $NaHCO_3$. The organic extract was dried ($MgSO_4$) and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with $CHCl_3$/MeOH (95/5, v/v) to give **15** (631 mg, 79%) as white crystals: mp 190˚C-192˚C; $[\alpha]^{20}_D$ = –41.9° (c, 0.35, $CHCl_3$); ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.07 (9H, s, *t*-Bu), 1.33 (1H, ddd, *J* = 9.5, 5.5, 1.9 Hz, H-6'a), 1.72 (1H, pseudo t, *J* ≈ 5.2 Hz H-5'), 1.80-1.83 (1H, m, H-6'b), 2.27-2.33 (2H, m, H-2'a, H-4'), 2.49 (1H, ddd, *J* = 13.7, 6.7, 1.8 Hz, H-2'b), 3.90-4.04 (2H, m, CH_2OSi), 4.42 (1H, d, *J* = 6.6 Hz, H-3'), 6.03 (2H, br s, NH_2), 7.35-7.71 (11H, m, Ph-H, H-8), 8.20 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 17.6, 19.3, 26.2, 26.9, 41.2, 42.7, 52.8, 65.2, 73.7, 119.7, 127.7, 129.8, 133.4, 135.5, 135.6, 135.7, 140.9, 150.8, 152.5, 155.1; FAB-MS m/z (relative intensity) 500.2 (MH^+, 100%). Anal. Calcd for $C_{28}H_{33}N_5O_2Si$: C, 67.30; H, 6.66; N, 14.02. Found: C, 67.11; H, 6.61; N, 14.06.

(1*S*,3*R*,4*R*,5*S*)-1-(6-Aminopurin-9-yl)-4-[(2,2-dimethyl-1,1-diphenyl-1-silapro-popoxy)methyl]-bicyclo[3.1.0]hexan-3-ol (17). Compound **15** (250 mg, 0.500 mmol) was dissolved in CH_2Cl_2 (2 mL) and treated with the Dess-Martin periodinane reagent (318 mg,

0.745 mmol) at 0˚C under argon. The reaction was allowed to reach room temperature and stirred for 3.5 h. After diluting with Et_2O (30 mL) the entire reaction mixture was poured into cold aqueous $NaHCO_3$ (10 mL) containing $Na_2S_2O_3$ (700 mg) and washed with brine. The organic solution was dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue was dissolved in THF (5 mL) and treated with 1M L-selectride® in THF (750 μL) at –78˚C under argon. After stirring for 60 min, the reaction was quenched with acetone (1 mL) and diluted with $CHCl_3$ (30 mL). The solution was extracted with aqueous NH_4Cl and then with brine, dried ($MgSO_4$), filtered, and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with $CHCl_3$/MeOH (90/10, v/v) to give **17** (202 mg, 81%) as a yellowish foam: $[\alpha]^{20}_D = -10.1°$ (c, 0.79, $CHCl_3$): ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.07 (10H, s, H-6'a, *t*-Bu), 1.60 (1H, br dd, *J* = 9.2, 5.8 Hz, H-5'), 1.72 (1H, ddd, *J* = 9.4, 4.5, 1.8 Hz, H-6'b), 2.13-2.19 (1H, m, H-4'), 2.26 (1H, dd, *J* = 13.9, 3.1 Hz, H-2'a), 2.38 (1H, dd, *J* = 13.9, 5.2 Hz, H-2'b), 4.03 (1H, dd, *J* = 10.4, 7.3 Hz, C*H*HOSi), 4.21 (1H, dd, *J* = 9.3, 4.8 Hz, H-3'), 4.29 (1H, dd, *J* = 10.4, 7.2 Hz, CH*H*OSi), 6.32 (2H, br s, NH_2), 7.35-7.71 (11H, m, Ph-H, H-8), 8.25 (1H, s, H-2): ^{13}C-NMR ($CDCl_3$, 100 MHz) δ 19.2, 23.0, 26.8, 27.0, 42.5, 43.5, 49.9, 63.9, 76.6, 119.7, 127.6, 129.7, 133.4, 135.5, 135.6, 140.6, 150.1, 152.3, 155.5; FAB-MS m/z (relative intensity) 500.4 (MH^+, 100%); HRMS (FAB) calc for ($C_{28}H_{34}N_5O_2Si^+$) 500.2482 (MH^+), found 500.2485.

9-{(1*S*,3*S*,4*S*,5*S*)-3-Azido-4-[(2,2-dimethyl-1,1-diphenyl-1-silapropopoxy)methyl]-bicyclo-[3.1.0]hexyl}purin-6-ylamine (19). Compound **17** (170 mg, 0.340 mmol) was co-evaporated 3 times with pyridine and dissolved in anhydrous pyridine (4 mL). After cooling to 0˚C, the solution was treated with MsCl (53 μL, 0.682 mmol) allowed to reach room temperature, and stirred for 1 h. The reaction was quenched with H_2O (1 mL) and evaporated *in vacuo*. The residue was diluted with EtOAc, washed with brine and H_2O, dried ($MgSO_4$), and evaporated *in vacuo*. The residue was then dissolved in DMF (10 mL) and reacted with NaN_3 (442 mg, 6.80 mmol) at 120 ˚C for 2 h. After reaching room temperature the reaction mixture was diluted with EtOAc and washed with H_2O and brine. The organic extract was dried ($MgSO_4$) and evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with hexane/EtOAc (1/1 → 1/2, v/v) to give **19** (125 mg, 70%) as white crystals: mp 174˚C-175˚C; $[\alpha]^{20}_D = -49.2°$ (c, 0.10, $CHCl_3$); IR (neat) 2103 cm^{-1}; ^{1}H-NMR ($CDCl_3$, 400 MHz) δ 1.10 (9H, s), 1.35 (1H, ddd, *J* = 9.4, 6.1, 1.9 Hz, H-6'a), 1.54 (1H, pseudo t, *J* ≈ 5.5 Hz, H-5'), 1.70 (1H, dd, *J* = 9.6, 4.8 Hz, H-6'b), 2.20 (1H, d, *J* = 13.9 Hz, H-2'a), 2.40 (1H, dd, *J* = 8.7, 6.2 Hz, H-4'), 2.56 (1H, ddd, *J* = 13.9, 7.8, 1.8 Hz, H-2'b), 3.97 (1H, dd, *J* = 10.4, 6.2 Hz, C*H*HOSi), 4.08 (1H, dd, *J* = 10.3, 9.2 Hz, CH*H*OSi), 4.25 (1H, d, *J* = 7.7 Hz, H-3'), 6.01 (2H, br, NH_2), 7.38-7.73 (11H, m, Ph-H, H-8), 8.17 (1H, s, H-2); ^{13}C- NMR ($CDCl_3$, 100 MHz) δ 16.1, 19.3, 25.9, 26.9, 37.3, 42.5, 50.1, 62.4, 64.7, 119.9, 127.8, 129.8, 133.3, 135.5, 135.6, 140.7, 150.8, 152.8, 155.4; FAB-MS m/z (relative intensity) 525.2 (100%). Anal. Calcd for $C_{28}H_{32}N_8OSi \cdot 0.7H_2O$: C, 62.59; H, 6.27; N, 20.85. Found: C, 62.62; H, 6.26; N, 20.81.

[(1*S*,3*S*,4*S*,5*S*)-5-(6-Aminopurin-9-yl)-3-azidobicyclo[3.1.0]hex-2-yl]methan-1-ol (7). A mixture of compound **19** (100 mg, 0.19 mmol) and NH_4F (35 mg, 0.945 mmol) was dissolved in MeOH (4 mL). After stirring at 60 ˚C for 24 h, the solution was evaporated *in vacuo*. The residue was purified by column chromatography on silica gel eluted with EtOAc/MeOH (90:10, v/v) to give **7** (50 mg, 93%) as white crystals. An analytical sample was recrystalized from EtOAc/MeOH: mp 217-218 ˚C (decomp.); $[\alpha]^{20}_D = -13.6°$ (c, 0.10, $CHCl_3$); IR (neat) 2093 $cm^{-}1$; ^{1}H-NMR (CD_3OD, 400 MHz) δ 1.41 (1H, ddd, *J* = 9.6, 6.0, 2.2 Hz, H-6'a), 1.50 (1H, pseudo t, *J* ≈ 5.5 Hz, H-1'), 1.87 (1H, ddd, *J* = 9.6, 4.8, 0.8 Hz, H-6'b), 2.28 (1H, t, *J* = 4.2 Hz, H-2'), 2.34 (1H, d, *J* = 13.8 Hz, H-4'a), 2.61 (1H, ddd, *J* = 13.8, 7.8, 2.2 Hz, H-4'b), 3.84 (1H, dd, *J* = 11.5, 4.4 Hz, C*H*HOH), 3.98 (1H, dd, *J* = 11.5, 4.2 Hz, CH*H*OH), 4.29 (1H, d, *J* = 7.7 Hz, H-3'), 8.16 (1H, s, H-8), 8.19 (1H, s, H-2); ^{13}C-NMR (CD_3OD, 100 MHz) δ 17.2, 28.0, 40.1, 44.5, 51.0, 65.5, 65.9, 120.3, 143.4, 151.2, 153.5, 157.4; FAB-MS m/z (relative intensity) 287.2 (MH^+, 100%); HRMS (FAB) calc for ($C_{12}H_{15}N_8O^+$) 287.1369 (MH^+), found 287.1380.

***N,N*-di-*n*-butylformamide dimethylacetal.** Di-*n*-butyl formamide (50 mL) and fresh dimethyl sulfate (26 mL) were mixed under argon and heated to reflux (100° C) during 4 hours, then cooled to ambient temperature and stirred overnight. The mixture was worked up with ice-cold absolute MeOH (150 mL) into which sodium (8 g) had been dissolved before. After the temperature returned

to ambient, the solvent was evaporated under reduced pressure, diethyl ether was added under vigorous stirring and the precipitate was filtered off and rinsed with more ether. The filtrate was evaporated under reduced pressure and the oily residue was distilled *in vacuo* (bp 110-120 °C under oil pump vacuum: early fractions contain *N,N*-di-*n*-butylformamide dimethyl acetal, late fractions contain di-*n*-butyl formamide) to give a clear colorless or pale yellow oil that can be safely stored under an inert atmosphere in the cold; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.89 (6H, t, J = 7.2 Hz, $N(CH_2CH_2CH_2CH_3)_2$), 1.30 (4H, q, J = 7.2 Hz, $N(CH_2CH_2CH_2CH_3)_2$), 1.40 (4H, q, J = 7.5 Hz, $N(CH_2CH_2CH_2CH_3)_2$), 2.59 (4H, t, J = 7.2 Hz, $N(CH_2CH_2CH_2CH_3)_2$), 3.30 (6H, s, $(OCH_3)_2$), 4.51 (1H, s, $NCH(OCH_3)_2$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.9, 20.4, 30.9, 47.0, 53.6, 112.6.

(1*R*,2*S*,4*S*,5*S*)-4-{6-[1-aza-2-(dibutylamino)vinyl]purin-9-yl}-2-azidobicyclo[3.1.0]-hexyl)methan-1-ol (20). *N*,*N*-di-*n*-butylformamide dimethylacetal (95 mg, 0.472 mmol) was added dropwise to a stirred solution of the azide derivative **3**[8] (54 mg, 0.189 mmol) in MeOH (1.2 mL) at room temperature. During 1 h, the reaction mixture was stirred and heated for a few seconds with the heat gun every 15 min. The volatiles were removed *in vacuo* and the residue was purified by silica gel column chromatography (cyclohexanes/EtOAc, 1/1 → 1/2 → 1/3 → 1/4 → 1/5, v/v) to give the protected amidine, which was co-evaporated from toluene to give **20** (80 mg, 99%) as a white solid: mp 113-117 ºC; ^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.76–0.84 (1H, m, H-6'a), 0.84–0.92 (1H, m, H-6'b), 0.90 (6H, t, J = 6.3 Hz, $N(CH_2CH_2CH_2CH_3)_2$), 1.25–1.41 (4H, m, $N(CH_2CH_2CH_2CH_3)_2$), 1.54–1.70 (4H, m, $N(CH_2CH_2CH_2CH_3)_2$), 1.65–1.70 (1H, m, H-5'), 1.86–1.96 (1H, m, H-3'a), 2.10 (1H, dd, J = 14.7, 8.4 Hz, H-3'b), 3.35 (2H, t, J = 7.2

Hz, N(C*H*$_2$CH$_2$CH$_2$CH$_3$)$_2$), 3.42 (1H, d, *J* = 11.7 Hz, C*H*HOH), 3.66 (2 H, t, *J* = 5.6 Hz, N(C*H*$_2$CH$_2$CH$_2$CH$_3$)$_2$), 4.34 (1H, d, *J* = 11.7 Hz, CH*H*OH), 4.82 (1H, t, *J* = 8.9 Hz, H-2'), 4.96 (1H, d, *J* = 6.9 Hz, H-4'), 8.24 (s, 1H, H-8), 8.44 (s, 1H, H-2), 8.91 (s, 1 H, N=C*H*NBu$_2$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 10.7, 13.5, 13.8, 19.6, 20.1, 26.2, 29.1, 30.8 , 36.2, 37.0, 45.1, 51.8, 56.4, 60.3, 63.3, 126.3, 141.1, 150.4, 152.0, 158.0, 160.1; HRMS (ESI$^+$) calcd for ($C_{21}H_{32}N_9O^+$) 426.2730 (MH^+), found 426.2727.

((1*S*,2*S*,3*S*,5*S*)-5-{6-[1-Aza-2-(dibutylamino)vinyl]purin-9-yl}-3-azidobicyclo[3.1.0]-hex-2-yl)methan-1-ol (21). To a stirred solution of the azidopurine **7** (54 mg, 0.189 mmol) in MeOH (1.2 mL) was added dropwise *N*,*N*-di-*n*-butylformamide dimethylacetal (95 mg, 0.472 mmol) and the reaction mixture was stirred at room temperature for 1h and every 15 min, the solution was heated for a few seconds with the heat gun. The volatiles were removed *in vacuo* and the residue was purified by silica gel column chromatography (cyhexane/EtOAc 1/1 → 1/2 → 1/3 → 1/4 → 1/5, v/v) to give the compound **22** (79 mg, 98 %) as a off-white oil: ^{1}H-NMR($CDCl_3$, 300 MHz) δ 0.88–0.94 (6 H, m, N(CH$_2$CH$_2$CH$_2$C<u>H</u>$_3$)$_2$) 1.26–1.39 (5H, m, H-6'a, N(CH$_2$CH$_2$C*H*$_2$CH$_3$)$_2$), 1.49 (1H, t, *J* = 5.3 Hz, H-6'b), 1.55–1.68 (4H, m, N(CH$_2$C*H*$_2$CH$_2$CH$_3$)$_2$), 1.78 (1H, dd, *J* = 9.5, 4.7 Hz, H-1'), 2.22 (1H, d, *J* = 13.5 Hz, H-4'a), 2.31 (1H, br. s, H-2'), 2.70 (1H, dd, *J* = 12.6, 8.1 Hz, H-4'b), 3.37 (2H, t, *J* = 7.2 Hz, N(C*H*$_2$CH$_2$CH$_2$CH$_3$)$_2$), 3.68 (2H t, *J* = 7.5 Hz, N(C*H*$_2$CH$_2$CH$_2$CH$_3$)$_2$), 3.83 (1H, br. s, C*H*HOH), 4.09 (1H, d, *J* = 12.0 Hz, CH*H*OH), 4.33 (1H, d, *J* = 7.5 Hz, H-3'), 6.68 (1H, br. s, OH), 7.91 (1H, s, H-8), 8.46 (1H, s, H-2), 8.96 (1H, s, N=C*H*NBu$_2$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.6, 13.8, 16.2, 19.6, 20.1, 27.2,

29.1, 30.8, 40.1, 43.1, 45.2, 49.4, 51.9, 64.5, 65.7, 126.0, 142.3, 151.2, 152.0, 158.3, 160.3; HRMS (ESI^+) calcd for ($C_{21}H_{32}N_9O^+$) 426.2730 (MH^+), found 426.2731.

*^{1}H-NMR, ^{13}C-NMR, and HRMS data for compounds **22-25***

(2*S*)-*N*-{(1*R*,2*S*,4*S*,5*S*)-4-[6-(Dimethylamino)purin-9-yl)-1-(hydroxymethyl)bicyclo-[3.1.0]hex-2-yl}-2-[(fluoren-9-ylmethoxy)carbonylamino]-3-(4-methoxyphenyl)-propanamide (22).

^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.51–0.60 (2H, m, H-6'a,b), 1.56–1.66 (1H, m, H-5'), 1.62 (1H, dd, *J* = 8.1, 3.6 Hz, H-3'a), 1.99–2.08 (1H, m, H-3'b), 2.90–3.07 (2H, m, *p*-MeOPhC*H*$_2$), 3.18 (1H, d, *J* = 12.2 Hz, C*H*HOH), 3.50 (1H, br s, NMe_2), 3.75 (3H, s, OCH_3), 3.87 (1H, d, *J* = 12.2 Hz, H-CH*H*OH), 4.13 (1H, t, *J* = 6.9 Hz, H aliphatic fluorene), 4.21– 4.41 (3H, m, C*H*$_2$-fluorene, Hα-tyrosyl), 4.95 (1H, d, *J* = 6.6 Hz, H-2'), 4.95 (1H, d, *J* = 6.6 Hz, H-4'), 5.82 (1H, br. s, N*H*Fmoc), 6.21 (1H, br s, 3'-N*H*), 6.80 (2H, d, *J* = 8.4, Ph(OMe)), 7.09 (2H, d, *J* = 6.6 Hz , Ph(OMe)), 7.22–7.29 (2H, m, fluorene), 7.34 (2H, dd, *J* = 7.2, 4.8 Hz, fluorene), 7.49 (2H, dd, *J* = 7.2, 4.2 Hz , fluorene), 7.71 (2H, d, *J* = 7.5 Hz, fluorene), 8.23 (1H, s, H8), 8.26 (1H, s, H2); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 9.5, 26.3, 35.3, 36.0, 37.8, 38.6, 47.0, 49.0, 55.1, 55.2, 56.5, 63.3, 67.1, 114.1, 120.0, 120.4, 124.9, 125.0 127.0, 127.7, 128.1, 130.3 137.3, 141.2, 143.6, 149.5, 151.8, 154.9, 156.1, 158.7, 172.1; HRMS (ESI^+) calcd for ($C_{39}H_{42}N_7O_5^+$) 688.3247 (MH^+), found 688.3248.

(2S)-*N*-((1*R*,2*S*,4*S*,5*S*)-4-{6-[1-aza-2-(dibutylamino)vinyl]purin-9-yl}-1-(hydroxymethyl)bicyclo-[3.1.0]hex-2-yl)-2-[(fluoren-9-ylmethoxy)carbonylamino]-3-(4-methoxyphenyl)propanamide (23).

^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.52–0.60 (2H, m, H-6'a,b), 0.89–0.96 (6H, m, $N(CH_2CH_2CH_2CH_3)_2$), 1.30–1.41 (4H, m, $N(CH_2CH_2CH_2CH_3)_2$), 1.56–1.70 (6H, m, $N(CH_2CH_2CH_2CH_3)_2$, H-5', H-3'a), 1.99–2.10 (1H, m, H-3'b), 2.83–3.09 (2H, m, *p*-MeOPhCH_2), 3.21 (1H, d, *J* = 12.0 Hz, C*H*HOH), 3.37 (2H, t, *J* = 7.2 Hz, $N(CH_2CH_2CH_2CH_3)_2$), 3.66–3.73 (2H, m, $N(CH_2CH_2CH_2CH_3)_2$), 3.73 (3H, s, OCH_3), 3.87 (1H, d, *J* = 12.0 Hz, CH*H*OH), 4.07–4.15 (1H, m, aliphatic fluorene), 4.31–4.39 (3H, m, CH_2-fluorene, Hα-tyrosyl), 4.90–4.98 (2H, m, H-2', H-4'), 5.74 (1H, br. s, N*H*Fmoc), 6.32 (1H, br. s, 2'-N*H*), 6.79 (2H, d, *J* = 8.4 Hz, Ph(OMe), 7.07 (2H, br. s, Ph(OMe)), 7.22–7.27 (2H, m, fluorene), 7.34 (2H, dd, *J* = 12.9, 6.9 Hz, fluorene), 7.47–7.50 (2H, m, fluorene), 7.71 (2H, d, *J* = 6.9 Hz, fluorene), 8.36 (1H, s, H-8), 8.49 (1H, s, H-2), 9.02 (1H, s, N=C*H*NBu_2); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 9.5, 13.6, 13.9, 19.7, 20.1, 26.2, 29.2, 30.9, 35.3, 36.1, 37.8, 45.2 , 46.9, 49.0, 51.9, 55.2, 55.3, 56.4, 63.2, 67.0, 114.1, 119.9, 124.9, 125.0, 126.2, 127.0, 127.7, 128.2, 130.3, 140.6, 141.2, 143.6, 150.8, 152.2, 158.4, 158.6, 160.1, 162.3, 172.0; HRMS (ESI^+) calcd for ($C_{46}H_{55}N_8O_5^+$) 799.4295 (MH^+), found 799.4297.

(2*S*)-*N*-{(1*S*,3*S*,4*S*,5*S*)-1-[6-(Dimethylamino)purin-9-yl]-4-(hydroxymethyl)bicyclo-[3.1.0]hex-3-yl}-2-(fluoren-9-ylmethoxy)carbonylamino]-3-(4-methoxyphenyl)propanamide (24).

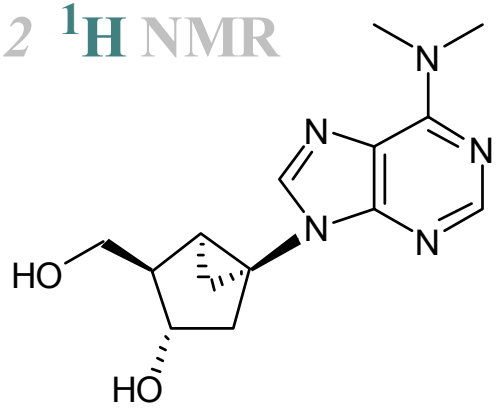
^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.58 (2H, br. s, H-6'a), 1.09–1.15 (1H, m, H-6'b), 1.67 (1H, dd, *J* = 4.7, 9.5 Hz, H-5'), 1.91 (1H, br. s, H4'), 2.00 (1H, d, *J* = 13.8 Hz, H-2'a), 2.72 (1H, ddd, *J* = 13.8, 9.0, 1.8 Hz, H-2'b), 2.88 (1H, br s, *p*-MeOPhC*H*H), 3.06 (1H, br s, *p*-MeOPhCH*H*), 3.51 (6H, br s, NMe_2), 3.77 (3H, s, OCH_3), 3.87 (1H, dd, *J* = 11.6 Hz, *J* = 3.2 Hz, C*H*HOH), 4.01 (1H, d, *J* = 11.6 Hz, CH*H*OH), 4.21 (1H, t, *J* = 6.9 Hz, H aliphatic fluorene), 4.18–4.24 (1H, m, Hα-tyrosyl), 4.32–4.45 (3H, m, CH_2-fluorene, H-3'), 5.55 (2H, br s, 3'-N*H*, N*H*Fmoc), 6.86 (2H, d, *J* = 8.4 Hz, Ph(OMe)), 7.12 (2H, d, *J* = 4.5 Hz, Ph(OMe)), 7.31 (2H, td, *J* = 7.5, 0.9 Hz, fluorene), 7.40 (2H, t, *J* = 7.5 Hz, fluorene), 7.55 (2H, d, *J* = 7.5 Hz, fluorene), 7.63 (1H, s, H-8), 7.77 (2H, d, *J* = 7.5 Hz, fluorene), 8.26 (1H, s, H-2); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 17.1, 27.4, 50.6, 38.1, 38.5, 40.9, 43.4, 47.0, 50.7, 53.6, 55.3, 56.6, 65.7, 67.2, 114.2, 120.1, 124.9, 125.0, 127.1, 127.8, 128.4, 130.3, 138.9, 141.3, 143.6, 150.1, 151.8, 155.0, 156.0, 158.8, 172.1; HRMS (ESI^+) calcd for ($C_{39}H_{42}N_7O_5^+$) 688.3247 (MH^+), found : 688.3248.

(2*S*)-*N*-((1*S*,3*S*,4*S*,5*S*)-1-{6-[1-Aza-2-(dibutylamino)vinyl]purin-9-yl}-4-(hydroxymethyl)bicyclo-[3.1.0]hex-3-yl)-2-[(fluoren-9-ylmethoxy)carbonylamino]-3-(4-methoxyphenyl)propanamide (25).

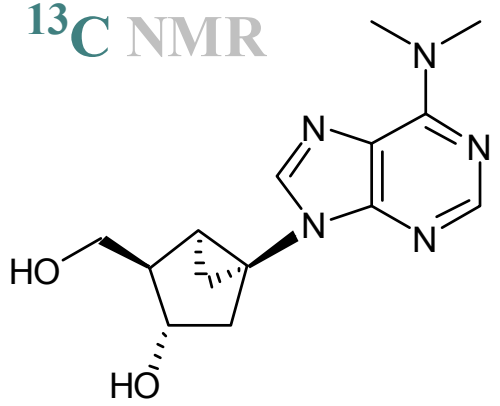
^{1}H-NMR ($CDCl_3$, 300 MHz) δ 0.63 (1H, br. s, H-6'a), 0.88–0.96 (6H, m, $N(CH_2CH_2CH_2CH_3)_2$), 1.10 (1H, pseudo t, *J* ≈ 7.0 Hz, H-6'b), 1.27–1.42 (4H, m, $N(CH_2CH_2CH_2CH_3)_2$), 1.55–1.69 (5H, m, $N(CH_2CH_2CH_2CH_3)_2$, H-5'), 1.95 (1H, s, H-4'), 2.03 (1H, d, *J* = 14.1 Hz, H-2'a), 2.71 (1H, dd, *J* = 12.6, 9.6 Hz, H-2'b), 2.87–2.94 (1H, m, *p*-MeOPhC*H*H), 3.03 (1H, br. s, *p*-MeOPhCH*H*), 3.37 (2H,

t, *J* = 7.1 Hz, N(C*H*$_2$CH$_2$CH$_2$CH$_3$)$_2$), 3.65–3.73 (2H, m, N(C*H*$_2$CH$_2$CH$_2$CH$_3$)$_2$), 3.75 (3H, s, OCH$_3$), 3.88 (1H, irregular t, *J* = 10.5, 7.5 Hz, C*H*HOH), 4.01 (1H, d, *J* = 11.4 Hz , CH*H*OH), 4.19 (1H, t, *J* = 6.9 Hz, aliphatic fluorene), 4.27–4.41 (4H, m, C*H*$_2$-fluorene, Hα-tyrosyl, H-3'), 5.88 (1H, br. s, N*H*Fmoc), 6.42 (1H, d, *J* = 6.9 Hz, 3'-N*H*), 6.83 (2H, d, *J* = 8.7 Hz, Ph(OMe)), 7.10 (2H, d, *J* = 5.7 Hz, Ph(OMe)), 7.25–7.30 (2H, m, fluorene), 7.37 (2H, t , *J* = 7.4 Hz ,fluorene), 7.53 (2H, d, *J* = 7.2 Hz, fluorene), 7.74 (2H, d, *J* = 8.1 Hz, fluorene), 7.75 (1H, s, H-8); 8.47 (1H, s, H-2), 8.95 (1H, s, N=C*H*NBu$_2$); ^{13}C-NMR ($CDCl_3$, 75 MHz) δ 13.6, 13.8, 17.1, 19.7, 20.1 , 27.3, 29.2, 30.9, 38.1, 40.8, 43.4, 45.2, 46.9, 50.5, 51.9, 53.6, 55.2, 56.5, 65.7, 67.2, 114.1, 120.0, 124.9, 125.0, 125.9, 127.0, 127.7, 128.4, 130.2, 141.2, 142.2, 143.5, 143.6, 151.2, 152.0, 158.2, 158.2, 158.7, 160.3, 170.3; HRMS (ESI$^+$) calcd for ($C_{46}H_{55}N_8O_5^+$) 799.4295 (MH+), found 799.4292.

12 **^{1}H NMR**



12 ^{13}C NMR



150

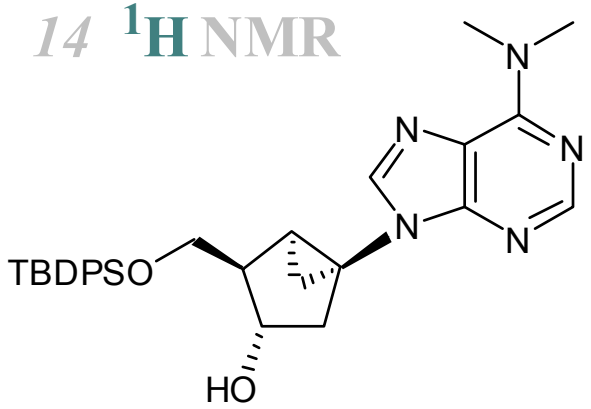
100

50

ppm (t1)

20

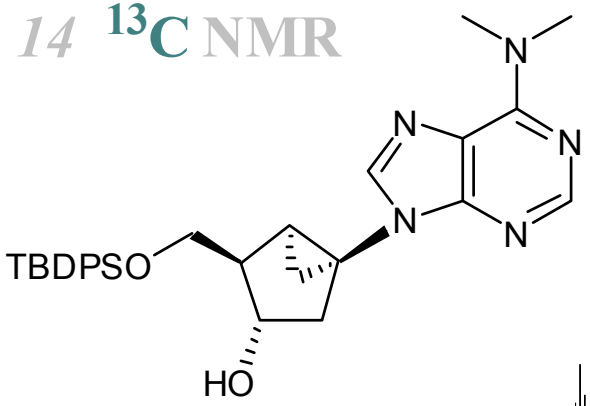
14 **^{1}H NMR**



8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

ppm (t1)

14 ^{13}C NMR



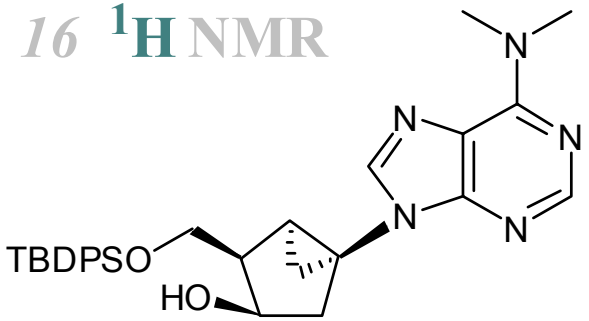
150

100

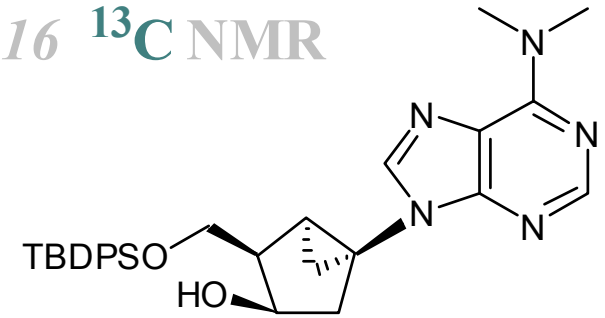
50

ppm (t1)

16 **^{1}H** NMR



16 ^{13}C NMR



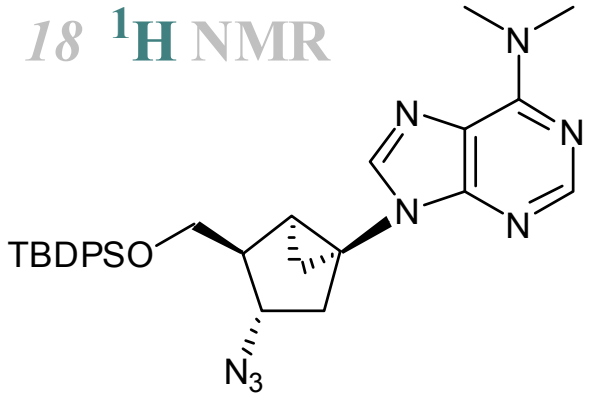
150

100

50

ppm (f1)

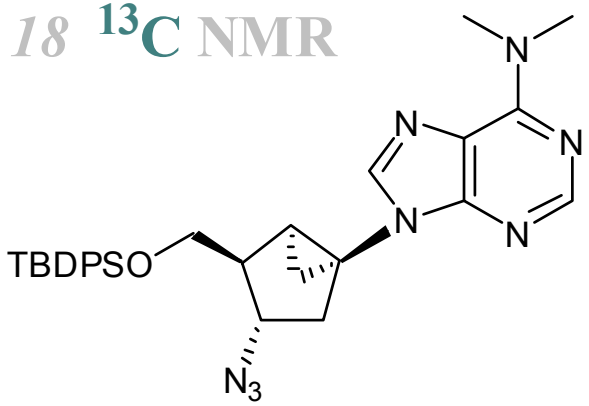
18 ^{1}H NMR



8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

ppm (t1)

18 ^{13}C NMR



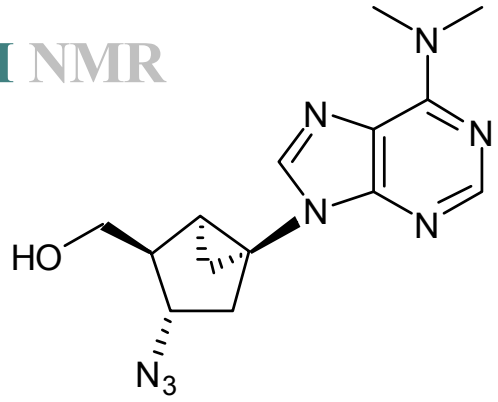
150

100

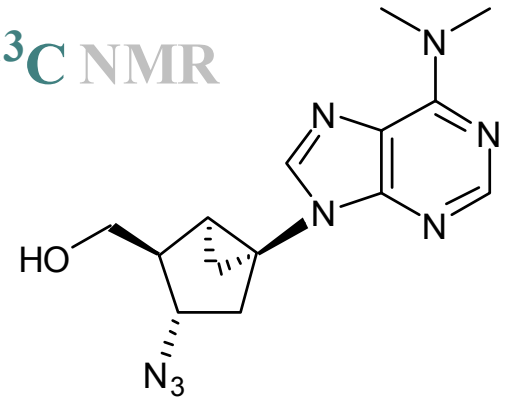
50

ppm (f1)

6 ^{1}H NMR



6 ^{13}C NMR



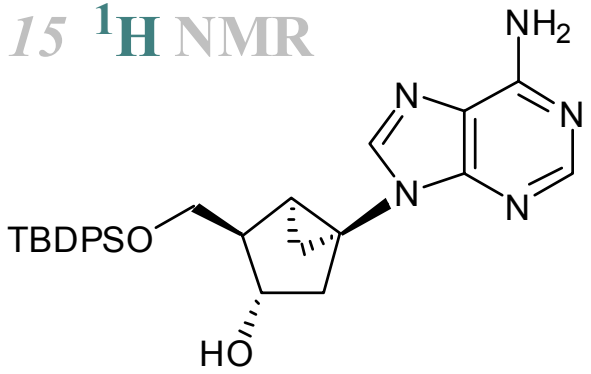
150

100

50

ppm (f1)

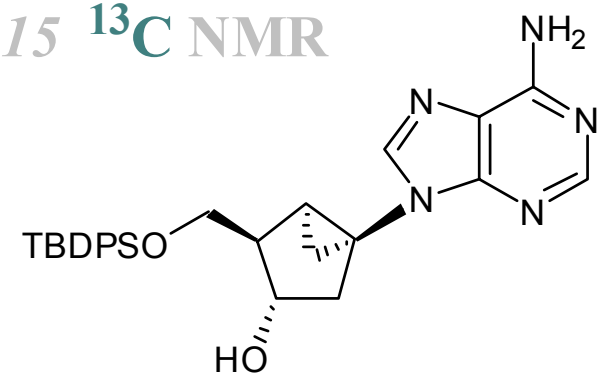
15 ^{1}H NMR



8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

ppm (f1)

15 ^{13}C NMR



150

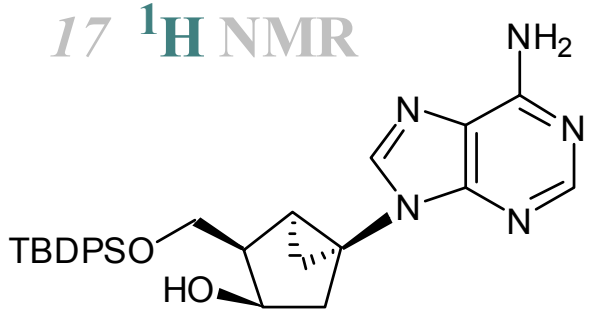
100

50

ppm (t1)

30

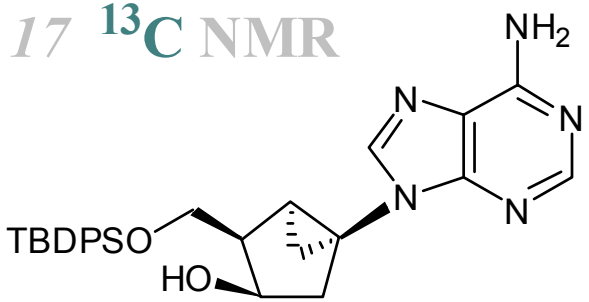
17 **^{1}H NMR**



8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

ppm (f1)

17 ^{13}C NMR



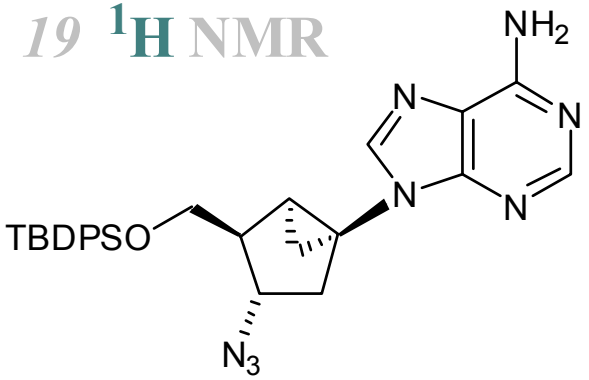
150

100

50

ppm (t1)

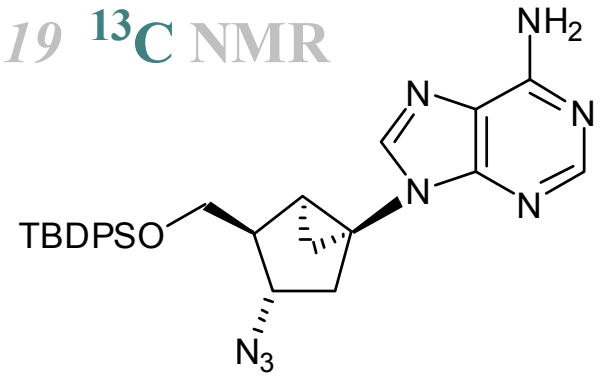
19 ^{1}H NMR



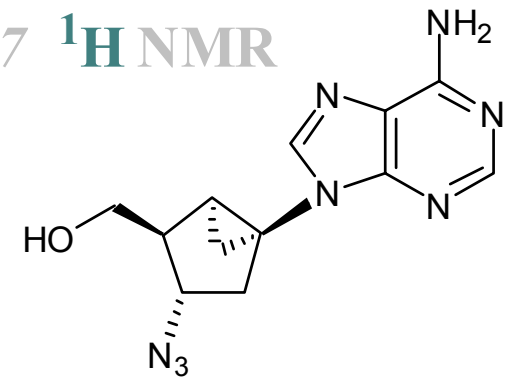
8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

ppm (f1)

19 ^{13}C NMR



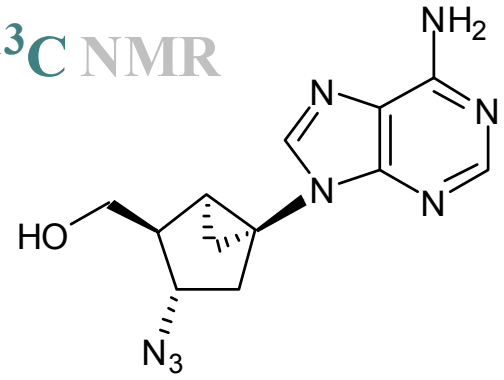
7 ^{1}H NMR



8.0 7.0 6.0 5.0 4.0 3.0 2.0 1.0

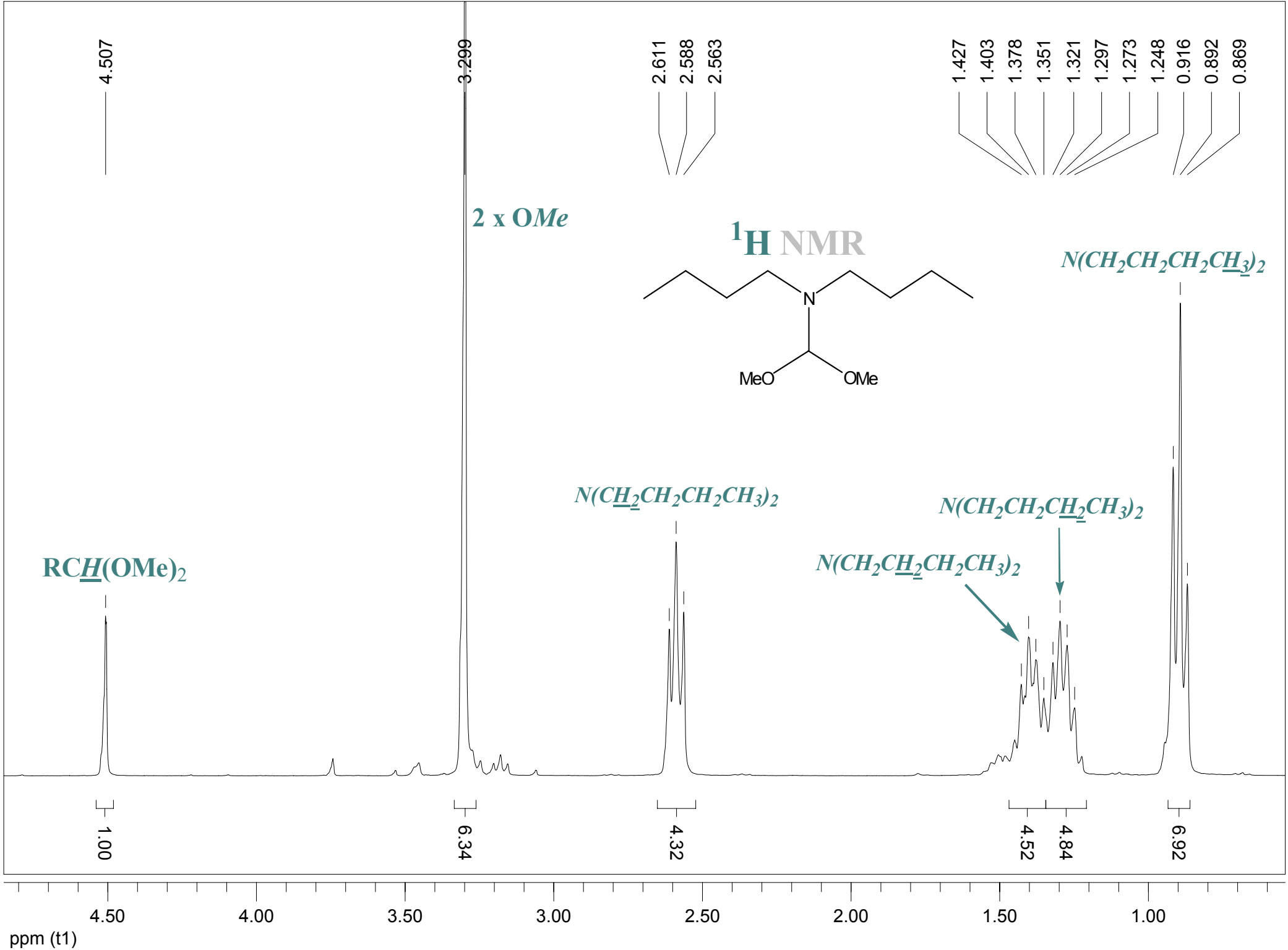
ppm (t1)

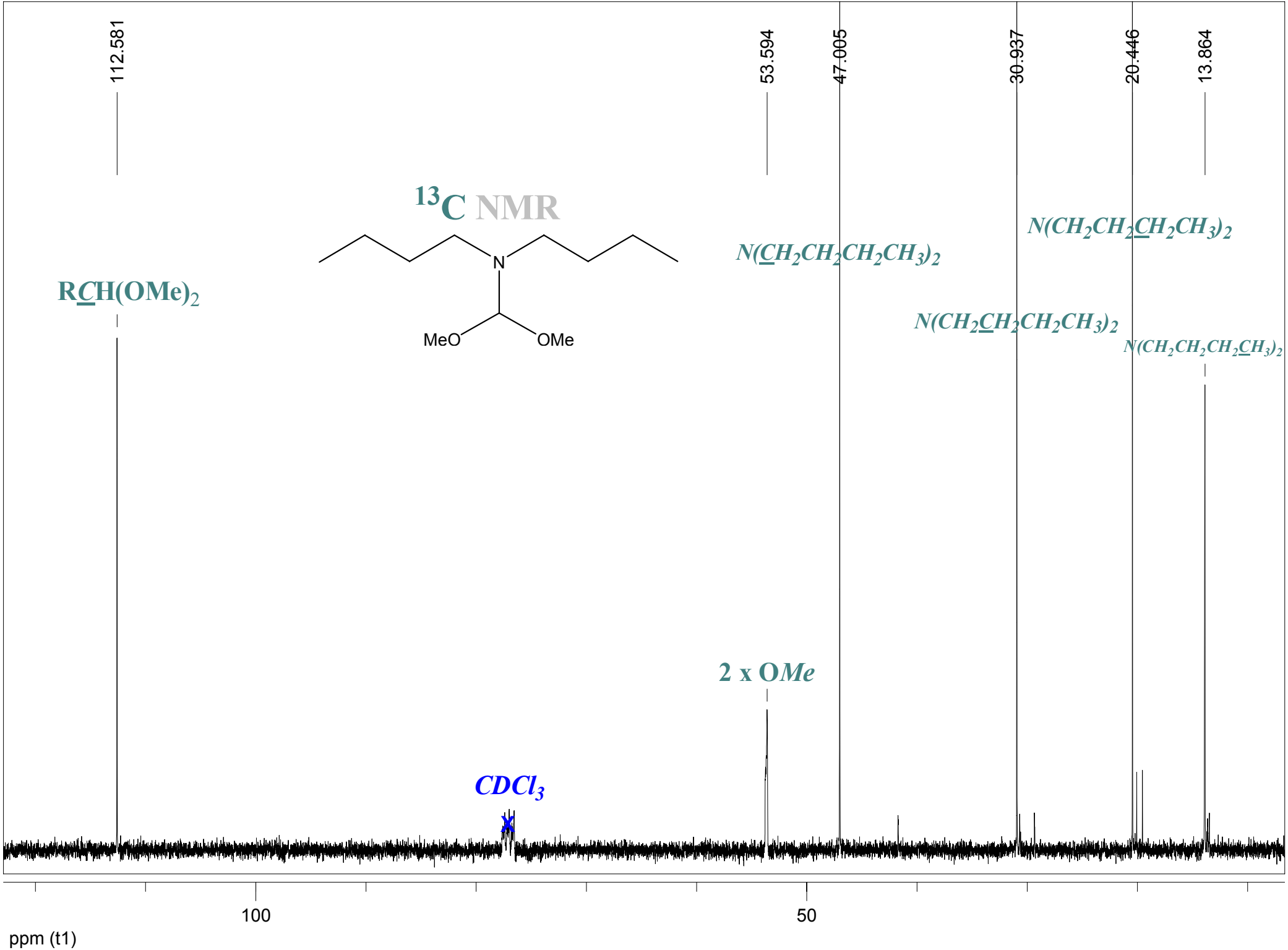
7 ^{13}C NMR

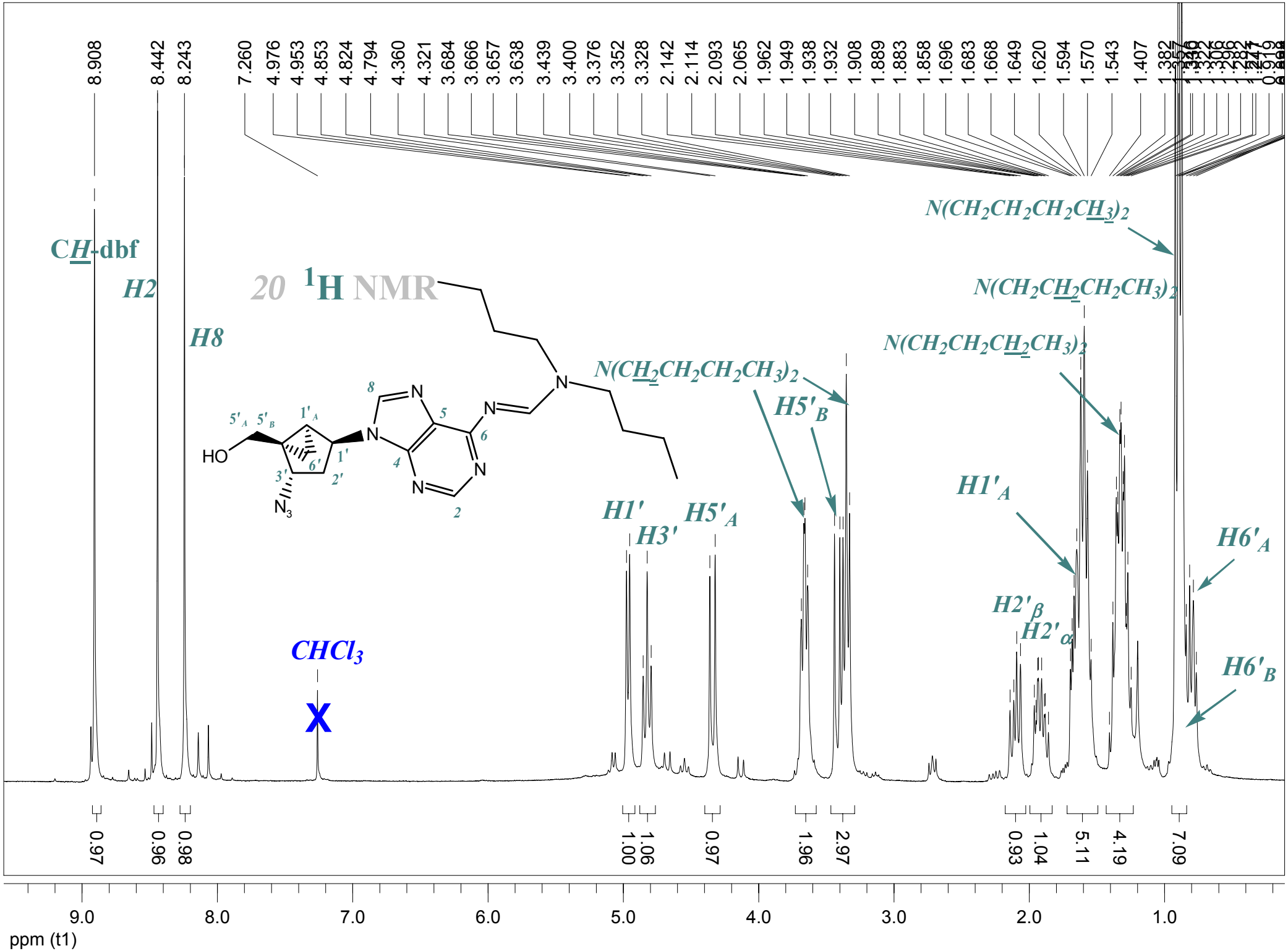


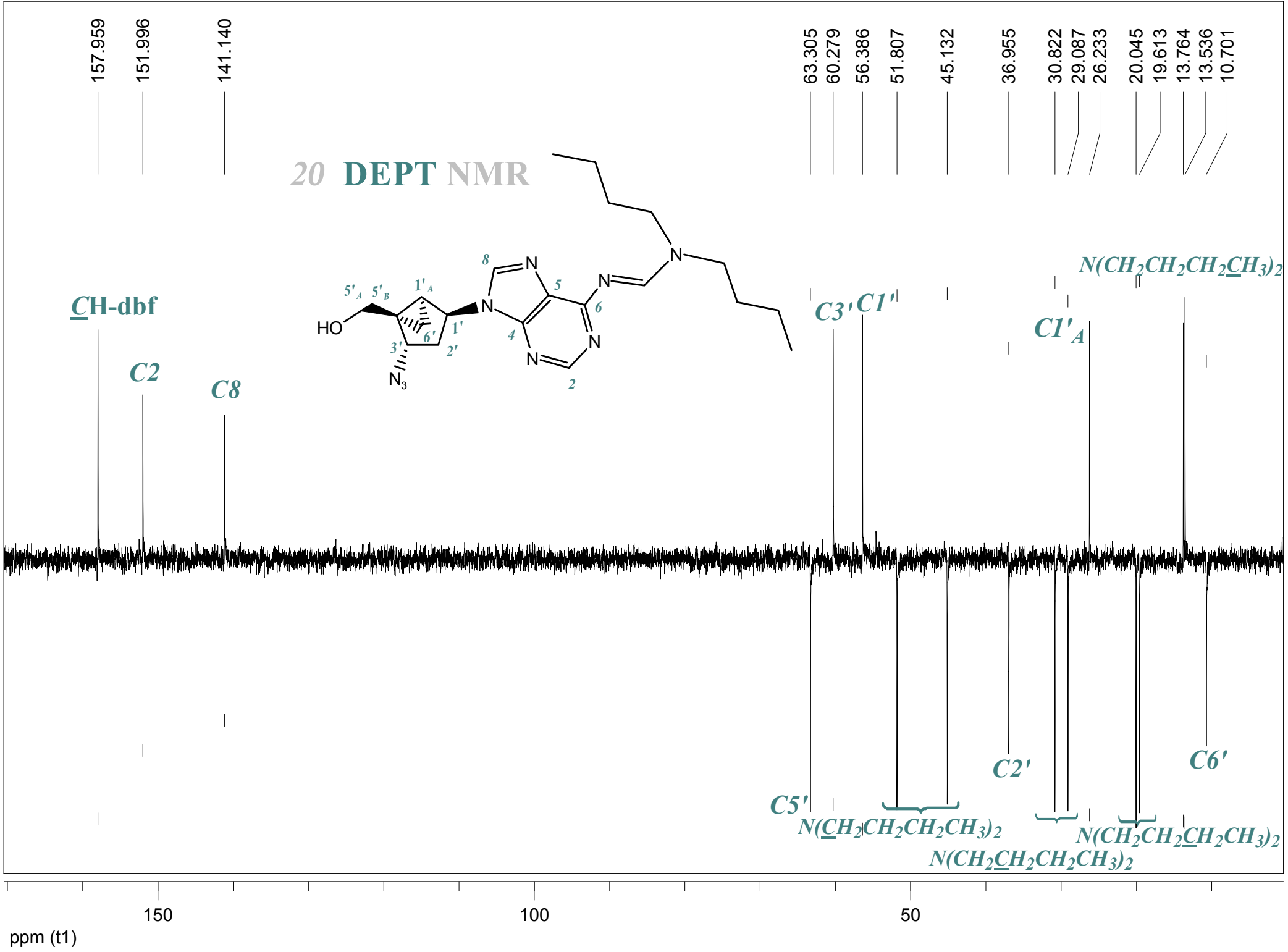
150 100 50 0

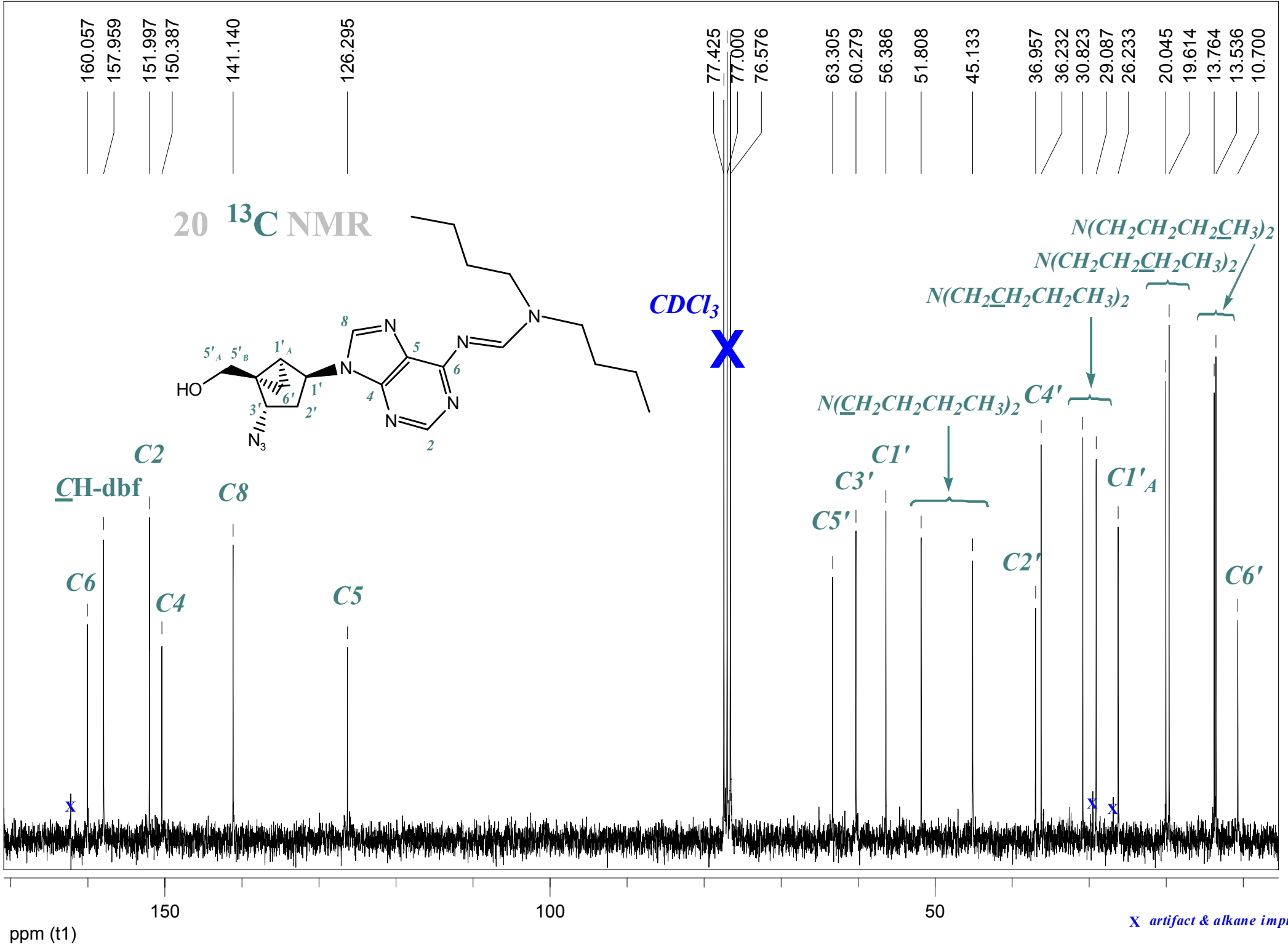
ppm (t1)

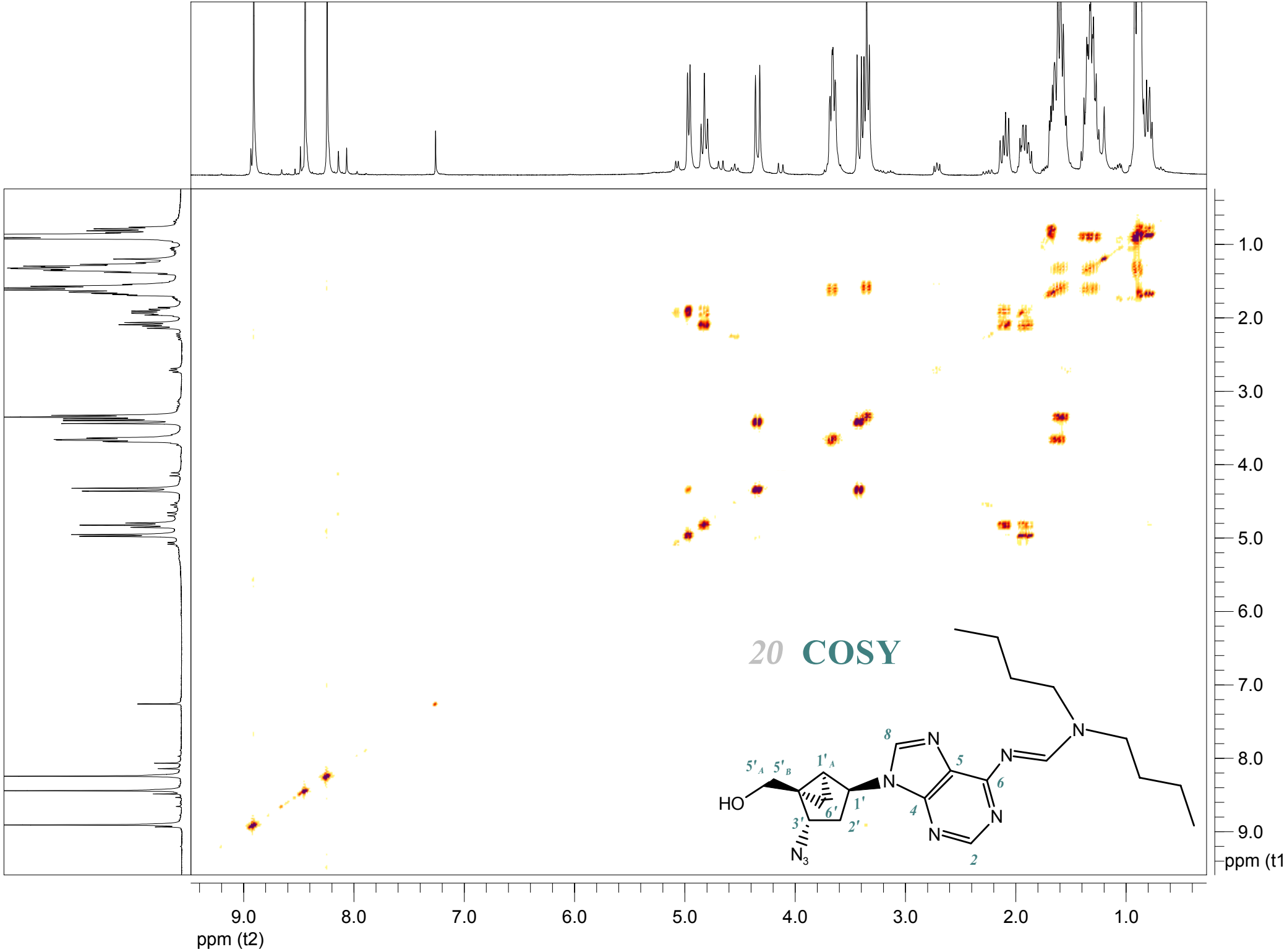

4.507
3.299
2.611
2.588
2.563
1.427
1.403
1.378
1.351
1.321
1.297
1.273
1.248
0.916
0.892
0.869
2 x OMe
1H NMR
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
RCH(OMe)2
N
MeO
OMe
1.00
6.34
4.32
4.52
4.84
6.92
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
ppm (t1)

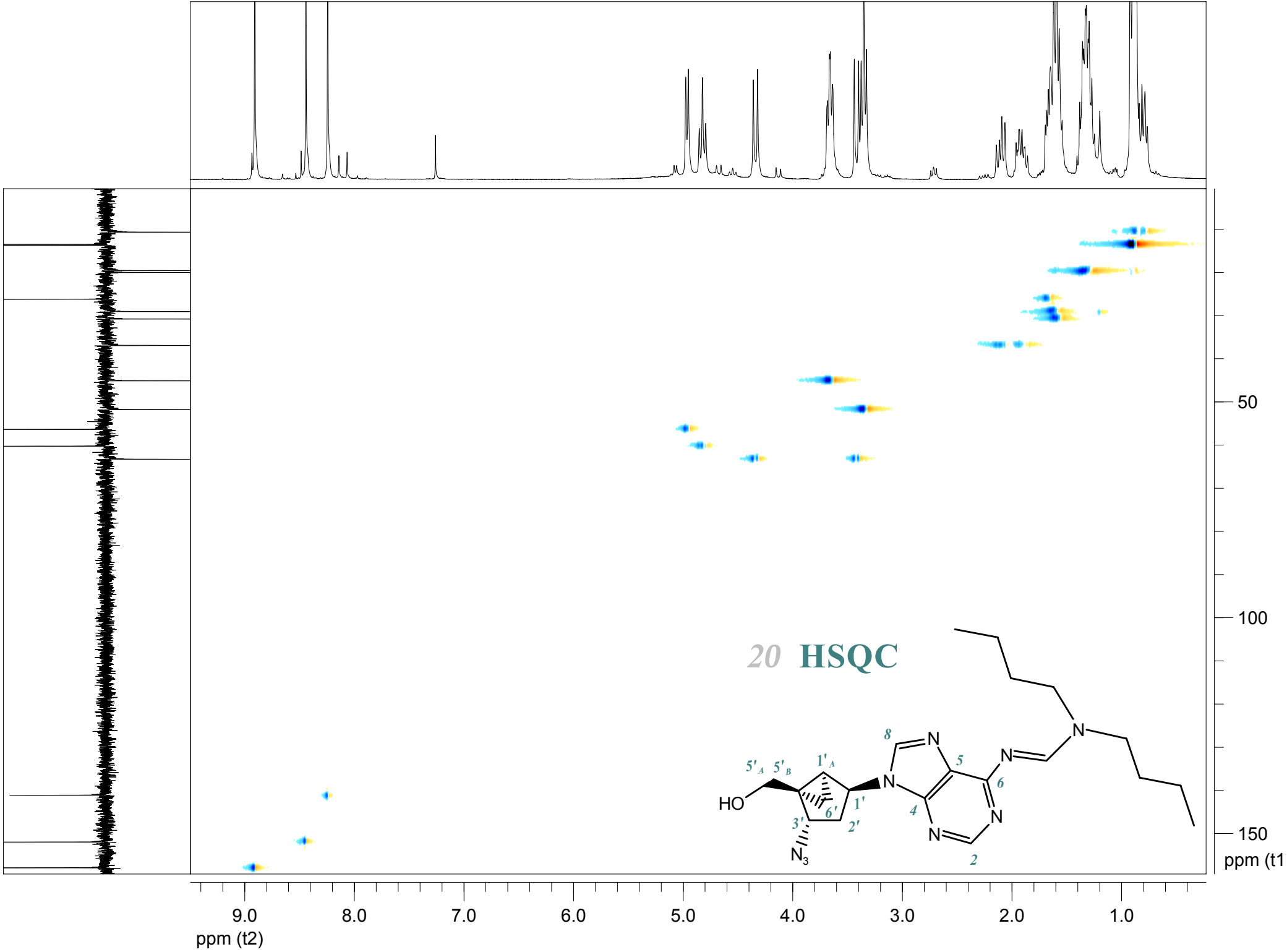

112.581
53.594
47.005
30.937
20.446
13.864
13C NMR
N
MeO
OMe
RCH(OMe)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
2 x OMe
CDCl3
100
50
ppm (t1)

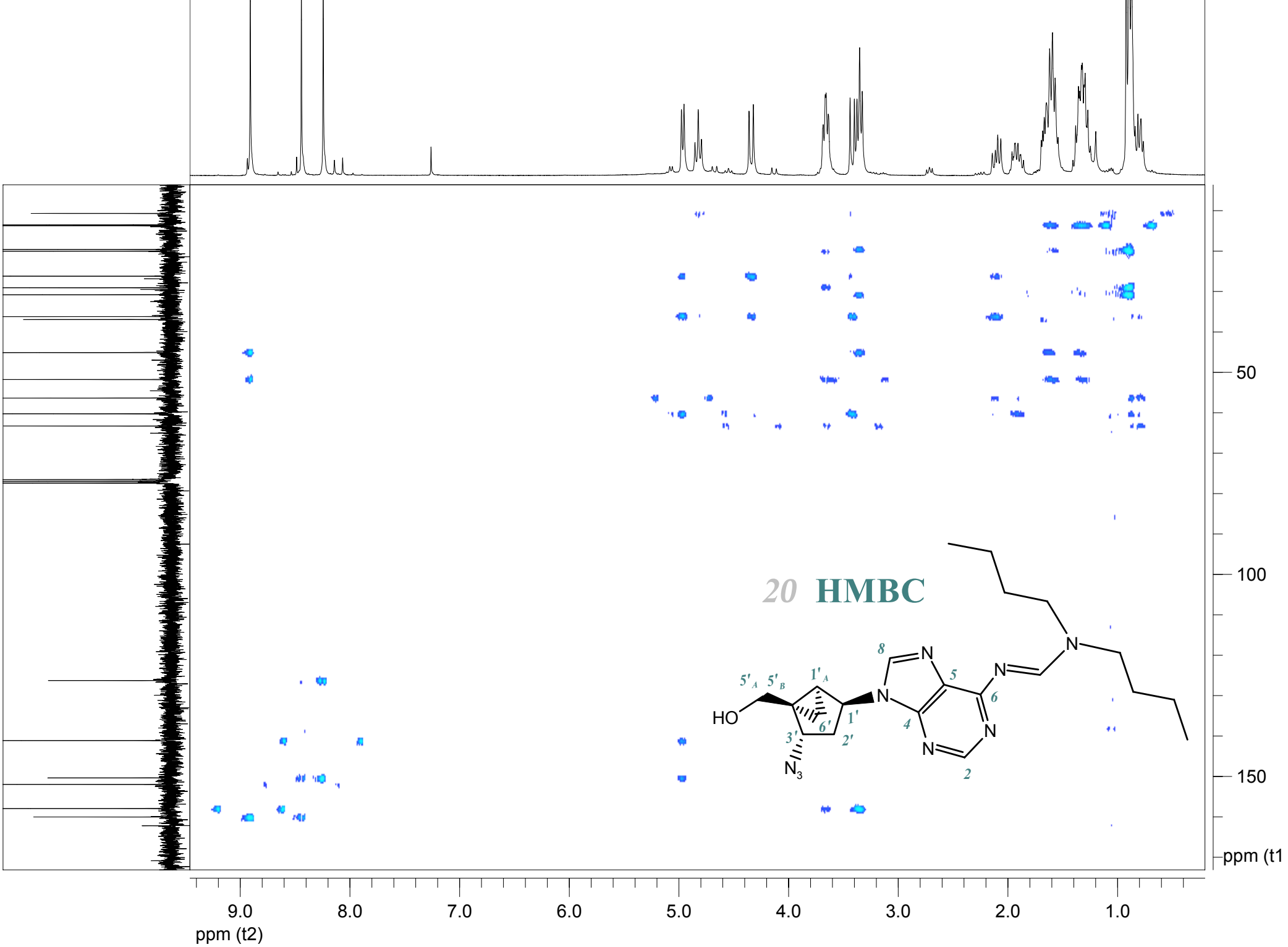

20 1H NMR
CH-dbf
H2
H8
CHCl3
N(CH2CH2CH2CH3)2
H1'
H3'
H5'A
H5'B
H1'A
H2'β
H2'α
H6'A
H6'B
8.908
8.442
8.243
7.260
4.976
4.953
4.853
4.824
4.794
4.360
4.321
3.684
3.666
3.657
3.638
3.439
3.400
3.376
3.352
3.328
2.142
2.114
2.093
2.065
1.962
1.949
1.938
1.932
1.908
1.889
1.883
1.858
1.696
1.683
1.668
1.649
1.620
1.594
1.570
1.543
1.407
1.382
0.97
0.96
0.98
1.00
1.06
0.97
1.96
2.97
0.93
1.04
5.11
4.19
7.09
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t1)

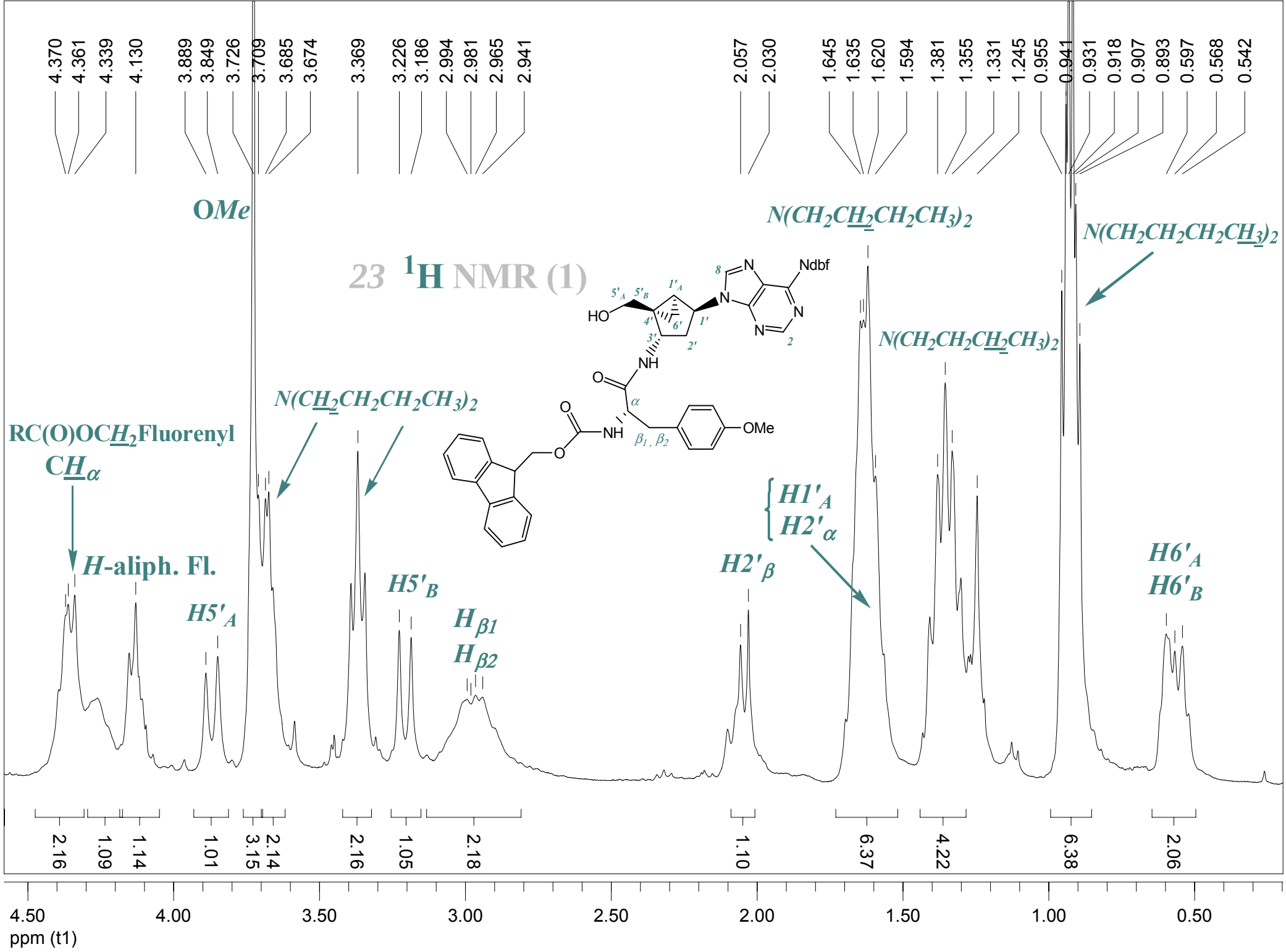

157.959
151.996
141.140
63.305
60.279
56.386
51.807
45.132
36.955
30.822
29.087
26.233
20.045
19.613
13.764
13.536
10.701
20 DEPT NMR
CH-dbf
C2
C8
C3'
C1'
C1'A
N(CH2CH2CH2CH3)2
C2'
C6'
C5'
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
HO
N3
150
100
50
ppm (t1)

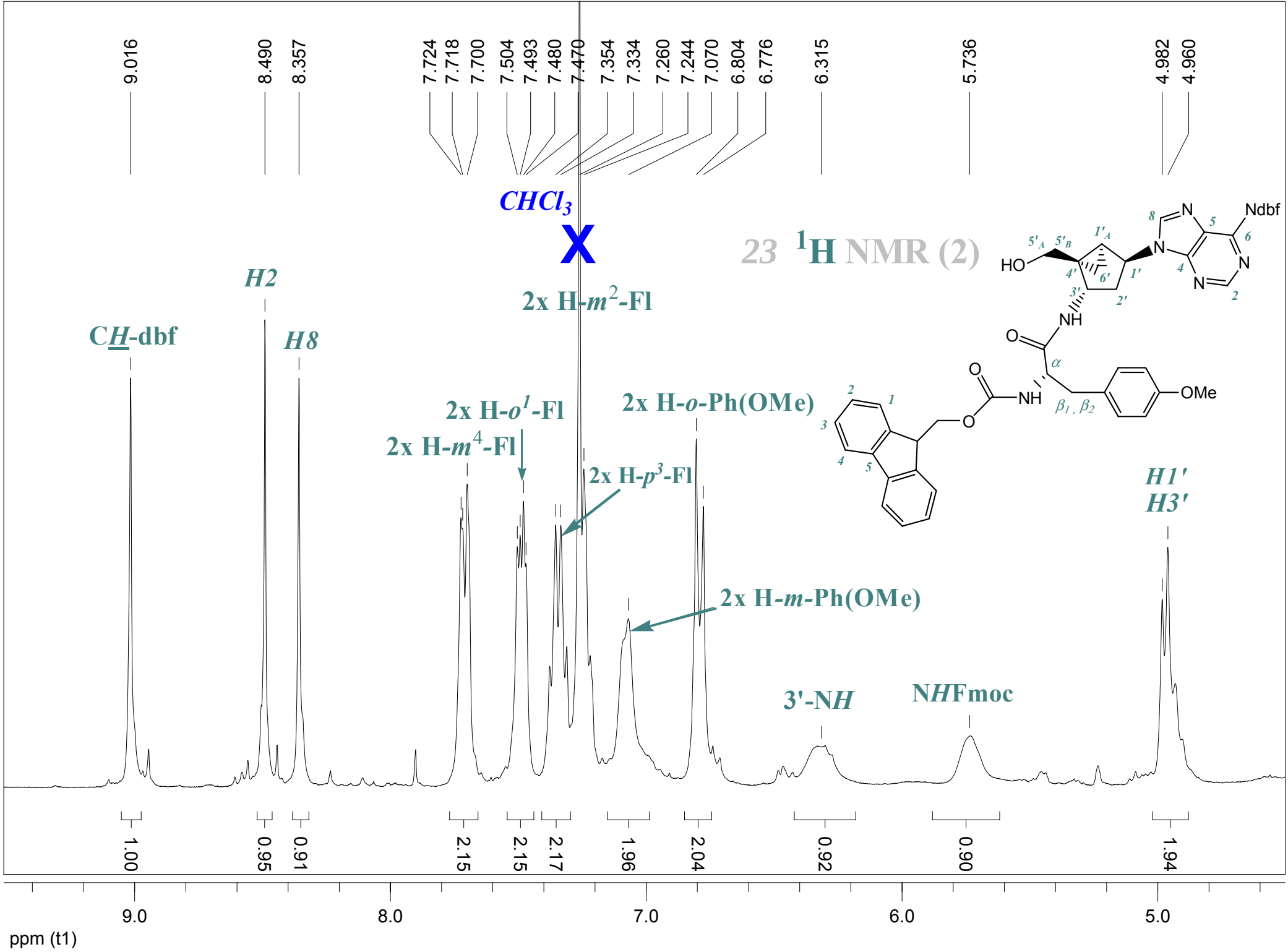

160.057
157.959
151.997
150.387
141.140
126.295
77.425
77.000
76.576
63.305
60.279
56.386
51.808
45.133
36.957
36.232
30.823
29.087
26.233
20.045
19.614
13.764
13.536
10.700
20 13C NMR
CDCl3
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
C4'
C1'
C3'
C5'
C1'A
C2'
C6'
C2
CH-dbf
C8
C6
C4
C5
HO
N3
150
100
50
ppm (t1)
X artifact & alkane impurities

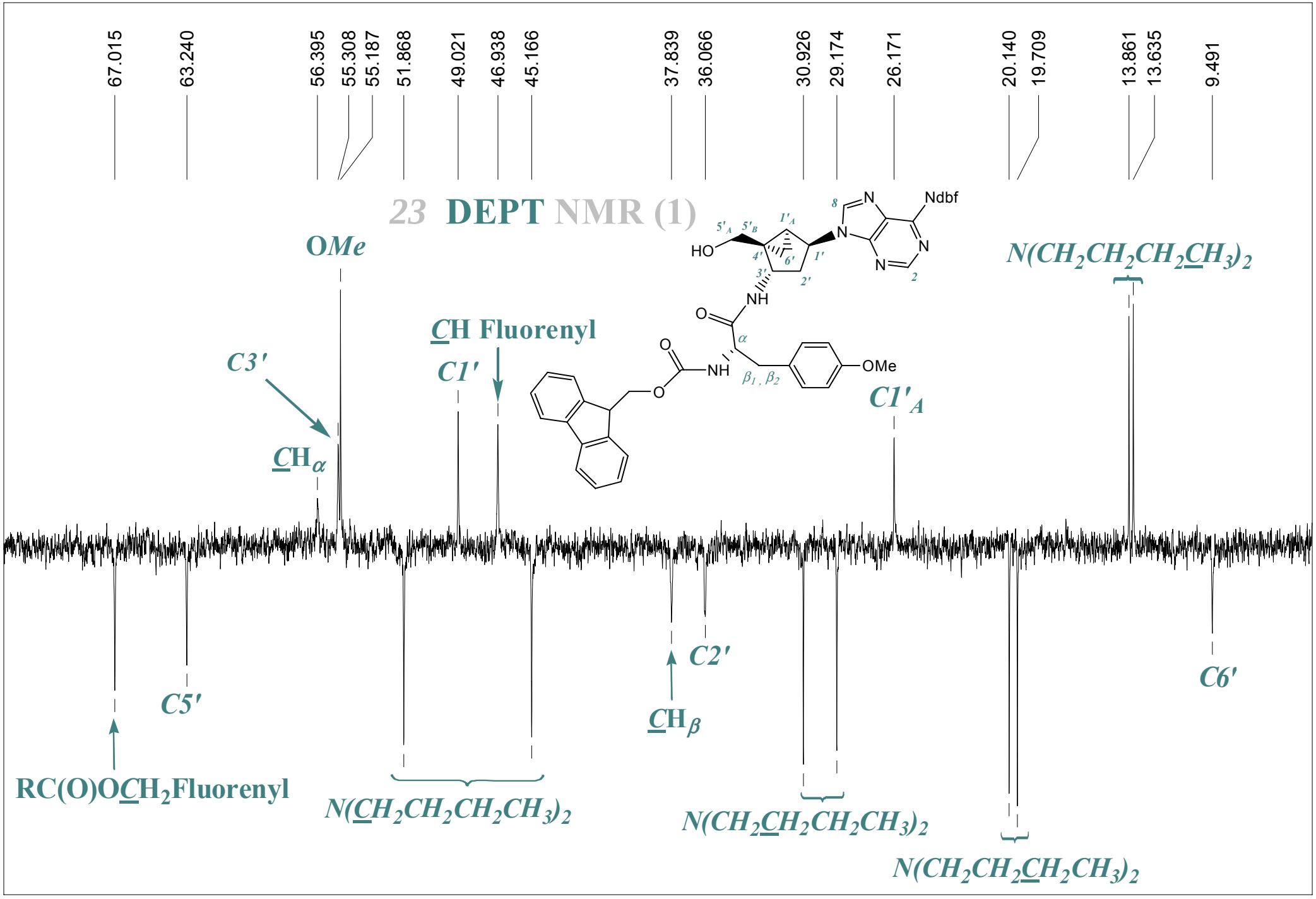

20 COSY
HO
N3
N
ppm (t2)
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


20 HSQC
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
50
100
150
ppm (t1
HO
N3
N

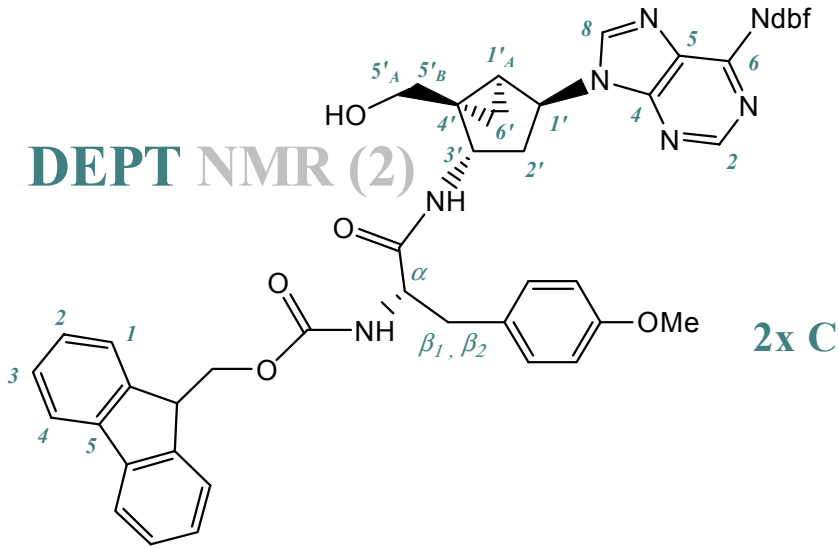

20 HMBC
HO
N3
N
50
100
150
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)


4.370
4.361
4.339
4.130
3.889
3.849
3.726
3.709
3.685
3.674
3.369
3.226
3.186
2.994
2.981
2.965
2.941
2.057
2.030
1.645
1.635
1.620
1.594
1.381
1.355
1.331
1.245
0.955
0.941
0.931
0.918
0.907
0.893
0.597
0.568
0.542
OMe
23 1H NMR (1)
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
RC(O)OCH2Fluorenyl
CHα
H-aliph. Fl.
H5'A
H5'B
Hβ1
Hβ2
H2'β
H1'A
H2'α
H6'A
H6'B
Ndbf
HO
NH
OMe
2.16
1.09
1.14
1.01
3.15
2.14
2.16
1.05
2.18
1.10
6.37
4.22
6.38
2.06
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)


9.016
8.490
8.357
7.724
7.718
7.700
7.504
7.493
7.480
7.470
7.354
7.334
7.260
7.244
7.070
6.804
6.776
6.315
5.736
4.982
4.960
CHCl3
23 1H NMR (2)
2x H-m2-Fl
H2
CH-dbf
H8
2x H-o1-Fl
2x H-m4-Fl
2x H-p3-Fl
2x H-o-Ph(OMe)
2x H-m-Ph(OMe)
H1'
H3'
3'-NH
NHFmoc
Ndbf
OMe
1.00
0.95
0.91
2.15
2.15
2.17
1.96
2.04
0.92
0.90
1.94
9.0
8.0
7.0
6.0
5.0
ppm (t1)


67.015
63.240
56.395
55.308
55.187
51.868
49.021
46.938
45.166
37.839
36.066
30.926
29.174
26.171
20.140
19.709
13.861
13.635
9.491
23 DEPT NMR (1)
OMe
CH Fluorenyl
C3'
C1'
CHα
C1'A
N(CH2CH2CH2CH3)2
C5'
C2'
CHβ
C6'
RC(O)OCH2Fluorenyl
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
Ndbf
HO
NH
OMe
70
60
50
40
30
20
10
ppm (t1)

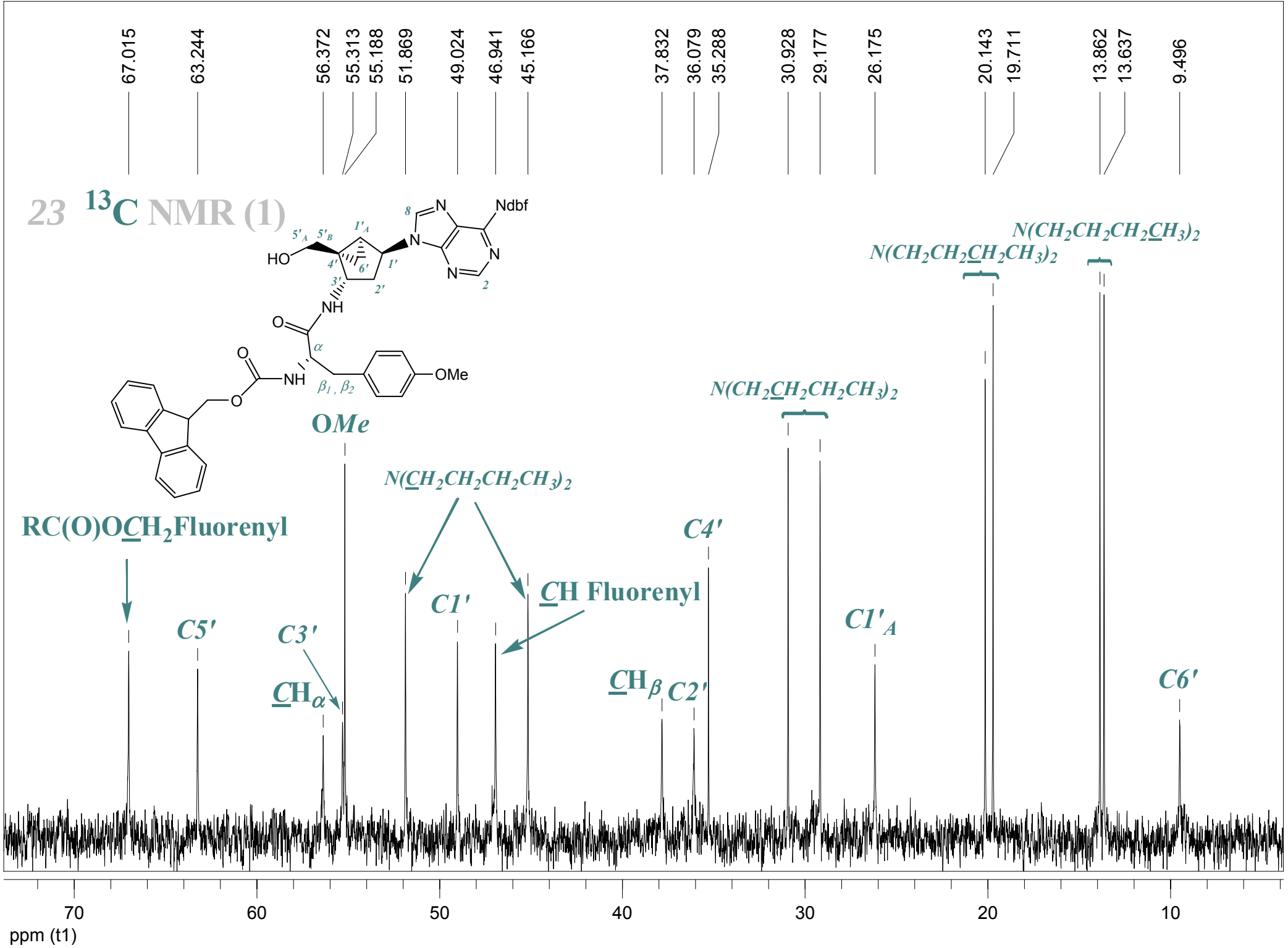
23 DEPT NMR (2)

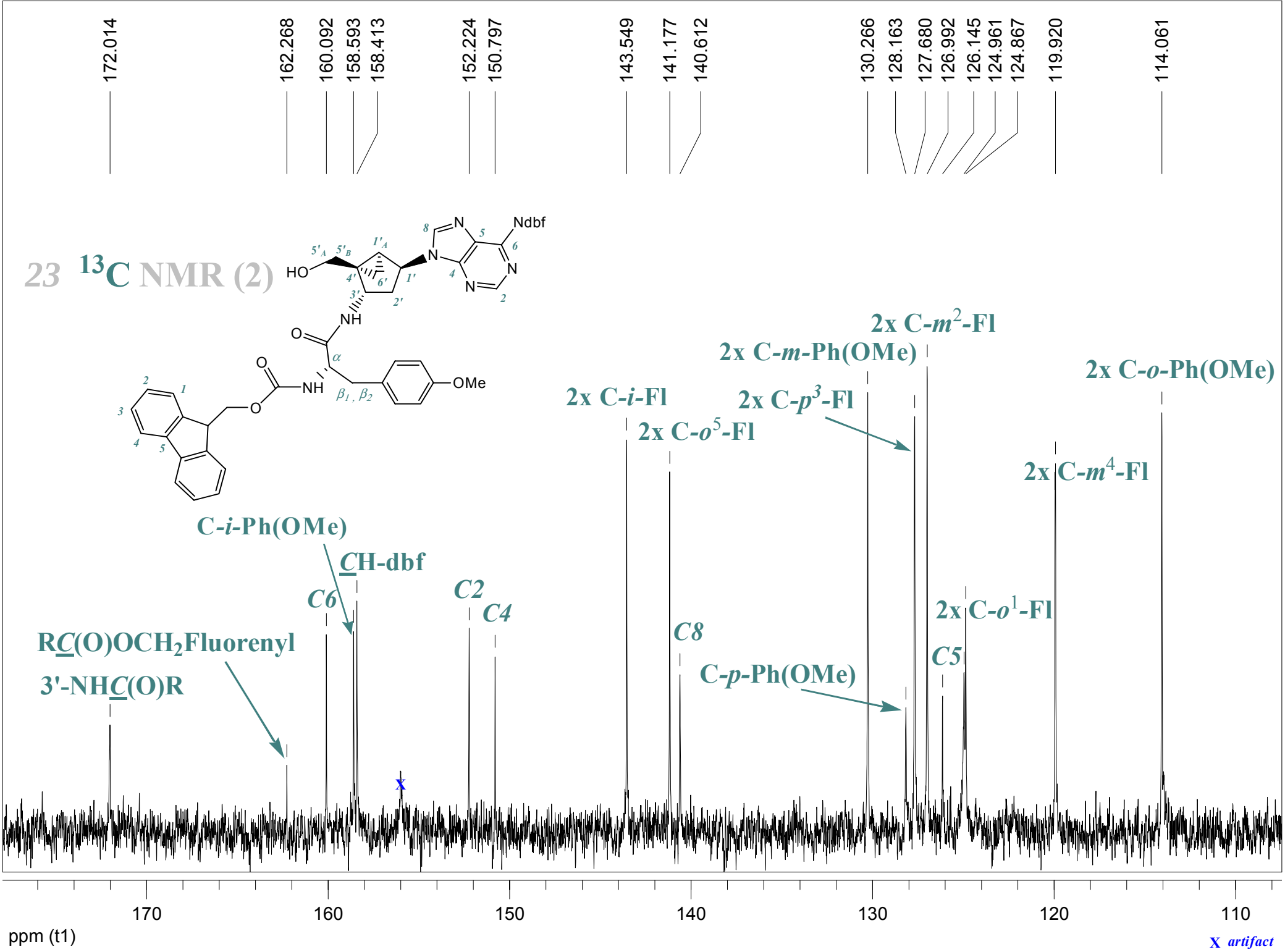


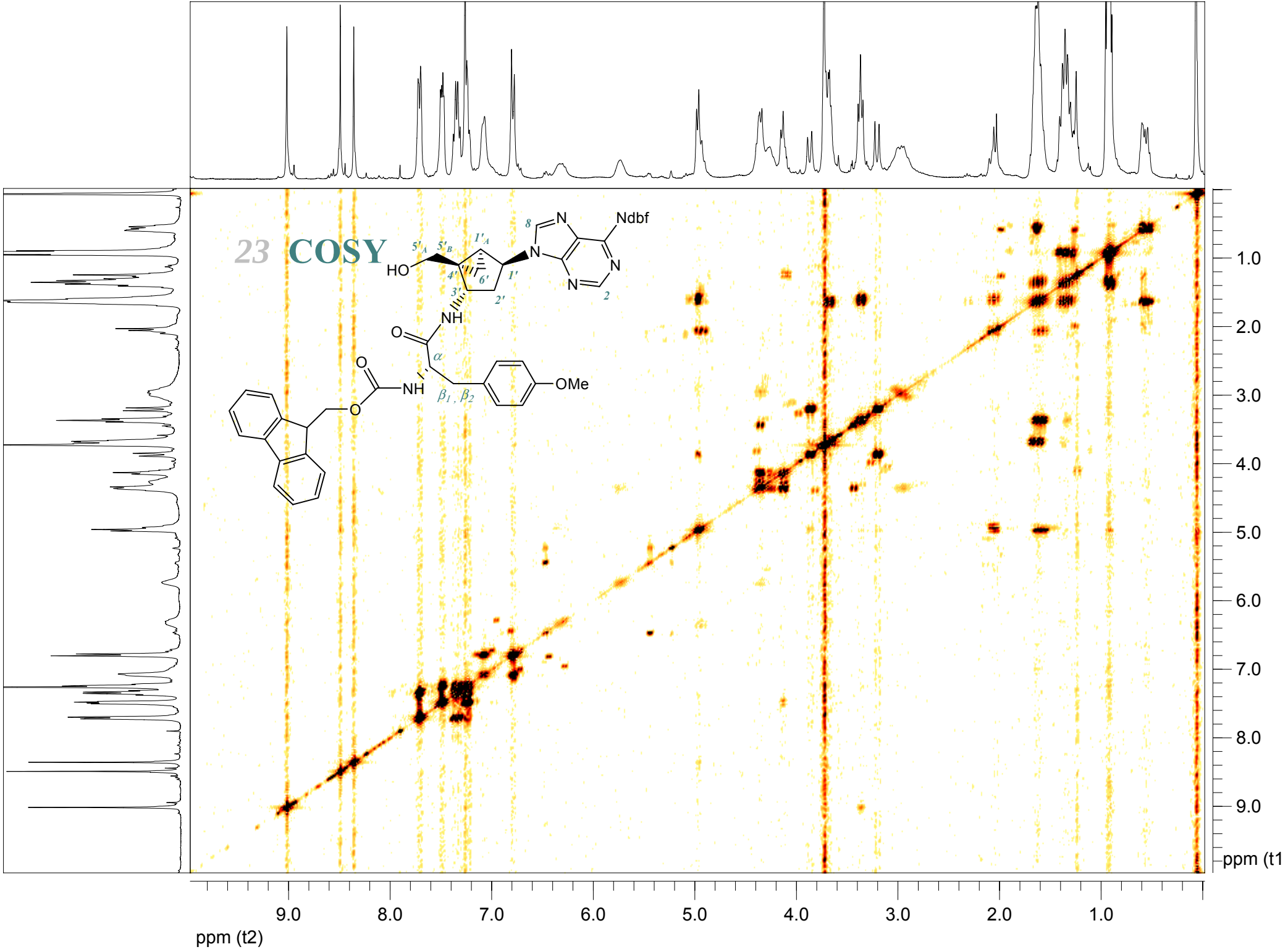
158.415
152.224
140.610
130.266
127.680
126.991
124.963
124.868
119.938
114.060

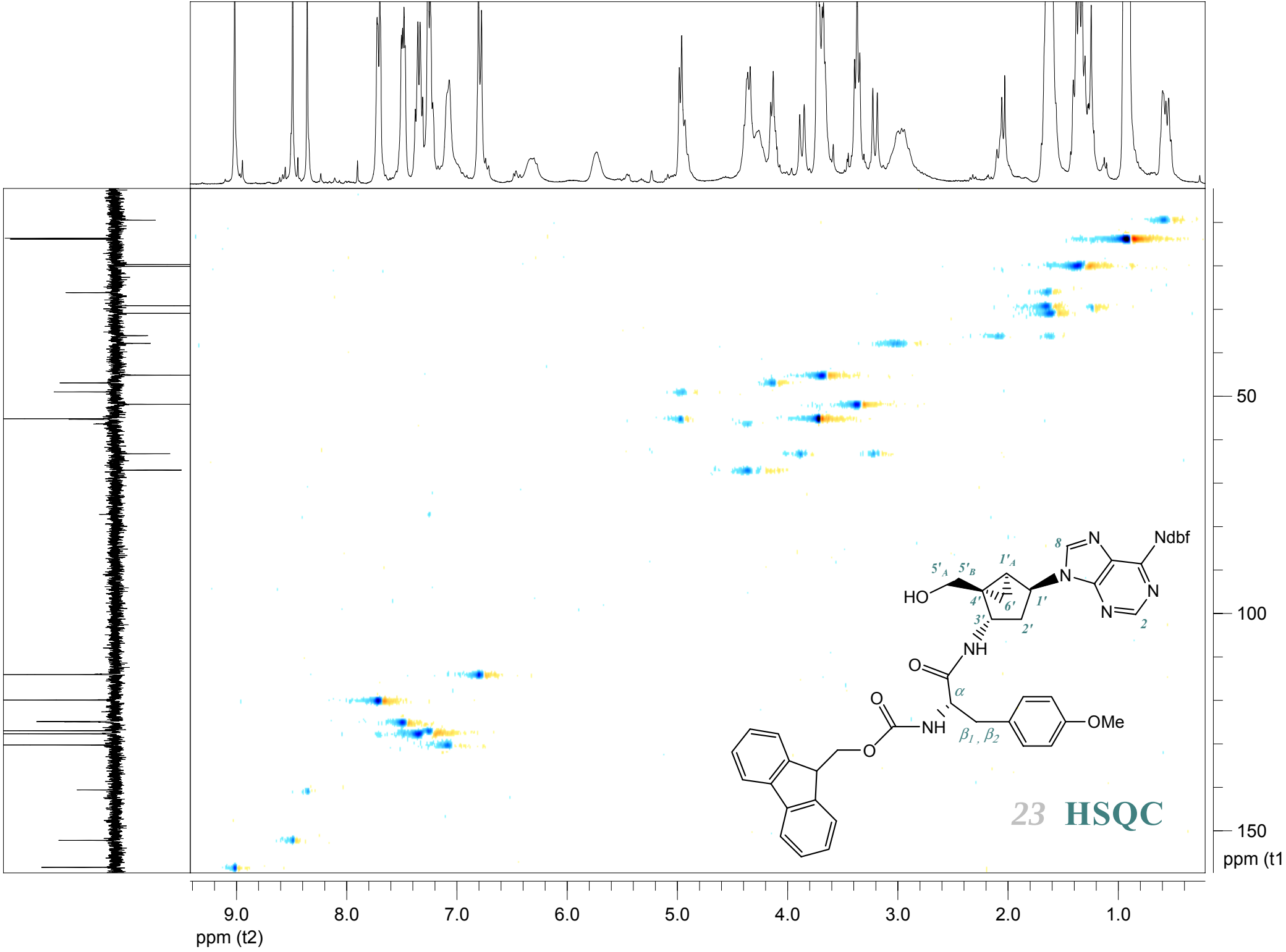
2x C-p^3-Fl
2x C-m^2-Fl
2x C-*m*-Ph(OMe)
2x C-*o*-Ph(OMe)
2x C-m^4-Fl
2x C-o^1-Fl
CH-dbf
C2
C8

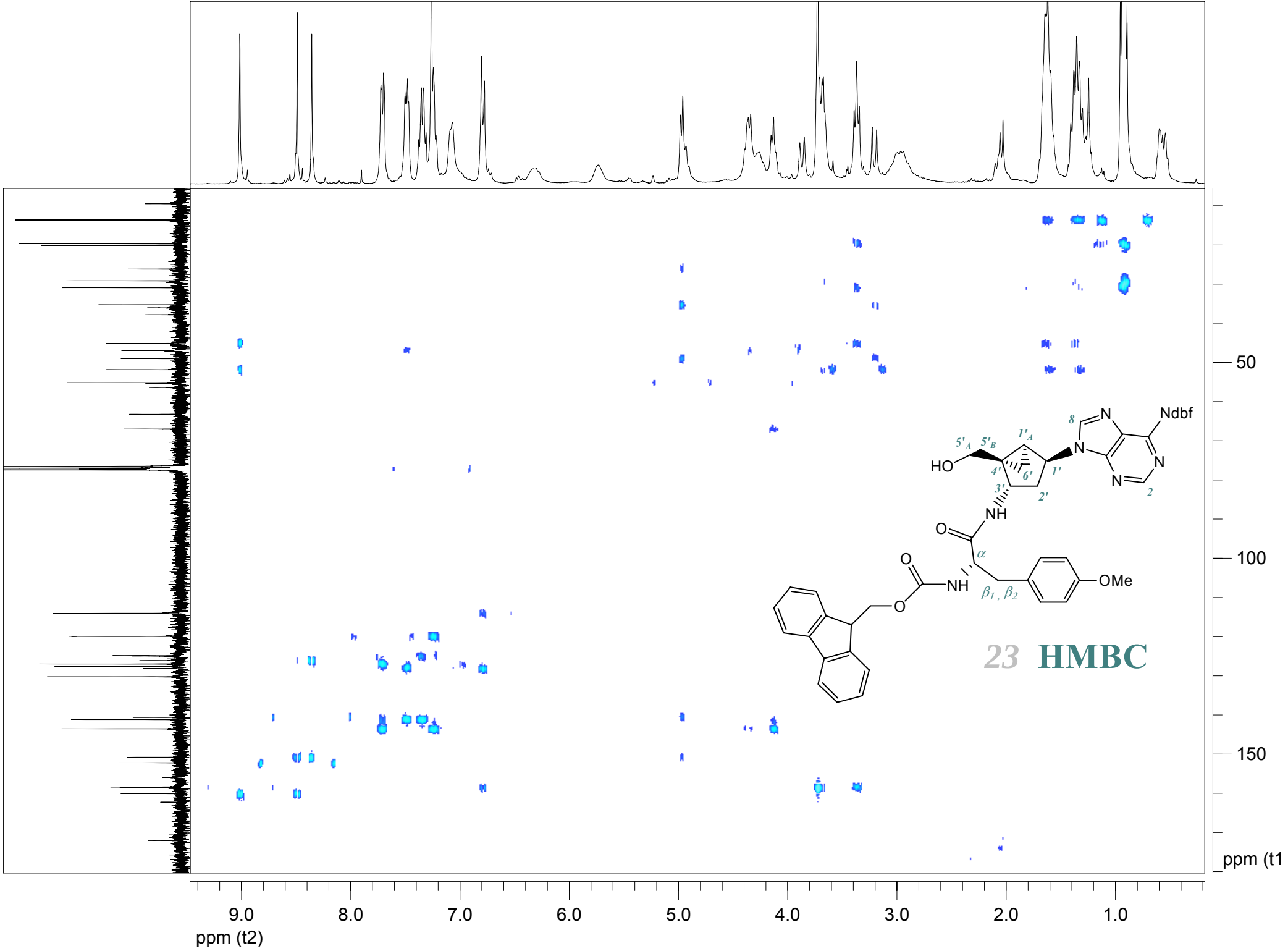
160 150 140 130 120 110
ppm (t1)

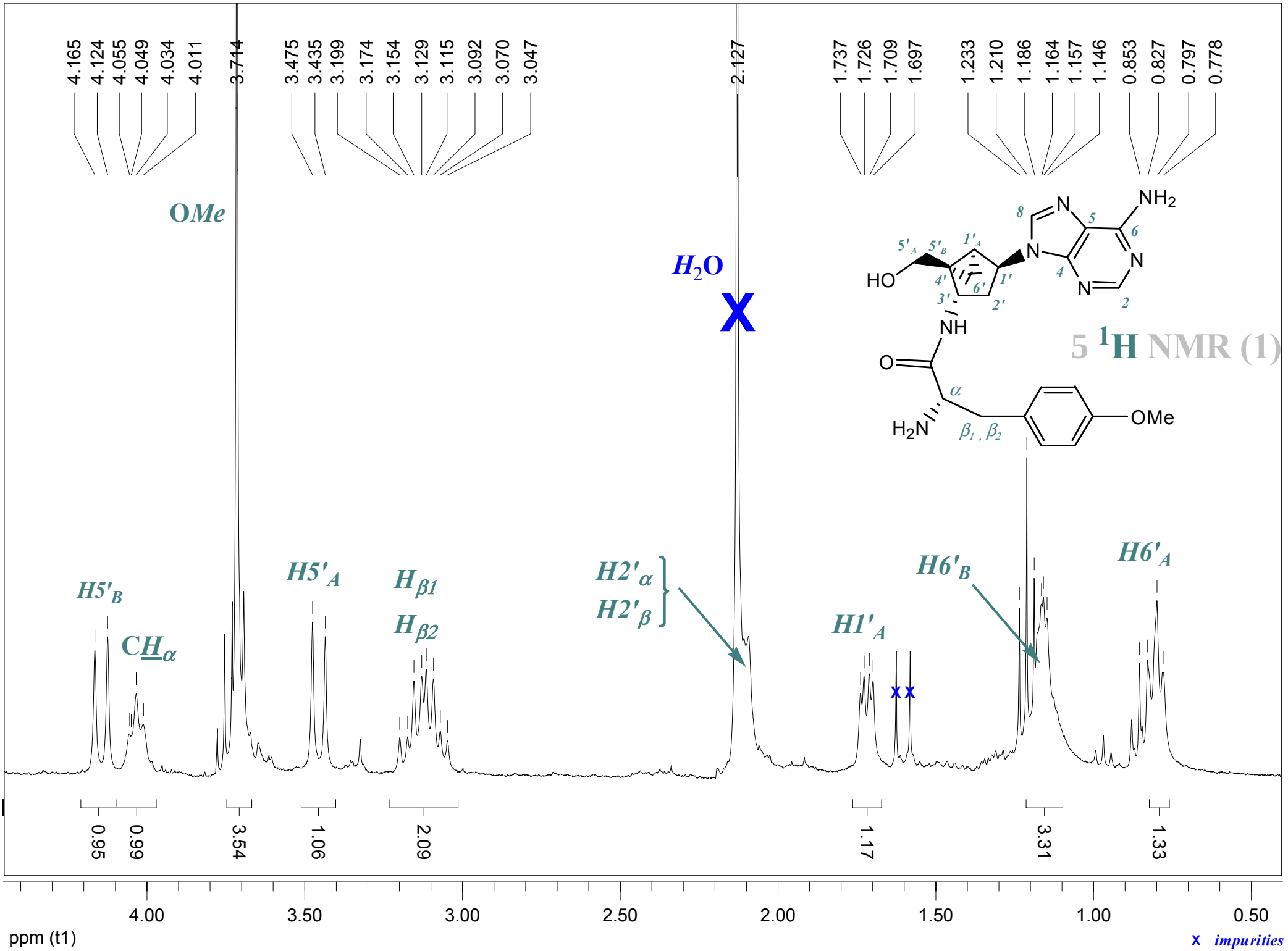

67.015
63.244
56.372
55.313
55.188
51.869
49.024
46.941
45.166
37.832
36.079
35.288
30.928
29.177
26.175
20.143
19.711
13.862
13.637
9.496
23 13C NMR (1)
Ndbf
HO
NH
OMe
OMe
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
RC(O)OCH2Fluorenyl
C5'
C3'
CHα
C1'
CH Fluorenyl
C4'
CHβ
C2'
C1'A
C6'
70
60
50
40
30
20
10
ppm (t1)

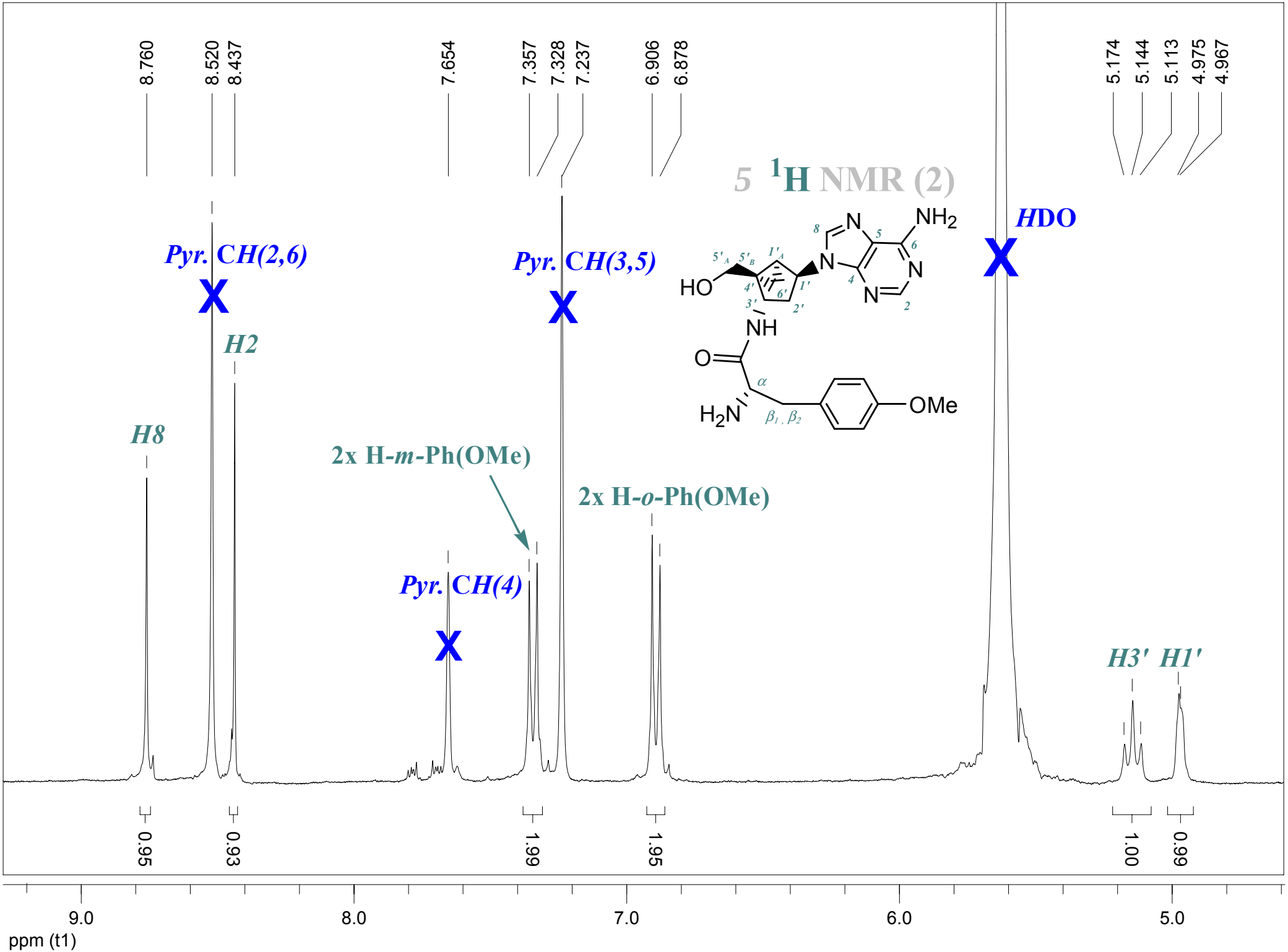

172.014
162.268
160.092
158.593
158.413
152.224
150.797
143.549
141.177
140.612
130.266
128.163
127.680
126.992
126.145
124.961
124.867
119.920
114.061
23 13C NMR (2)
Ndbf
HO
NH
O
α
NH
OMe
β1 , β2
2x C-m2-Fl
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
2x C-i-Fl
2x C-p3-Fl
2x C-o5-Fl
2x C-m4-Fl
C-i-Ph(OMe)
CH-dbf
C6
C2
C4
C8
2x C-o1-Fl
C5
RC(O)OCH2Fluorenyl
C-p-Ph(OMe)
3'-NHC(O)R
x
170
160
150
140
130
120
110
ppm (t1)
x artifact

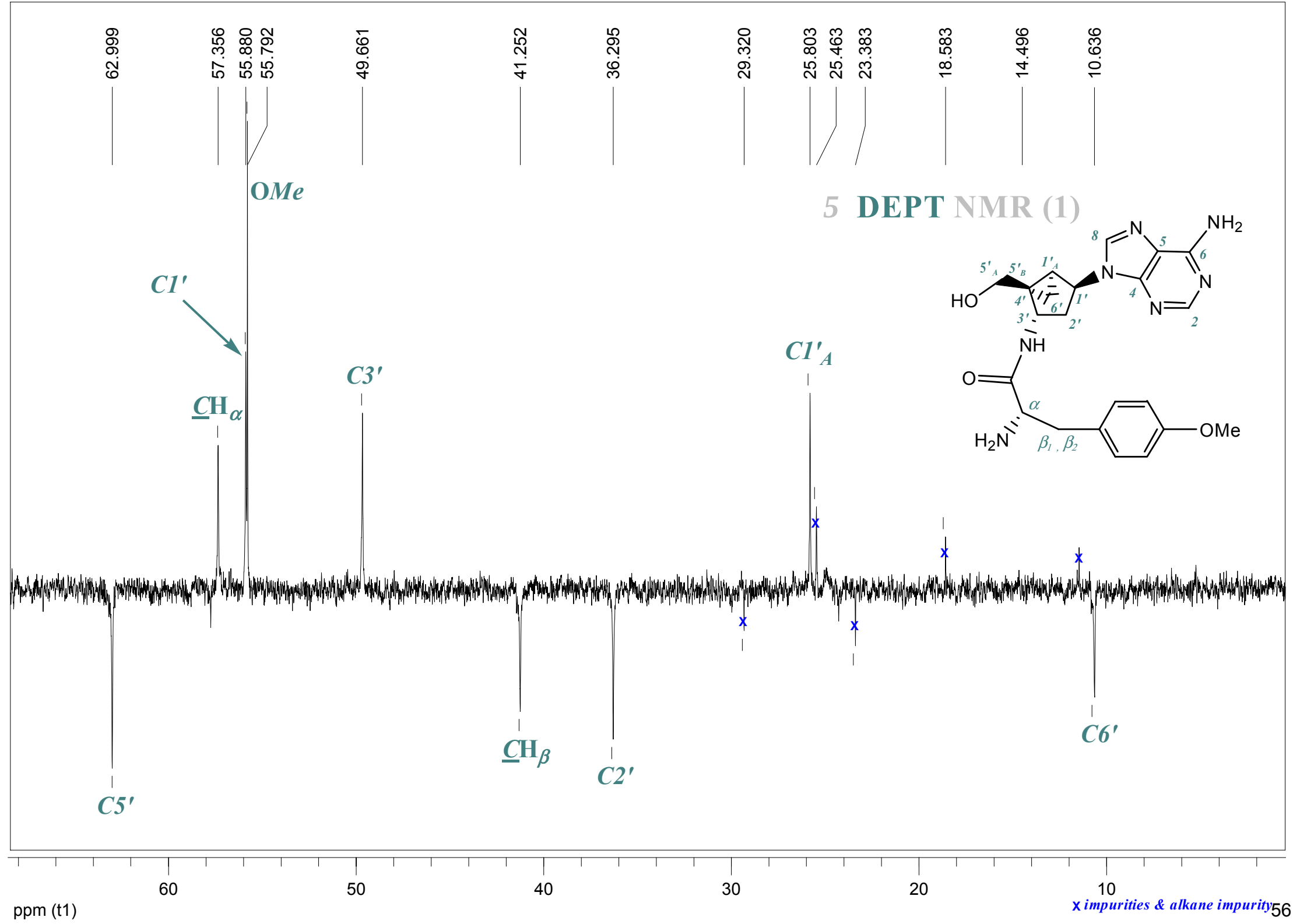

23 COSY
Ndbf
HO
NH
NH
OMe
ppm (t2)
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0


9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
50
100
150
ppm (t1
HO
Ndbf
NH
O
OMe
23 HSQC

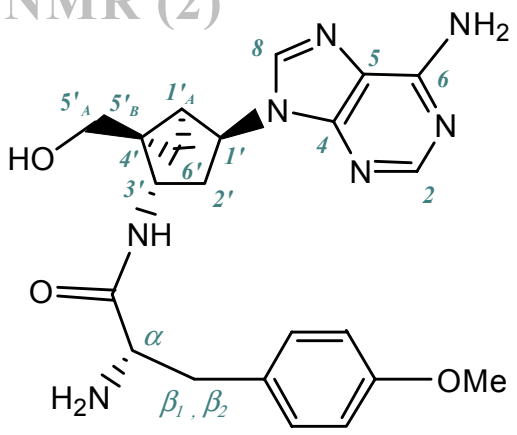

Ndbf
HO
NH
O
NH
O
O
OMe
23 HMBC
50
100
150
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)


4.165
4.124
4.055
4.049
4.034
4.011
3.714
3.475
3.435
3.199
3.174
3.154
3.129
3.115
3.092
3.070
3.047
2.127
1.737
1.726
1.709
1.697
1.233
1.210
1.186
1.164
1.157
1.146
0.853
0.827
0.797
0.778
OMe
H2O
5 1H NMR (1)
H5'B
CHα
H5'A
Hβ1
Hβ2
H2'α
H2'β
H1'A
H6'B
H6'A
0.95
0.99
3.54
1.06
2.09
1.17
3.31
1.33
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)
x impurities


8.760
8.520
8.437
7.654
7.357
7.328
7.237
6.906
6.878
5.174
5.144
5.113
4.975
4.967
5 1H NMR (2)
Pyr. CH(2,6)
H2
Pyr. CH(3,5)
HDO
H8
2x H-m-Ph(OMe)
2x H-o-Ph(OMe)
Pyr. CH(4)
H3' H1'
0.95
0.93
1.99
1.95
1.00
0.99
9.0
8.0
7.0
6.0
5.0
ppm (t1)


62.999
57.356
55.880
55.792
49.661
41.252
36.295
29.320
25.803
25.463
23.383
18.583
14.496
10.636
OMe
C1'
CHα
C3'
C1'A
C5'
CHβ
C2'
C6'
5 DEPT NMR (1)
NH2
HO
NH
O
OMe
H2N
60
50
40
30
20
10
ppm (t1)
x impurities & alkane impurity

5 DEPT NMR (2)



152.965 149.513 139.921 137.400 131.381 124.673 114.709

2x C-*m*-Ph(OMe)

2x C-*o*-Ph(OMe)

Pyr. CH(3,5)

Pyr. CH(2,6)

Pyr. CH(4)

C2

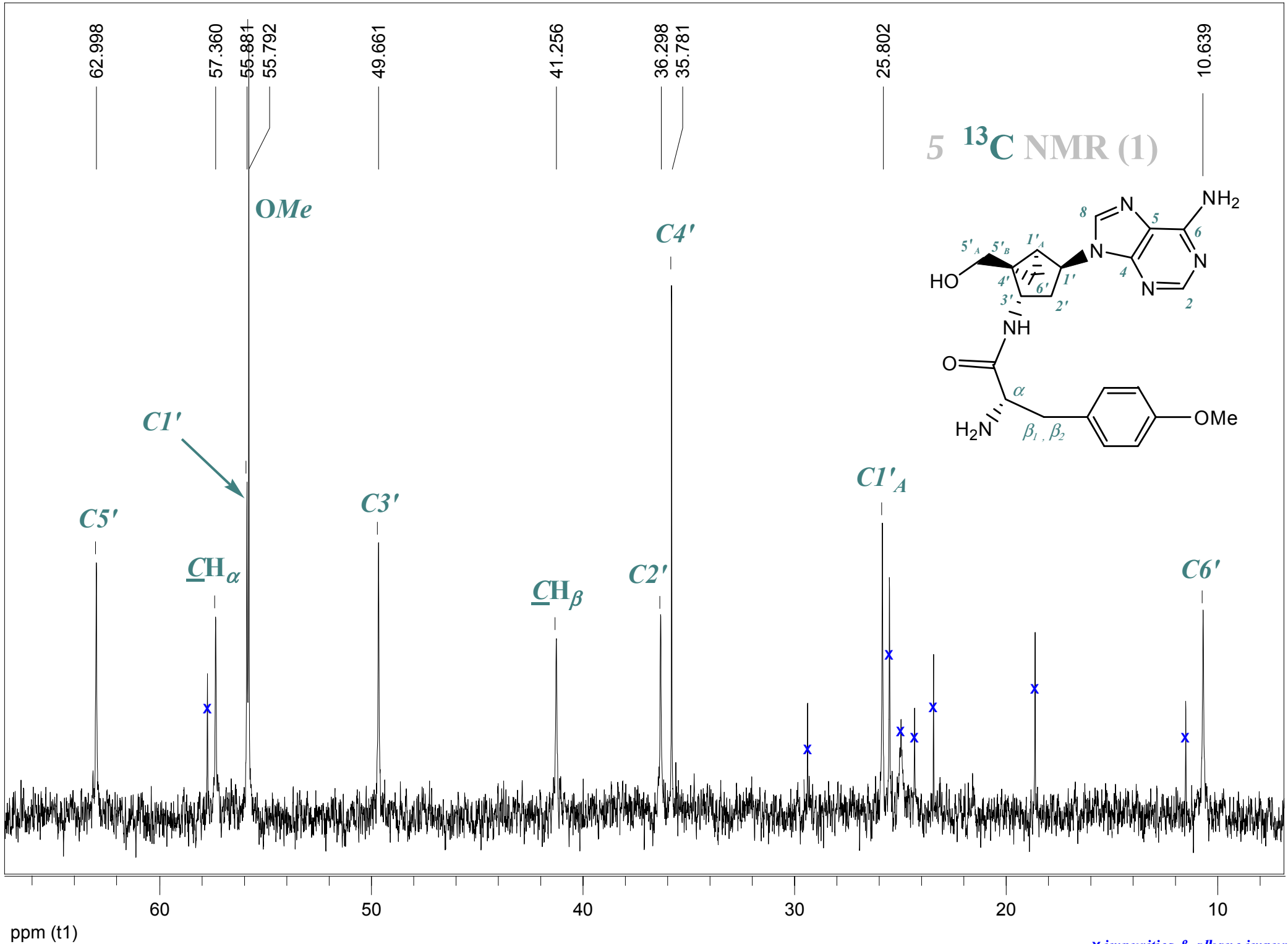
C8

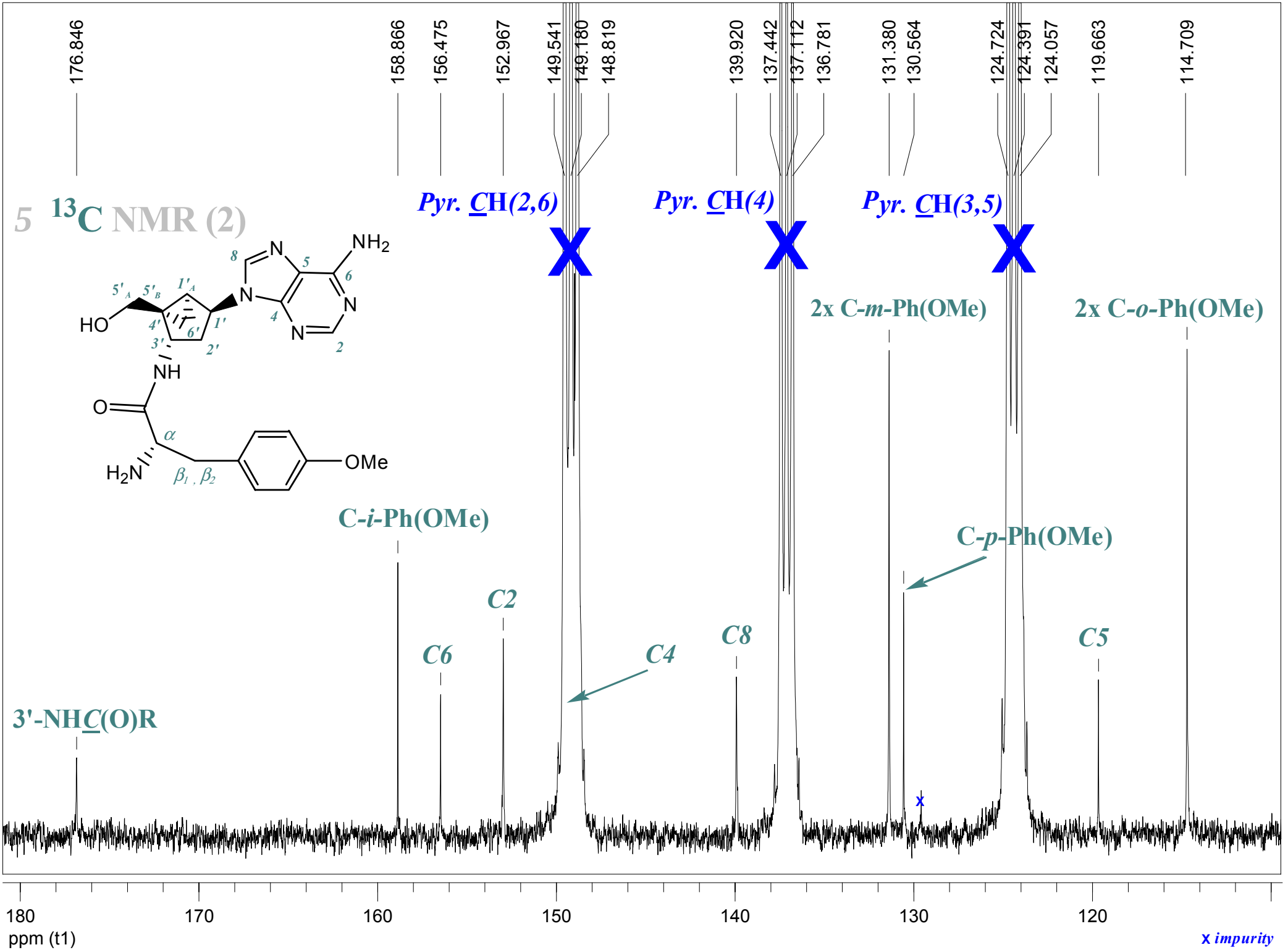
x

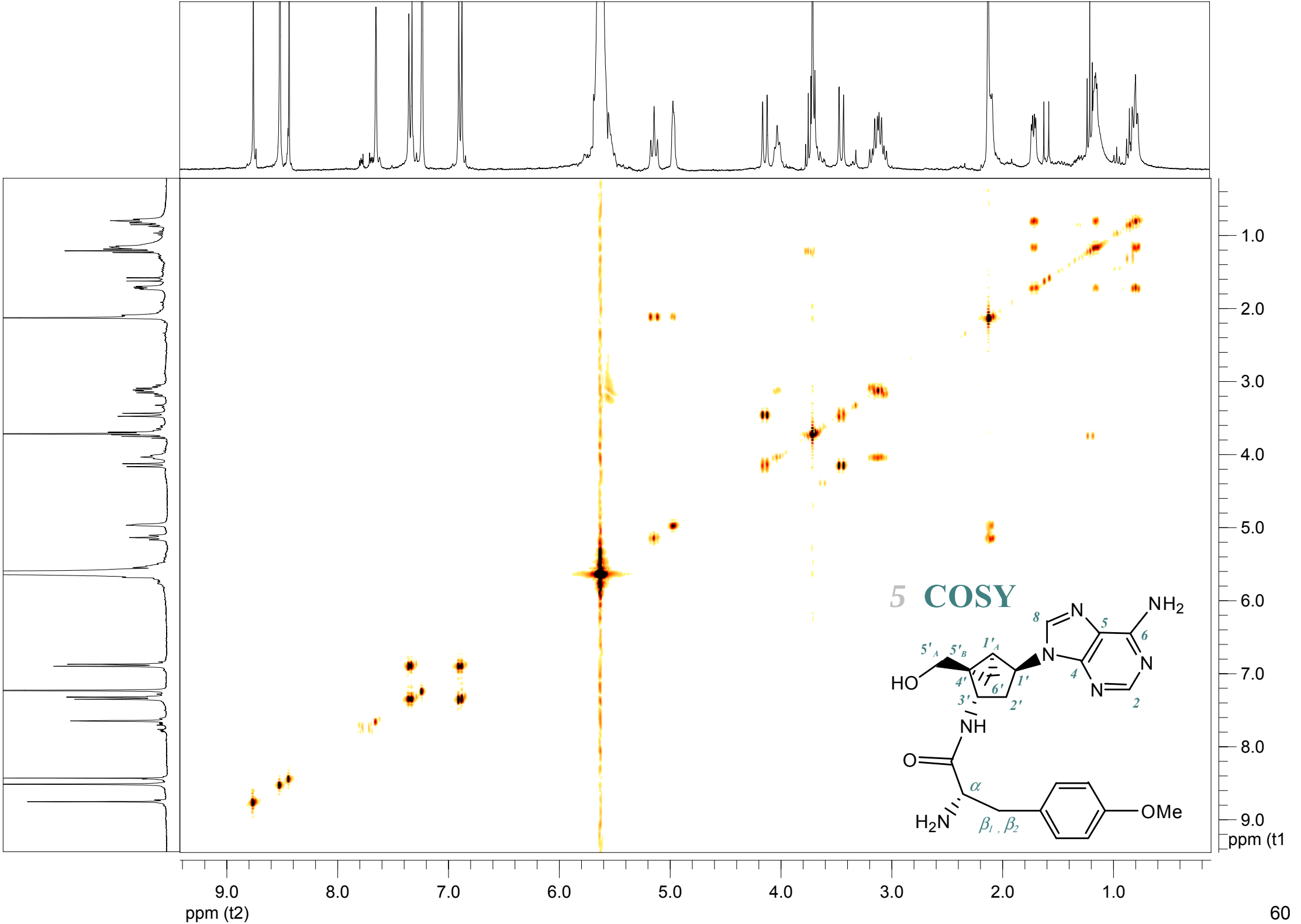
160 150 140 130 120 110 100

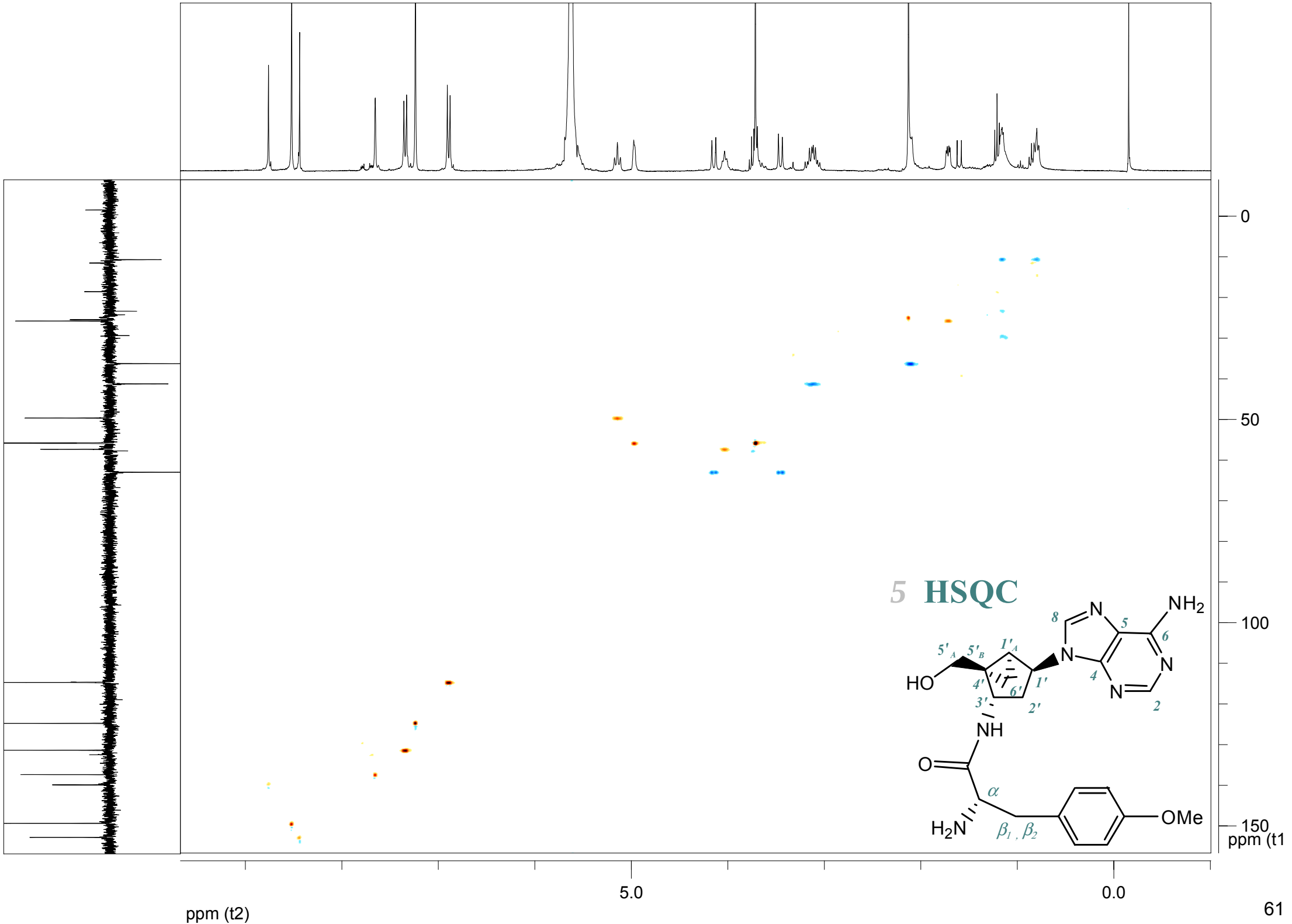
ppm (t1)

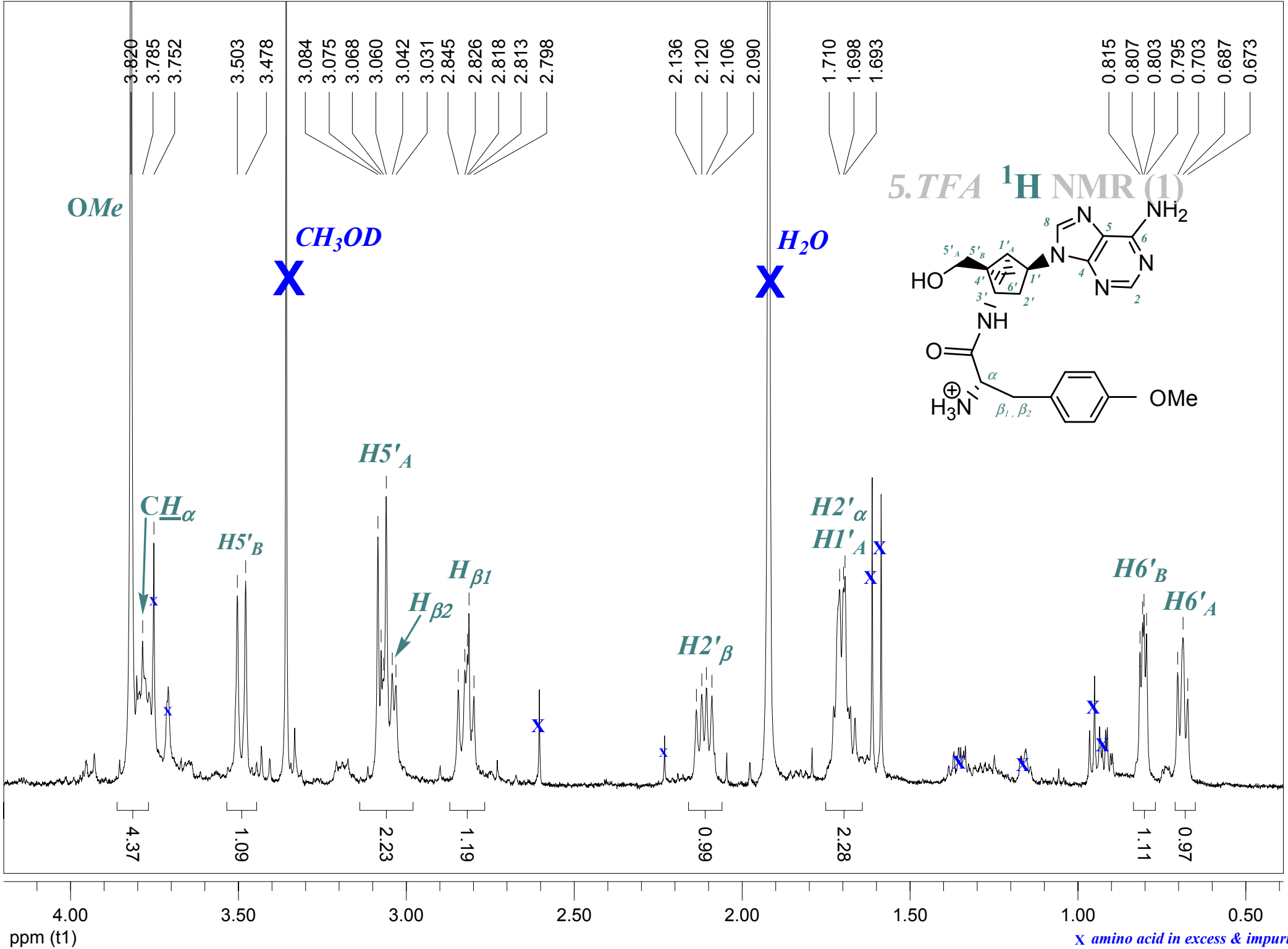
x *impurity*

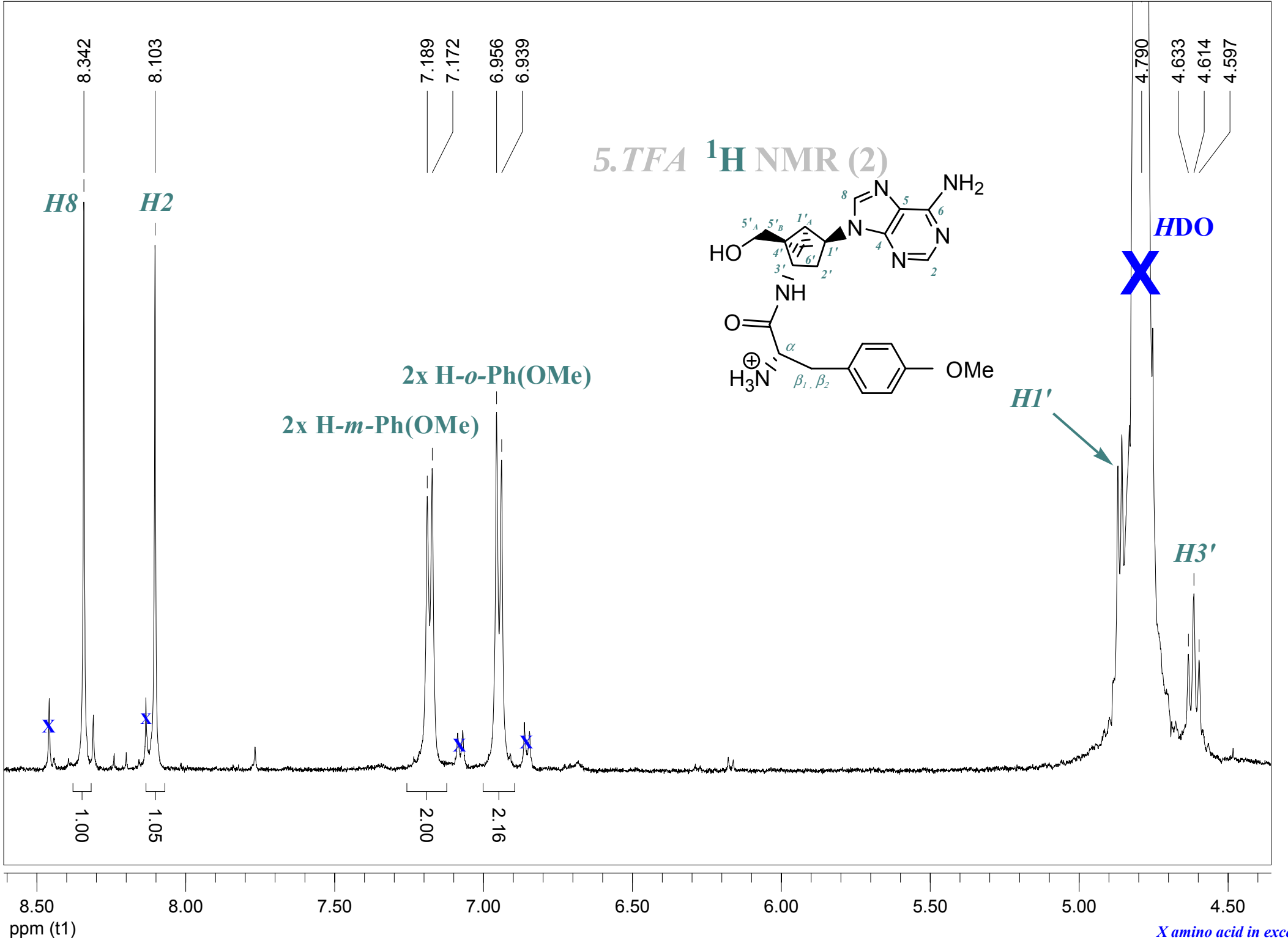

62.998
57.360
55.881
55.792
49.661
41.256
36.298
35.781
25.802
10.639
5 13C NMR (1)
OMe
C4'
C1'
C5'
C3'
CHα
CHβ
C2'
C1'A
C6'
NH2
HO
NH
O
OMe
H2N
60
50
40
30
20
10
ppm (t1)
x impurities & alkane impurity

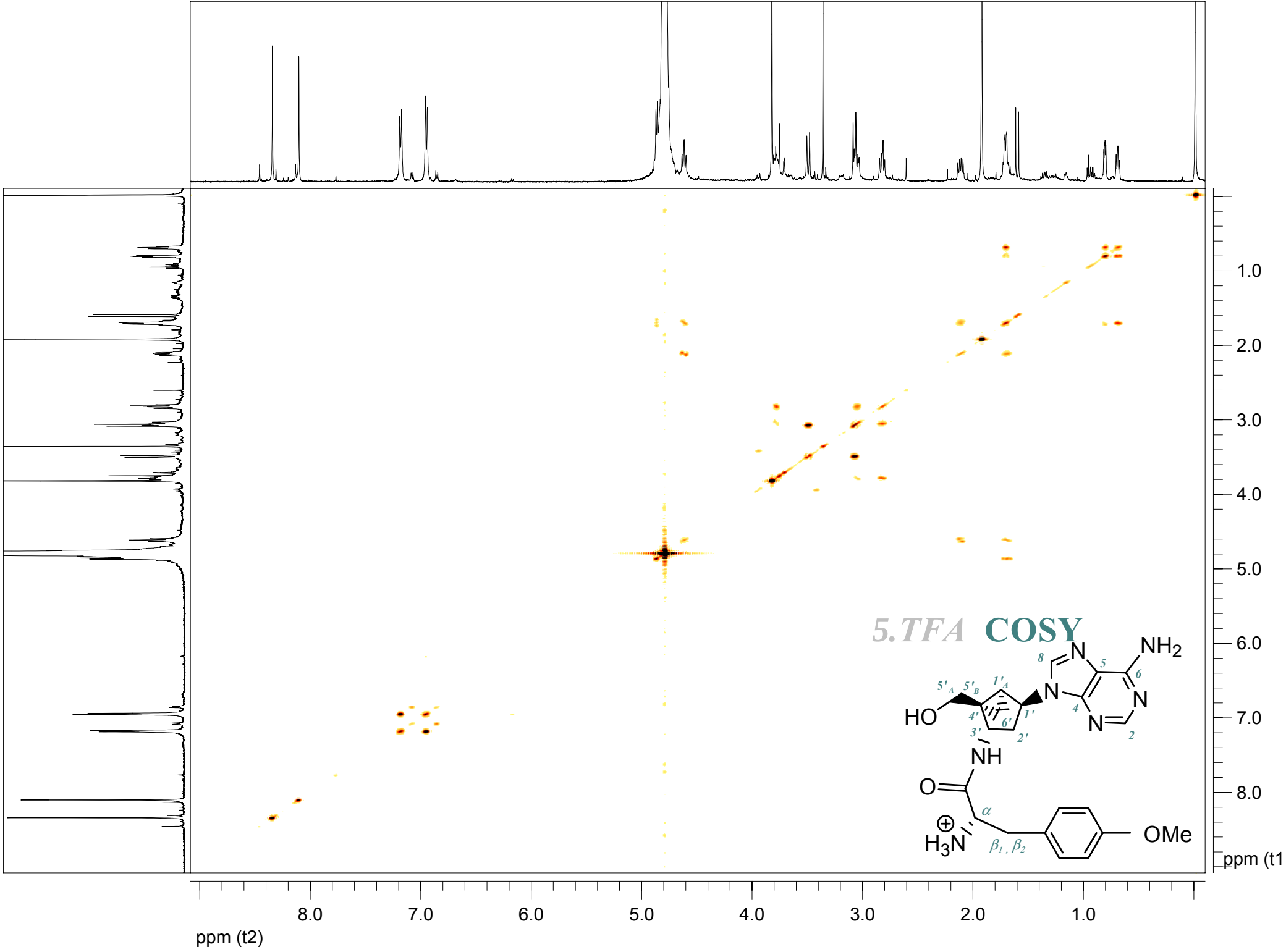

176.846
158.866
156.475
152.967
149.541
149.180
148.819
139.920
137.442
137.112
136.781
131.380
130.564
124.724
124.391
124.057
119.663
114.709
5 13C NMR (2)
Pyr. CH(2,6)
Pyr. CH(4)
Pyr. CH(3,5)
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
C-i-Ph(OMe)
C-p-Ph(OMe)
C2
C6
C4
C8
C5
3'-NHC(O)R
x
180
170
160
150
140
130
120
ppm (t1)
x impurity

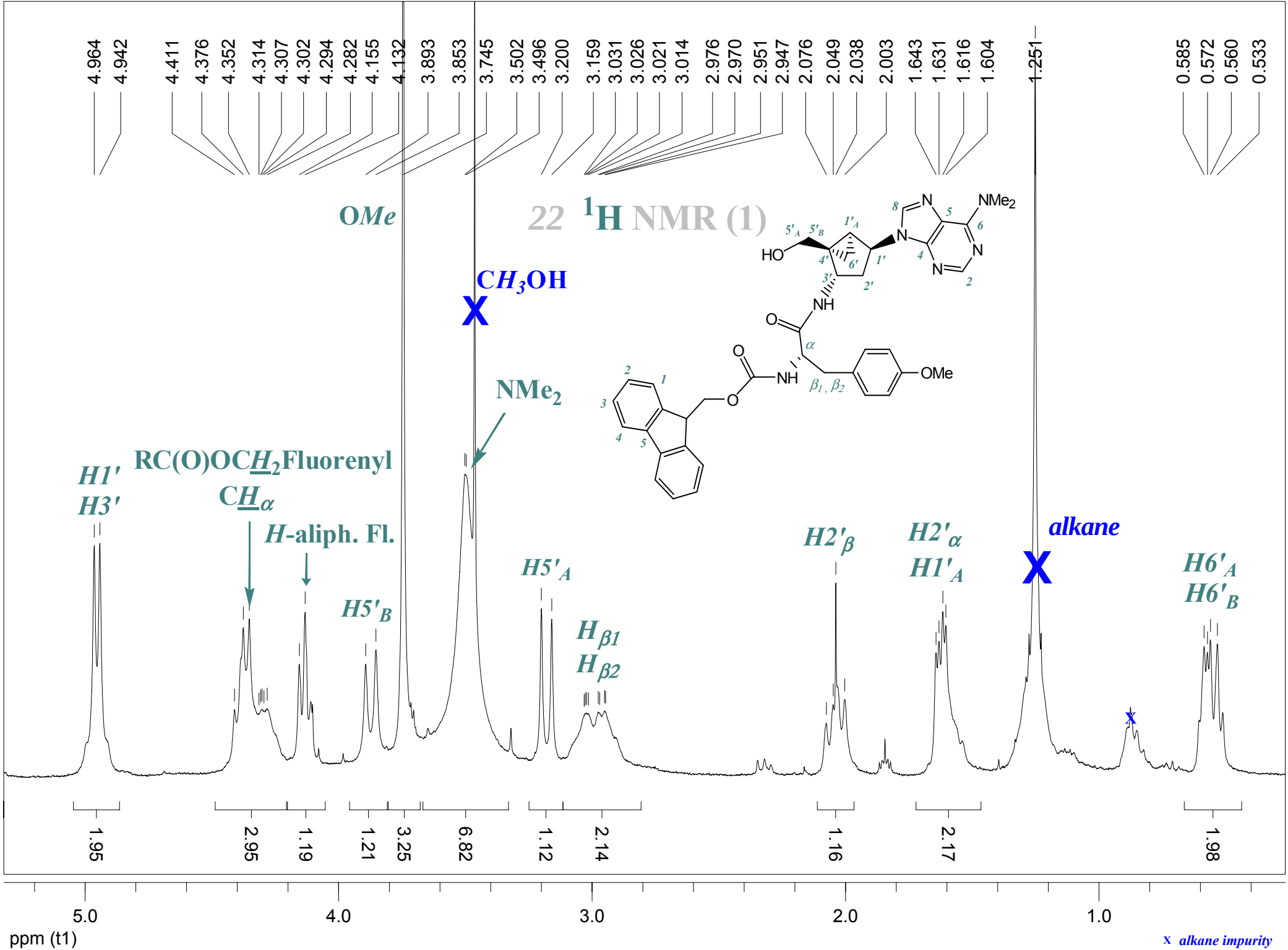

5 COSY
NH2
N
HO
NH
O
OMe
H2N
α
β1 , β2
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
ppm (t1

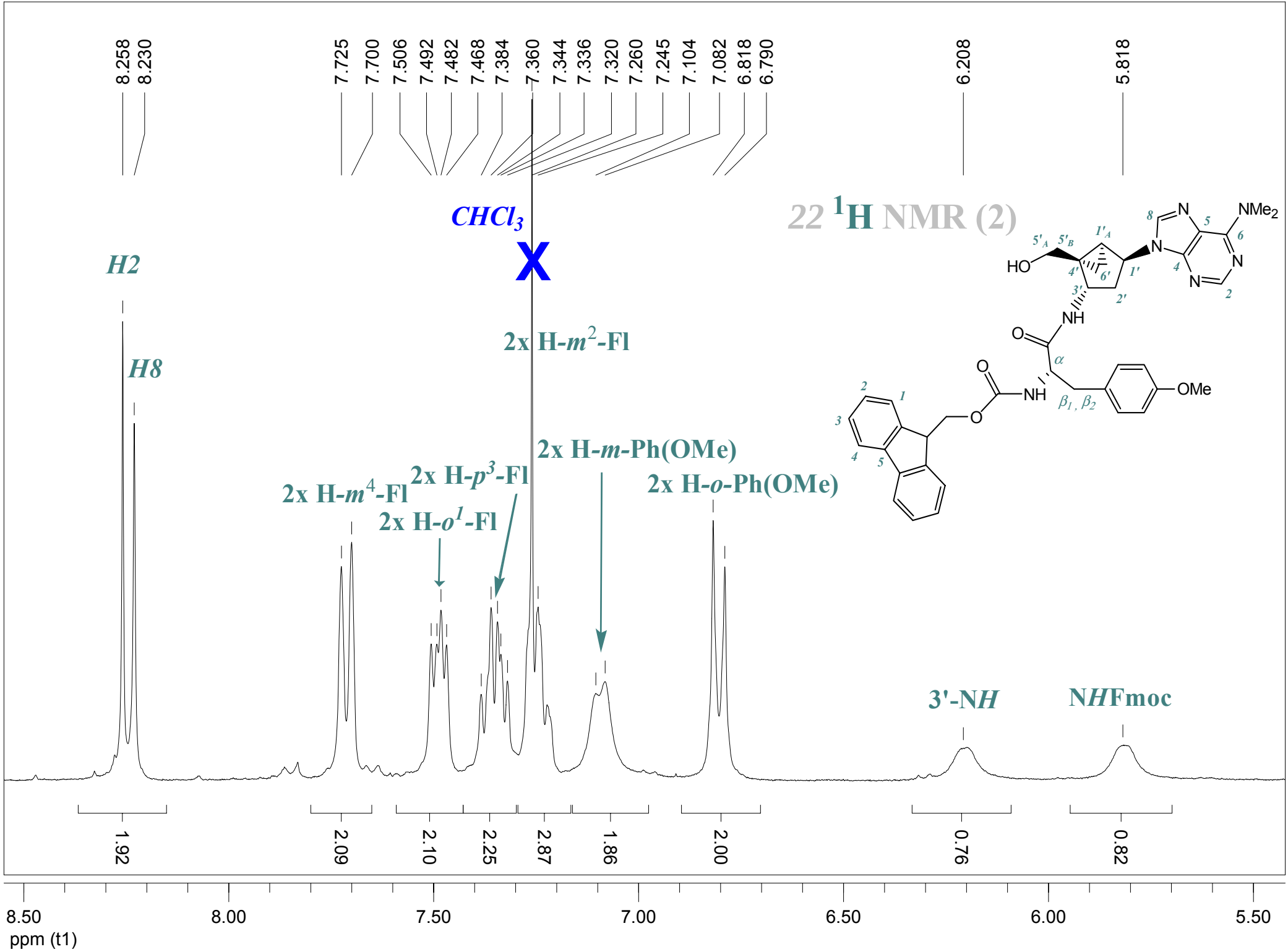

5 HSQC
0
50
100
150
ppm (t1
5.0
0.0
ppm (t2)
NH2
N
HO
NH
O
OMe
H2N

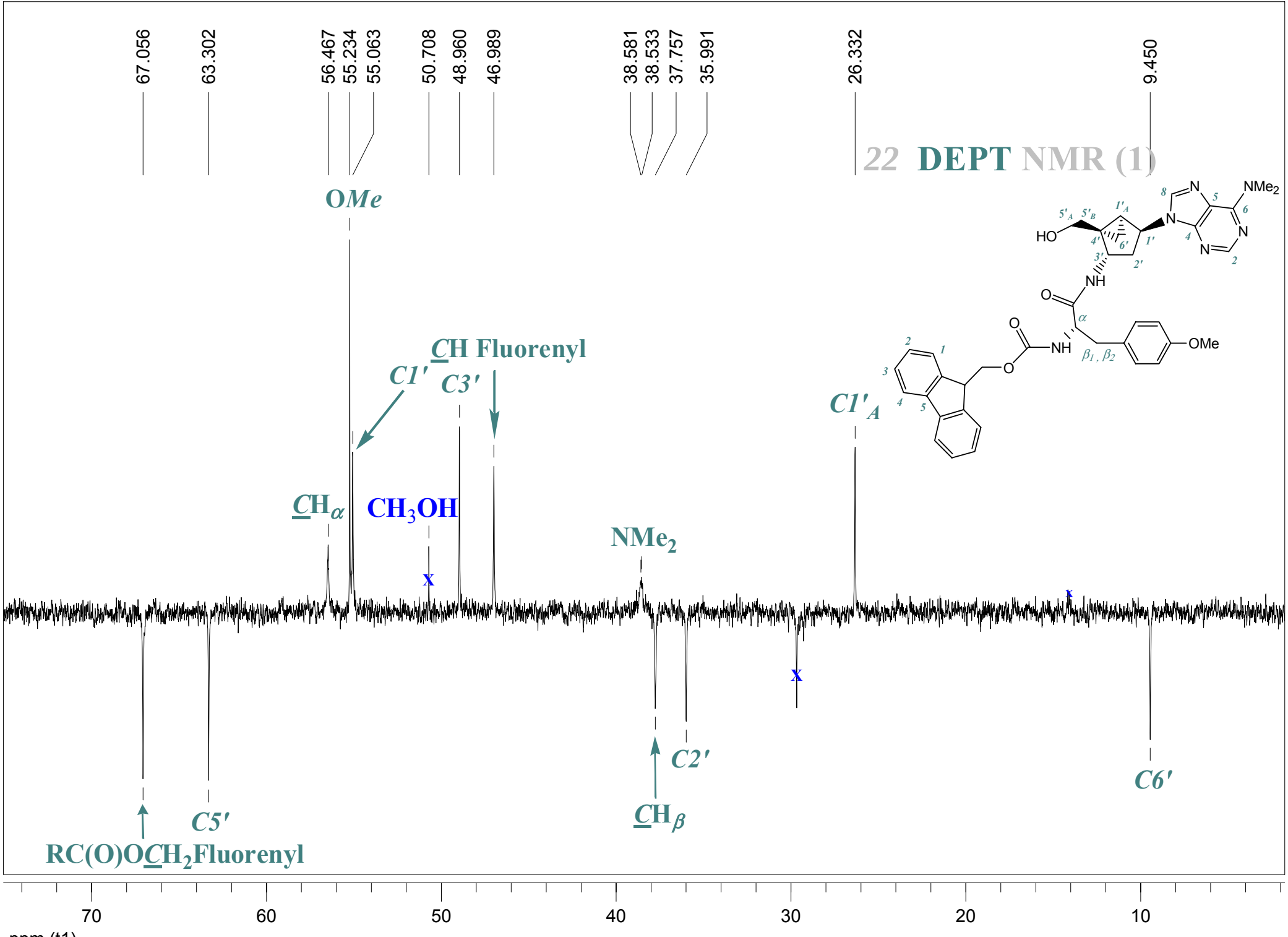

3.820
3.785
3.752
3.503
3.478
3.084
3.075
3.068
3.060
3.042
3.031
2.845
2.826
2.818
2.813
2.798
2.136
2.120
2.106
2.090
1.710
1.698
1.693
0.815
0.807
0.803
0.795
0.703
0.687
0.673
OMe
CH3OD
H2O
5.TFA 1H NMR (1)
CHα
H5'B
H5'A
Hβ1
Hβ2
H2'β
H2'α
H1'A
H6'B
H6'A
4.37
1.09
2.23
1.19
0.99
2.28
1.11
0.97
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)
x amino acid in excess & impurities

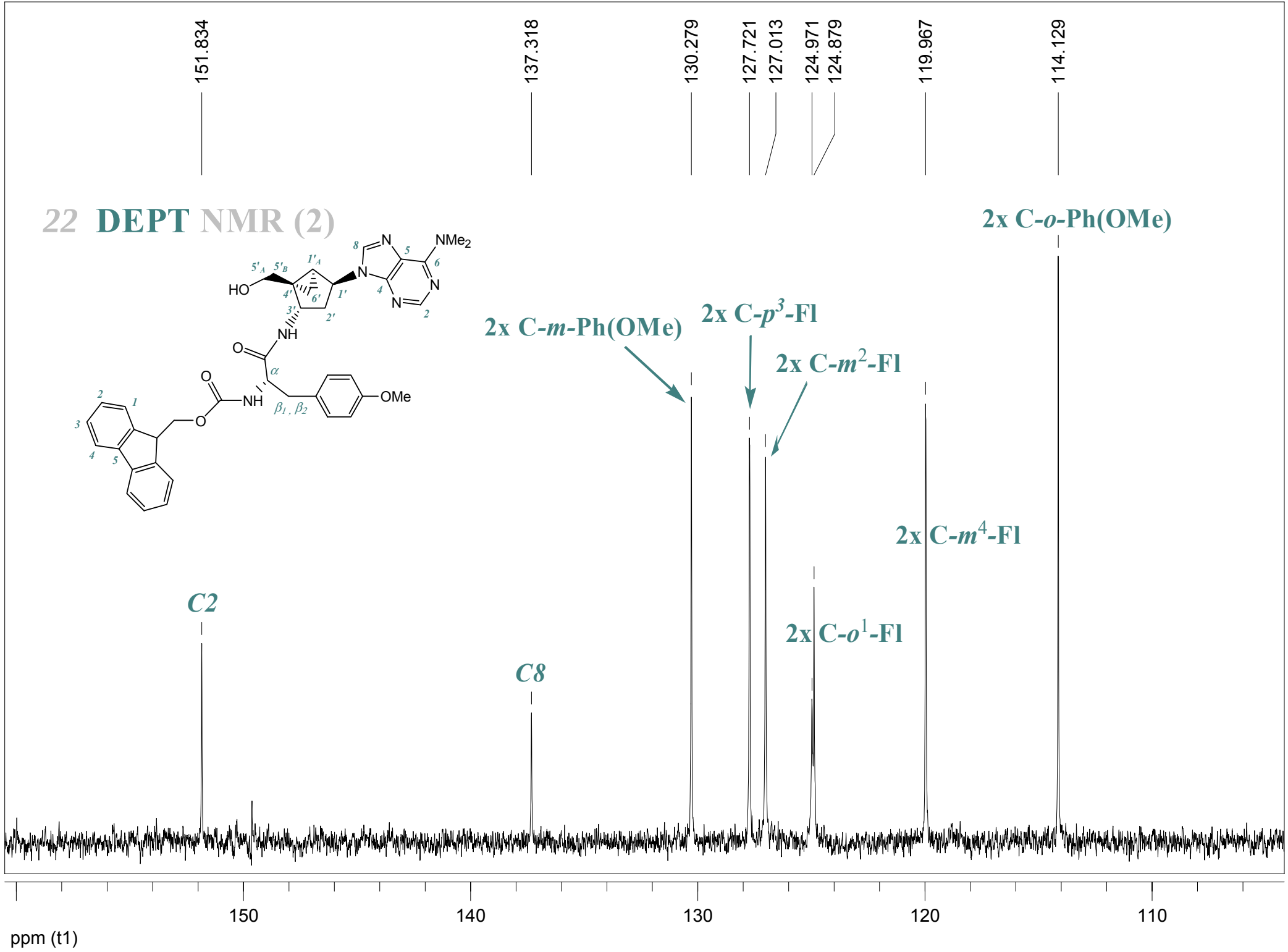

5. TFA 1H NMR (2)
8.342
8.103
7.189
7.172
6.956
6.939
4.790
4.633
4.614
4.597
H8
H2
HDO
2x H-o-Ph(OMe)
2x H-m-Ph(OMe)
H1'
H3'
1.00
1.05
2.00
2.16
8.50
8.00
7.50
7.00
6.50
6.00
5.50
5.00
4.50
ppm (t1)
X amino acid in excess

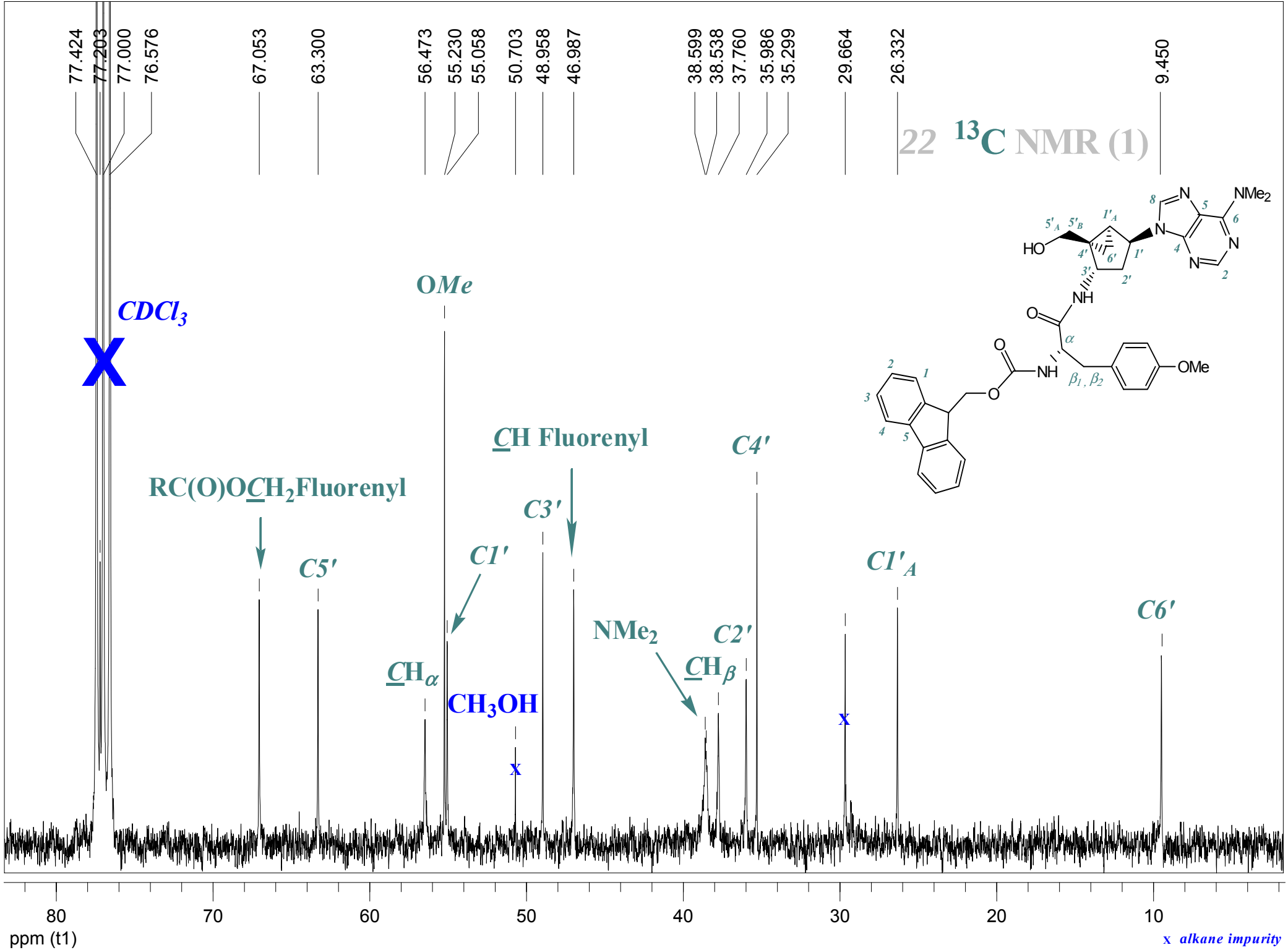

5.TFA COSY
NH2
HO
NH
O
OMe
ppm (t2)
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0

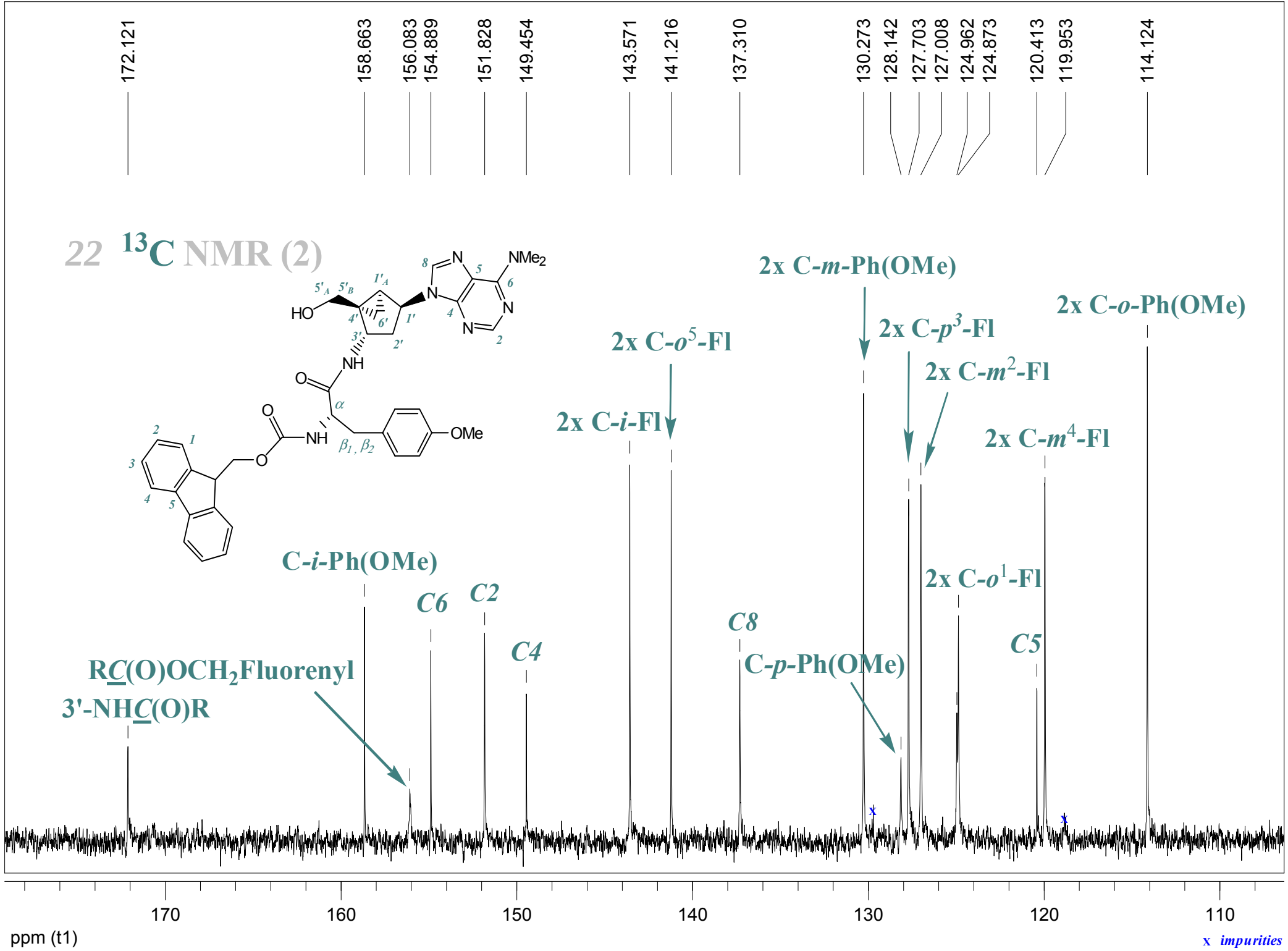

4.964
4.942
4.411
4.376
4.352
4.314
4.307
4.302
4.294
4.282
4.155
4.132
3.893
3.853
3.745
3.502
3.496
3.200
3.159
3.031
3.026
3.021
3.014
2.976
2.970
2.951
2.947
2.076
2.049
2.038
2.003
1.643
1.631
1.616
1.604
1.251
0.585
0.572
0.560
0.533
OMe
22 1H NMR (1)
CH3OH
NMe2
H1'
H3'
RC(O)OCH2Fluorenyl
CHα
H-aliph. Fl.
H5'B
H5'A
Hβ1
Hβ2
H2'β
H2'α
H1'A
alkane
H6'A
H6'B
1.95
2.95
1.19
1.21
3.25
6.82
1.12
2.14
1.16
2.17
1.98
5.0
4.0
3.0
2.0
1.0
ppm (t1)
x alkane impurity

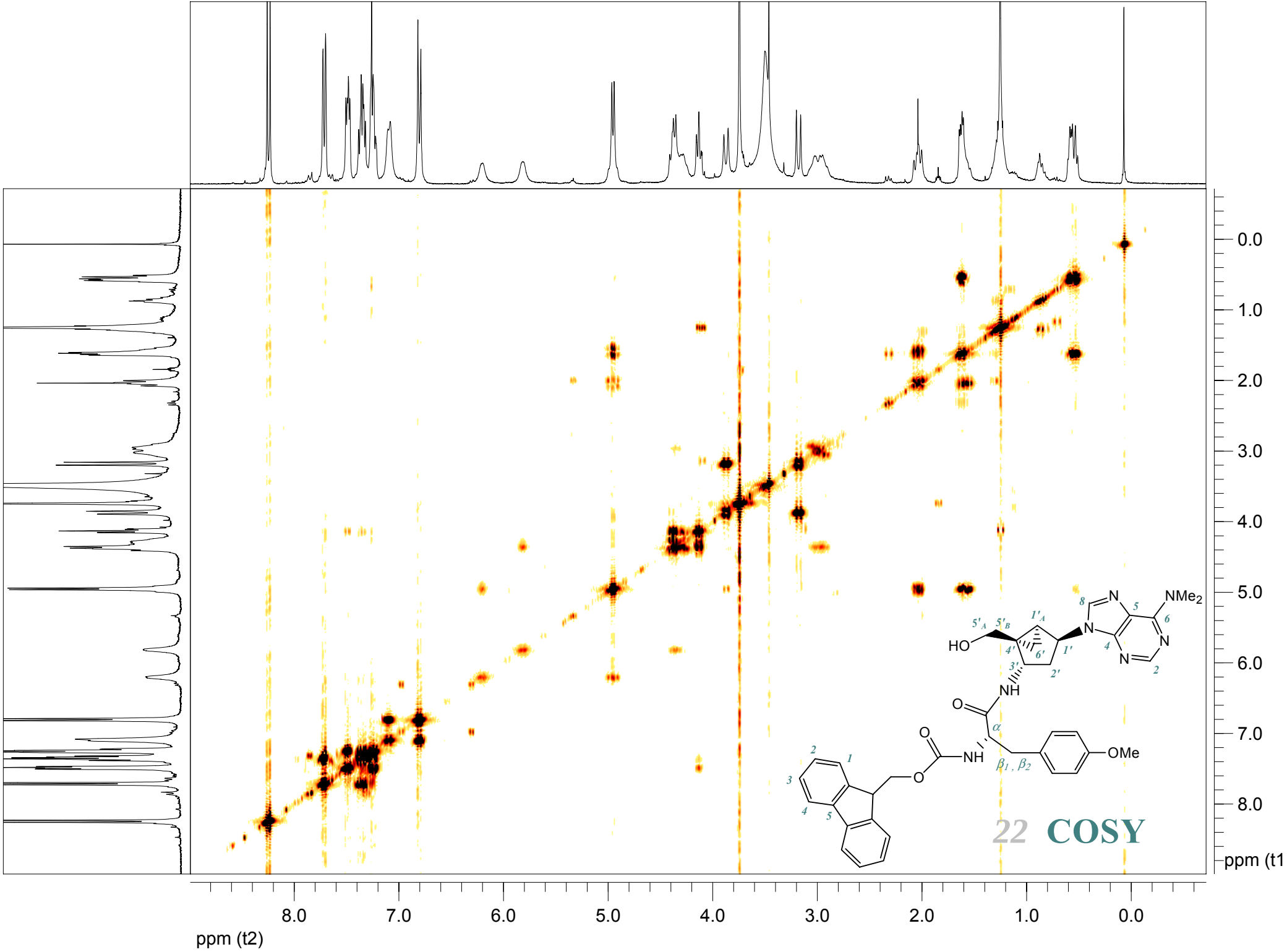

8.258
8.230
7.725
7.700
7.506
7.492
7.482
7.468
7.384
7.360
7.344
7.336
7.320
7.260
7.245
7.104
7.082
6.818
6.790
6.208
5.818
22 1H NMR (2)
CHCl3
H2
H8
2x H-m2-Fl
2x H-m4-Fl
2x H-p3-Fl
2x H-o1-Fl
2x H-m-Ph(OMe)
2x H-o-Ph(OMe)
3'-NH
NHFmoc
1.92
2.09
2.10
2.25
2.87
1.86
2.00
0.76
0.82
8.50
8.00
7.50
7.00
6.50
6.00
5.50
ppm (t1)

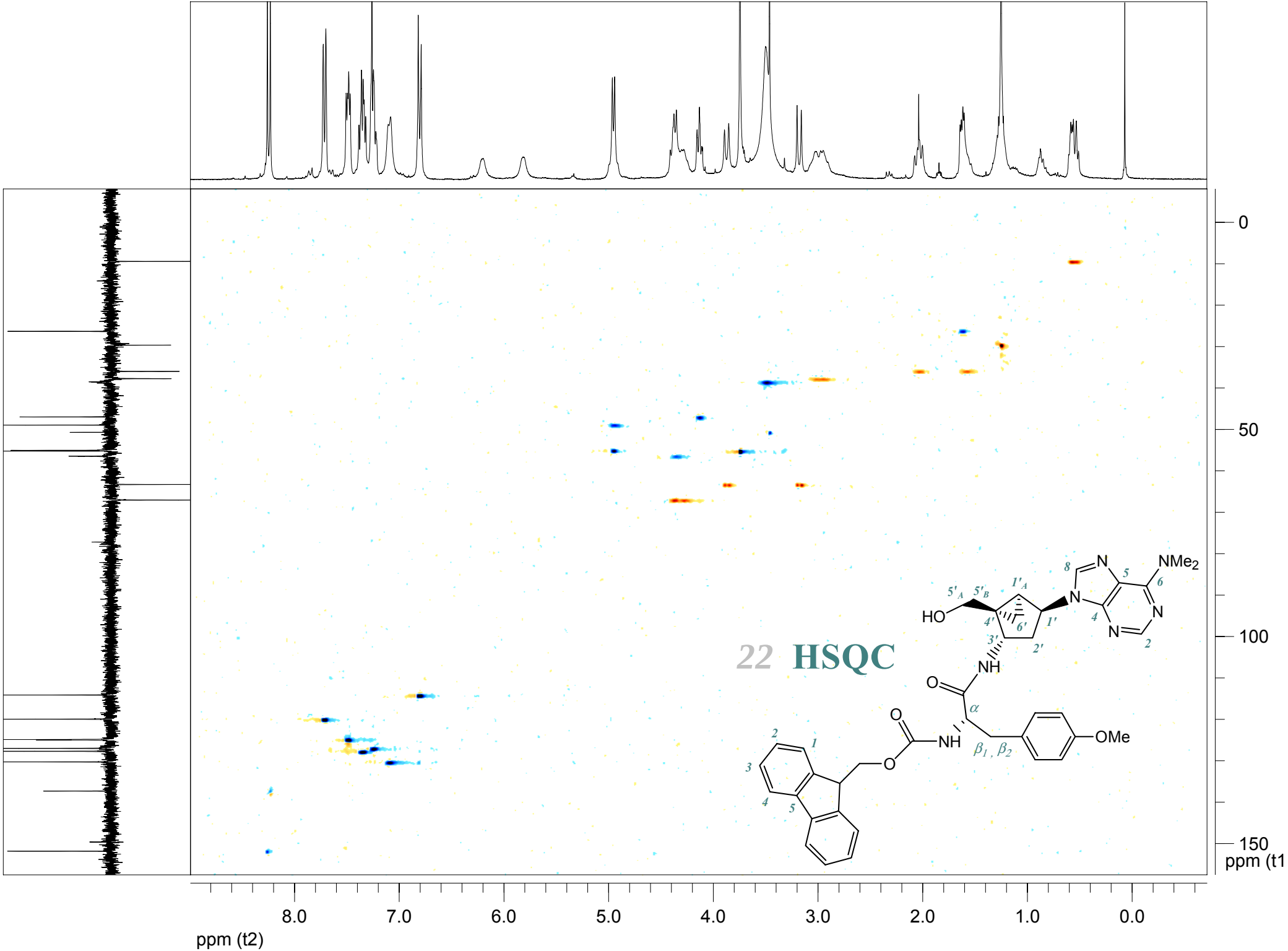

67.056
63.302
56.467
55.234
55.063
50.708
48.960
46.989
38.581
38.533
37.757
35.991
26.332
9.450
22 DEPT NMR (1)
OMe
CH Fluorenyl
C1'
C3'
CHα
CH3OH
NMe2
C1'A
C2'
C5'
CHβ
C6'
RC(O)OCH2Fluorenyl
70
60
50
40
30
20
10
ppm (t1)
x alkane impurity

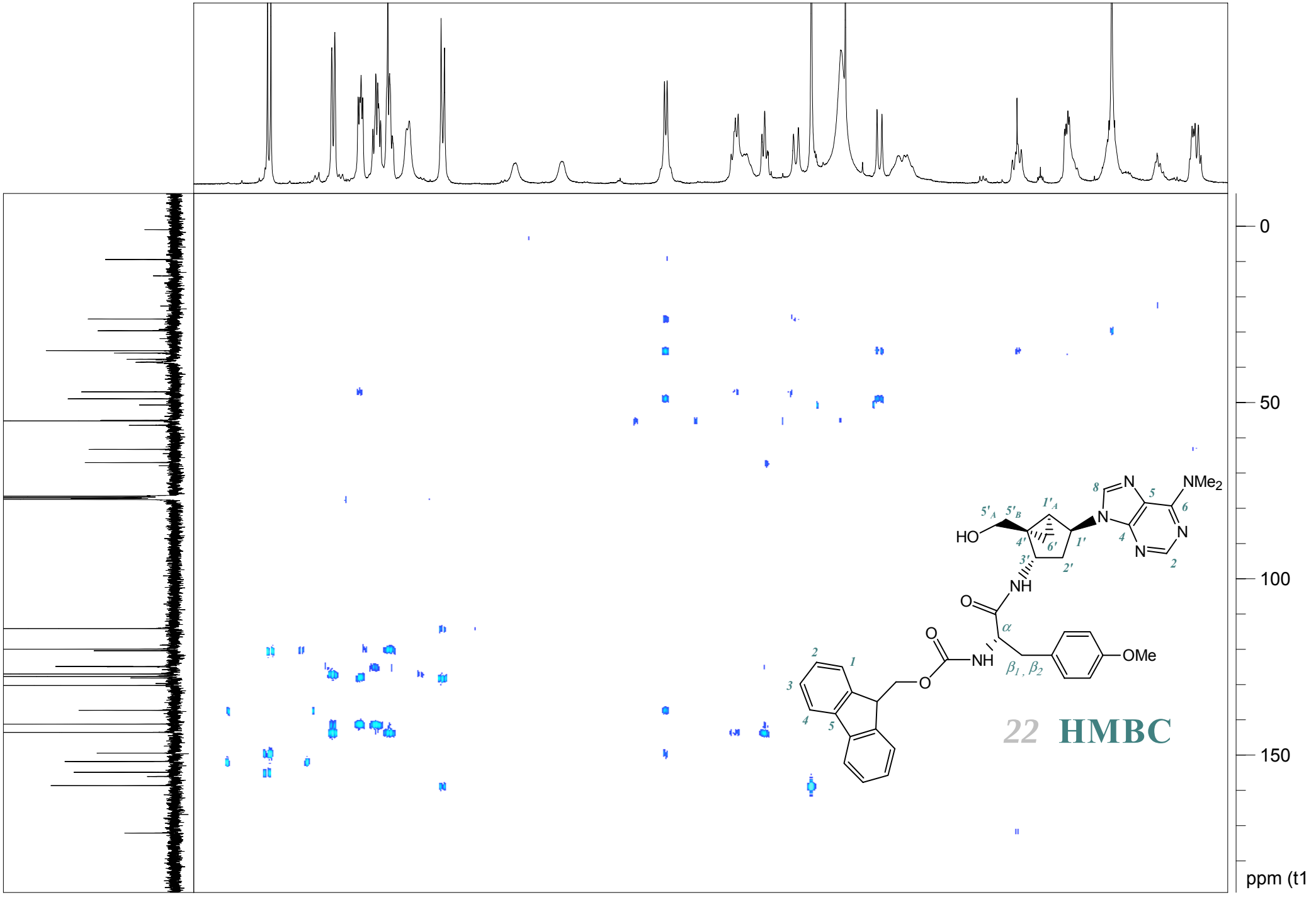

151.834
137.318
130.279
127.721
127.013
124.971
124.879
119.967
114.129
22 DEPT NMR (2)
2x C-o-Ph(OMe)
2x C-m-Ph(OMe)
2x C-p3-Fl
2x C-m2-Fl
2x C-m4-Fl
2x C-o1-Fl
C2
C8
NMe2
HO
NH
OMe
150
140
130
120
110
ppm (t1)

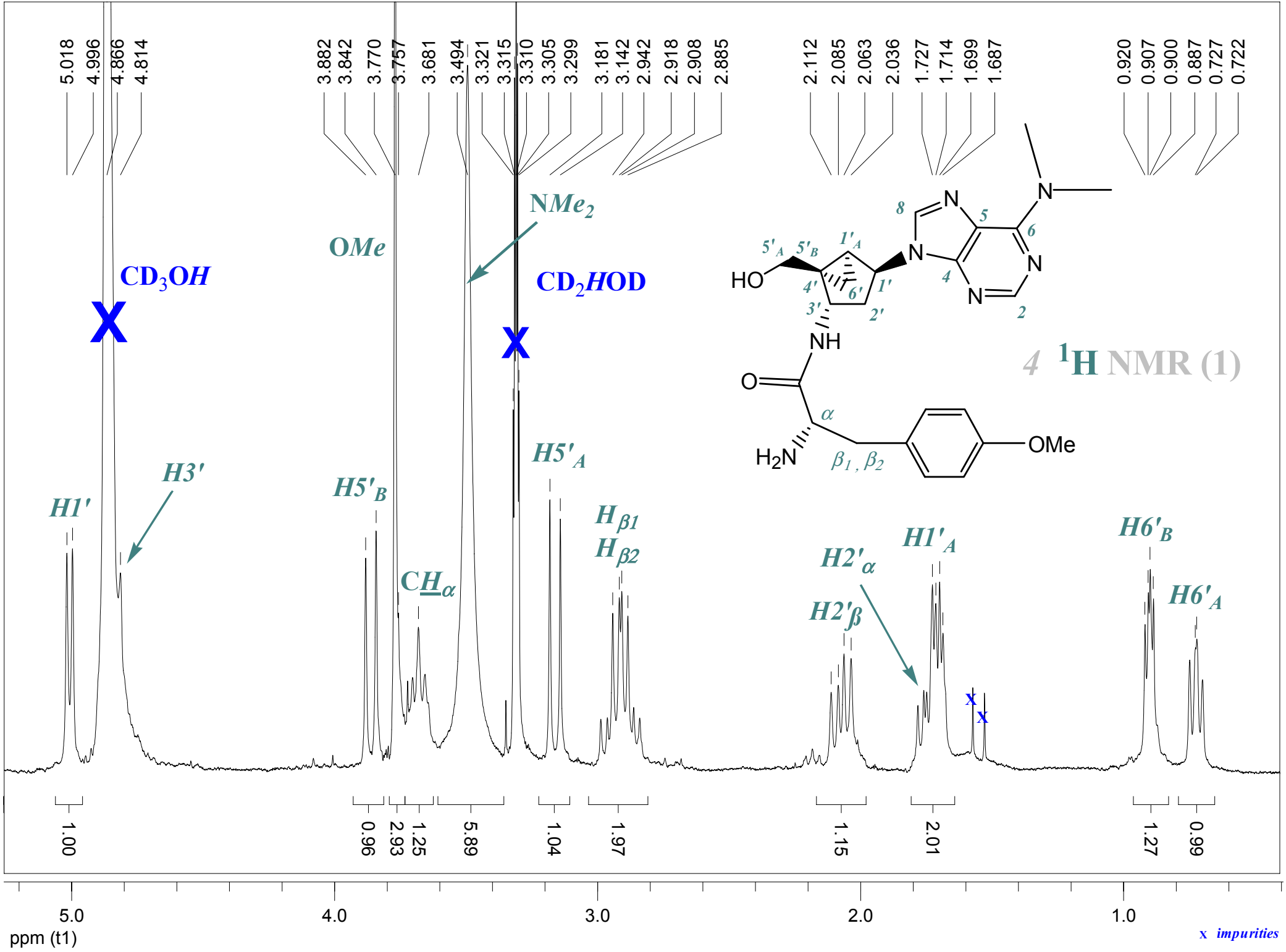

77.424
77.203
77.000
76.576
67.053
63.300
56.473
55.230
55.058
50.703
48.958
46.987
38.599
38.538
37.760
35.986
35.299
29.664
26.332
9.450
22 13C NMR (1)
CDCl3
OMe
CH Fluorenyl
C4'
RC(O)OCH2Fluorenyl
C3'
C5'
C1'
C1'A
C6'
NMe2
C2'
CHα
CHβ
CH3OH
x
x
80
70
60
50
40
30
20
10
ppm (t1)
x alkane impurity

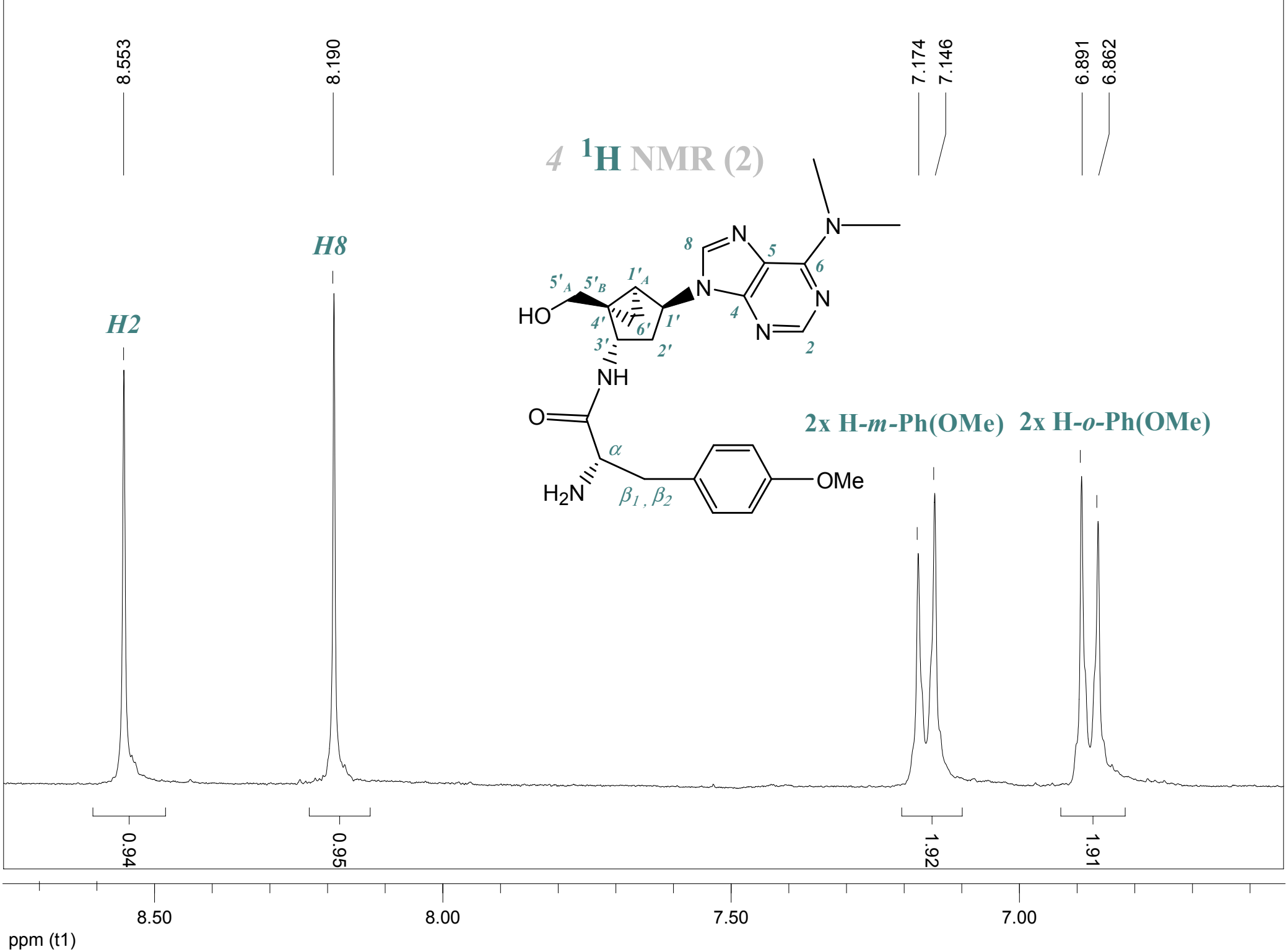

172.121
158.663
156.083
154.889
151.828
149.454
143.571
141.216
137.310
130.273
128.142
127.703
127.008
124.962
124.873
120.413
119.953
114.124
22 13C NMR (2)
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
2x C-p3-Fl
2x C-o5-Fl
2x C-m2-Fl
2x C-i-Fl
2x C-m4-Fl
C-i-Ph(OMe)
C6
C2
2x C-o1-Fl
C8
C4
C5
C-p-Ph(OMe)
RC(O)OCH2Fluorenyl
3'-NHC(O)R
170
160
150
140
130
120
110
ppm (t1)
x impurities

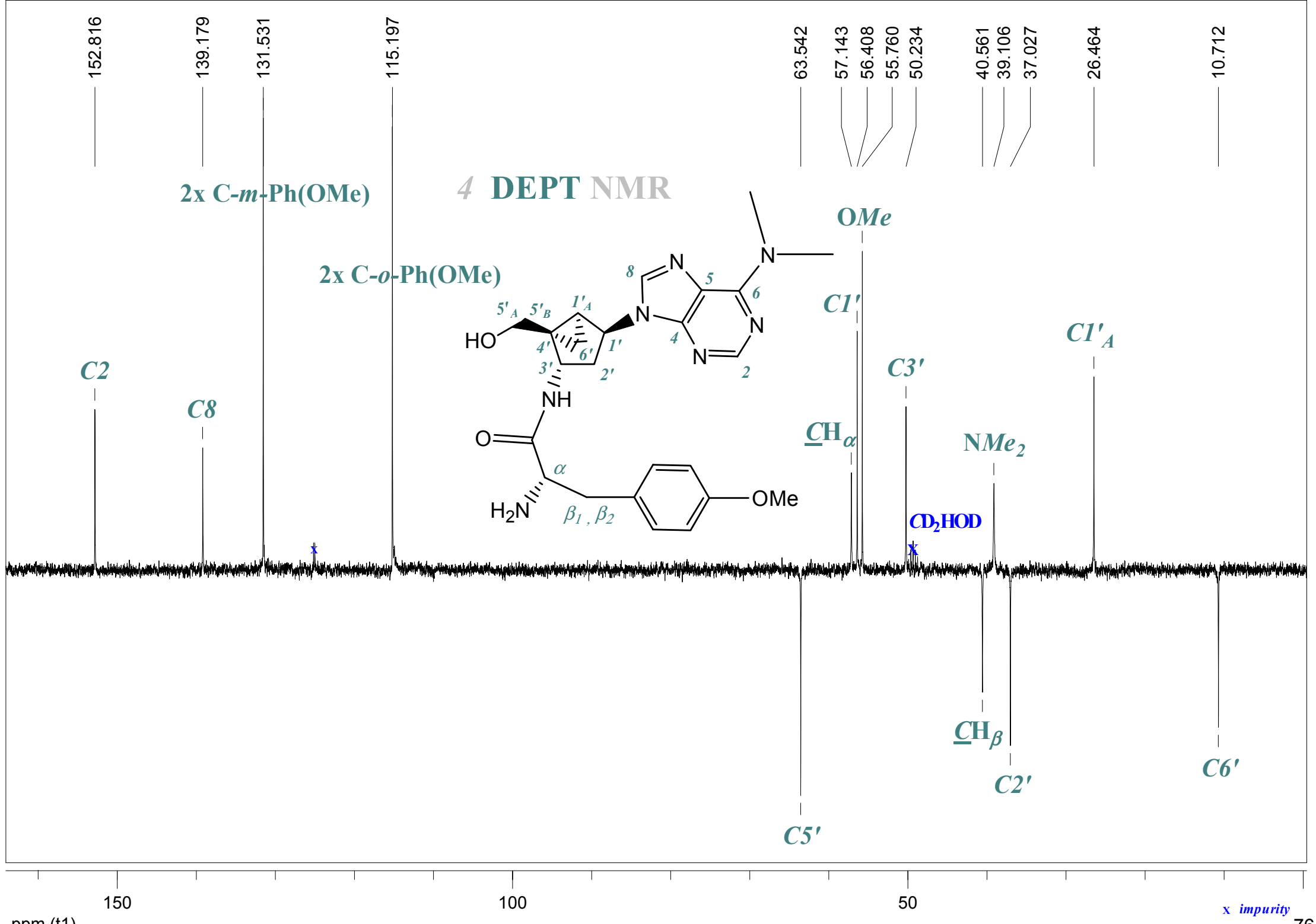

8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t2)
ppm (t1
HO
NMe2
NH
O
OMe
22 COSY

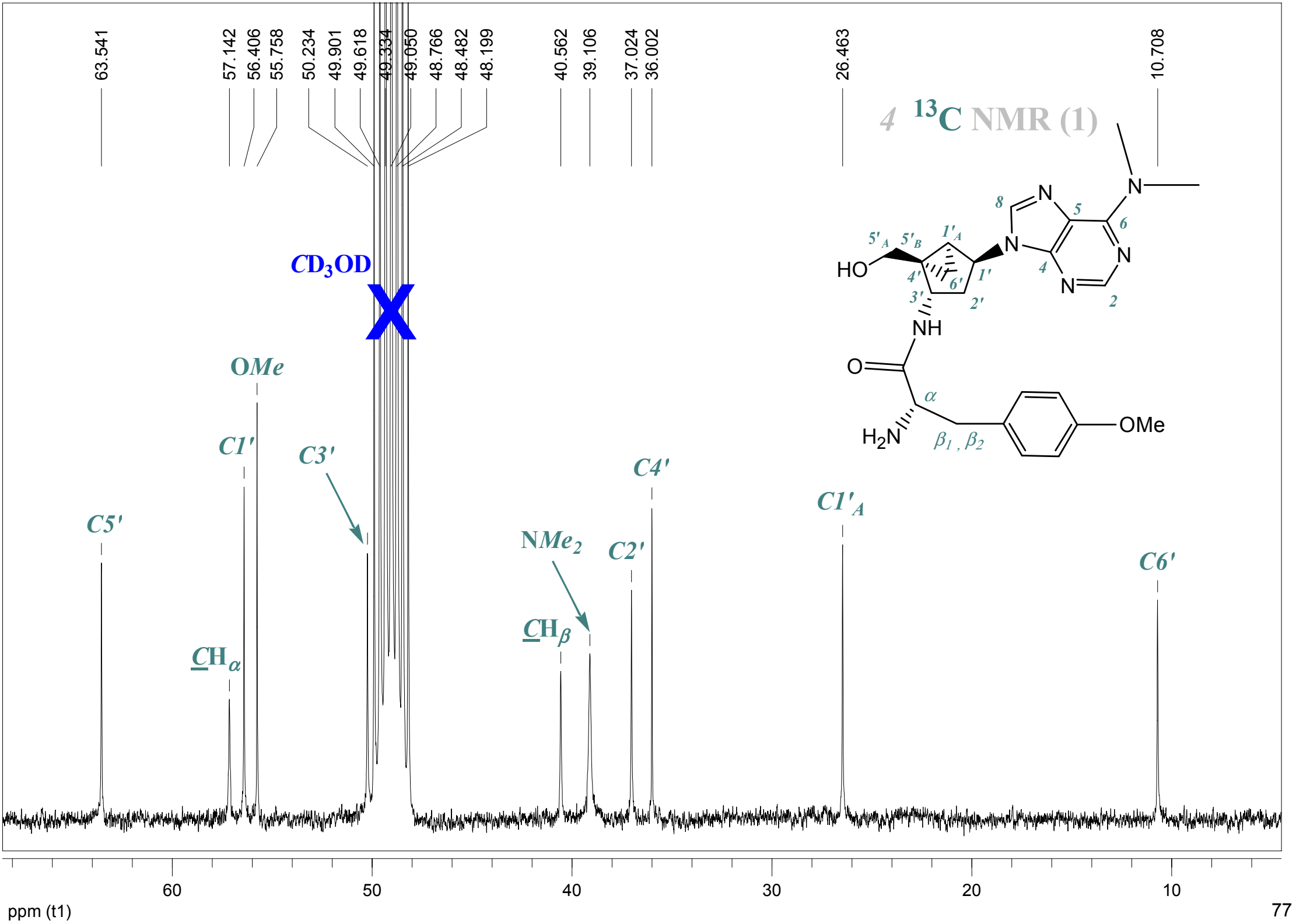

22 HSQC
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t2)
0
50
100
150
ppm (t1
NMe2
HO
NH
OMe
O

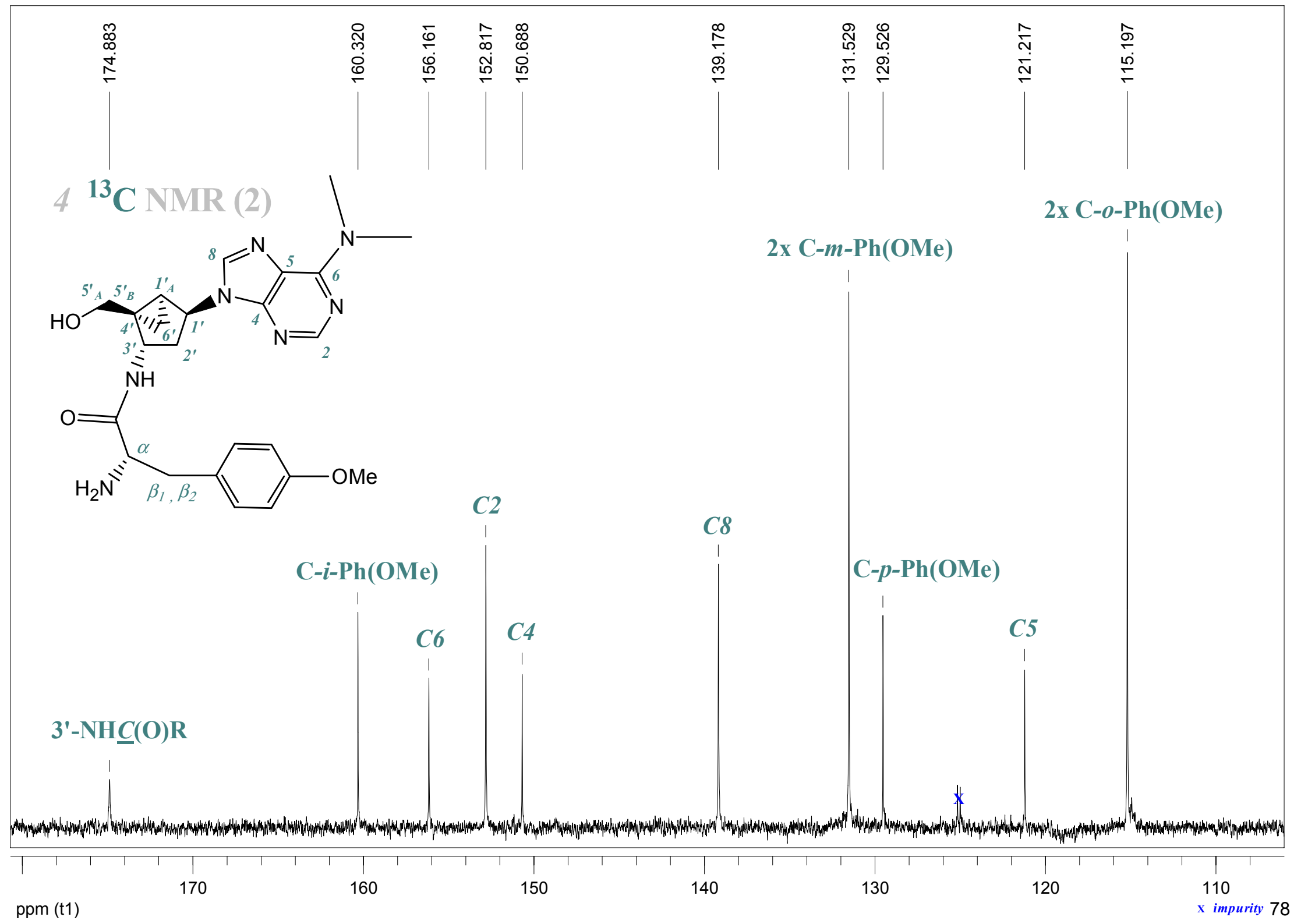

0
50
100
150
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
NMe2
HO
NH
O
OMe
22 HMBC

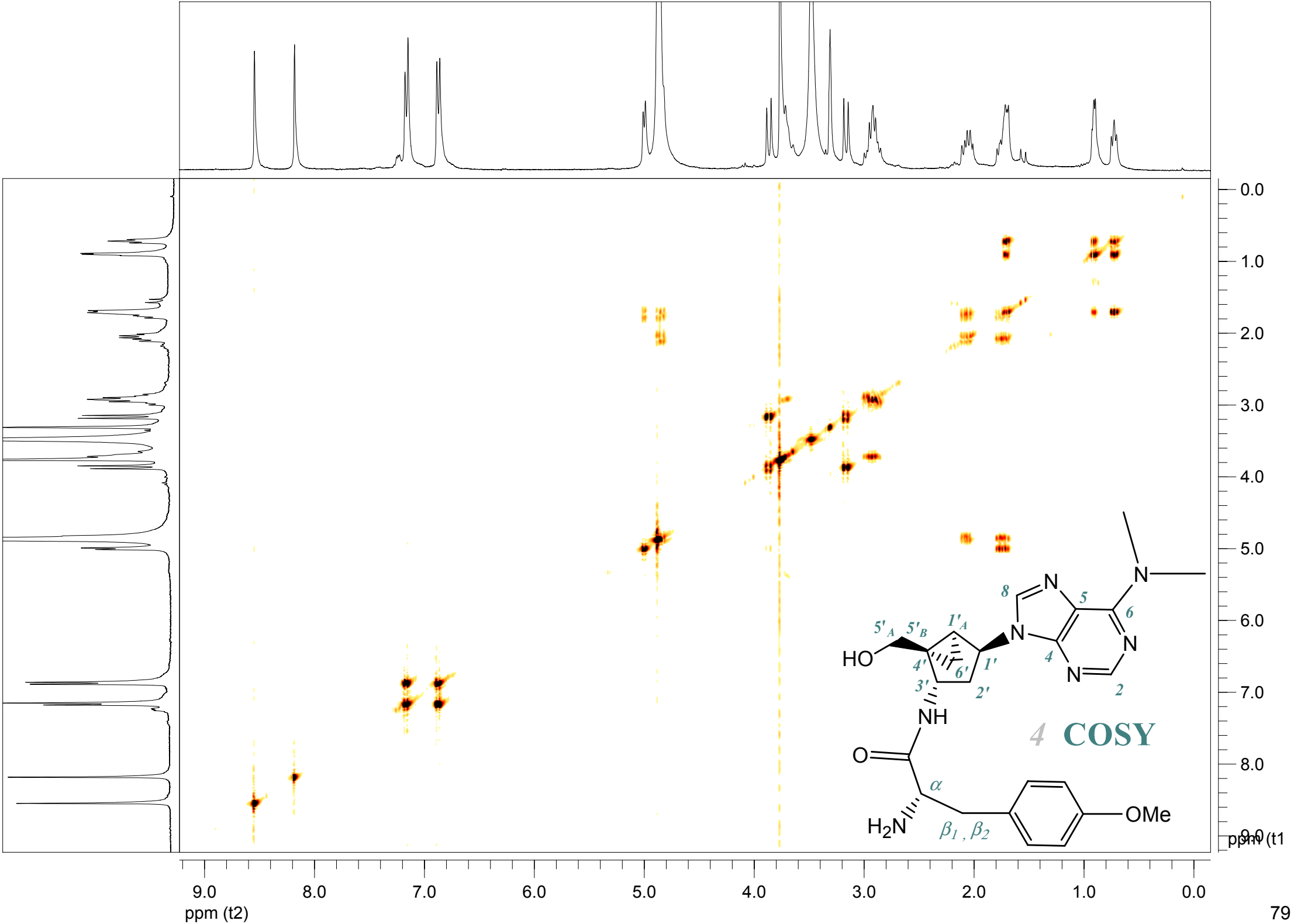

5.018
4.996
4.866
4.814
3.882
3.842
3.770
3.757
3.681
3.494
3.321
3.315
3.310
3.305
3.299
3.181
3.142
2.942
2.918
2.908
2.885
2.112
2.085
2.063
2.036
1.727
1.714
1.699
1.687
0.920
0.907
0.900
0.887
0.727
0.722
CD3OH
OMe
NMe2
CD2HOD
H1'
H3'
H5'B
CHα
H5'A
Hβ1
Hβ2
H2'α
H2'β
H1'A
H6'B
H6'A
4 1H NMR (1)
HO
NH
O
H2N
OMe
α
β1 , β2
1.00
0.96
2.93
1.25
5.89
1.04
1.97
1.15
2.01
1.27
0.99
5.0
4.0
3.0
2.0
1.0
ppm (t1)
x impurities

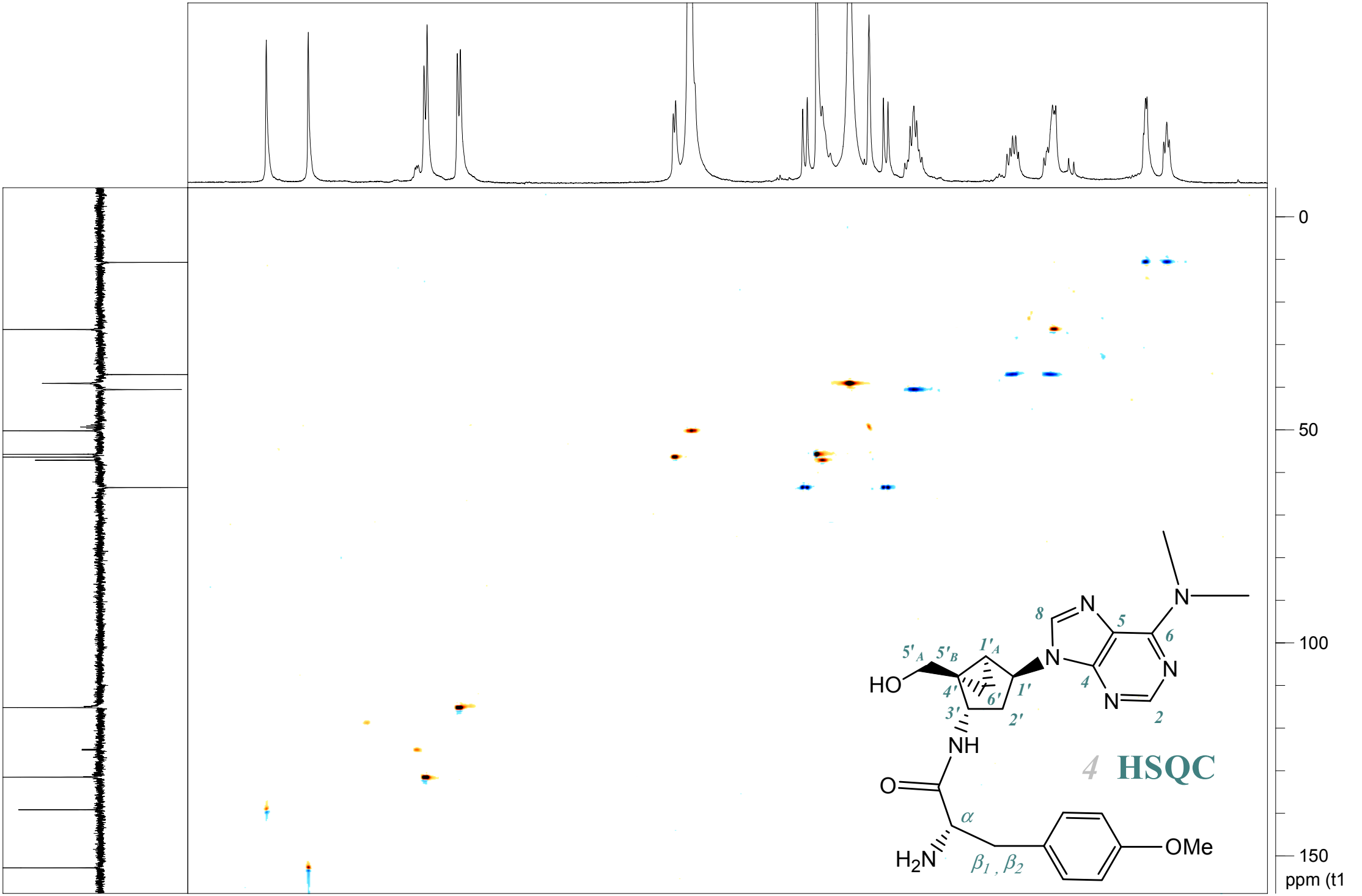

8.553
8.190
7.174
7.146
6.891
6.862
4 1H NMR (2)
H2
H8
2x H-m-Ph(OMe)
2x H-o-Ph(OMe)
0.94
0.95
1.92
1.91
8.50
8.00
7.50
7.00
ppm (t1)

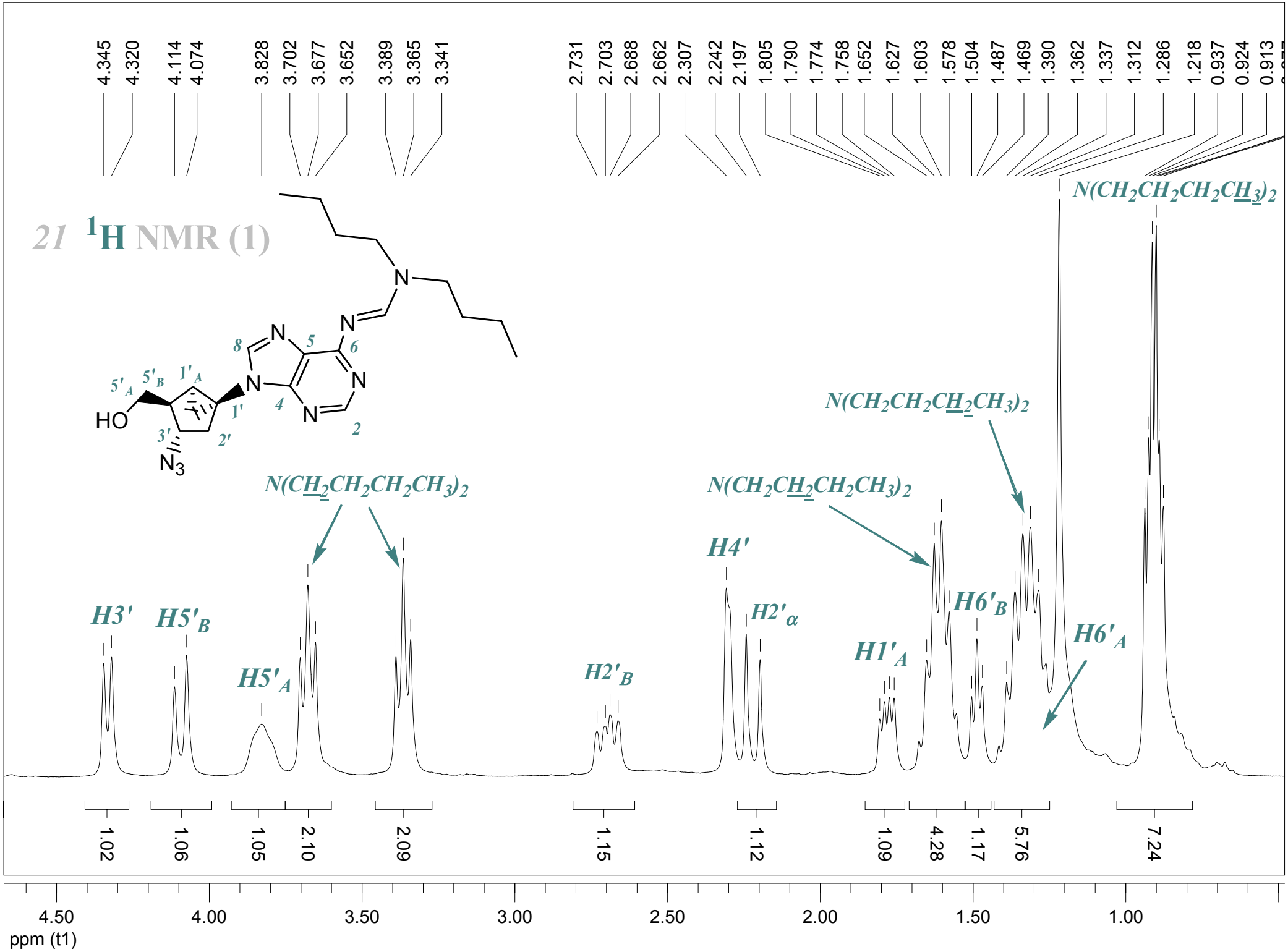

152.816
139.179
131.531
115.197
63.542
57.143
56.408
55.760
50.234
40.561
39.106
37.027
26.464
10.712
4 DEPT NMR
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
OMe
C1'
C1'A
C3'
C2
C8
CHα
NMe2
CD2HOD
CHβ
C2'
C6'
C5'
HO
NH
O
H2N
α
β1 , β2
OMe
150
100
50
ppm (t1)
x impurity

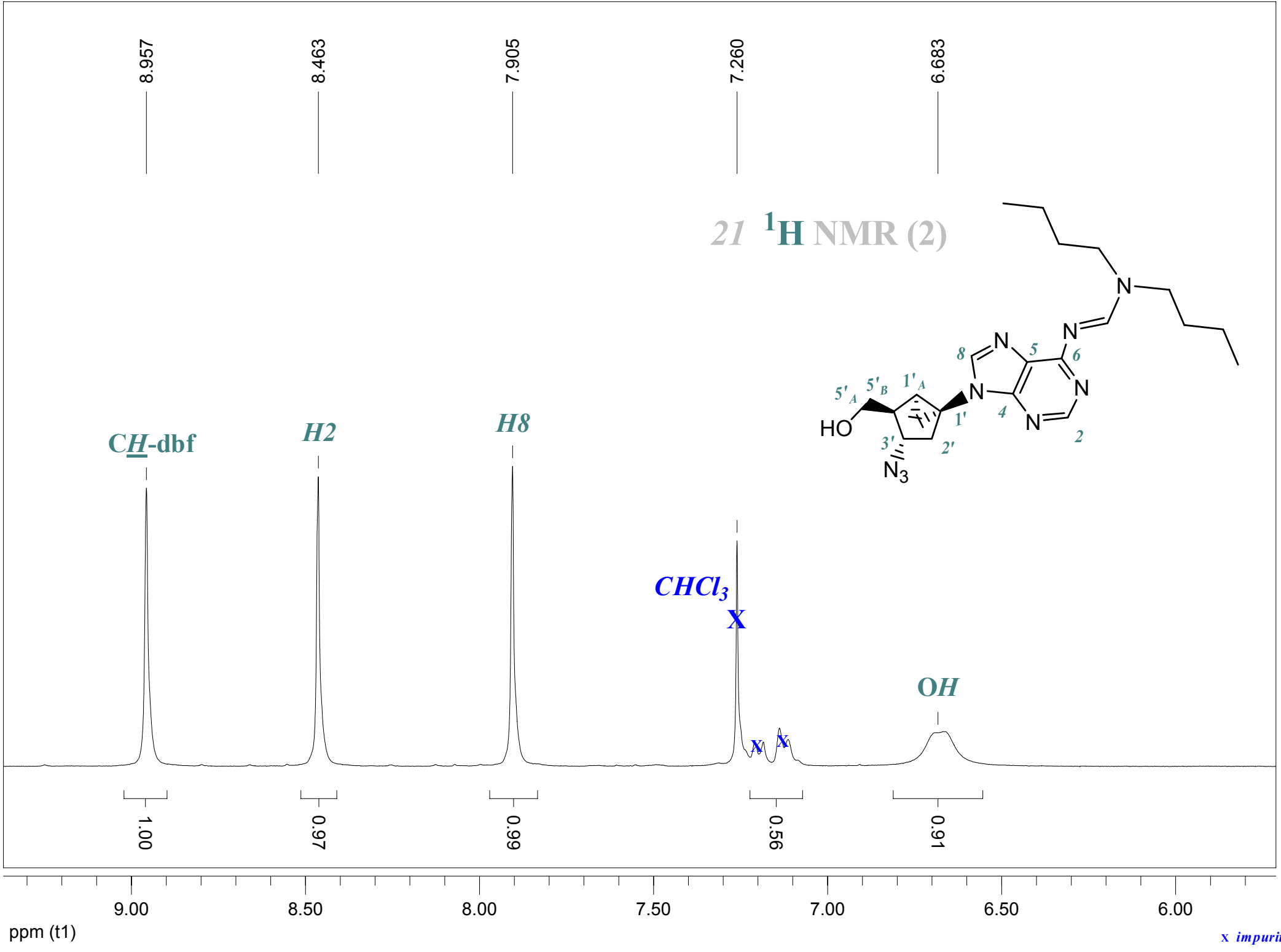

63.541
57.142
56.406
55.758
50.234
49.901
49.618
49.334
49.050
48.766
48.482
48.199
40.562
39.106
37.024
36.002
26.463
10.708
4 13C NMR (1)
CD3OD
OMe
C1'
C3'
C5'
CHα
NMe2
CHβ
C2'
C4'
C1'A
C6'
HO
NH
O
H2N
α
β1 , β2
OMe
60
50
40
30
20
10
ppm (t1)

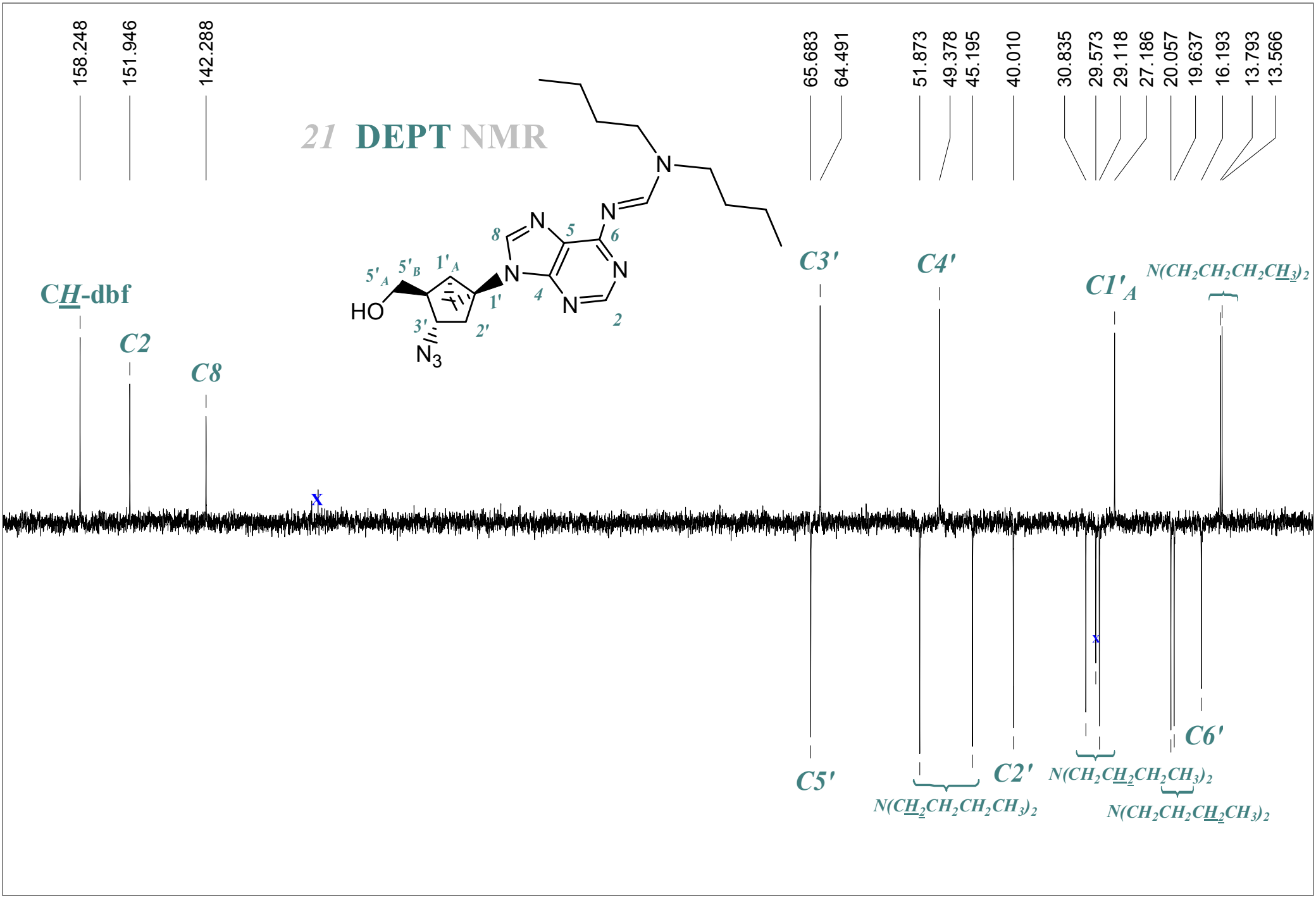

174.883
160.320
156.161
152.817
150.688
139.178
131.529
129.526
121.217
115.197
4 13C NMR (2)
2x C-o-Ph(OMe)
2x C-m-Ph(OMe)
C2
C8
C-i-Ph(OMe)
C-p-Ph(OMe)
C6
C4
C5
3'-NHC(O)R
x
170
160
150
140
130
120
110
ppm (t1)
x impurity

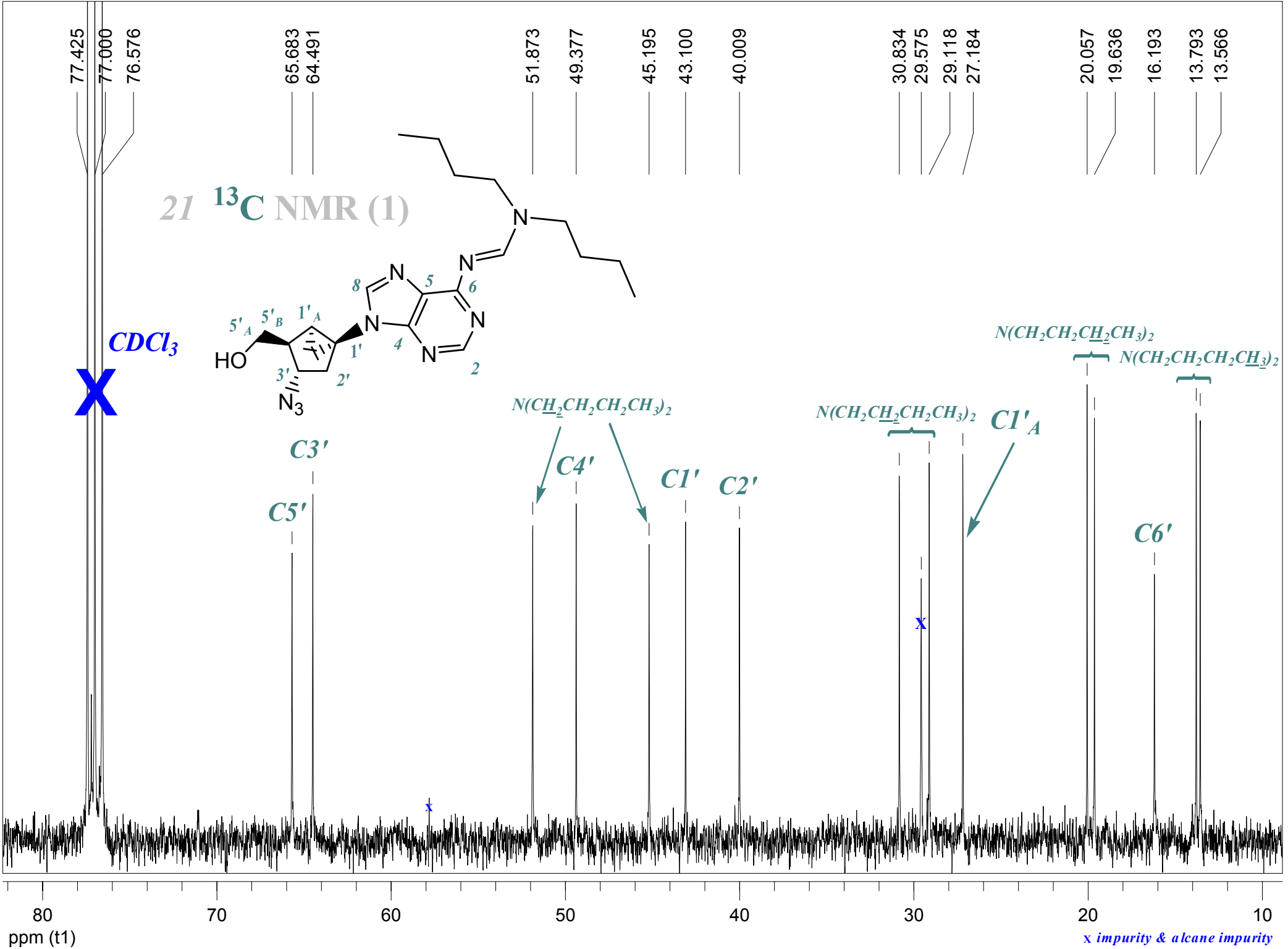

9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t2)
ppm (t1
HO
NH
O
H_2N
OMe
α
β_1 , β_2
4 COSY

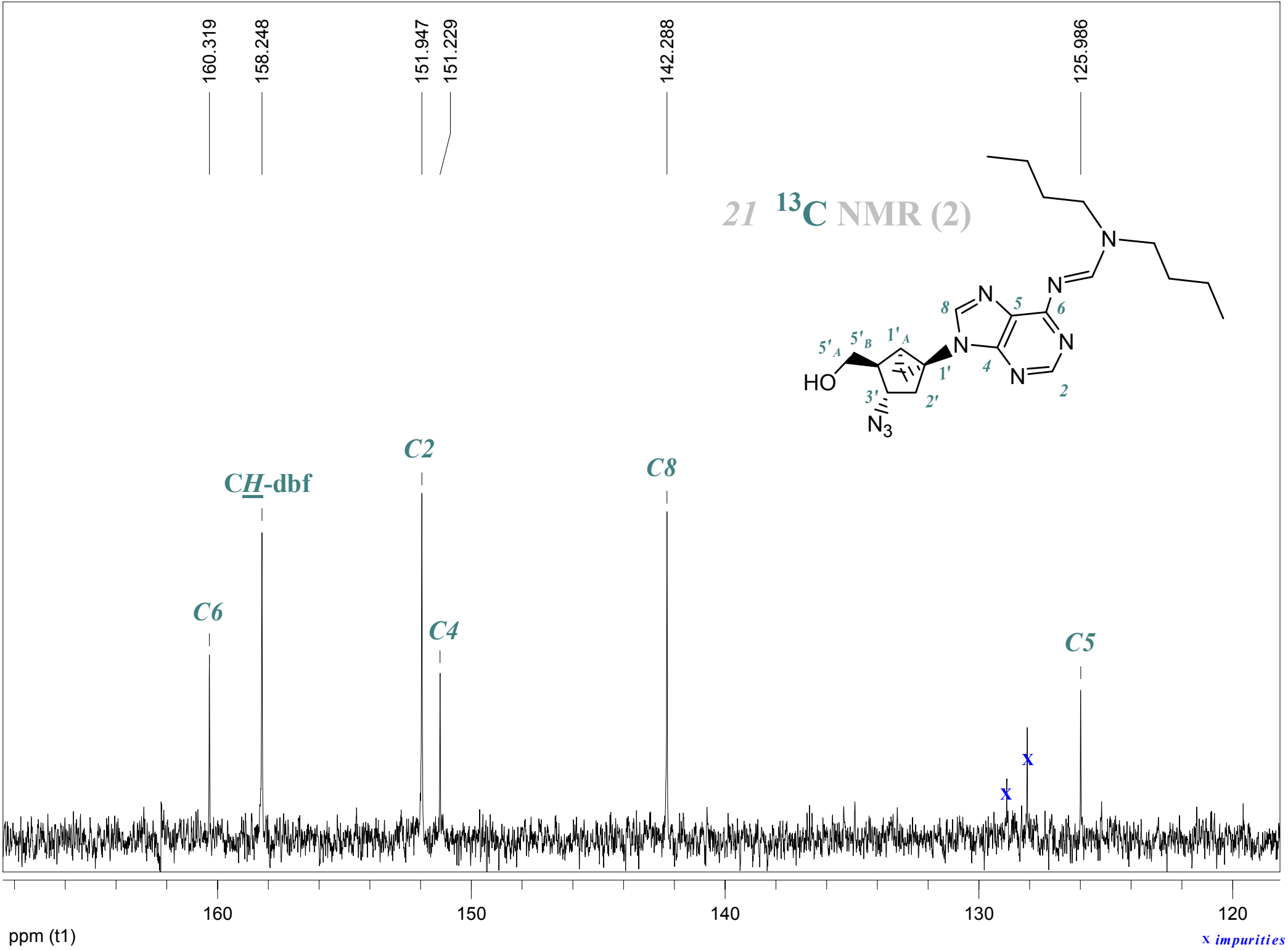

0
50
100
150
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0.0
ppm (t2)
HO
5'A 5'B
1'A
4'
6'
1'
3'
2'
NH
O
α
H2N
β1 , β2
OMe
N
8
5
6
4
2
4 HSQC

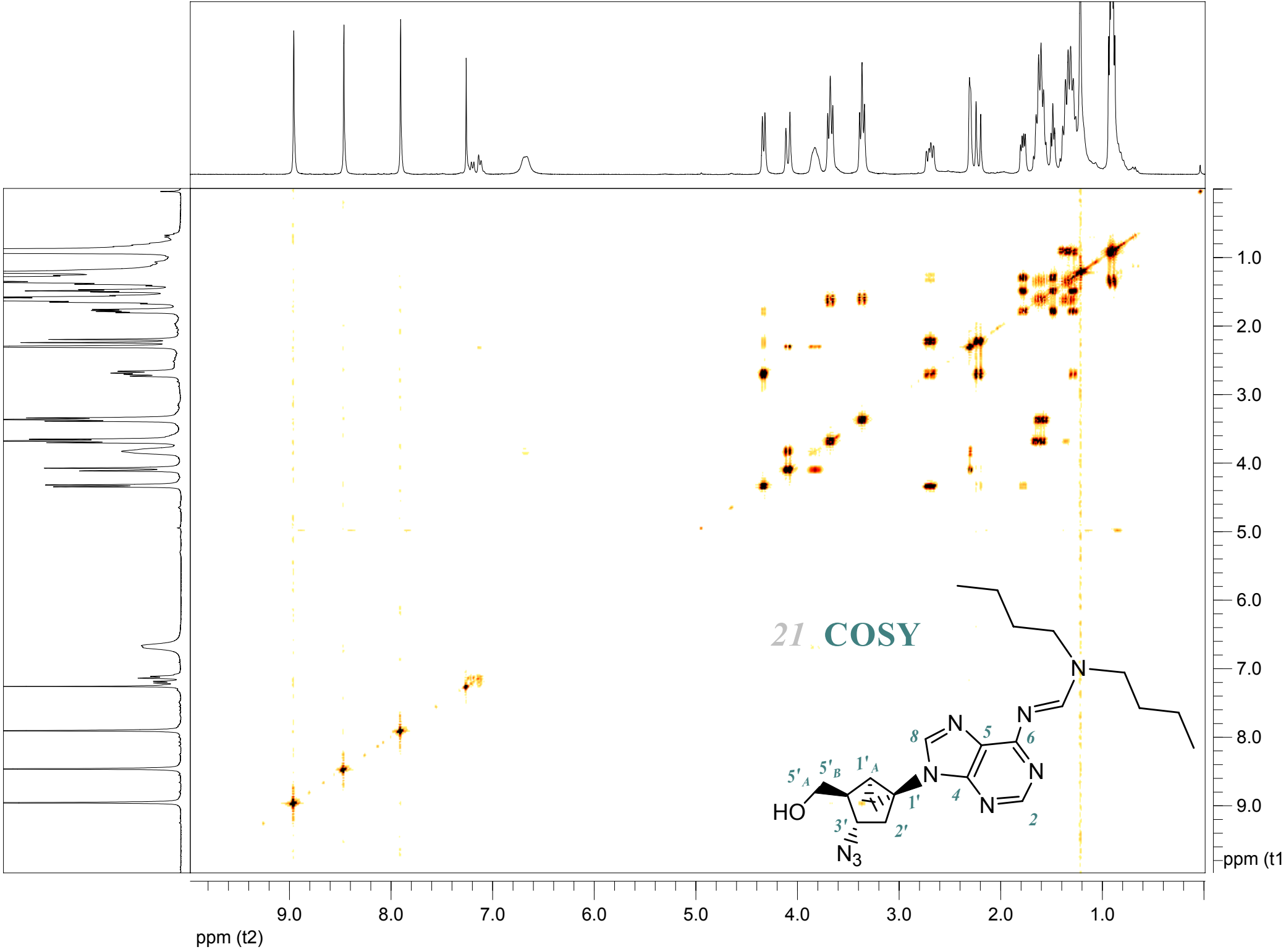

21 1H NMR (1)
4.345
4.320
4.114
4.074
3.828
3.702
3.677
3.652
3.389
3.365
3.341
2.731
2.703
2.688
2.662
2.307
2.242
2.197
1.805
1.790
1.774
1.758
1.652
1.627
1.603
1.578
1.504
1.487
1.469
1.390
1.362
1.337
1.312
1.286
1.218
0.937
0.924
0.913
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
H3'
H5'B
H5'A
H2'B
H4'
H2'α
H1'A
H6'B
H6'A
1.02
1.06
1.05
2.10
2.09
1.15
1.12
1.09
4.28
1.17
5.76
7.24
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
ppm (t1)

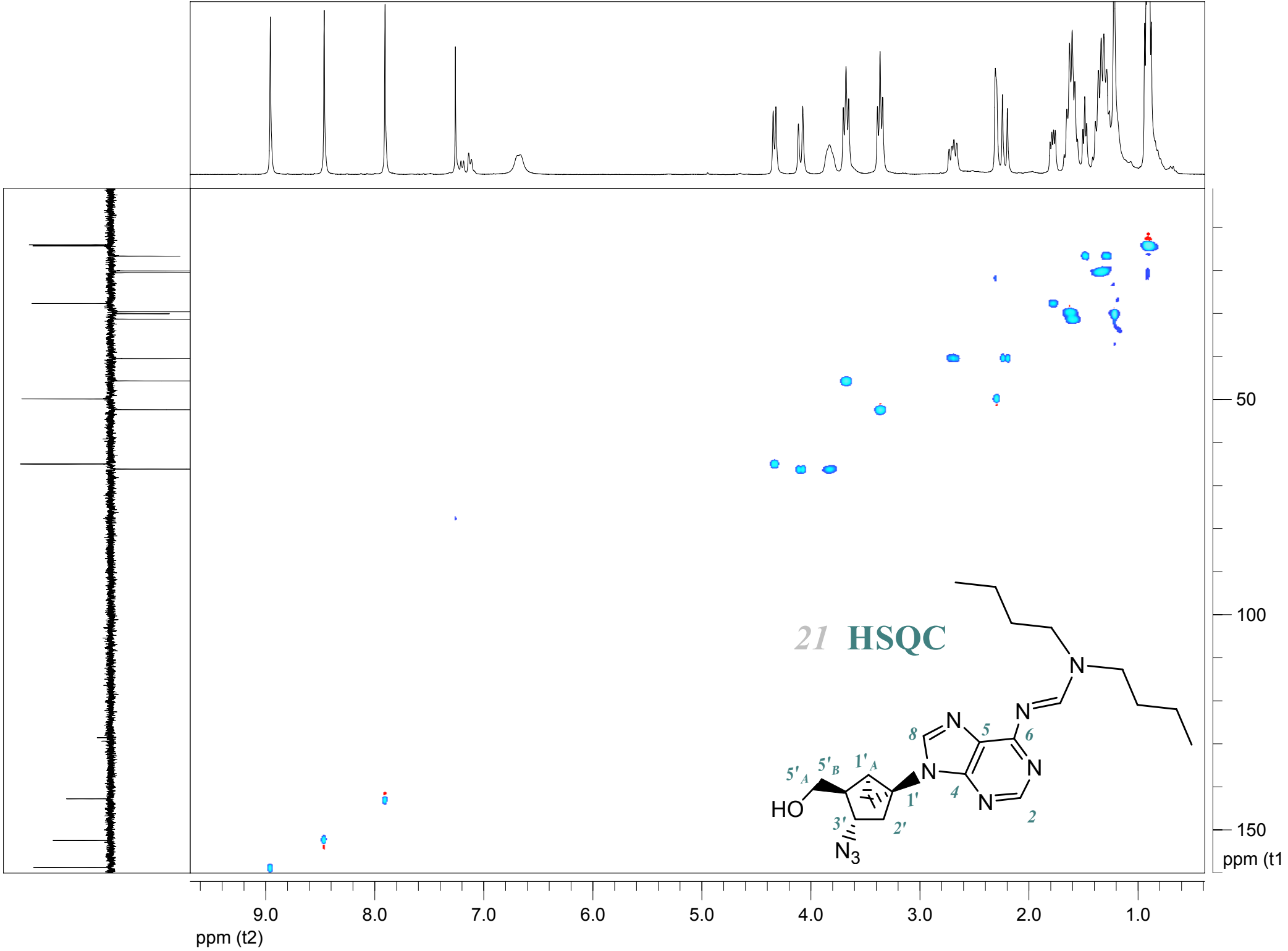

8.957
8.463
7.905
7.260
6.683
21 ¹H NMR (2)
CH-dbf
H2
H8
CHCl3
X
OH
1.00
0.97
0.99
0.56
0.91
9.00
8.50
8.00
7.50
7.00
6.50
6.00
ppm (t1)
x impurities

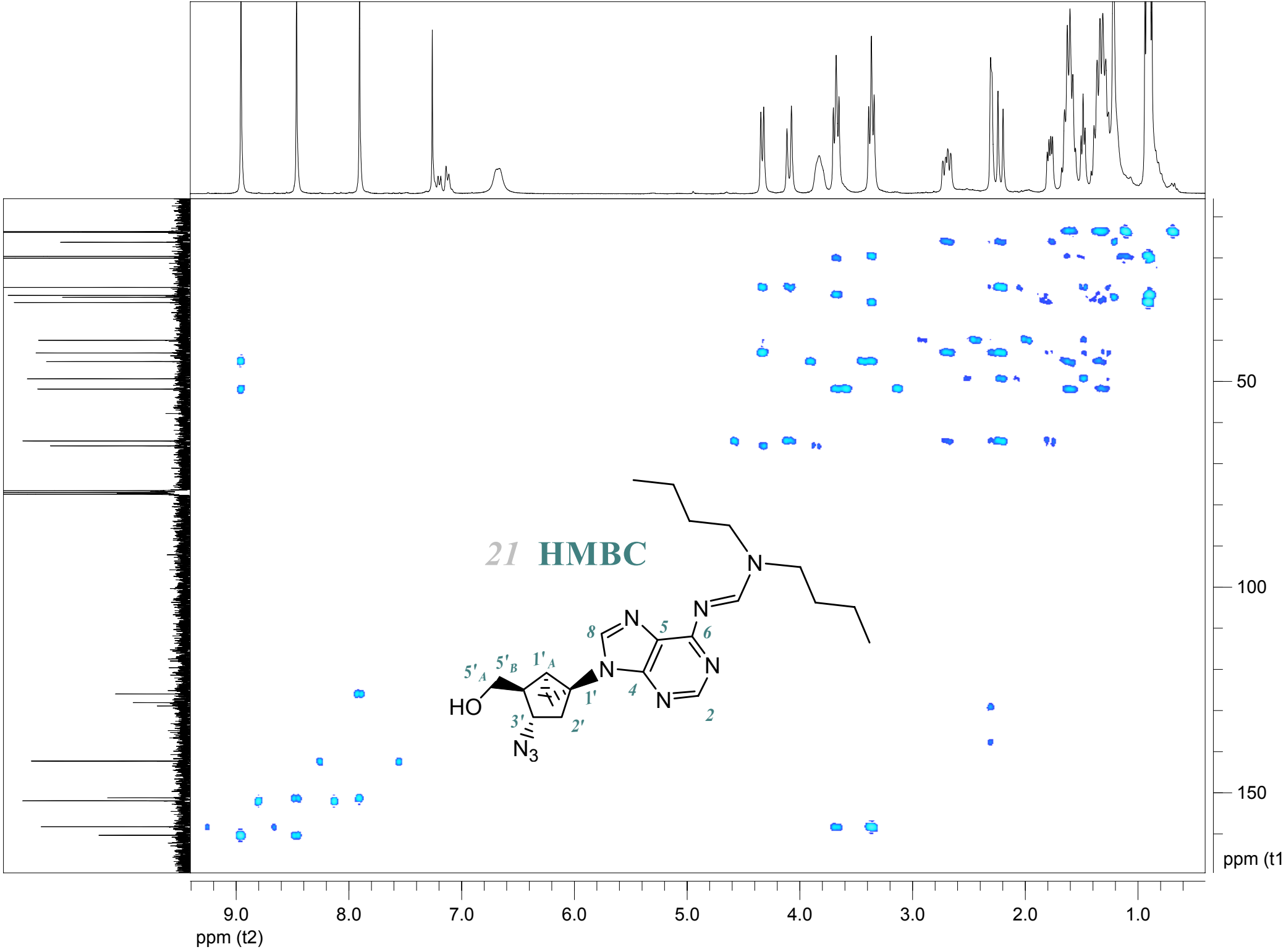

158.248
151.946
142.288
65.683
64.491
51.873
49.378
45.195
40.010
30.835
29.573
29.118
27.186
20.057
19.637
16.193
13.793
13.566
21 DEPT NMR
CH-dbf
C2
C8
C3'
C4'
C1'A
N(CH2CH2CH2CH3)2
C5'
C2'
C6'
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
x
150
100
50
ppm (t1)
x impurity & alkane impurity

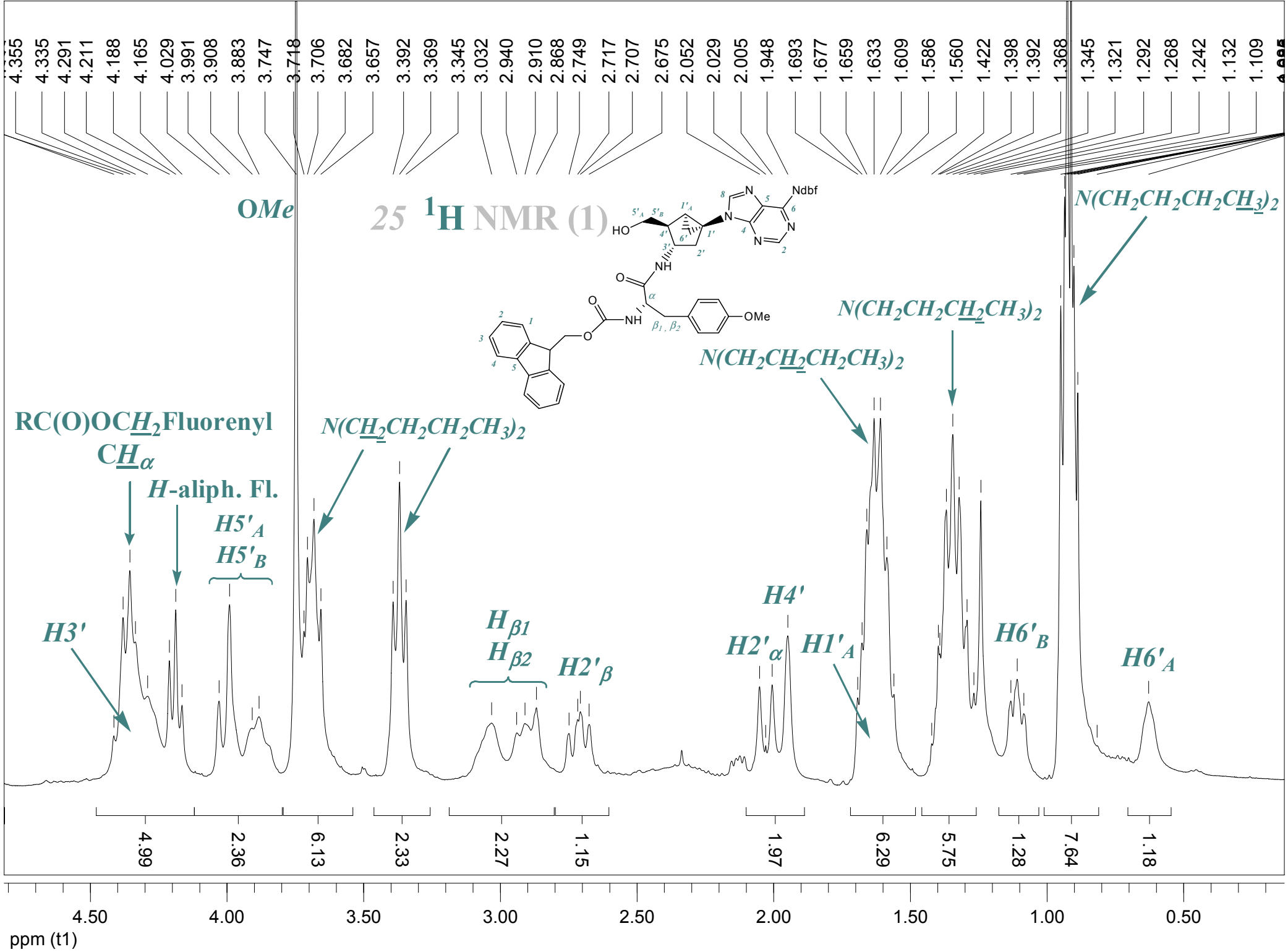

77.425
77.000
76.576
65.683
64.491
51.873
49.377
45.195
43.100
40.009
30.834
29.575
29.118
27.184
20.057
19.636
16.193
13.793
13.566
21 13C NMR (1)
CDCl3
C3'
C5'
C4'
C1'
C2'
C1'A
C6'
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
HO
N3
80
70
60
50
40
30
20
10
ppm (t1)
x impurity & alcane impurity

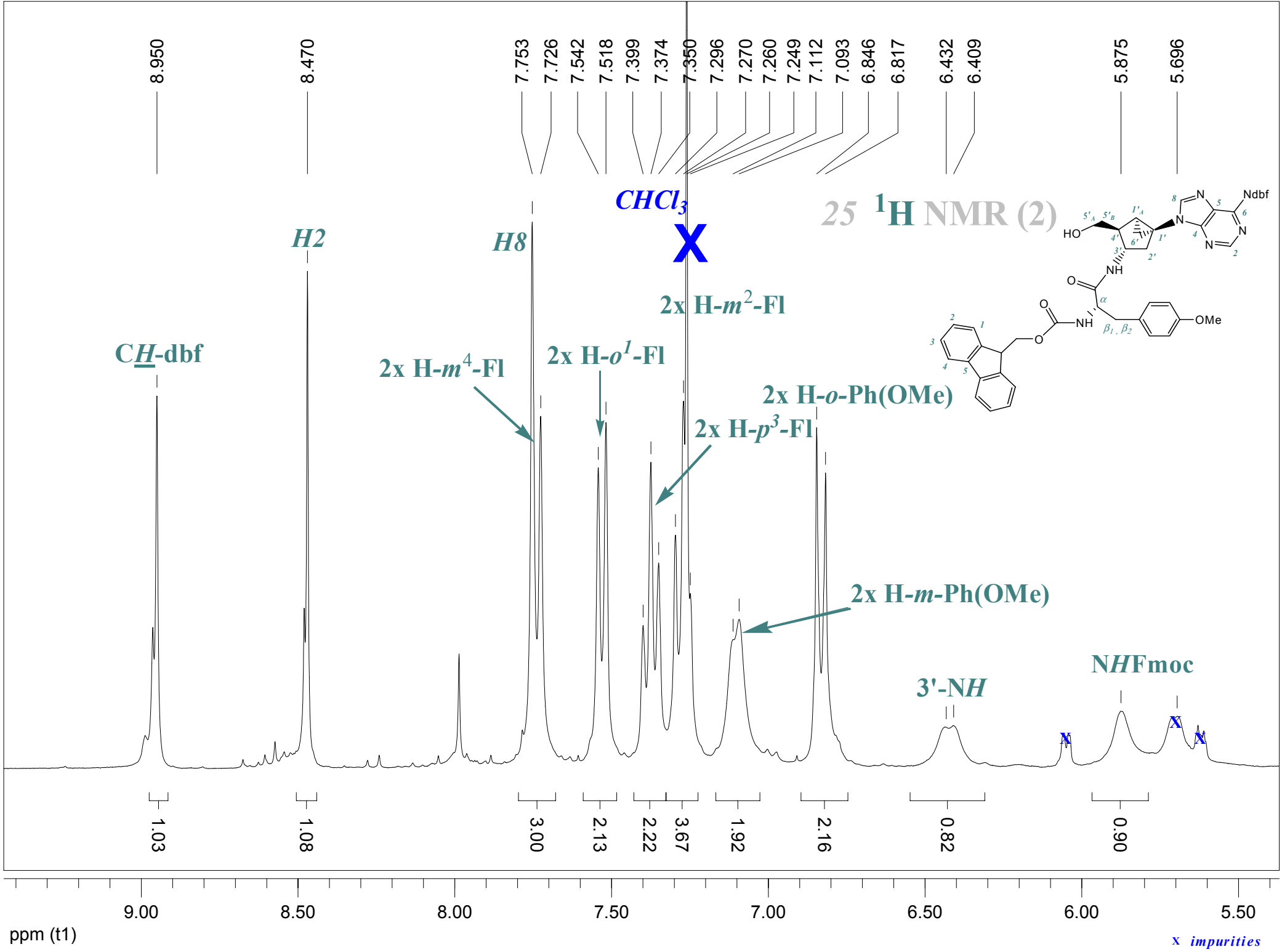

160.319
158.248
151.947
151.229
142.288
125.986
21 13C NMR (2)
C2
CH-dbf
C8
C6
C4
C5
x
x
x
160
150
140
130
120
ppm (t1)
x impurities

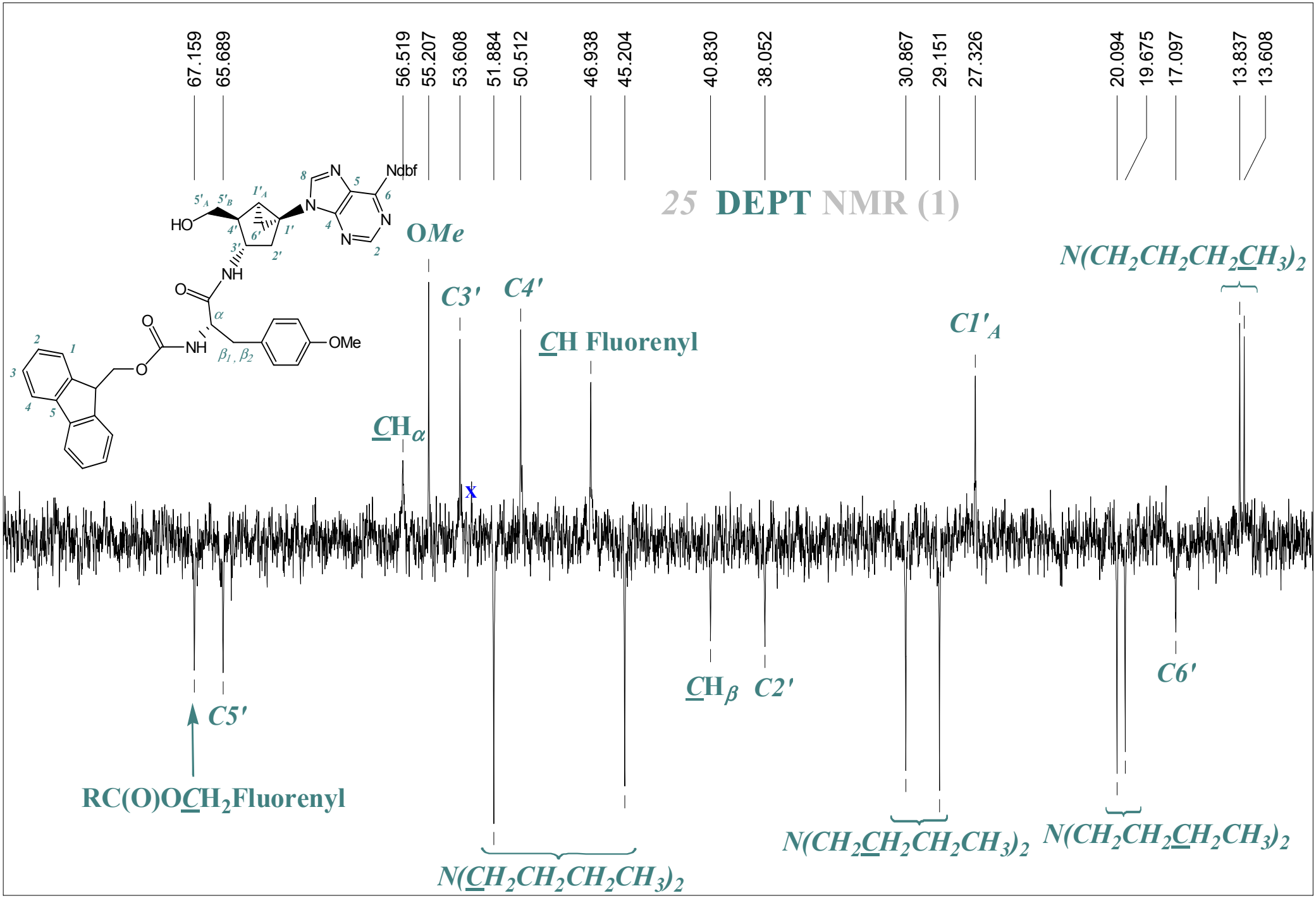

21 COSY
ppm (t2)
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
HO
N3
N

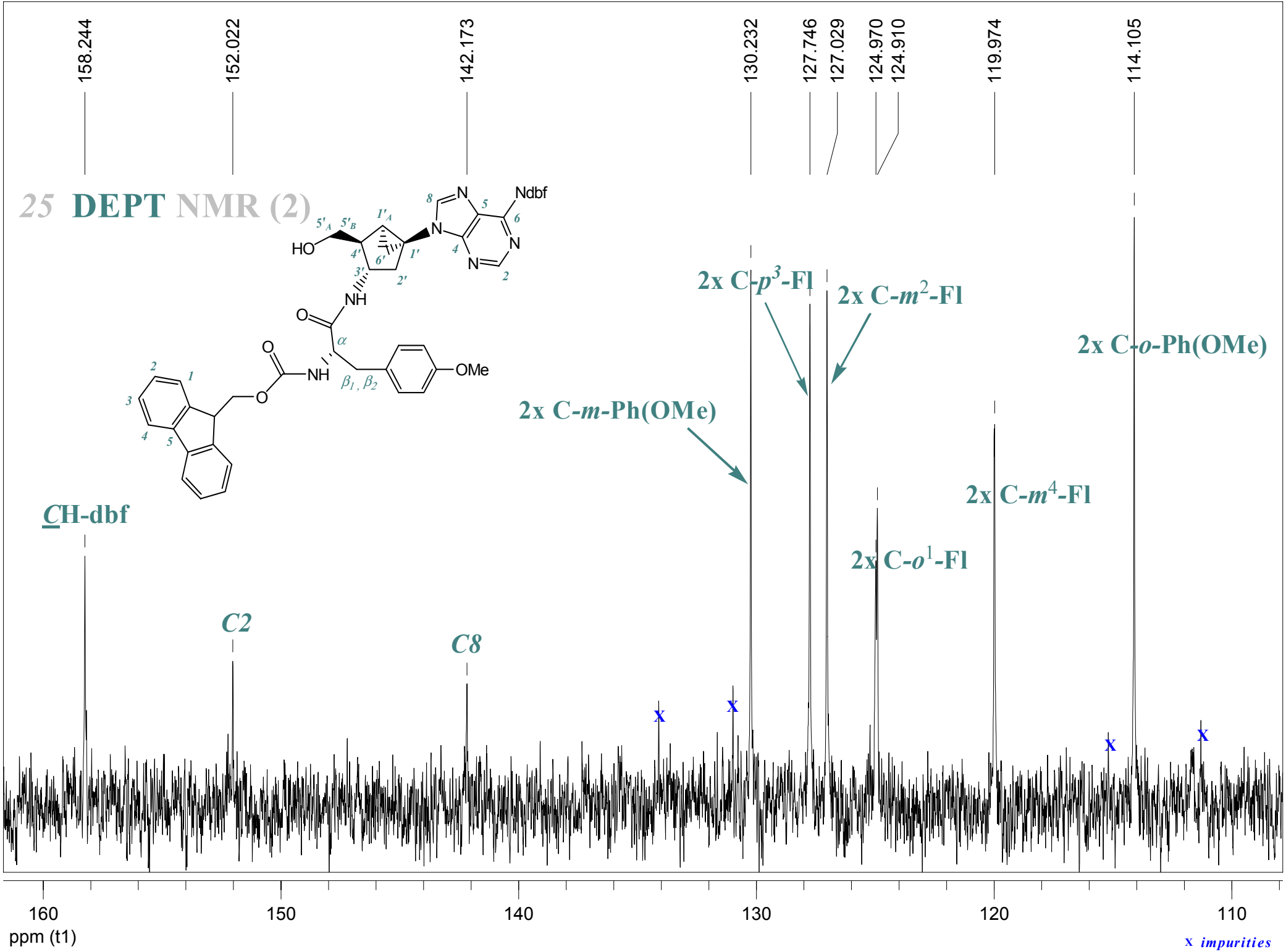

21 HSQC
50
100
150
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
HO
N3
N

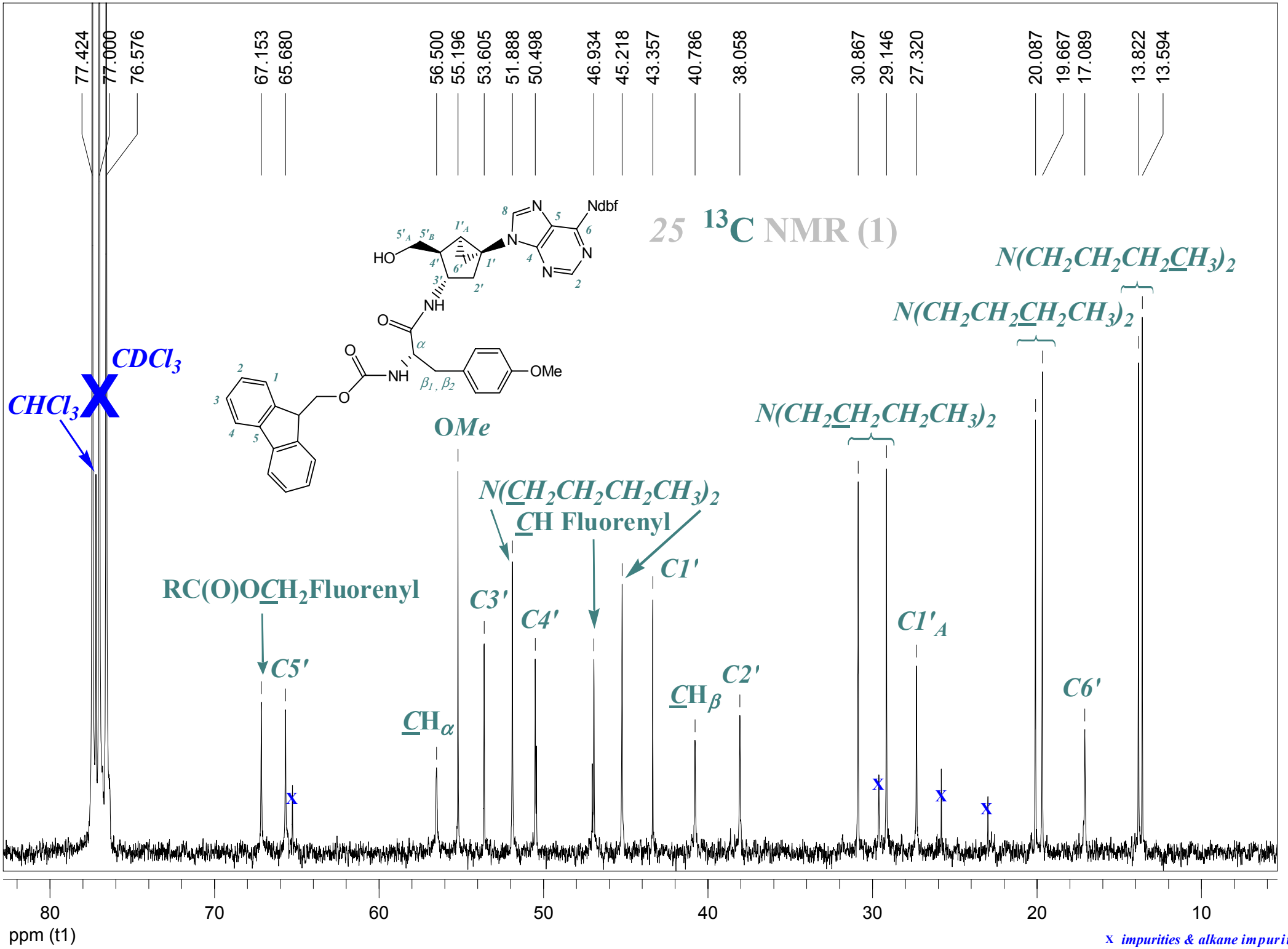

21 HMBC
HO
N3
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
50
100
150
ppm (t1

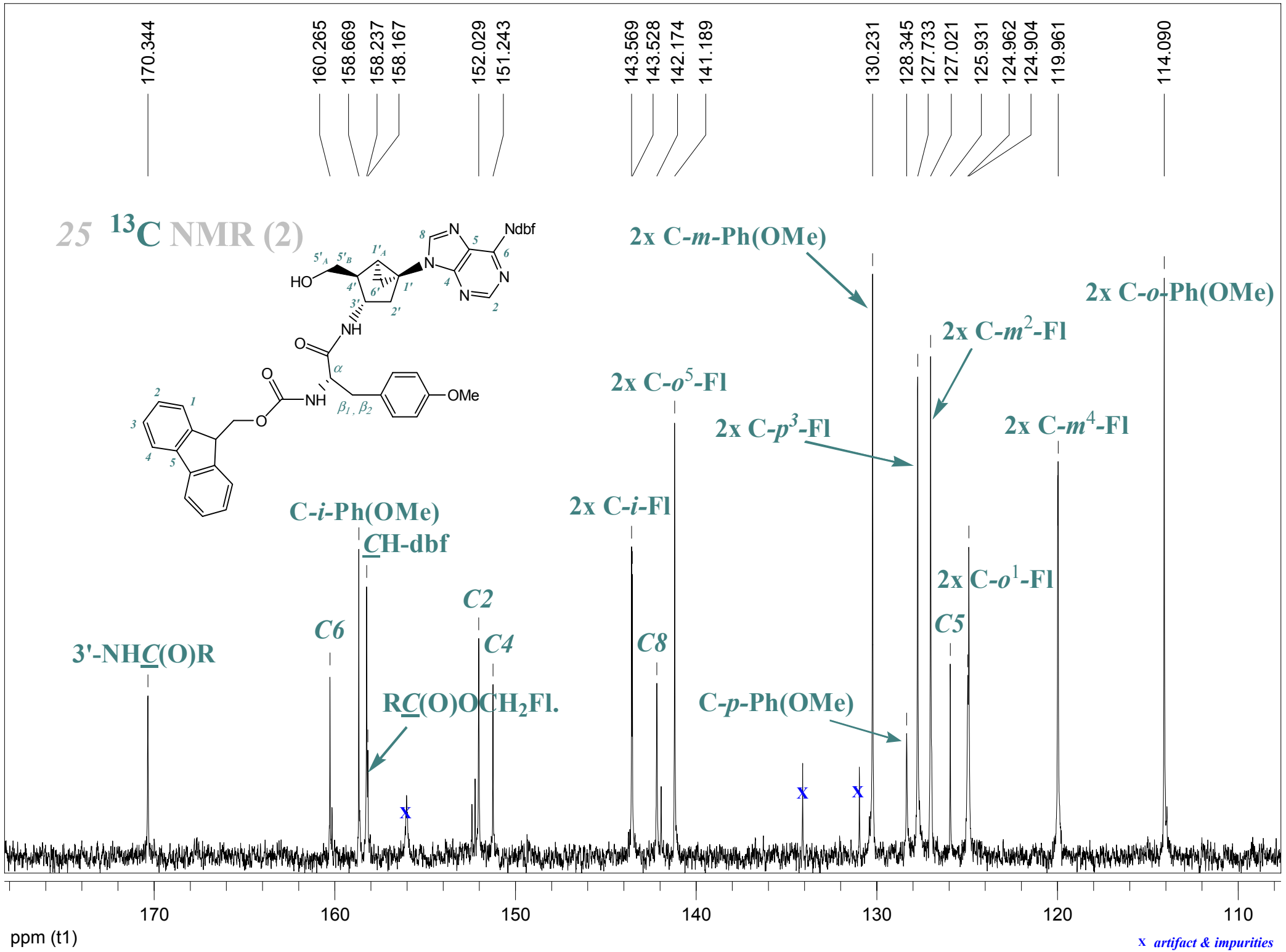

25 1H NMR (1)
OMe
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
RC(O)OCH2Fluorenyl
CHα
H-aliph. Fl.
H5'A
H5'B
H3'
Hβ1
Hβ2
H2'β
H4'
H2'α
H1'A
H6'B
H6'A
4.99
2.36
6.13
2.33
2.27
1.15
1.97
6.29
5.75
1.28
7.64
1.18
4.50
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)

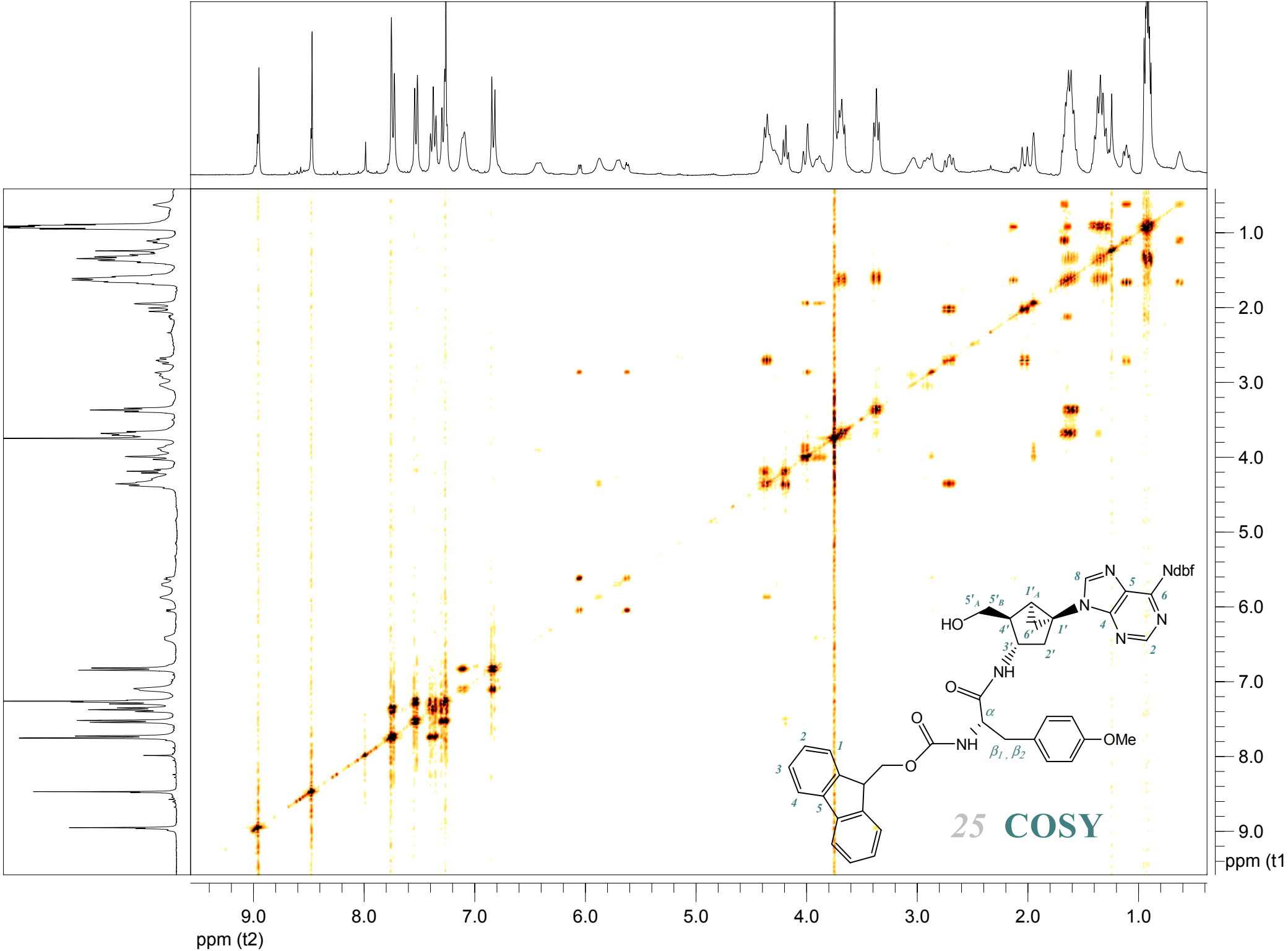

8.950
8.470
7.753
7.726
7.542
7.518
7.399
7.374
7.350
7.296
7.270
7.260
7.249
7.112
7.093
6.846
6.817
6.432
6.409
5.875
5.696
CHCl3
25 1H NMR (2)
H2
H8
2x H-m2-Fl
CH-dbf
2x H-m4-Fl
2x H-o1-Fl
2x H-o-Ph(OMe)
2x H-p3-Fl
2x H-m-Ph(OMe)
3'-NH
NHFmoc
1.03
1.08
3.00
2.13
2.22
3.67
1.92
2.16
0.82
0.90
9.00
8.50
8.00
7.50
7.00
6.50
6.00
5.50
ppm (t1)
x impurities

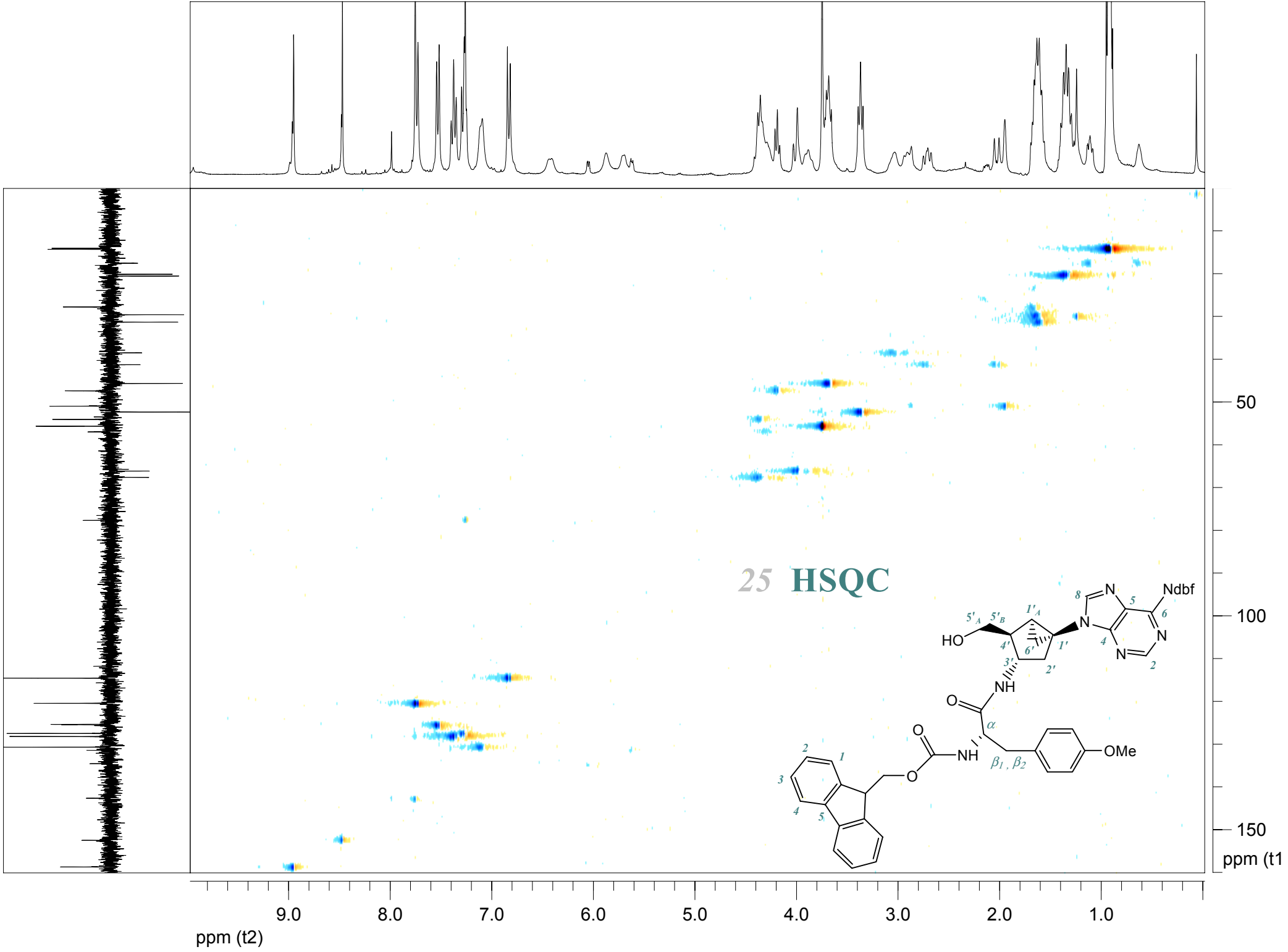

67.159
65.689
56.519
55.207
53.608
51.884
50.512
46.938
45.204
40.830
38.052
30.867
29.151
27.326
20.094
19.675
17.097
13.837
13.608
25 DEPT NMR (1)
OMe
C3'
C4'
CH Fluorenyl
C1'A
N(CH2CH2CH2CH3)2
CHα
x
C5'
RC(O)OCH2Fluorenyl
CHβ
C2'
C6'
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
N(CH2CH2CH2CH3)2
70
60
50
40
30
20
ppm (t1)
x impurities

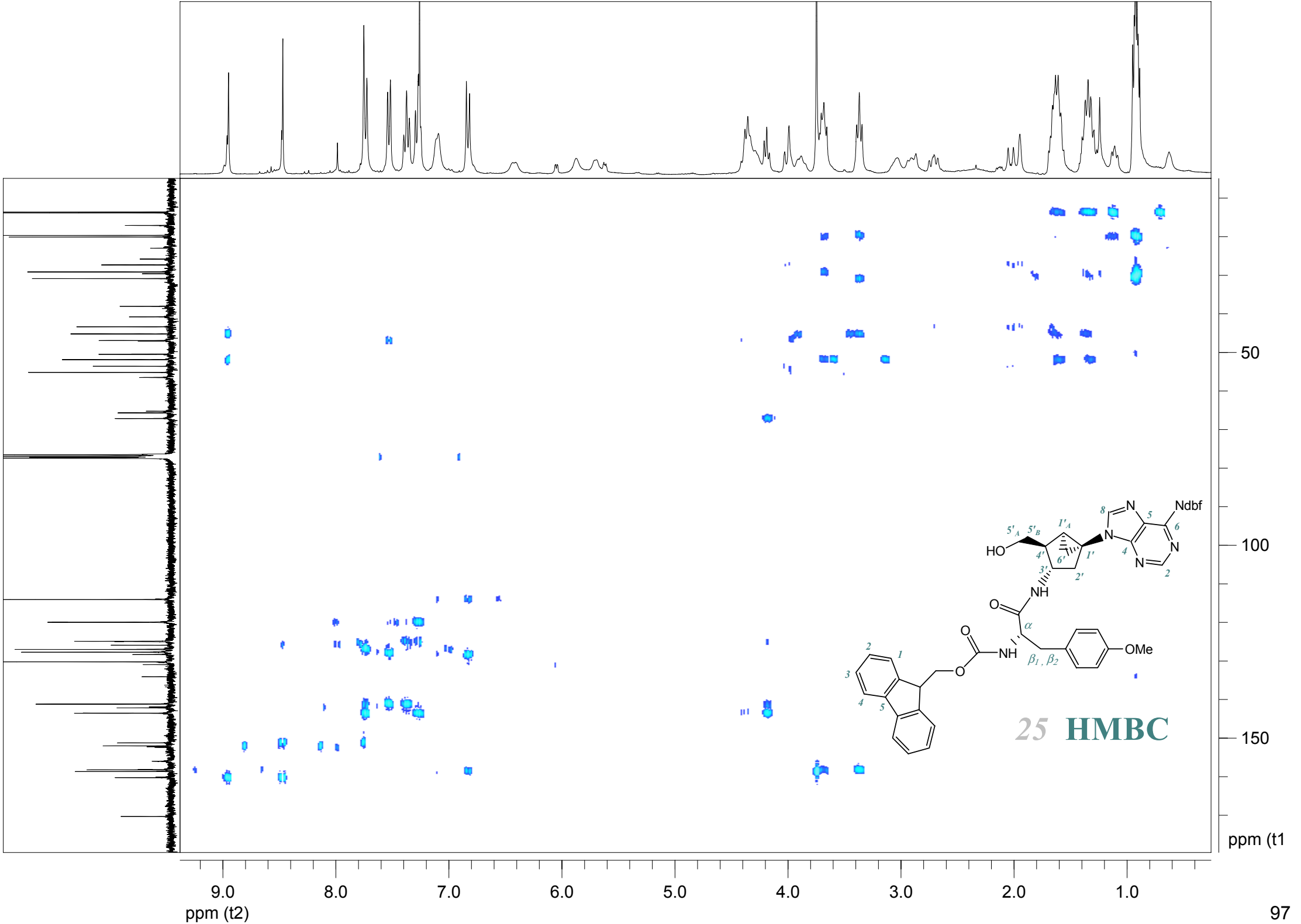

158.244
152.022
142.173
130.232
127.746
127.029
124.970
124.910
119.974
114.105
25 DEPT NMR (2)
Ndbf
HO
NH
O
NH
OMe
2x C-p3-Fl
2x C-m2-Fl
2x C-o-Ph(OMe)
2x C-m-Ph(OMe)
2x C-m4-Fl
2x C-o1-Fl
CH-dbf
C2
C8
x
160
150
140
130
120
110
ppm (t1)
x impurities

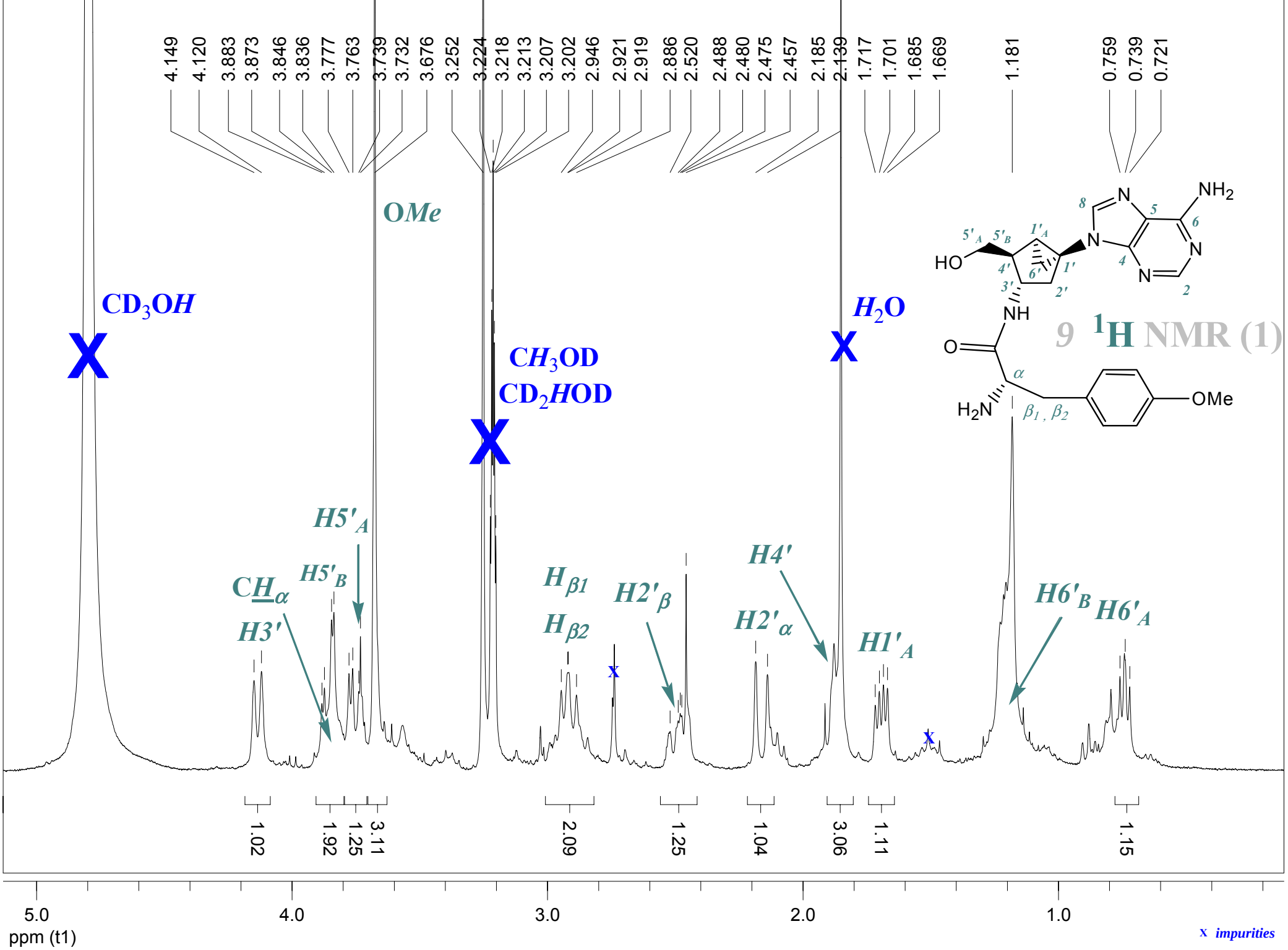

77.424
77.000
76.576
67.153
65.680
56.500
55.196
53.605
51.888
50.498
46.934
45.218
43.357
40.786
38.058
30.867
29.146
27.320
20.087
19.667
17.089
13.822
13.594
25 13C NMR (1)
CDCl3
CHCl3
OMe
N(CH2CH2CH2CH3)2
CH Fluorenyl
RC(O)OCH2Fluorenyl
C5'
C3'
C4'
C1'
C1'A
C2'
CHα
CHβ
C6'
Ndbf
HO
NH
OMe
80
70
60
50
40
30
20
10
ppm (t1)
x impurities & alkane impurity

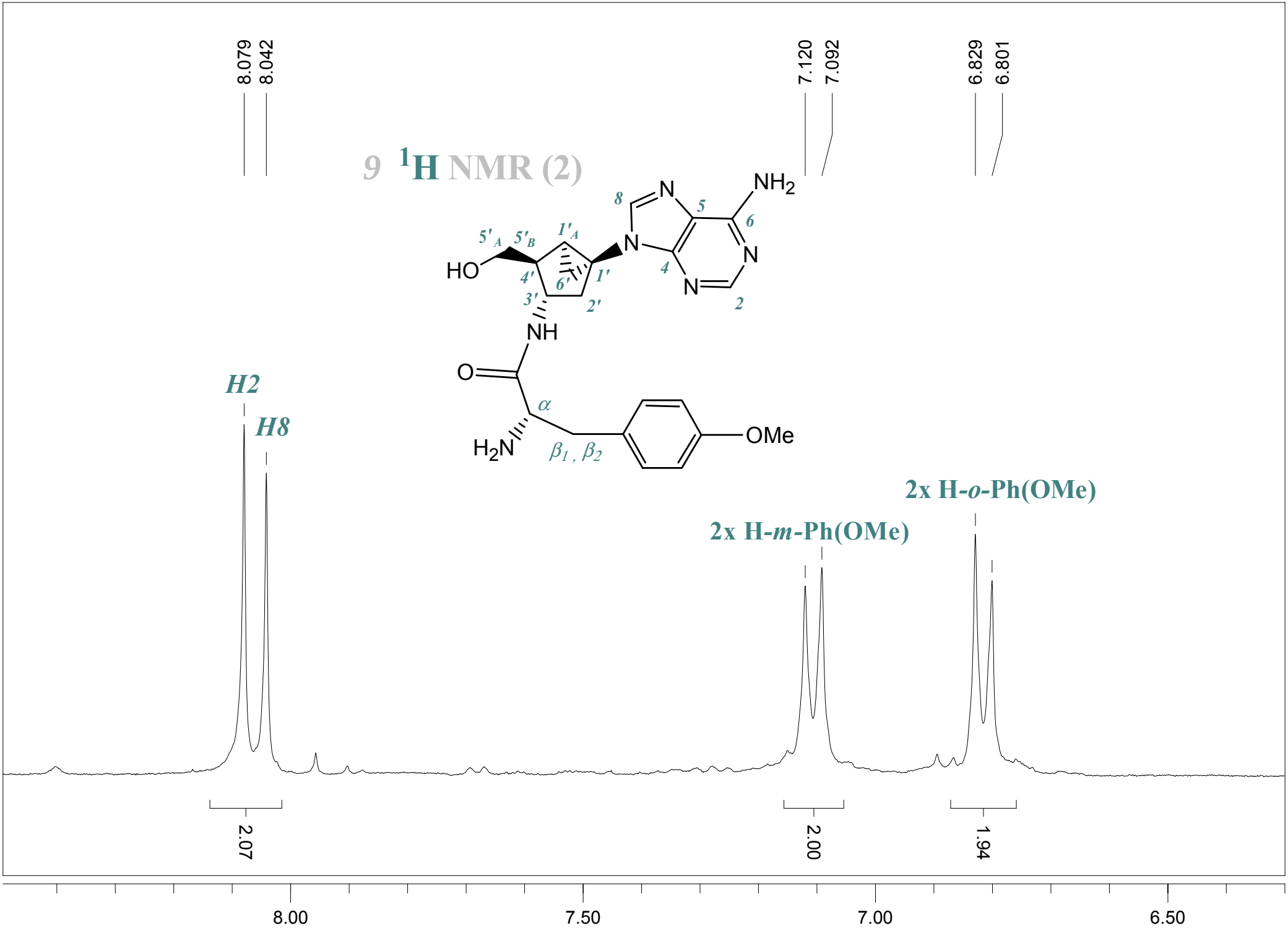

170.344
160.265
158.669
158.237
158.167
152.029
151.243
143.569
143.528
142.174
141.189
130.231
128.345
127.733
127.021
125.931
124.962
124.904
119.961
114.090
25 13C NMR (2)
Ndbf
HO
NH
OMe
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
2x C-m2-Fl
2x C-o5-Fl
2x C-p3-Fl
2x C-m4-Fl
C-i-Ph(OMe)
CH-dbf
2x C-i-Fl
2x C-o1-Fl
C2
C6
C4
C8
C5
3'-NHC(O)R
RC(O)OCH2Fl.
C-p-Ph(OMe)
x
x
x
170
160
150
140
130
120
110
ppm (t1)
x artifact & impurities

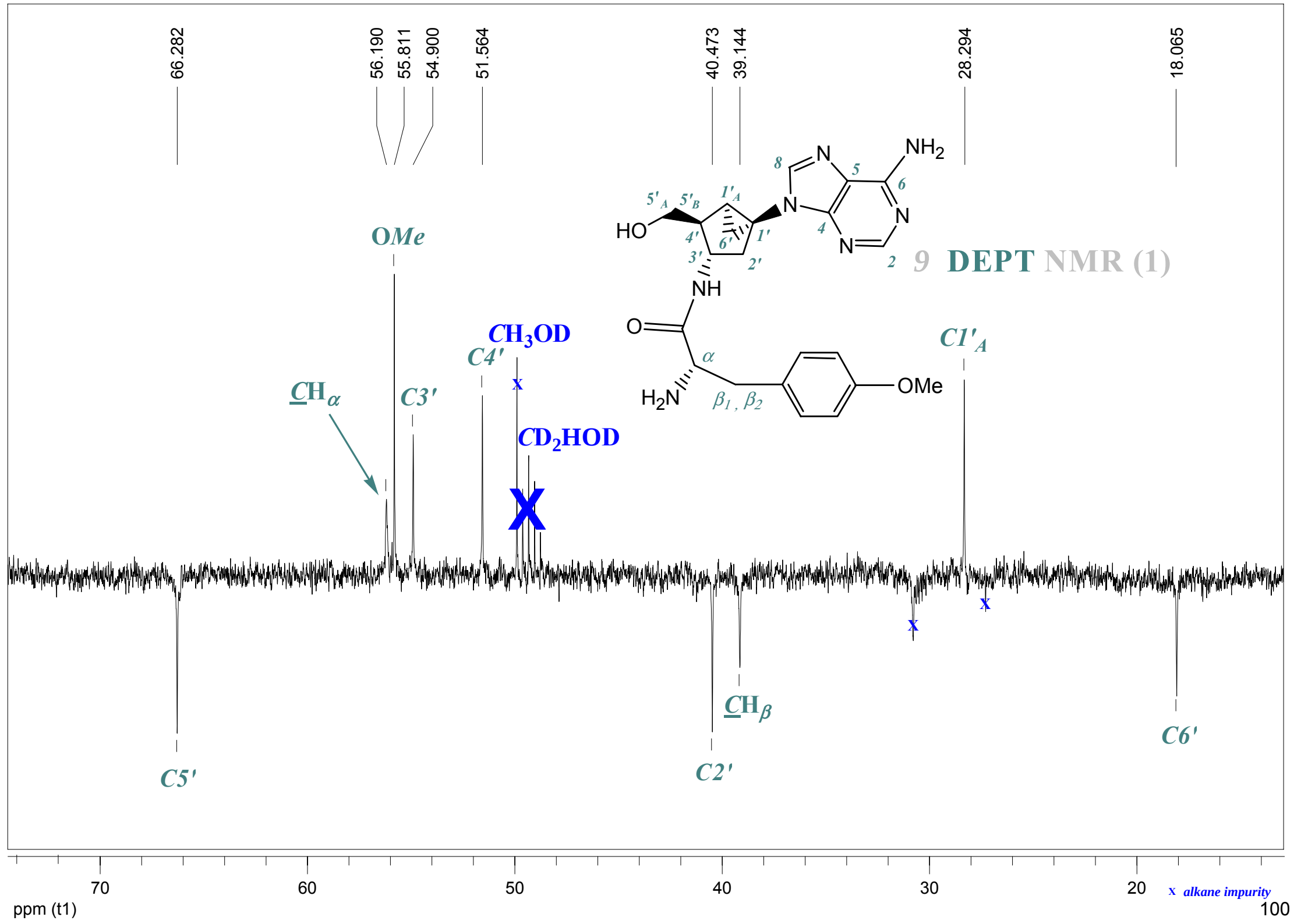

9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
ppm (t1
Ndbf
HO
NH
OMe
25 COSY


25 HSQC
Ndbf
HO
NH
O
NH
OMe
50
100
150
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)

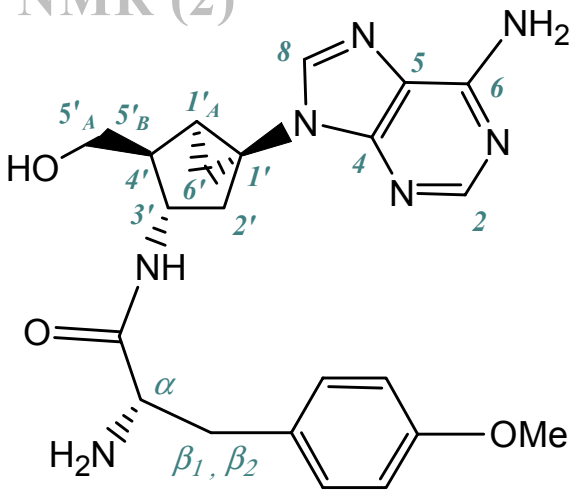

50
100
150
ppm (t1
9.0
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
Ndbf
HO
NH
O
NH
OMe
25 HMBC


4.149
4.120
3.883
3.873
3.846
3.836
3.777
3.763
3.739
3.732
3.676
3.252
3.224
3.218
3.213
3.207
3.202
2.946
2.921
2.919
2.886
2.520
2.488
2.480
2.475
2.457
2.185
2.139
1.717
1.701
1.685
1.669
1.181
0.759
0.739
0.721
OMe
CD3OH
CH3OD
CD2HOD
H2O
H5'A
H5'B
CHα
H3'
Hβ1
Hβ2
H2'β
H4'
H2'α
H1'A
H6'B
H6'A
1.02
1.92
1.25
3.11
2.09
1.25
1.04
3.06
1.11
1.15
5.0
4.0
3.0
2.0
1.0
ppm (t1)
x impurities
9 1H NMR (1)


9 1H NMR (2)
8.079
8.042
7.120
7.092
6.829
6.801
H2
H8
2x H-m-Ph(OMe)
2x H-o-Ph(OMe)
2.07
2.00
1.94
8.00
7.50
7.00
6.50
ppm (t1)


66.282
56.190
55.811
54.900
51.564
40.473
39.144
28.294
18.065
OMe
CH3OD
C4'
CHα
C3'
CD2HOD
C1'A
CHβ
C5'
C2'
C6'
9 DEPT NMR (1)
x alkane impurity
70
60
50
40
30
20
ppm (t1)
100

9 DEPT NMR (2)



153.506

143.180

131.697

115.347

2x C-*m*-Ph(OMe)

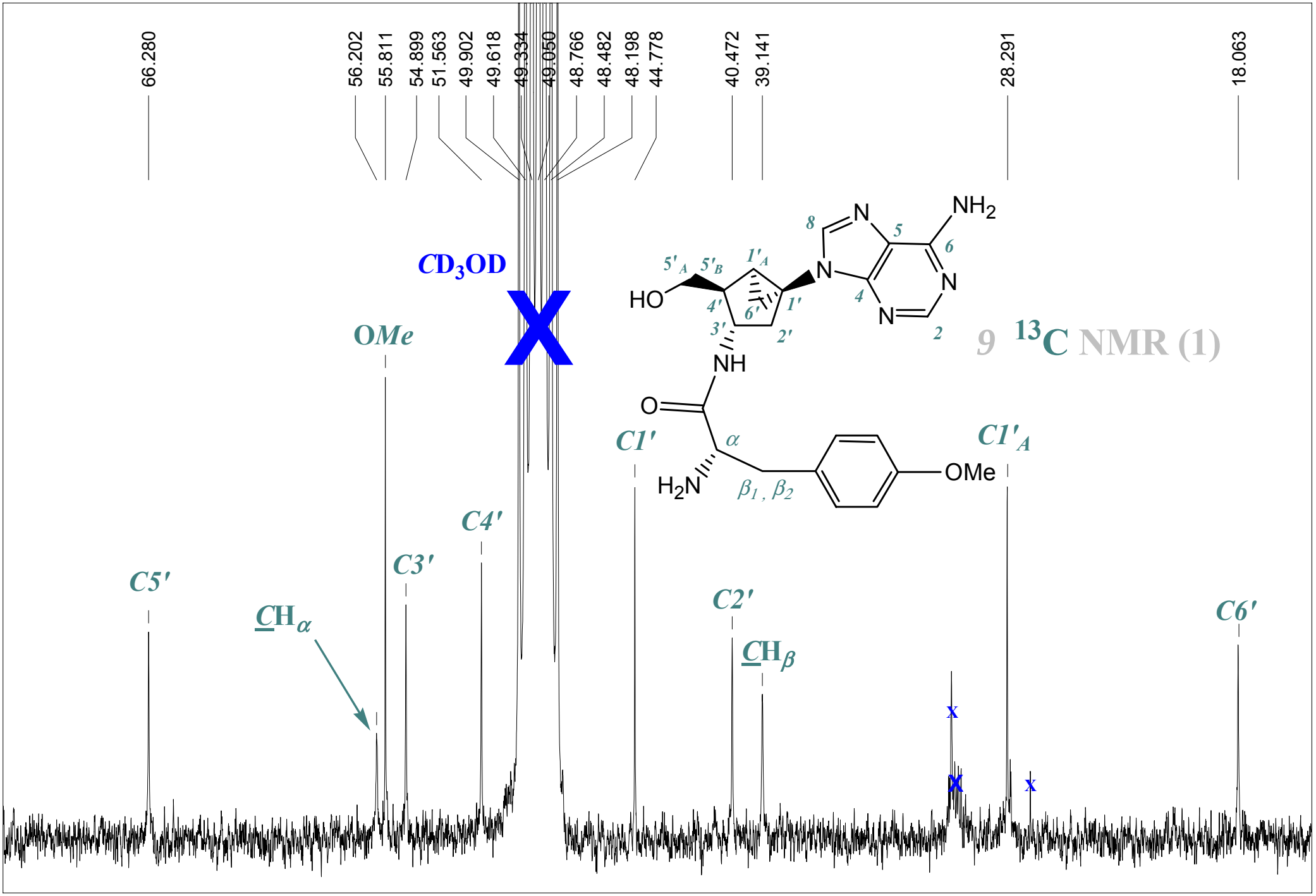
2x C-*o*-Ph(OMe)

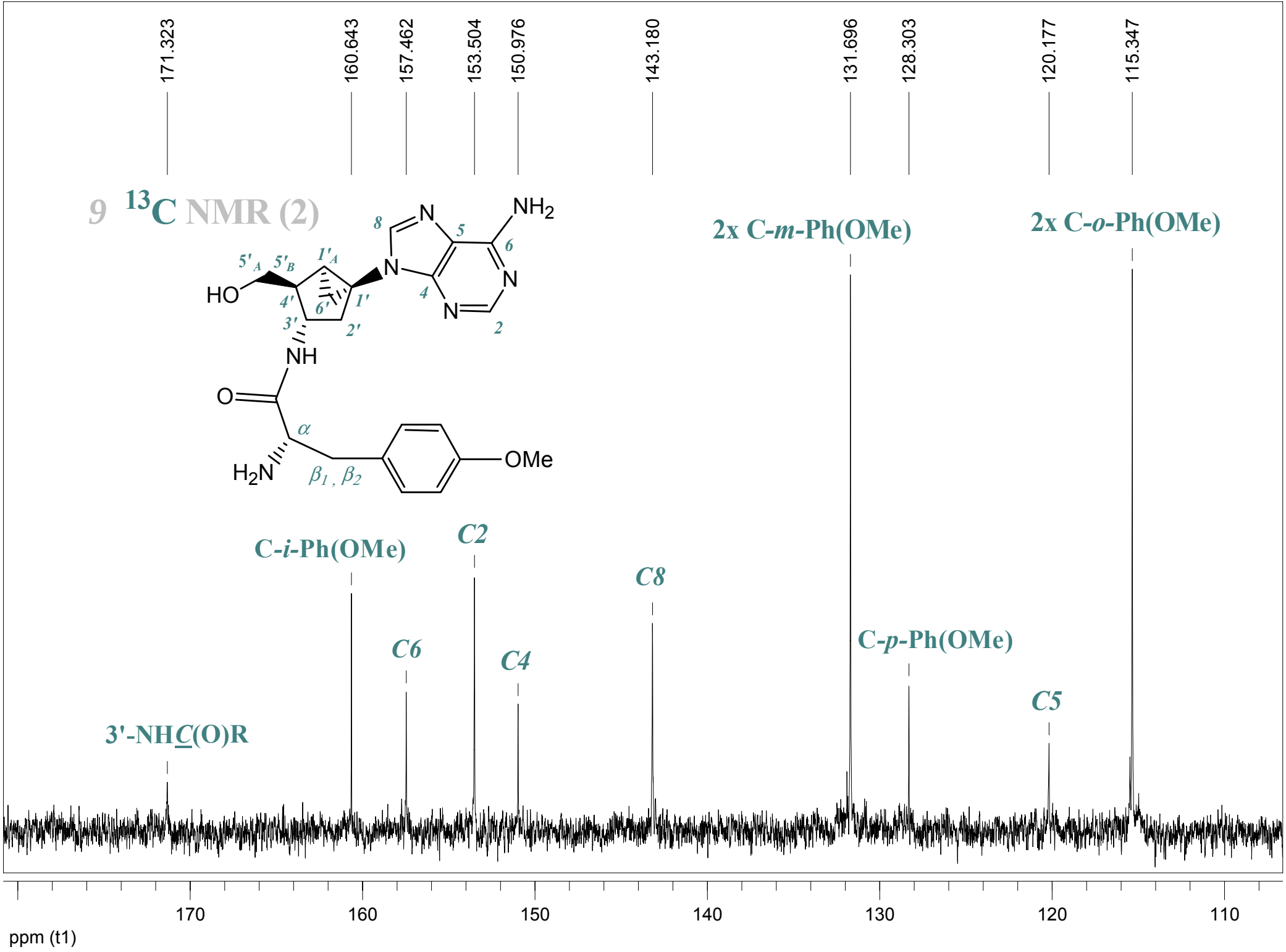
C2

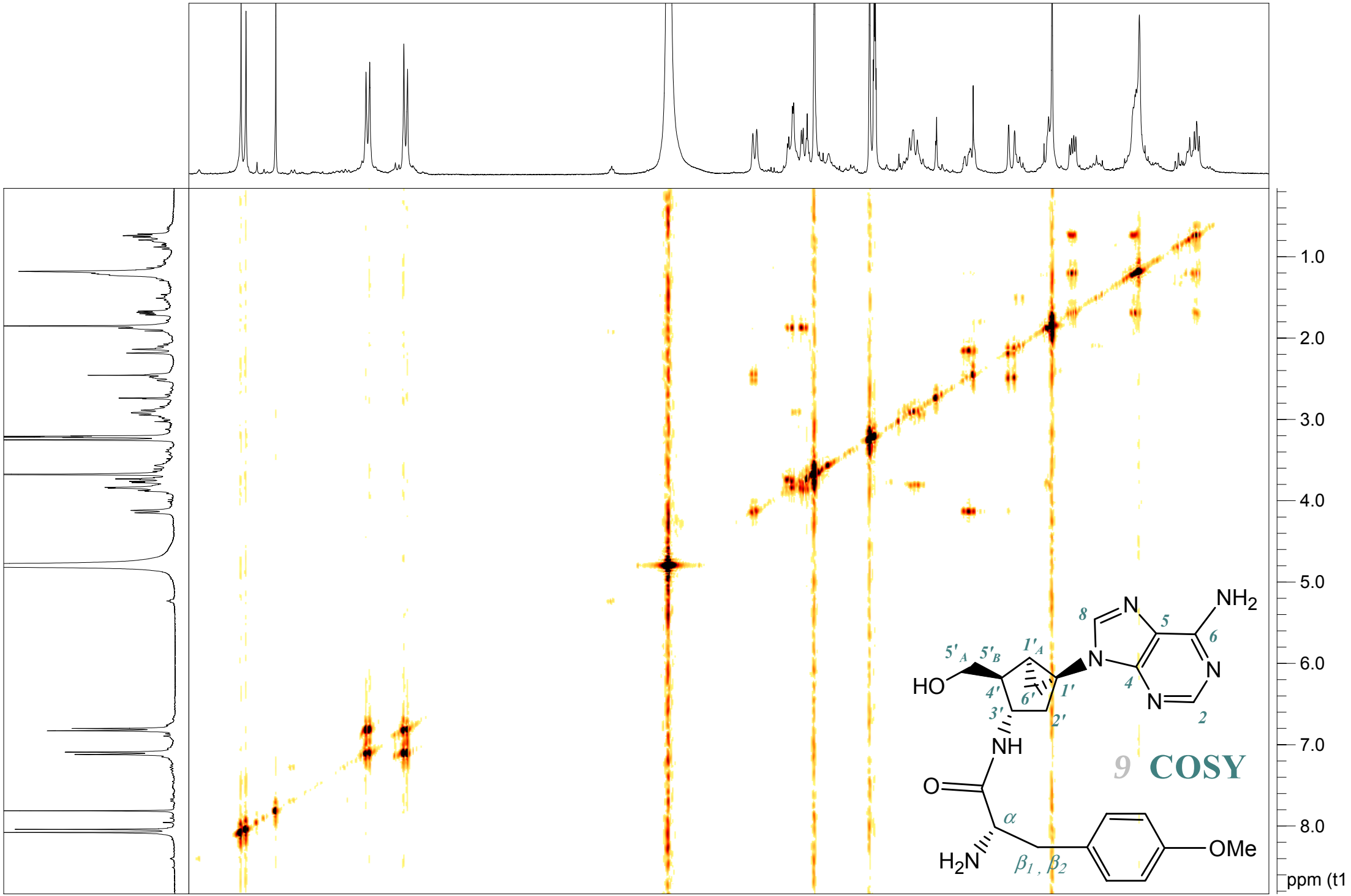
C8

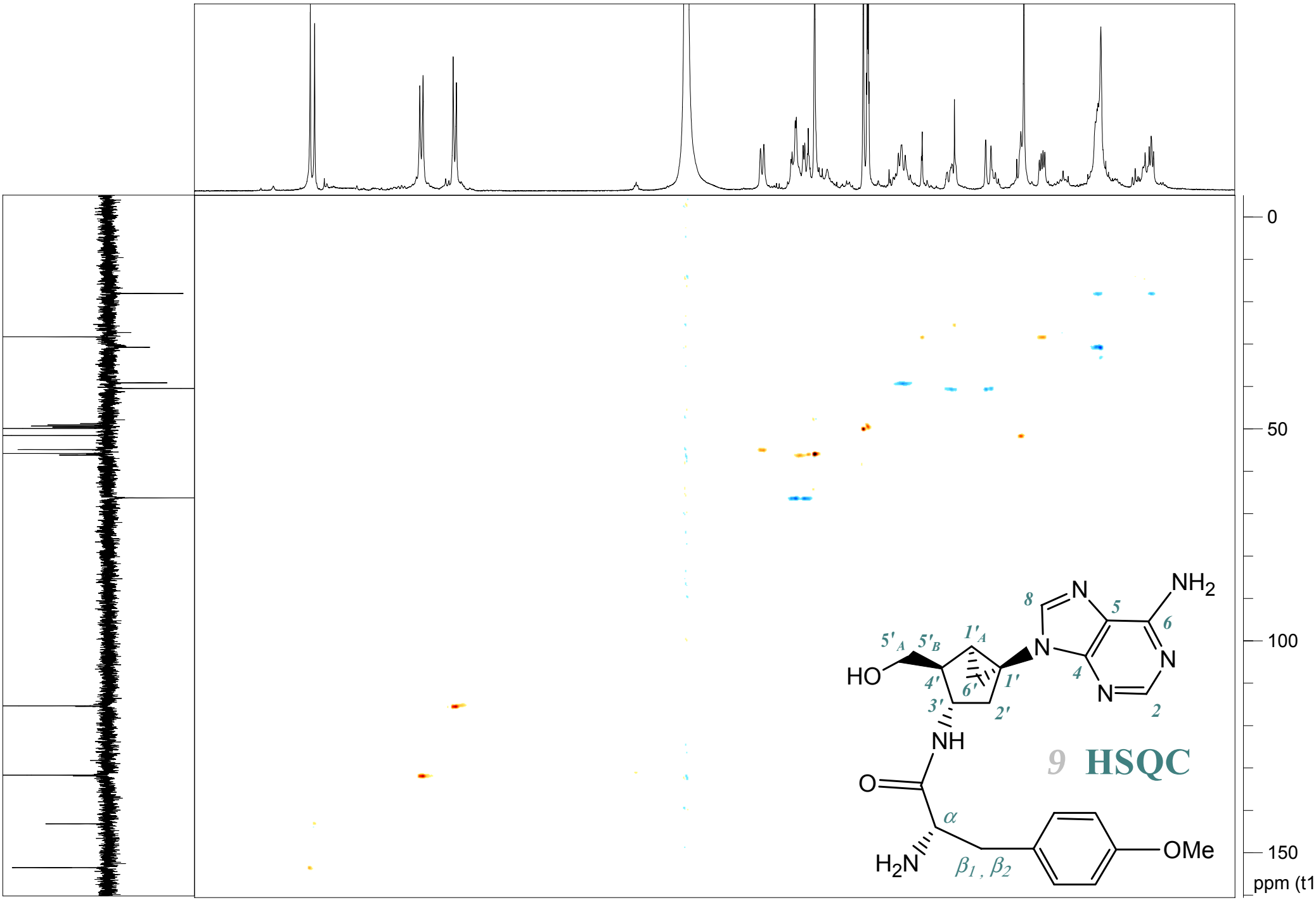
160 150 140 130 120 110

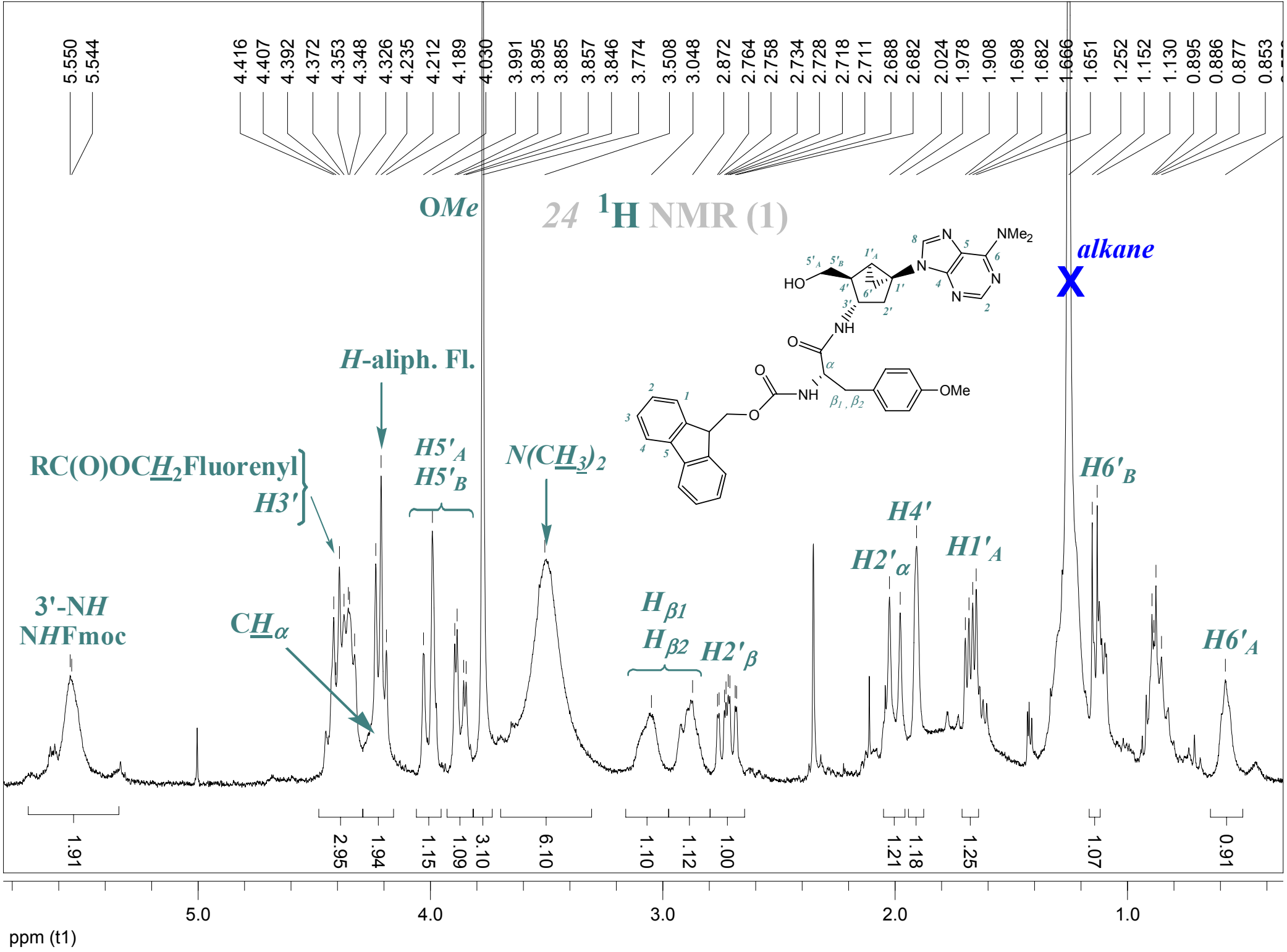
ppm (t1)

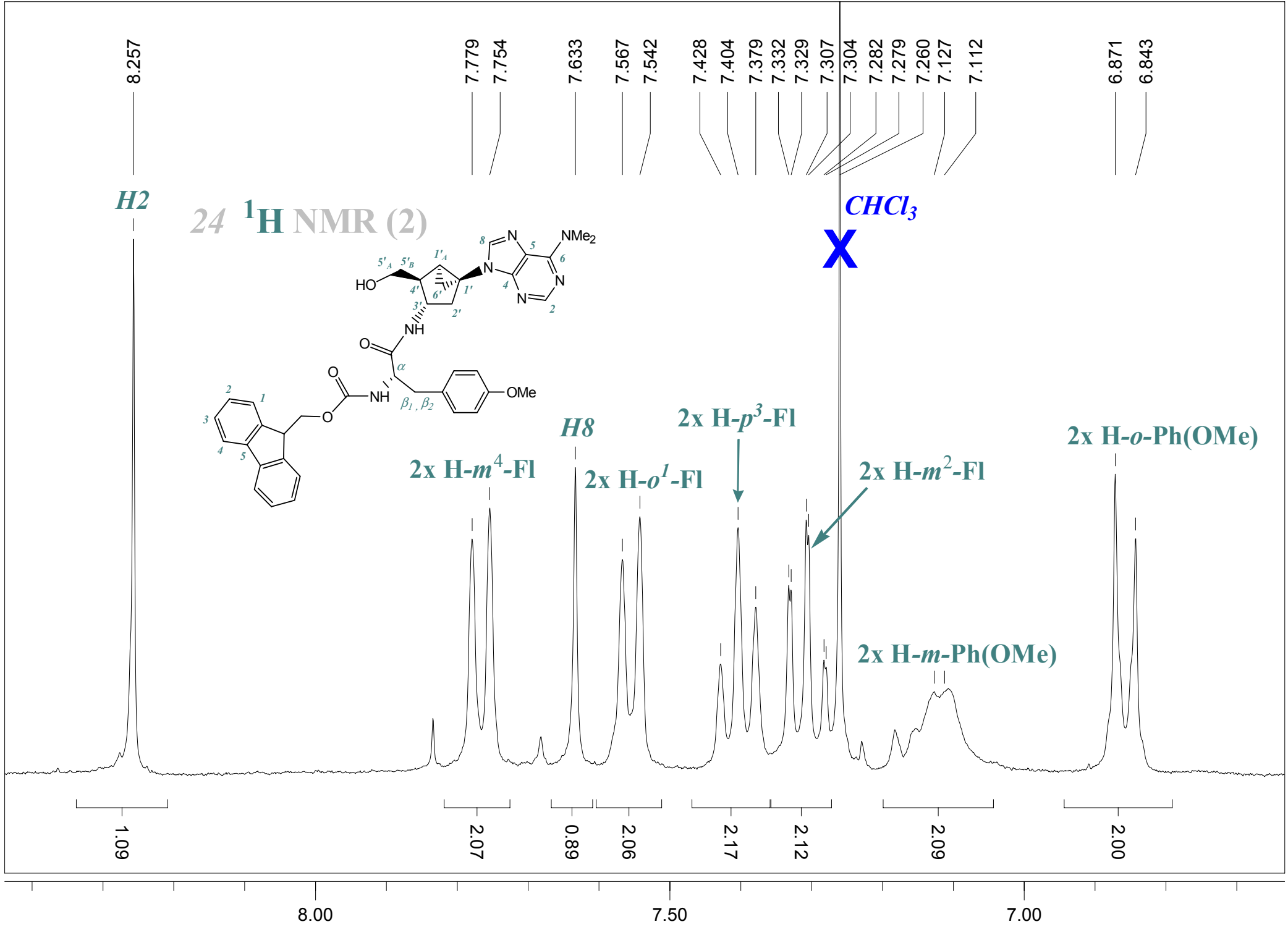

66.280
56.202
55.811
54.899
51.563
49.902
49.618
49.334
49.050
48.766
48.482
48.198
44.778
40.472
39.141
28.291
18.063
CD3OD
OMe
C5'
CHα
C3'
C4'
C1'
C2'
CHβ
C1'A
C6'
9 13C NMR (1)
70
60
50
40
30
20
ppm (t1)
x alkane impurities

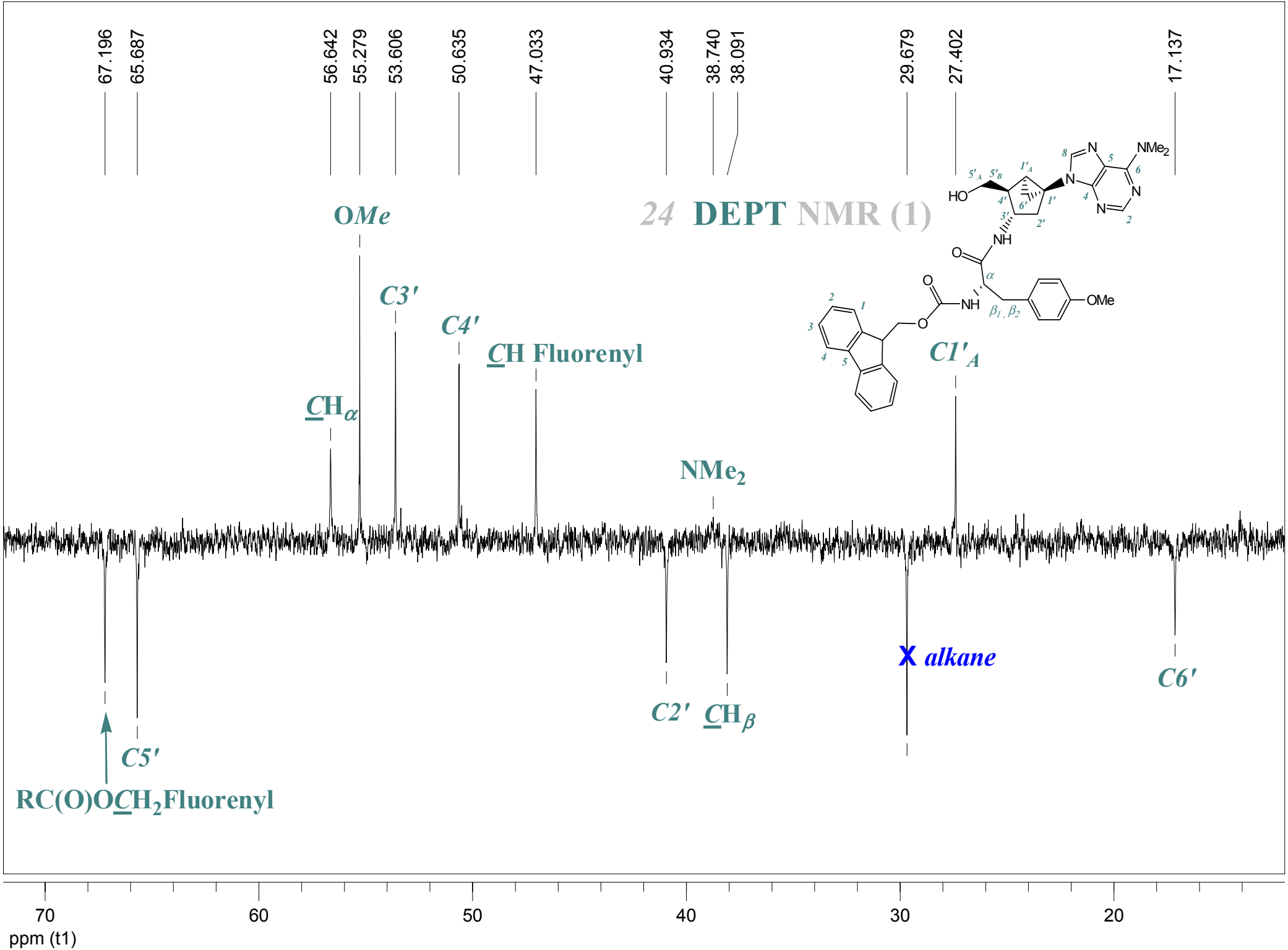

171.323
160.643
157.462
153.504
150.976
143.180
131.696
128.303
120.177
115.347
9 13C NMR (2)
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
C-i-Ph(OMe)
C2
C8
C6
C4
C-p-Ph(OMe)
C5
3'-NHC(O)R
170
160
150
140
130
120
110
ppm (t1)

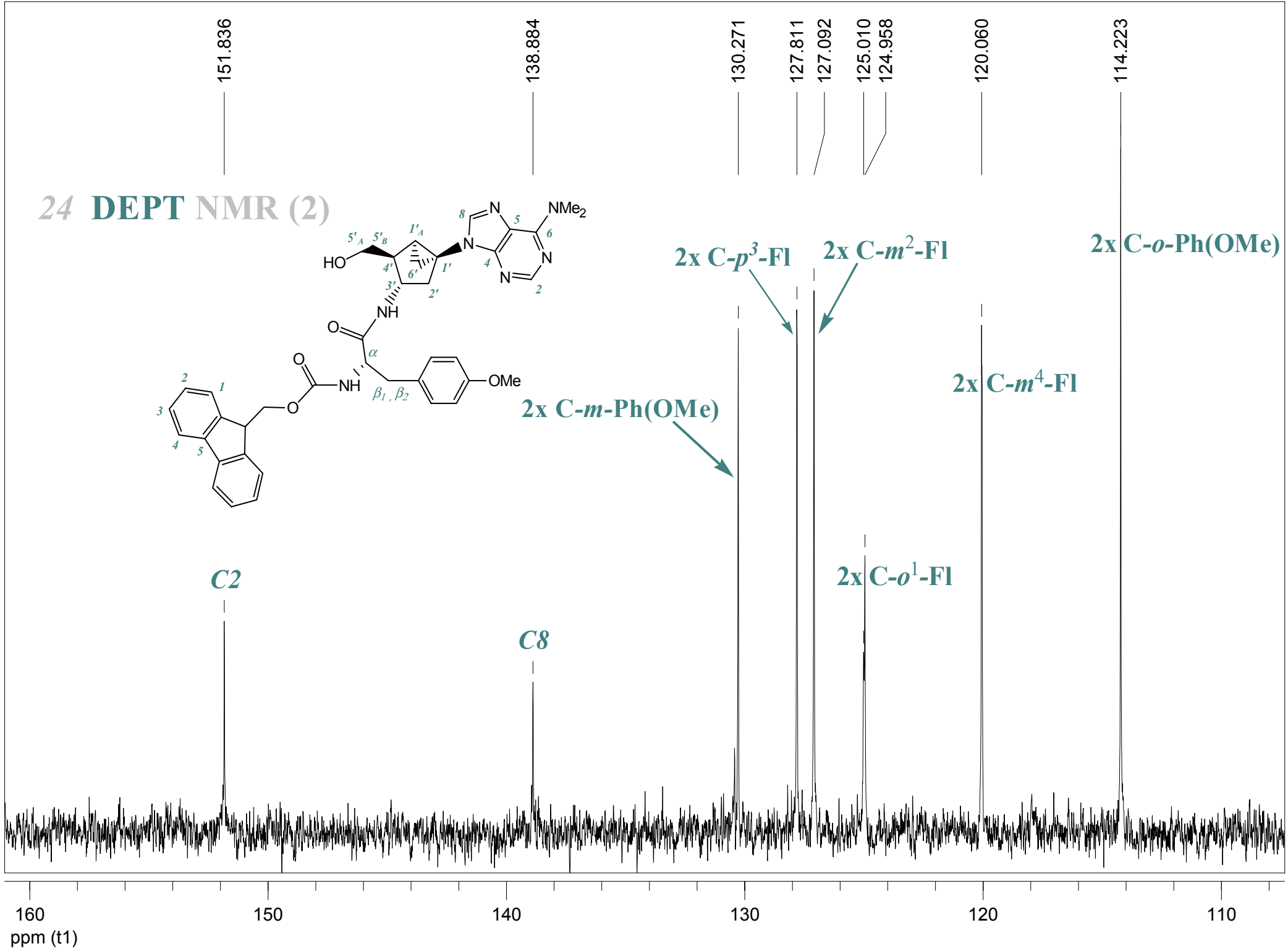

8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
ppm (t1
HO
NH
O
NH2
OMe
9 COSY

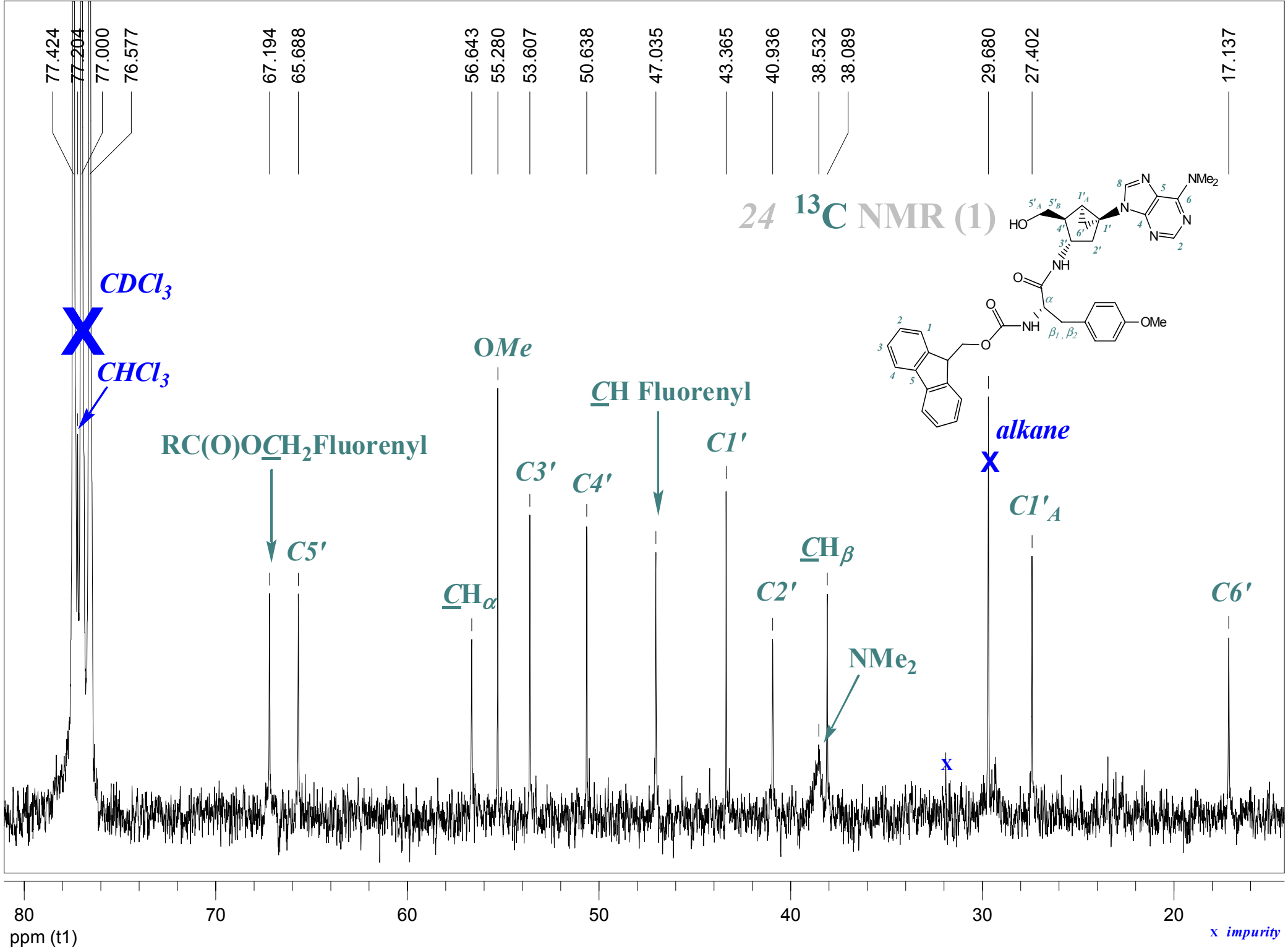

0
50
100
150
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
HO
5'A
5'B
1'A
1'
2'
3'
4'
6'
NH
O
α
H2N
β1 , β2
OMe
N
NH2
8
5
6
4
2
9 HSQC

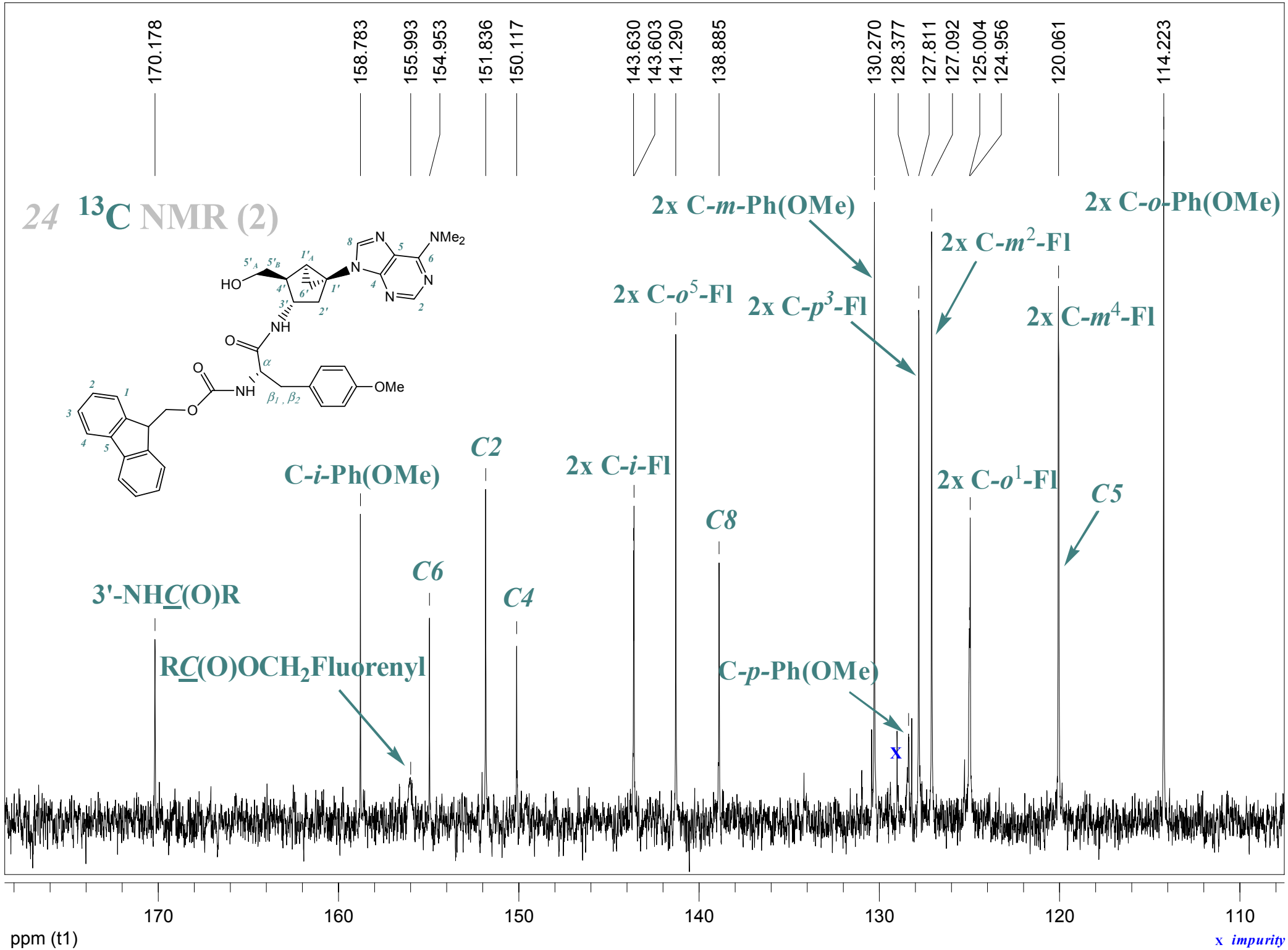

5.550
5.544
4.416
4.407
4.392
4.372
4.353
4.348
4.326
4.235
4.212
4.189
4.030
3.991
3.895
3.885
3.857
3.846
3.774
3.508
3.048
2.872
2.764
2.758
2.734
2.728
2.718
2.711
2.688
2.682
2.024
1.978
1.908
1.698
1.682
1.666
1.651
1.252
1.152
1.130
0.895
0.886
0.877
0.853
OMe
24 1H NMR (1)
alkane
H-aliph. Fl.
RC(O)OCH2Fluorenyl
H3'
H5'A
H5'B
N(CH3)2
H6'B
H4'
H2'α
H1'A
3'-NH
NHFmoc
CHα
Hβ1
Hβ2
H2'β
H6'A
1.91
2.95
1.94
1.15
1.09
3.10
6.10
1.10
1.12
1.00
1.21
1.18
1.25
1.07
0.91
5.0
4.0
3.0
2.0
1.0
ppm (t1)

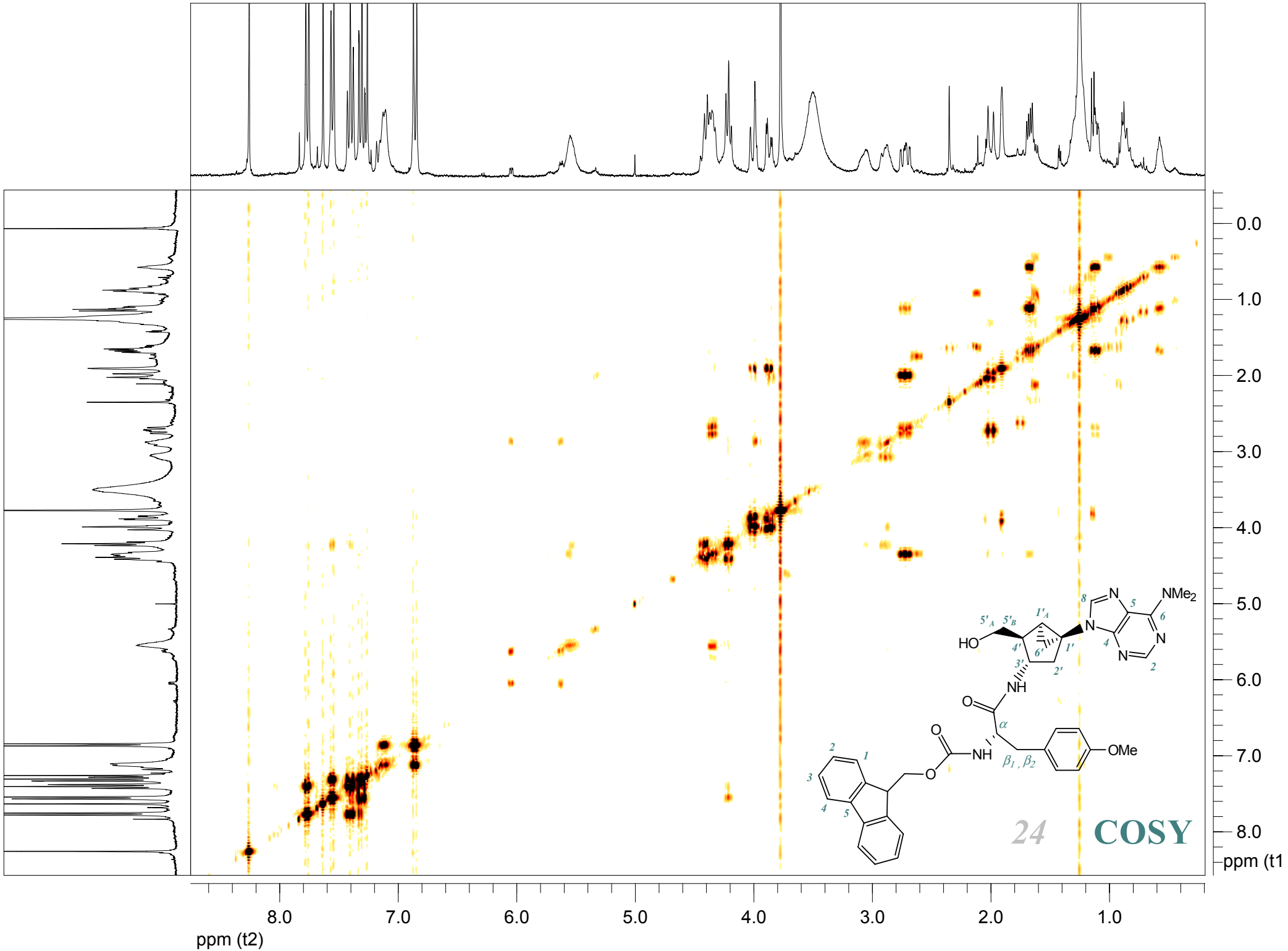

24 1H NMR (2)
8.257
7.779
7.754
7.633
7.567
7.542
7.428
7.404
7.379
7.332
7.329
7.307
7.304
7.282
7.279
7.260
7.127
7.112
6.871
6.843
H2
CHCl3
H8
2x H-m4-Fl
2x H-o1-Fl
2x H-p3-Fl
2x H-m2-Fl
2x H-o-Ph(OMe)
2x H-m-Ph(OMe)
1.09
2.07
0.89
2.06
2.17
2.12
2.09
2.00
8.00
7.50
7.00
ppm (t1)

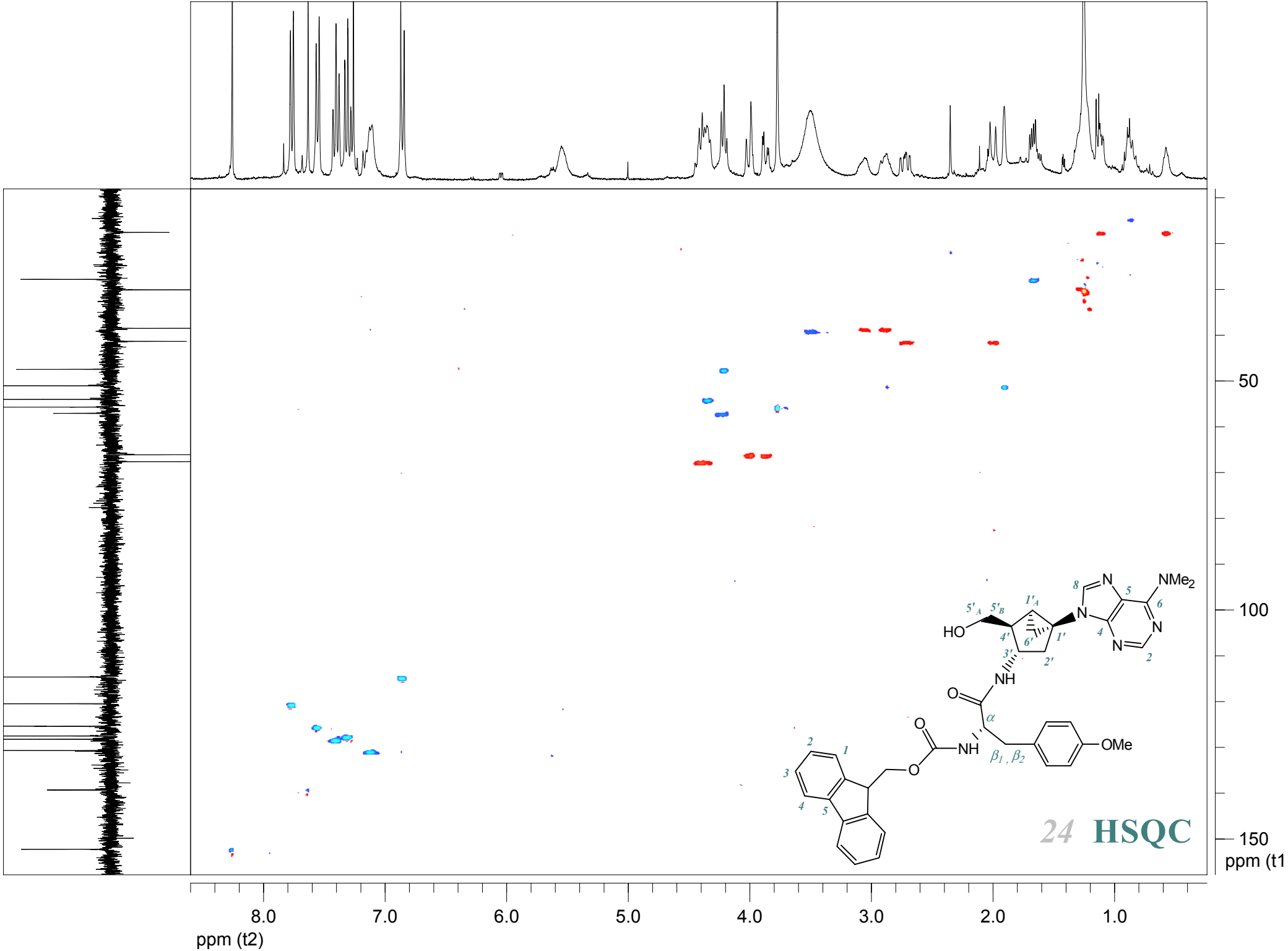

67.196
65.687
56.642
55.279
53.606
50.635
47.033
40.934
38.740
38.091
29.679
27.402
17.137
24 DEPT NMR (1)
OMe
C3'
C4'
CH Fluorenyl
CHα
NMe2
C1'A
X alkane
C6'
C2'
CHβ
C5'
RC(O)OCH2Fluorenyl
70
60
50
40
30
20
ppm (t1)

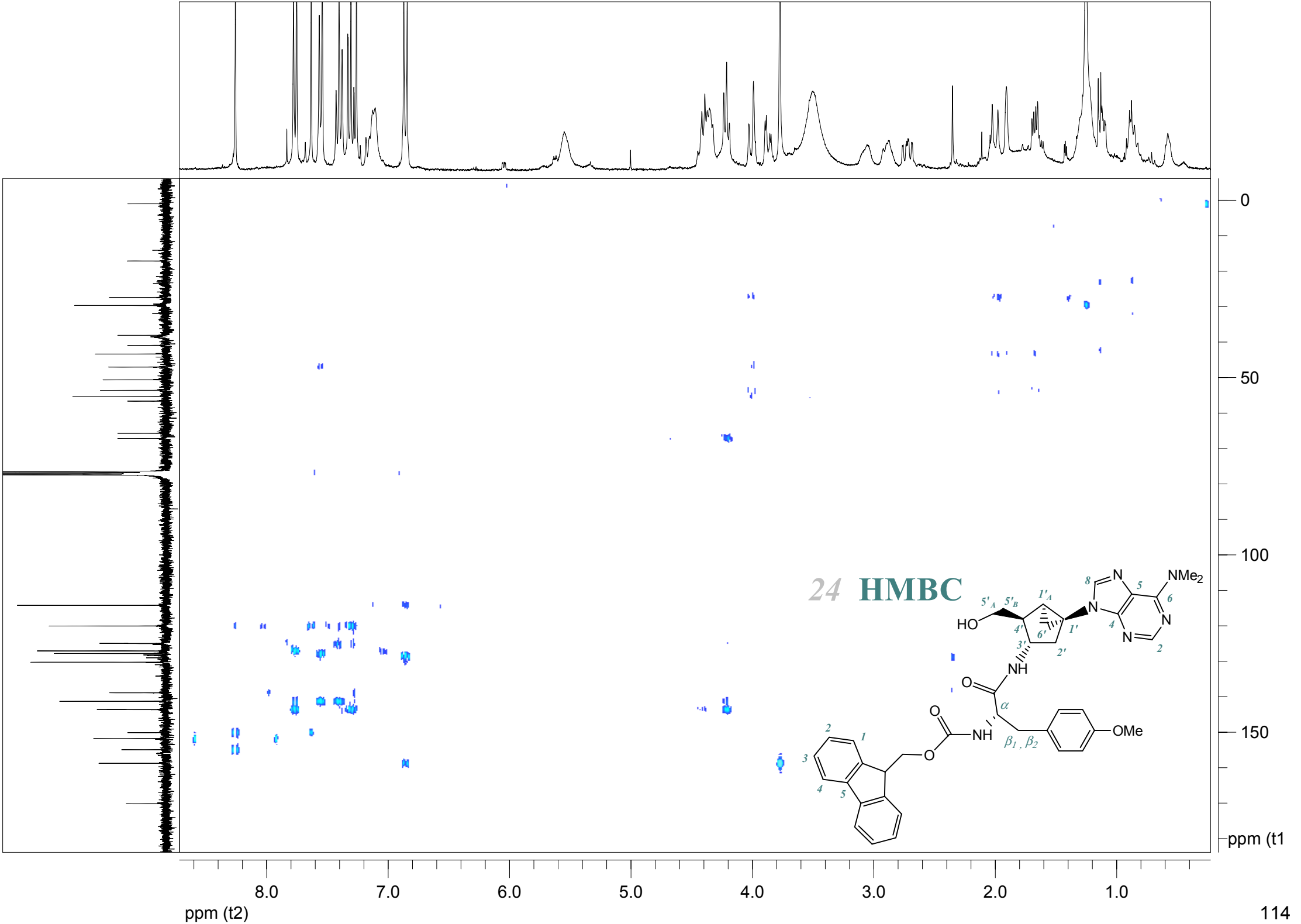

151.836
138.884
130.271
127.811
127.092
125.010
124.958
120.060
114.223
24 DEPT NMR (2)
2x C-p3-Fl
2x C-m2-Fl
2x C-o-Ph(OMe)
2x C-m4-Fl
2x C-m-Ph(OMe)
2x C-o1-Fl
C2
C8
160
150
140
130
120
110
ppm (t1)

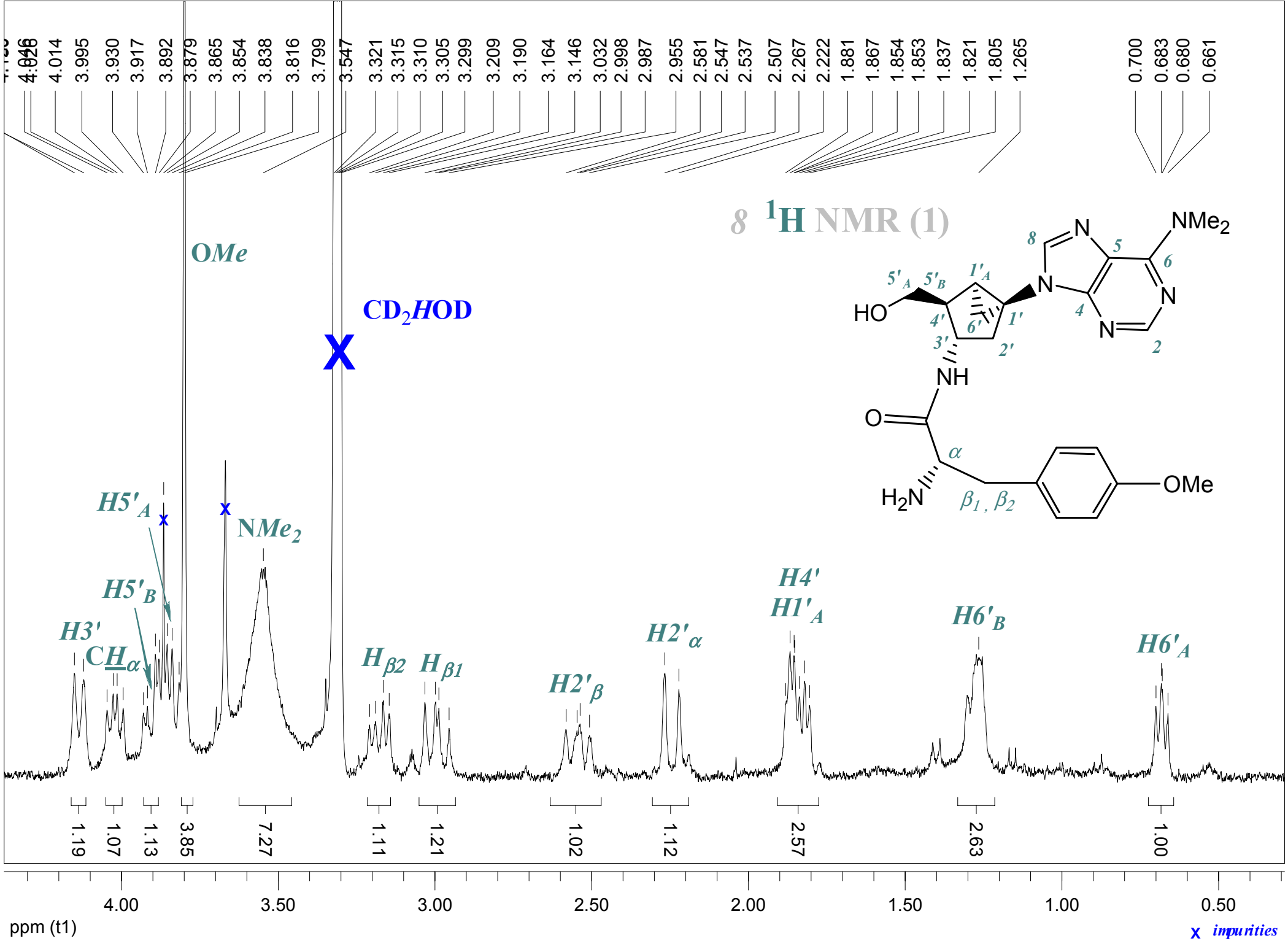

77.424
77.204
77.000
76.577
67.194
65.688
56.643
55.280
53.607
50.638
47.035
43.365
40.936
38.532
38.089
29.680
27.402
17.137
24 13C NMR (1)
CDCl3
CHCl3
OMe
CH Fluorenyl
RC(O)OCH2Fluorenyl
C3'
C4'
C1'
alkane
C1'A
C5'
CHα
CHβ
C2'
C6'
NMe2
x
80
70
60
50
40
30
20
ppm (t1)
x impurity

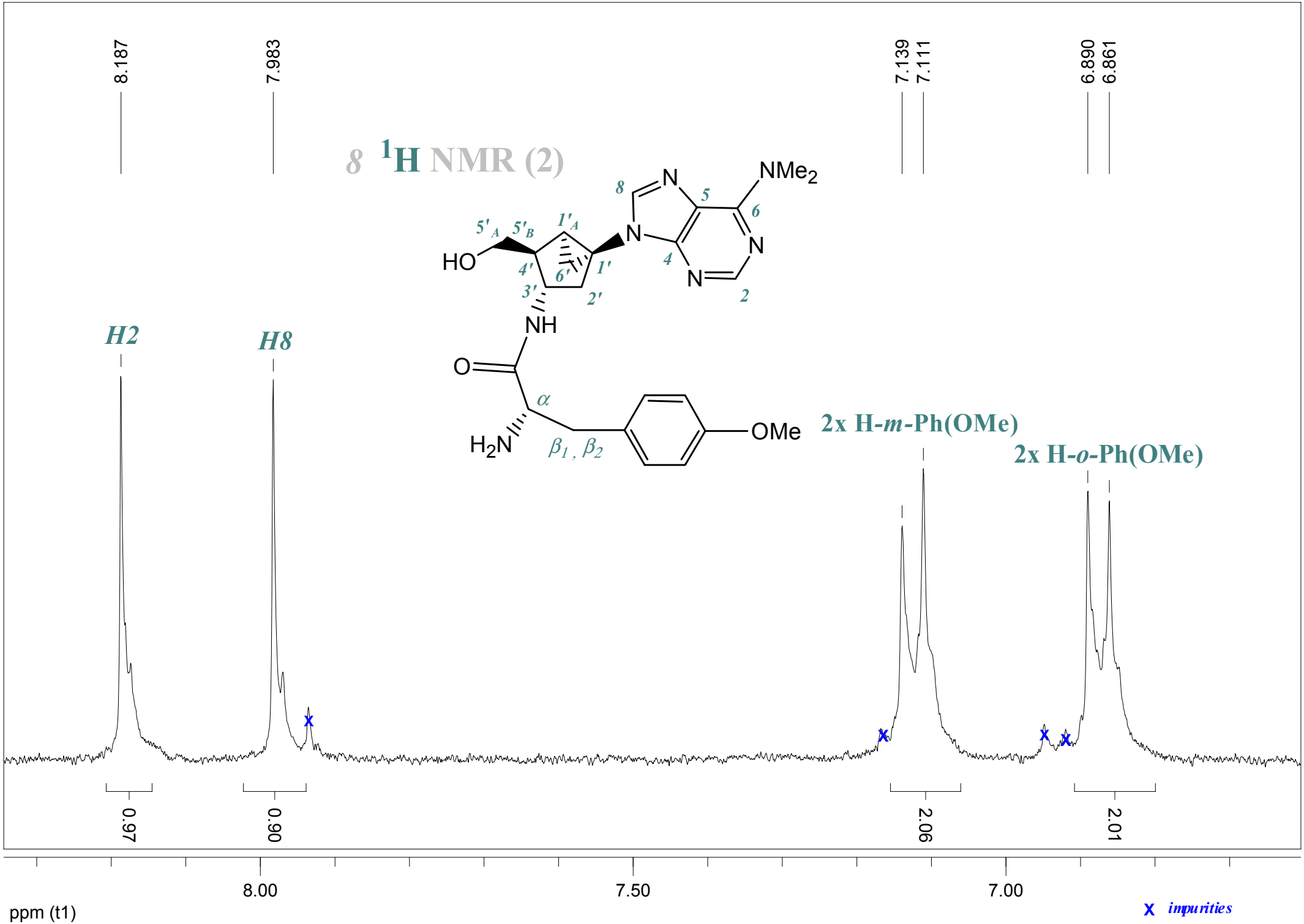

24 13C NMR (2)
170.178
158.783
155.993
154.953
151.836
150.117
143.630
143.603
141.290
138.885
130.270
128.377
127.811
127.092
125.004
124.956
120.061
114.223
2x C-m-Ph(OMe)
2x C-o-Ph(OMe)
2x C-m2-Fl
2x C-o5-Fl
2x C-p3-Fl
2x C-m4-Fl
C2
C-i-Ph(OMe)
2x C-i-Fl
2x C-o1-Fl
C5
C8
C6
C4
3'-NHC(O)R
RC(O)OCH2Fluorenyl
C-p-Ph(OMe)
x
170
160
150
140
130
120
110
ppm (t1)
x impurity

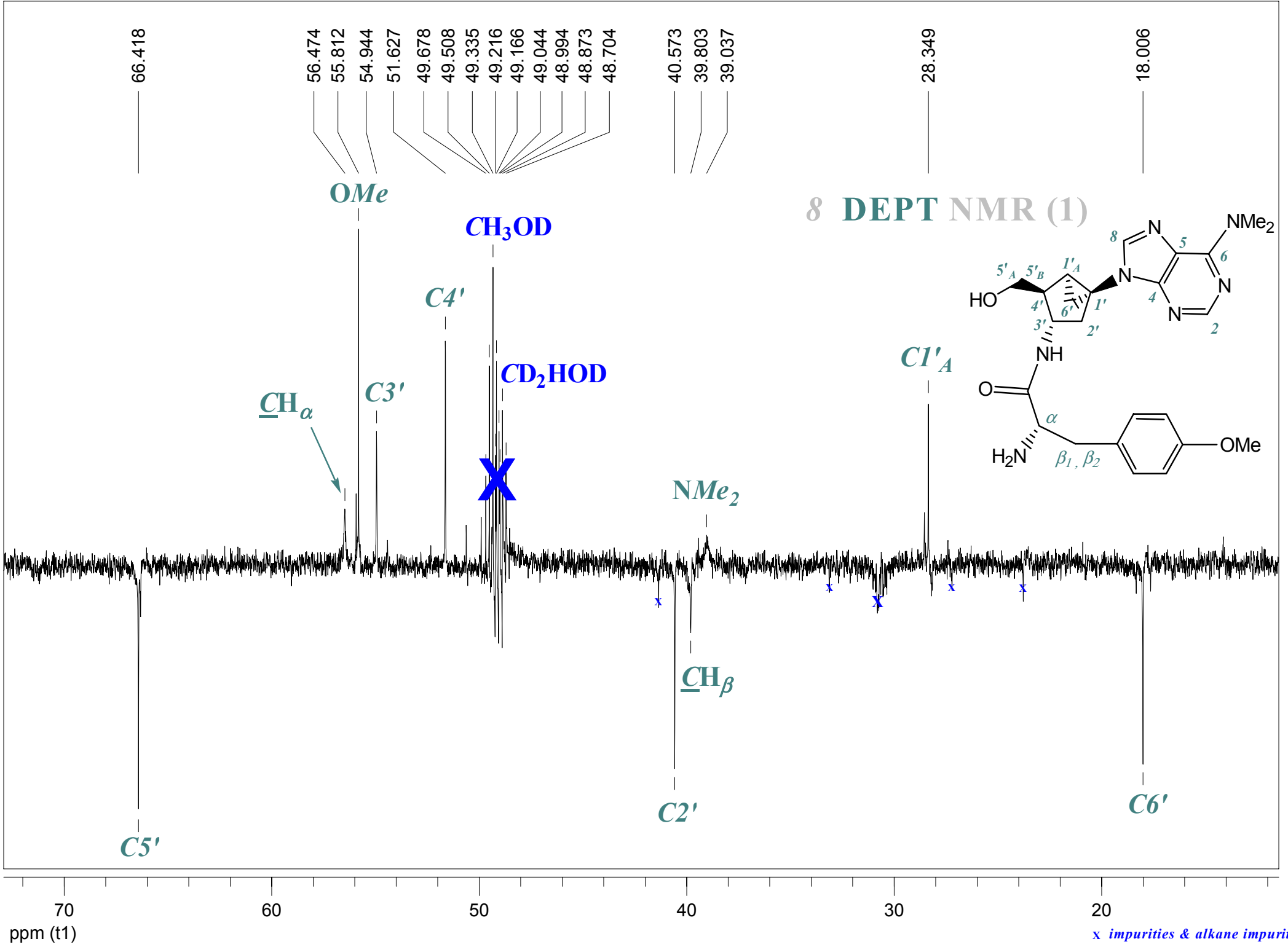

0.0
1.0
2.0
3.0
4.0
5.0
6.0
7.0
8.0
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
HO
NH
NH
O
O
O
OMe
NMe2
N
24
COSY


8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
50
100
150
ppm (t1
24 HSQC

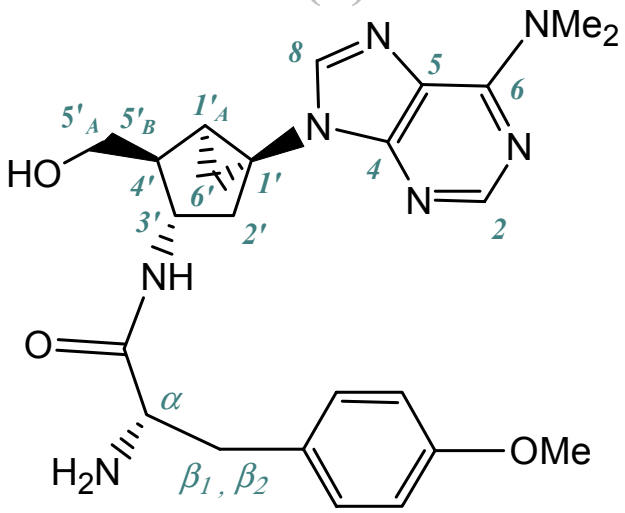

24 HMBC
HO
NH
O
NH
OMe
NMe2
ppm (t2)
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
0
50
100
150


8 1H NMR (1)
OMe
CD2HOD
NMe2
H5'A
H5'B
H3'
CHα
Hβ2
Hβ1
H2'β
H2'α
H4'
H1'A
H6'B
H6'A
1.19
1.07
1.13
3.85
7.27
1.11
1.21
1.02
1.12
2.57
2.63
1.00
4.00
3.50
3.00
2.50
2.00
1.50
1.00
0.50
ppm (t1)
x impurities

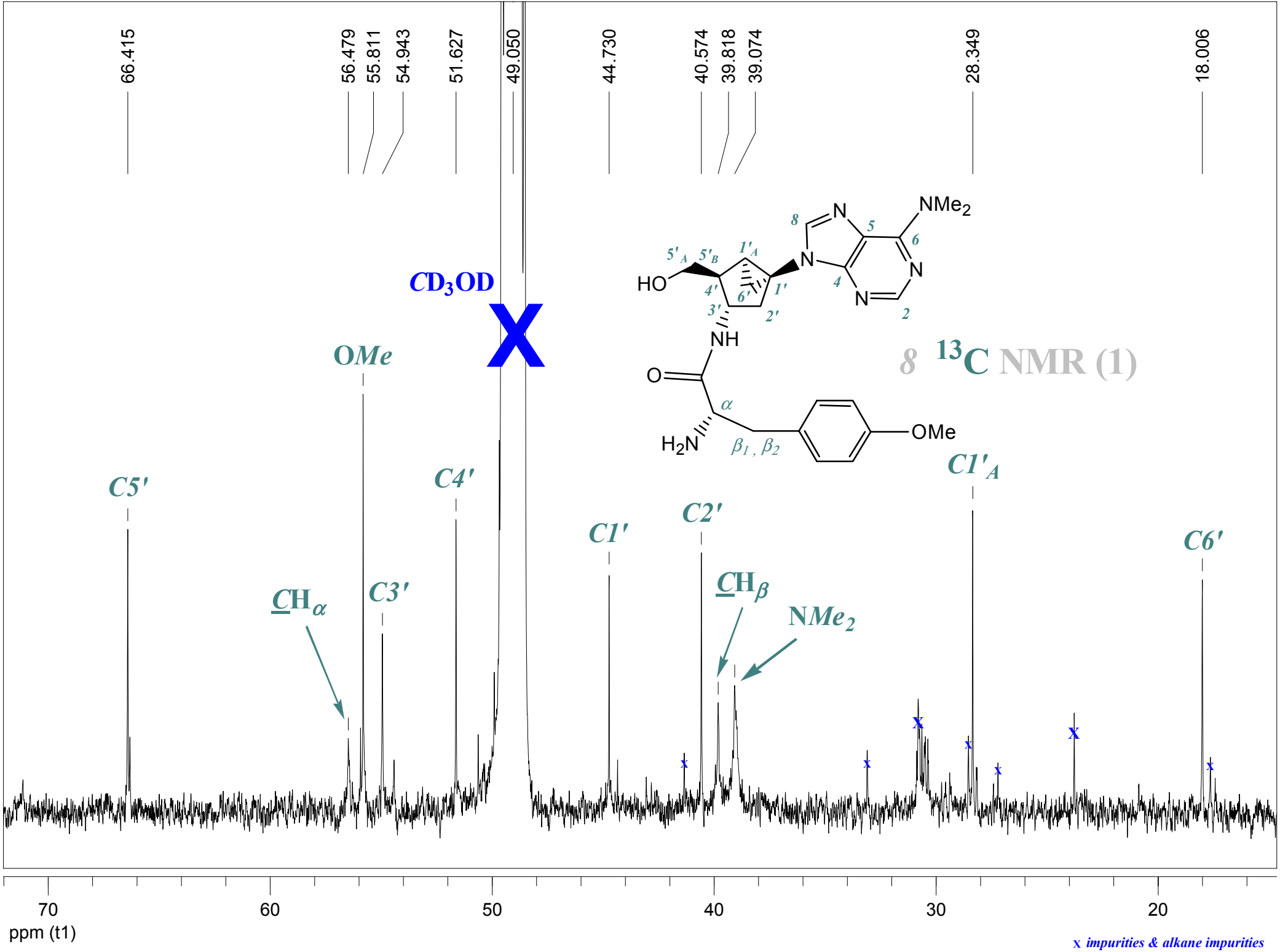

8.187
7.983
7.139
7.111
6.890
6.861
8 1H NMR (2)
NMe2
HO
NH
O
OMe
H2N
H2
H8
2x H-m-Ph(OMe)
2x H-o-Ph(OMe)
0.97
0.90
2.06
2.01
8.00
7.50
7.00
ppm (t1)
x impurities

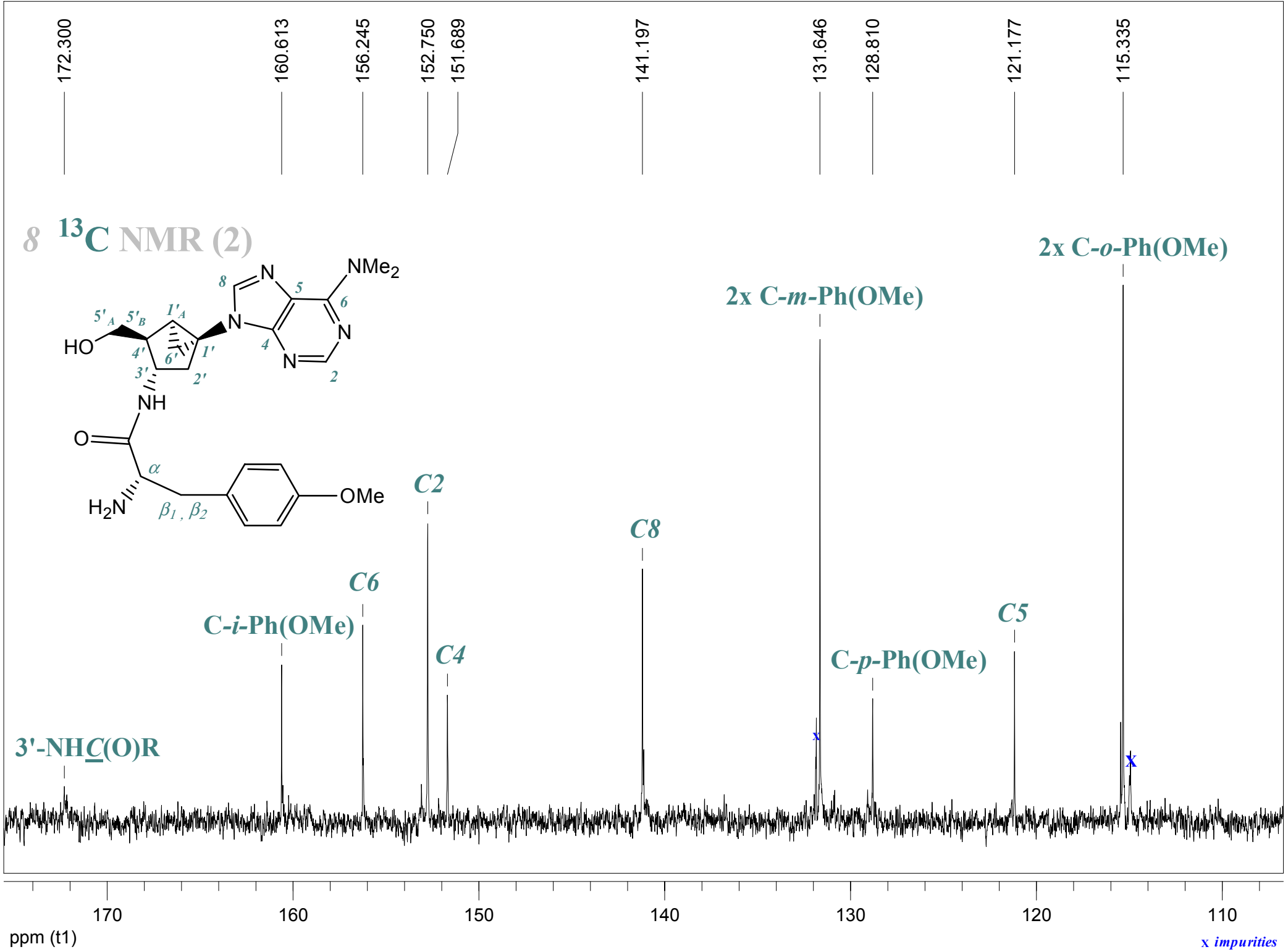

66.418
56.474
55.812
54.944
51.627
49.678
49.508
49.335
49.216
49.166
49.044
48.994
48.873
48.704
40.573
39.803
39.037
28.349
18.006
OMe
CH3OD
C4'
CD2HOD
CHα
C3'
C1'A
NMe2
CHβ
C5'
C2'
C6'
8 DEPT NMR (1)
NMe2
HO
NH
O
OMe
H2N
70
60
50
40
30
20
ppm (t1)
x impurities & alkane impurity

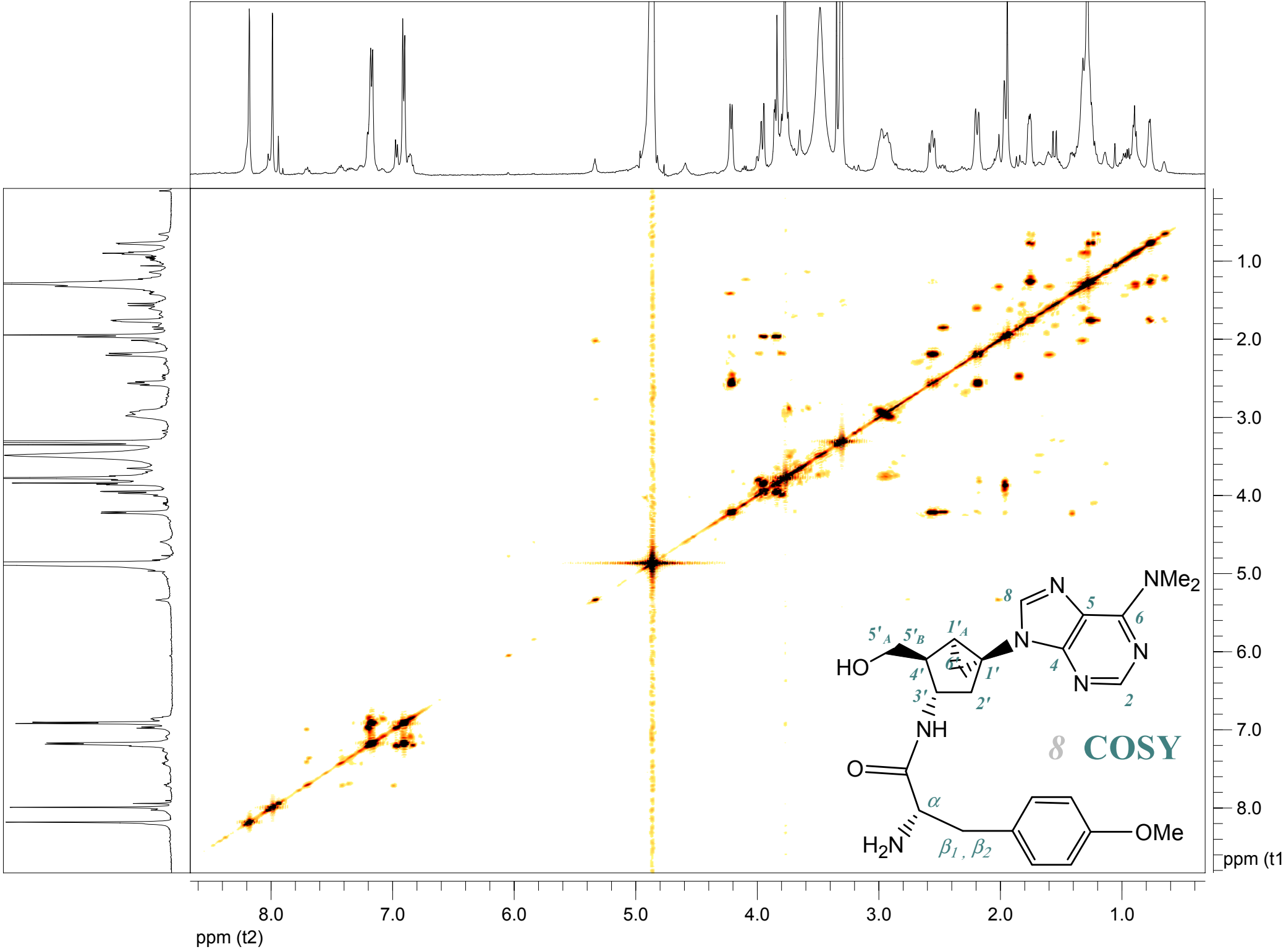
8 DEPT NMR (2)

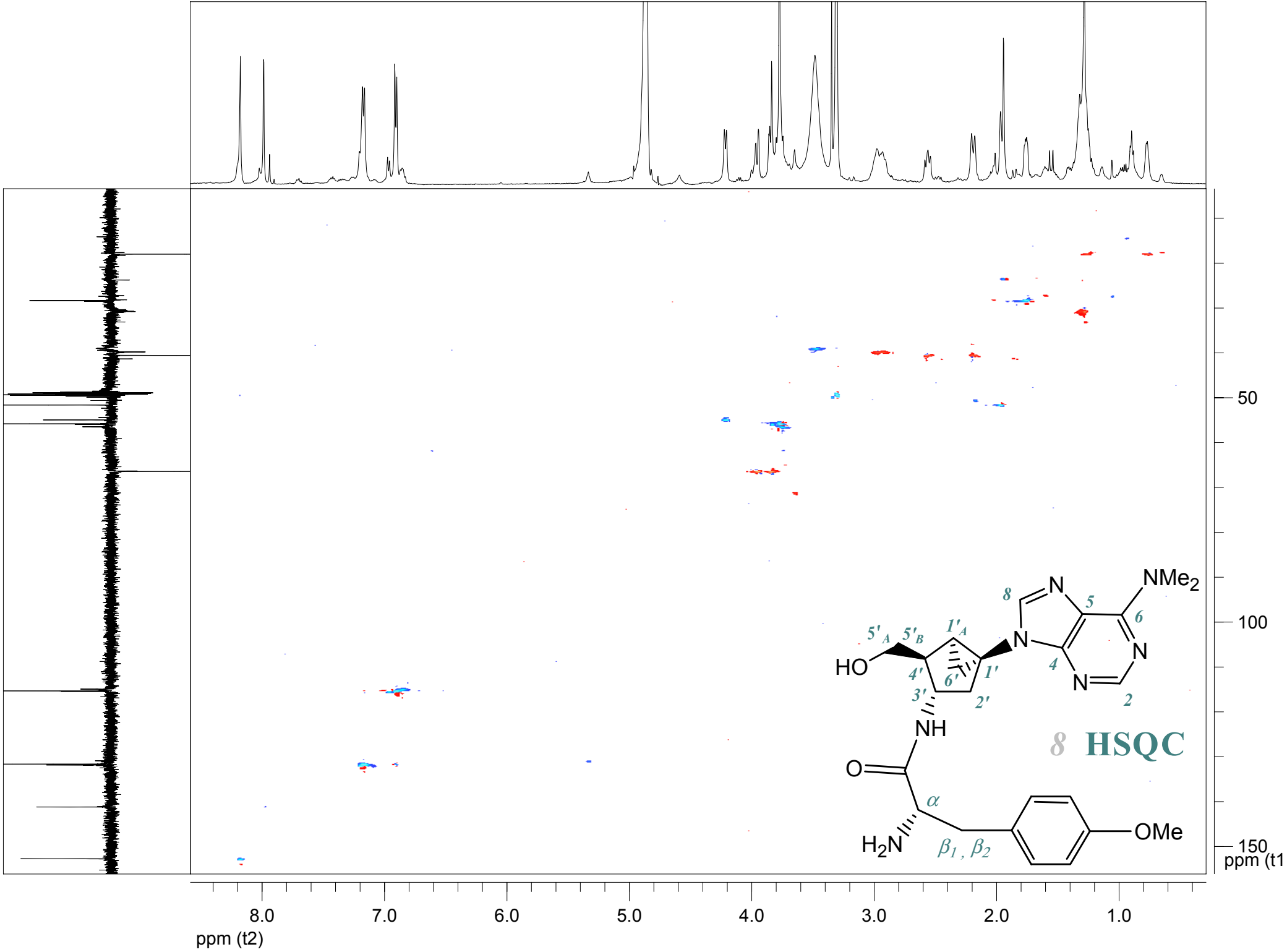

NMe2
N
8
5
6
N
4
N
2
5'A
5'B
1'A
HO
4'
6'
1'
3'
2'
NH
O
α
H2N
β1 , β2
OMe

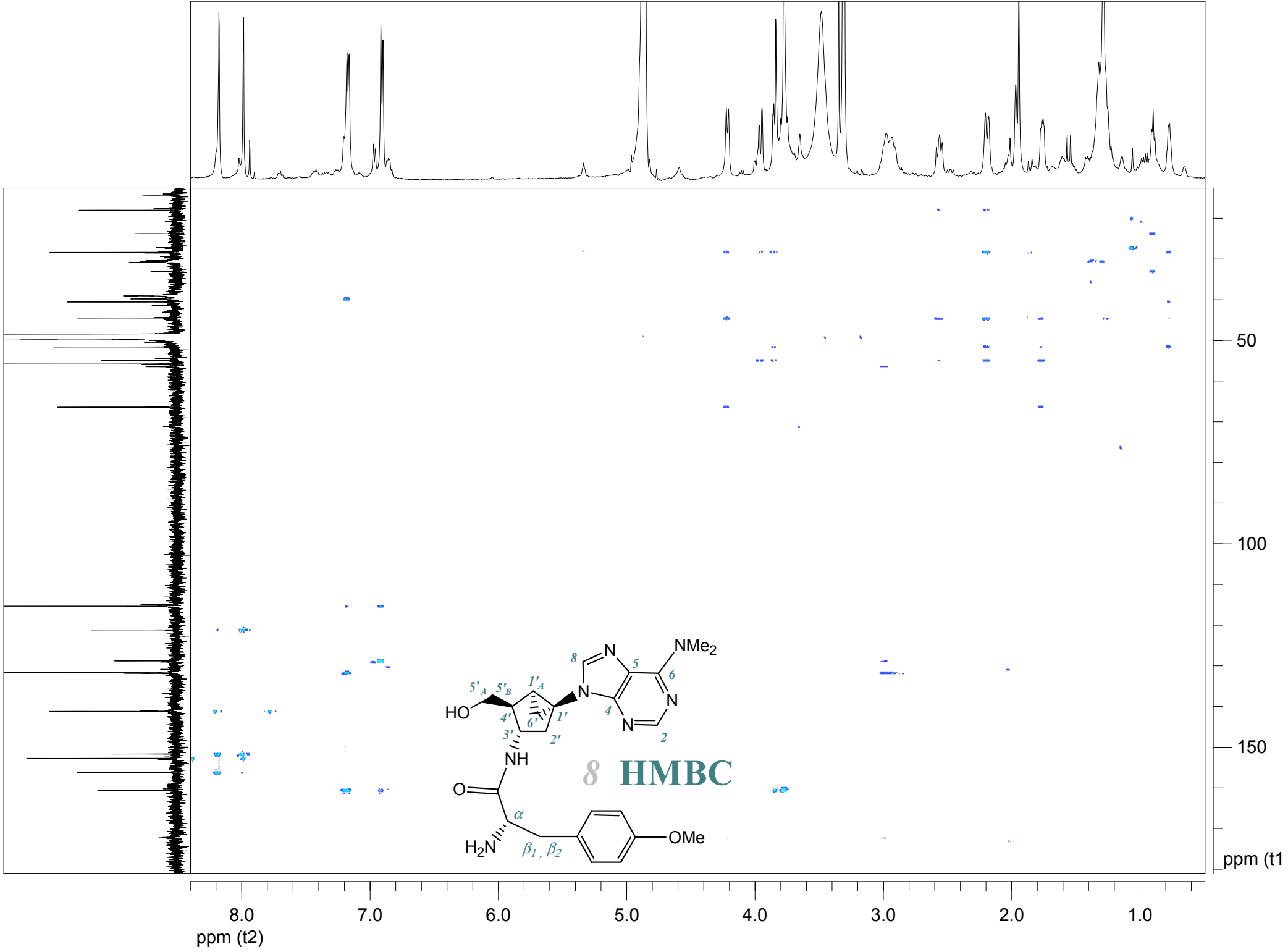
152.749
141.200
131.647
115.335
2x C-*m*-Ph(OMe)
2x C-*o*-Ph(OMe)
C2
C8
x
x
x
160
150
140
130
120
110
100
ppm (t1)
x impurities


66.415
56.479
55.811
54.943
51.627
49.050
44.730
40.574
39.818
39.074
28.349
18.006
CD3OD
OMe
C5'
C4'
C1'
C2'
C1'A
C6'
CHα
C3'
CHβ
NMe2
NMe2
OMe
HO
NH
O
H2N
α
β1 , β2
8 13C NMR (1)
70
60
50
40
30
20
ppm (t1)
x impurities & alkane impurities


172.300
160.613
156.245
152.750
151.689
141.197
131.646
128.810
121.177
115.335
8 13C NMR (2)
NMe2
HO
NH
O
OMe
H2N
2x C-o-Ph(OMe)
2x C-m-Ph(OMe)
C2
C8
C6
C5
C-i-Ph(OMe)
C4
C-p-Ph(OMe)
3'-NHC(O)R
170
160
150
140
130
120
110
ppm (t1)
x impurities


8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
ppm (t1
NMe2
HO
NH
O
OMe
H2N
α
β1 , β2
8 COSY


8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)
50
100
150
ppm (t1
NMe2
HO
NH
O
OMe
H2N
α
β1 , β2
8 HSQC


8 HMBC
NMe2
HO
NH
OMe
50
100
150
ppm (t1
8.0
7.0
6.0
5.0
4.0
3.0
2.0
1.0
ppm (t2)