Electronic Supplementary Material (ESI) for Chemical Communications

A 1,3-Phenyl-Linked Hydantoin Oligomer Scaffold as a β-Strand Mimetic

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Supporting Information

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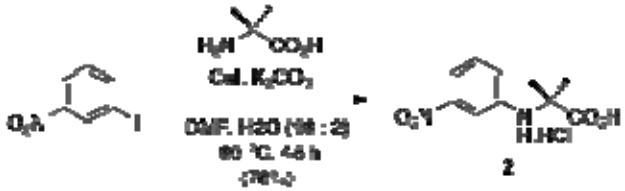
Part I. General Experimental Section

All experiments were carried out under an atmosphere of nitrogen, using anhydrous solvents, unless otherwise stated. All chemicals were purchased from Sigma-Aldrich and used as received. Analytical thin layer chromatography was carried out on Merck Kieselgel 60 F_{254} plates with visualisation by ultraviolet light. Flash column chromatography was performed using Merck Kieselgel 60 (230-400 mesh). Infra-red spectra were recorded on a Perkin Elmer System 100 with a Universal ATR attachment accessory as neat films. Maximum absorbances (ν_{max}) are quoted in wavenumbers (cm^{-1}) and the abbreviations used are: w, weak; m, medium; s, strong. NMR spectra were recorded on Brucker DPX 300 (^{1}H, 300 MHz; ^{13}C, 75 MHz), Brucker DPX 400 (^{1}H, 400 MHz; ^{13}C, 100 MHz) or Brucker Avance III 500 (^{1}H, 500 MHz; ^{13}C, 125 MHz) spectrometers as indicated. NMR chemical shifts (δ) are quoted in ppm relative to the residual non-deuterated solvent peak of chloroform (^{1}H δ 7.26, ^{13}C δ 77.0) and coupling constants (*J*) are quoted to the nearest 0.1 Hertz (Hz). Spectral data is reported as follows: chemical shift, integration, multiplicity (s, singlet; d, doublet; t, triplet; m, multiplet; or as a combination of these), coupling constant(s) and assignment. ^{1}H assignment is supported by COSY spectra where necessary. ^{13}C assignment is supported by APT and HSQC spectra correlations where necessary. Melting points were recorded on a Reichert Köfler micro heating stage melting point apparatus and are uncorrected. High-resolution mass spectra were recorded on a Kratos Concept 1H spectrometer using peak matching to stable reference.

Part II. Synthesis and Characterisation

2-Methyl-2-(3-nitrophenylamino)propanoic acid hydrochloride (2)



1-Iodo-3-nitrobenzene (2.0 g, 8.03 mmol), 2-aminoisobutyric acid (1.66 g, 16.1 mmol, 2 equiv.) and potassium carbonate (2.22 g, 16.1 mmol, 2 equiv.) were placed in a 250 mL RBF under nitrogen. DMF (80 mL, 0.1 M) was added followed by water (1.60 mL, 2% w/v) and the mixture sonicated for 5 mins. Copper (I) iodide (76 mg, 0.402 mmol, 0.05 equiv.) was then added and the mixture heated to 80 °C for 48 hours with vigorous stirring. The reaction mixture was concentrated *in vacuo* and the residue dissolved in water (75 mL), basified with saturated sodium hydrogen carbonate solution (25 mL) and washed with diethyl ether (5 x 100 mL). The aqueous layer was acidified with concentrated hydrochloric acid and extracted with ethyl actetate (5 x 100 mL). The combined organic extracts were washed with water (3 x 500 mL) and brine (3 x 500 mL), dried ($MgSO_4$) and concentrated *in vacuo* to give the title compound as a yellow solid (1.62 g, 78%). M.p. 128 – 129 °C; ν_{max} (neat)/cm^{-1} 3390 (m, N-H), 2995 (w, O-H), 1703 (s, C=O), 1537 (s, C=C), 1350 (s, N-O), 732 (s, C-H), 671 (s, C-H); δ_H (500 MHz, $CDCl_3$) 1.65 (6H, s, C(C*H*$_3$)$_2$), 5.30 (1H, s, N*H*), 6.87 (1H, ddd, *J* 8.2, 2.3, 0.8 Hz, Ar C*H*), 7.31 (1H, t, *J* 8.2 Hz, Ar C*H*), 7.44 (1H, t, *J* 2.3 Hz, Ar C*H*), 7.62 (1H, ddd, *J* 8.2, 2.3, 0.8 Hz, Ar C*H*); δ_C (125 MHz, $CDCl_3$) 25.8 ((*C*H$_2$)$_2$), 57.5 (*C*(CH$_3$)$_2$), 109.5 (Ar *C*H), 113.6 (Ar *C*H), 120.8 (Ar *C*H), 129.9 (Ar *C*H), 145.9 (Ar *C*), 149.1 (Ar *C*), 180.0 (*C*=O); HRMS (ESI) *m/z* found 225.0873, $C_{10}H_{13}N_2O_4$ (M+H) requires 225.0875 (Δ = 3.0 ppm).

2-Methyl-2-(3-nitrophenylamino)-*N*-phenylpropanamide (3)

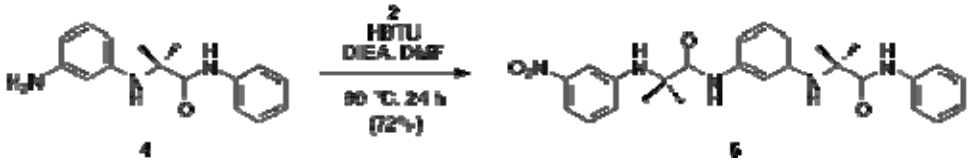
2-methyl-2-(3-nitrophenylamino)propanoic acid hydrochloride **2** (1.50 g, 5.76 mmol) was placed in a dry 100 mL RBF under nitrogen. DMF (5.76 mL, 0.1 M) was added followed by DIEA (2.00 mL, 11.5 mmol, 2 equiv.) and HBTU (2.62 g, 6.91 mmol, 1.2 equiv.) and the mixture stirred for 5 minutes. Aniline (629 µl, 6.91 mmol, 1.2 equiv.) was then added and the mixture heated to 90 °C for 24 hours. The reaction mixture was concentrated *in vacuo* and the residue dissolved in ethyl

acetate (300 mL). This was washed with water (3 x 300 mL), 5% lithium chloride solution (3 x 300 mL) and brine (3 x 300 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude residue by flash column chromatography (ethyl acetate: hexane, 3:7) provided the title compound as a yellow solid (1.59 g, 98%). M.p. 160 – 161 ^oC; ν_{max} (neat)/cm^{-1} 3336 (m, N-H), 1669 (s, C=O), 1527 (s, C=C), 1505 (s, C=C), 1353 (s, N-O), 749 (s, C-H), 694 (s, C-H); δ_H (500 MHz, $CDCl_3$) 1.65 (6H, s, C(CH_3)$_2$), 4.29 (1H, s, N*H*), 6.91 (1H, ddd, *J* 8.2, 2.3, 0.6 Hz, Ar C*H*), 7.14 (1H, t, *J* 7.4 Hz, Ar C*H*), 7.32 – 7.37 (3H, m, Ar C*H*), 7.52 (2H, dd, *J* 8.7, 1.1 Hz, Ar C*H*), 7.56 (1H, t, *J* 2.3 Hz, Ar C*H*), 7.68 (1H, ddd, *J* 8.2, 2.3, 0.6 Hz, Ar C*H*), 8.66 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 25.7 ((CH_2)$_2$), 59.1 (*C*(CH_3)$_2$), 111.0 (Ar *C*H), 114.3 (Ar *C*H), 119.9 (Ar *C*H), 120.9 (Ar *C*H), 124.6 (Ar *C*H), 129.1 (Ar *C*H), 130.2 (Ar *C*H), 137.5 (Ar *C*), 145.4 (Ar *C*), 149.2 (Ar *C*), 172.9 (*C*=O); HRMS (ESI) *m*/*z* found 300.1347, $C_{16}H_{18}N_3O_3$ (M+H) requires 300.1348 (Δ = 2.0 ppm).

2-(3-Aminophenylamino)-2-methyl-*N*-phenylpropanamide (4)

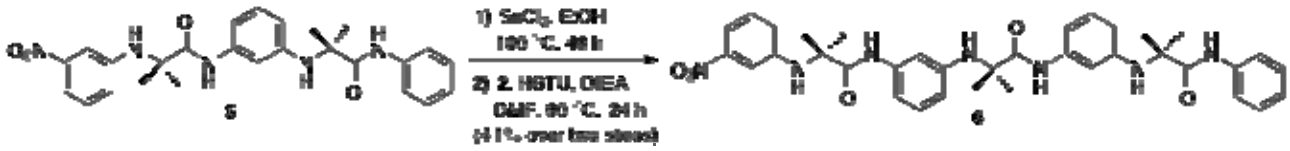
2-methyl-2-(3-nitrophenylamino)-*N*-phenylpropanamide (100 mg, 0.334 mmol) was placed in a 50 mL RBF under nitrogen. Methanol (3.35 mL, 0.1 M) was added followed by acetic acid (400 µl, 6.69 mmol, 20 equiv.) and the mixture cooled to 0 $^{\circ}C$ in an ice bath before zinc powder (218 mg, 3.34 mmol, 10 equiv.) was added. The mixture was allowed to warm to room temperature and stirred vigorously for 3 hours. The reaction mixture was filtered though a pad of celite, concentrated *in vacuo* and the residue dissolved in ethyl acetate (15 mL). This was washed with saturated sodium hydrogen carbonate solution (3 x 15 mL), water (3 x 15 mL) and brine (3 x 15 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude residue by flash column chromatography (ethyl acetate: hexane, 3:2) provided the title compound as a pale yellow solid (80 mg, 90%). M.p. 175 – 177 ^oC; ν_{max} (neat)/cm^{-1} 3341 (w, N-H), 3262 (w, N-H), 1595 (s, C=O), 1220 (s, C-C), 754 (s, C-H), 695 (s, C-H); δ_H (500 MHz, $CDCl_3$) 1.59 (6H, s, C(CH_3)$_2$), 3.57 (2H, s, N*H*), 3.83 (1H, s, N*H*), 5.96 (1H, t, *J* 1.6 Hz, Ar C*H*), 6.09 (1H, dd, *J* 7.9, 1.6 Hz, Ar C*H*), 6.18 (1H, dd, *J* 7.9, 1.6 Hz, Ar C*H*), 6.97 (1H, t, *J* 7.9 Hz, Ar C*H*), 7.12 (1H, t, *J* 7.8 Hz, Ar C*H*), 7.34 (2H, t, *J* 7.8 Hz, Ar C*H*), 7.56 (2H, d, *J* 7.8 Hz, Ar C*H*), 9.01 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 25.9 ((CH_2)$_2$), 58.9 (*C*(CH_3)$_2$), 102.9 (Ar *C*H), 107.0 (Ar *C*H), 107.2 (Ar *C*H), 119.8 (Ar *C*H), 124.2 (Ar *C*H), 130.0 (Ar *C*H), 130.1 (Ar *C*H), 138.0 (Ar *C*), 145.7 (Ar *C*), 147.5 (Ar *C*), 174.4 (*C*=O); HRMS (ESI) *m*/*z* found 270.1602, $C_{16}H_{20}N_3O$ (M+H) requires 270.1606 (Δ = 3.0 ppm).

2-Methyl-*N*-(3-(2-methyl-1-oxo-1-(phenylamino)propan-2-ylamino)phenyl)-2-(3-nitrophenylamino)propanamide (5)



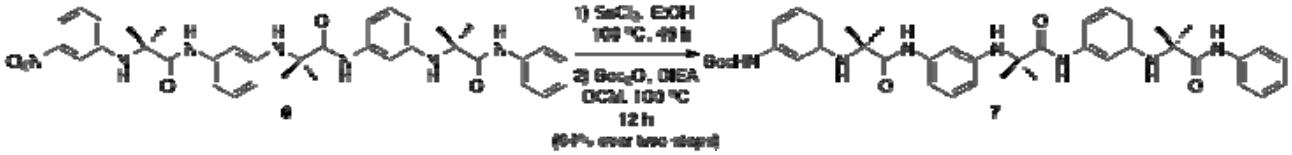
2-Methyl-2-(3-nitrophenylamino)propanoic acid hydrochloride (1.04 g, 4.14 mmol) was placed in a dry 250 mL RBF under nitrogen. DMF (40 mL, 0.1 M) was added followed by DIEA (1.44 mL, 8.27 mmol, 2 equiv.) and HBTU (1.72 g, 4.55 mmol, 1.1 equiv.) and the mixture stirred for 5 mins. 2-(3-aminophenylamino)-2-methyl-*N*-phenylpropanamide (1.07 g, 4.14 mmol, 1 equiv.) was then added and the mixture heated to 90 °C for 24 hrs. The reaction mixture was concentrated *in vacuo* and the residue dissolved in DCM (50 mL). This was washed with water (3 x 50 mL), 5% lithium chloride solution (3 x 50 mL) and brine (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude residue by flash column chromatography (gradient elution from ethyl acetate: hexane 3:7 - 0:1) provided the title compound as a yellow solid (1.42 g, 72%). M.p. 87 – 89 °C; ν_{max} (neat)/cm^{-1} 3334 (w, N-H), 2160 (w, N-H), 1672 (s, C=O), 1599 (s, C-C), 1520 (s, C=C), 1347 (s, N-O), 736 (s, C-H), 692 (s, C-H); δ_H (500 MHz, $CDCl_3$) 1.58 (6H, s, C(C*H*$_3$)$_2$), 1.62 (6H, s, C(C*H*$_3$)$_2$), 3.98 (1H, s, N*H*), 4.31 (1H, s, N*H*), 6.38 (1H, ddd, *J* 8.2, 2.4, 0.7 Hz, Ar C*H*), 6.80 (1H, ddd, *J* 8.2, 2.4, 0.7 Hz, Ar C*H*), 6.86 (1H, ddd, *J* 8.2, 2.4, 0.7 Hz, Ar C*H*), 7.10 (1H, s, Ar C*H*), 7.12 (2H, d, *J* 2.4 Hz, Ar C*H*), 7.28 (1H, d, *J* 1.6 Hz, Ar C*H*), 7.30 (1H, d, *J* 1.0 Hz, Ar C*H*), 7.32 (1H, s, Ar C*H*), 7.48 (1H, d, *J* 1.0 Hz, Ar C*H*), 7.50 (1H, d, *J* 1.2 Hz, Ar C*H*), 7.51 (1H, t, *J* 2.4 Hz, Ar C*H*), 7.64 (1H, ddd, *J* 8.2, 2.4, 0.7 Hz, Ar C*H*), 8.59 (1H, s, N*H*), 8.87 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 25.7 ((*C*H$_3$)$_2$), 25.8 ((*C*H$_3$)$_2$), 58.9 (*C*(CH$_3$)$_2$), 59.1 (*C*(CH$_3$)$_2$), 108.1 (Ar *C*H), 110.8 (Ar *C*H), 111.1 (Ar *C*H), 112.0 (Ar *C*H), 114.2 (Ar *C*H), 119.8 (Ar *C*H), 121.0 (Ar *C*H), 124.2 (Ar *C*H), 128.9 (Ar *C*H), 129.8 (Ar *C*H), 130.1 (Ar *C*H), 137.8 (Ar *C*), 138.5 (Ar *C*), 145.3 (Ar *C*), 145.4 (Ar *C*), 149.1 (Ar *C*), 173.1 (*C*=O), 173.9 (*C*=O); HRMS (ESI) *m*/*z* found 476.2296, $C_{26}H_{30}N_5O_4$ (M+H) requires 476.2230 (Δ = 2.0 ppm).

2-Methyl-N-(3-(2-methyl-1-(3-(2-methyl-1-oxo-1-(phenylamino)propan-2-ylamino)phenylamino)-1-oxopropan-2-ylamino)phenyl)-2-(3-nitrophenylamino)propanamide (6)



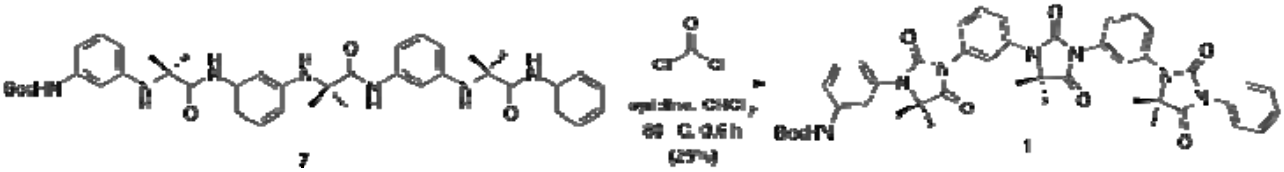
2-Methyl-N-(3-(2-methyl-1-oxo-1-(phenylamino)propan-2-ylamino)phenyl)-2-(3-nitrophenylamino)propanamide (1.20 g, 2.53 mmol) was placed in a 40 mL pressure tube under nitrogen. Ethanol (25 mL, 0.1 M) was added followed by tin (II) chloride (4.8 g, 25.3 mmol, 10 equiv.), the tube was sealed and the mixture heated to 100 °C for 48 hours. Ethyl acetate (50 mL) was added and the mixture washed with saturated hydrogen carbonate solution (3 x 50 mL), water (3 x 50 mL) and brine (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo* to leave a pale yellow solid (1.12 g, quantitative). The pale yellow solid (1.12 g, 2.53 mmol) was transferred to a dry 100 mL RBF under nitrogen. DMF (25 mL, 0.1 M) was added followed by 2-methyl-2-(3-nitrophenylamino)propanoic acid hydrochloride (660 mg, 2.53 mmol, 1 equiv.), DIEA (880 µl, 5.06 mmol, 2 equiv.) and HBTU (1.15 g, 3.04 mmol, 1.2 equiv.) and the mixture heated to 90 °C for 24 hours. The reaction mixture was concentrated *in vacuo* and the residue dissolved in DCM (50 mL). This was washed with water (3 x 50 mL), 5% lithium chloride solution (3 x 50 mL) and brine (3 x 50 mL), dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude residue by flash column chromatography (gradient elution from ethyl acetate: hexane 2:3 - 0:1) provided the title compound as a yellow solid (670 mg, 41% over two steps). M.p. 101 – 103 °C; ν_{max} (neat)/cm^{-1} 3339 (w, N-H), 2925 (w, N-H), 1674 (s, C=O), 1607 (s, C=O), 1516 (s, C=C), 1365 (m, N-O), 1156 (s, C-H), 691 (s, C-H); δ_H (500 MHz, $CDCl_3$) 1.56 (6H, s, C(CH_3)$_2$), 1.58 (6H, s, C(CH_3)$_2$), 1.62 (6H, C(CH_3)$_2$), 3.95 (1H, s, N*H*), 3.97 (1H, s, N*H*), 4.29 (1H, s, N*H*), 6.34 (2H, ddd, *J* 8.2, 2.4, 1.1 Hz, Ar C*H*), 6.71 (1H, ddd, *J* 4.0, 2.0, 0.7 Hz, Ar C*H*), 6.73 (1H, ddd, *J* 4.0, 2.4, 0.7 Hz, Ar C*H*), 6.87 (1H, ddd, *J* 8.2, 2.4, 0.7 Hz, Ar C*H*), 7.07 (2H, td, *J* 8.2, 2.4 Hz, Ar C*H*), 7.11 (1H, dt, *J* 7.5, 1.1 Hz, Ar C*H*), 7.15 (1H, t, *J* 2.1 Hz, Ar C*H*), 7.21 (1H, t, *J* 2.1 Hz, Ar C*H*), 7.29 (1H, d, *J* 1.5 Hz, Ar C*H*), 7.31 (1H, dd, *J* 1.8, 0.9 Hz, Ar C*H*), 7.32 (1H, s, Ar C*H*), 7.49 (1H, d, *J* 1.2 Hz, Ar C*H*), 7.51 (1H, d, *J* 1.2 Hz, Ar C*H*), 7.52 (1H, t, *J* 2.4 Hz, Ar C*H*), 7.65 (1H, ddd, *J* 8.2, 2.0, 0.7 Hz, Ar C*H*), 8.57 (1H, s, N*H*), 8.80 (1H, s, N*H*), 8.90 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 25.7 ((CH_3)$_2$), 25.8 ((CH_3)$_2$), 25.8 ((CH_3)$_2$), 58.9 (*C*(CH_3)$_2$), 59.9 (*C*(CH_3)$_2$), 59.1 (*C*(CH_3)$_2$), 108.3 (Ar *C*H), 108.4 (Ar *C*H), 110.8 (Ar *C*H), 111.1 (Ar *C*H), 111.2 (Ar *C*H), 111.5 (Ar *C*H), 111.9 (Ar *C*H), 114.3 (Ar *C*H), 119.9 (Ar *C*H), 121.0 (Ar *C*H), 124.2 (Ar *C*H), 129.7 (Ar *C*H), 129.8 (Ar *C*H), 130.1 (Ar *C*H), 137.9 (Ar *C*), 138.4 (Ar *C*), 138. 7 (Ar *C*), 145.2 (Ar *C*), 145.4 (Ar *C*), 149.1 (Ar *C*), 173.0 (*C*=O), 173.9 (*C*=O), 174.0 (*C*=O); HRMS (ESI) *m*/*z* found 652.3236, $C_{36}H_{42}N_7O_5$ (M+H) requires 652.3247 (Δ = 2.0 ppm).

***tert*-Butyl 3-(2-methyl-1-(3-(2-methyl-1-(3-(2-methyl-1-oxo-1-(phenylamino)propan-2-ylamino)phenylamino)-1-oxopropan-2-ylamino)phenylamino)-1-oxopropan-2-ylamino)phenylcarbamate (7)**



2-Methyl-N-(3-(2-methyl-1-(3-(2-methyl-1-oxo-1-(phenylamino)propan-2-ylamino)phenylamino)-1-oxopropan-2-ylamino)phenyl)-2-(3-nitrophenylamino)propanamide (50 mg, 0.077 mmol) was placed in a dry 4 mL pressure vial under nitrogen. Ethanol (0.8 mL, 0.1 M) was added followed by tin (II) chloride (146 mg, 0.770 mmol, 10 equiv.), the vial was sealed and the mixture heated to 100 °C for 48 hours. Ethyl acetate (15 mL) was added and the solution washed with saturated hydrogen carbonate solution (3 x 15 mL), water (3 x 15 mL) and brine (3 x 15 mL), dried ($MgSO_4$) and the solvent evaporated off to leave a pale orange solid (47 mg, quantitative). The pale orange solid (47 mg, 0.077 mmol) was transferred to a dry 4 mL pressure vial under nitrogen. Chloroform (0.8 mL, 0.1 M) was added followed by DIEA (32 µl, 0.185 mmol, 2.4 equiv.) and di-*tert*-butyl dicarbonate (20 mg, 0.092 mmol, 1.2 equiv.), the vial was sealed and the mixture heated to 100 °C for 12 hours. Purification of the crude reaction mixture by flash column chromatography (ethyl acetate: hexane, 1:1) provided the title compound as a pale yellow solid (52 mg, 94% over two steps). M.p. 110 – 112 °C; ν_{max} (neat)/cm^{-1} 3337 (w, N-H), 2980 (w, N-H), 2931 (w, N-H), 1676 (s, C=O), 1607 (s, C=O), 1516 (s, C=C), 1157 (s, C-C), 757 (C-H), 692 (C-H); δ_H (500 MHz, $CDCl_3$) 1.52 (12H, s, C(C*H*$_3$)$_3$), 1.55 (6H, s, C(C*H*$_3$)$_2$), 1.56 (6H, s, C(C*H*$_3$)$_2$), 1.57 (6H, s, C(C*H*$_3$)$_2$), 3.92 (2H, s, N*H*), 3.98 (1H, s, N*H*), 6.27 (1H, dd, *J* 8.1, 1.8 Hz, Ar C*H*), 6.30 (1H, dd, *J* 8.1, 1.8 Hz, Ar C*H*), 6.34 (1H, dd, *J* 9.9, 1.8 Hz, Ar C*H*), 6.50 (1H, s, N*H*), 6.70 (3H, ddd, *J* 10.2, 1.9, 1.4, Ar C*H*), 6.94 (1H, s, C*H*), 7.05 (3H, t, *J* 9.0 Hz, Ar C*H*), 7.10 (1H, d, *J* 7.4 Hz, Ar C*H*), 7.25 (2H, dd, *J* 5.0, 2.3 Hz, Ar C*H*), 7.31 (2H, ddd, *J* 7.4, 1.9, 0.8, Ar C*H*), 7.50 (2H, dd, *J* 8.7, 1.2 Hz, Ar C*H*), 8.83 (1H, s, N*H*), 8.85 (1H, s, N*H*), 8.90 (1H, s, N*H*); δ_C (125 MHz, $CDCl_3$) 25.8 ((*C*H$_3$)$_2$), 25.8 ((*C*H$_3$)$_2$), 26. 9 ((*C*H$_3$)$_2$), 28.3 ((*C*H$_3$)$_3$), 58.9 (*C*(CH$_3$)$_2$), 80.6 (O*C*(CH$_3$)$_3$), 106.7 (Ar *C*H), 108.5 (Ar *C*H), 109.9 (Ar *C*H), 110.5 (Ar *C*H), 111.2 (Ar *C*H), 111.4 (Ar *C*H), 119.8 (Ar *C*H), 124.1 (Ar *C*H), 128.9 (Ar *C*H), 129.7 (Ar *C*H), 129.7 (Ar *C*H), 137. 9 (Ar *C*), 138.8 (Ar *C*), 139.3 (Ar *C*), 145.1 (Ar *C*), 145.2 (Ar *C*), 152.7 (Ar *C*), 174.0 (*C*=O), 174.1 (*C*=O), 174.2(*C*=O); HRMS (ESI) *m*/*z* found 722.4049, $C_{41}H_{52}N_7O_5$ (M+H) requires 722.4030 (Δ = 3.0 ppm).

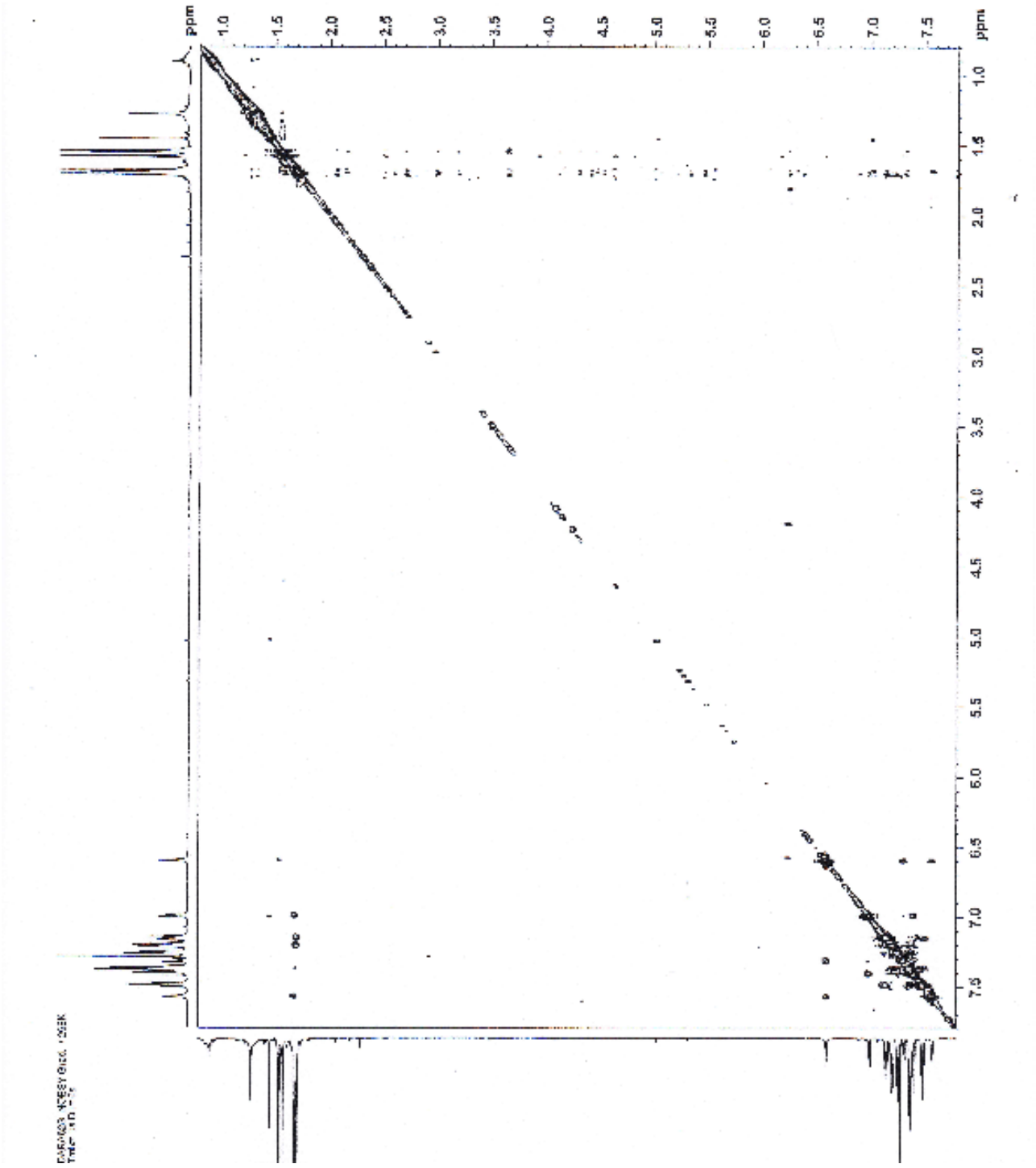
***tert*-Butyl 3-(3-(3-(3-(3-(5,5-dimethyl-2,4-dioxo-3-phenylimidazolidin-1-yl)phenyl)-5,5-dimethyl-2,4-dioxoimidazolidin-1-yl)phenyl)-5,5-dimethyl-2,4-dioxoimidazolidin-1-yl)phenylcarbamate (1)**



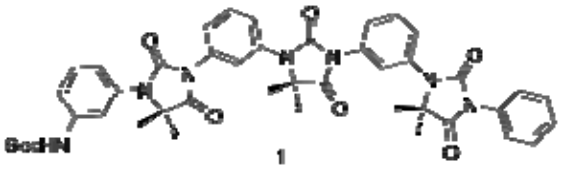
tert-Butyl 3-(2-methyl-1-(3-(2-methyl-1-(3-(2-methyl-1-oxo-1-(phenylamino)propan-2-ylamino)phenylamino)-1-oxopropan-2-ylamino)phenylamino)-1-oxopropan-2-ylamino)phenylcarbamate (60 mg, 0.083 mmol) was placed in a dry 4 mL pressure vial under nitrogen. Chloroform (2 mL) was added followed by pyridine (101 µl, 1.25 mmol, 15 equiv.) and phosgene (20% solution in toluene, 263 µl, 0.499 mmol, 6 equiv.), the vial was sealed and the mixture heated to 80 °C for 30 mins. The mixture was allowed to cool then partitioned between saturated sodium hydrogen carbonate solution (2 mL). The organic layer was extracted, dried ($MgSO_4$) and concentrated *in vacuo*. Purification of the crude residue by flash column chromatography (diethyl ether: hexane, 4:1) provided the title compound as a white solid (17 mg, 25%). M.p. 227 – 228 °C; ν_{max} (neat)/cm^{-1} 2978 (w, N-H), 1805 (s, C=O), 1713 (s, C=O), 1596 (s, C=O), 1486 (m, C=C), 1148 (s, C-C), 748 (C-H), 693 (C-H); δ_H (500 MHz, $CDCl_3$) 1.55 (9H, s, C(C*H*$_3$)$_3$), 1.69 (6H, s, C(C*H*$_3$)$_2$), 1.71 (12H, C(C*H*$_3$)$_2$), 6.60 (1H, s, N*H*), 6.99 (1H, ddd, *J* 7.8, 1.9, 0.9 Hz, Ar C*H*), 7.15 (2H, ddd, *J* 8.0, 1.8, 1.0 Hz, Ar C*H*), 7.19 – 7.22 (3H, m, Ar C*H*), 7.26 (2H, dd, *J* 8.6, 1.1 Hz, Ar C*H*), 7.31 (1H, dd, *J* 8.3, 1.2 Hz, Ar C*H*), 7.35 – 7.39 (4H, m, Ar C*H*), 7.40 (1H, d, *J* 3.6 Hz, Ar C*H*), 7.49 (2H, td, *J* 8.0, 1.8 Hz, Ar C*H*), 7.58 (1H, s, Ar C*H*); δ_C (125 MHz, $CDCl_3$) 26.3 ((*C*H$_3$)$_2$), 26.3 (*C*H$_3$)$_2$), 26.4(*C*H$_3$)$_2$), 28.3 (*C*H$_3$)$_3$), 64.5 (*C*(CH$_3$)$_2$), 64.6 (*C*(CH$_3$)$_2$), 64.6 (*C*(CH$_3$)$_2$), 81.1 (O*C*(CH$_3$)$_3$), 118.6 (Ar *C*H), 118.9 (Ar *C*H), 122.8 (Ar *C*H), 123.1 (Ar *C*H), 123.7 (Ar *C*H), 123.8 (Ar *C*H), 123.9 (Ar *C*H), 124.0 (Ar *C*H), 125.4 (Ar *C*H), 125.5 (Ar *C*H), 125.5 (Ar *C*H), 128.8 (Ar *C*H), 130.0 (Ar *C*H), 133.7 (Ar *C*), 133.9 (Ar *C*), 139.9 (Ar *C*), 143.8 (Ar *C*), 145.1 (Ar *C*), 145.2 (Ar *C*), 151.3 (*C*=O), 151.8 (*C*=O), 152.3 (*C*=O), 155.5 (*C*=O), 156.9 (*C*=O), 157.0 (*C*=O); HRMS (ESI) *m*/*z* found 800.3406, $C_{44}H_{46}N_7O_8$ (M+H) requires 800.3408 (Δ = 2.0 ppm).

Part III. NOSEY NMR data for compound 1

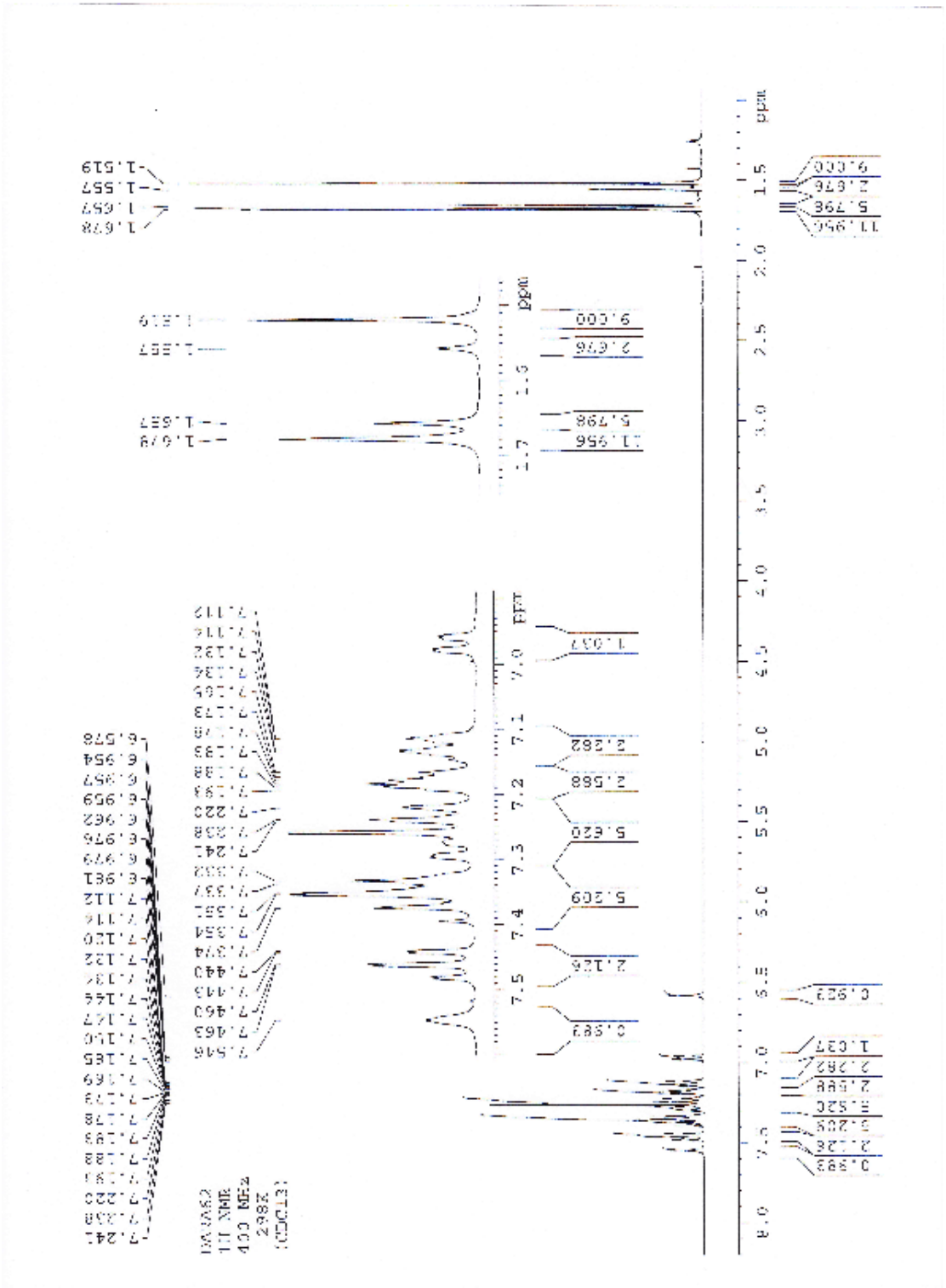
NOESY NMR spectra of samples dissolved in $CDCl_3$ (Aldrich) were recorded at 298K on a Bruker AX500 spectrometer using a 5 mm BBO probe head and TOPSPIN 2.1 software. The manufacturers standard noesygpph pube program was used with 2048 x 256 data points, 8 scans per increment, a spectral width of 9.5 ppm in both dimensions and a mixing time of 1 s with a 6s pre-acquisition delay. Spectra were apodised using 90° shift square sine functions in both directions.

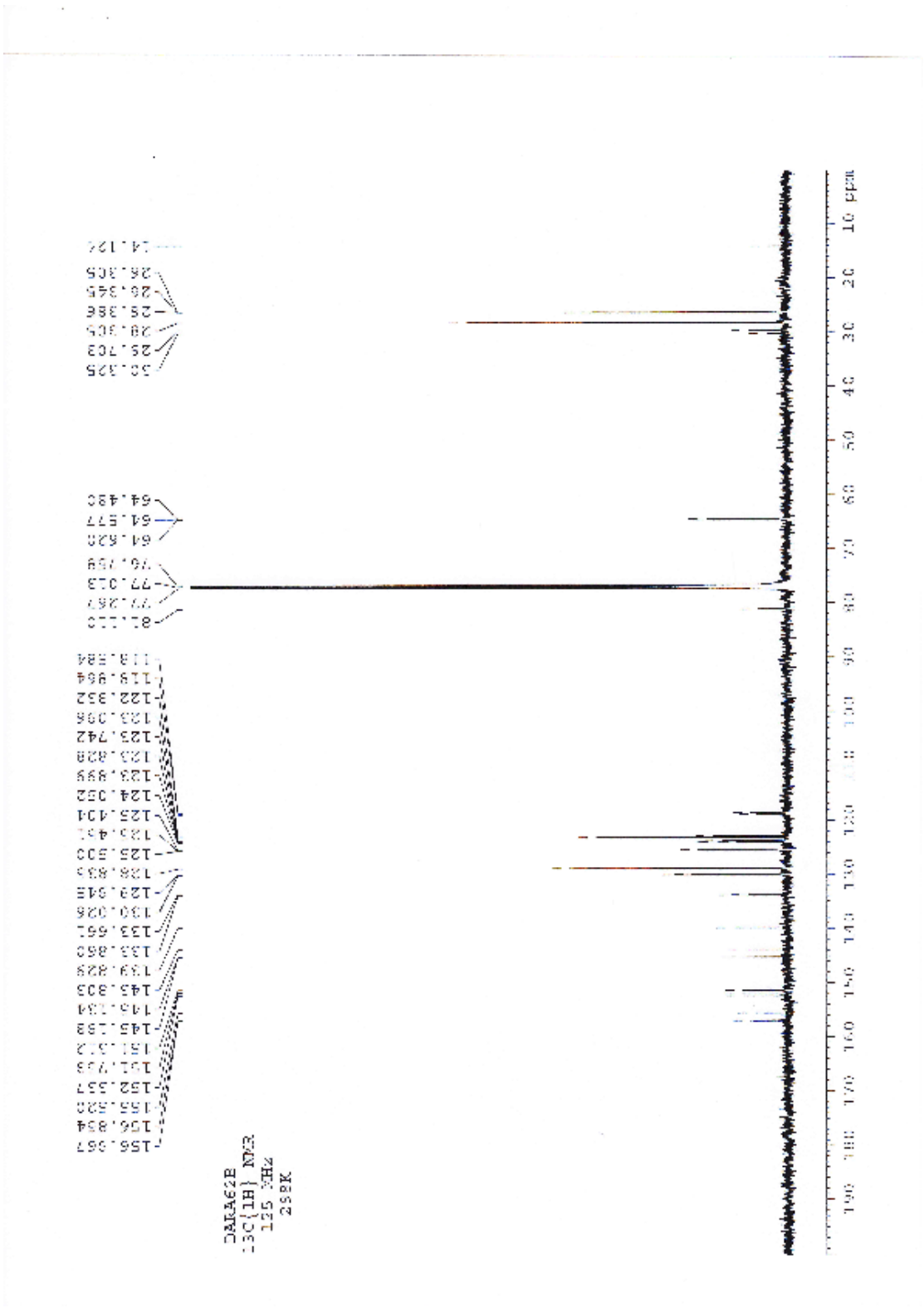


Part IV. NMR data for compounds 1-7



1




DARA62B
13C{1H} NMR
125 MHz
298K
14.124
28.305
28.345
28.386
29.305
29.763
30.325
64.480
64.577
64.820
76.759
77.013
77.267
82.112
118.384
119.964
122.352
123.096
125.742
125.829
125.899
126.052
126.434
126.451
126.500
126.833
129.043
130.028
133.661
133.860
139.829
145.805
146.134
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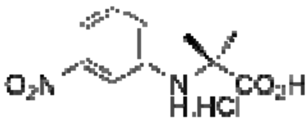
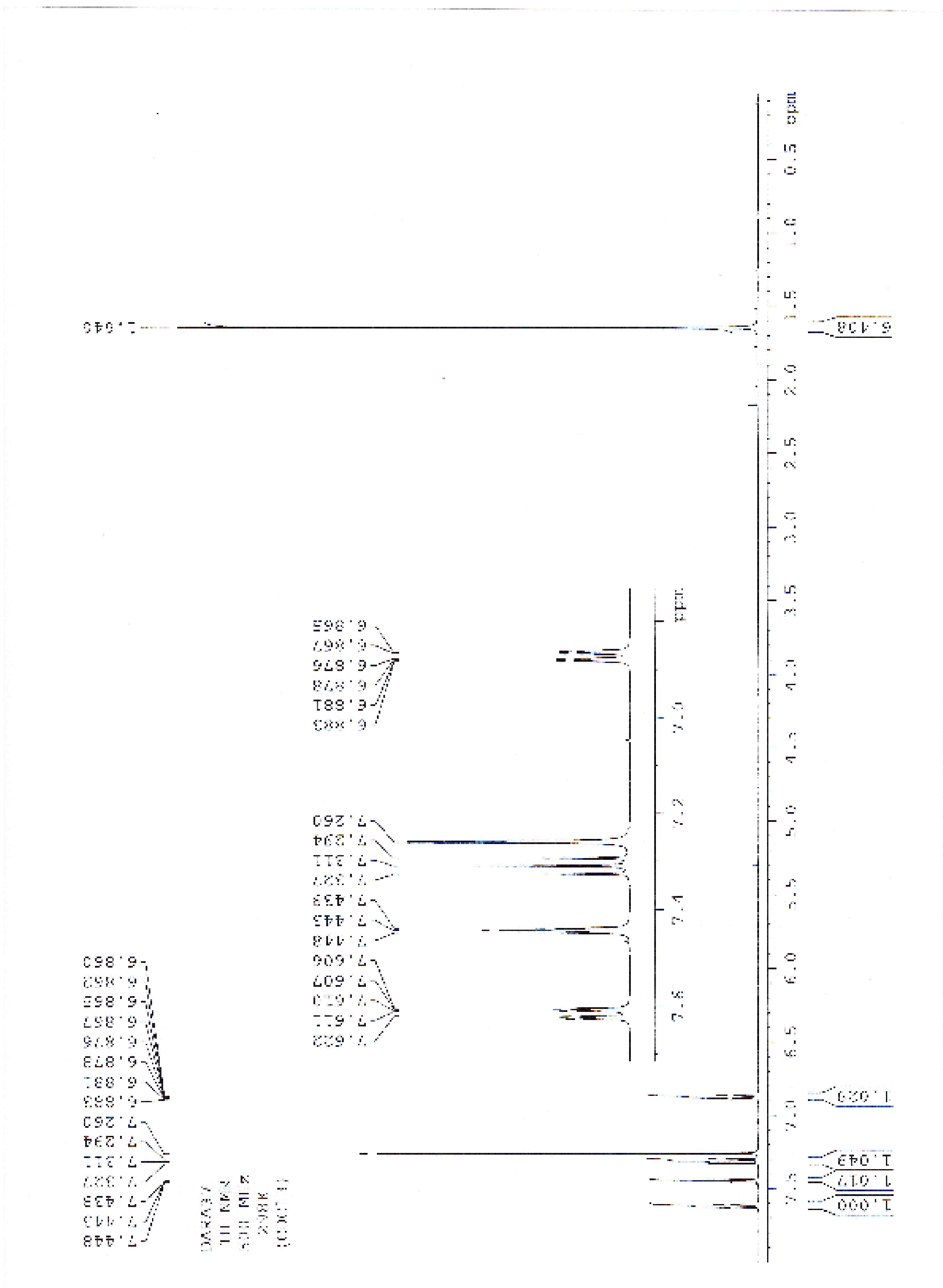
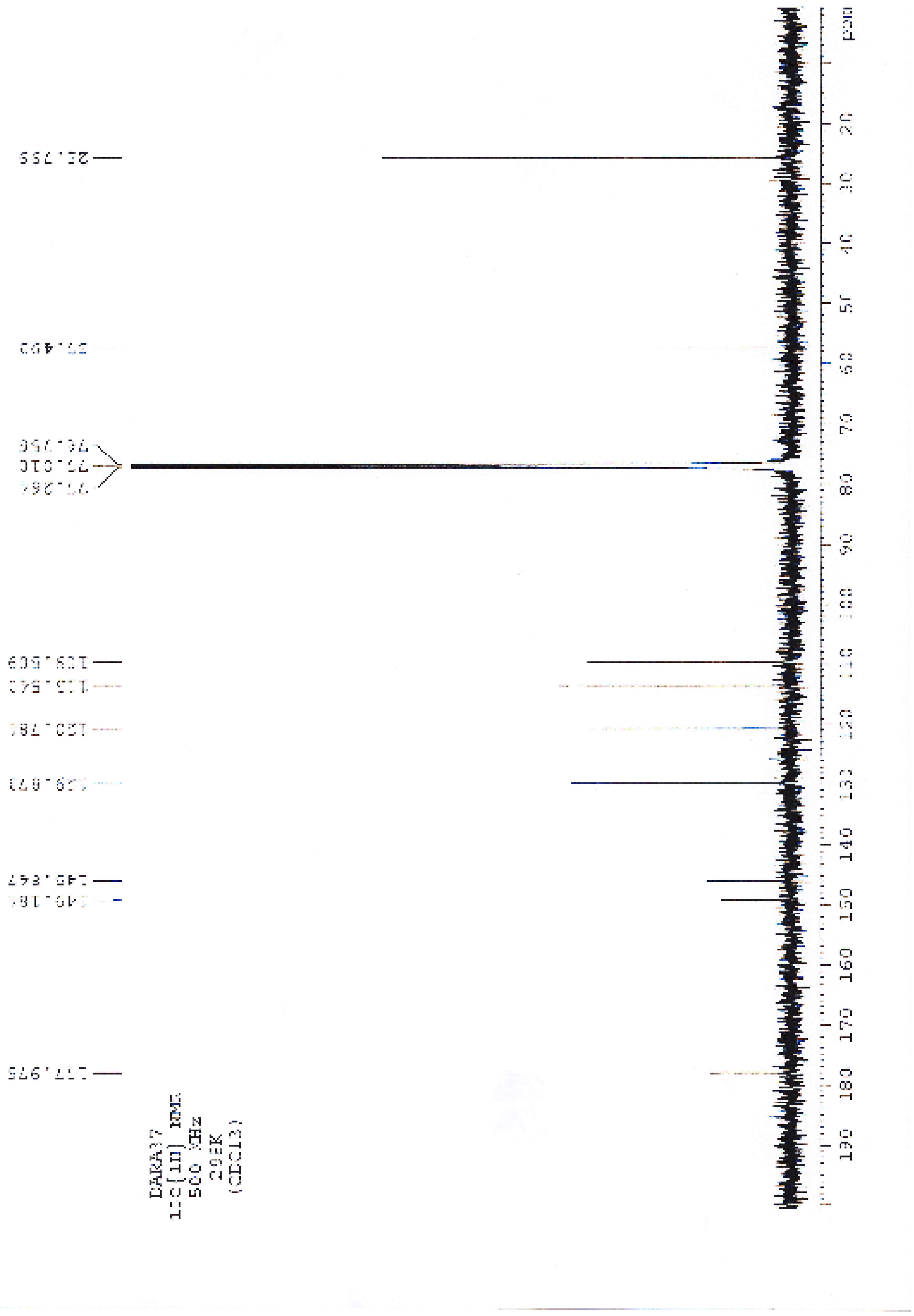
151.735
152.557
155.520
156.854
156.867
10 ppm

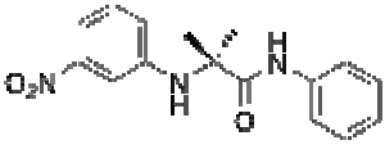


2



Electronic Supplementary Material (ESI) for Chemical Communications





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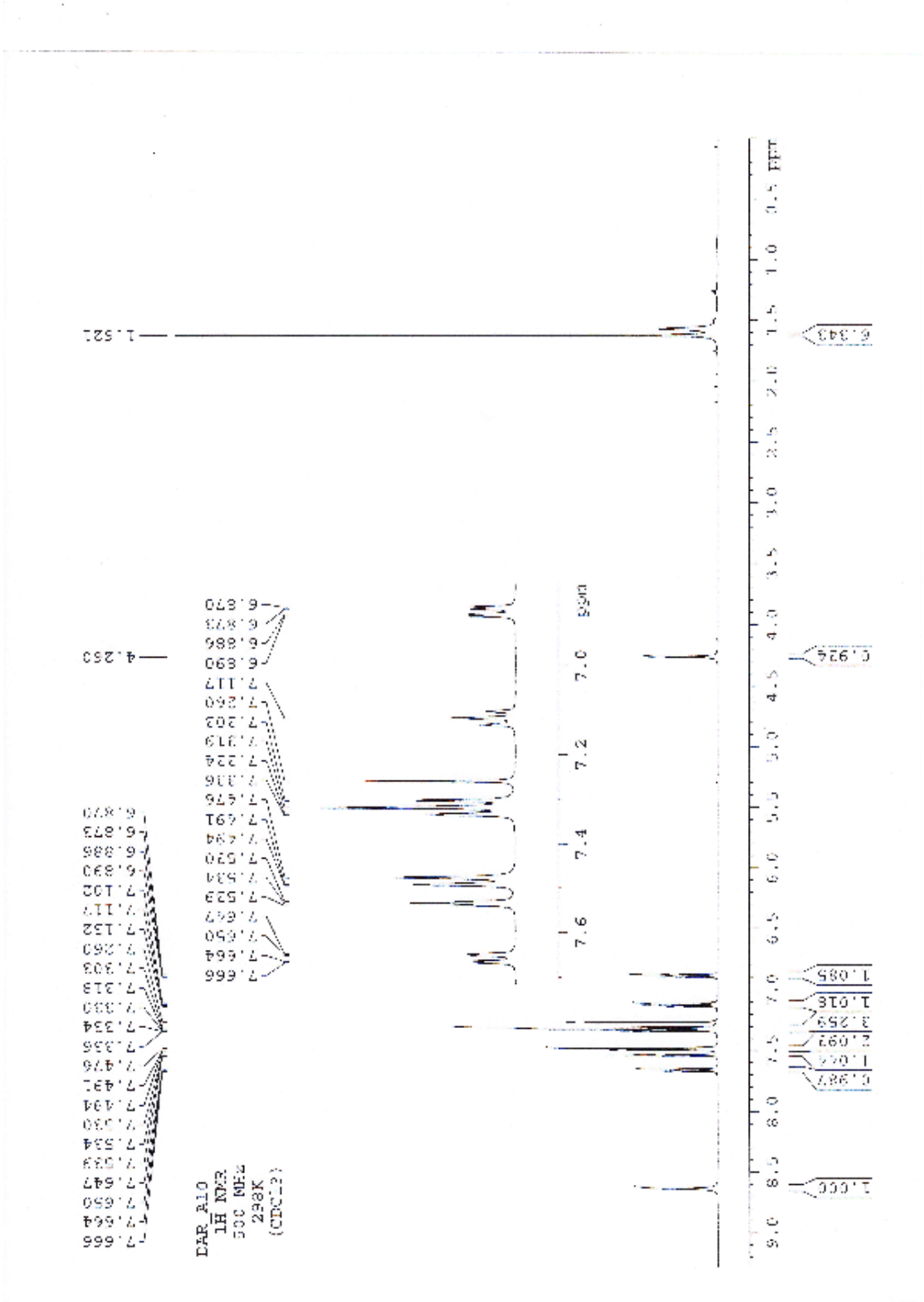

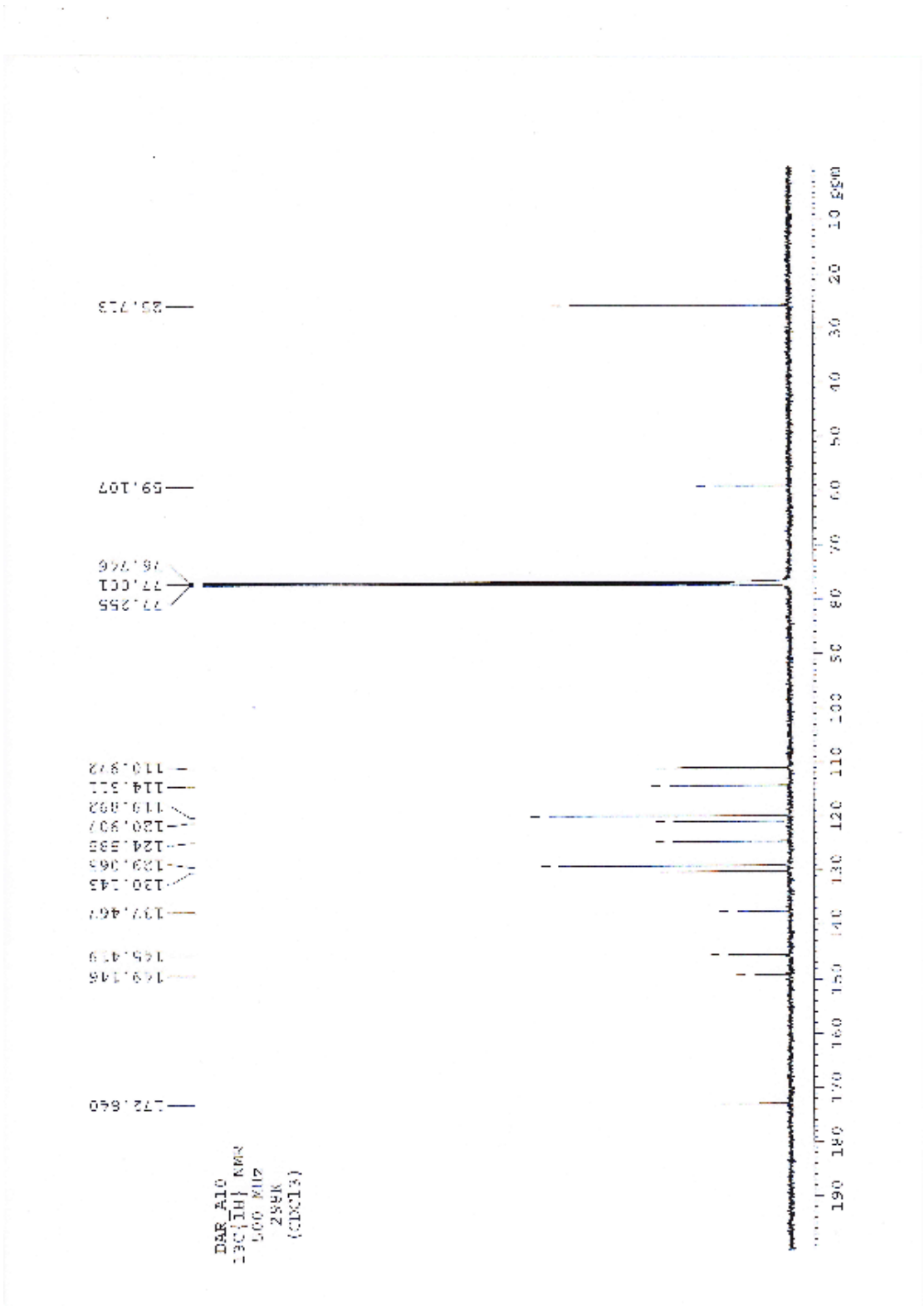

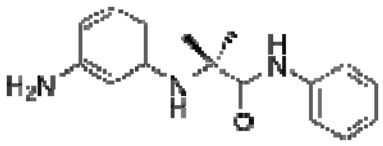

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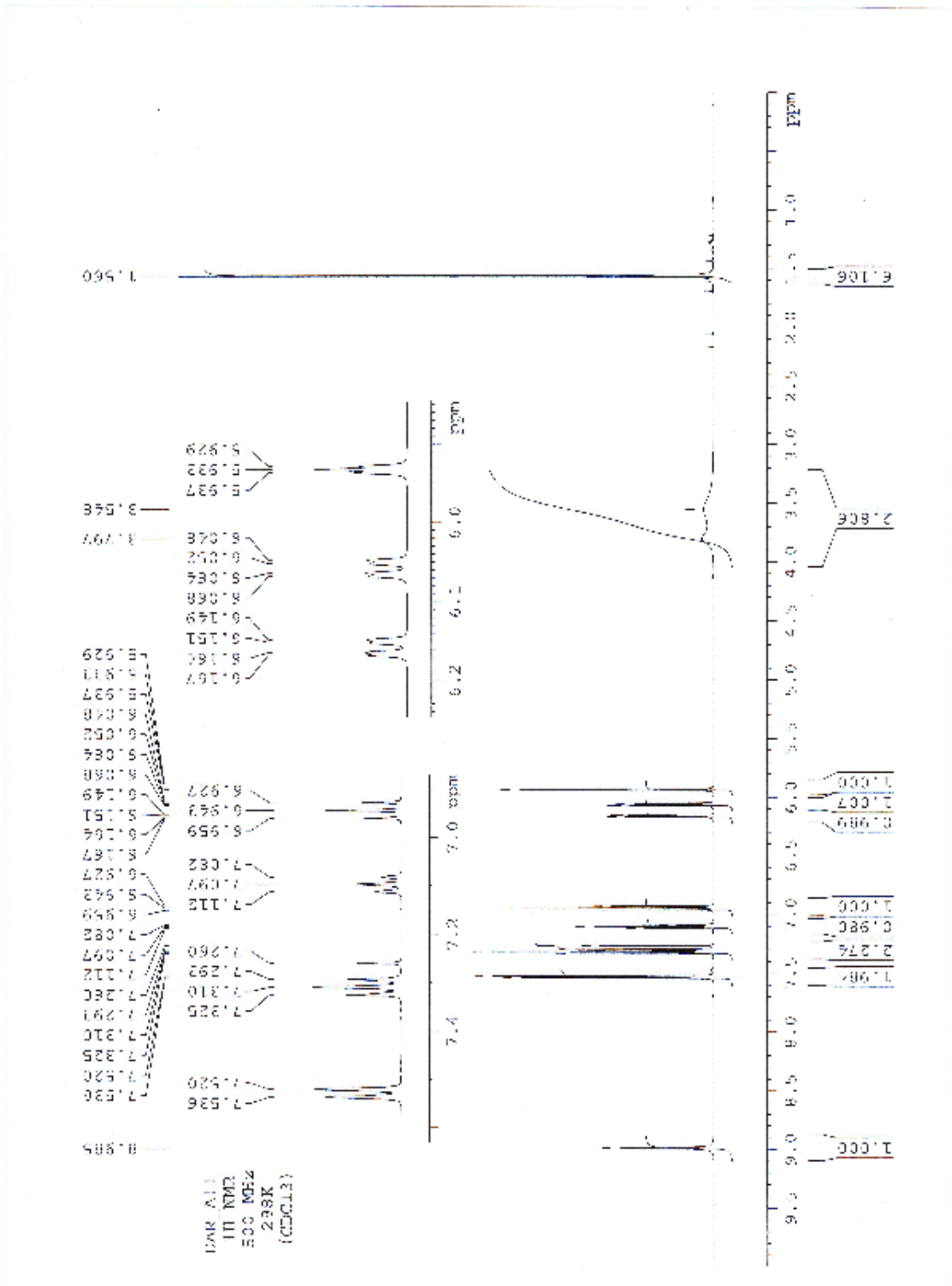

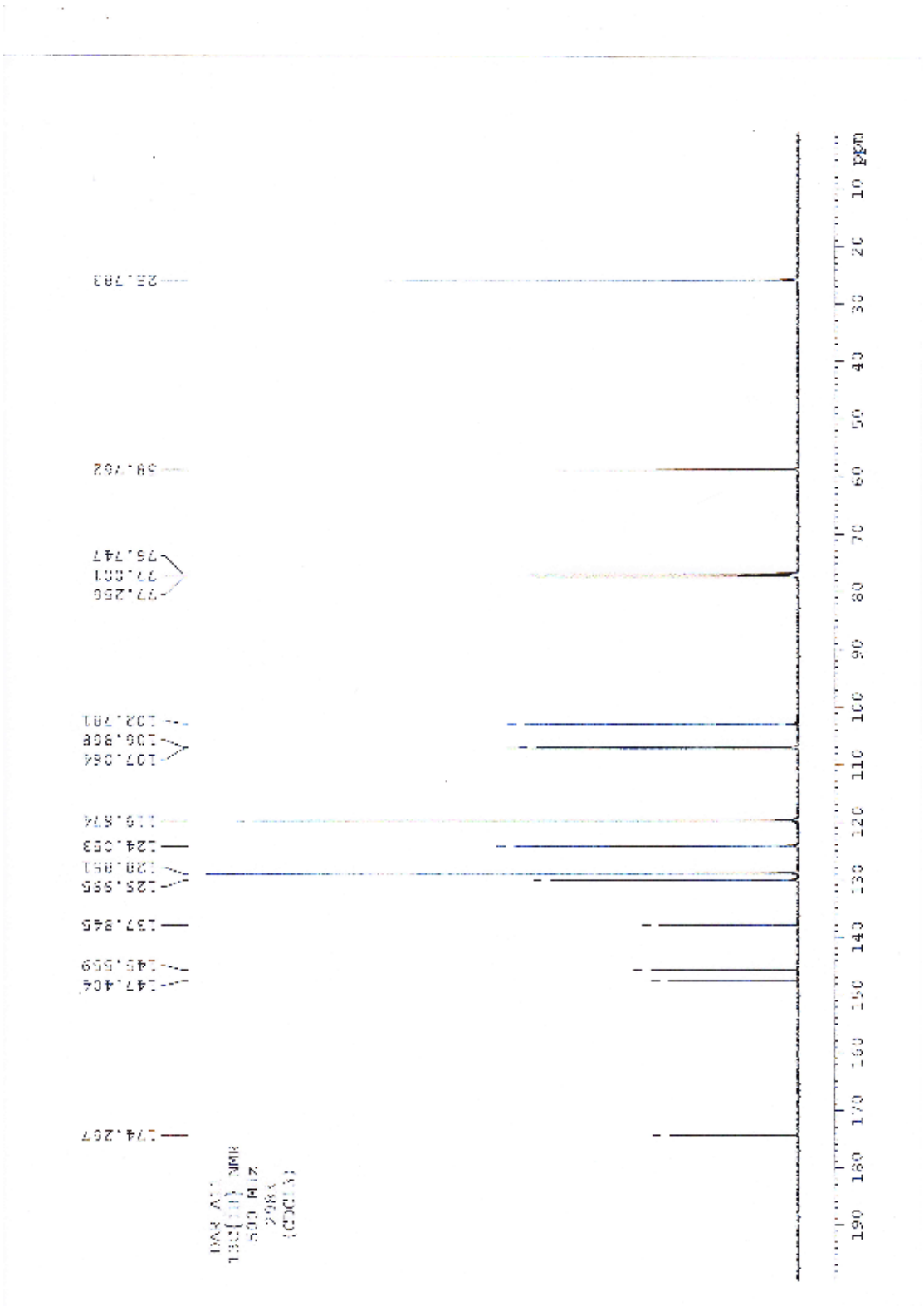

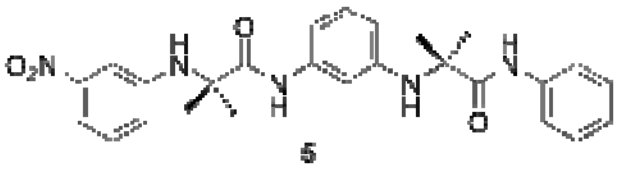

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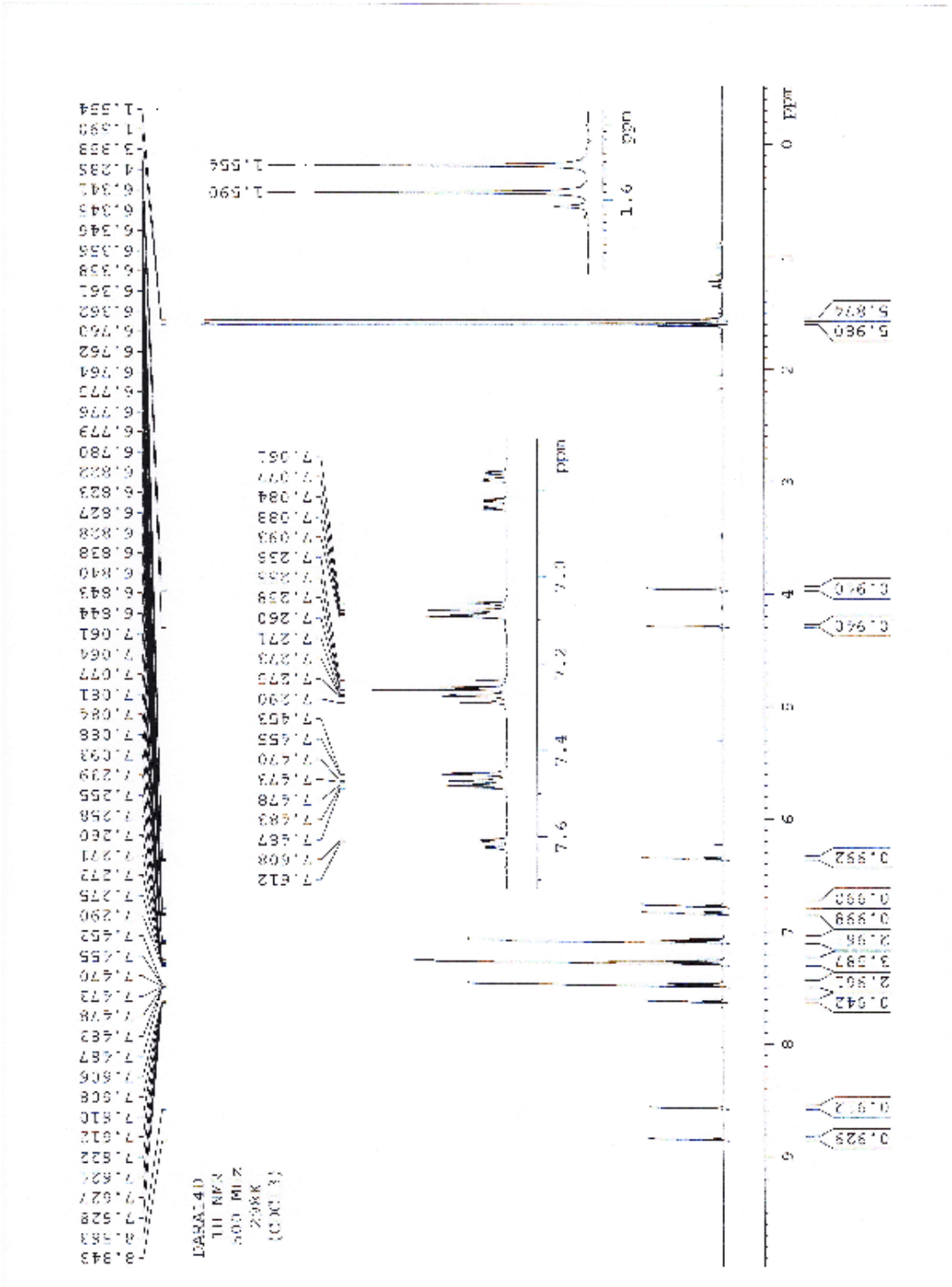
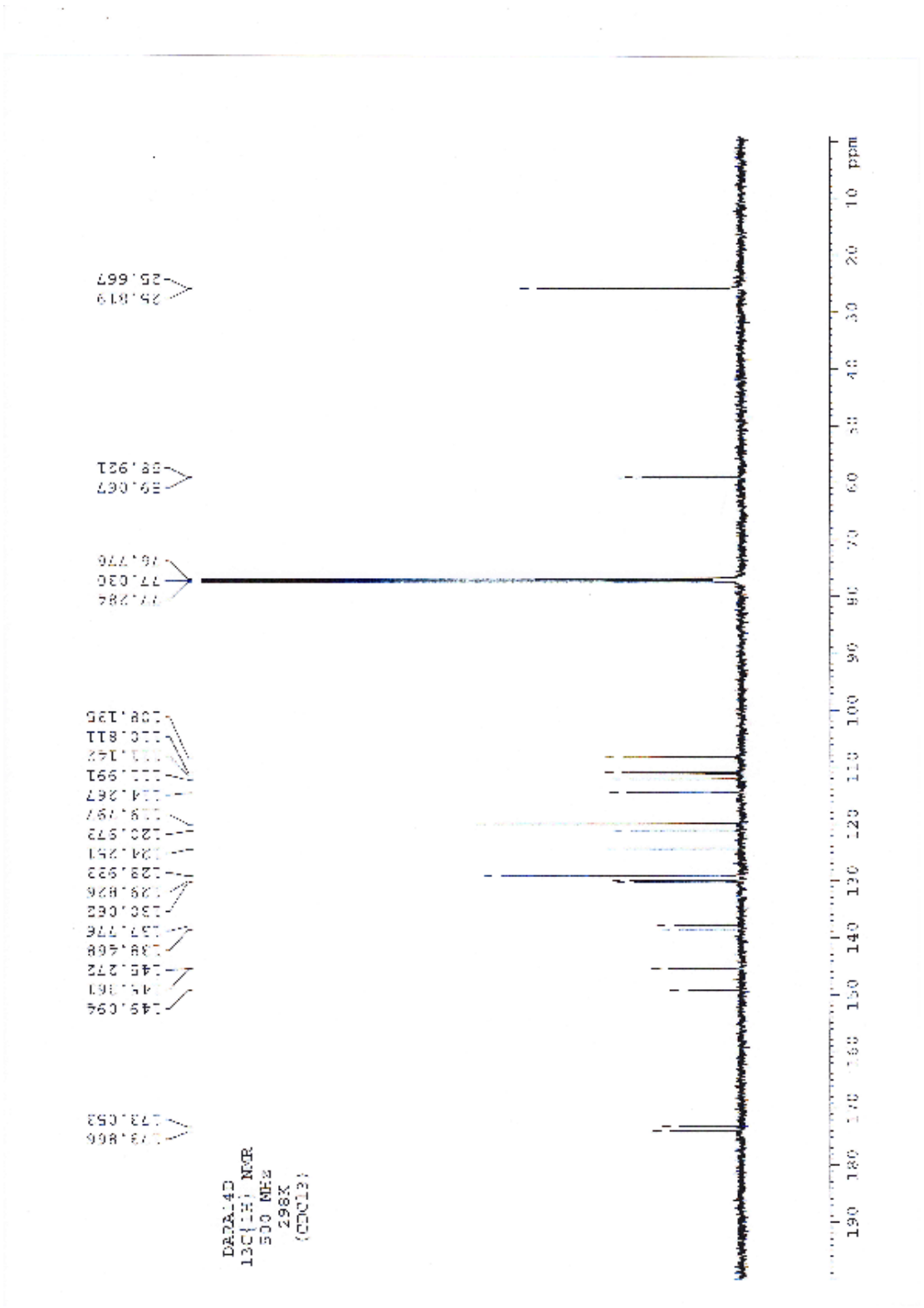
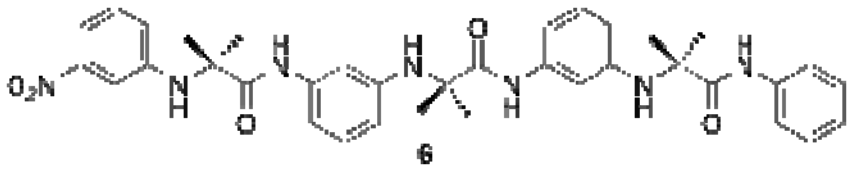
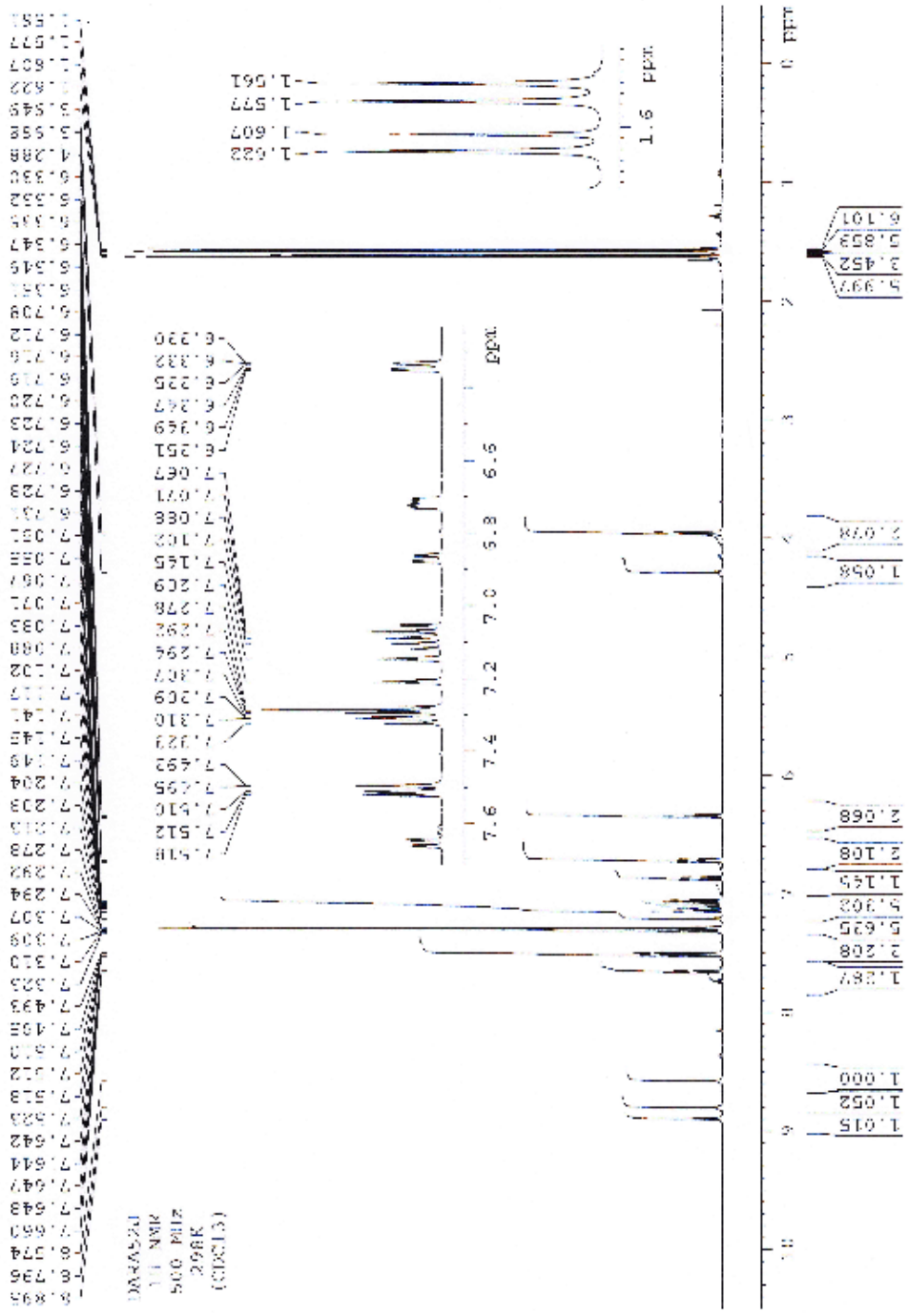
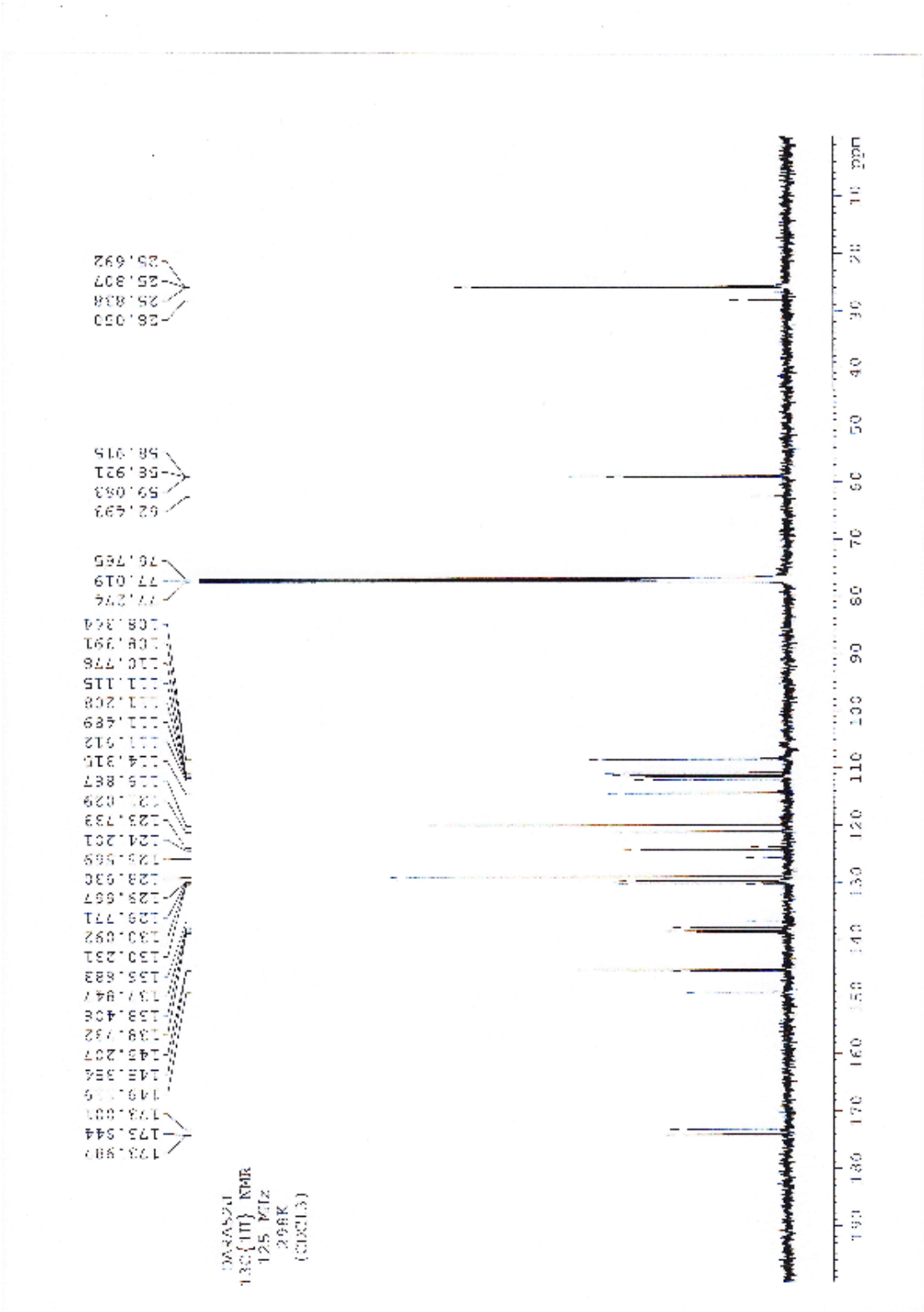


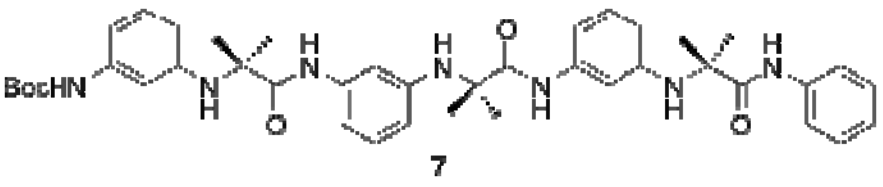




6




25.692
25.807
25.838
26.050
58.915
59.083
62.499
76.765
77.019
77.276
173.987
175.544
DMSO
13C{1H} NMR
125 MHz
298K
(CD3)2SO



7