Electronic Supplementary Material (ESI) for Physical Chemistry Chemical Physics.

Supporting Information 2: Quantitative analysis of zero-field splitting parameter distributions in Gd(III) complexes

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Contents:

General

Unless otherwise stated, reactions were performed under ambient atmosphere using solvents and reagents as commercially received, except THF (HPLC grade) which was distilled from sodium/benzophenone prior to use. Gd-DOTA (**2**) was commercially obtained. If inert atmosphere was needed, argon was used that was passed through anhydrous $CaCl_2$ prior to use. The solvents used for extraction and chromatography were of technical grade and were distilled prior to their use. For the preparation of the aqueous solutions, deionized water was used. Semi-saturated aqueous solution of $NaHCO_3$ was prepared by mixing a saturated aqueous solution of $NaHCO_3$ with an aliquot of water. The proton-exchange resin (Dowex® 50WX4 hydrogen form, Sigma-Aldrich, 91 g) was subsequently washed with THF (3 × 200 mL), EtOH (2 × 100 mL), H_2O (2 × 150 mL), and EtOH (200 mL) and then dried over P_4O_{10} at ~0.05 mbar for 5 days to obtain a purified and dry proton-exchange resin (30 g).

The temperatures given for the reactions refer to the bath temperature. Solvents were removed at a bath temperature of about 40 °C and reduced pressure. The products were dried at room temperature at ~0.05 mbar. The pH/pD values of the solutions were determined using pH indicator strips (resolution: 0.3 pH or 0.5 pH).

Column chromatography was carried out on silica gel 60 (0.035 − 0.070 mm) applying slight pressure with argon gas. In the procedures reported below, the size of the column is given as diameter × length. Unless otherwise stated, the material was loaded onto the column dissolved in a small quantity of the eluent. Analytical thin layer chromatography (TLC) was performed on silica gel 60 containing fluorescent indicator F254. The solid support for the silica gel layer was aluminum foil. The compound spots were detected with UV light of λ = 254 nm. The compositions of solvent mixtures are given in volume ratios.

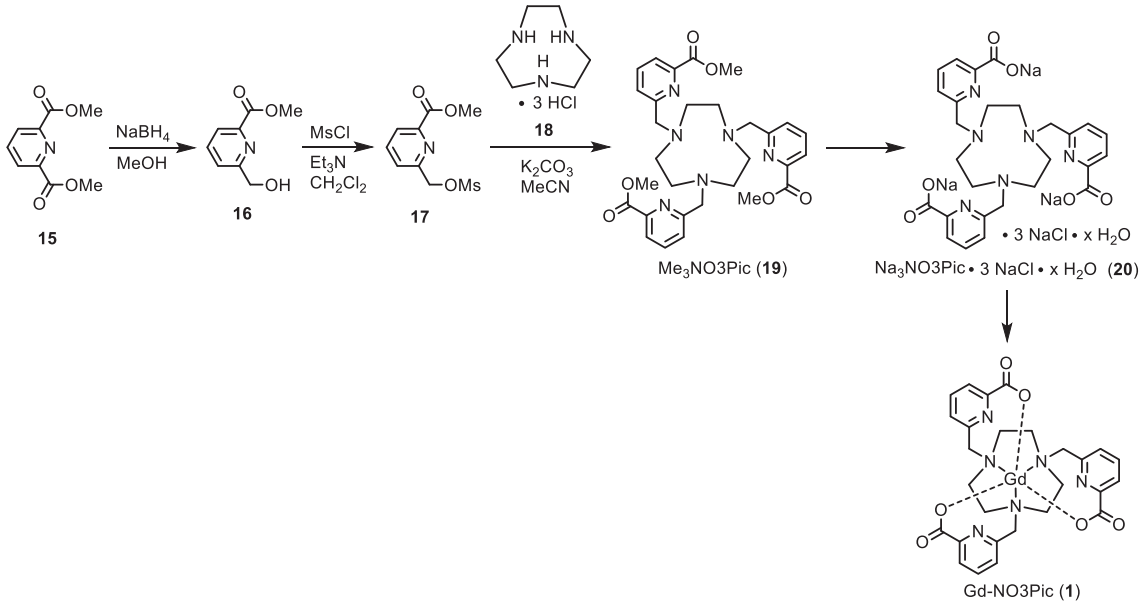
For centrifugation, a centrifuge with a relative centrifugal force of 6500rpm/4000g was used.

NMR spectra were recorded at room temperature. NMR spectra were calibrated using the solvent signal as an internal standard [$CDCl_3$: δ (^{1}H) = 7.25, δ (^{13}C) = 77.0; DMSO-d_6: δ (1H) = 2.49, δ (^{13}C) = 39.5; CD_3OD: δ (1H) = 3.31, δ (13C) = 49.0; D_2O: δ (1H) = 4.79]. For ^{13}C NMR experiments in D_2O, a drop of MeOH was added as the internal standard [δ ($^{13}C)_{MeOH}$ = 49.5]. Signal assignments are supported by DEPT-135, COSY, HMBC, and HMQC experiments.

ESI MS spectra were recorded using an Esquire 3000 ion trap mass spectrometer (Bruker Daltonik) equipped with a standard ESI source. Accurate MS experiments were performed using a FT-ICR mass spectrometer APEX III (Bruker Daltonik) interfaced to an external

ESI ion source.

Synthesis of Gd-NO3Pic (1)



The procedures reported by Huang et al.[1] and by Storr et al.[2] for the synthesis of mesylate **17** and the procedure reported by Gateau et al.[3] for the syntheses of Et_3NO3Pic (ethyl analogon of Me_3NO3Pic (**19**)) and Gd-NO3Pic (**1**) were the basis for our work. We applied some modifications.

Methyl 6-(hydroxymethyl)picolinate (16). This reaction was performed under argon. $NaBH_4$ (1.02 g, 26.9 mmol) was added portionwise within 10 min to a suspension of dimethyl pyridine-2,6-dicarboxylate (**15**) (3.00 g, 15.4 mmol) in MeOH (100 mL) under cooling with an ice water bath (caution: gas evolution). During the adding of $NaBH_4$ the colorless suspension turned into a slightly pink solution. The solution was stirred, while still in the cooling bath, for 10 min. Then, the cooling bath was removed and the solution was stirred at room temperature for 165 min. During the stirring the color of the solution changed from pinkish to colorless. Under cooling with an ice water bath, hydrochloric acid (37 wt.%, 4 mL) was added to lower the pH of the solution from 9 to 2, upon which a colorless precipitate formed. The solvent of the suspension was removed. The residual colorless solid was dissolved in water (20 mL). A saturated aqueous solution of $NaHCO_3$ (28 mL) was added to rise the pH of the solution to 8 (caution: vigorous gas evolution). The aqueous solution was extracted with CH_2Cl_2 (3 × 40 mL). The combined organic phases were dried over Na_2SO_4, the suspension was filtered, and the solvent of the filtrate was removed. Column chromatography (3.5 cm × 32 cm, CH_2Cl_2/MeOH 10:1) of the residual colorless solid (2.35 g) gave methyl 6-(hydroxymethyl)picolinate (**16**) (1.84 g, 71%; R_f = 0.50) as a

colorless solid and dimethyl pyridine-2,6-dicarboxylate (**15**) (417 mg, 14%; R_f = 0.78) as a colorless solid. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.02 (d, ^3J = 7.7 Hz, 1H, H_{Ar} para to CH_2OH), 7.85 (apparent t, ^3J = 7.7 Hz, ^3J = 7.8 Hz, 1H, H_{Ar} meta to CH_2OH), 7.53 (d, ^3J = 7.8 Hz, 1H, H_{Ar} ortho to CH_2OH), 4.86 (s, 2H, CH_2), 3.98 (s, 3H, CH_3), 2.99 (s br, 1H, OH). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.5 (C=O), 160.1 ($\underline{C}_{Ar}CH_2OH$), 146.9 ($\underline{C}_{Ar}C$=O), 137.8 ($C_{Ar}H$ meta to CH_2OH), 124.0 ($C_{Ar}H$ ortho to CH_2OH), 123.9 ($C_{Ar}H$ para to CH_2OH), 64.5 (CH_2), 52.9 (CH_3). MS (ESI): *m/z* = 189.9 $[M + Na]^+$.

Mesylate 17. This reaction was performed in dried glassware under argon. Triethylamine (2.0 mL, 14.4 mmol) and MsCl (0.6 mL, 7.8 mmol) were added successively to a solution of methyl 6-(hydroxymethyl)picolinate (**16**) (760 mg, 4.55 mmol) in dry CH_2Cl_2 (50 mL) under cooling with an ice water bath. The yellow solution was stirred, while still in the cooling bath, for 2 h, during which time the color of the solution changed to dark yellow. The dark yellow solution was poured into a mixture of semi-saturated aqueous solution of $NaHCO_3$ (50 mL). The organic phase was separated, and the aqueous phase was extracted with CH_2Cl_2 (3 × 25 mL). The combined organic phases were washed with semi-saturated aqueous $NaHCO_3$ solution (2 × 20 mL) and dried over $MgSO_4$. The suspension was filtered, and the solvents of the filtrate were removed. Column chromatography (3.0 cm × 32 cm, CH_2Cl_2/Et_2O 1:1) of the residual beige solid (1.15 g) gave mesylate **17** (783 mg, 70%; R_f = 0.33) as a colorless solid. Because of the poor solubility in CH_2Cl_2/Et_2O 1:1, the beige solid was loaded onto the column dissolved in a small quantity of CH_2Cl_2. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.10 (d, ^3J = 7.8 Hz, 1H, H_{Ar} para to CH_2OMs), 7.92 (t, ^3J = 7.8 Hz, 1H, H_{Ar} meta to CH_2OMs), 7.68 (d, ^3J = 7.8 Hz, 1H, H_{Ar} ortho to CH_2OMs), 5.42 (s, 2H, CH_2), 3.99 (s, 3H, OCH_3), 3.14 (s, 3H, OMs). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.1 (C=O), 154.4 ($\underline{C}_{Ar}CH_2$), 147.7 ($\underline{C}_{Ar}C$=O), 138.3 ($C_{Ar}H$ meta to CH_2OMs), 125.2 ($C_{Ar}H$ ortho to CH_2OMs), 124.9 ($C_{Ar}H$ para to CH_2OMs), 70.9 (CH_2), 53.0 (OCH_3), 38.0 (O_3SCH_3). MS (ESI): *m/z* = 267.9 $[M + Na]^+$.

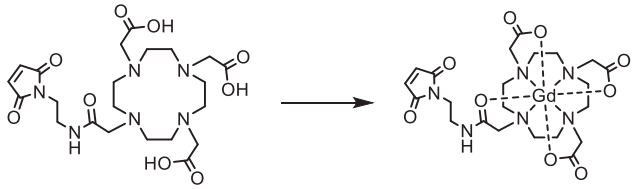
Me_3NO3Pic (19). A solution of mesylate **17** (233 mg, 0.95 mmol) in acetonitrile (2 mL) was added dropwise to a suspension of 1,4,7-triazacyclononane trihydrochloride (**18**) (77 mg, 0.32 mmol) and K_2CO_3 (266 mg, 1.92 mmol) in acetonitrile (15 mL). This suspension was heated to reflux (oil bath temperature 96 °C) for 22.5 h. The pale yellow suspension was filtered. The solvent of the filtrate was removed. The residual yellow oil (212 mg) was dissolved in CH_2Cl_2 (20 ml) and this solution was washed with semi-saturated aqueous $NaHCO_3$ solution (2 × 10 mL) and dried over Na_2SO_4. The suspension was filtered and the solvents were removed giving Me_3NO3Pic (**19**) (101 mg, 56%) as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.99 (d, ^3J = 7.7 Hz, 3H, H_{Ar} para to CH_2N), 7.80 (apparent t, ^3J = 7.7 Hz, ^3J = 7.5 Hz, 3H, H_{Ar} meta to CH_2N), 7.76 (d, ^3J = 7.5 Hz, 3H, H_{Ar} ortho to CH_2N),

3.97 (s, 9H, OCH_3), 3.94 (s, 6H, $ArCH_2$), 2.88 (s, 12H, $C\underline{H}_2C\underline{H}_2$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 165.9 (C=O), 161.4 ($\underline{C}_{Ar}CH_2N$), 147.2 ($\underline{C}_{Ar}C=O$), 137.2 ($C_{Ar}H$ meta to CH_2N), 126.3 ($C_{Ar}H$ ortho to CH_2N), 123.5 ($C_{Ar}H$ para to CH_2N), 64.7 ($Ar\underline{C}H_2$), 56.1 ($\underline{C}H_2\underline{C}H_2$), 52.9 ($OCH_3$). MS (ESI): *m/z* = 599.2 $[M + Na]^+$, 577.2 $[M + H]^+$.

[Na_3NO3Pic]•3 NaCl•x H_2O (20). Me_3NO3Pic (**19**) (94 mg, 163 µmol) was dissolved in EtOH (2 mL) and water (1.5 mL). An aqueous NaOH solution (2 M, 0.5 mL, 1.0 mmol) was added and the yellow solution was stirred at room temperature for 31.5 h. Aqueous hydrochloric acid (2 M, 0.25 mL, 0.5 mmol) was added to lower the pH of the solution to 11.5. Removal of the solvents gave [Na_3NO3Pic]•3 NaCl•x H_2O (**20**) (124 mg, containing 131 µmol of the structural motif $[NO3Pic]^{3-}$ as determined by quantitative ^1H NMR spectroscopy;[4,5] yield 80%) as a pale yellow solid. ^1H NMR (500 MHz, D_2O): δ = 7.85 (t, ^3J = 7.7 Hz, 3H, H_{Ar} meta to CH_2N), 7.79 (d, ^3J = 7.7 Hz, 3H, H_{Ar} para to CH_2N), 7.40 (d, ^3J = 7.7 Hz, 3H, H_{Ar} ortho to CH_2N), 3.85 (s, 6H, $ArCH_2$), 2.87 (s, 12H, $C\underline{H}_2C\underline{H}_2$). ^{13}C NMR (125 MHz, D_2O): δ = 173.7 (C=O), 157.2 ($\underline{C}_{Ar}CH_2N$), 154.1 ($\underline{C}_{Ar}C=O$), 139.1 ($C_{Ar}H$ meta to CH_2N), 126.7 ($C_{Ar}H$ ortho to CH_2N), 123.3 ($C_{Ar}H$ para to CH_2N), 62.3 ($Ar\underline{C}H_2$), 52.6 ($\underline{C}H_2\underline{C}H_2$). MS (ESI): *m/z* = 601.1 $[Na_3NO3Pic + H]^+$, 623.1 $[Na_3NO3Pic + Na]^+$.

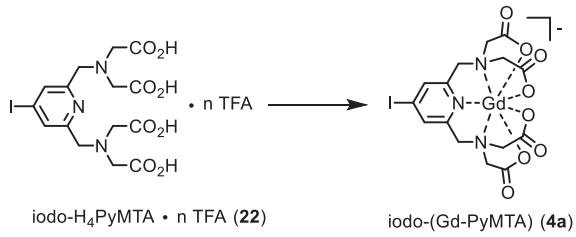
Gd-NO3Pic (1). A solution of [Na_3NO3Pic]•3 NaCl•x H_2O (**20**) in D_2O (150 µL, containing 3.89 µmol of the structural motif $[NO3Pic]^{3-}$) was mixed with a solution of $GdCl_3$ in D_2O (50 mM, 74 µL, 3.70 µmol). The resulting solution was diluted with D_2O (to a total volume of 778 µL) to obtain a 5 mM solution of Gd-NO3Pic (**1**) in D_2O containing NaCl. The pD of the solution was 7.5. MS (ESI): *m/z* = 712.1 $[M + Na]^+$.

Synthesis of Gd-maleimide-DOTA (3)

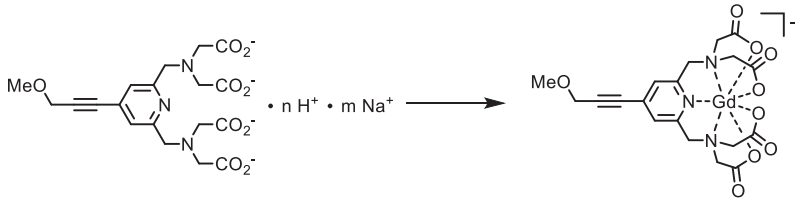


Gd-maleimide-DOTA (3). A solution of $GdCl_3$ in D_2O (0.1 M, 46.3 µL, 4.63 µmol) was added to a solution of maleimide-H_3DOTA (**21**) (purity 94 wt.% as determined with quantitative ^1H NMR spectroscopy, 4.049 mg, 4.84 µmol) in D_2O (500 µL). A solution of NaOD in D_2O (0.10 M, 250 µL, 25 µmol) was added to rise the pD of the solution to 8.2. The solution was diluted with D_2O (233.3 µL) to obtain a 4.5 mM solution of Gd-maleimide-DOTA (**3**) in D_2O. MS (ESI): *m/z* = 704.2 $[M + Na]^+$.

Synthesis of R-(Gd-PyMTA) (4)



iodo-H_4PyMTA • n TFA (**22**) iodo-(Gd-PyMTA) (**4a**)

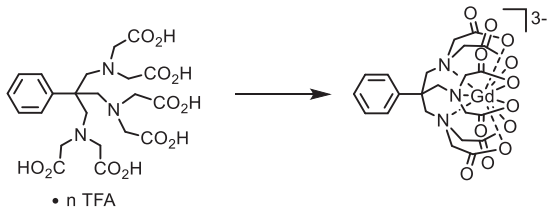


MOMethynyl-(H_nNa_mPyMTA) (**23**) MOMethynyl-(Gd-PyMTA) (**4b**)

The syntheses of iodo-H_4PyMTA•n TFA (**22**), iodo-(Gd-PyMTA) (**4a**), and MOMethynyl-H_nNa_mPyMTA (**23**) were reported in our previous work.[4,6,7]

MOMethynyl-(Gd-PyMTA) (4b). A solution of $GdCl_3$ in D_2O (0.1 M, 331.1 µL, 33.11 µmol) was added to a solution of MOMethynyl-H_nNa_mPyMTA (**23**) in D_2O (1743 µL, containing 34.85 µmol of the structural motif [MOMethynyl-PyMTA]$^{4-}$ as determined by quantitative ^{1}H NMR spectroscopy[4,5]). The solution was diluted with D_2O (1411 µL) to obtain a 10.0 mM solution of MOMethynyl-(Gd-PyMTA) (**4b**). A part of the obtained solution (100 µL) was mixed with a solution of NaOD in D_2O (0.10 M, 33 µL, 3.3 µmol), a solution of NaCl in D_2O (0.10 M, 37 µL), and D_2O (330 µL) to obtain a 2.0 mM solution of MOMethynyl-(Gd-PyMTA) (**4b**) in D_2O containing NaCl. The pD of the solution was 8.2. MS (ESI): *m/z* = 590.9 [M]$^-$.

Synthesis of Gd-TAHA (5)



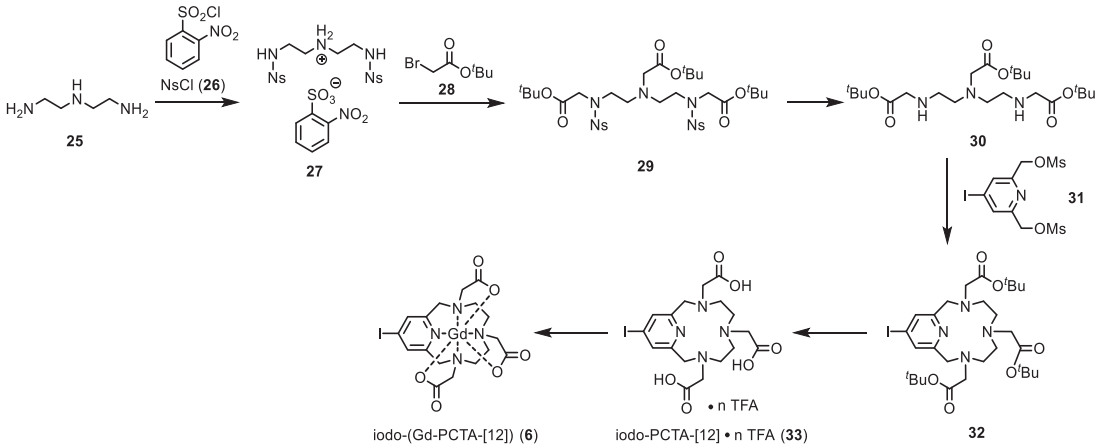
H_6TAHA • n TFA (**24**) Gd-TAHA (**4a**)

The synthesis of H_6TAHA•n TFA (**24**) was reported in our previous work.[6]

Gd-TAHA (5). H_6TAHA•n TFA (**24**) (10.053 mg, containing 15.63 µmol of the structural motif H_6TAHA) was dissolved in D_2O (600 µL). A part of the obtained solution (100 µL, containing 2.60 µmol of the structural motif [TAHA]$^{6-}$) was mixed with a solution of $GdCl_3$•6

H_2O in D_2O (0.05 M, 49 µL, 2.45 µmol). A solution of NaOD in D_2O (0.10 M, 130 µL, 13 µmol) was added to rise the pD of the solution to 6.5. The solution was diluted with D_2O (to a total volume of 520 µL) to obtain a 5.0 mM solution of Gd-TAHA (**5**) in D_2O containing $Na(O_2CCF_3)$. MS (ESI): *m/z* = 680.9 $[M + 2 H]^-$.

Synthesis of iodo-(Gd-PCTA-[12]) (6)



The strategy reported by Ferroud et al.[8] for the synthesis of Gd-PCTA-[12] with a substituent in meta position of the pyridine ring was applied to synthesize iodo-(Gd-PCTA-[12]) (**6**). The procedure reported by Favre-Réguillon et al.[9] for the nosylation of 1,4,7-triazaheptane and the procedures reported by Ferroud et al.[8] for the synthesis of dinosylate **29**, diamine **30** and PCTA-[12] were the basis for our work. We applied some modifications. The synthesis of mesylate **31** was reported in our previous work.[4]

For nosylation of diethylenetriamine (**25**) the procedure reported by Favre-Réguillon et al.[9] for the threefold nosylation of was applied. However, we isolated only the dinosylation product in form of the salt 1,7-dinosyl-1,4,7-triazaheptane • NsOH (**27**). Obviously, hydrolysis of 2-nitrobenzenesulfonyl chloride (NsCl) (**26**) was competing with N-nosylation.

For denosylation *p*-toluenethiol was used instead of benzenethiol because of the toxicity of the latter.

1,7-Dinosyl-1,4,7-triazaheptane•NsOH (27). A solution of 2-nitrobenzenesulfonyl chloride (NsCl) (**26**) (30.9 g, 140 mmol) in THF (300 mL) was added dropwise within 2 h to a suspension of diethylenetriamine (**25**) (4.4 mL, 41 mmol) and $NaHCO_3$ (23.7 g, 282 mmol) in THF (300 mL) under cooling with an ice water bath, during which time the color of the suspension changed to yellow. The cooling bath was removed and the suspension was stirred at room temperature for 69 h. The suspension was filtered. The solvent of the filtrate was removed. The residual orange brown solid was recrystallized twice in CH_2Cl_2 (140 mL,

each time). 1,7-Dinosyl-1,4,7-triazaheptane•NsOH (**27**) (8.45 g, 68%) was obtained as pale brown solid. ^{1}H NMR (500 MHz, DMSO-d_6): δ = 8.68 (br s, 2H, H_2N^+), 8.32 (t, ^{3}J = 5.7 Hz, 2H, NsN<u>H</u>), 8.02 (m, 4H, H_{Ar} of NNs ortho to NO_2 and H_{Ar} of NNs ortho to SO_2NH), 7.91 (m, 4H, H_{Ar} of NNs para to NO_2 and H_{Ar} of NNs para to SO_2NH), 7.84 (m, 1H, H_{Ar} of NsO^- ortho to NO_2), 7.56 (m, 2H, H_{Ar} of NsO^- para to NO_2 and H_{Ar} of NsO^- para to SO_3^-), 7.50 (m, 1H, H_{Ar} of NsO^- ortho SO_3^-), 3.18 (apparent q, J ~ 6 Hz, 4H, NsNHC<u>H</u>$_2$CH$_2$), 3.07 (apparent pent, J ~ 6 Hz , 4H, NsNHCH$_2$C<u>H</u>$_2$). ^{13}C NMR (125 MHz, DMSO-d_6): δ = 147.8 ($C_{Ar}NO_2$ of NsO^-), 147.7 ($C_{Ar}NO_2$ of NNs), 139.3 ($C_{Ar}SO_3^-$), 134.5 (C_{Ar}H of NNs para to NO_2), 132.9 (C_{Ar}H of NNs para to SO_2NH), 131.8 ($C_{Ar}SO_2N$), 130.7 (C_{Ar}H of NsO^- para to NO_2), 130.0 (C_{Ar}H of NsO^- ortho to SO_3^-), 129.6 (C_{Ar}H of NNs ortho to SO_2NH), 129.0 (C_{Ar}H of NsO^- ortho to NO_2), 124.7 (C_{Ar}H of NNs ortho to NO_2), 122.3 (C_{Ar}H of NsO^- para to SO_3^-), 46.5 (<u>C</u>H$_2$CH$_2$NHNs), 39.0 (CH$_2$<u>C</u>H$_2$NHNs). MS (ESI): *m/z* = 496.1 [1,7-dinosyl-1,4,7-triazaheptane + Na]$^+$, 474.1 [1,7-dinosyl-1,4,7-triazaheptane + H]$^+$.

Dinosylate 29. *Tert*-butyl bromoacetate (**28**) (3.8 mL, 26 mmol) was added dropwise within 5 min to a suspension of 1,7-dinosyl1,4,7-triazaheptane•NsOH (**27**) (2.01 g, 2.97 mmol) and K_2CO_3 (17.5 g, 127 mmol) in acetonitrile (100 mL). This suspension was heated to reflux for 2 h and then stirred at room temperature for 17 h. The suspension was filtered. The solvent of the filtrate was removed. Column chromatography (7.0 cm × 30 cm, ethyl acetate/*n*-hexane 1:1) of the residual yellow oil gave dinosylate **29** (1.44 g, 59%; R_f = 0.26) as a viscous yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 8.07 (m, 2H, H_{Ar} ortho to NO_2), 7.66 (m, 4H, H_{Ar} para to NO_2 and H_{Ar} para to SO_2N), 7.57 (m, 2H, H_{Ar} ortho to SO_2N), 4.15 (s, 4H, NsNC<u>H</u>$_2$CO$_2$*t*Bu), 3.45 (t, ^{3}J = 6.9 Hz, 4H, NsNC<u>H</u>$_2$CH$_2$), 3.23 (s, 2H, (CH$_2$)$_2$NC<u>H</u>$_2$CO$_2$*t*Bu), 2.86 (t, ^{3}J = 6.9 Hz, 4H, NsNCH$_2$C<u>H</u>$_2$), 1.43 (s, 9H, (CH$_2$)$_2$NCH$_2$CO$_2$<u>*t*Bu</u>), 1.33 (s, 18H, NsNCH$_2$CO$_2$<u>*t*Bu</u>). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.2 ((CH$_2$)$_2$NCH$_2$<u>C</u>O$_2$*t*Bu), 167.8 (NsNCH$_2$<u>C</u>O$_2$*t*Bu), 147.9 ($C_{Ar}NO_2$), 133.4 (C_{Ar}H para to NO_2), 133.3 ($C_{Ar}SO_2N$), 131.8 (C_{Ar}H para to SO_2N), 130.9 (C_{Ar}H ortho to NO_2), 123.9 (C_{Ar}H ortho to SO_2N), 82.2 (NsNCH$_2$CO$_2$<u>C</u>(CH$_3$)$_3$), 81.4 ((CH$_2$)$_2$NCH$_2$CO$_2$<u>C</u>(CH$_3$)$_3$), 56.2 ((CH$_2$)$_2$N<u>C</u>H$_2$CO$_2$*t*Bu), 53.1 (NsNCH$_2$<u>C</u>H$_2$), 49.4 (NsN<u>C</u>H$_2$CO$_2$*t*Bu), 46.7 (NsN<u>C</u>H$_2$CH$_2$), 28.1 ((CH$_2$)$_2$NCH$_2$CO$_2$C(<u>C</u>H$_3$)$_3$), 27.8 (NsNCH$_2$CO$_2$C(<u>C</u>H$_3$)$_3$). MS (ESI) *m/z*: 838.4 [M + Na]$^+$, 816.4 [M + H]$^+$.

Amine 30. A solution of *p*-toluenethiol (189 mg, 1.52 mmol) in DMF (1.4 mL) was added to a suspension of dinosylate **29** (200 mg, 0.25 mmol) and Na_2CO_3 (317 mg, 3.00 mmol) in DMF (5 mL). This black-yellow suspension was stirred at 50 °C for 5 h. After 4 h the color of the solution turned into yellow. The suspension was stirred at room temperature for another 19.5 h. The solvent of the reaction mixture was removed at reduced pressure. Et_2O (15 mL) was added to the yellow residue and the ethereal solution was washed with

water (3 × 5 mL). Removal of the solvents gave a yellow viscous oil. The components of this oil were separated by column chromatography (4.5 cm × 6 cm). Eluting first with pentane/Et_2O 10:1 gave a mixture of (2-nitrophenyl)(*p*-tolyl)sulfane (R_f(pentane/Et_2O 10:1) = 0.36) and 1,2-di-*p*-tolyldisulfane (R_f(pentane/Et_2O 10:1) = 0.83). Then, the eluent was changed to THF, and amine **30** (93 mg, 85%; R_f(pentane/Et_2O 10:1) = 0, R_f(THF) = 0.90) was obtained as a yellow-orange oil. ^{1}H NMR of amine **30** (500 MHz, $CDCl_3$): δ = 3.32 (s, 2H, $(CH_2)_2NC\underline{H}_2CO_2{}^t$Bu), 3.29 (s, 4H, $HNC\underline{H}_2CO_2{}^t$Bu), 2.79 (t, ^3J = 6.0 Hz, 4H each, $NHC\underline{H}_2CH_2$), 2.65 (t, ^3J = 6.0 Hz, 4H each, $NHCH_2C\underline{H}_2$), 1.44 (s, 18H, $HNCH_2CO_2(C\underline{H}_3)_3$), 1.43 (s, 9H, $(CH_2)_2NCH_2CO_2C(C\underline{H}_3)_3$). ^{13}C NMR of amine **30** (125 MHz, $CDCl_3$): δ = 171.6 ($HNCH_2\underline{C}O_2{}^t$Bu), 170.9 ($(CH_2)_2NCH_2\underline{C}O_2{}^t$Bu), 80.9 ($HNCH_2CO_2\underline{C}(CH_3)_3$), 80.8 ($(CH_2)_2NCH_2CO_2\underline{C}(CH_3)_3$), 55.7 ($(CH_2)_2N\underline{C}H_2CO_2{}^t$Bu), 54.1 ($NHCH_2\underline{C}H_2$), 51.6 ($HN\underline{C}H_2CO_2{}^t$Bu), 47.3 ($NH\underline{C}H_2CH_2$), 28.2 ($(CH_2)_2NCH_2CO_2C(\underline{C}H_3)_3$), 28.1($HNCH_2CO_2C(\underline{C}H_3)_3$). MS of amine **30** (ESI) *m/z*: 468.4 $[M + Na]^+$, 446.4 $[M + H]^+$. ^{1}H NMR of (2-nitrophenyl)(*p*-tolyl)sulfane (500 MHz, $CDCl_3$): δ = 8.21 (dd, ^4J = 1.5 Hz, ^3J = 8.2 Hz, H_{Ar} ortho to NO_2), 7.46 (half of an AA'XX' spin system, 2H, H_{Ar} meta to CH_3), 7.31 (apparent td, ^4J = 1.5 Hz, ^3J = 7.2 Hz, ^3J = 8.5 Hz, H_{Ar} para to S), 7.28 (half of an AA'XX' spin system, 2H, H_{Ar} ortho to CH_3), 7.18 (apparent td, ^{4}J = 1.3 Hz, ^3J = 7.2 Hz, ^3J = 8.4 Hz, H_{Ar} para to NO_2), 6.84 (dd, ^4J = 1.3 Hz, ^3J = 8.3 Hz, H_{Ar} ortho to S), 2.42 (s, 3H, CH_3). ^{1}H NMR 1,2-di-*p*-tolyldisulfane (500 MHz, $CDCl_3$): δ = 7.38 (half of an AA'XX' spin system, 4H, H_{Ar} ortho to S), 7.10 (half of an AA'XX' spin system, 4H, H_{Ar} ortho to CH_3), 2.31 (s, 6H, CH_3).

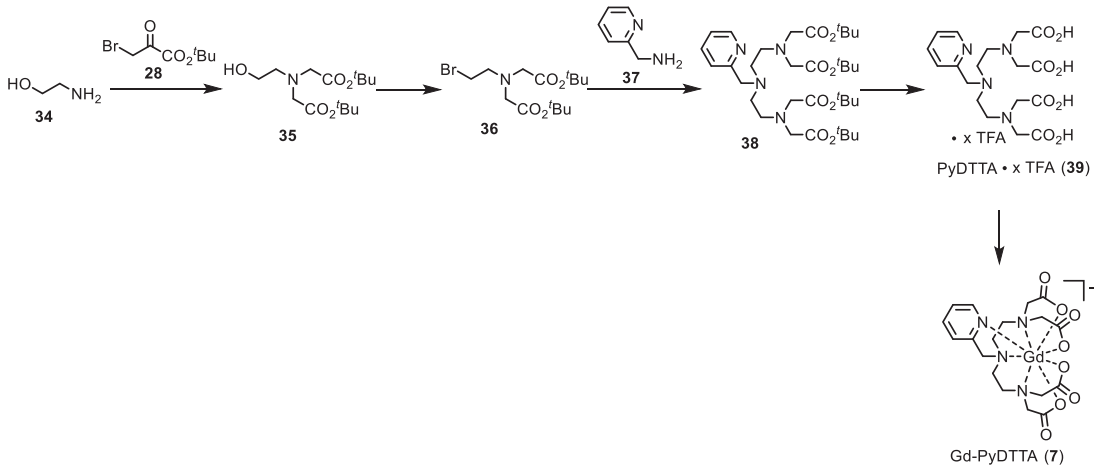
4-Iodo-PCTA-[12] *tert*-butyl ester (32). Mesylate **31** (99 mg, 0.24 mmol) was added to a solution of amine **30** (105 mg, 0.24 mmol) and triethylamine (328 µL, 2.37 mmol) in acetonitrile (10 mL). The yellow solution was stirred at room temperature for 46.5 h. The solvents were removed. The residual yellow solid was dissolved in CH_2Cl_2 and the resulting solution was washed with H_2O (5 × 7 mL). The washing was performed in a centrifuge tube: The CH_2Cl_2 phase and the aqueous phase were mixed well. Centrifugation of the resulting yellow emulsion at 9000 rpm for 2 min separated the mixture into two phases, a yellow CH_2Cl_2 phase and a colorless aqueous phase. The aqueous phase was removed with the help of a glass pipette. The solvent of the CH_2Cl_2 phase was removed. Centrifugal thin layer chromatography using a chromatotron (stationary phase: aluminiumoxid 60 neutral F254; layer thickness: 2 mm; plate diameter: 24 cm; eluent: THF; the separation on the plate was monitored using UV light with λ = 254 nm) of the residual yellow oil (97 mg) gave 4-iodo-PCTA-[12] *tert*-butyl ester (**32**) (19 mg, 12%; R_f = 0.59) contaminated with a small amount of unidentified components. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 7.54 (s, 2H, H_{Ar}), 3.94 (s, 4H, $ArC\underline{H}_2$), 3.41 (s, 4H, $ArCH_2NC\underline{H}_2CO_2{}^t$Bu), 3.12 (s br, 2H, $(CH_2CH_2)_2N\underline{C}H_2CO_2{}^t$Bu), 2.78 (m, 4H, $ArCH_2NC\underline{H}_2CH_2$), 2.62 (m, 4H, $ArCH_2NCH_2C\underline{H}_2$), 1.47 (s, 18H,

$ArCH_2NCH_2CO_2C(C\underline{H}_3)_3$), 1.41 (s, 9H, $(CH_2CH_2)_2NCH_2CO_2C(C\underline{H}_3)_3$). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.7 ($(CH_2CH_2)_2NCH_2\underline{C}O_2{}^t$Bu), 170.6 ($ArCH_2NCH_2\underline{C}O_2{}^t$Bu), 158.7 ($\underline{C}_{Ar}CH_2$), 131.4 ($C_{Ar}H$), 106.5 ($C_{Ar}I$), 81.1 ($ArCH_2NCH_2CO_2\underline{C}(CH_3)_3$), 80.8 ($(CH_2CH_2)_2NCH_2CO_2\underline{C}(CH_3)_3$), 59.8 ($C_{Ar}\underline{C}H_2$), 58.2 ($ArCH_2N\underline{C}H_2CO_2{}^t$Bu), 57.5 ($(CH_2CH_2)_2N\underline{C}H_2CO_2{}^t$Bu), 50.2 ($ArCH_2N\underline{C}H_2CH_2$), 50.1 ($ArCH_2NCH_2\underline{C}H_2$), 28.2 ($ArCH_2NCH_2CO_2C(\underline{C}H_3)_3$), 28.1 ($(CH_2CH_2)_2NCH_2CO_2C(\underline{C}H_3)_3$). MS (ESI) *m/z*: 697.3 $[M+Na]^+$, 675.3 $[M+H]^+$.

4-Iodo-PCTA-[12]•n TFA (33). 4-Iodo-PCTA-[12] *tert*-butyl ester (**32**) (15 mg, ca. 22 µmol), as it had been received in the experiment described above, was dissolved in trifluoroacetic acid (TFA) (1 mL) and the resulting orange solution was stirred at room temperature for 1 h. The volatile components were removed at room temperature by lowering the pressure to 10 mbar. The residue was dissolved in TFA (1 mL) and the resulting orange solution was stirred at room temperature for 1 h. The solution was concentrated at room temperature at reduced pressure. The residual solution was added dropwise to Et_2O (3 mL), whereupon a colorless solid precipitated. The precipitate was separated via centrifugation (9000 rpm, 1 min), washed with Et_2O, and dried at reduced pressure. 4-Iodo-PCTA-[12]•n TFA (**33**) (12 mg) contaminated with a small amount of unidentified components was obtained as a colorless solid. ^1H NMR (500 MHz, D_2O): δ = 7.92 (s, 2H, ArH), 4.79 (s, covered by the signal of H_2O; evidence comes from HMQC and HMBC NMR spectra, $ArC\underline{H}_2$), 4.19 (s, 4H, $ArCH_2NC\underline{H}_2CO_2H$), 3.62 (s, 2H, $(CH_2CH_2)_2NC\underline{H}_2CO_2H$), 3.53 (s br, 4H, $ArCH_2NC\underline{H}_2CH_2$), 2.97 (s br, 4H, $ArCH_2NCH_2C\underline{H}_2$). ^{13}C NMR (125 MHz, D_2O): δ = 175.3 ($(CH_2CH_2)_2NCH_2\underline{C}O_2H$), 170.0 ($ArCH_2NCH_2\underline{C}O_2H$), 163.6 (q, ^2J = 35.6 Hz, CO_2H of TFA), 151.3 ($\underline{C}_{Ar}CH_2$), 132.3 ($C_{Ar}H$), 116.9 (q, ^1J = 291.8 Hz, CF_3 of TFA), 109.5 ($C_{Ar}I$), 59.4 ($C_{Ar}\underline{C}H_2$), 57.8 ($ArCH_2N\underline{C}H_2CO_2H$), 55.3 ($(CH_2CH_2)_2N\underline{C}H_2COOH$), 55.1 ($ArCH_2N\underline{C}H_2CH_2$), 51.7 ($ArCH_2NCH_2\underline{C}H_2$). MS (ESI, positive) *m/z*: 507.2 $[M + H]^+$. MS (ESI, negative) *m/z*: 619.1 $[M + CF_3COO]^-$, 505.1 $[M - H]^-$.

Iodo-(Gd-PCTA-[12]) (6). 4-Iodo-PCTA-[12]•n TFA (**33**) was used as obtained in the experiment described above. A solution of $GdCl_3$ in D_2O (50 mM, 129.7 µL, 6.486 µmol) was added into a solution of 4-iodo-PCTA-[12]•n TFA (**33**) in D_2O (500 µL, containing 6.83 µmol of the structural motif $[4\text{-iodo-PCTA-[12]}]^{3-}$ as determined by quantitative ^1H NMR spectroscopy[4,5]). A solution of NaOD in D_2O (0.1 M, 425.6 µL, 42.56 µmol) was added to inrease the pD to 9.0. The solution was diluted with D_2O (to a total volume of 1365.6 µL) to obtain a 5.0 mM solution of iodo-(Gd-PCTA-[12]) (**6**) in D_2O. Accurate MS (ESI): *m/z* calcd for $[M + Na]^+$ $C_{17}H_{20}GdIN_4O_6Na^+$, 683.95607; found, 683.95601.

Synthesis of Gd-PyDTTA (7)



The procedure reported by Williams et al.[10] for the synthesis of bromide **36** and the procedure reported by Bridger et al.[11] for the synthesis of PyDTTA ester **38** were the basis for our work. We applied some modifications.

Alcohol 35. *Tert*-butyl bromoacetate (**28**) (1.3 mL, 8.92 mmol) was added dropwise to a suspension of 2-aminoethanol (**34**) (250 µL, 4.14 mmol) and $NaHCO_3$ (784 mg, 9.33 mmol) in DMF (10 mL) cooled with an ice water bath. The suspension was stirred, while still in the cooling bath, for 1.5 h. Then, the cooling bath was removed, and the reaction mixture was stirred at room temperature for 21.5 h. After removal of the solvent, the colorless residue was dissolved in a mixture of Et_2O (25 mL), saturated aqueous solution of $NaHCO_3$ (15 mL), and H_2O (10 mL). The phases were separated. The organic phase was washed with a saturated aqueous solution of $NaHCO_3$ (3 × 10 mL). The aqueous phase was extracted with Et_2O (3 × 20 mL). The combined organic phases were dried over Na_2SO_4. The suspension was filtered and the solvent of the filtrate was removed giving alcohol **35** (957 mg, 80%) as a colorless oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.77 (t, ^3J = 5.6 Hz, 1H, OH), 3.51 (apparent q, ^3J ~ 5 Hz, 2H, HOC$\underline{H}_2$), 3.42 (s, 4H, CH_2CO), 2.87 (t, ^3J = 5.0 Hz, 2H, $HOCH_2C\underline{H}_2$), 1.45 (s, 18H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 171.5 (C=O), 81.5 ($\underline{C}(CH_3)_3$), 59.3 ($HOCH_2$), 57.0 ($HOCH_2\underline{C}H_2$), 56.6 ($\underline{C}H_2CO$), 28.1 (CH_3). MS (ESI): *m/z* = 312.2 $[M + Na]^+$, 290.2 $[M + H]^+$.

Bromide 36. PPh_3 (2.51 g, 9.56 mmol) was added in portions within 5 min to a solution of alcohol **35** (2.49 g, 8.61 mmol) in CH_2Cl_2 (25 mL). The resulting solution was cooled with an ice water bath and then N-bromosuccinimide (1.71 g, 9.60 mmol) was added in portions within 5 min maintaining the cooling. During this addition the color of the solution changed to yellow. The reaction mixture was stirred, while still in the cooling bath, for 1.7 h. The volatile components were removed at reduced pressure. Et_2O (45 mL) was added to the

residual yellow oil, whereupon a yellow solid precipitated. The yellow solid was removed through filtration and the solvent of the filtrate was removed. Column chromatography (5.0 cm × 22 cm, CH_2Cl_2/Et_2O 1:1) of the residual yellow oil (2.52 g) gave bromide **36** (1.12 g, 37%; R_f = 0.9) contaminated with a small amount of unidentified components as a yellow oil. ^{1}H NMR (500 MHz, $CDCl_3$): δ = 3.46 (s, 4H, CH_2CO), 3.42 (t, ^3J = 7.0 Hz, 2H, $BrC\underline{H}_2CH_2$), 3.11 (t, ^3J = 7.0 Hz, 2H, $BrCH_2C\underline{H}_2$), 1.44 (s, 18H, CH_3). ^{13}C NMR (125 MHz, $CDCl_3$): δ = 170.5 (C=O), 81.3 ($\underline{C}Me_3$), 56.6 ($BrCH_2\underline{C}H_2$), 56.5 ($\underline{C}H_2CO$), 30.3 ($BrCH_2$), 28.1 (CH_3). MS (ESI): *m/z* = 374.2 $[M + Na]^+$, 352.2 $[M + H]^+$.

PyDTTA *tert*-butyl ester (38). A suspension of bromide **36** (1.00 g, 2.84 mmol; as obtained in the experiment described above), 2-picolylamine (**37**) (968 µL, 946 µmol) and K_2CO_3 (3.98 g, 28.8 mmol) in acetonitrile (35 mL) was stirred under reflux for 24 h. The solvent was removed at reduced pressure. The residue was dissolved in Et_2O (15 mL) and H_2O (20 mL). The organic phase was separated, and the aqueous phase was extracted with Et_2O (5 × 10 mL). The combined organic phases were dried over Na_2SO_4 and filtered, and the solvents were removed. Column chromatography (3.5 cm × 39.5 cm, CH_2Cl_2/MeOH 10:1) of the residual oil (850 mg) gave PyDTTA *tert*-butyl ester (**38**) (339 mg, 55%; R_f = 0.25) as a yellow oil and bromide **36** (229 mg, 23%; R_f = 0.86) as a yellow oil. ^{1}H NMR (500 MHz, CD_2Cl_2); *marks slightly broadened signals: δ = 8.49* (d, ^3J = 4.2 Hz, 1H, H_{Ar} ortho to N), 7.68* (t-like, ^3J = 7.6 Hz, 1H, H_{Ar} para to N), 7.52* (d, ^3J = 6.0 Hz, 1H, H_{Ar} ortho to CH_2), 7.19* (t-like, ^3J = 6.0 Hz, 1H, H_{Ar} para to CH_2), 4.10 (broad s, 2H, $ArC\underline{H}_2$), 3.38 (s, 8H, CH_2CO), 2.93 (broad s, 8H, $C\underline{H}_2C\underline{H}_2$), 1.42 (s, 36H, CH_3). ^{1}H NMR (500 MHz, $CDCl_3$): δ =8.49 (slightly broadened d, ^3J = 4.2 Hz, 1H, H_{Ar} ortho to N), 7.65 (broad t, ^3J = 7.0 Hz, 1H, H_{Ar} para to N), 7.53 (broad s, 1H, H_{Ar} ortho to CH_2), 7.16 (broad s, 1H, H_{Ar} para to CH_2), 3.97 (very broad s, $ArCH_2$), 3.40 (s, 8H, CH_2CO), 2.96 (broad s, 8H, $C\underline{H}_2C\underline{H}_2$), 1.40 (s, 36H, CH_3). ^{13} C NMR (125 MHz, $CDCl_3$): 170.6 (C=O), 170.1 ($\underline{C}_{Ar}CH_2$), 148.9 ($C_{Ar}H$ ortho to N), 136.7 (C_{Ar} para to N), 123.6 (C_{Ar} ortho to CH_2), 122.4 (C_{Ar} para to CH_2), 81.1 ($\underline{C}Me_3$), 55.9 ($\underline{C}H_2CO$), 52.9 ($\underline{C}H_2\underline{C}H_2$), 50.7 ($Ar\underline{C}H_2$), 28.1 ($CH_3$). MS (ESI): *m/z* = 651.5 $[M + H]^+$.

PyDTTA•x TFA (39). PyDTTA *tert*-butyl ester (**38**) (301 mg, 462 µmol), was dissolved in TFA (15 mL) and the dark yellow solution was stirred at room temperature for 1 h. The volatile components were removed at room temperature by lowering the pressure to 10 mbar, giving a brown oil. This oil was dissolved in TFA (15 mL) and the yellow orange solution was stirred at room temperature for 1 h. The solution was concentrated by removing the volatile components at reduced pressure. This concentrated solution was added dropwise into Et_2O (13 mL), whereupon a beige solid precipitated. The precipitate was separated via centrifugation (9000 rpm, 1 min) and dissolved in H_2O (5 mL). Removal of the solvent through freeze-drying provided a brown solid (209 mg) containing PyDTTA•x

TFA (**39**) (228 µmol of the structural motif $[PyDTTA]^{4-}$; yield: 49%) and ca. 6 mol% of an unidentified component, as was quantified by quantitative ^{1}H NMR spectroscopy.[4,5] . ^{1}H NMR (500 MHz, D_2O): δ = 8.74 (d, ^{3}J = 5.9 Hz, 1H, H_{Ar} ortho to N), 8.56 (dt, ^{3}J = 8.0 Hz, ^{4}J = 1.1 Hz, 1H, H_{Ar} para to N), 8.07 (d, ^{3}J = 8.0 Hz, 1H, H_{Ar} ortho to CH_2), 7.99 (t-like, ^{3}J = 7.5 Hz, 1H, H_{Ar} para to CH_2), 4.18 (s, 2H, Ar$\underline{C}H_2$), 4.03 (8H, s, CH_2CO), 3.55 and 3.07 (2t, ^{3}J = 6.7 Hz, 4H each, $C\underline{H}_2C\underline{H}_2$). ^{13}C NMR (125 MHz, D_2O): 169.5 (C=O), 163.5 (q, ^{2}J = 35.8 Hz, C=O of TFA), 152.4 ($\underline{C}_{Ar}CH_2$), 148.2 ($C_{Ar}H$ para to N), 142.6 ($C_{Ar}H$ ortho to N), 128.1 (C_{Ar} ortho to CH_2), 127.2 (C_{Ar} para to CH_2), 116.9 (q, ^{1}J = 291.8 Hz, CF_3 of TFA), 56.6 ($\underline{C}H_2CO$), 55.0 (Ar$\underline{C}H_2$), 53.2 and 48.6 ($\underline{C}H_2\underline{C}H_2$). MS (ESI): *m/z* = 427.2 $[M + H]^+$.

Gd-PyDTTA (7). A solution of $GdCl_3$•6 H_2O in D_2O (0.05 M, 87.8 µL, 4.39 µmol) was added to a solution of PyDTTA•x TFA **39** (125 µL, contains 4.63 µmol of the structural motif $[PyDTTA]^{4-}$ as determined by quantitative ^{1}H NMR spectroscopy[4,5]). A solution of NaOD in D_2O (0.10 M, 390.8 µL, 39.08 µmol) was added to rise the pD of the solution to 7. The pale yellow solution was diluted with D_2O (to a total volume of 925 µL) to obtain a 5.0 mM solution of Gd-PyDTTA (**7**) in D_2O containing $Na(O_2CCF_3)$. MS (ESI): *m/z* = 579.9 $[M - Na]^-$.

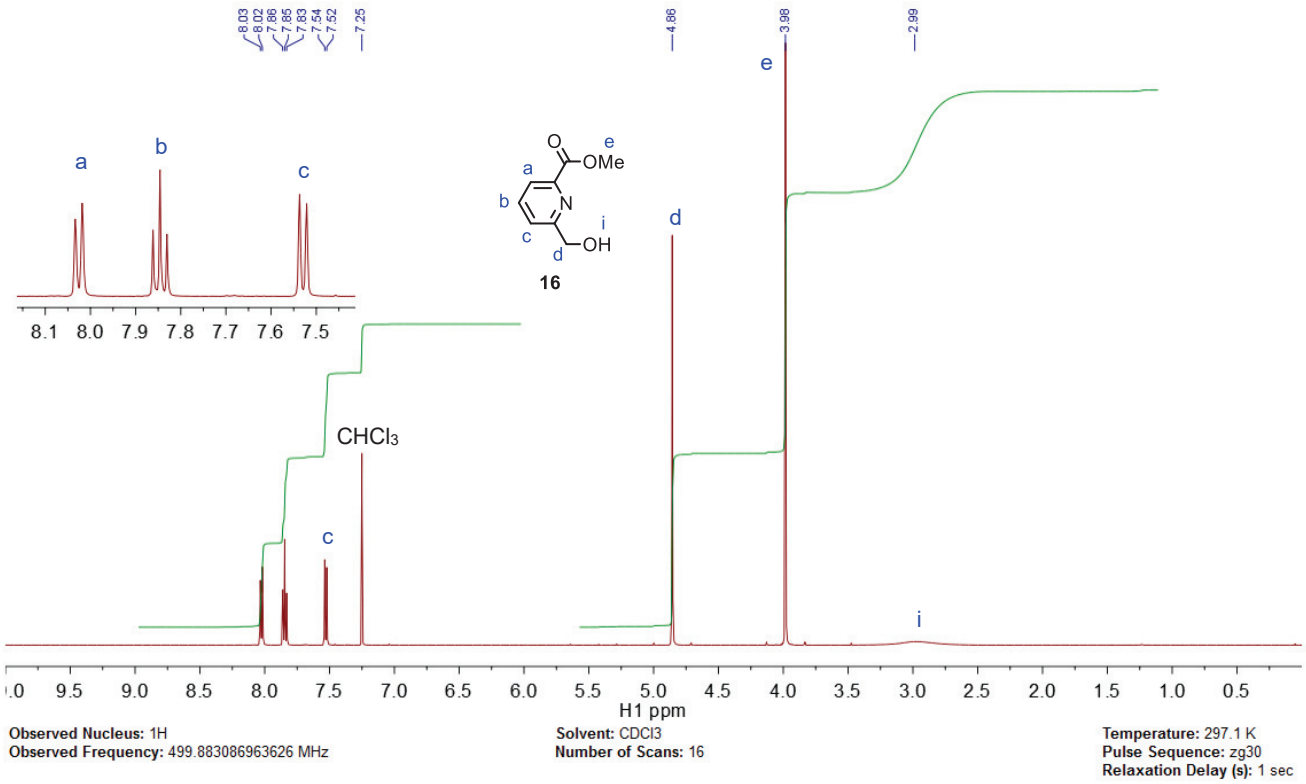


Figure SII-1: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of methyl 6-(hydroxymethyl)picolinate (**16**).

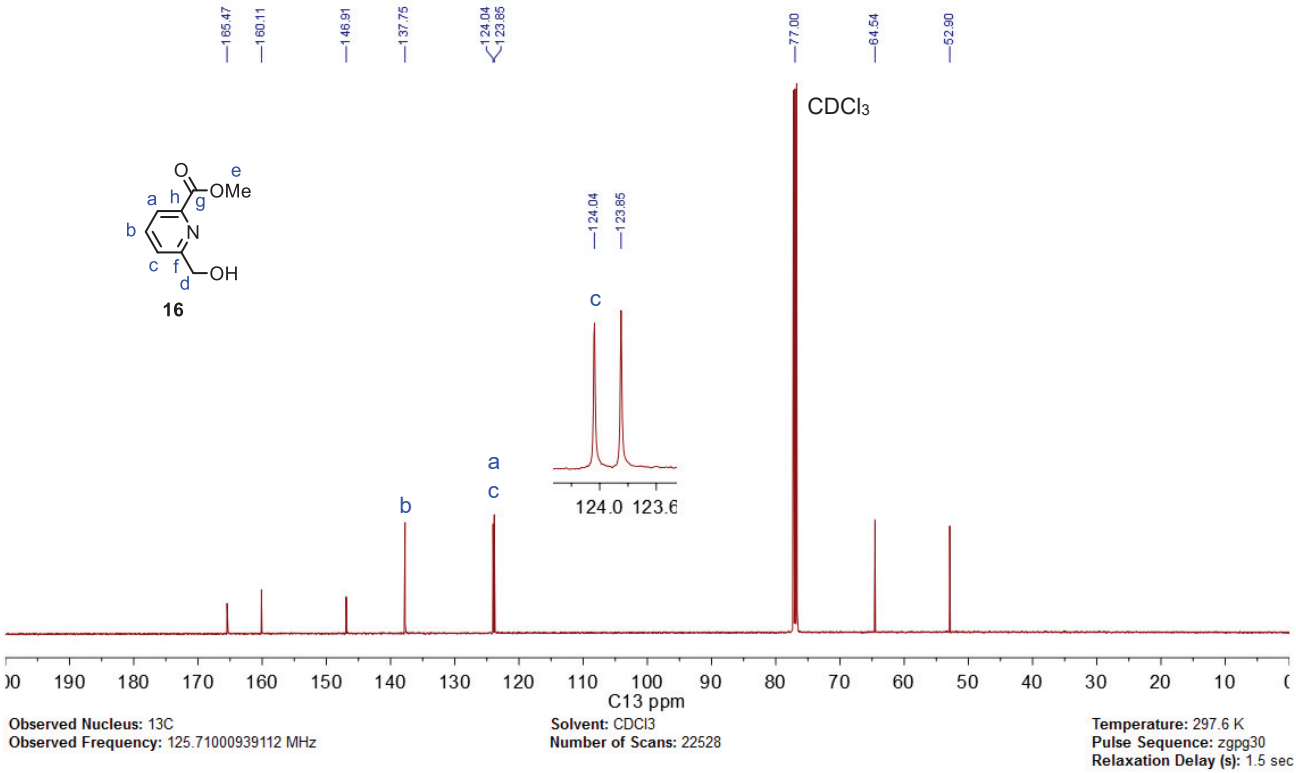


Figure SII-2: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of methyl 6-(hydroxymethyl)picolinate (**16**).

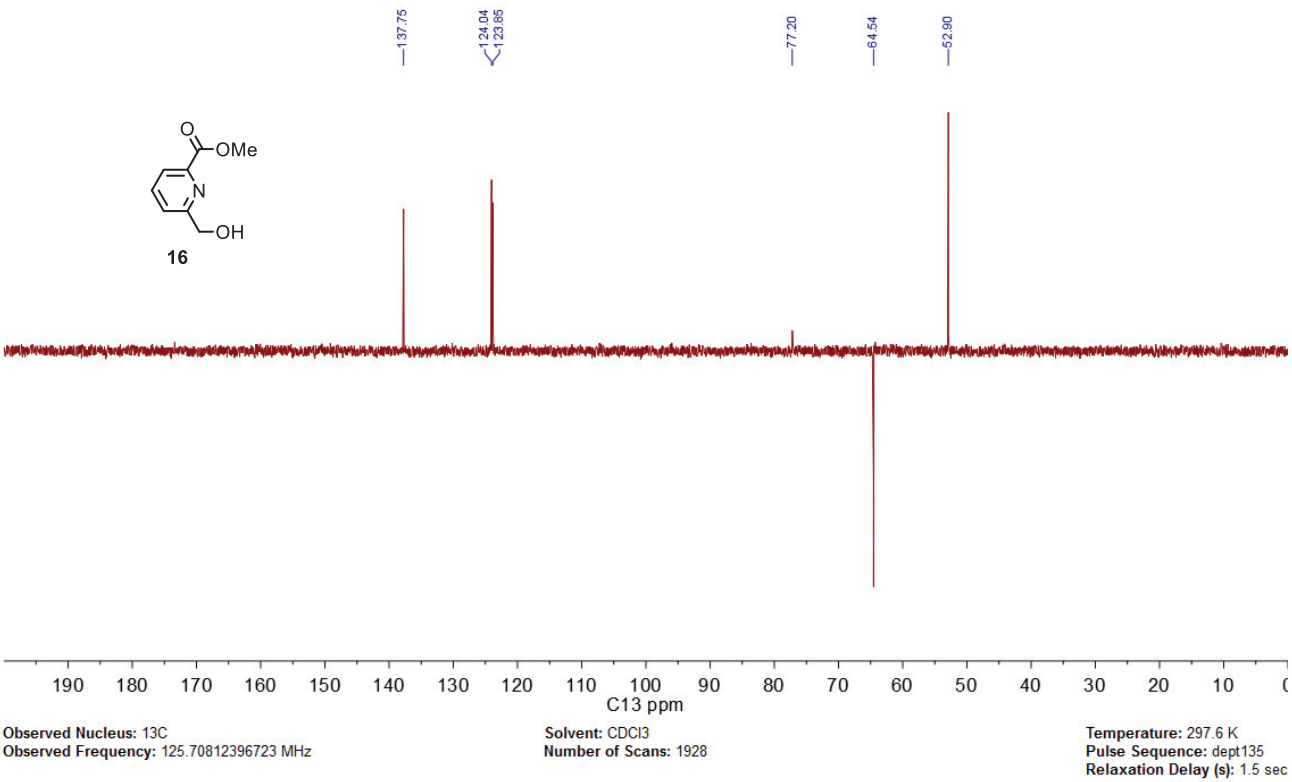


Figure SII-3: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of methyl 6-(hydroxymethyl)picolinate (**16**).

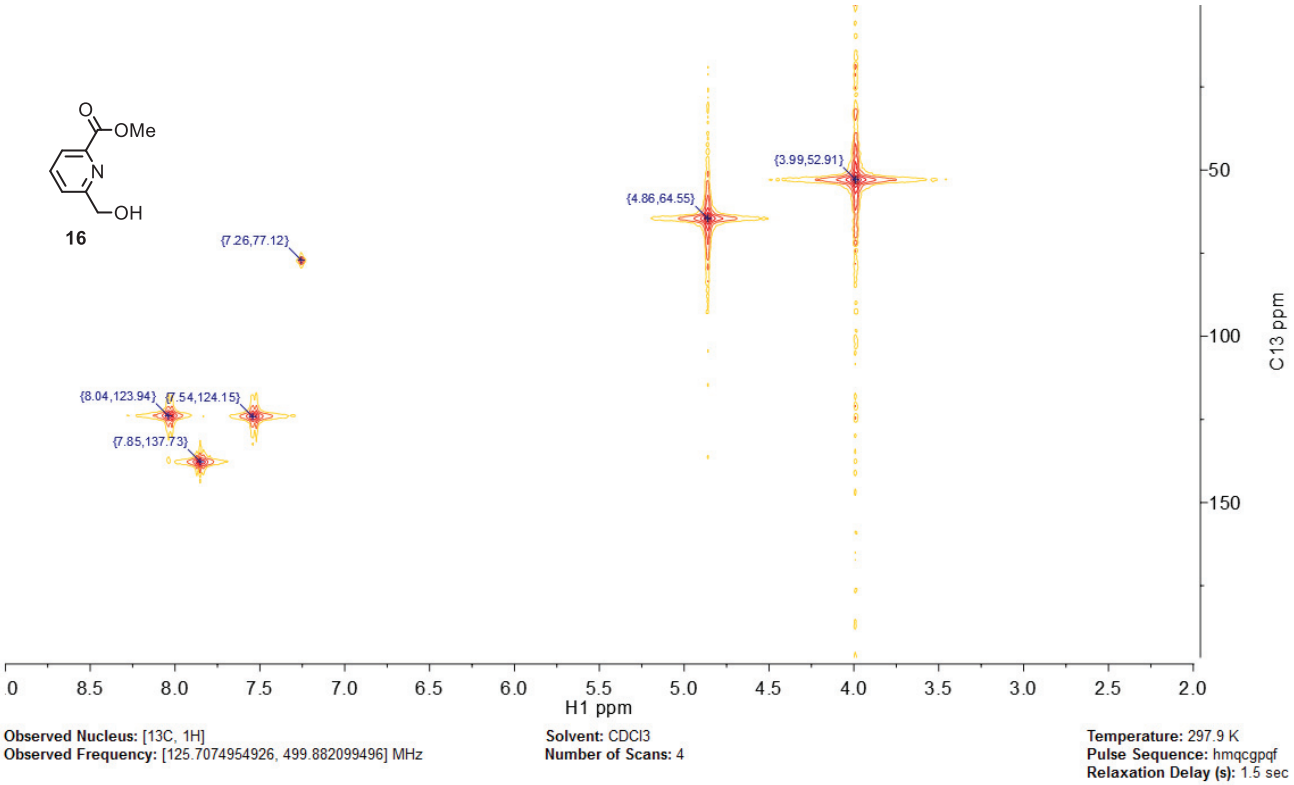


Figure SII-4: HMQC spectrum (500 MHz/125 MHz, $CDCl_3$) of methyl 6-(hydroxymethyl)picolinate (**16**).

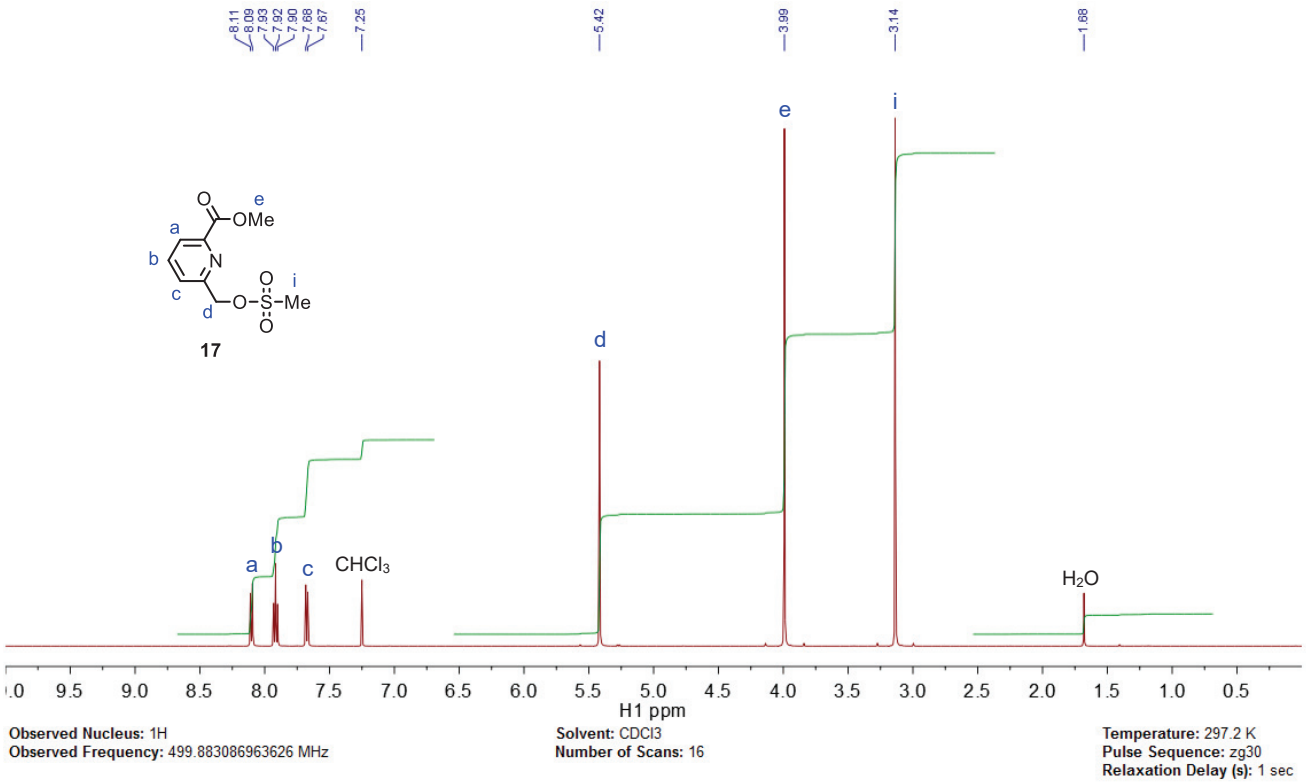


Figure SII-5: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of mesylate **17**.

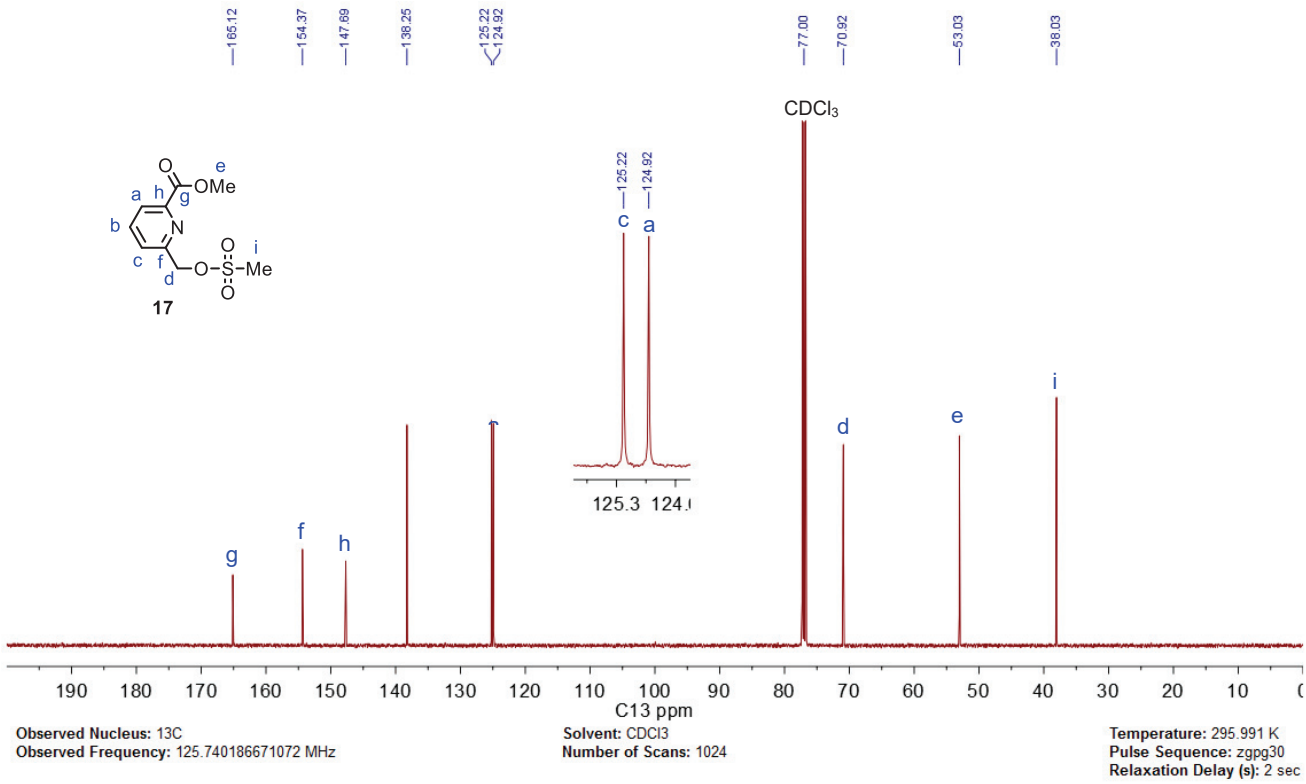


Figure SII-6: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of mesylate **17**.

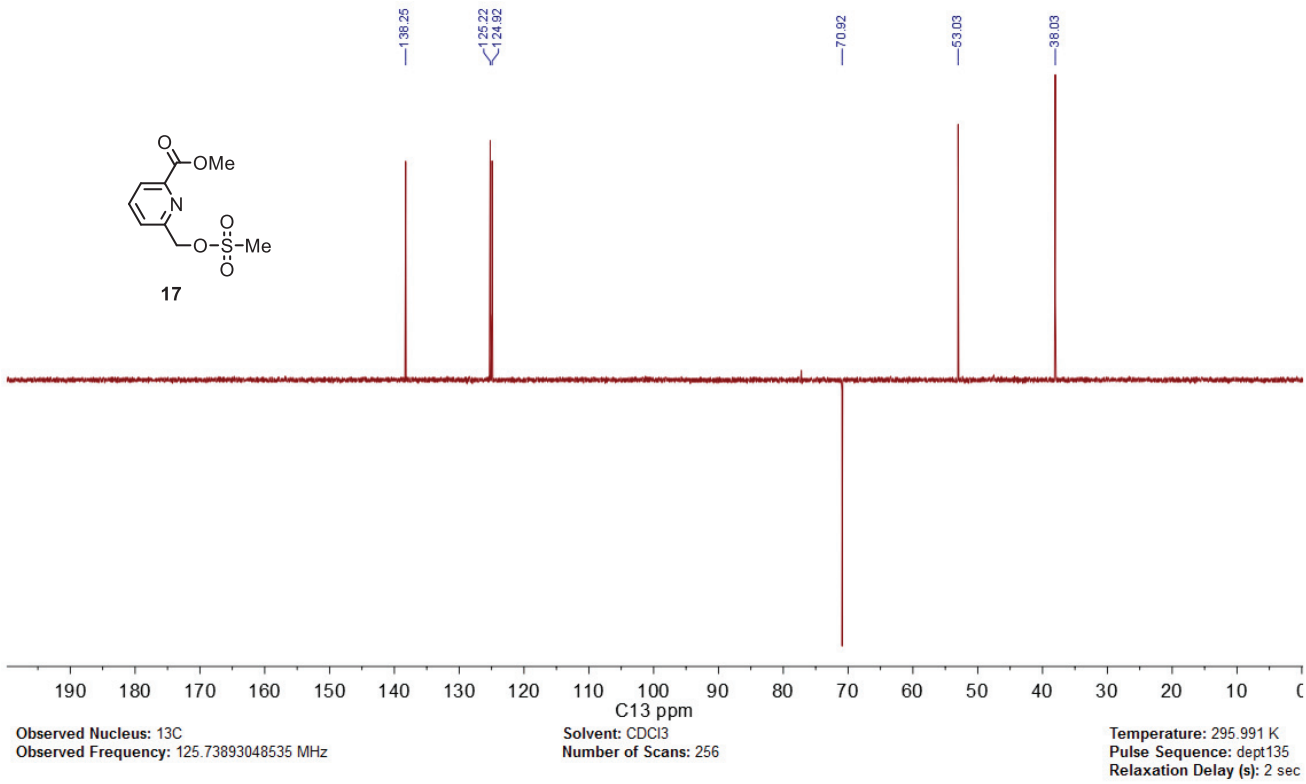


Figure SII-7: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of mesylate **17**.

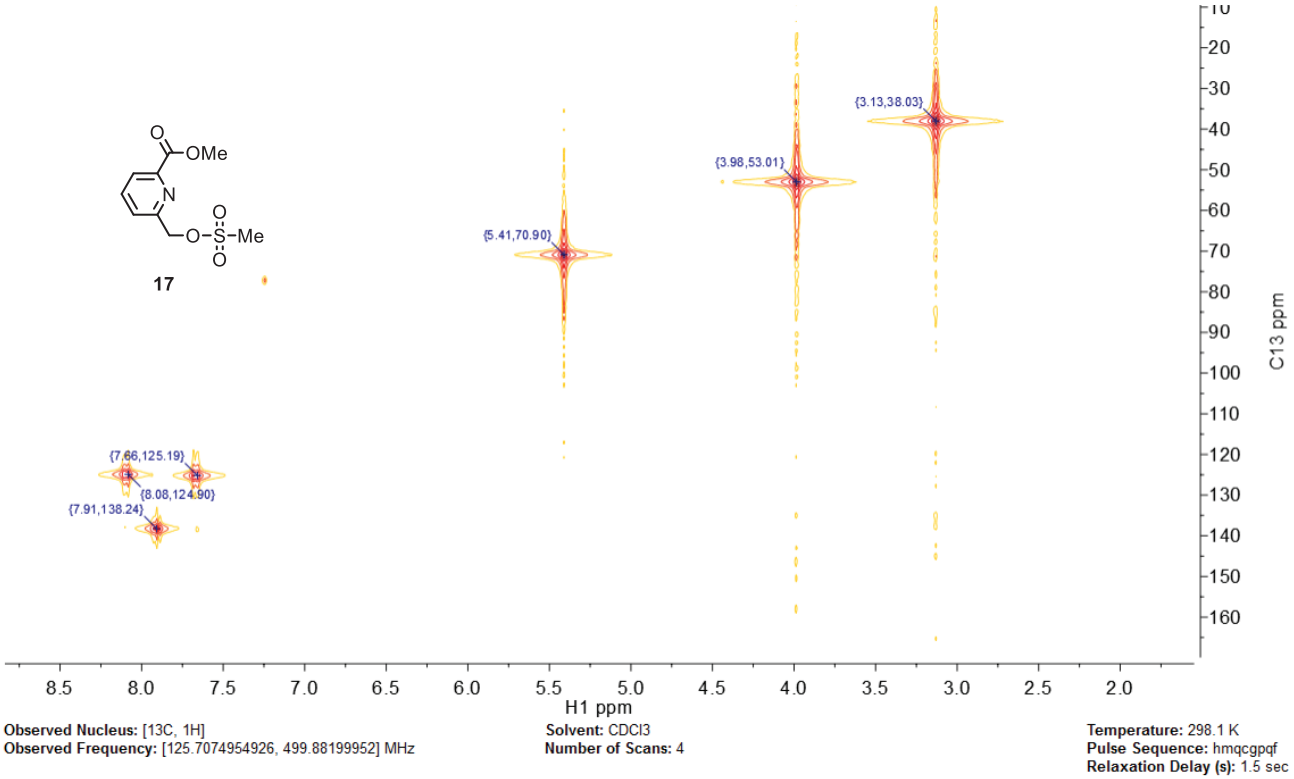


Figure SII-8: HMQC spectrum (500 MHz/125 MHz, $CDCl_3$) of mesylate **17**.

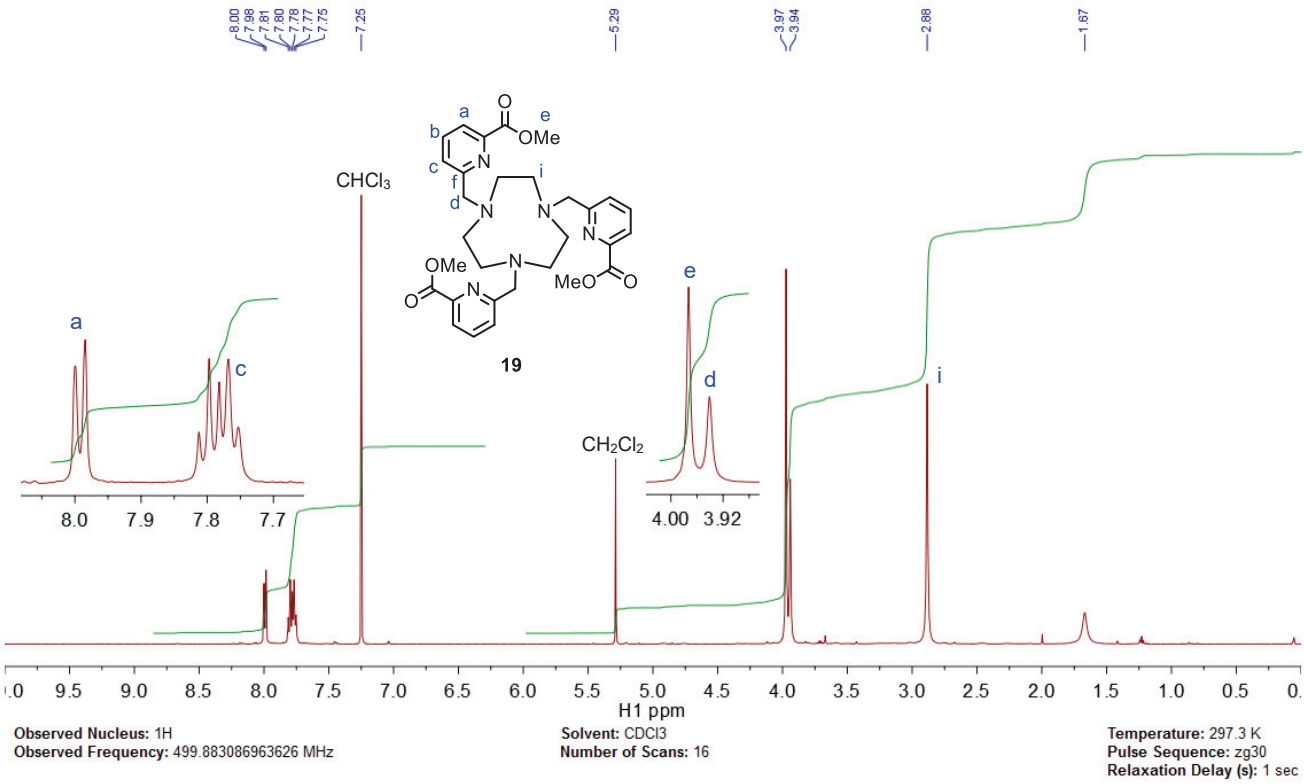


Figure SII-9: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of NO3Pic methyl ester **19**.

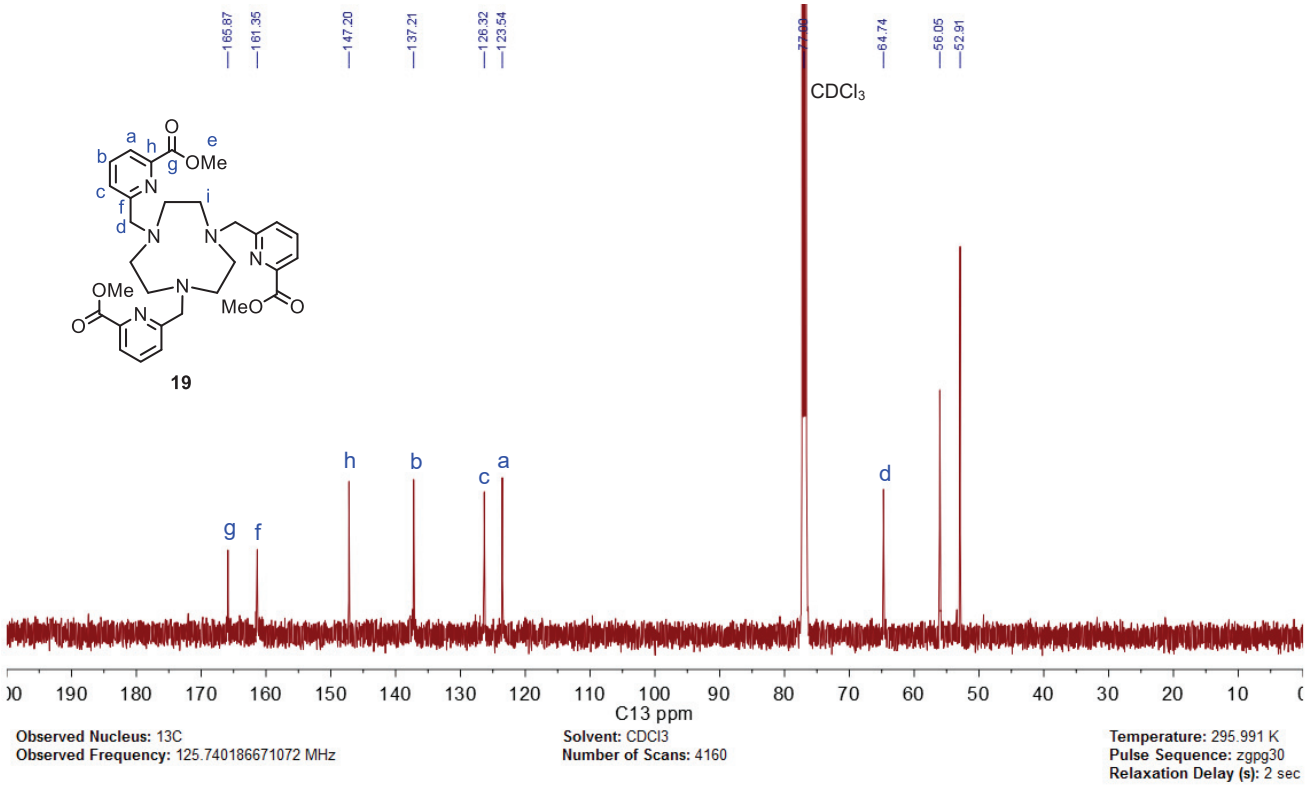


Figure SII-10: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of NO3Pic methyl ester **19**.

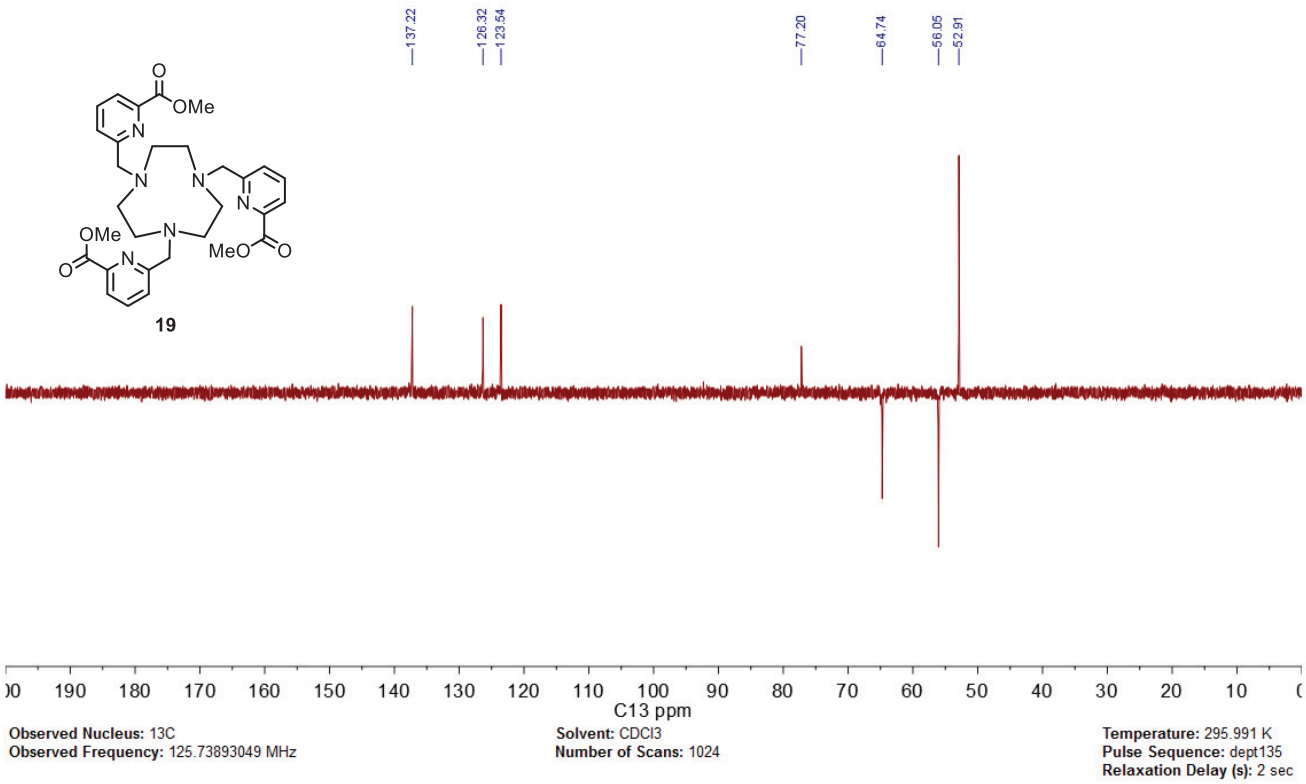


Figure SII-11: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of NO3Pic methyl ester **19**.

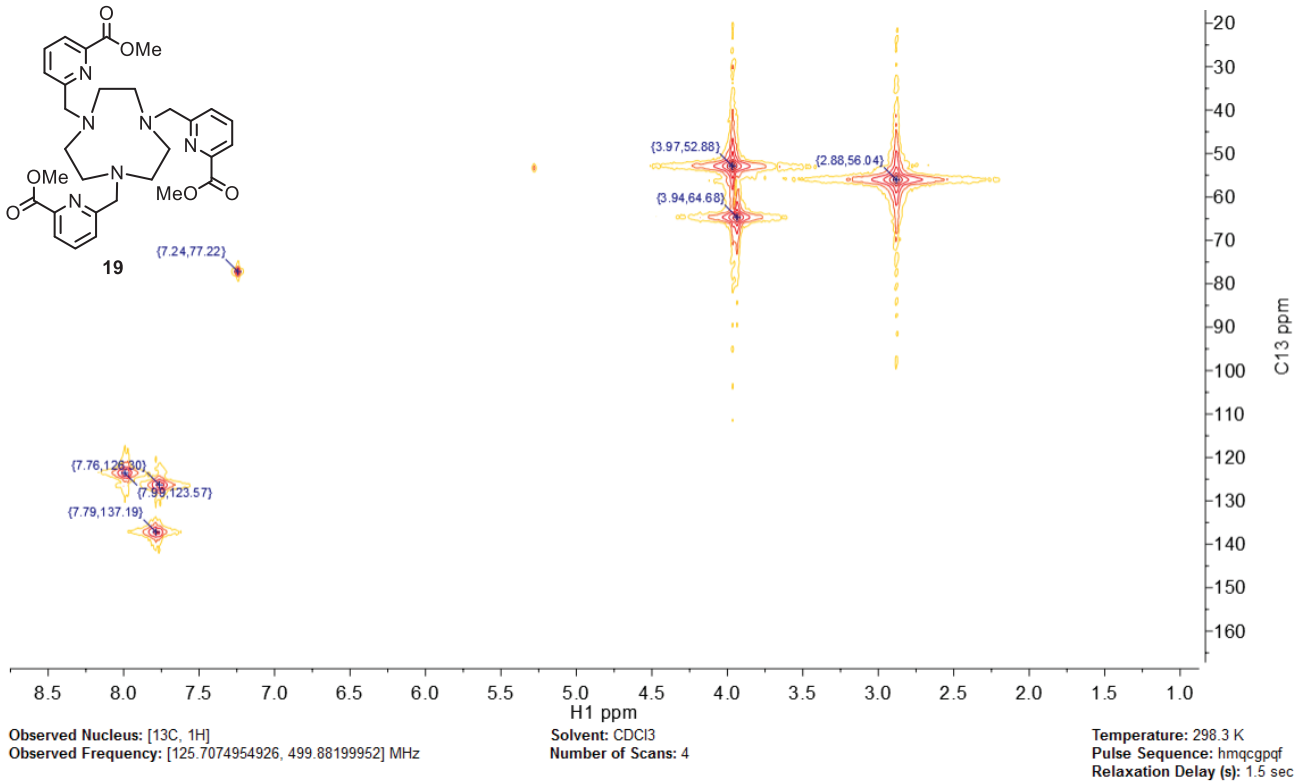


Figure SII-12: HMQC spectrum (500 MHz/125 MHz, $CDCl_3$) of NO3Pic methyl ester **19**.

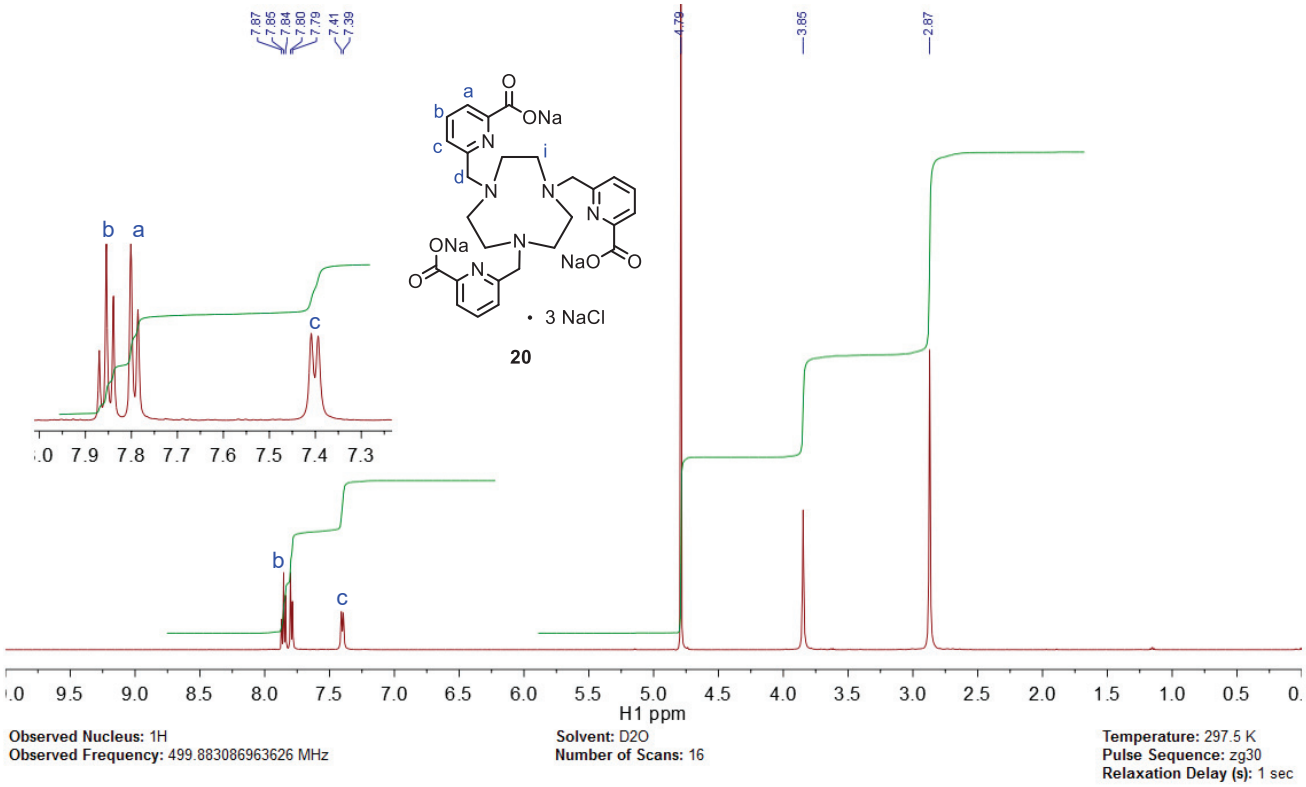


Figure SII-13: ^{1}H NMR spectrum (500 MHz, D_2O) of [Na_3NO3Pic]•3 NaCl•x H_2O (**20**).

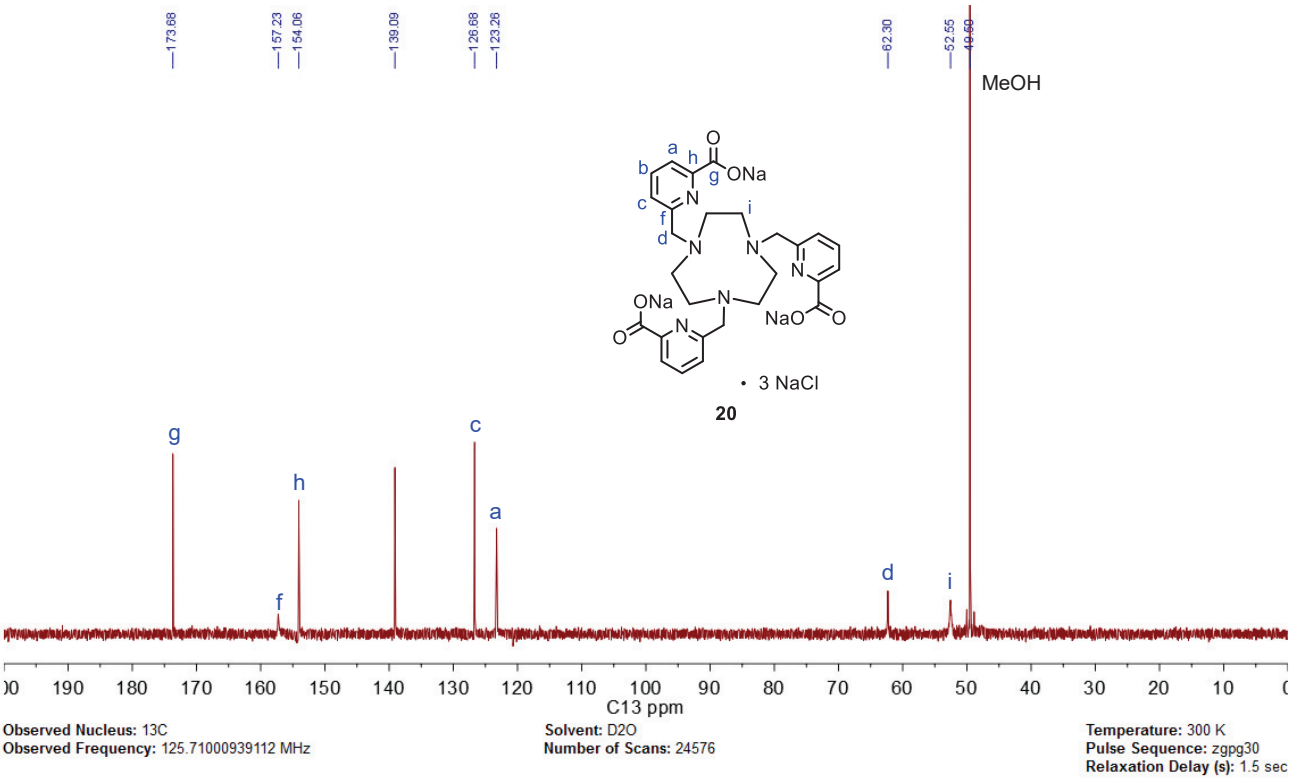


Figure SII-14: ^{13}C NMR spectrum (125 MHz, D_2O) of $[Na_3NO3Pic]$•3 NaCl•x H_2O. A drop of MeOH was added as reference for the chemical shift.

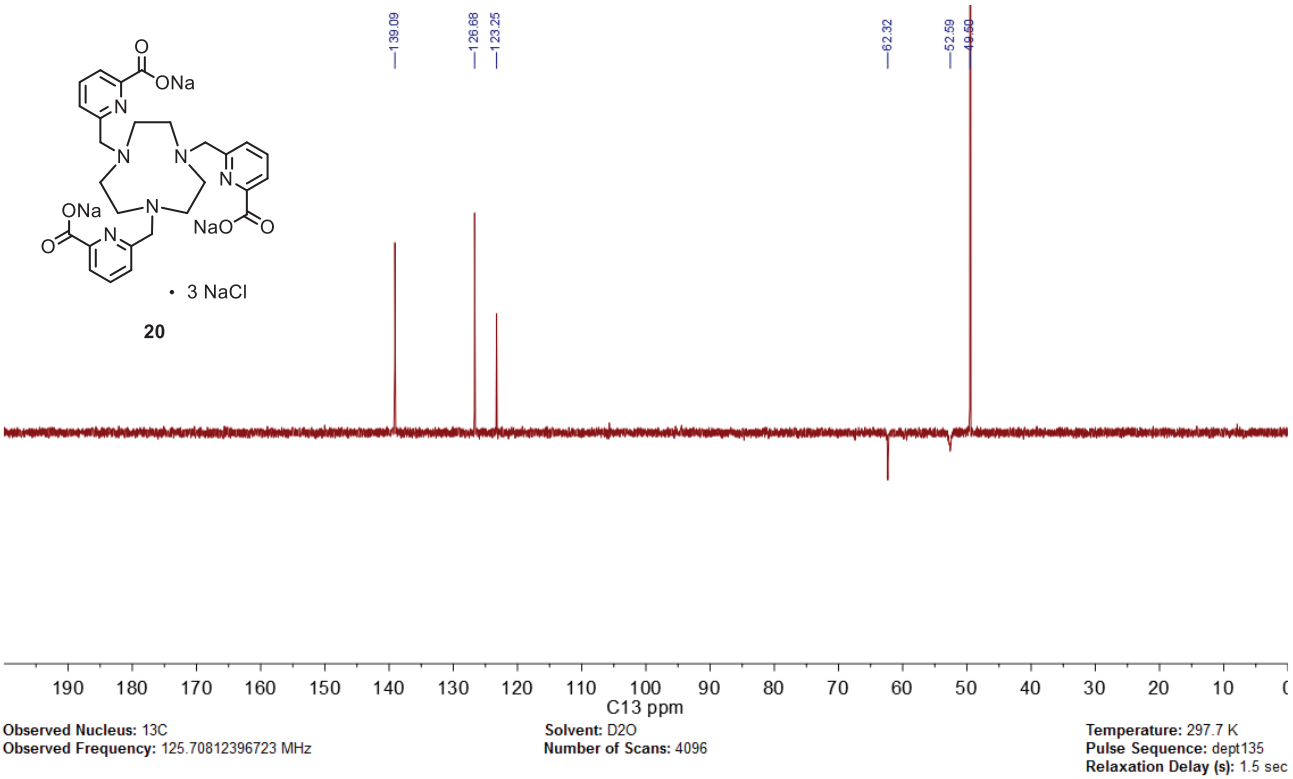


Figure SII-15: ^{13}C DEPT 135 NMR spectrum (125 MHz, D_2O) of [Na_3NO3Pic]•3 NaCl•x H_2O. A drop of MeOH was added as reference for the chemical shift.

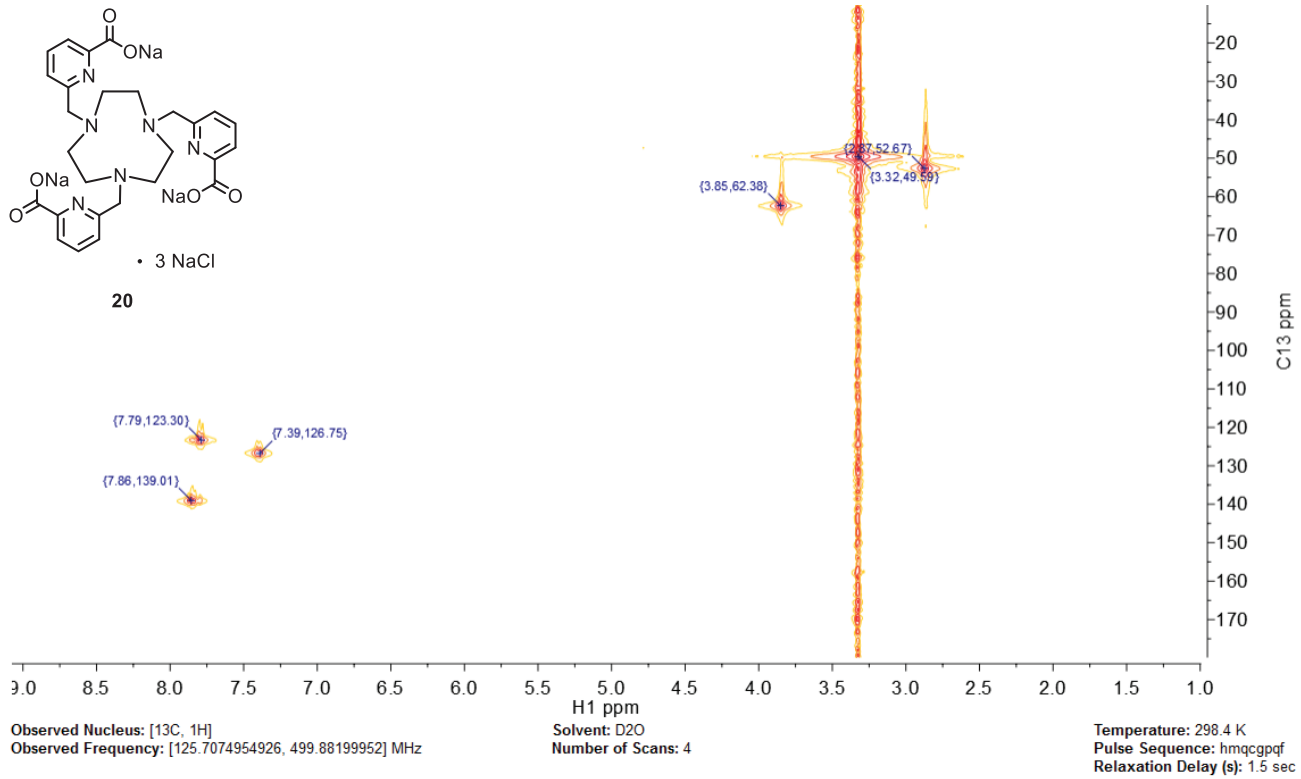


Figure SII-16: HMQC spectrum (500 MHz/125 MHz, D_2O) of [Na_3NO3Pic]•3 NaCl•x H_2O. A drop of MeOH was added as reference for the chemical shift.

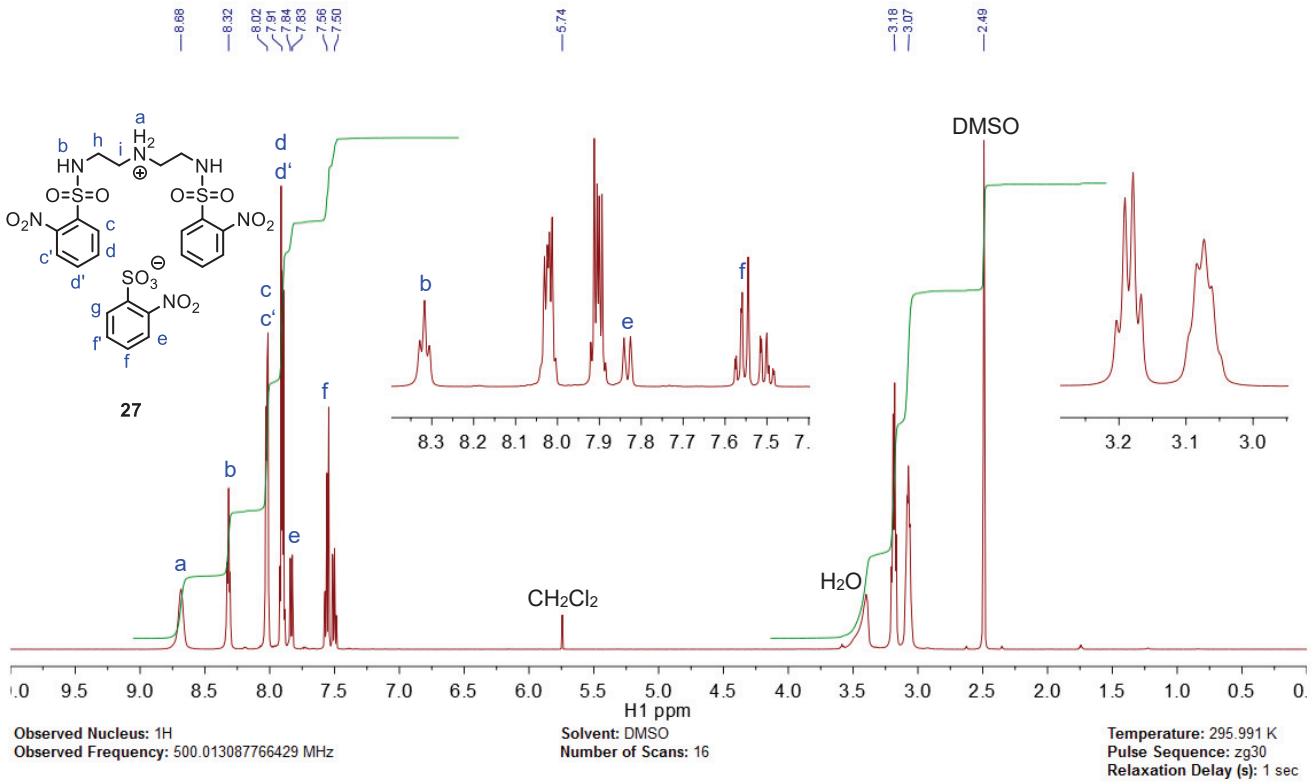


Figure SII-17: ^{1}H NMR spectrum (500 MHz, DMSO-d_6) of 1,7-dinosyl-1,4,7-triazaheptane•NsOH (**27**).

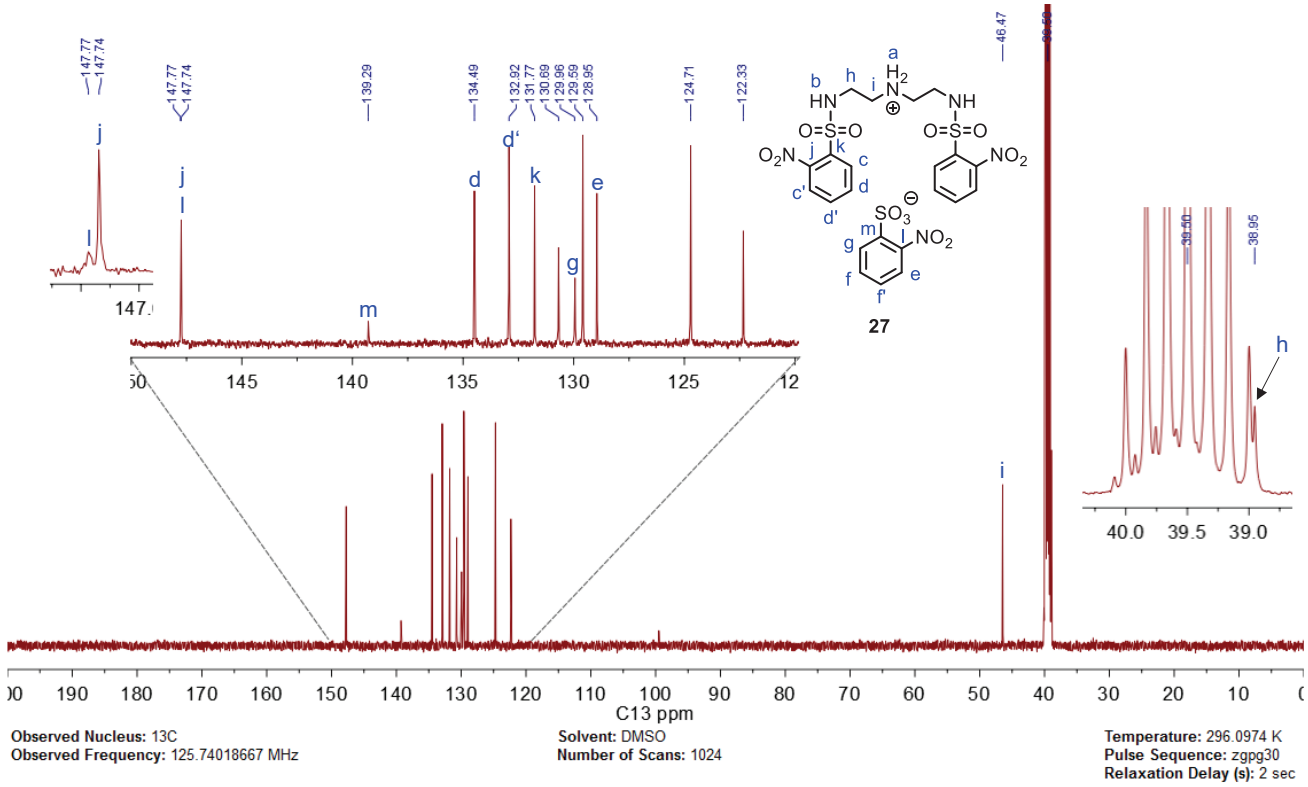


Figure SII-18: ^{13}C NMR spectrum (125 MHz, DMSO-d_6) of 1,7-dinosyl-1,4,7-triazaheptane•NsOH (**27**).

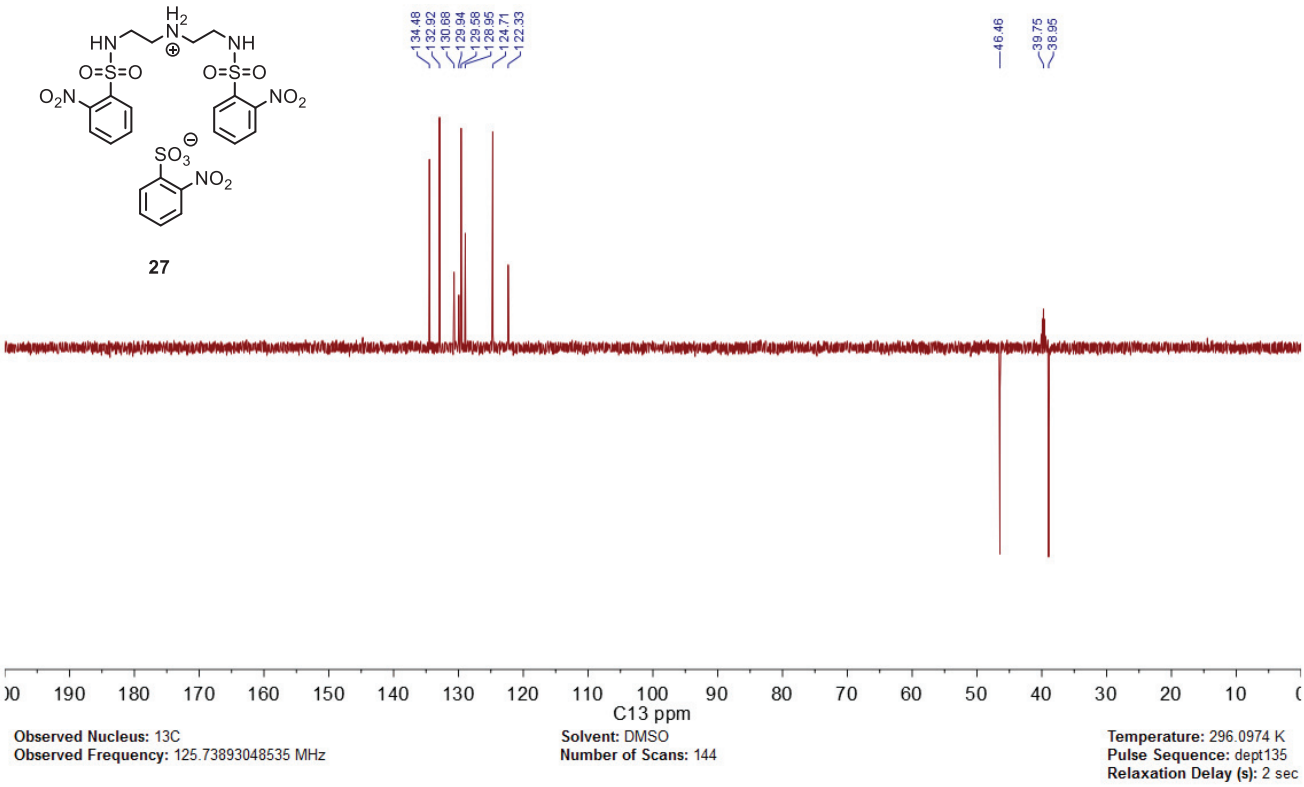
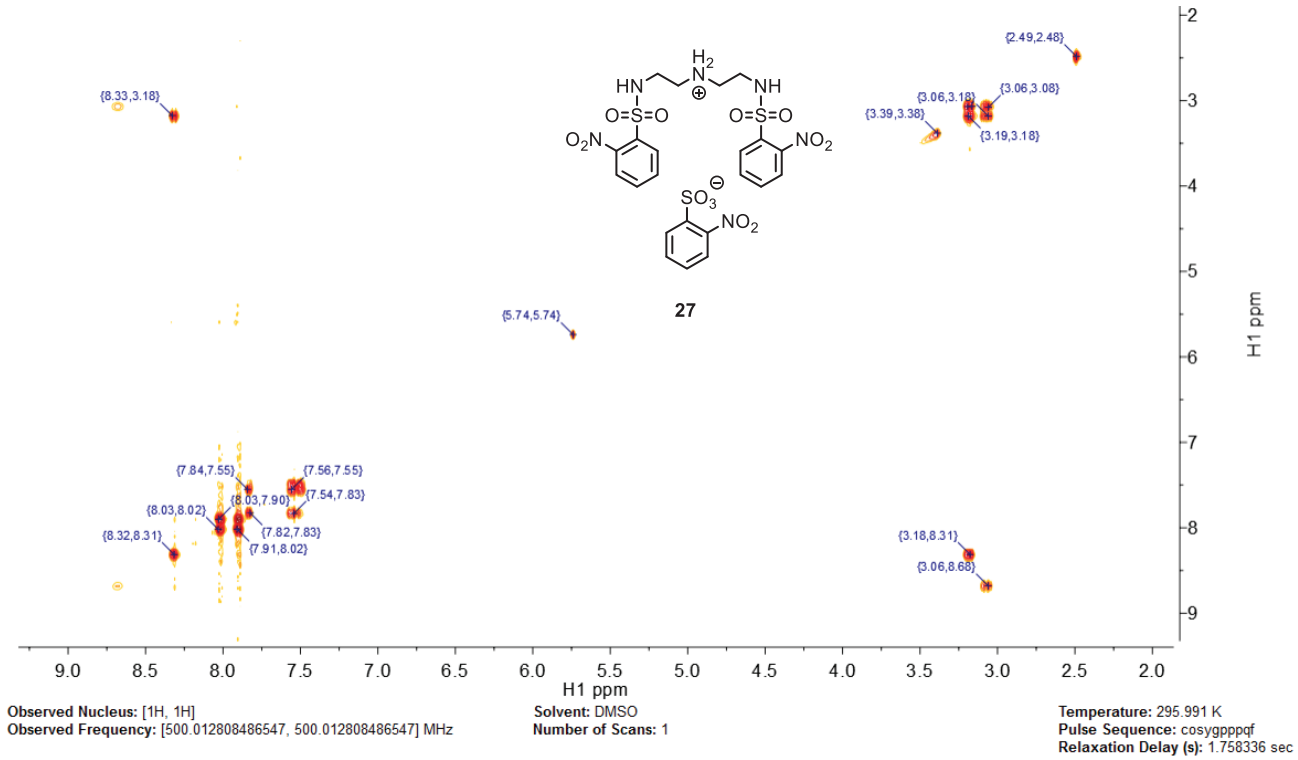


Figure SII-19: ^{13}C DEPT 135 NMR spectrum (125 MHz, DMSO-d_6) of 1,7-dinosyl-1,4,7-triazaheptane•NsOH (**27**).



27

Figure SII-20: COSY NMR spectrum (500 MHz, DMSO-d_6) of 1,7-dinosyl-1,4,7-triazaheptane•NsOH (**27**).

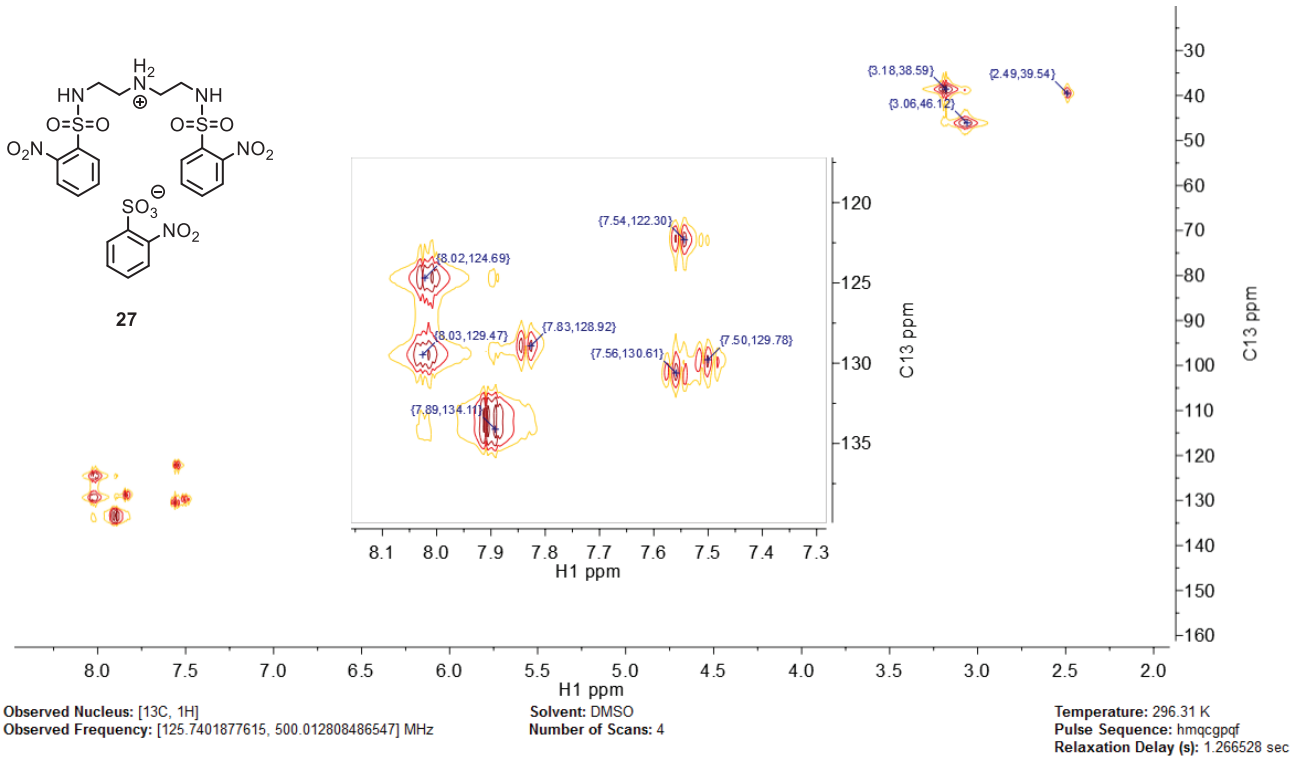


Figure SII-21: HMQC NMR spectrum (500 MHz, 125 MHz, DMSO-d_6) of 1,7-dinosyl-1,4,7-triazaheptane•NsOH (**27**).

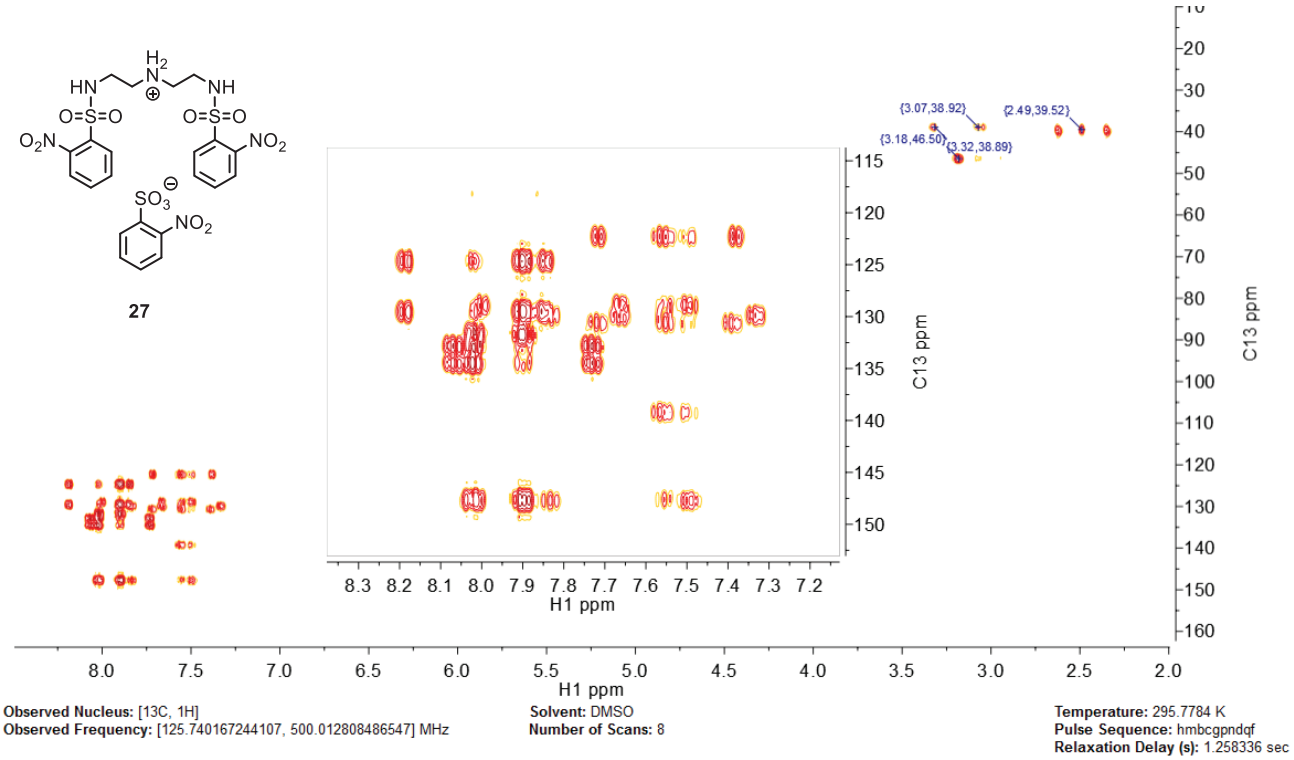


Figure SII-22: HMBC NMR spectrum (500 MHz, 125 MHz, DMSO-d_6) of 1,7-dinosyl-1,4,7-triazaheptane•NsOH (**27**).

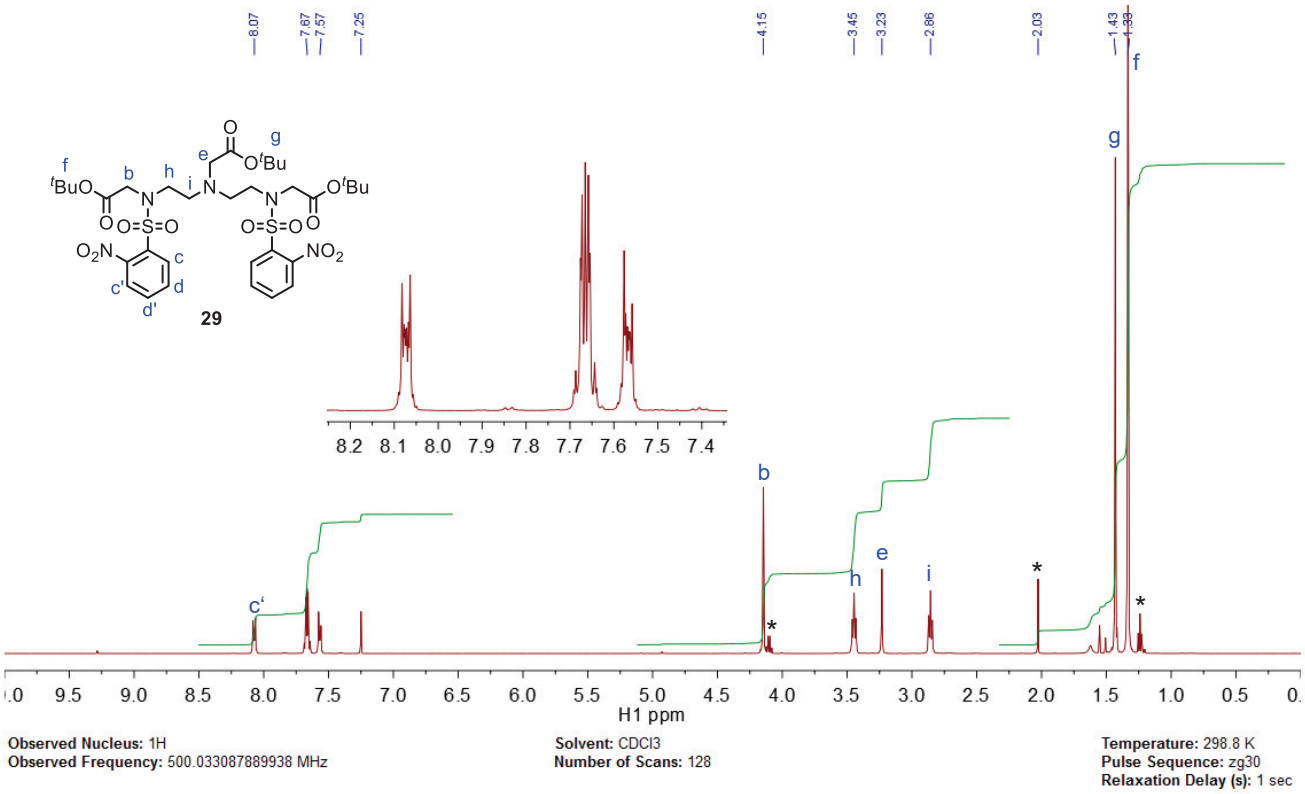


Figure SII-23: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of dinosylate **29**. *Signals of ethyl acetate.

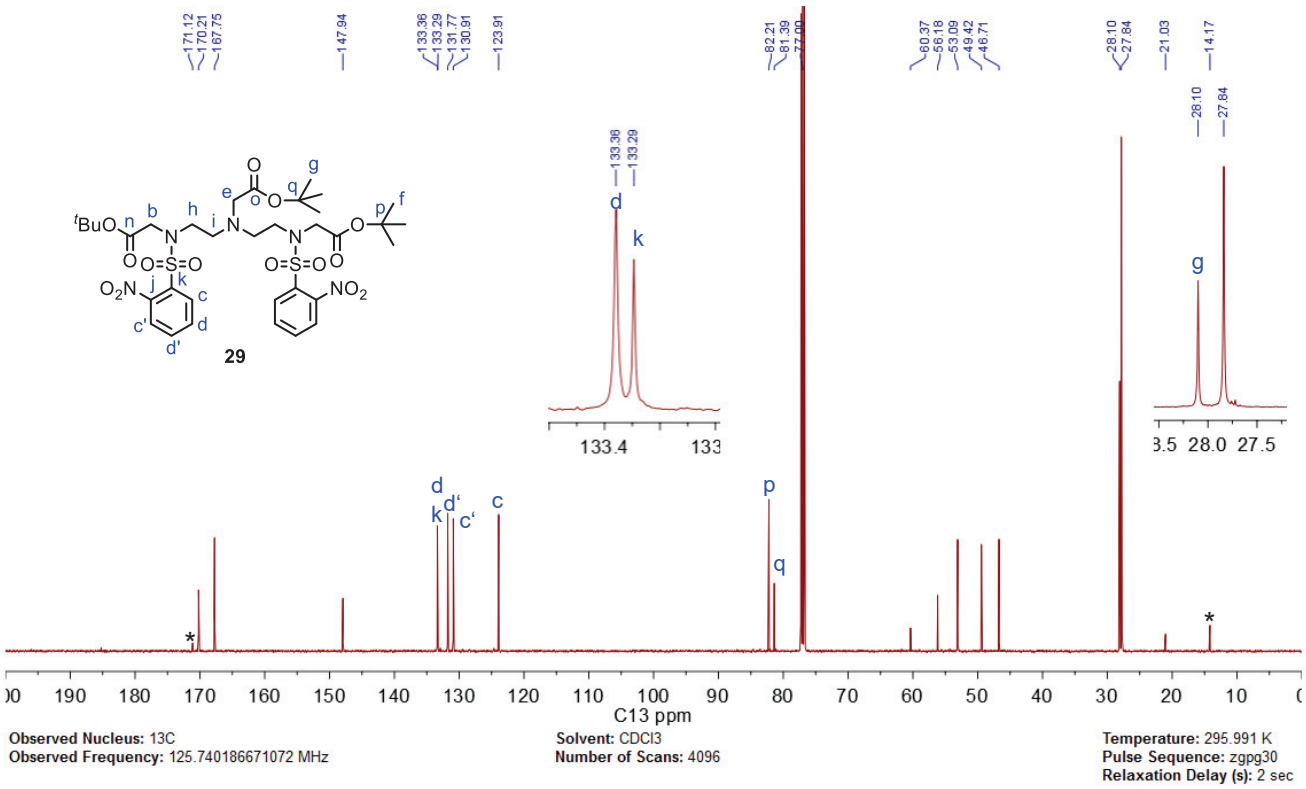


Figure SII-24: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of dinosylate **29**. *Signals of ethyl acetate.

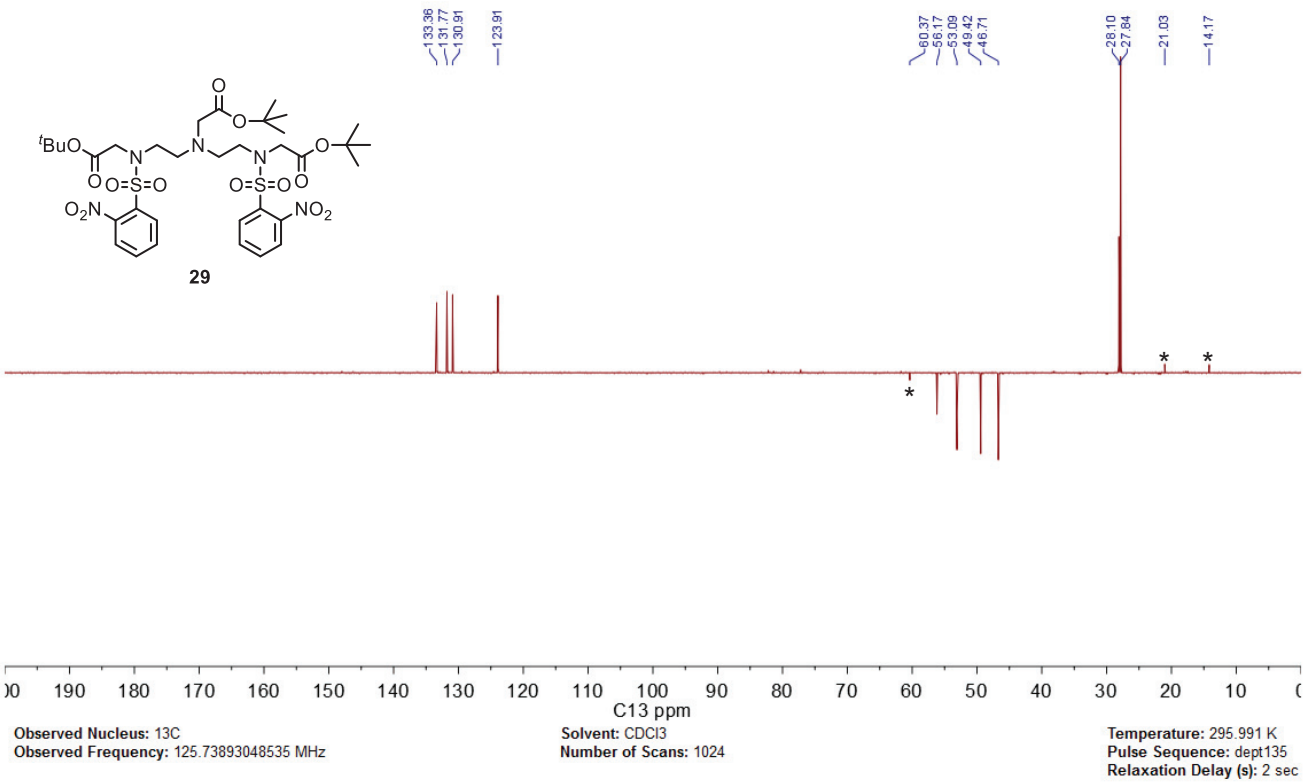


Figure SII-25: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of dinosylate **29**. *Signals of ethyl acetate.

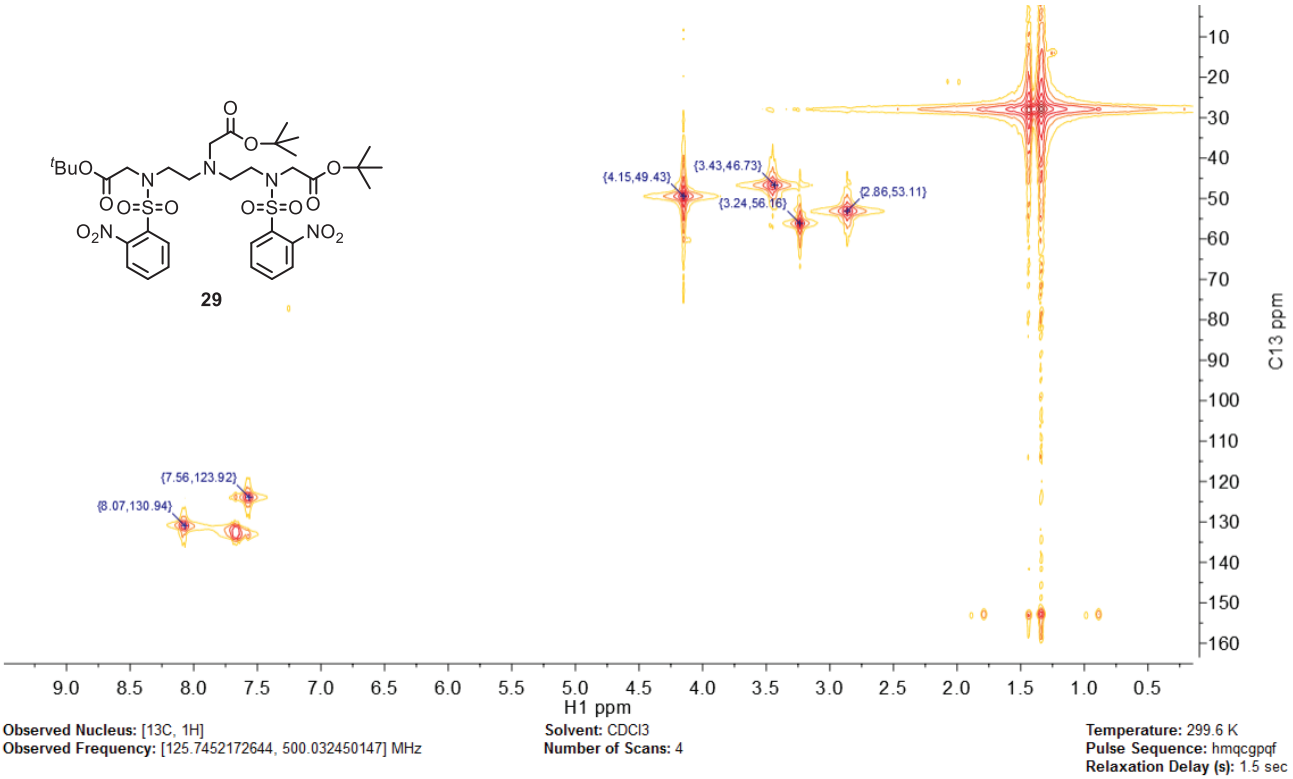


Figure SII-26: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of dinosylate **29**.

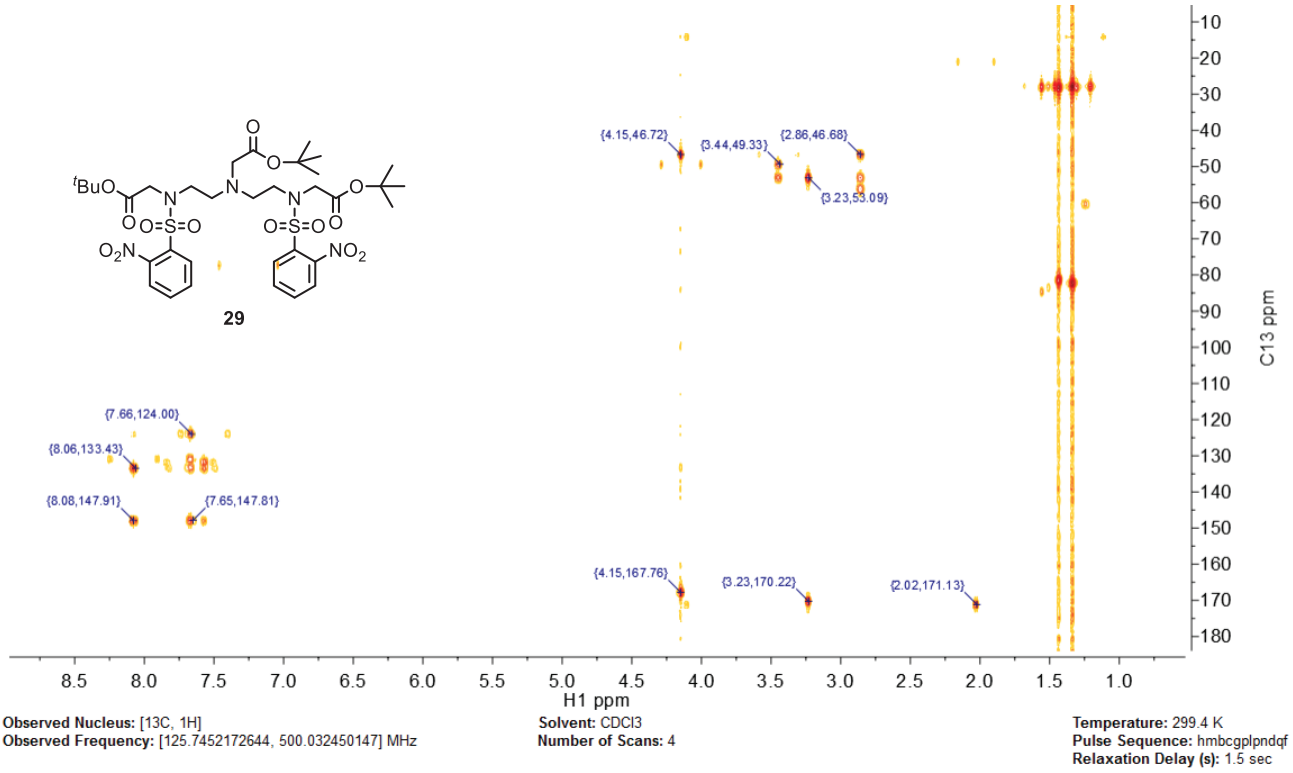


Figure SII-27: HMBC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of dinosylate **29**.

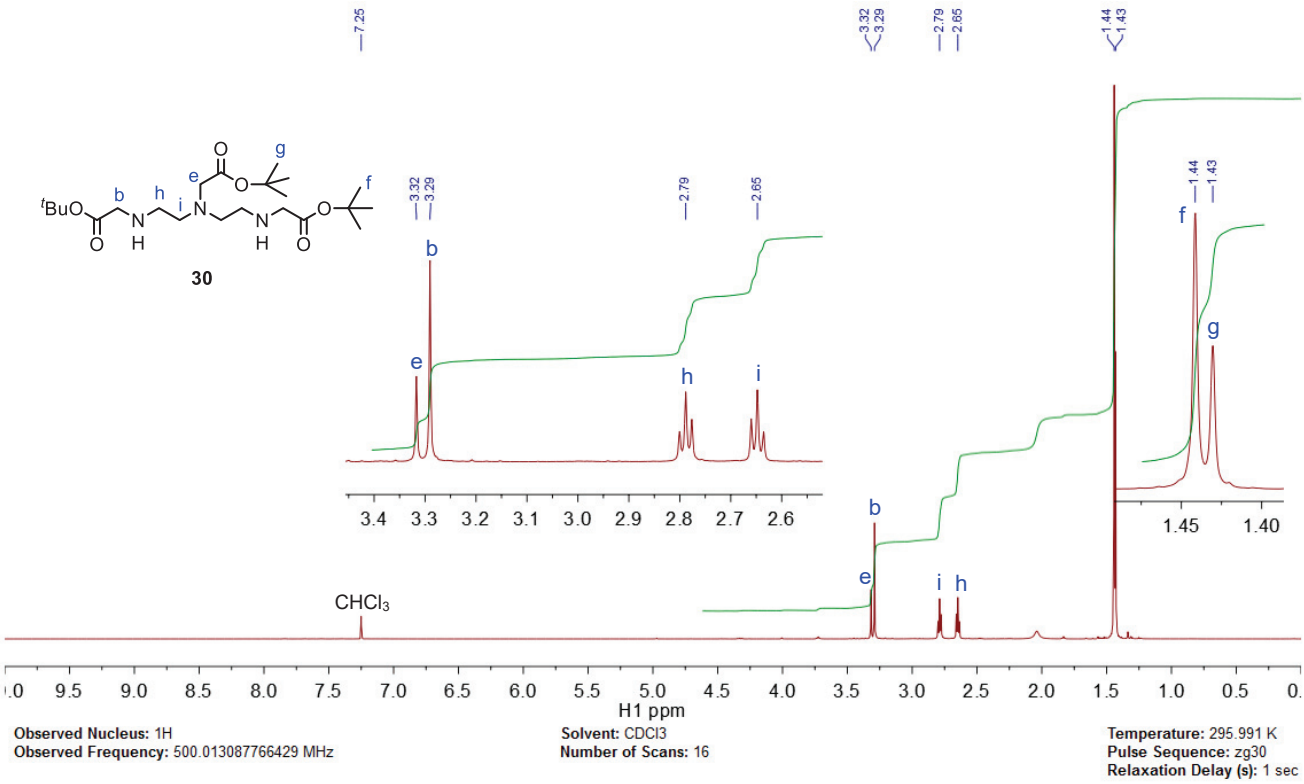


Figure SII-28: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of amine **30**.

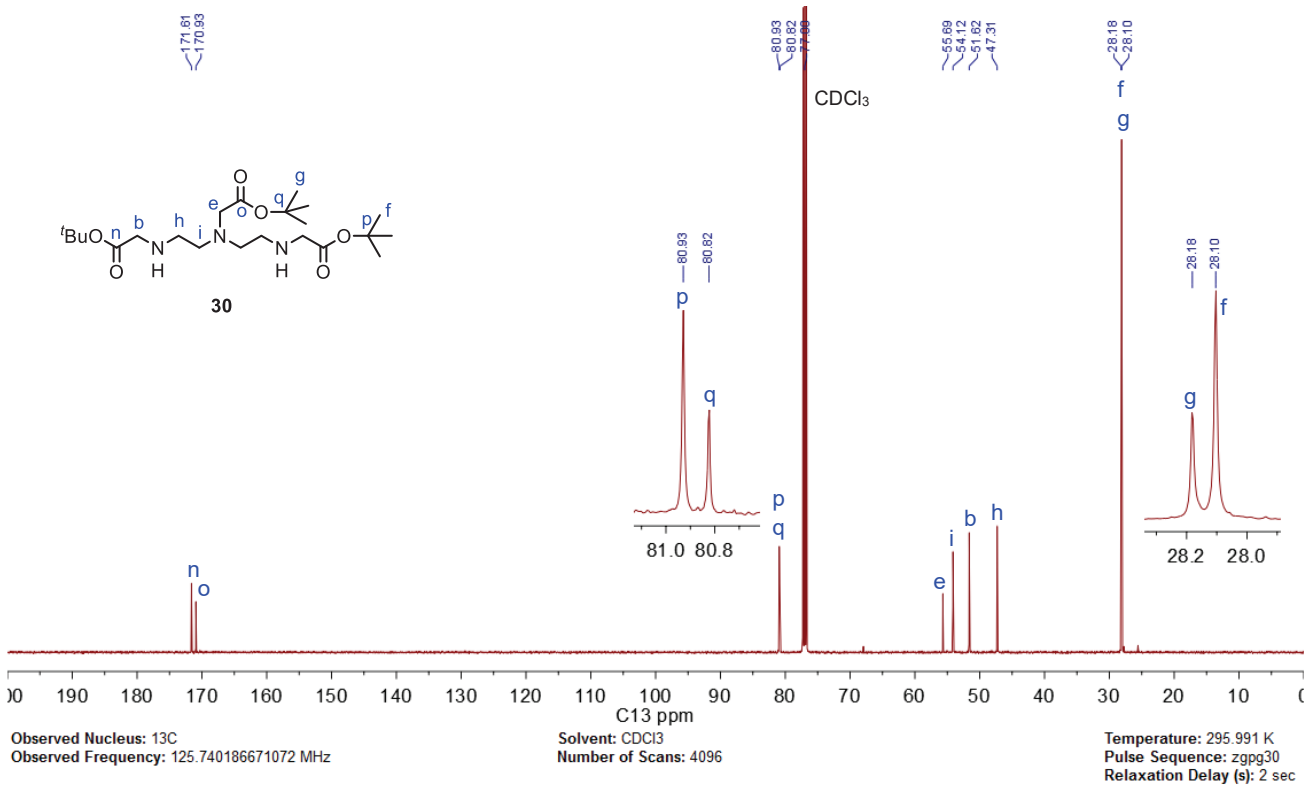


Figure SII-29: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of amine **30**.

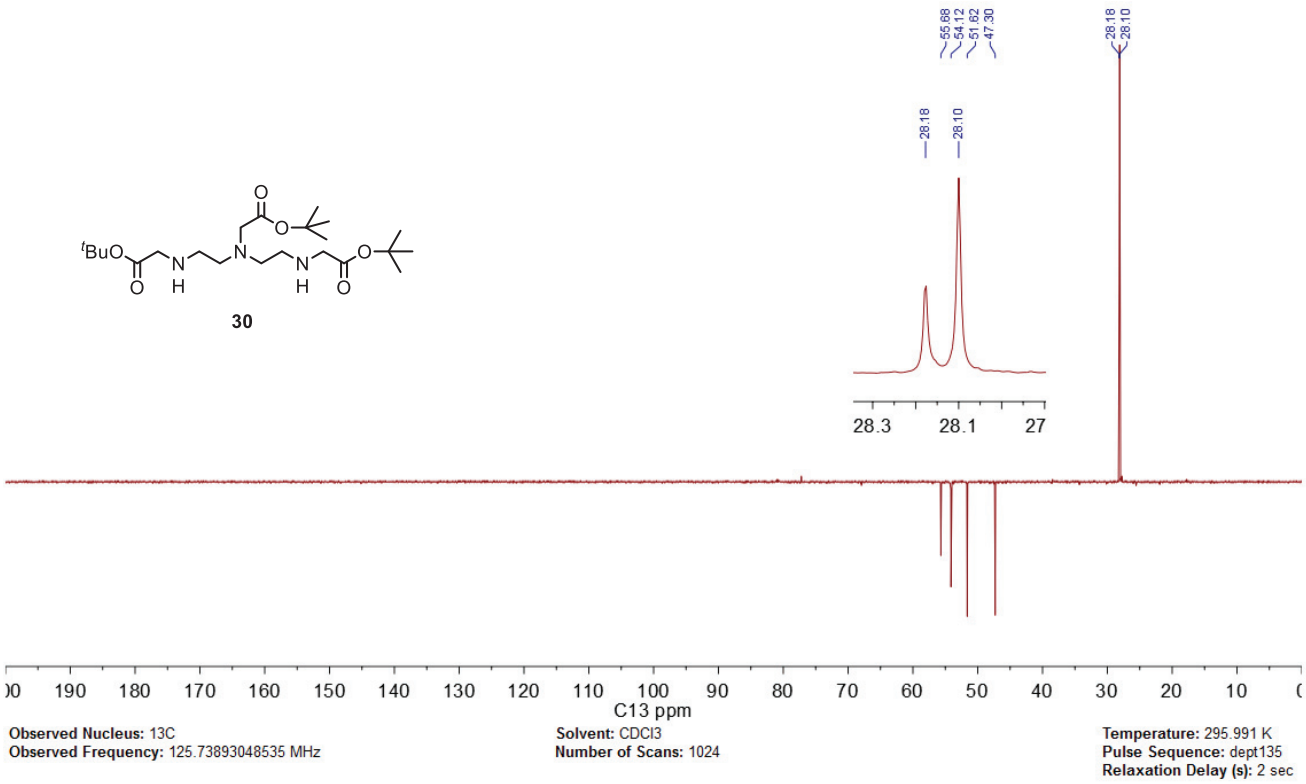


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Figure SII-30: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of amine **30**.

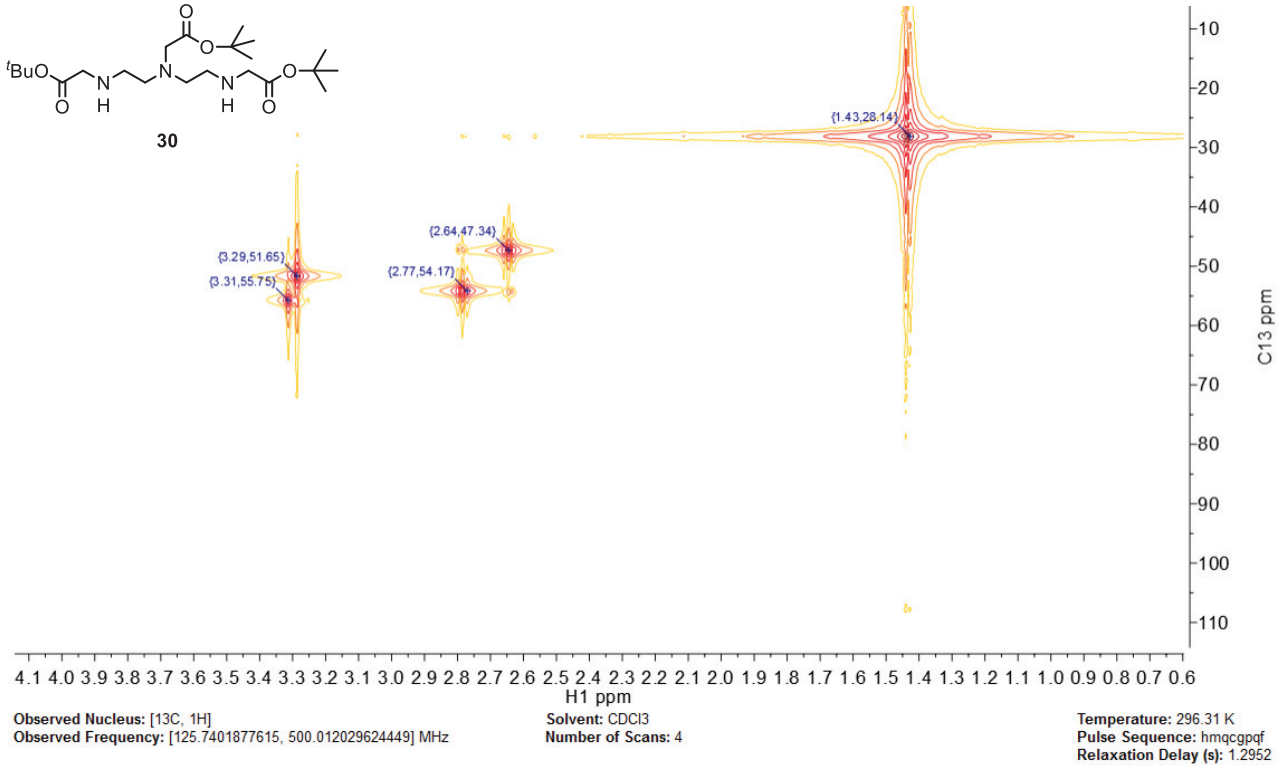

Figure SII-31: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of amine **30**.

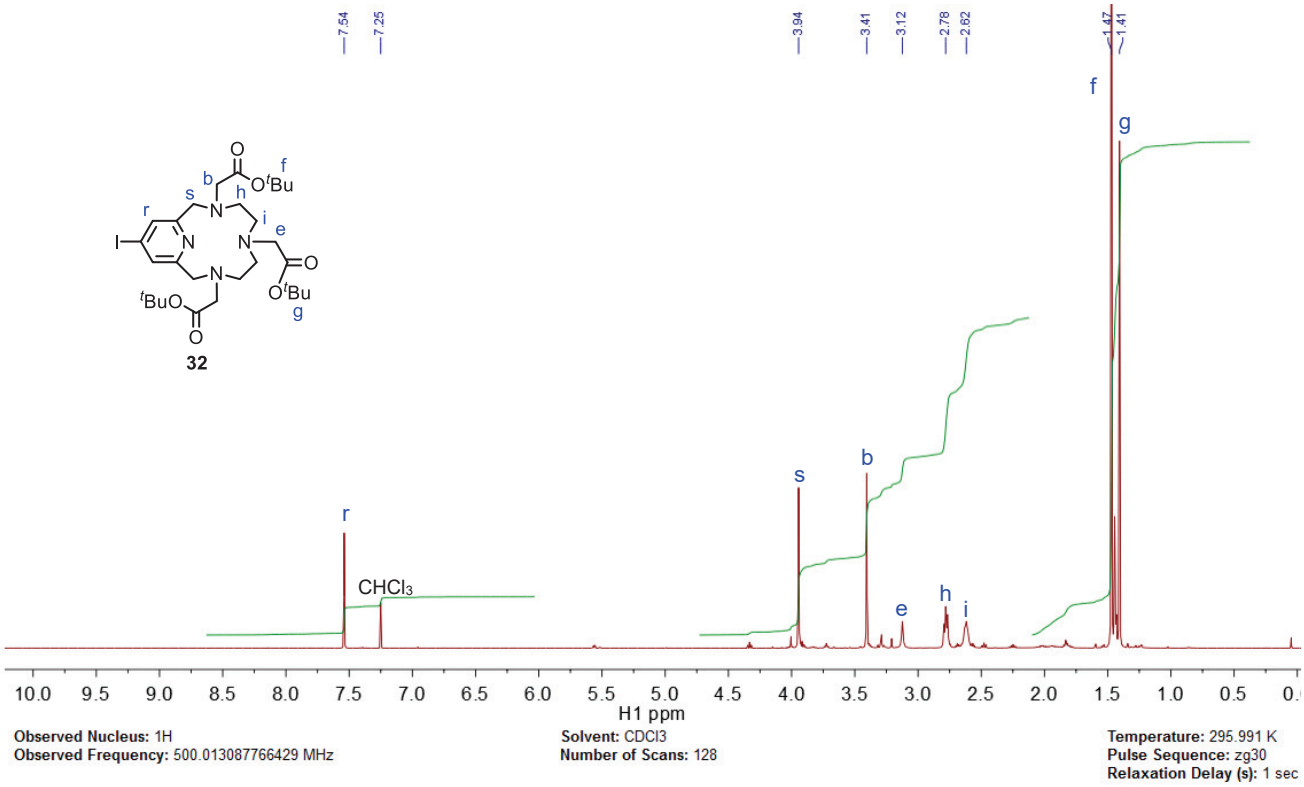

Figure SII-32: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of 4-iodo-PCTA *tert*-butyl ester (**32**) contaminated with unidentified component(s).

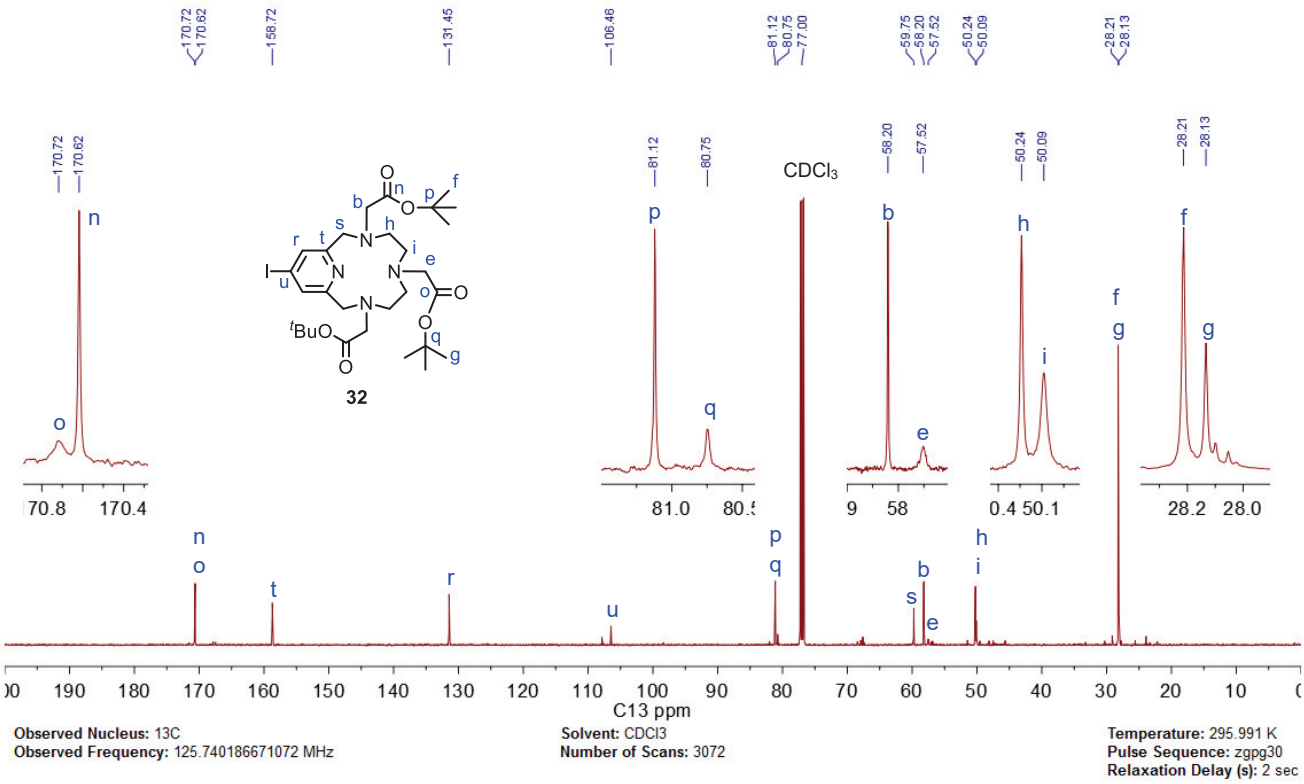

Figure SII-33: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of 4-iodo-PCTA *tert*-butyl ester (**32**) contaminated with unidentified component(s).

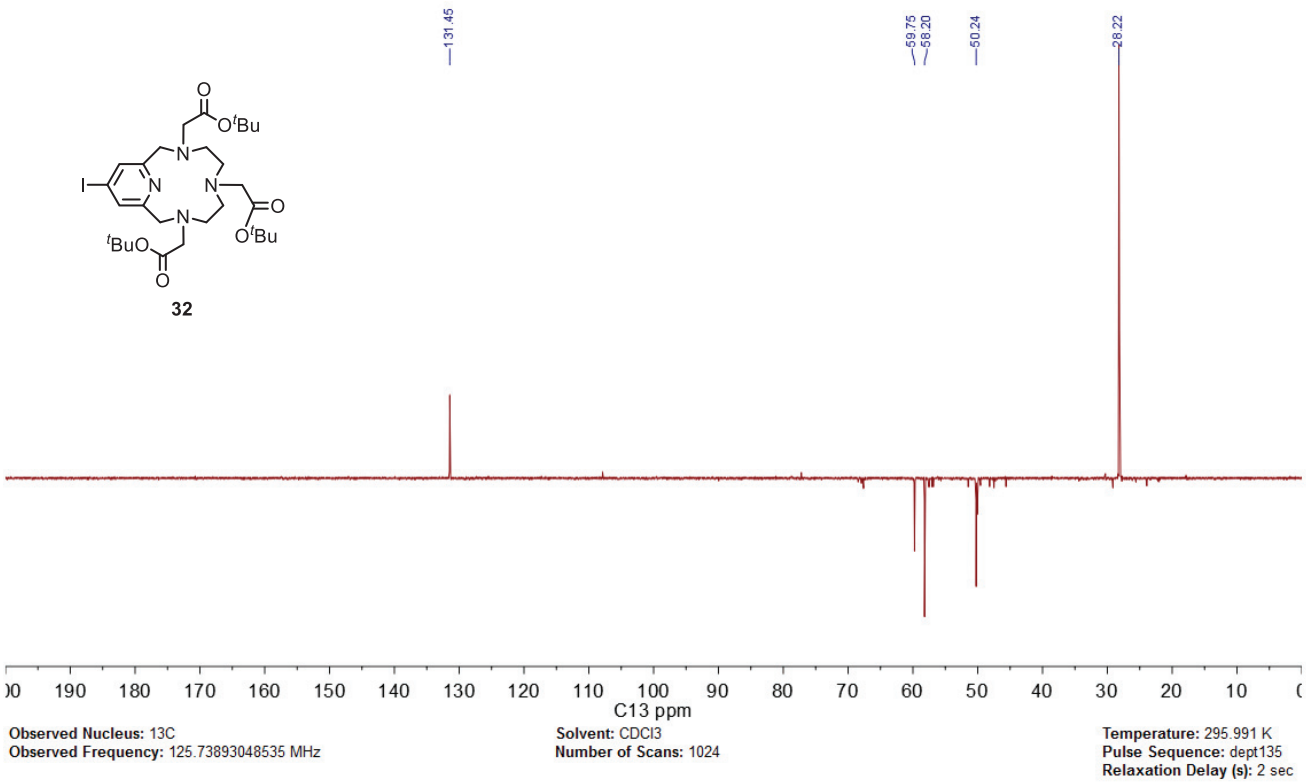

Figure SII-34: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of 4-iodo-PCTA *tert*-butyl ester (**32**) contaminated with unidentified component(s).

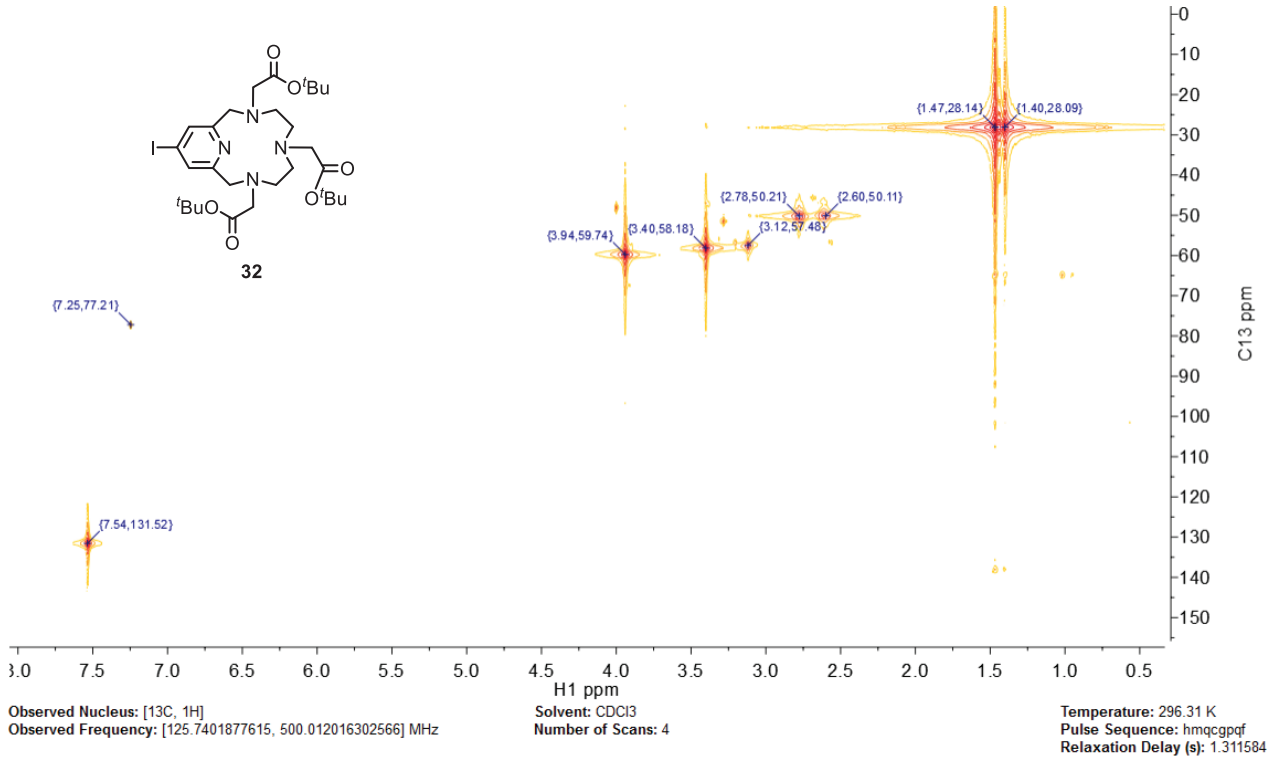

Figure SII-35: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of 4-iodo-PCTA *tert*-butyl ester (**32**) contaminated with unidentified component(s).

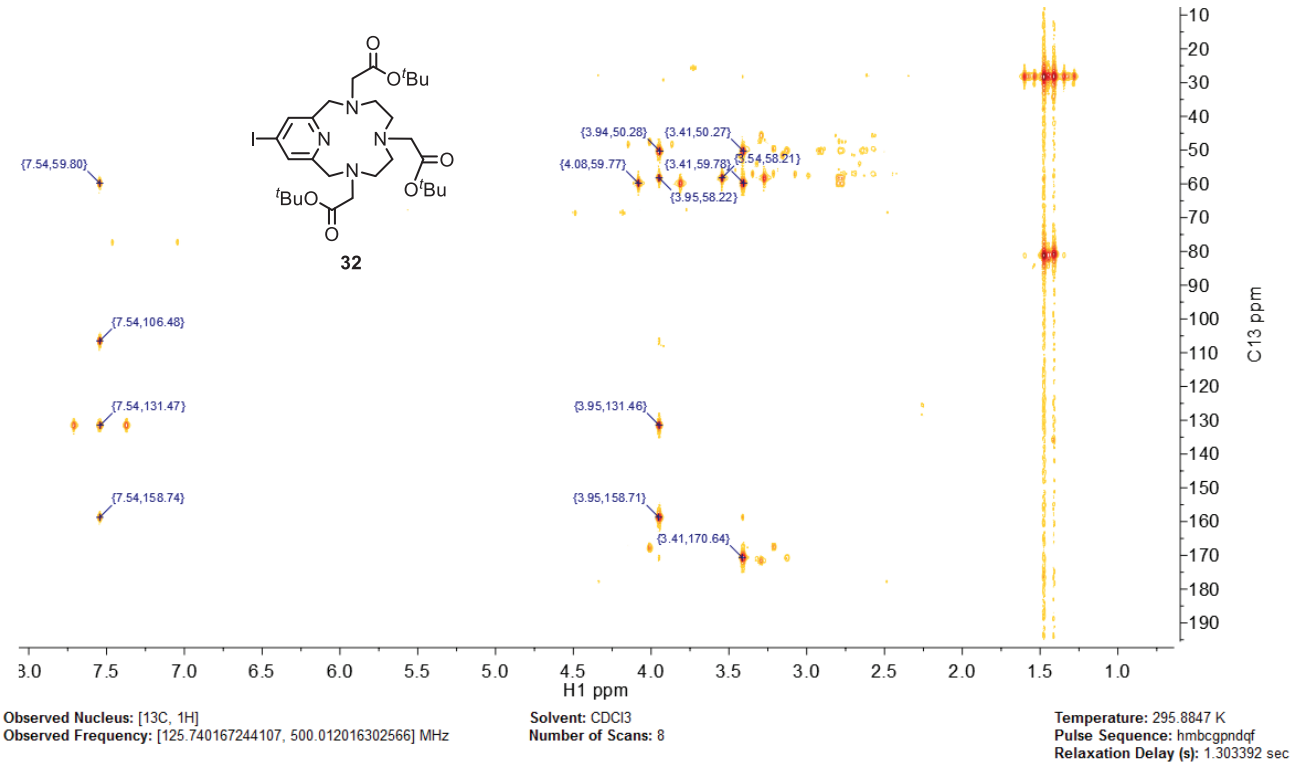

Figure SII-36: HMBC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of 4-iodo-PCTA *tert*-butyl ester (**32**) contaminated with unidentified component(s).

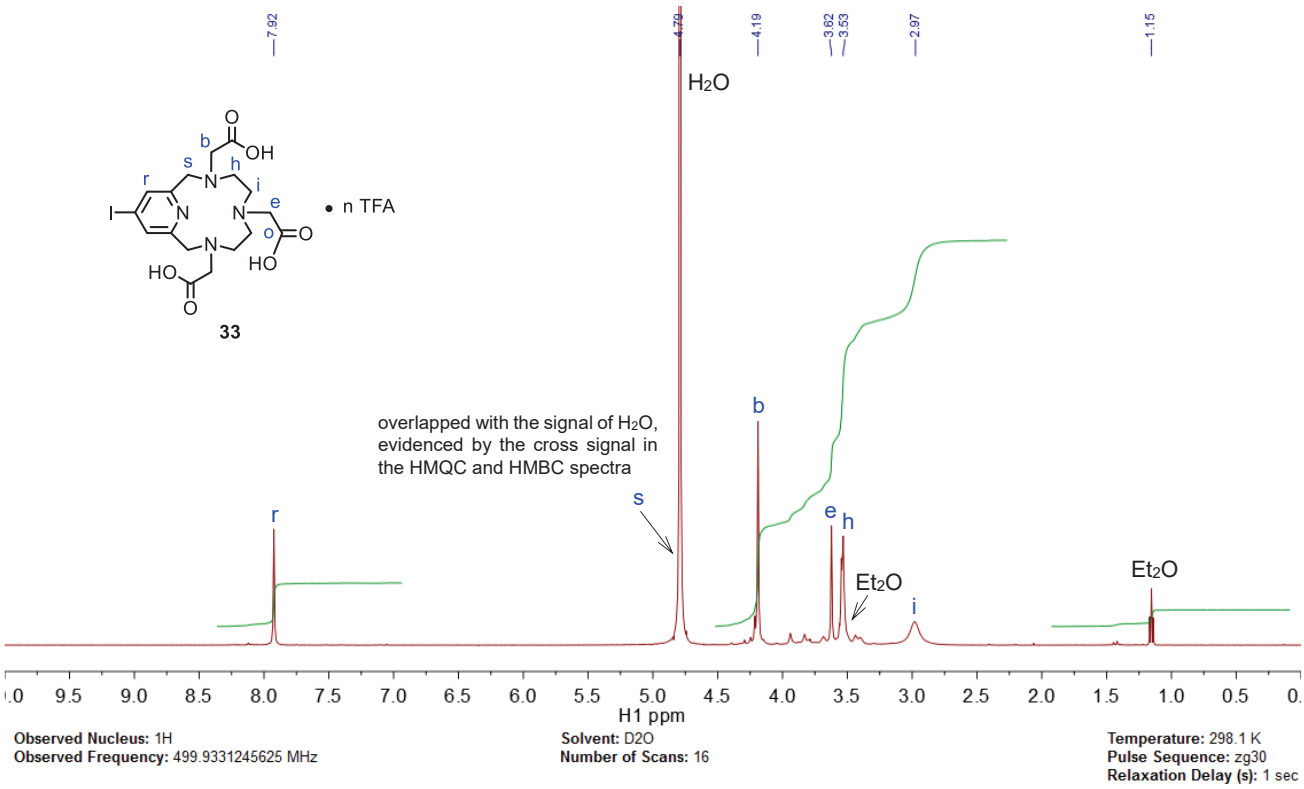

Figure SII-37: ^{1}H NMR spectrum (500 MHz, D_2O) of 4-Iodo-PCTA•n TFA (**33**) contaminated with unidentified component(s).

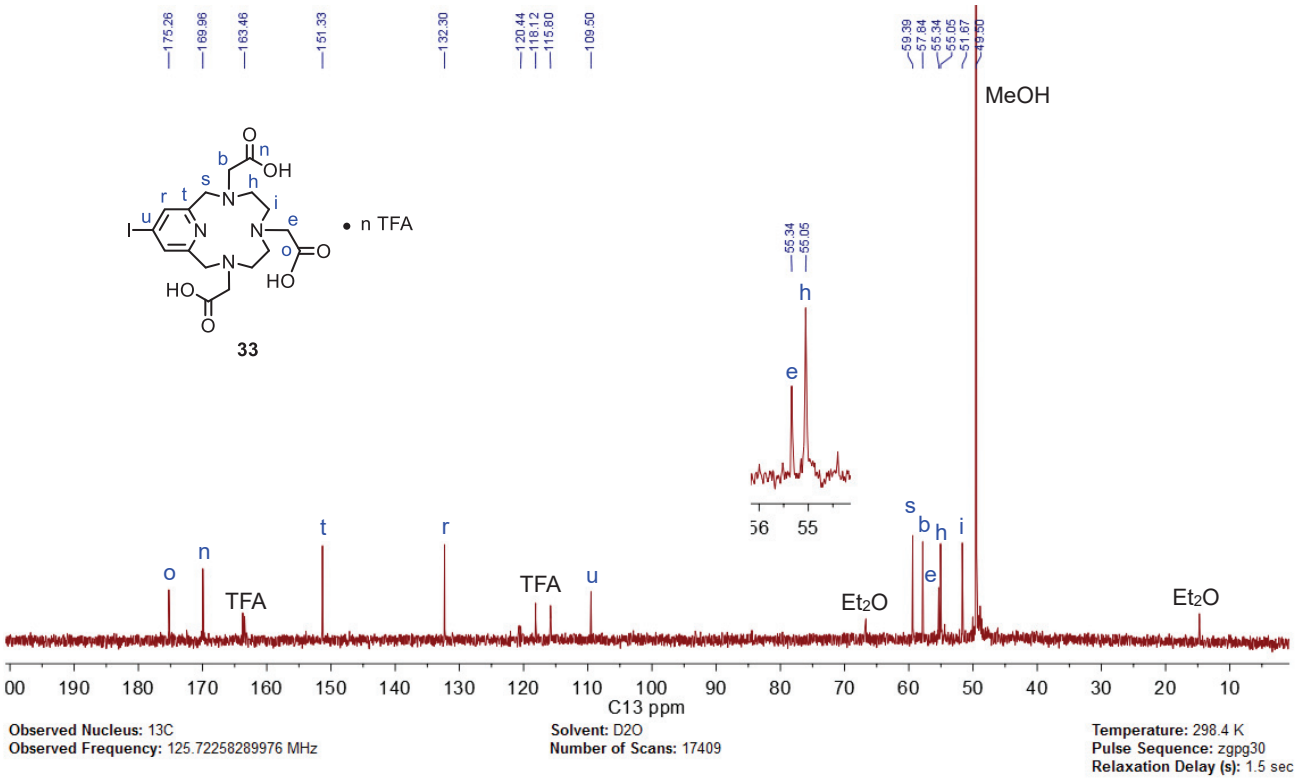

Figure SII-38: ^{13}C NMR spectrum (125 MHz, D_2O) of 4-Iodo-PCTA•n TFA (**33**) contaminated with unidentified component(s).

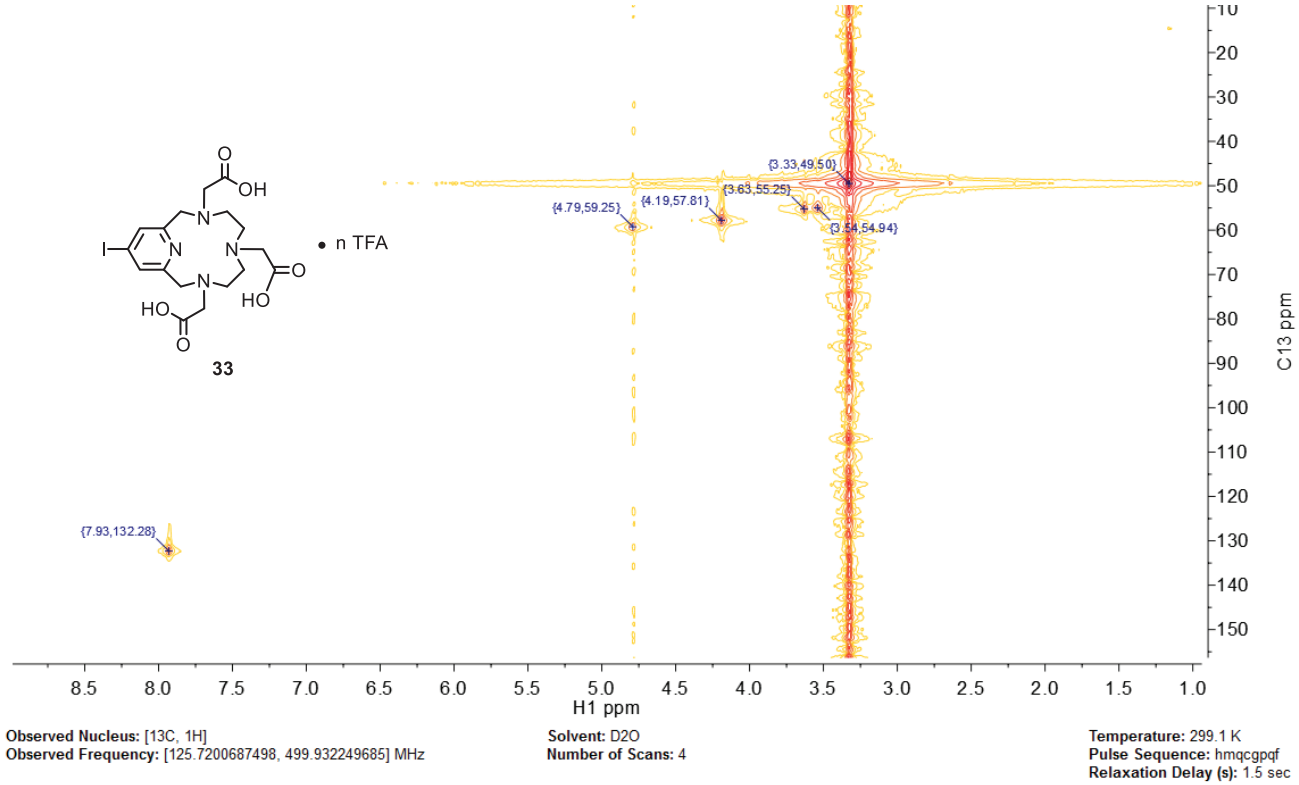

Figure SII-39: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of 4-Iodo-PCTA•n TFA (**33**) contaminated with unidentified component(s).

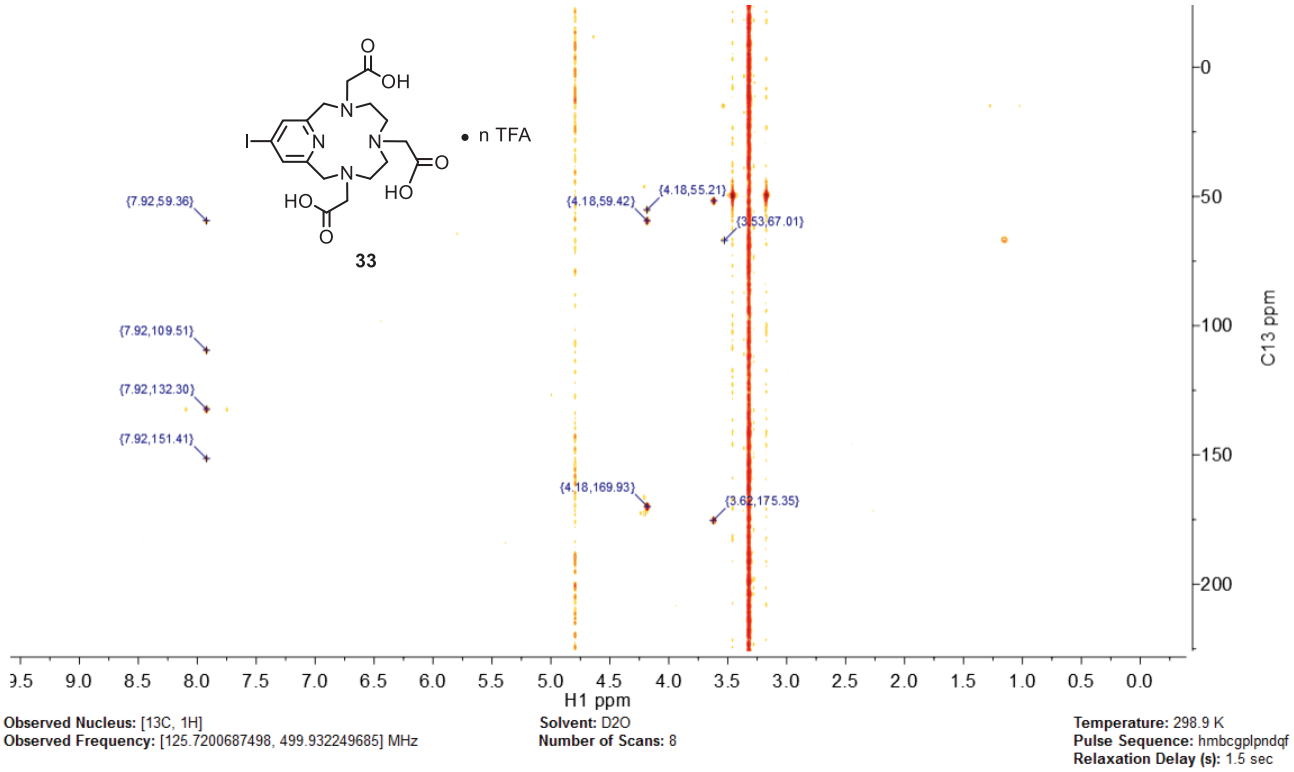

Figure SII-40: HMBC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of 4-Iodo-PCTA•n TFA (**33**) contaminated with unidentified component(s).

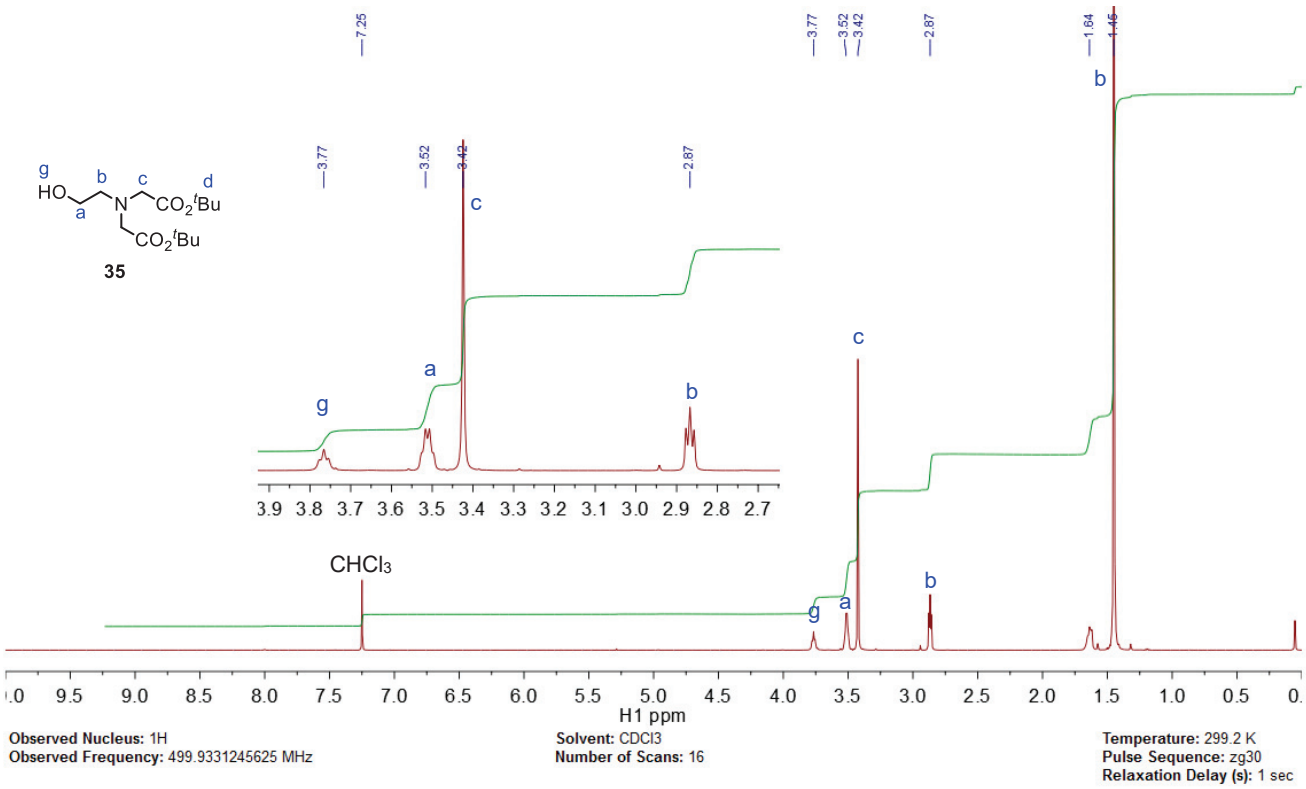

Figure SII-41: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of alcohol **35**.

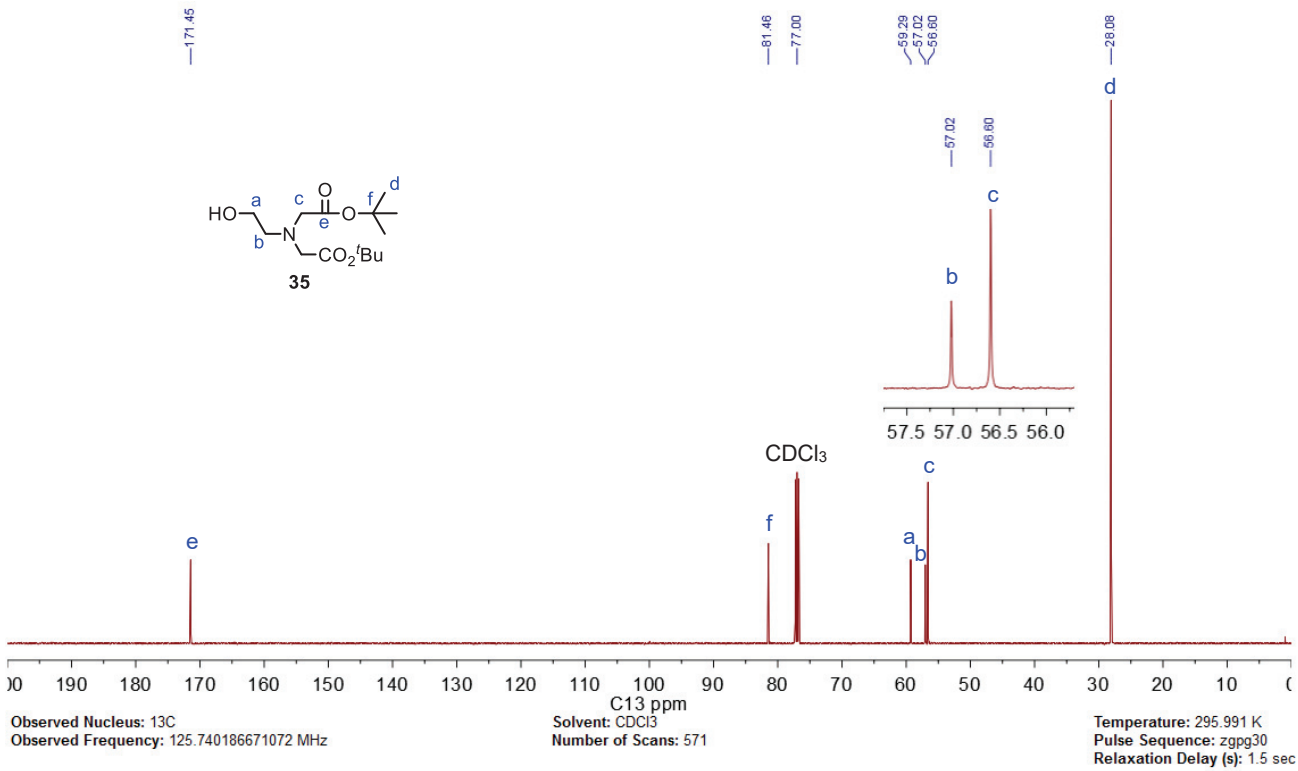

Figure SII-42: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of alcohol **35**.

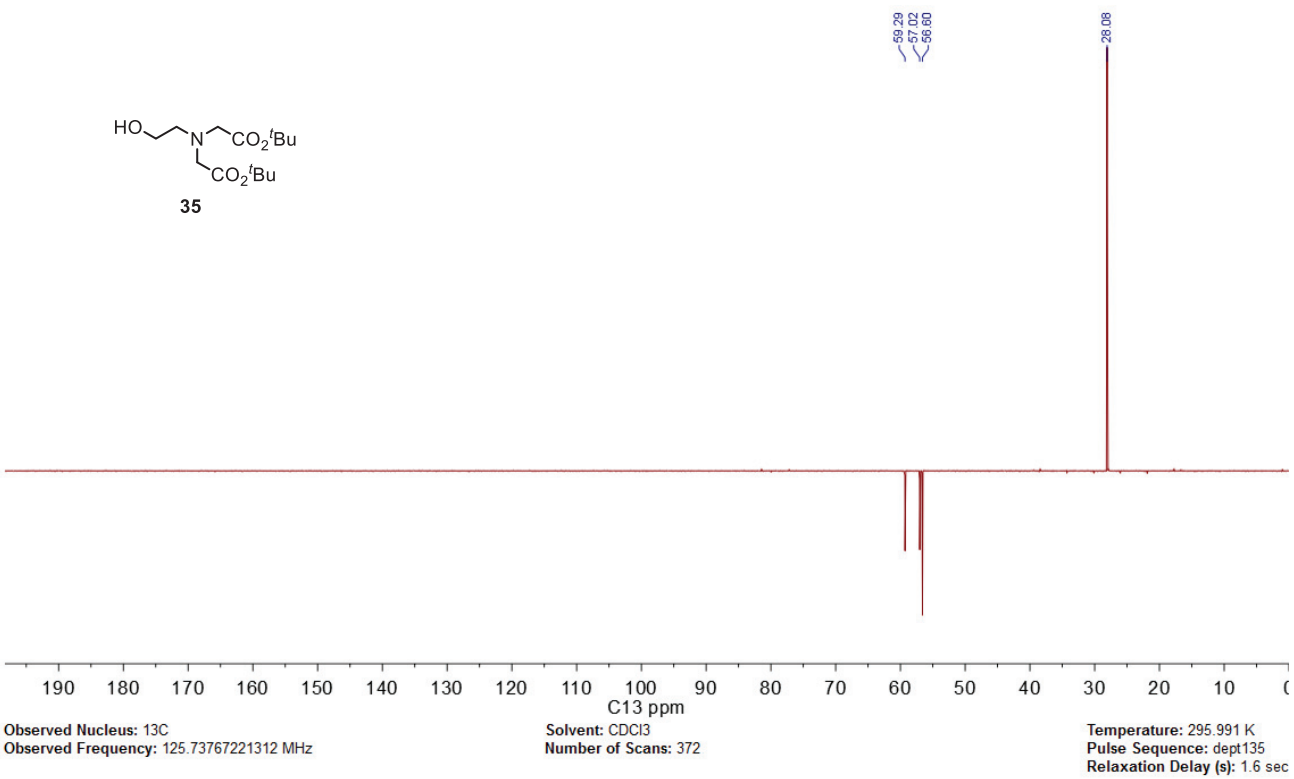

Figure SII-43: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of alcohol **35**.

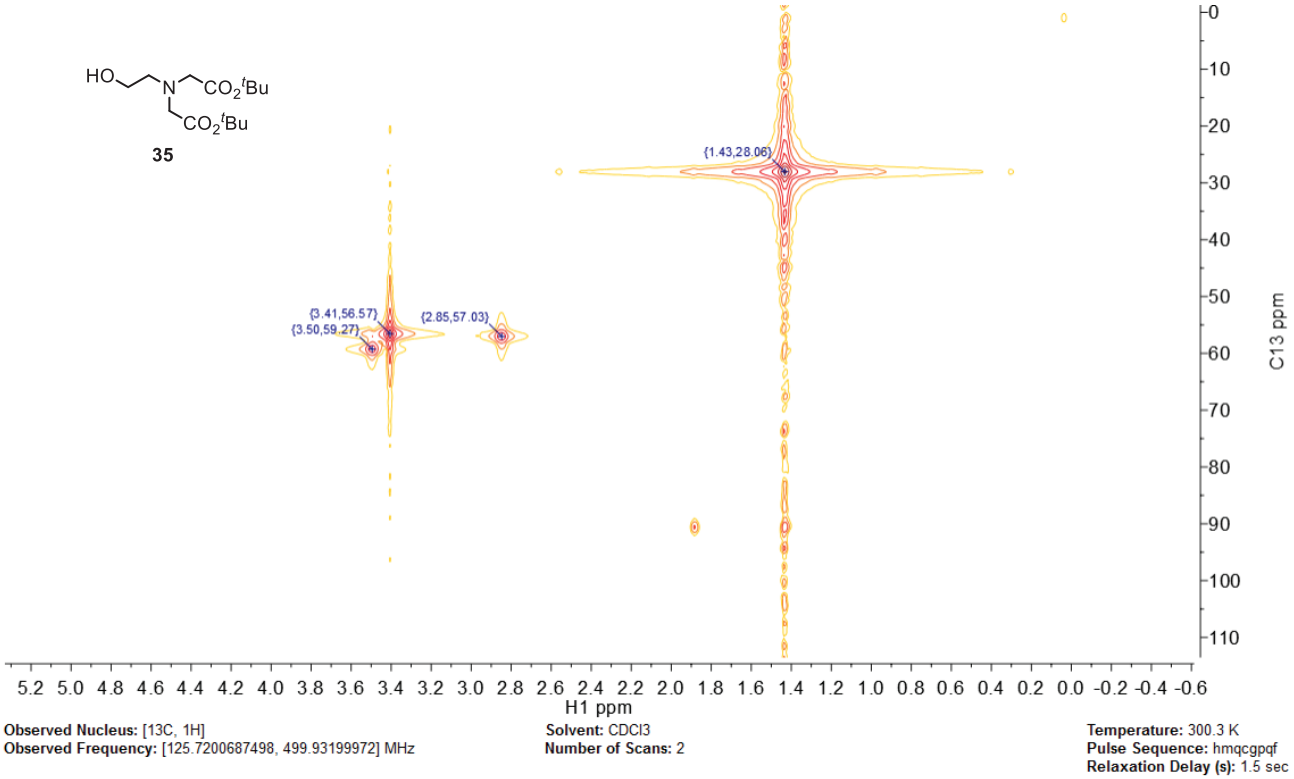

Figure SII-44: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of alcohol **35**.

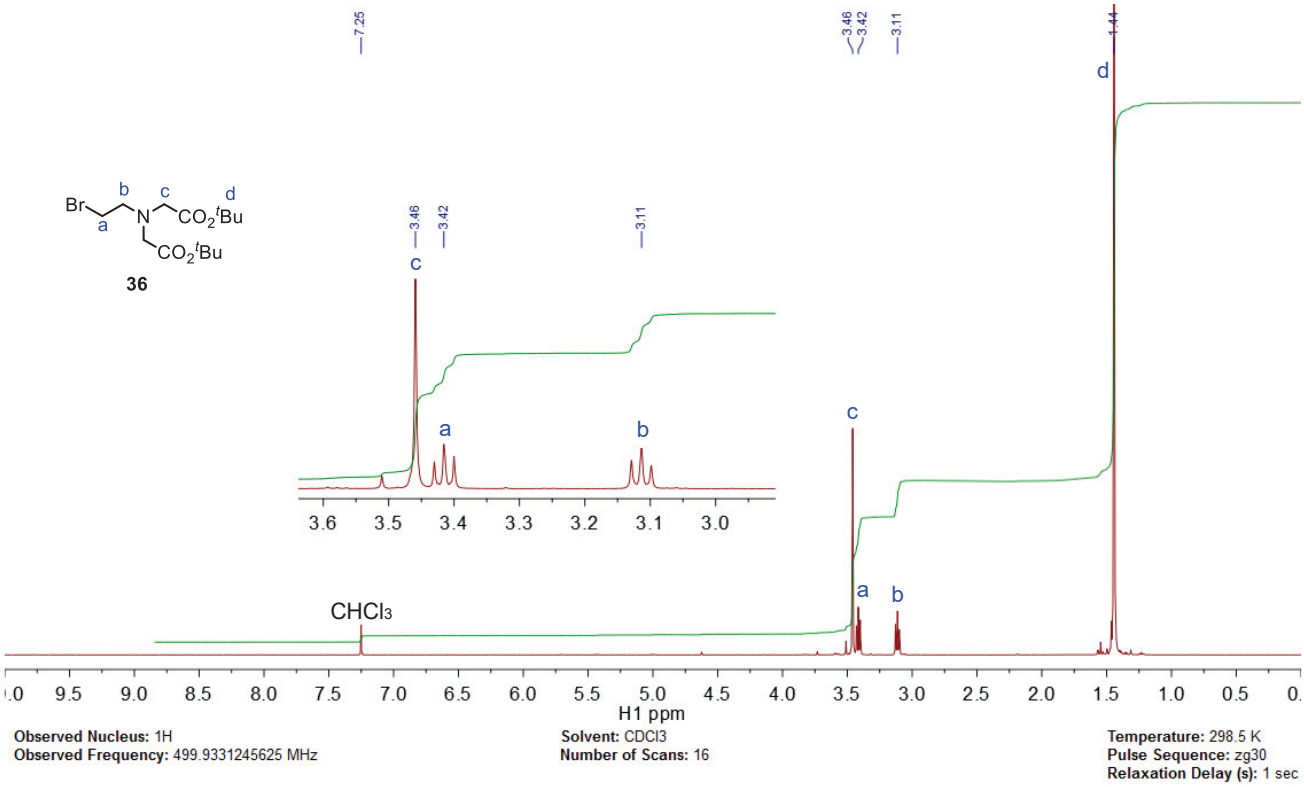

Figure SII-45: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of bromide **36**.

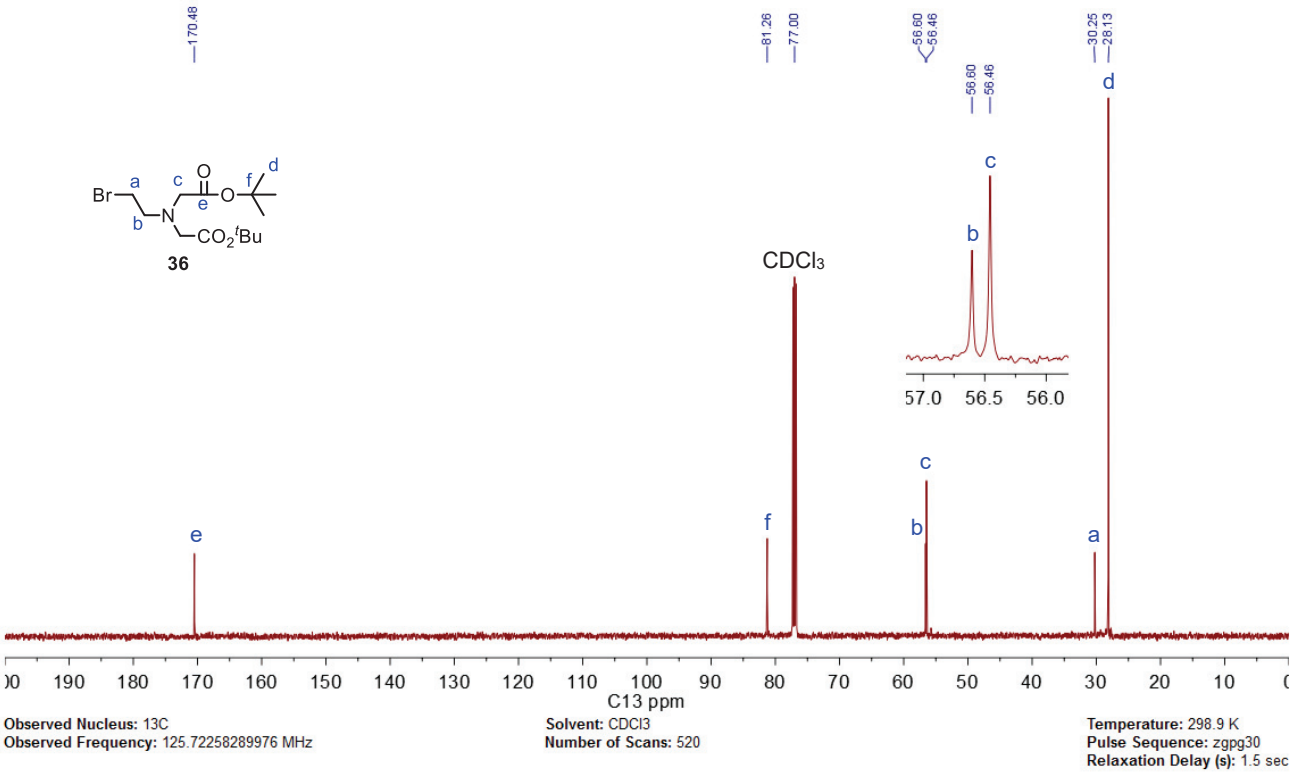

Figure SII-46: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of bromide **36**.

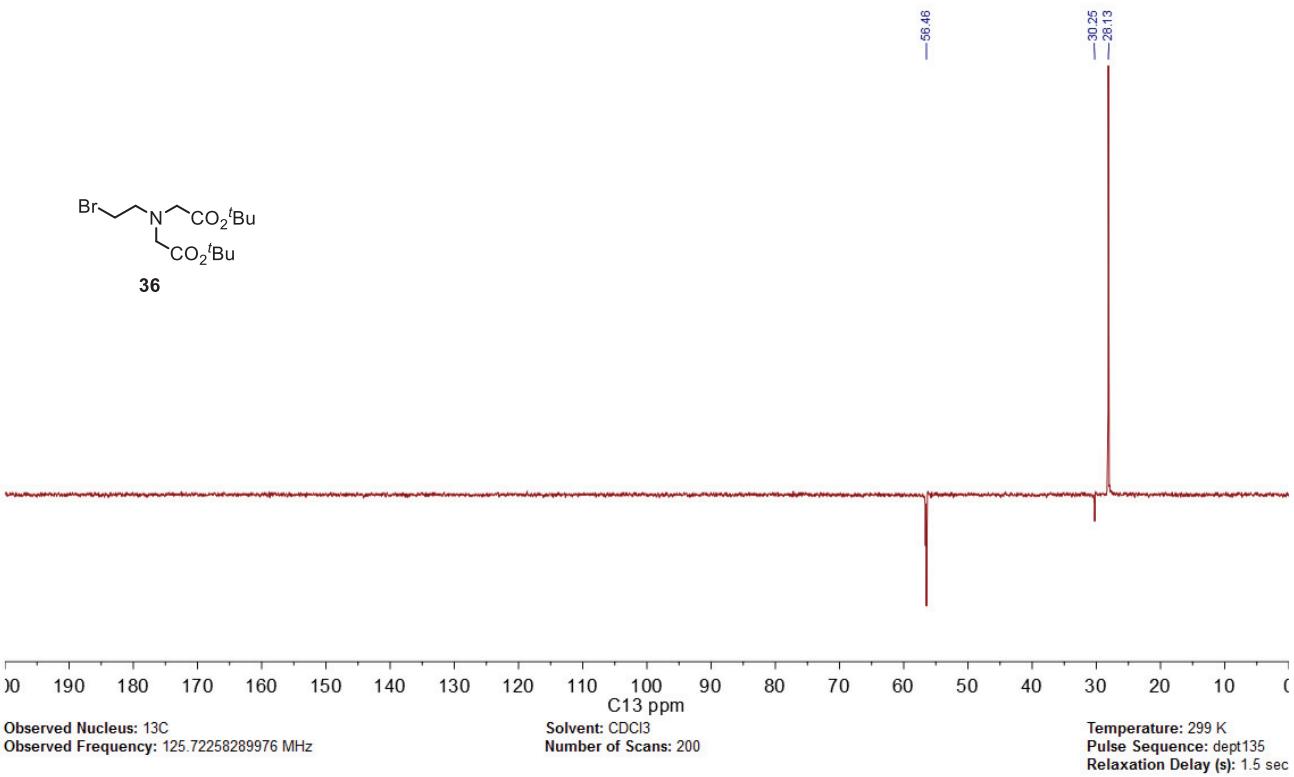

Figure SII-47: ^{13}C DEPT 135 NMR spectrum (125 MHz, $CDCl_3$) of bromide **36**.

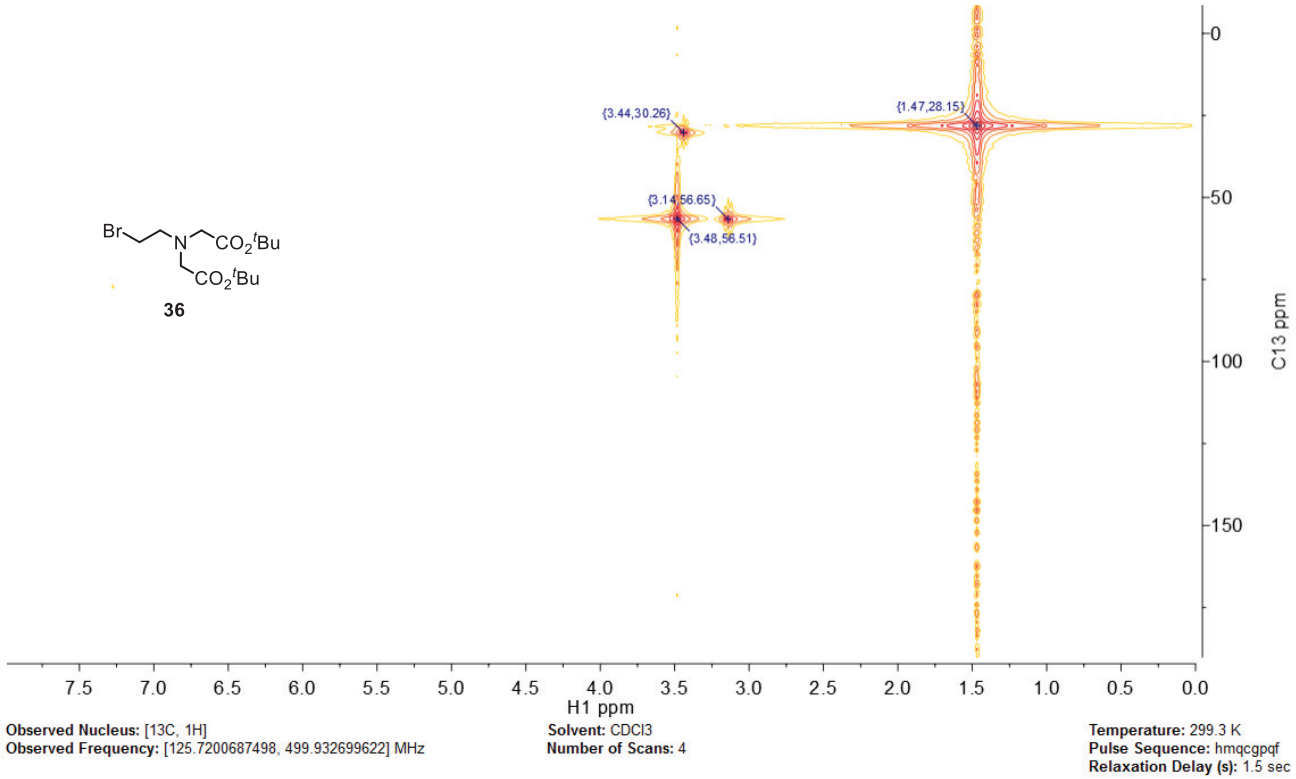

Figure SII-48: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of bromide **36**.

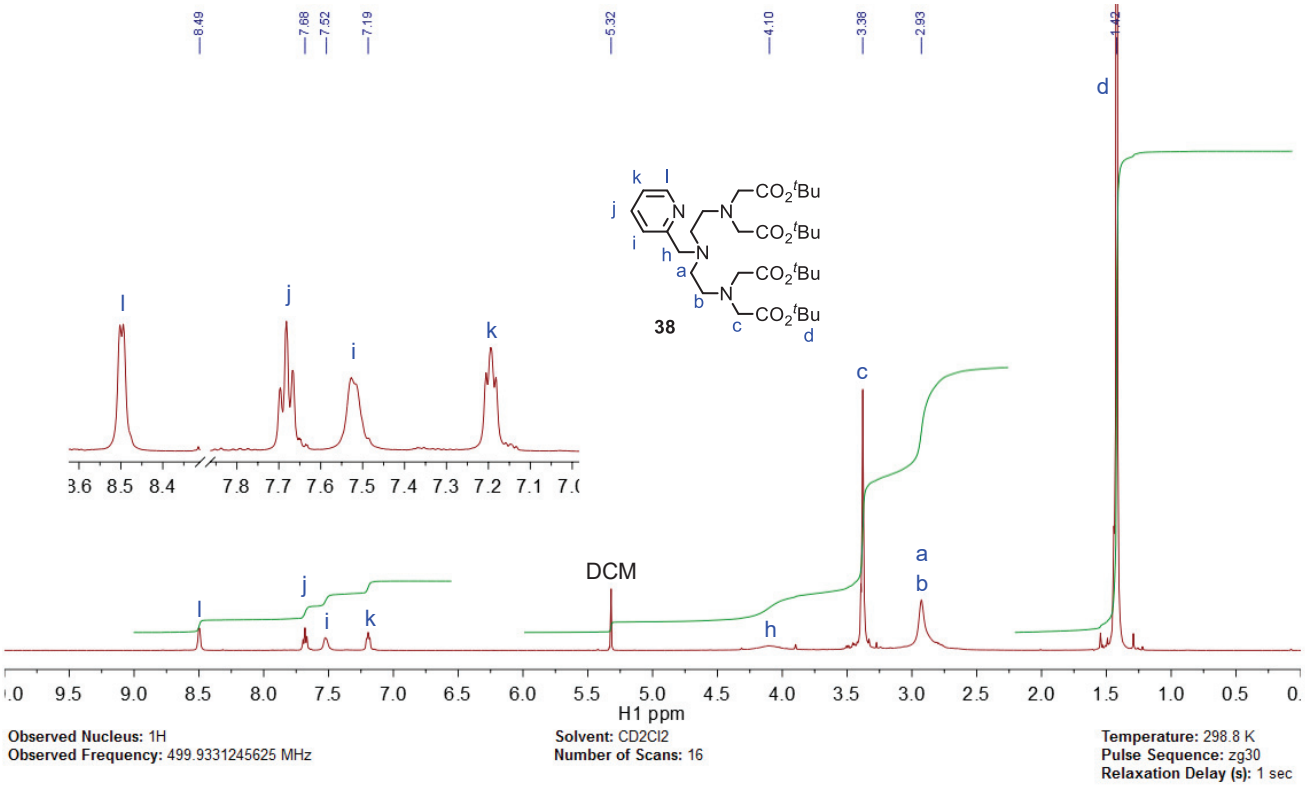

Figure SII-49: ^{1}H NMR spectrum (500 MHz, CD_2Cl_2) of PyDTTA *tert* butyl ester (**38**).

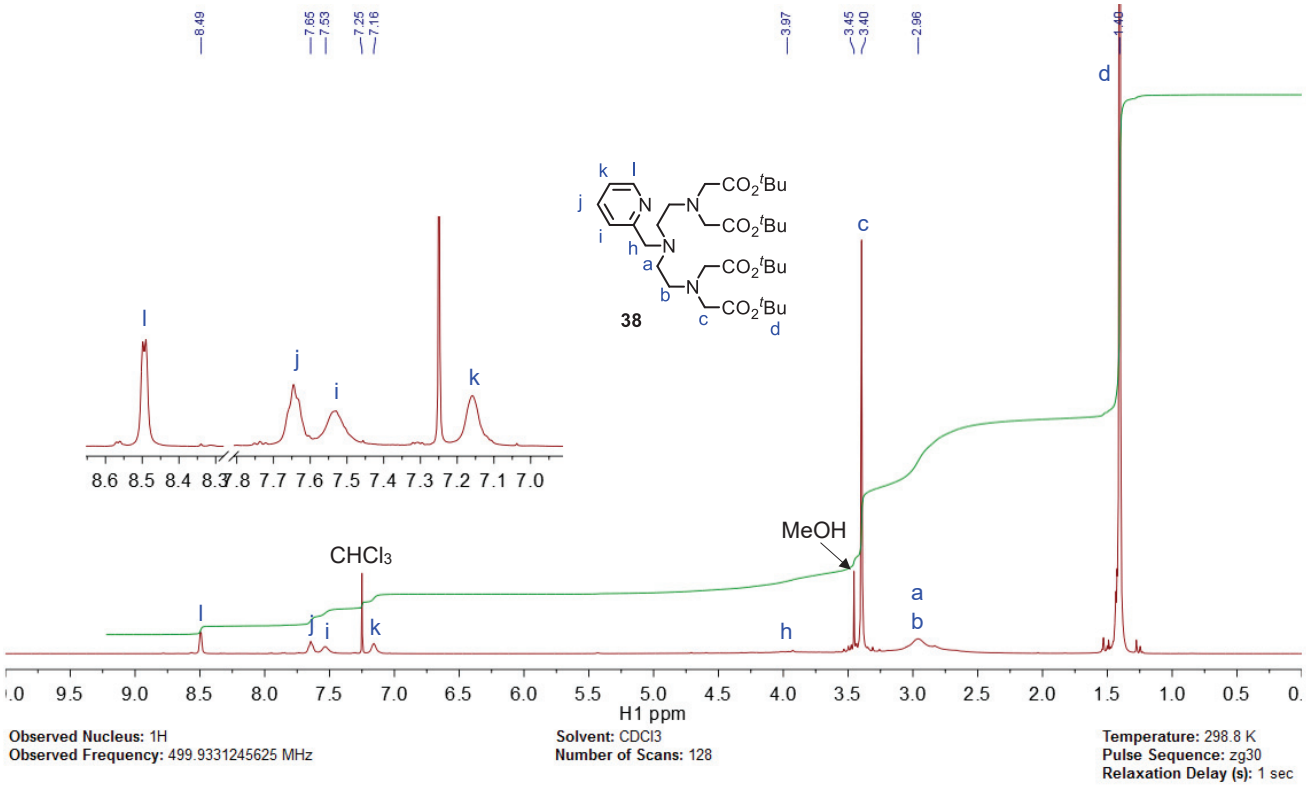

Figure SII-50: ^{1}H NMR spectrum (500 MHz, $CDCl_3$) of PyDTTA *tert* butyl ester (**38**).

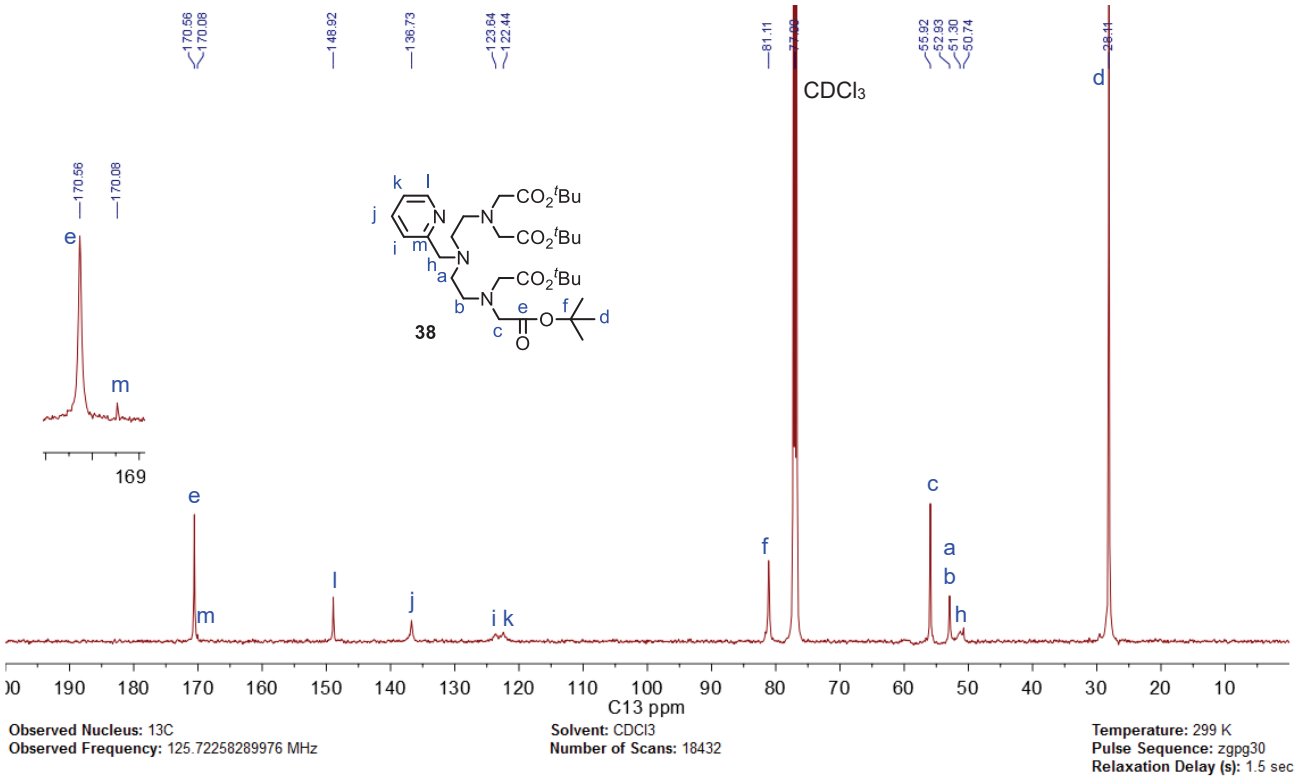

Figure SII-51: ^{13}C NMR spectrum (125 MHz, $CDCl_3$) of PyDTTA *tert* butyl ester (**38**).

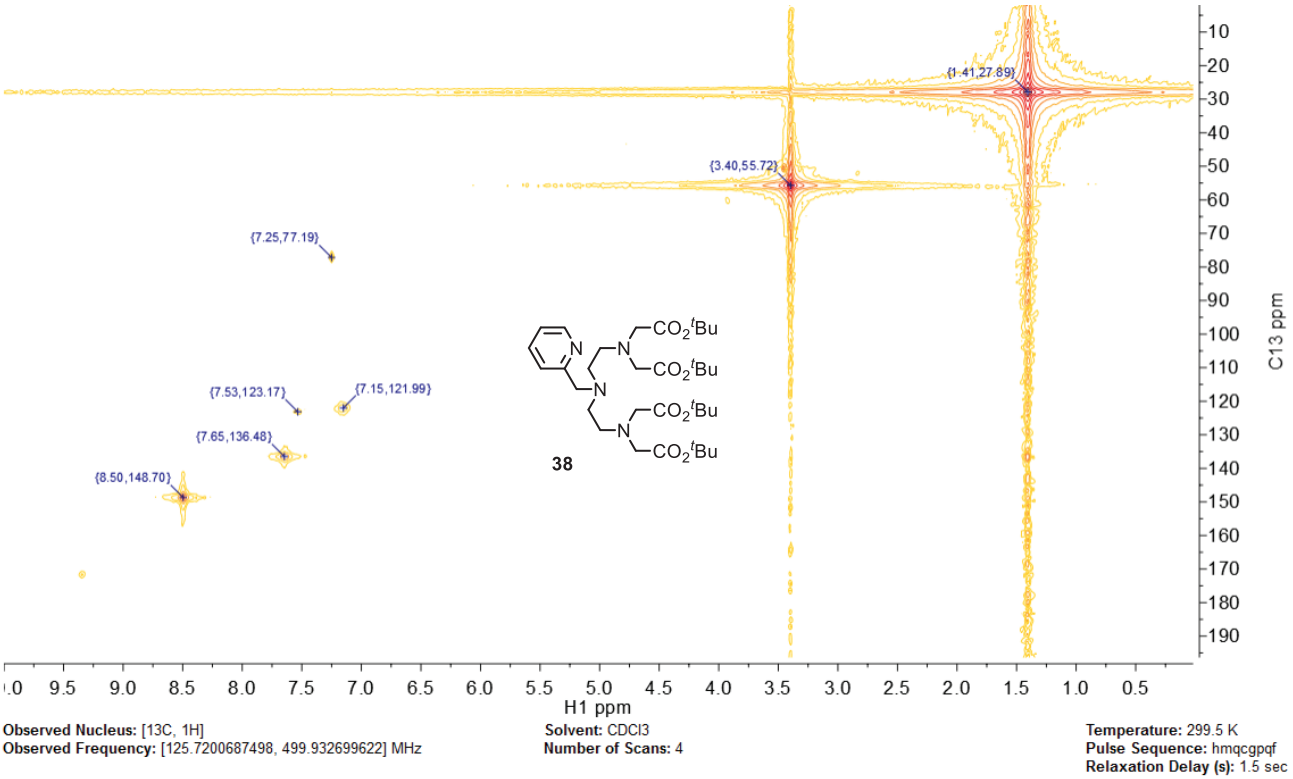

Figure SII-52: HMQC NMR spectrum (500 MHz, 125 MHz, $CDCl_3$) of PyDTTA *tert* butyl ester (**38**).

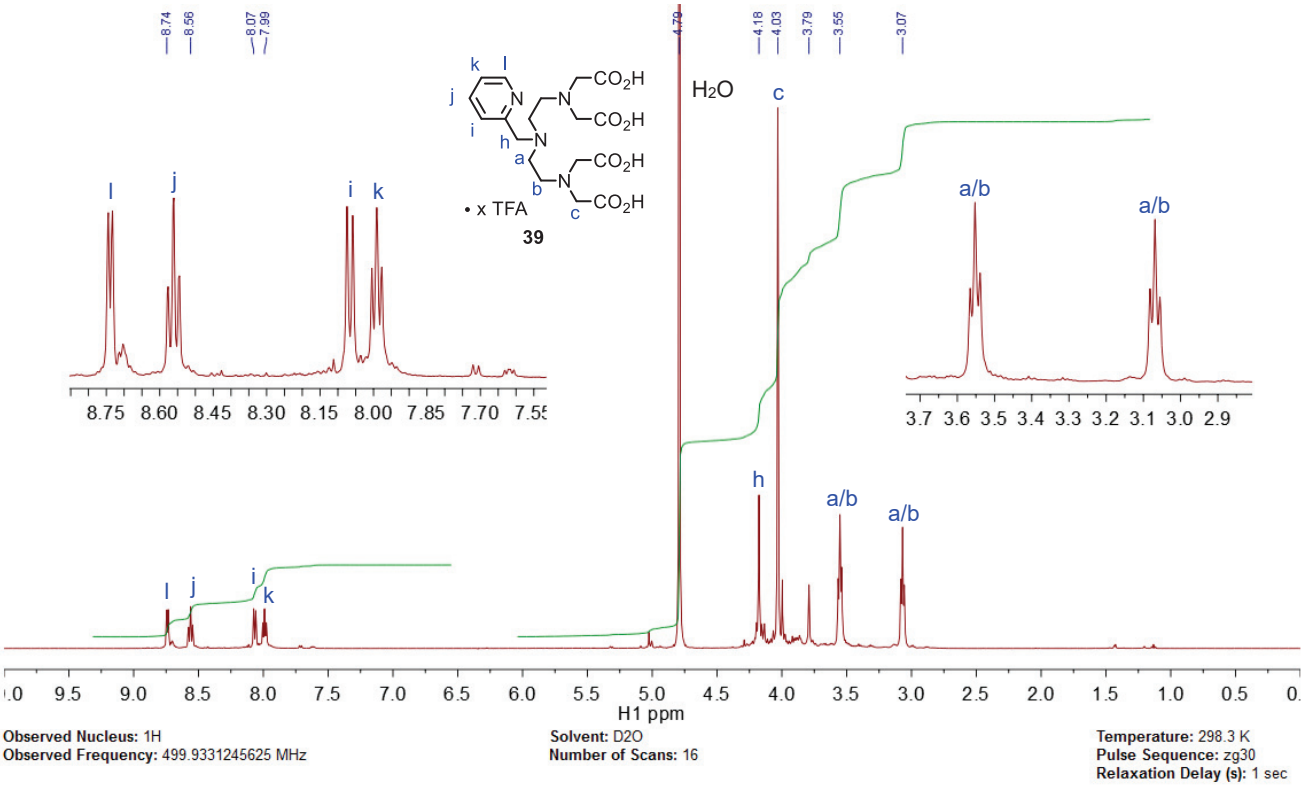

Figure SII-53: ^{1}H NMR spectrum (500 MHz, D_2O) of PyDTTA PyDTTA•x TFA (**39**) contaminated with unidentified component(s)

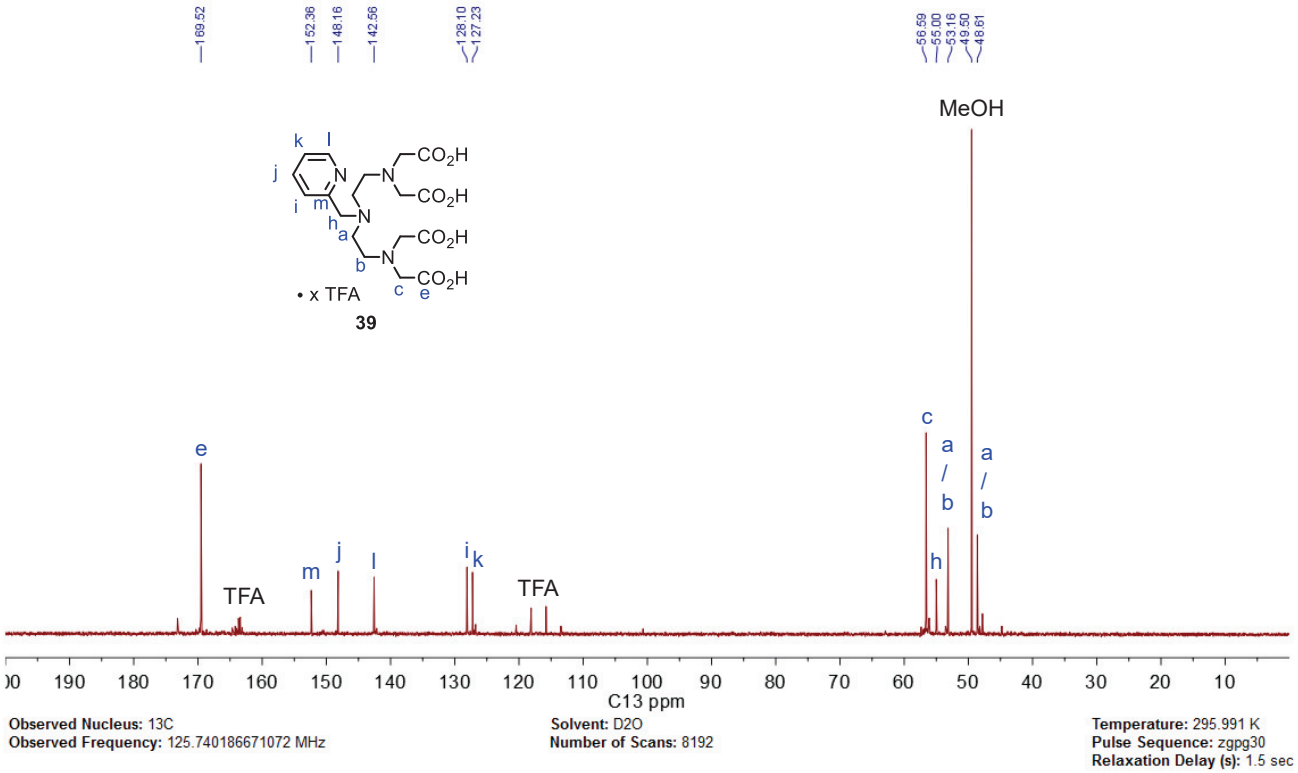

Figure SII-54: ^{13}C NMR spectrum (500 MHz, D_2O) of PyDTTA PyDTTA•x TFA (**39**) contaminated with unidentified component(s).

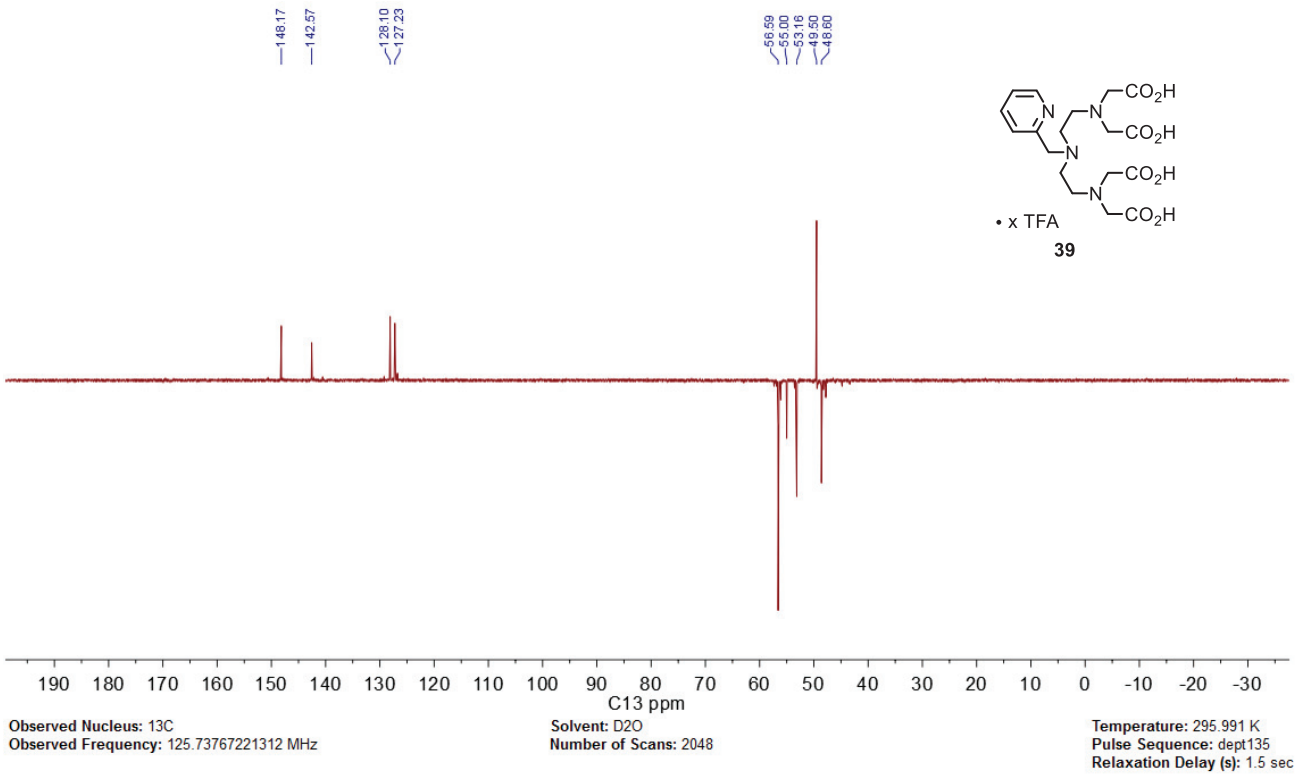

Figure SII-55: ^{13}C DEPT 135 NMR spectrum (500 MHz, D_2O) of PyDTTA PyDTTA•x TFA (**39**) contaminated with unidentified component(s).

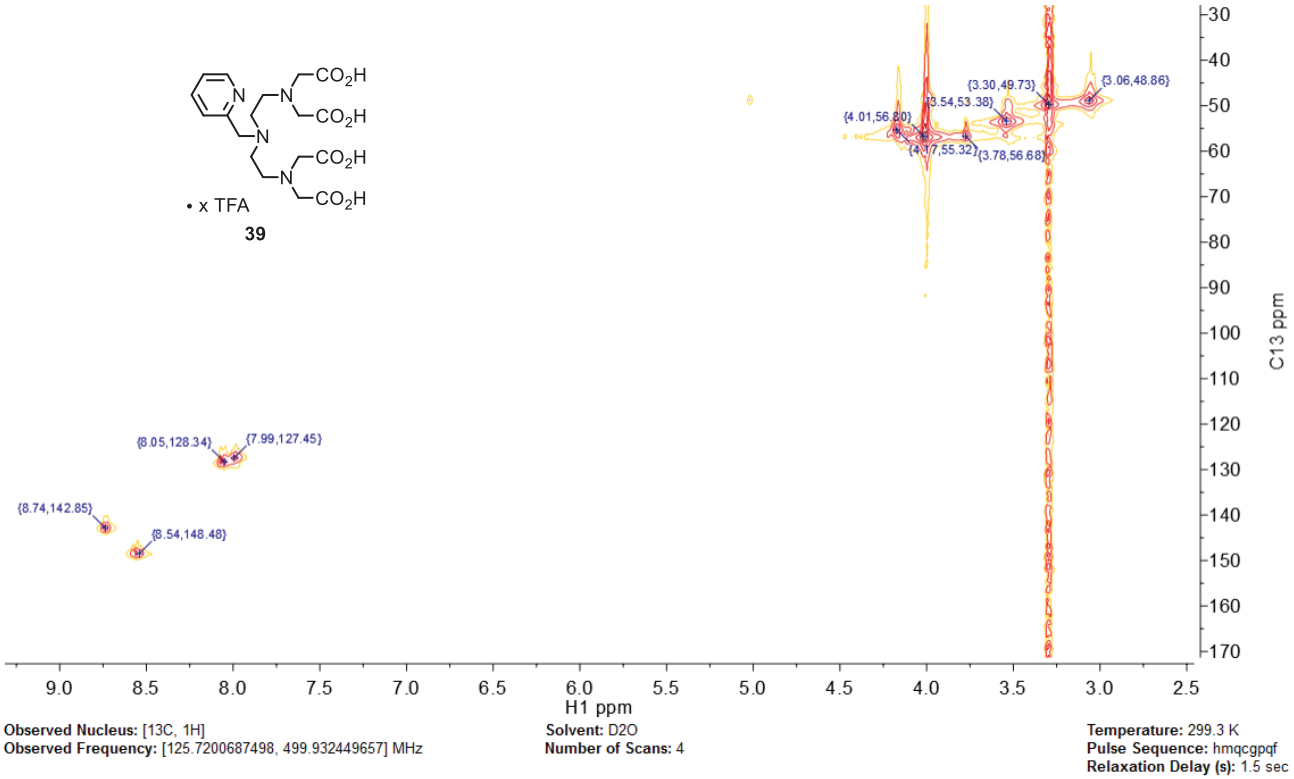

Figure SII-56: HMQC NMR spectrum (500 MHz, 125 MHz, D_2O) of PyDTTA PyDTTA•x TFA (**39**) contaminated with unidentified component(s).

References

1 L. Huang, J. C. Jr. Quada, and J. W. Lown, *Bioconjugate Chem.*, 1995, **6**, 21–33.

2 T. Storr, B. R. Cameron, R. A. Gossage, H. Yee, R. T. Skerlj, M. C. Darkes, S. P. Fricker, G. J. Bridger, N. A. Davies, M. T. Wilson, K. P. Maresca and J. Zubieta, *Eur. J. Inorg. Chem.*, 2005, 2685–2697.

3 C. Gateau, M. Mazzanti, J. Pecaut, F. A. Dunand and L. Helm, *Dalton Trans.*, 2003, 2428–2433.

4 M. Qi, M. Hülsmann and A. Godt, *Synthesis*, 2016, **48**, 3773–3784.

5 S. K. Bharti and R. Roy, *TrAC*, 2012, **35**, 5–26.

6 K. Keller, M. Zalibera, M. Qi, V. Koch, J. Wegner, H. Hintz, A. Godt, G. Jeschke, A. Savitsky and M. Yulikov, *Phys. Chem. Chem. Phys.*, 2016, **18**, 25120–25135.

7 J. A. Clayton, M. Qi, A. Godt, D. Goldfarb, S. Han and M. S. Sherwin, *Phys. Chem. Chem. Phys.*, 2017, **19**, 5127–5136.

8 C. Ferroud, H. Borderies, E. Lasri, A. Guy and M. Port, *Tetrahedron Lett.*, 2008, **49**, 5972–5975.

9 A. Favre-Réguillon, F. Segat-Dioury, L. Nait-Bouda, C. Cosma, J.-M. Siaugue, J. Foos and A. Guy, *Synlett.*, 2000, **2000**, 868–871.

10 M. A. Williams and H. Rapoport, *J. Org. Chem.*, 1993, **58**, 1151–1158.

11 G. Bridger, B. Cameron, S. Fricker, M. Abrams, R. Skerlj and I. Baird, *Pharmaceutical compositions comprising metal complexes*, 2002, US patent, US20020049190 A1.