Supporting Information

Aryl-linked Diphenylimidazolidin-2-ones as Non-Peptidic β-Strand Mimetics

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CONTENTS

1. General Information

Reactions were carried out under a nitrogen or argon atmosphere in oven-dried glassware unless otherwise stated. Standard inert atmosphere techniques were used in handling all air and moisture sensitive reagents.

1.1. Solvent & reagents

Anhydrous tetrahydrofuran and dichloromethane (from commercial sources) were obtained by filtration through activated alumina (powder ~150 mesh, pore size 58 Å, basic, Sigma-Aldrich) columns, or were dried on an MB-SPS-800 dry solvent system. Other solvents and reagents were used directly as received from commercial suppliers. Petrol refers to distilled light petroleum of fraction (30 ˚C – 40 ˚C).

1.2. Chromatography

Flash column chromatography was carried out using VWR Kieselgel 60 silica gel (60-63 μm). Thin-layer chromatography was carried out using Merck Kieselgel 60 F254 (230-400 mesh) fluorescent treated silica, visualized under UV light (250 nm) and by staining with aqueous potassium permanganate solution.

1.3. Spectroscopy

^{1}H and ^{13}C NMR spectra were recorded using a Bruker 500, 400, 300 or 250 MHz spectrometer running Topspin™ software and are quoted in ppm for measurement against a tetramethylsilane (TMS) or residual solvent peaks as internal standards. Chemical shifts (δ) are given in parts per million (ppm), and coupling constants (*J*) are given in Hertz (Hz). The ^{1}H NMR spectra are reported as follows: δ / ppm (number of protons, multiplicity, coupling constant *J* / Hz (where appropriate), assignment). Multiplicity is abbreviated as follows: s = singlet, br = broad, d = doublet, dd = doublet of doublets, t = triplet, dt = doublet of triplet, q = quartet, dq = doublet of quartet, quint. = quintet, sept. = septet, m = multiplet, v = very. Compound names are those generated by ChemBioDraw™ (CambridgeSoft) following IUPAC nomenclature. However, the NMR assignment numbering used is arbitrary and does not follow any particular convention. Numbering of compounds is illustrated on the spectra themselves; *vide infra*. The ^{13}C NMR spectra are reported in δ / ppm. Two-dimensional (COSY, HSQC, HMBC) NMR spectroscopy was used to assist the assignment of signals in the ^{1}H and ^{13}C NMR spectra. IR spectra were recorded on a Bruker Tensor 27 FT-IR spectrometer from a thin film deposited onto a sodium chloride plate or a diamond ATR

module. Only selected maximum absorbances (ν_{max}) of the most intense peaks are reported (cm^{-1}). Low-resolution mass spectra were recorded on a Waters LCT premier XE Micromass spectrometer (ESI). High-resolution mass spectra were recorded on a Bruker MicroTof mass spectrometer (ESI) by the internal service at the Department of Organic Chemistry, University of Oxford. Melting points were recorded using a Leica Galen III hot-stage microscope apparatus and are reported uncorrected in degrees Celsius (˚C).

2. Practical experimental

General procedure (a) Coupling of 1-iodo-3-nitrobenzene to α-amino alcohols

According to a literature procedure,[1] dimethyl sulfoxide (0.60 M) and 2-amino propan-1-ol (1.5 eq.) were added to 1-iodo-3-nitrobenzene (1.0 eq.), copper iodide (0.1 eq.), L-proline (0.2 eq.) and potassium carbonate (2.0 eq.) and the mixture then heated for 36 h at 80 ˚C. The reaction mixture was diluted with ethyl acetate (0.05 M), partitioned with water (0.05 M) and extracted with ethyl acetate (3 x 0.05 M). The organic layers were combined, dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography.

General procedure (b) TBS Protection of primary alcohols

TBSCl (2.0 eq.) was added to a stirred solution of 2-((3-nitrophenyl)amino)propan-1-ol (1.0 eq.), imidazole (3.0 eq.) and 4-dimethylaminopyridine (0.1 eq.) in *N*,*N*-dimethylformamide (0.30 M). The reaction mixture was stirred overnight at room temperature and then diluted with dichloromethane (0.03 M), partitioned with ammonium chloride (0.03 M), and extracted with dichloromethane (3 x 0.03 M). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography.

General procedure (c) Coupling of isocyanates with aryl amines

Phenyl isocyanate (2.0 eq.) was added to a stirred solution of N-(1-((*tert*-butyldimethylsilyl)oxy)propan-2-yl)-3-nitroaniline (1.0 eq.) and 4-dimethylaminopyridine (0.1 eq.) in dichloromethane (0.20 M). The reaction mixture was stirred at room temperature for 48 h then diluted with dichloromethane (0.03 M), partitioned with pH 7 buffer solution (0.03 M), and extracted with dichloromethane (3 x 0.03 M). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography.

General procedure (d) Removal of the tert-butyldimethylsilane group

Tetra-*n*-butylammonium fluoride (1.2 eq.) was added dropwise to a stirred solution of 1-(1-((*tert*-butyldimethylsilyl)oxy)propan-2-yl)-1-(3-nitrophenyl)-3-phenylurea (1.0 eq.) and acetic acid (1.2 eq.) in tetrahydrofuran (0.10 M). The reaction mixture was stirred at room temperature overnight then diluted with dichloromethane (0.03 M), partitioned with ammonium chloride (0.03 M) and extracted with dichloromethane (3 x 0.03 M). The combined organic layers were dried ($MgSO_4$), filtered and concentrated *in vacuo*. The residue was purified by flash column chromatography.

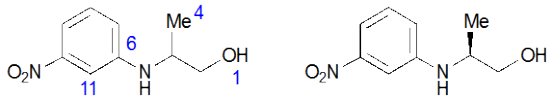
General procedure (e) Formation of an imidazolidin-2-one ring

Based on a literature procedure,[2] diisopropyl azodicarbonate (1.5 eq.) was added dropwise to a stirred solution of urea (1.0 eq.) and triphenylphosphane (1.5 eq.) in tetrahydrofuran (0.1 M). After stirring at room temperature for thirty minutes, the solution was concentrated *in vacuo*. The residue was purified by flash column chromatography.

General procedure (f) The synthesis of isocyanates from anilines

Aryl amine (1.0 eq.) was dissolved in dichloromethane (0.10 M) then water (0.10 M) and sodium bicarbonate (2.0 eq.) were added. Triphosgene (0.4 eq.) was added to the *vigorously* stirred solution. After 30 mins the aqueous and organic layers were separated, the aqueous layer extracted with dichloromethane (3 x 0.03 M) and the combined organic layers dried (Na_2SO_4). Following filtration the isocyanates were used immediately in the next step.

(±)- & (S)-2-((3-Nitrophenyl)amino)propan-1-ol (1)



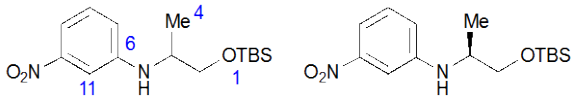
According to general procedure (a) 1-iodo-3-nitrobenzene and (±)-2-amino-propan-1-ol gave the title compound **± 1** (180 mg, 0.92 mmol, 76 %). Similarly (*S*)-2-amino-propan-1-ol gave the title compound **1** (1.18 g, 6.00 mmol, 75 %) also as a viscous deep orange oil; chromatography: 1 : 1, ethyl acetate : petrol; $[\alpha]_D^{25}$ + 9.1 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.48 (1H, ddd, *J* 8.1, 2.1, 0.8, H9), 7.40 (1H, dt, *J* 2.2, 1.1, H11), 7.24 (1H, dt, *J* 8.1, 1.1, H8), 6.89 (1H, ddd, *J* 8.2, 2.4, 0.8, H7), 4.14 (1H, br, H5), 3.74 (1H, dd, *J* 10.6, 4.1, H2), 3.67 (1H, m, H3), 3.59 (1H, dd, *J* 10.5, 5.2, H2'), 2.22 (1H, br, H1), 1.22 (3H, d, *J* 6.4, H4); δ_C (100 MHz, $CDCl_3$) 149.4 (C10), 148.4 (C6), 129.9 (C8), 119.6 (C7), 112.1 (C9), 107.0 (C11), 65.9 (C2), 50.4 (C3), 17.2 (C4); IR ν_{max} (CH_2Cl_2) 3399, 2968, 2872, 1621, 1526, 1347, 735; HRMS (ESI) found 195.0772, $C_9H_{11}N_2O_3$ $[M-H]^-$ requires 195.0775.

(±)-2-((3-Nitrophenyl)amino)propyl phenylcarbamate (6)

Phenyl isocyanate (17 µl, 0.16 mmol) and 4-dimethylaminopyridine (1.7 mg, 1.4 µmol) were added to a solution of 2-((3-nitrophenyl)amino)propan-1-ol **1** (28 mg, 0.14 mmol) in

dichloromethane (0.5 mL) and stirred at room temperature for 5 h. The reaction mixture was diluted with dichloromethane (10 mL), partitioned with ammonium chloride (10 mL), and extracted with dichloromethane (3 x 10 mL). The organic layers were dried ($MgSO_4$), filtered, and concentrated *in vacuo*. The residue was purified by flash column chromatography (19 : 1, petrol : Et_2O) to afford the title compound **6** (33 mg, 0.11 mmol, 73 %) as a viscous yellow oil; δ_H (400 MHz, $CDCl_3$) 7.50 (1H, dd, *J* 8.0, 2.0, H14), 7.45 (1H, t, *J* 2.2, H16), 7.37 – 7.35 (2H, br, m, H3), 7.32 – 7.27 (2H, m, H2), 7.25 (1H, t, *J* 8.1, H13), 7.07 (1H, t, *J* 7.2, H1), 6.90 (1H, dd, *J* 8.2, 2.3, H12), 6.75 (1H, br, H5), 4.31 (1H, dd, *J* 11.2, 6.1, H7), 4.19 (1H, d, *J* 7.9, H10), 4.13 (1H, dd, *J* 1.2, 4.8, H7'), 3.87 (1H, m, H8), 1.29 (3H, d, *J* 6.5, H9); δ_C (100 MHz, $CDCl_3$) 153.6 (C6), 149.5 (C15), 148.0 (C11), 137.6 (C4), 130.0 (C13), 129.2 (C2), 123.9 (C1), 119.1 (C12), 118.9, br (C3), 112.1 (C14), 106.9 (C16), 68.0 (C1), 48.3 (C2), 17.6 (C3); IR ν_{max} ($CHCl_3$) 3393, 2975, 1714, 1620, 1601, 1526, 1444, 1348, 1220, 1065, 757; HRMS (ESI) found 316.1295, $C_{16}H_{18}N_3O_4$ $[M+H]^+$ requires 316.1292.

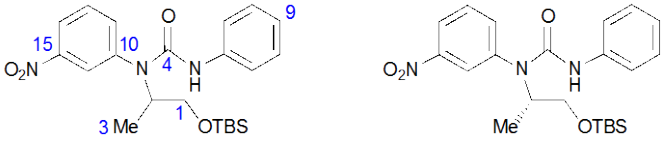
(±)- & (S)-N-(1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-3-nitroaniline (2)



According to general procedure (b) alcohol **± 1** was protected using TBSCl to give the title compound **± 2** (178 mg, 0.57 mmol, 93 %). Similarly alcohol **1** gave the title compound **2** (1.69 g, 5.44 mmol, 96 %) also as a yellow oil; chromatography: 19 : 1, petrol : ether; $[\alpha]_D^{25}$ – 12.5 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.48 (1H, dd, *J* 8.1, 2.2, H9), 7.39 (1H, t, *J* 2.2, H11), 7.25 (1H, t, *J* 8.1, H8), 6.85 (1H, dd, *J* 8.2, 2.4, H7), 4.20 (1H, br, H5), 3.71 – 3.69 (3H, m, H2, H3), 1.22 (3H, d, *J* 6.1, H4), 0.90 (9H, s, Si*t*-Bu), 0.06 (3H, s, SiMe), 0.04 (3H, s, SiMe); δ_C (100 MHz, $CDCl_3$) 149.6 (C10), 148.5 (C6), 129.8 (C8), 119.5 (C7), 111.8 (C9), 106.9 (C11), 66.2 (C2), 50.0 (C3), 26.0 (Si*t*-Bu), 18.4 (Si*t*-Bu), 17.3 (C4), – 5.3 (SiMe); IR

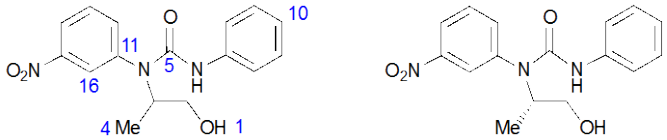
ν_{max} (CH_2Cl_2) 3407, 2955, 2930, 2857, 1623, 1529, 1471, 1347, 1255, 1107, 836, 778, 735; HRMS (ESI) found 311.1776, $C_{15}H_{27}N_2O_3Si$ $[M+H]^+$ requires 311.1785.

(±)- & (S)-1-(1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-1-(3-nitrophenyl)-3-phenylurea (3)



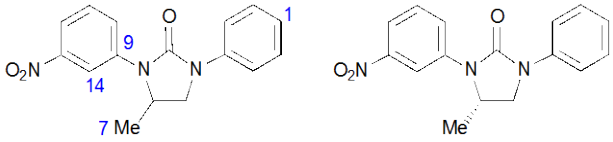
According to general procedure (c) secondary amine **± 2** and phenyl isocyanate gave starting material **± 2** (16 mg, 3.7 μmol, 9 %) and the title compound **± 3** (202 mg, 0.47 mmol, 82 %). Similarly amine **2** and phenyl isocyanate gave starting material **2** (117 mg, 0.38 mmol, 7 %) and the title compound **3** (2.17 g, 5.07 mmol, 93 %) also as a yellow oil; chromatography: 19 : 1 then 2 : 1, petrol : ether; $[\alpha]_D^{25}$ + 19.1 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.30 (1H, m, H15), 8.28 (1H, m, H13), 7.73 (1H, dt, *J* 7.9, 1.4, H11), 7.66 (1H, t, *J* 7.9, H12), 7.24 (2H, s, H7), 7.23 (2H, s, H8), 7.00 (1H, m, H9), 6.04 (1H, br, H5), 4.70 (1H, m, H2), 3.72 (1H, dd, *J* 10.8, 4.4, H1), 3.58 (1H, dd, *J* 10.8, 8.1, H1'), 1.11 (3H, d, *J* 7.0, H6), 0.90 (9H, s, Si*t*-Bu), 0.10 (3H, s, SiMe), 0.08 (3H, s, SiMe); δ_C (100 MHz, $CDCl_3$) 153.1 (C4), 149.2 (C14), 140.4 (Q Ar), 138.6 (Q Ar), 137.4 (C11), 130.5 (C12), 129.0 (C8), 126.0 (C15), 123.5, 123.4 (C13, C9), 120.0 (C7), 65.1 (C1), 54.7 (C2), 26.0 (Si*t*-Bu), 18.4 (Si*t*-Bu), 15.9 (C3), – 5.2 (SiMe), – 5.3 (SiMe); IR ν_{max} (CH_2Cl_2) 2954, 2929, 2857, 1664, 1527, 1440, 1349, 1316, 1240, 1102, 1081, 835, 777, 751, 691; HRMS (ESI) found 430.2145, $C_{22}H_{32}N_3O_4Si$ $[M+H]^+$ requires 430.2157.

(±)- & (S)-1-(1-Hydroxypropan-2-yl)-1-(3-nitrophenyl)-3-phenylurea (4)



According to general procedure (d) silyl ether **± 3** was deprotected to give the title compound **± 4** (631 mg, 2.00 mmol, 92 %). Similarly urea **3** gave the title compound **4** (1.30 g, 4.12 mmol, 65 %) also as a yellow oil. Chromatography: 7 : 1, ether : petrol to 20 : 1, ether : methanol; $[\alpha]_D^{25}$ – 21.0 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.27 (1H, d, *J* 8.16, H14), 8.21 (1H, t, *J* 1.9, H16), 7.73 (1H, d, *J* 7.9, H12), 7.64 (1H, t, 8.0, H13), 7.26 – 7.21 (4H, m, Ar-H), 7.07 – 7.03 (1H, m, H10), 6.18 (1H, s, H6), 4.76 – 4.67 (1H, m, H3), 3.67 (1H, dd, *J* 11.6, 3.9, H2), 3.34 (1H, t, *J* 10.5, H2'), 3.33 (1H, br, H1), 1.04 (3H, d, *J* 7.0, H4); δ_C (66 MHz, $CDCl_3$) 155.9 (C5), 149.5 (C15), 139.8 (Q Ar), 138.6 (Q Ar), 137.8 (H12), 131.3 (H13), 129.3 (H9), 126.3 (H16), 124.2 (C14/C10), 124.1 (C14/C10), 120.7 (C8), 65.3 (C2), 55.0 (C2), 16.0 (C4); IR ν_{max} ($CHCl_3$) 3403, 2976, 2933, 2876, 1656, 1596, 1527, 1442, 1350, 1326, 1240, 753, 692; HRMS (ESI) found 316.1285, $C_{16}H_{18}N_3O_4$ $[M+H]^+$ requires 316.1292.

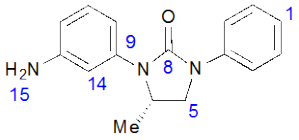
(±)- & (S)-4-Methyl-3-(3-nitrophenyl)-1-phenylimidazolidin-2-one (5)



According to general procedure (e) alcohol **± 4** was recrystallised from acetonitrile to give the title compound **± 5** (147 mg, 0.49 mmol, 71 %) as yellow powder, m.p. 163 – 165. Similarly alcohol **4** gave the title compound **5** (943 mg, 3.18 mmol, 79 %) also as a yellow powder, m.p. 179 – 181. Chromatography: 9 : 1, dichloromethane : petrol; $[\alpha]_D^{25}$ + 13.6 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.31 (1H, m, H11), 8.03 (1H, ddd, *J* 8.2, 1.3, 0.8, H14), 7.98 (1H, ddd, *J* 8.2, 1.3, 0.8, H10), 7.61 – 7.59 (2H, m, H3), 7.56 (1H, t, *J* 8.3, H11), 7.40 (2H, t, *J* 7.7, H2), 7.14 (1H, t, *J* 7.1, H1), 4.59 (1H, m, H6), 4.20 (1H, t, *J* 8.8, H5), 3.62 (1H, dd, 8.8, 5.3, H5'), 1.47 (3H, d, *J* 6.0, H7); δ_C (100 MHz, $CDCl_3$) 154.6 (C8), 148.8 (C13), 139.7 (Q Ar), 139.6 (Q Ar), 129.8 (C11), 129.1 (C2), 126.8 (C10), 123.7

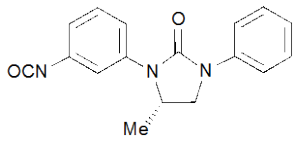
(C1), 118.4 (C3), 118.3 (C12), 114.9 (14), 49.9 (C5), 48.5 (C6), 19.2 (C7); IR ν_{max} ($CHCl_3$) 2988, 1700, 1598, 1526, 1503, 1480, 1402, 1345, 1273, 1219, 1165, 735, 690, 673; HRMS (ESI) found 298.1180, $C_{16}H_{16}N_3O_3$ $[M+H]^+$ requires 298.1186.

(S)-3-(3-Aminophenyl)-4-methyl-1-phenylimidazolidin-2-one (7)



Palladium on carbon (0.5 % Pd by weight) was added to a stirred solution of nitro compound **5** (943 mg, 3.18 mmol) in ethanol (10 mL). The solution was degassed, stirred overnight under an atmosphere of hydrogen and then filtered over Celite™. The solvent was removed *in vacuo*, leaving title compound **7** (840 mg, 3.15 mmol, 99 %) as a viscous brown oil; $[\alpha]_D^{25}$ + 20.1 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 7.59 (2H, dd, *J* 8.7, 1.0, H3), 7.35 (2H, dd, *J* 8.7, 7.5, H2), 7.14 (1H, t, *J* 8.0, H11), 7.07 (1H, tt, *J* 7.4, 1.01, H1), 6.98 (1H, t, *J* 2.1, H9), 6.72 (1H, ddd, *J* 8.1, 2.0, 0.7, H10), 6.46 (1H, ddd, *J* 8.0, 2.2, 0.7, H12), 4.36 (1H, m, H6), 4.03 (1H, t, *J* 8.8, H5), 3.71 (2H, br, H15), 3.48 (1H, dd, *J* 8.8, 5.8, H5), 1.35 (3H, d, *J* 6.1, H6); δ_C (100 MHz, $CDCl_3$) 155.3 (C8), 147.3 (C13), 140.3 (Q Ar), 139.2 (Q Ar), 129.6 (C11), 128.9 (C2), 122.8 (C1), 118.0 (C3), 111.7 (C10), 111.4 (C12), 109.4 (C14), 49.9 (C5), 48.9 (C6), 19.5 (C7); IR ν_{max} ($CDCl_3$) 3450, 2975, 1692, 1598, 1495, 1481, 1402, 1299, 1248, 908, 724, 689; HRMS (ESI) found 268.1440, $C_{16}H_{18}N_3O$ $[M+H]^+$ requires 268.1444.

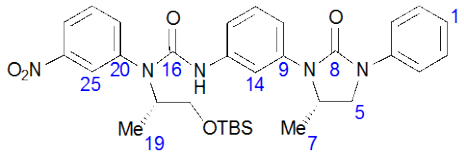
(S)-3-(3-Isocyanatophenyl)-4-methyl-1-phenylimidazolidin-2-one (8)



According to general procedure (f) aniline **7** gave the title compound **8** (821 mg, 2.80 mmol, 100 %) as a viscous grey-green oil; $[\alpha]_D^{25}$ + 18.0 (*c* 0.90, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.62 (1H, s), 7.59 (1H, s), 7.42 – 7.25 (5H, m), 7.00 (1H, t, *J* 7.3), 6.87 (1H, d, *J* 7.2), 4.48 – 4.35 (1H, m), 4.07 (1H, t, *J* 8.8), 3.51 (1H, dd, *J* 8.8, 5.5), 1.39 (3H, d, *J* 6.1); δ_C (66 MHz, $CDCl_3$)

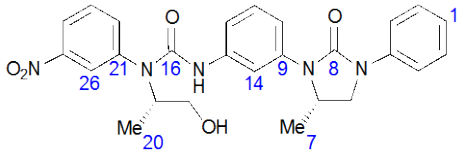
154.7 (C=O), 139.8, 139.4, 134.0, 129.8, 128.9, 124.7, 123.1 (NCO), 120.1, 118.1, 118.0, 117.8, 49.7, 48.5, 19.1; IR ν_{max} ($CDCl_3$) 3064, 2977, 2883, 2258, 1829, 1704, 1598, 1402, 1274, 1175, 935, 815, 754, 687.

1-((S)-1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea (9)



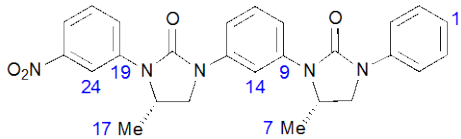
According to general procedure (c) isocyanate **8** and amine **2** gave the title compound **9** (665 mg, 1.10 mmol, 39 %) as a viscous yellow oil; chromatography: 4 : 1, ether : petrol; $[\alpha]_D^{25}$ + 29.1 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.26 (1H, t, *J* 1.9, H25), 8.24 (1H, dd, *J* 7.9, 2.1, 1.1, H23), 7.69 (1H, ddd, *J* 7.8, 1.6, 1.3, H21), 7.61 (1H, t, *J* 7.9, H22), 7.54 – 7.51 (2H, m, H3), 7.42 (1H, t, *J* 2.0, H14), 7.35 – 7.30 (2H, m, H2), 7.25 (1H, t, *J* 8.1, H11), 7.15 (1H, ddd, *J* 8.1, 1.9, 0.8, Ar-H), 7.06 (1H, dt, *J* 7.7, 1.0, H1), 7.04 (1H, dt, *J* 5.8, 1.0, Ar-H), 6.17 (1H, br, H15), 4.74 – 4.66 (1H, m, H18), 4.45 – 4.36 (1H, m, H6), 4.04 (1H, t, *J* 8.8, H5), 3.69 (1H, dd, *J* 10.8, 4.5, H17), 3.55 (1H, dd, *J* 10.8, 8.0, H17'), 3.48 (1H, dd, *J* 8.8, 5.9, H5'), 1.34 (3H, d, *J* 6.1, H7), 1.09 (3H, d, *J* 7.0, H19), 0.89 (9H, s, Si*t*-Bu), 0.09, 0.07 (3H, s, SiMe); δ_C (100 MHz, $CDCl_3$) 155.2 (C=O), 154.1 (C=O), 149.1 (C24), 140.1 (Q Ar), 140.0 (Q Ar), 139.4 (Q Ar), 138.6 (Q Ar), 137.4 (C21), 130.6 (C22), 129.2 (C2), 128.9 (C11), 126.1 (C25), 123.5 (C23), 123.0 (C1), 118.0 (C3), 116.6 (Ar), 116.1 (Ar), 113.8 (C14), 65.0 (C17), 54.6 (C18), 49.9 (C5), 48.9 (C6), 26.0 (C17), 19.4 (C7), 18.4 ($SiCMe_3$), 15.8 ($SiCMe_3$), – 5.3 (SiMe), – 5.4 (SiMe); IR ν_{max} ($CDCl_3$) 3336, 2955, 2930, 2857, 1697, 1674, 1600, 1530, 1492, 1407, 1350, 1241, 837, 755, 691; HRMS (ESI) found 626.2758, $C_{32}H_{41}N_5NaO_5Si$ $[M+Na]^+$ requires 626.2769.

1-((S)-1-Hydroxypropan-2-yl)-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea (10)



According to general procedure (d) silyl alcohol **9** gave the title compound **10** (451 mg, 0.92 mmol, 96 %) as a viscous yellow oil; chromatography 50 : 1, dichloromethane : methanol; $[\alpha]_D^{25}$ – 27.5 (*c* 0.80, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.12 (1H, t, *J* 1.9, H26), 8.10 (1H, ddd, *J* 8.1, 2.1, 0.9, H24), 7.64 (1H, ddd, *J* 7.7, 1.7, 1.1, H22), 7.51 (1H, t, *J* 8.1, H23), 7.46 – 7.43 (2H, m, H3), 7.42 (1H, t, *J* 2.0, H14), 7.34 – 7.30 (2H, m, H2), 7.27 (1H, t, *J* 3.9, H11), 7.20 (1H, ddd, *J* 8.2, 1.8, 1.0), 7.06 (1H, tt, *J* 7.4, 1.1, H1), 6.98 (1H, ddd, *J* 8.0, 1.8, 1.0), 6.59 (1H, br, H15), 4.56 – 4.48 (1H, m, H19), 4.40 – 4.31 (1H, m, H6), 4.02 (1H, t, *J* 8.9, H5), 3.65 (1H, dt, *J* 11.5, 3.8, H18), 3.60 – 3.52 (1H, m, H18'), 3.49 – 3.47 (1H, m, H17), 3.44 (1H, dd, *J* 8.8, H5'), 1.32 (3H, d, *J* 6.1, H7), 1.10 (3H, d, *J* 7.0, H20); δ_C (100 MHz, $CDCl_3$) 155.4 (C=O), 155.1 (C=O), 149.0 (C25), 140.4 (Q Ar), 140.0 (Q Ar), 139.4 (Q Ar), 138.4 (Q Ar), 137.1 (C22), 130.7 (23), 129.2 (C11), 128.9 (C2), 125.6 (C26), 123.3 (C24), 123.0 (Ar), 117.9 (C3), 116.8 (Ar), 116.3 (C1), 114.8 (C14), 64.6 (C18), 56.3 (C19), 49.9 (C5), 48.8 (C6), 19.4 (C8), 15.5 (C20); IR ν_{max} ($CDCl_3$) 3326, 2976, 2933, 2878, 1692, 1662, 1599, 1527, 1489, 1406, 1349, 1295, 1240, 909, 729, 691; HRMS (ESI) found 512.1888, $C_{26}H_{27}N_5NaO_5$ $[M+Na]^+$ requires 512.1904.

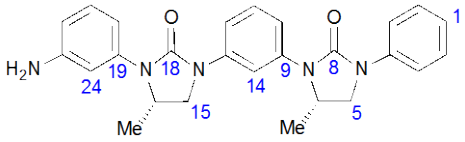
(S)-4-Methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-3-(3-nitrophenyl)imidazolidin-2-one (11)



According to general procedure (e) alcohol **10** was recrystallized from acetonitrile to give the title compound **11** (267 mg, 0.57 mmol, 58 %) as white crystals, m.p. 208 (decomposition); chromatography: 8 : 1, ether : petrol; $[\alpha]_D^{25}$ + 8.6 (*c* 1.00, $CHCl_3$); δ_H (400 MHz, $CDCl_3$) 8.32

(1H, t, *J* 2.1, H24), 7.96 (2H, m, H22, H20), 7.90 (1H, t, *J* 2.0, H14), 7.60 – 7.57 (2H, m, H3), 7.53 (1H, t, *J* 8.2, H21), 7.40 – 7.34 (4H, m, Ar-H), 7.20 (1H, dt, *J* 7.2, Ar-H), 7.08 (1H, tt, *J* 7.4, 1.0, H1), 4.58 – 4.47 (2H, m, $NCH_2C\underline{H}CH_3$), 4.18 (1H, t, *J* 8.9, $NC\underline{H}_2CHCH_3$), 4.09 (1H, t, *J* 8.5, $NC\underline{H}_2CHCH_3$), 3.62 (1H, dd, *J* 9.0, 5.4, $NC\underline{H}_2CHCH_3$), 3.53 (1H, dd, *J* 8.9, 5.8, $NC\underline{H}_2CHCH_3$), 1.43 (3H, d, *J* 5.9, $NCH_2CHC\underline{H}_3$), 1.41 (3H, d, *J* 6.0, $NC\underline{H}_2CHC\underline{H}_3$); δ_C (100 MHz, $CDCl_3$) 155.2 (C=O), 154.6 (C=O), 148.8 (C23), 140.3 (Q Ar), 140.1 (Q Ar), 139.6 (Q Ar), 139.0 (Q Ar), 129.8 (C21), 129.3 (Ar), 129.0 (C2), 126.9 (C20), 123.1 (C1), 118.4 (C22), 118.2 (C3), 116.2 (Ar), 115.2 (C24), 113.8 (Ar), 111.6 (C14), 59.0, 49.9 (C5, C15) 48.8, 48.5 (C6, C16), 19.4, 19.2 (C7, C17); IR ν_{max} ($CHCl_3$) 2976, 2881, 1703, 1599, 1529, 1498, 1482, 1458, 1401, 1378, 1269, 749; HRMS (ESI) found 494.1793, $C_{26}H_{25}N_5NaO_4$ $[M+Na]^+$ requires 494.1799.

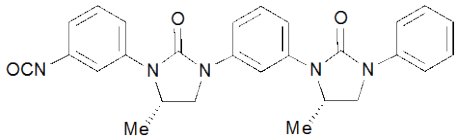
(S)-3-(3-Aminophenyl)-4-methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)imidazolidin-2-one (12)



Nitro aromatic **11** (141 mg, 0.30 mmol) was dissolved in a mixture of toluene (5 mL) and ethanol (3 mL) and a drop of acetic acid was added. Palladium on carbon (0.9 % Pd by weight) was added and the reaction was stirred under hydrogen for three hours. The palladium was removed using Celite™ and then purification with flash column chromatography was performed (50 : 1, dichloromethane : methanol) giving the title product **12** (117 mg, 0.26 mmol, 89 %) as a viscous brown oil; $[\alpha]_D^{25}$ + 8.2 (*c* 0.85, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 7.89 (1H, m, H14), 7.60 – 7.56 (2H, m, H3), 7.38 – 7.34 (4H, m, H2, H12, H10), 7.32 – 7.20 (1H, m, H11), 7.14 (1H, t, *J* 8.0, H21), 7.08 (1H, tt, *J* 7.4, 1.10, H1), 6.96 (1H, t, *J* 2.1, H24), 6.71 (1H, ddd, *J* 8.0, 2.1, 0.7, H22), 6.48 (1H, ddd, *J* 7.9, 2.2, 0.6, H20), 4.53 – 4.47 (1H, m $NCH_2C\underline{H}CH_3$), 4.42 – 4.35 (1H, m, $NCH_2C\underline{H}CH_3$), 4.09 (1H, t, *J* 8.8, $NC\underline{H}_2CHCH_3$), 4.08

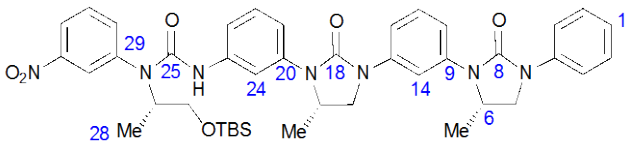
(1H, t, *J* 8.7, NC<u>H</u>$_2$CHCH$_3$), 3.72 (2H, br, H25), 3.55 (1H, dd, *J* 8.8, 5.8, NC<u>H</u>$_2$CHCH$_3$), 3.52 (1H, dd, *J* 8.7, 5.7, NC<u>H</u>$_2$CHCH$_3$), 1.40 (3H, d, *J* 6.1, NCH$_2$CHC<u>H</u>$_3$), 1.36 (1H, d, *J* 6.1, NCH$_2$CHC<u>H</u>$_3$); δ_C (125 MHz, $CDCl_3$) 155.3 (C=O), 155.3 (C=O), 147.3 (Q Ar), 141.0 (Q Ar), 140.2 (Q Ar), 139.1 (Q Ar), 138.9 (Q Ar), 138.2 (Q Ar), 129.8 (Ar), 129.2 (C21), 129.0 (C2), 123.0 (C1), 118.2 (C3), 116.0 (C11), 113.5 (Ar), 112.0 (C22), 111.6 (C20), 111.3 (C14), 109.6 (C24), 50.0, 50.0, (C5, C15), 49.0, 48.9 (C6, C16), 19.5, 19.5 (C7, C17); IR ν_{max} ($CHCl_3$) 3359, 2975, 2932, 2877, 2245, 1694, 1599, 1493, 1481, 1398, 1378, 1263, 908, 725, 689; HRMS (ESI) found 464.2046, $C_{26}H_{27}N_5NaO_2$ $[M+Na]^+$ requires 464.2057.

(S)-3-(3-Isocyanatophenyl)-4-methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)imidazolidin-2-one (13)



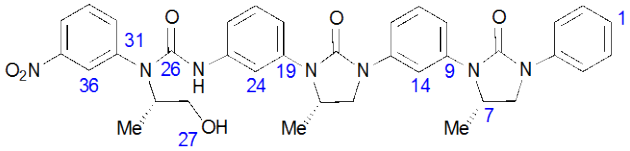
According to general procedure (f) aniline **12** gave the title compound **13** (110 mg, 0.24 mmol, 91 %) as a pale brown oil; $[\alpha]_D^{25}$ + 14.4 (*c* 0.25, $CHCl_3$); δ_H (250 MHz, $CDCl_3$) 7.91 (1H, s, Ar-H), 7.63 – 7.59 (2H, m, Ar-H), 7.41 – 7.21 (8H, m, Ar-H), 7.10 (1H, t, *J* 7.3, Ar-H), 6.87 (1H, d, *J* 7.5, Ar-H), 4.56 – 4.34 (2H, m, H6, H16), 4.15 – 4.03 (2H, m, H5, H15), 3.60 – 3.49 (2H, m, H5', H15'), 1.41 (3H, d, *J* 6.2, CH_3), 1.38 (3H, d, *J* 6.1, CH_3); δ_C (66 MHz, $CDCl_3$) 155.6, 155.2, 140.9, 140.5, 139.8, 139.3, 134.5, 130.2, 129.6, 129.3, 125.1, 123.4, 120.7, 118.8, 118.5, 118.5, 116.4, 113.9, 111.7, 50.3, 50.2, 49.1, 49.0, 19.8, 19.6; IR ν_{max} ($CHCl_3$) 2977, 2933, 2881, 2265, 1703, 1599, 1497, 1481, 1458, 1401, 1378, 1269, 755.

1-((S)-1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-3-(3-((S)-5-methyl-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-2-oxoimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea (14)



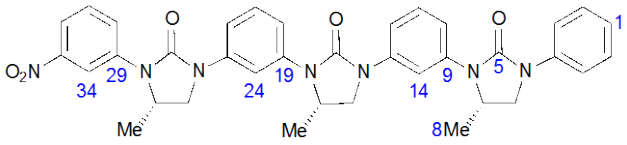
According to general procedure (c) amine **2** and isocyanate **13** gave the title compound **14** (117 mg, 0.15 mmol, 67 %) as a yellow oil; chromatography: 5 : 1, ether : petrol; $[\alpha]_D^{25}$ + 25.0 (*c* 0.75, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 8.27 – 8.24 (2H, m, H34, H32), 7.83 (1H, m, H24), 7.69 (1H, d, *J* 7.9, H30), 7.61 (1H, t, *J* 8.0, H31), 7.58 – 7.56 (2H, m, H3), 7.40 (1H, t, *J* 1.8, H14), 7.37 – 7.28 (4H, m, Ar-H), 7.27 – 7.23 (1H, m, Ar-H), 7.19 (1H, dt, *J* 7.6, 1.7, Ar-H), 7.16 (1H, d, *J* 8.1, Ar-H), 7.09 – 7.05 (2H, m, Ar-H), 6.16 (1H, br, H25), 4.73 – 4.67 (1H, m, H27), 4.49 – 4.43 (1H, m, NC<u>H</u>CH_2CH_3), 4.42 – 4.37 (1H, m, NC<u>H</u>CH_2CH_3), 4.07 (1H, t, *J* 8.8, NCHC<u>H</u>$_2CH_3$), 4.06 (1H, t, *J* 8.7, NCHC<u>H</u>$_2CH_3$), 3.69 (1H, dd, *J* 10.8, 4.4, H26), 3.56 – 3.49 (3H, m, H26, NCHC<u>H</u>$_2CH_3$, NCHC<u>H</u>$_2CH_3$), 1.38 (3H, d, *J* 6.1, NCHCH_2C<u>H</u>$_3$), 1.33 (3H, d, *J* 6.2, NCHCH_2C<u>H</u>$_3$), 1.09 (3H, d, *J* 7.0, H28), 0.89 (9H, s, Si*t*-Bu), 0.08 (3H, s, SiMe), 0.07 (3H, s, SiMe); δ_C (125 MHz, $CDCl_3$) 155.2, 155.2 (C=O), 154.1 (C25), 149.1 (C29), 140.8 (C19), 140.2, (Q Ar) 140.1 (C4), 139.4 (Q Ar), 138.8 (C23), 138.5 (Q Ar), 137.4 (C26), 130.6 (C31) 129.3 (Ar), 129.2 (Ar), 129.0 (C2), 126.1 (C26), 123.5 (C32), 123.0 (Ar), 118.2 (C3), 116.8 (Ar), 116.2 (Ar), 116.1 (Ar), 113.9 (C14), 113.5 (Ar), 111.4 (C24), 65.0 (C26), 54.5 (C27), 50.0, 50.0 (C5, C15), 49.0, 48.8 (C6, C16), 26.0 (Si*t*-Bu), 19.4, 19.4 (C7, C17), 18.4 (Si*t*-Bu), 15.9 (C28), – 5.3, – 5.5 (SiMe); IR ν_{max} ($CHCl_3$) 3338, 2955, 2939, 2857, 1702, 1600, 1530, 1493, 1458, 1402, 1350, 1298, 1270, 838, 778, 754, 691; HRMS (ESI) found 800.3561, $C_{42}H_{51}N_7NaO_6Si$ $[M+Na]^+$ requires 800.3562.

1-((S)-1-Hydroxypropan-2-yl)-3-(3-((S)-5-methyl-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-2-oxoimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea (15)



According to general procedure (d) silyl alcohol **14** gave the title compound **15** (53 mg, 8.0 μmol, 79 %) as a viscous pale yellow oil; chromatography 50 : 1, dichloromethane : methanol; $[\alpha]_D^{25}$ + 3.5 (*c* 1.00, $CHCl_3$); δ_H (500 MHz, $CDCl_3$) 8.11 (2H, m, H36, H34), 7.74 (1H, t, *J* 1.8, H24), 7.61 (1H, dt, *J* 7.9, 1.5, H32), 7.56 – 7.53 (2H, m, H3), 7.47 (1H, t, *J* 8.4, H33), 7.41 (1H, t, *J* 1.7, H14), 7.37 – 7.33 (2H, m, H2), 7.32 – 7.27 (2H, m,), 7.23 (1H, d, *J* 8.8), 7.19 (1H, dd, *J* 7.6, 1.6), 7.17 (1H, dd, *J* 7.6, 1.4) 7.08 (1H, tt, *J* 7.4, 1.0, H1), 6.96 (1H, d, *J* 7.9), 6.60 (1H, br, H25), 4.51 – 4.44 (1H, m, H29), 4.36 – 4.27 (2H, m, $NCH_2C\underline{H}CH_3$), 4.03 (1H, t, *J* 8.9, $NC\underline{H}_2CHCH_3$), 3.98 (1H, t, 8.7, $NC\underline{H}_2CHCH_3$), 3.65 – 3.54 (2H, m, H29, $NC\underline{H}_2CHCH_3$), 3.46 (1H, dd, *J* 8.8, 5.7, $NC\underline{H}_2CHCH_3$), 3.46 (1H, dd, *J* 8.9, 5.8, $NC\underline{H}_2CHCH_3$), 3.40 (1H, br, H27), 1.30 (3H, d, *J* 6.1, $NCH_2CHC\underline{H}_3$), 1.27 (3H, d, *J* 6.1, $NCH_2CHC\underline{H}_3$), 1.10 (3H, d, *J* 7.0, H30); δ_C (125 MHz, $CDCl_3$) 155.4 (C=O), 155.3 (C=O), 155.0 (C26), 149.0 (C35), 140.6 (C19), 140.6 (Q Ar), 140.1 (C31), 139.4 (C4), 138.8 (C23), 138.3 (Q Ar), 137.0 (C32), 130.6 (Ar), 129.2 (Ar), 129.2 (Ar), 129.0 (C2), 125.6 (C36), 123.2 (C34), 123.1 (C1), 118.2 (C3), 116.9 (Ar), 116.3 (Ar), 116.2 (Ar), 114.8 (C14), 113.3 (Ar), 111.4 (C24), 64.5 (C28), 56.6 (C29), 50.0, 49.8 (C15, C5), 48.9, 48.6 (C6, C16), 19.3, 19.3 (C7, C17), 15.5 (C30); IR ν_{max} ($CHCl_3$) 3337, 2976, 2932, 2877, 1698, 1600, 1530, 1492, 1403, 1380, 1350, 1316, 1270, 1243, 753, 691; HRMS (ESI) found 686.2703, $C_{36}H_{37}N_7NaO_6$ $[M+Na]^+$ requires 686.2698.

(S)-4-Methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-3-(3-((S)-4-methyl-3-(3-nitrophenyl)-2-oxoimidazolidin-1-yl)phenyl)imidazolidin-2-one (16)



According to general procedure (e) alcohol **15** gave the title compound **16** (20 mg, 3.1 μmol, 54 %) as a pale cream powder, m.p. 294 – 295; chromatography: 6 : 1, ether : petrol and then 100 : 1, dichloromethane : methanol; $[\alpha]_D^{25}$ – 20.0 (*c* 0.35, pyridine); δ_H (500 MHz, pyridine-d_5) 8.45 (1H, t, *J* 2.2, H34), 8.45 (1H, s, H14), 8.39 (1H, s, H24), 7.97 (1H, t, *J* 2.2, H32/30), 7.96 (1H, t, *J* 2.2, H32/30), 7.91 (2H, s, *J* 7.9, H3), 7.66-7.61 (2H, m, H22, H12), 7.54-7.46 (5H, m, H10, H11, H20, H21, H31), 7.44 (1H, t, *J* 8.0, H1), 4.53-4.45 (2H, m, H27, H17), 4.45-4.39 (1H, m, H7), 4.10 (1H, t, *J* 9.0, H26a), 4.03 (1H, t, *J* 8.8, H16a), 3.91 (1H, t, *J* 9.0, H6a), 3.54 (1H, dd, *J* 9.0, 5.0, H26b), 3.50 (1H, dd, *J* 8.8, 6.0, H16b), 3.36 (1H, dd, *J* 9.0, 5.7, H6b), 1.28 (3H, d, *J* 6.3, H18), 1.27 (3H, d, *J* 6.3, H8), 1.22 (3H, d, *J* 6.0, H28); δ_C (125 MHz, pyridine-d_5) 155.7 (C15, C5), 155.1 (C25), 149.5 (C33), 142.1, 141.6, 141.6, 140.8, 140.2, 140.1 (C29, C23, C19, C13, C9, C4), 130.4 (C31/C21), 129.9 (C11), 129.8 (C31/C21), 129.6 (C2), 126.6 (C30), 123.3 (C1), 118.7 (C3), 118.4 (C32), 117.1 (C20), 116.7 (C10), 116.0 (C34), 114.5 (C22), 114.2 (C12), 112.9 (C24), 112.7 (C14), 50.3 (C16), 50.2 (C26), 50.2 (C6), 49.3 (C22, C17), 48.8 (C7), 19.6 (C18/C8), 19.5 (C18/C8), 19.1 (C28); IR ν_{max} 1695, 1600, 1524, 1499, 1483, 1460, 1411, 1377, 1355, 1278, 1231, 781, 754, 673; HRMS (ESI) found 668.2602, $C_{36}H_{35}N_7NaO_5$ $[M+Na]^+$ requires 668.2592.

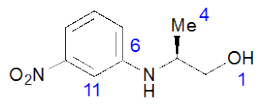
3. References

[1] H. Zhang, Q. Cai, and D. Ma, “Amino Acid Promoted CuI-Catalyzed C−N Bond Formation between Aryl Halides and Amines or N-Containing Heterocycles,” *J. Org. Chem.*, vol. 70, no. 13, pp. 5164–5173, 2005.

[2] T. H. Kim, G.-J. Lee, and M.-H. Cha, “Investigation of the Mitsunobu Reaction of N-(2-Hydroxyethyl)-N′-Phenyl-Ureas,” *Synthetic Communications*, vol. 29, no. 16, pp. 2753–2758, 1999.

4. NMR Spectra

2-((3-Nitrophenyl)amino)propan-1-ol: 1

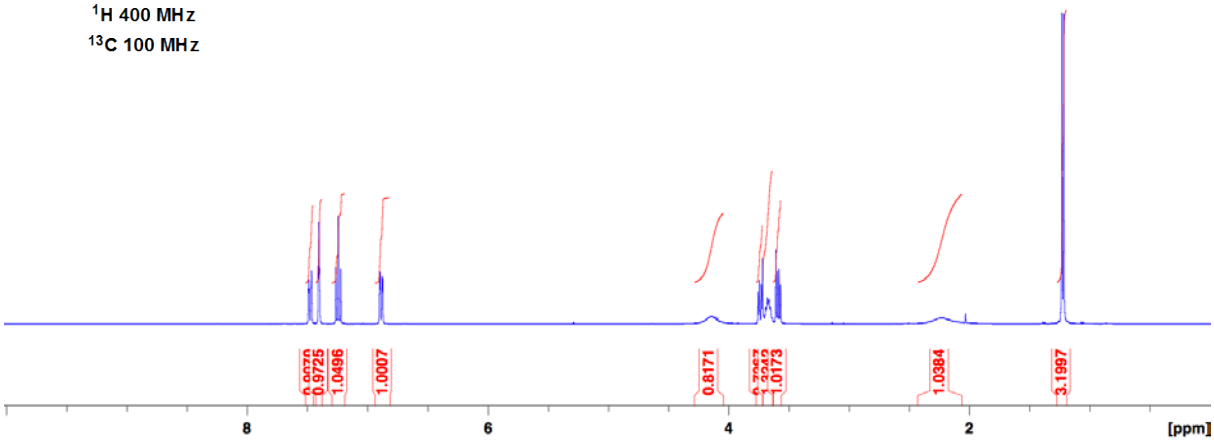


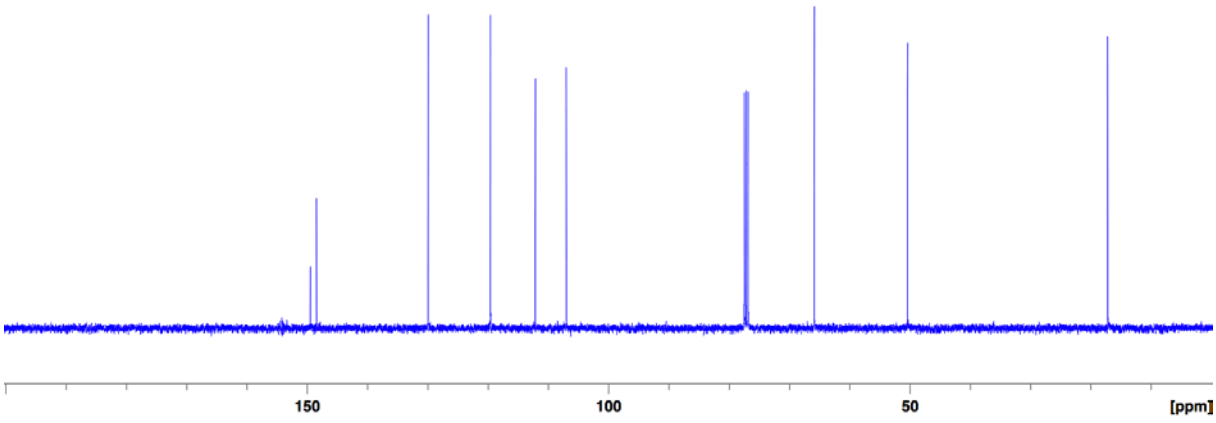
1

$CDCl_3$

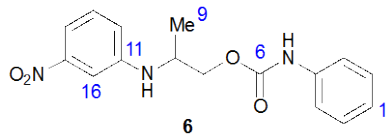
^1H 400 MHz

^{13}C 100 MHz





2-((3-Nitrophenyl)amino)propyl phenylcarbamate: 6

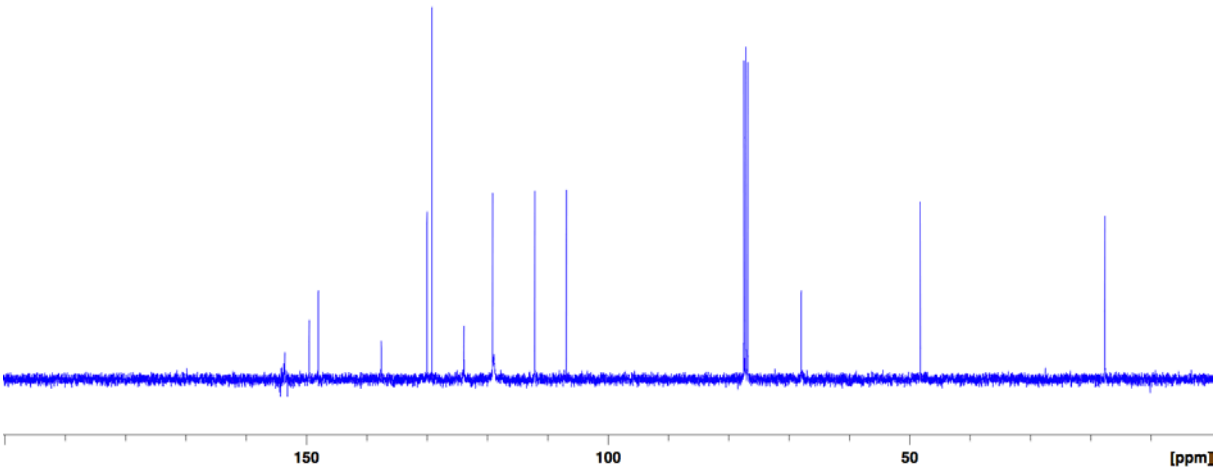


6

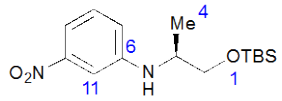
$CDCl_3$

^1H 400 MHz

^{13}C 100 MHz



N-(1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-3-nitroaniline: 2

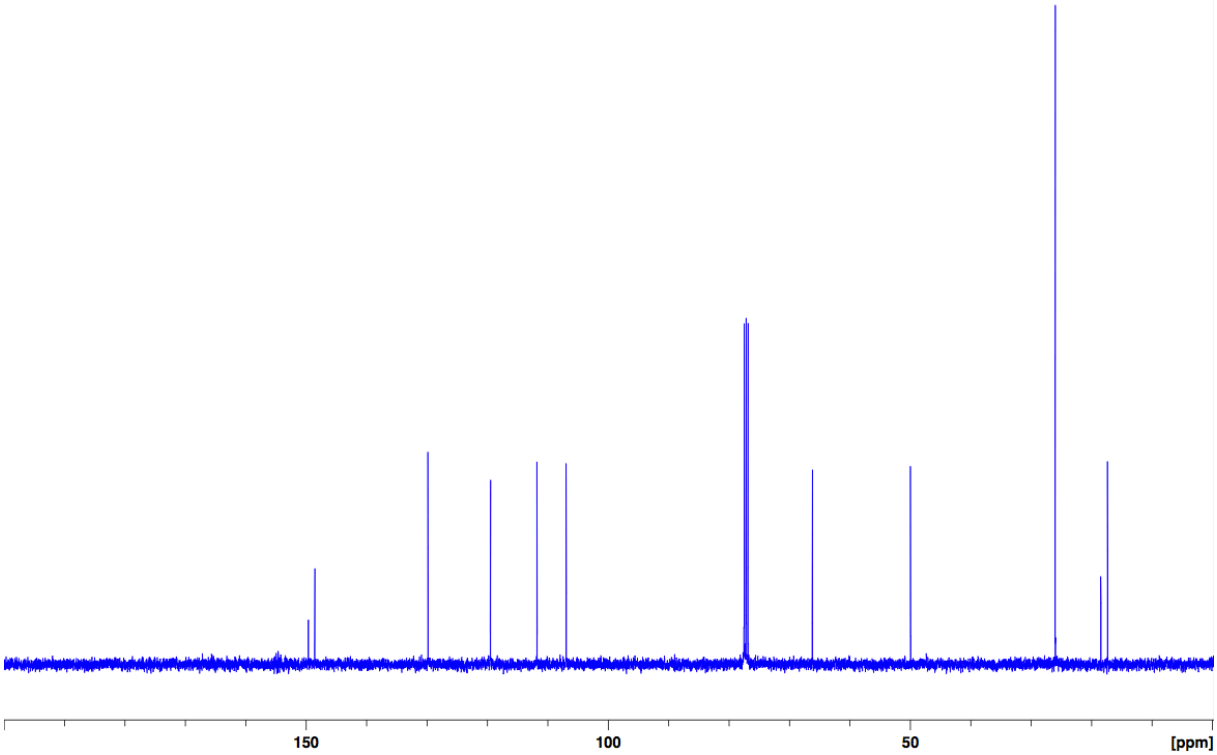


2

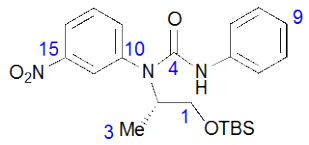
$CDCl_3$

^1H 400 MHz

^{13}C 100 MHz



1-(1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-1-(3-nitrophenyl)-3-phenylurea: 3

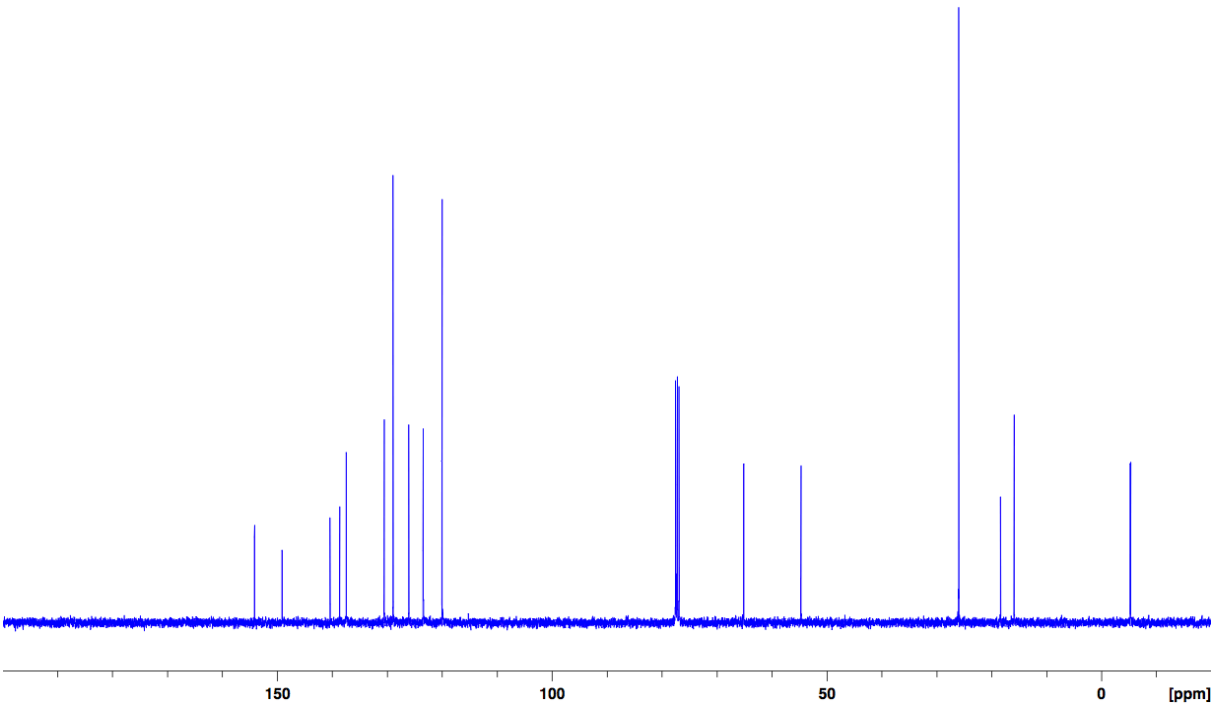


3

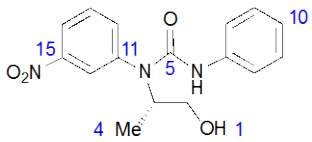
$CDCl_3$

^{1}H 400 MHz

^{13}C 100 MHz



1-(1-Hydroxypropan-2-yl)-1-(3-nitrophenyl)-3-phenylurea: 4

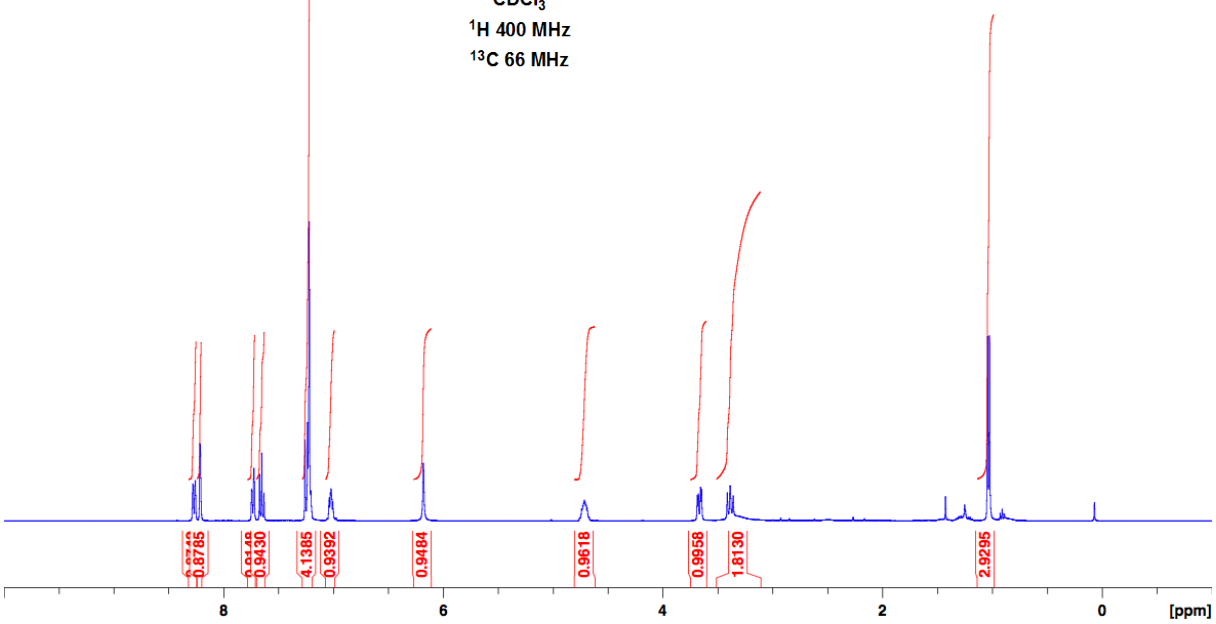


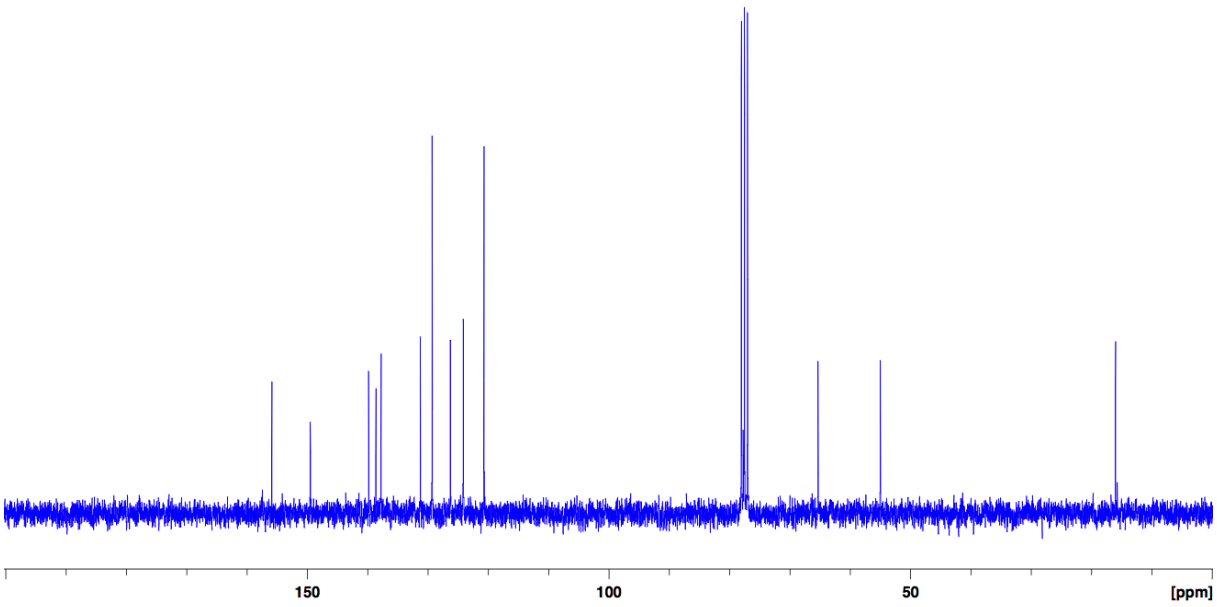
4

$CDCl_3$

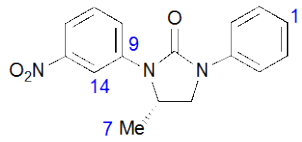
^1H 400 MHz

^{13}C 66 MHz





4-Methyl-3-(3-nitrophenyl)-1-phenylimidazolidin-2-one: 5

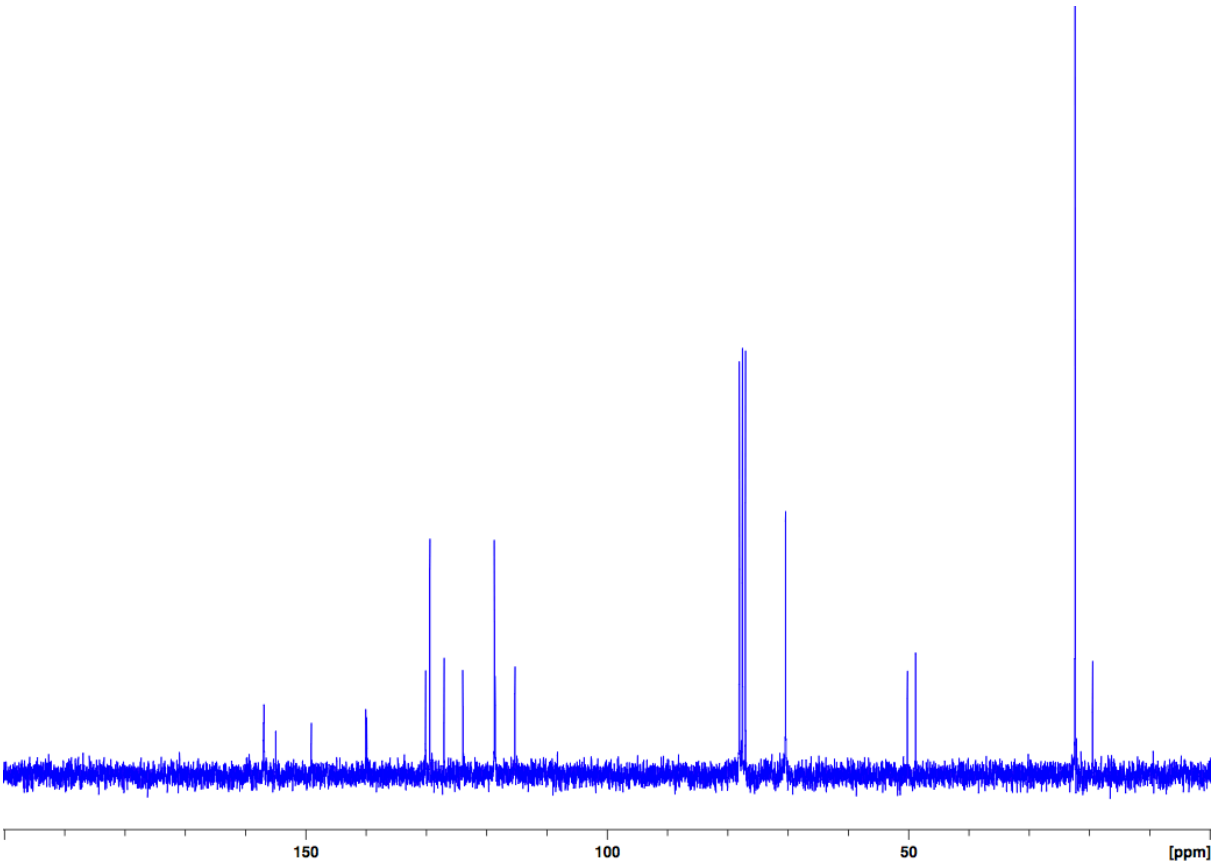


5

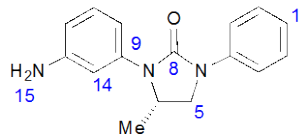
$CDCl_3$

^1H 400 MHz

^{13}C 100 MHz



(S)-3-(3-Aminophenyl)-4-methyl-1-phenylimidazolidin-2-one: 7

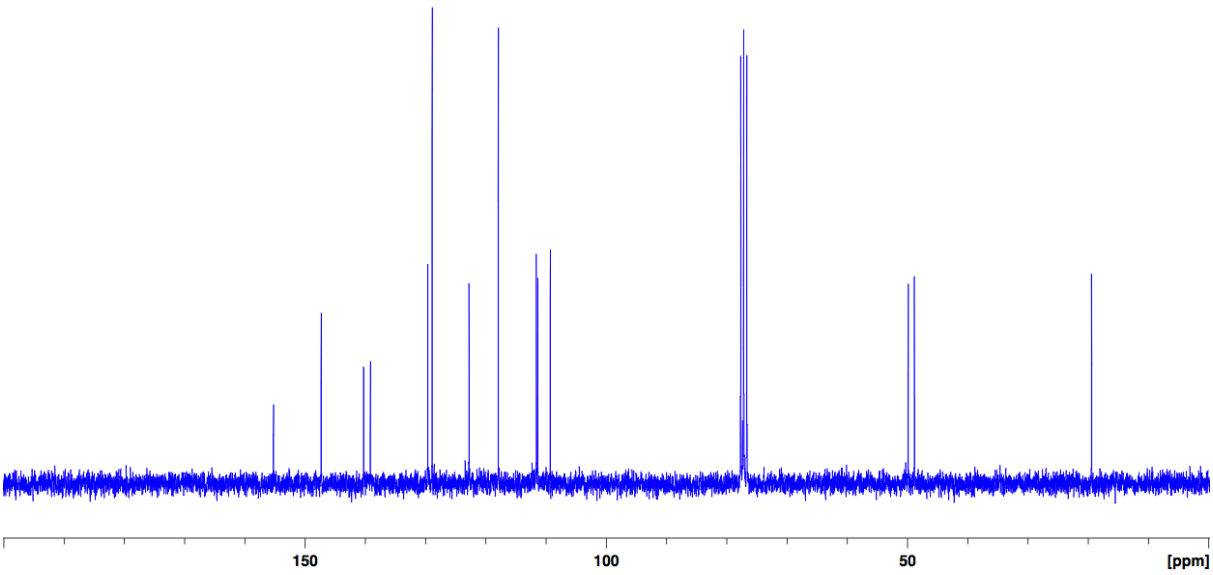


7

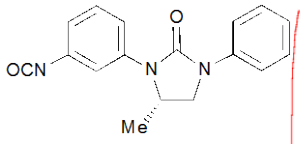
$CDCl_3$

^{1}H 400 MHz

^{13}C 100 MHz



(S)-3-(3-Isocyanatophenyl)-4-methyl-1-phenylimidazolidin-2-one: 8

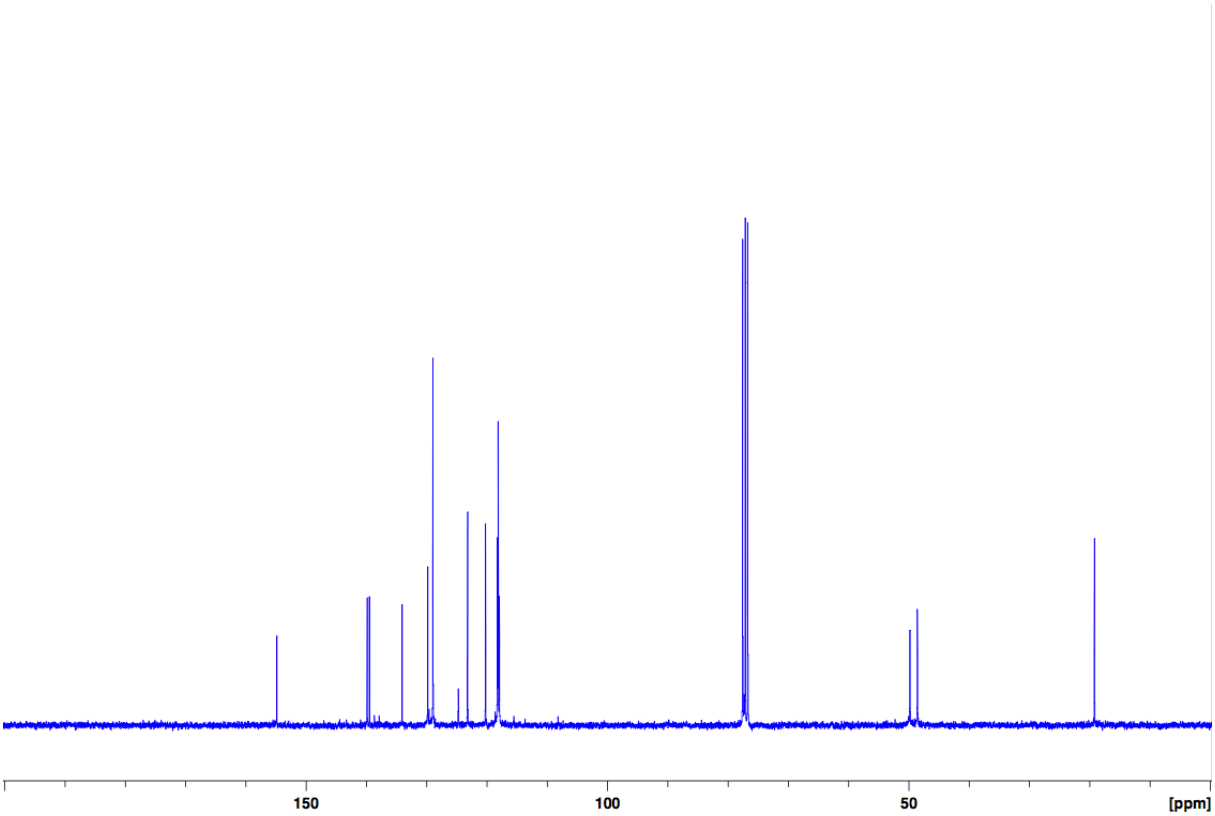


8

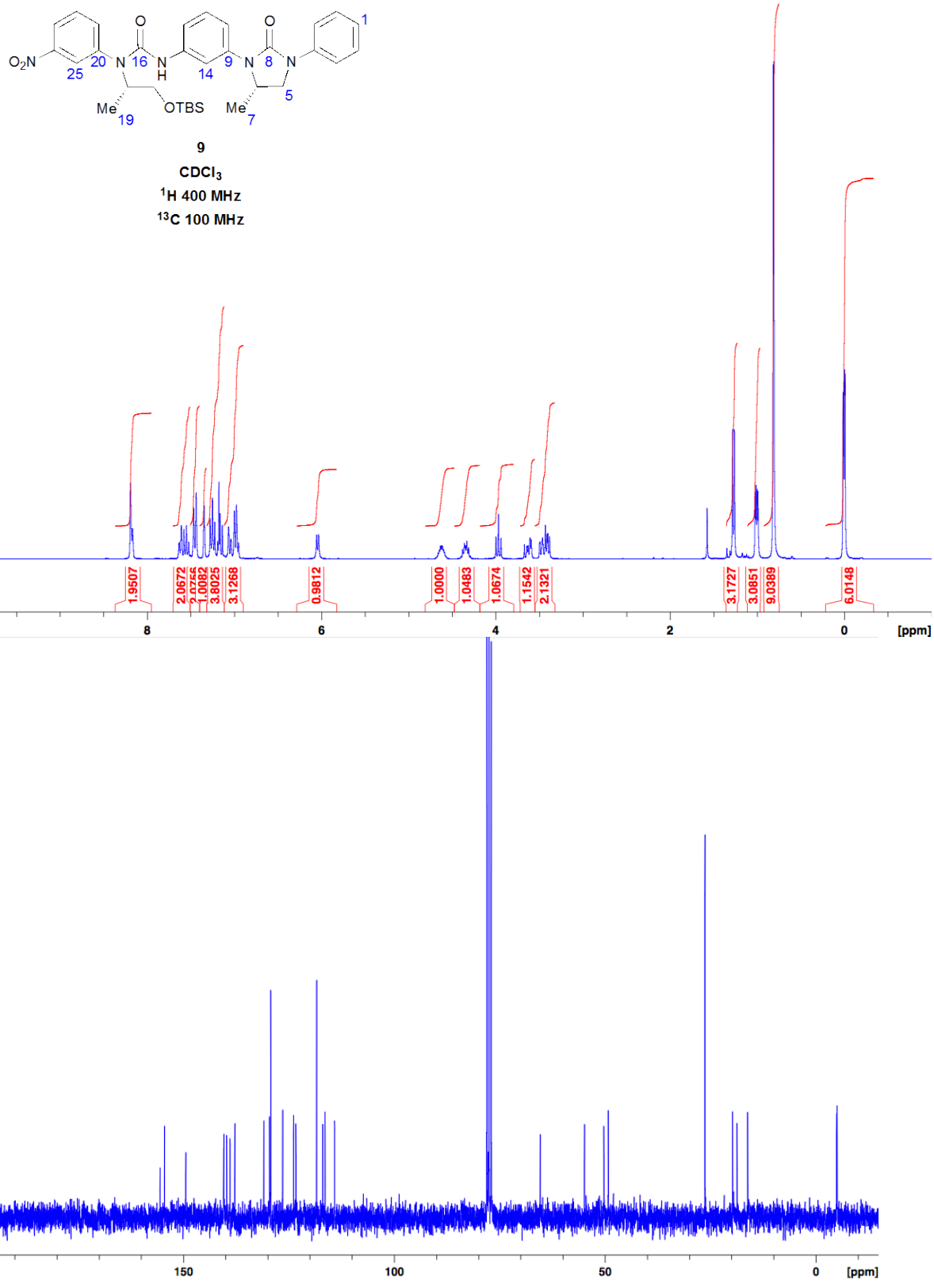
$CDCl_3$

^{1}H 250 MHz

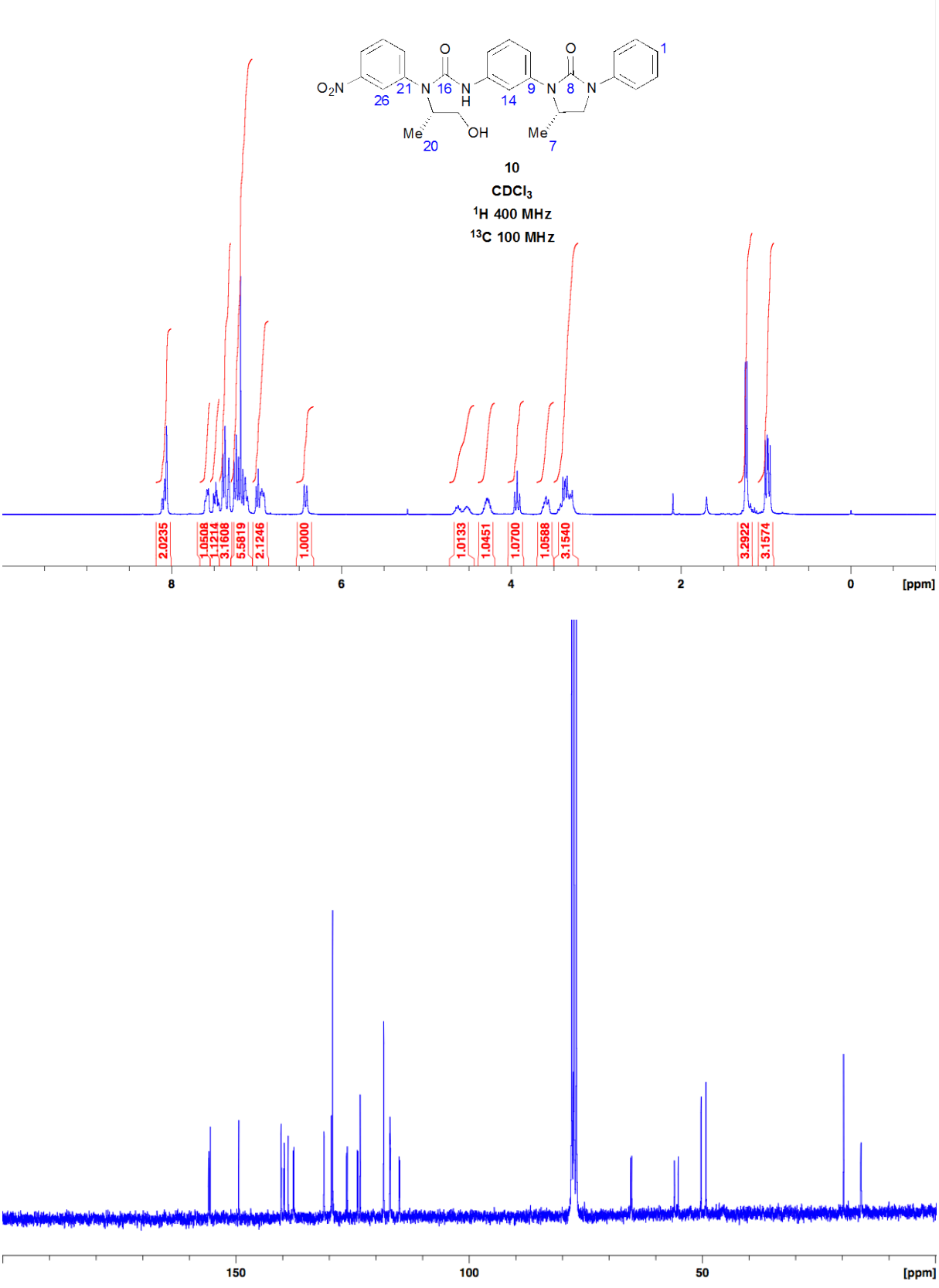
^{13}C 66 MHz



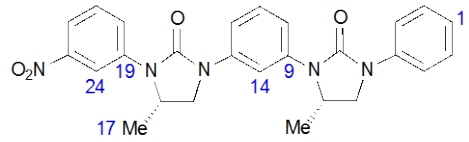
1-((S)-1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea: 9



1-((S)-1-Hydroxypropan-2-yl)-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea: 10



(S)-4-Methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-3-(3-nitrophenyl)imidazolidin-2-one: 11

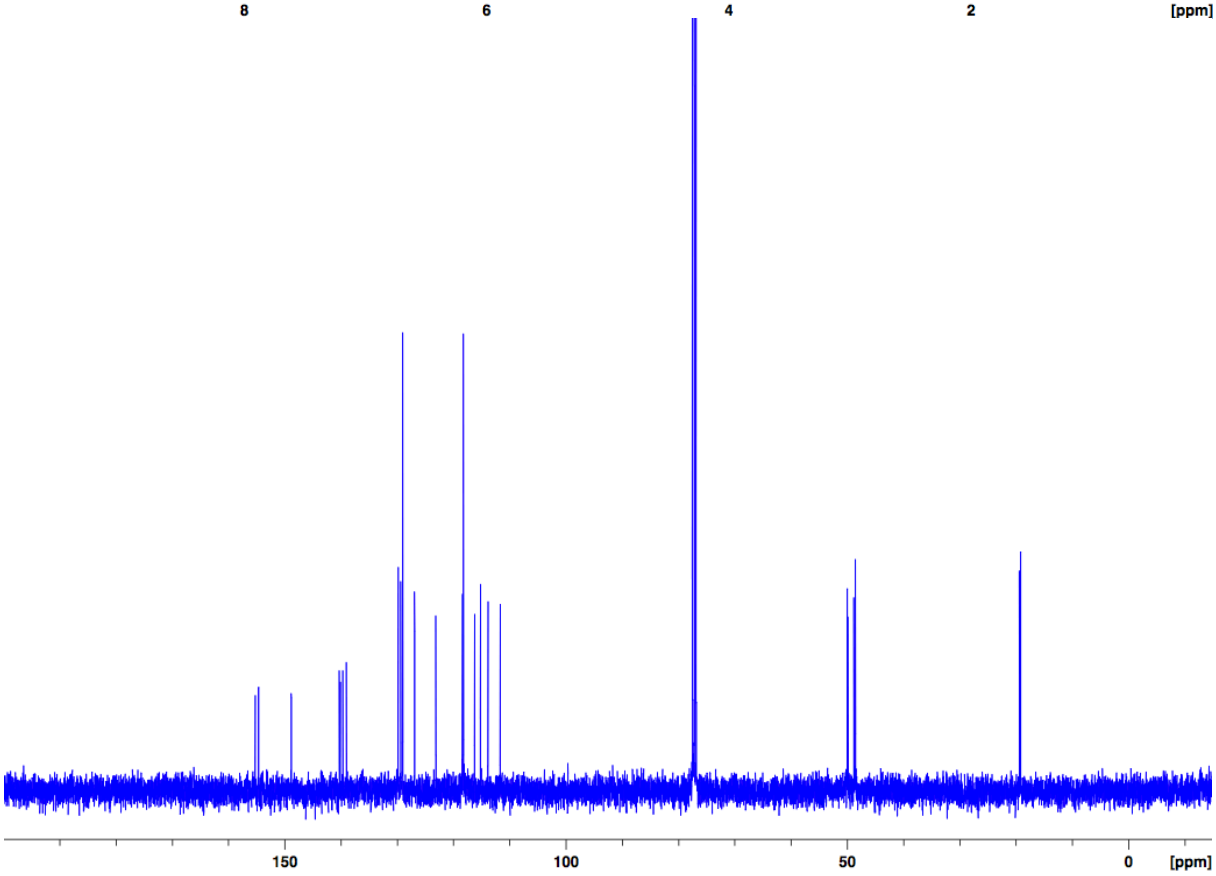


11

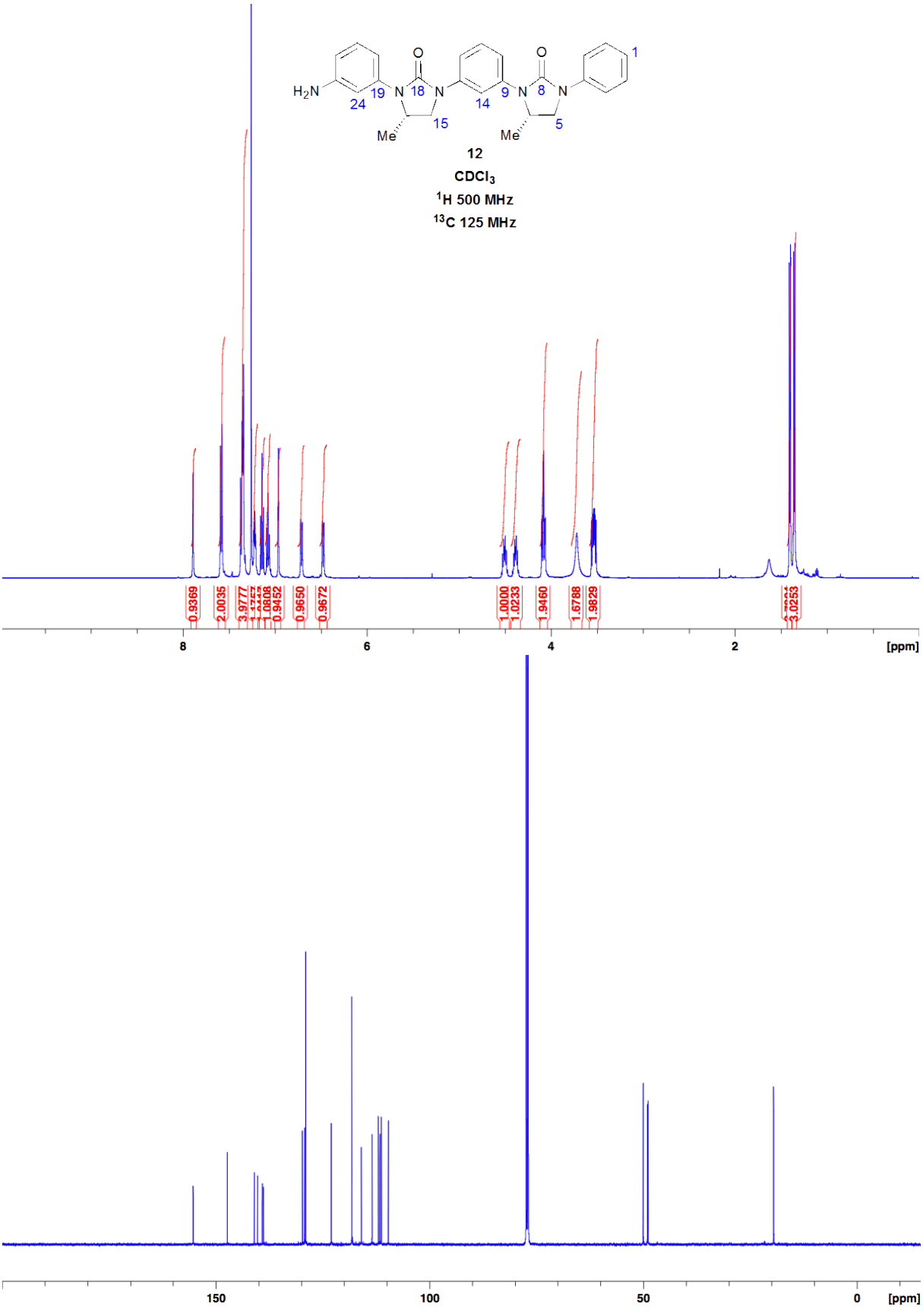
$CDCl_3$

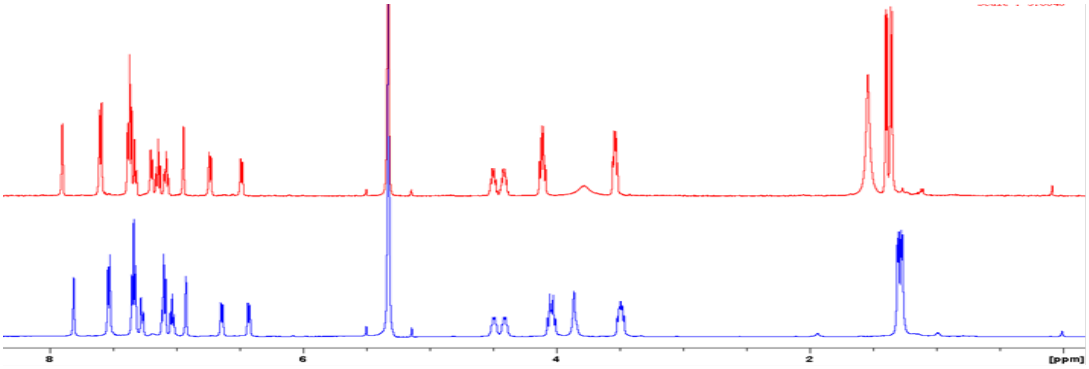
^{1}H 400 MHz

^{13}C 100 MHz



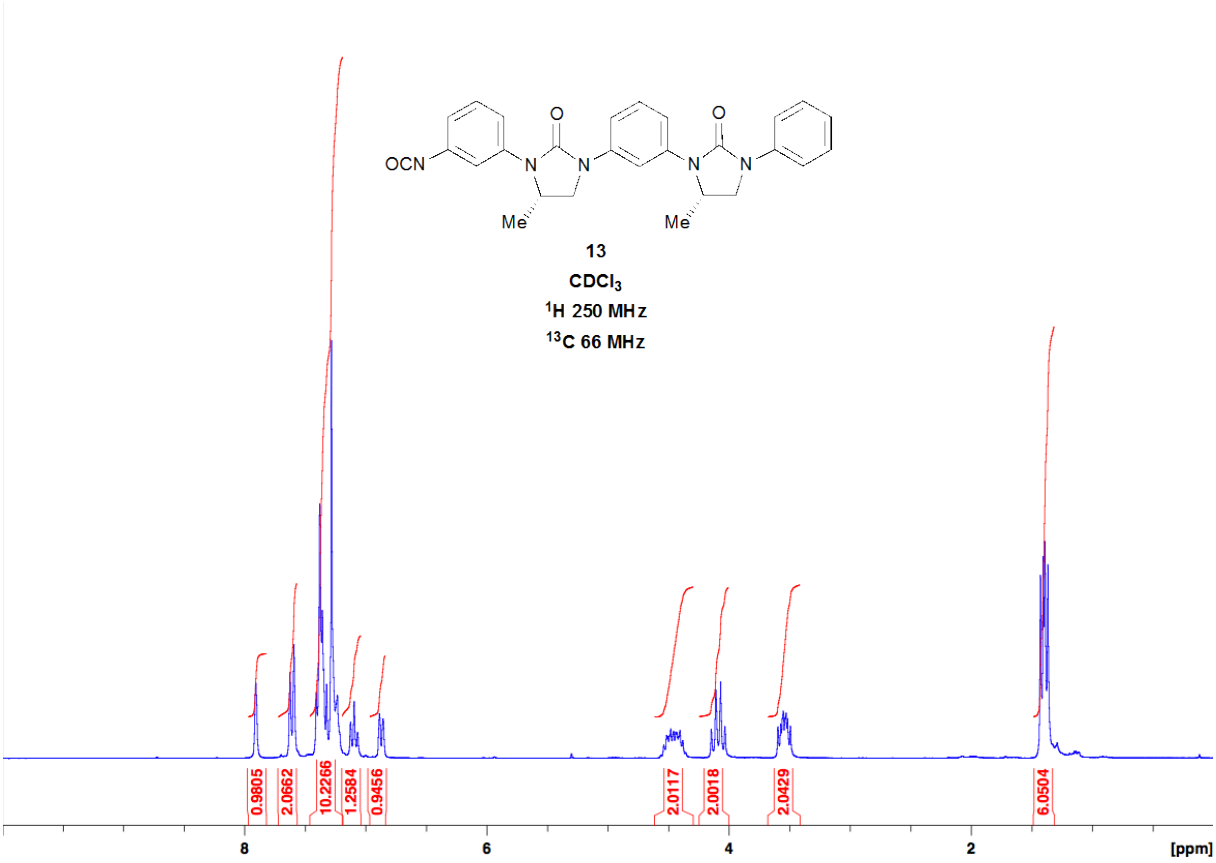
(S)-3-(3-Aminophenyl)-4-methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)imidazolidin-2-one: 12

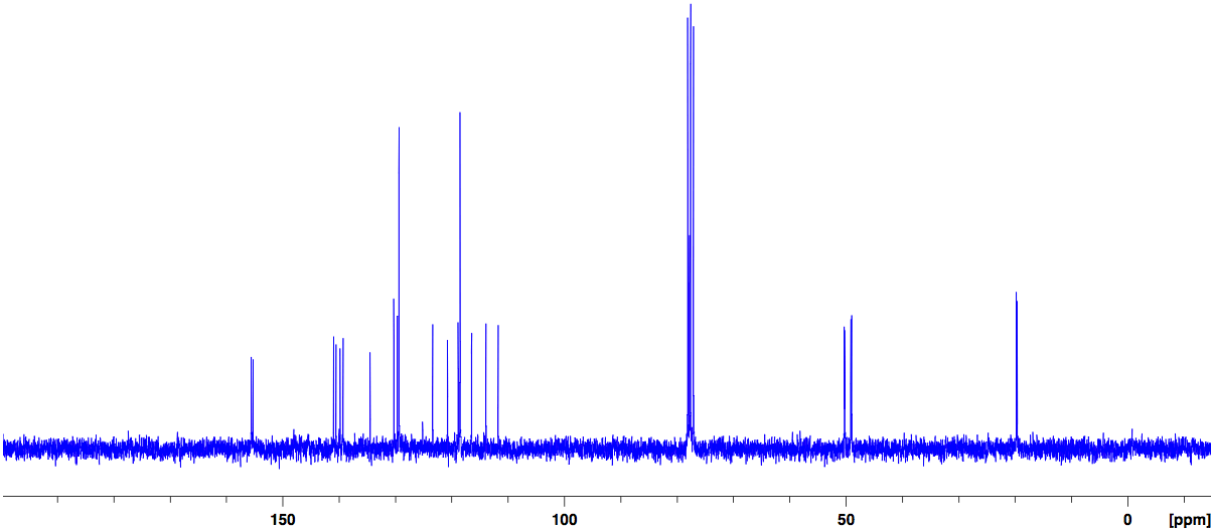




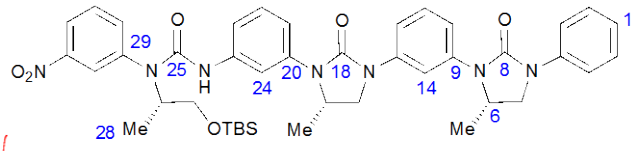
Spectra of **12** in dichloromethane-d_2 at 298 K (blue) and 218 K (red).

(S)-3-(3-Isocyanatophenyl)-4-methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)imidazolidin-2-one: 13

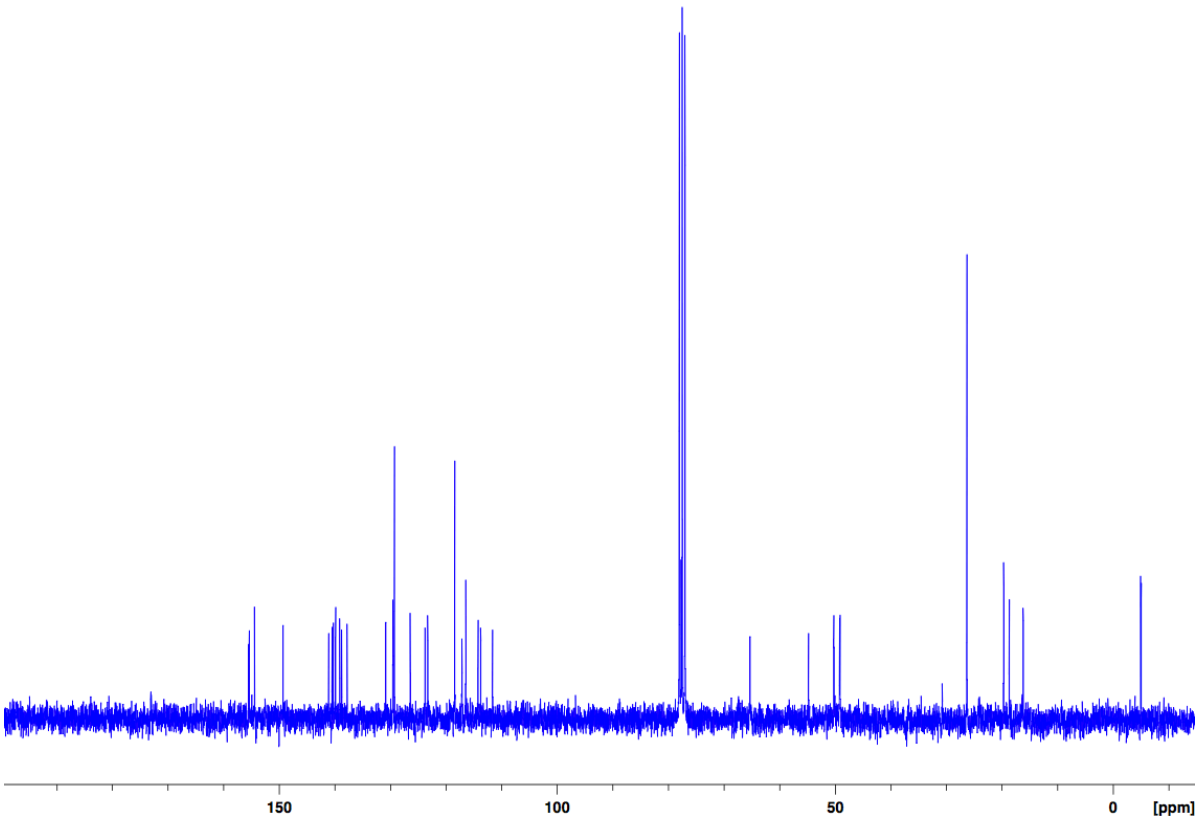




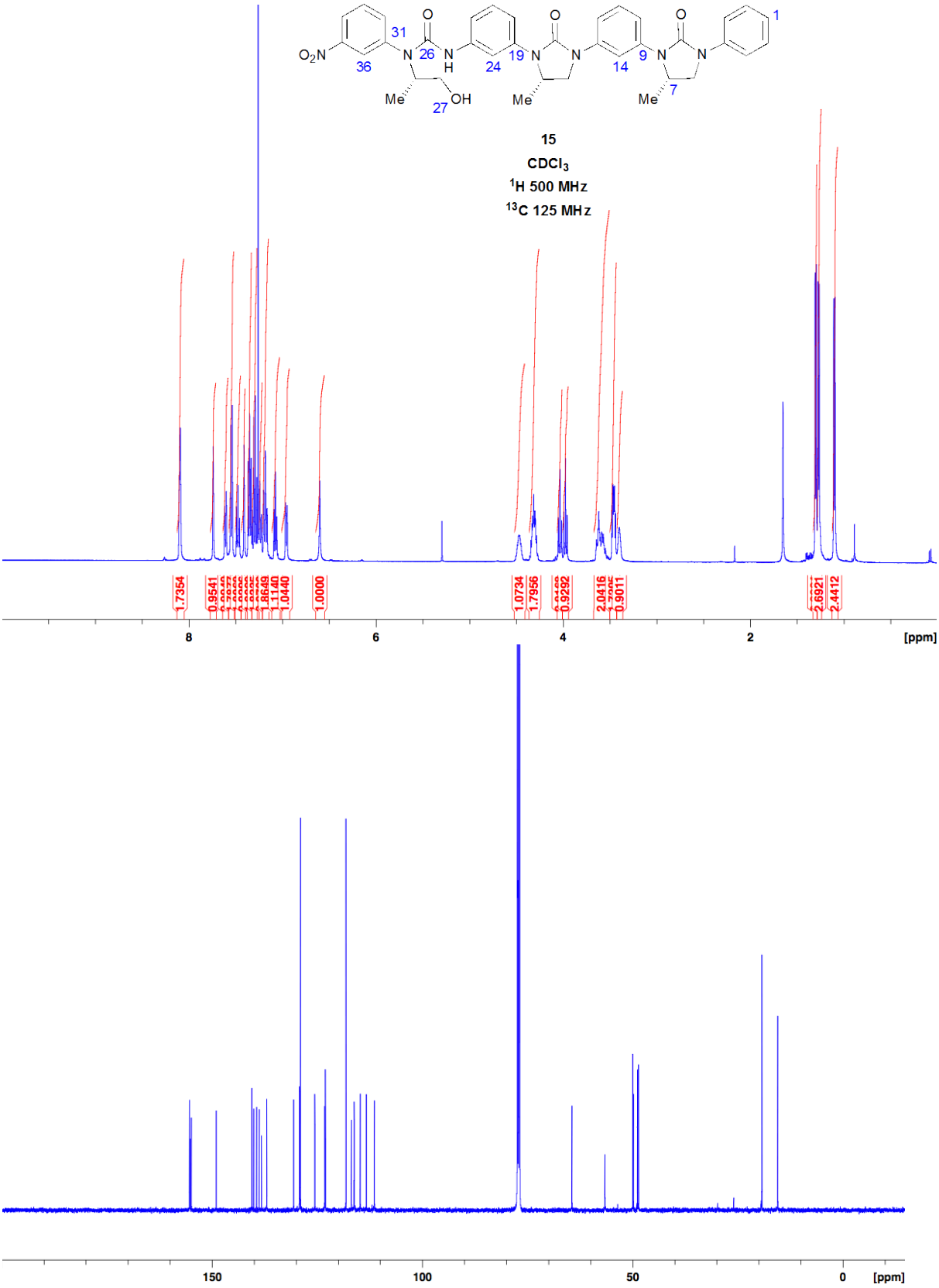
1-((S)-1-((tert-Butyldimethylsilyl)oxy)propan-2-yl)-3-(3-((S)-5-methyl-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-2-oxoimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea: 14



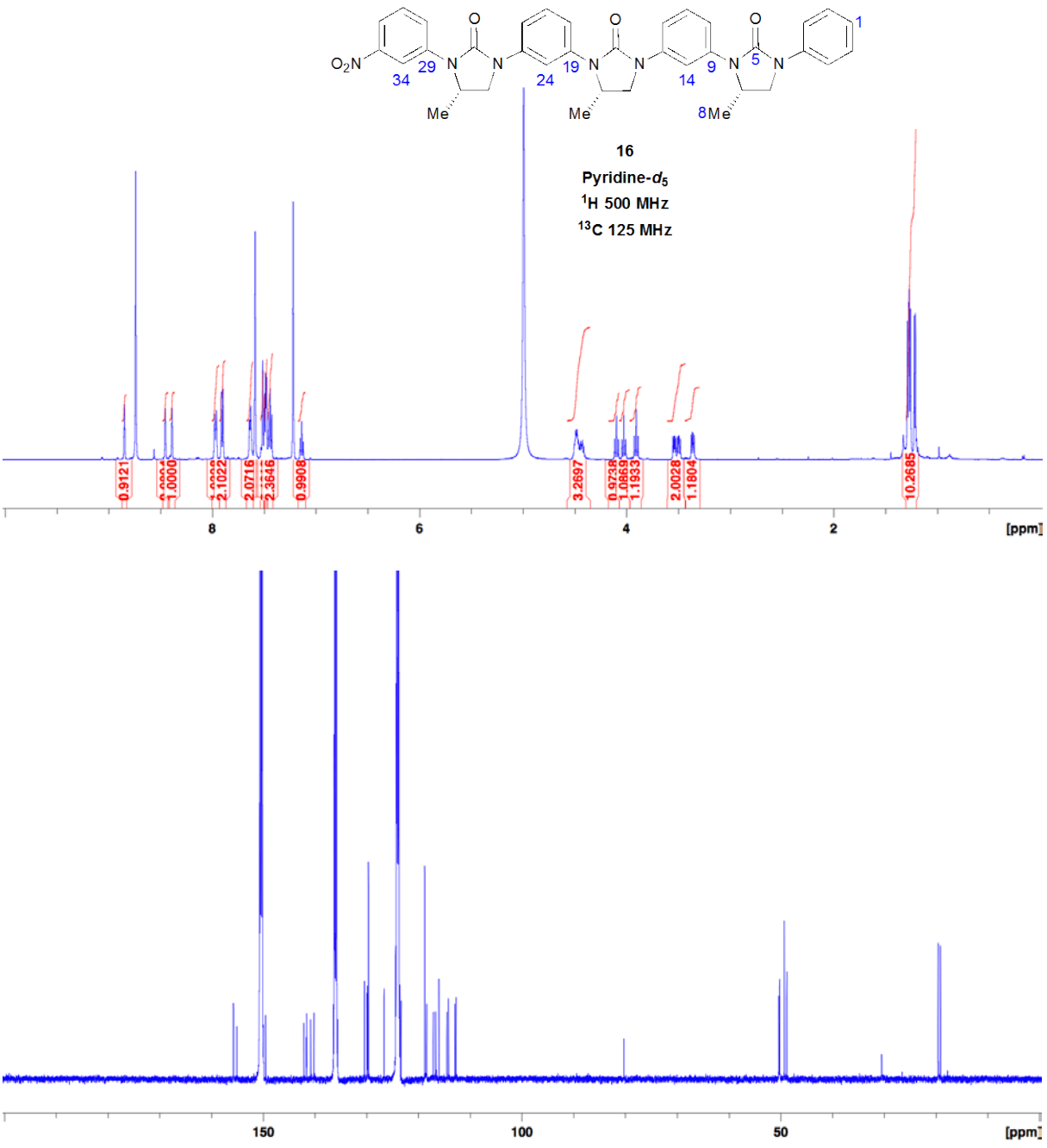
14
$CDCl_3$
^1H 500 MHz
^{13}C 125 MHz

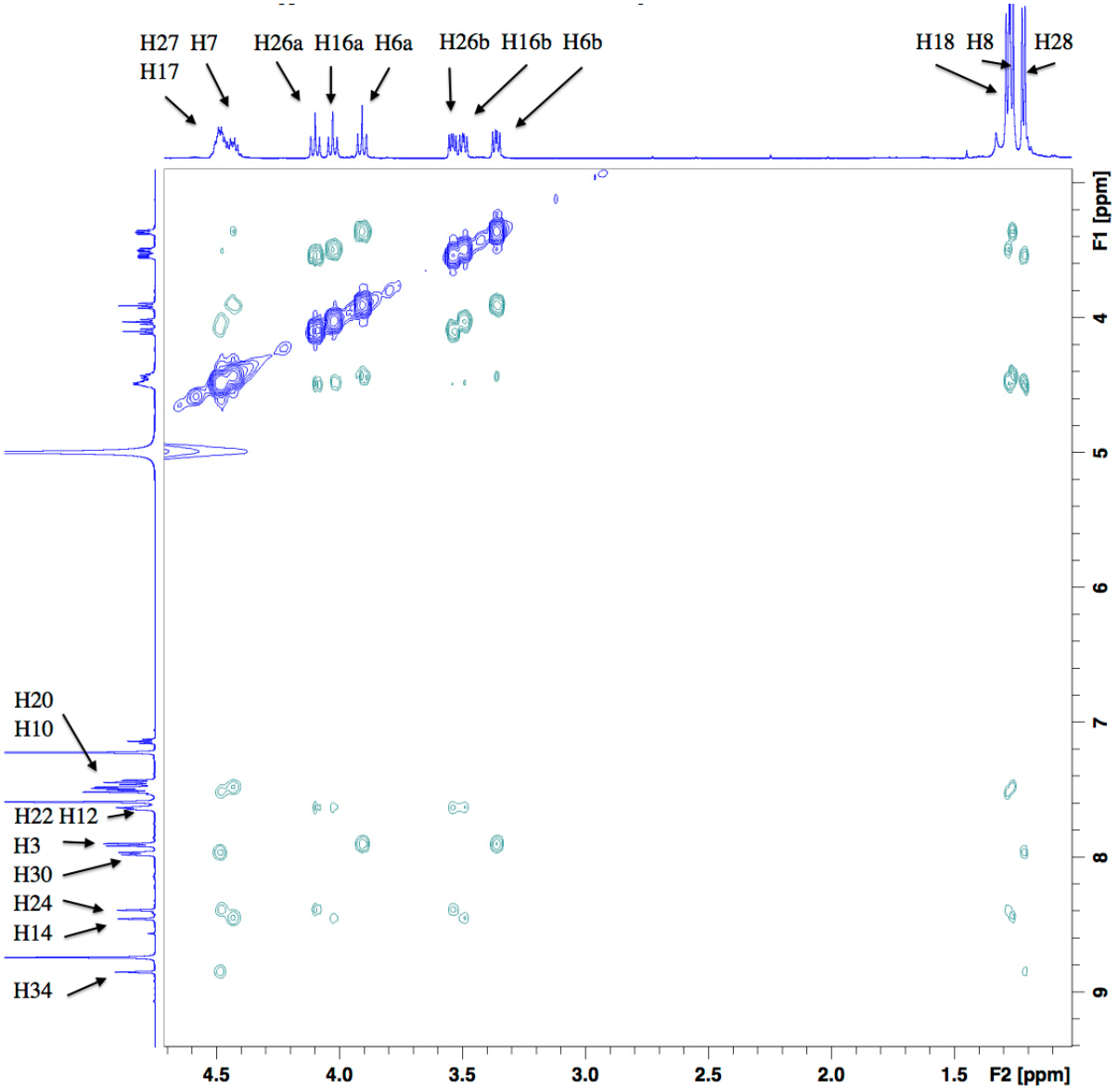


1-((S)-1-Hydroxypropan-2-yl)-3-(3-((S)-5-methyl-3-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-2-oxoimidazolidin-1-yl)phenyl)-1-(3-nitrophenyl)urea: 15



(S)-4-Methyl-1-(3-((S)-5-methyl-2-oxo-3-phenylimidazolidin-1-yl)phenyl)-3-(3-((S)-4-methyl-3-(3-nitrophenyl)-2-oxoimidazolidin-1-yl)phenyl)imidazolidin-2-one: 16





16

Pyridine-d_5

^{1}H NOESY 500 MHz