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Supplementary Information

Thermal and photochemical annulation of vinyl azides to 2-aminoimidazoles.

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Chemistry General Methods. Reagents were obtained from commercial sources and were used directly. Reactions involving air- or moisture-sensitive reagents were carried out under a nitrogen atmosphere. If not specified, reactions were carried out at ambient temperature. The light-mediated reactions were carried out in 2 dram borosilicate glass vials irradiated with Kessil LED lights (PR160-456 nm, www.Kessil.com). Microwave reactions were carried out in an Anton Paar Monowave 450 in G4 glass reaction vials. Heat block reactions were carried out in a Mettler Toledo Easy Max 102 using 4 dram borosilicate glass vials with PTFE faced silicone septa. Silica gel column chromatography was carried out using a Teledyne Isco Combiflash Rf with UV detection at 254 nm.

Analytical Chemistry Methods. 1H NMR spectra were recorded on a Bruker spectrometer operating at 400 MHz; chemical shifts are reported in parts per million (ppm) relative to TMS. LCMS analysis was conducted on a Waters Acquity BEH C18 column (2x50mm, 1.7m) operating at 40 ^{o}C. The gradient employed was mobile phase A: Water + 0.20% v/v Formic Acid and mobile phase B: Acetonitrile + 0.15% v/v Formic Acid. UV detection was provided by summed absorbance signal from 210 to 350nm scanning at 40Hz. Mass spectrometry utilized Waters Acquity system operating in alternating positive/negative electrospray mode. High-resolution mass spectrometry (HRMS) samples were analyzed on an on an Acquity UPLC CSH C18 column (100mm x 2.1mm i.d. 1.7µm packing diameter) at 50 degrees centigrade. MS analysis utilized Waters XEVO G2-XS Qtof in positive electrospray mode with Scan Range 100 to 1200 AMU. The solvents employed were: A = 0.1% v/v solution of Formic Acid in Water; B = 0.1% v/v solution of Formic Acid in Acetonitrile. An error of less than 5 ppm is deemed consistent with the proposed molecular formula.

X-ray Crystallography Methods. The crystal and molecular structures were determined from three-dimensional X-ray diffraction data collected at 150(2) K. All measurements were made using a Bruker D8 Venture diffractometer equipped with an Incoatec microfocus 3.0 (Cu) source (λ = 1.54178 Å). Mixtures of ω and φ scans were employed in each case. A numerical absorption correction was applied based on measured crystal faces. The structures were solved using SHELXT-2018/2 and refined by full-matrix least-squares procedures using SHELXL-2018/3. Co-ordinates and anisotropic atomic displacement parameters were refined for all non-hydrogen atoms. For the hydrogens associated with the nitrogen atoms, atomic co-ordinates and isotropic atomic displacement parameters were freely refined. All other hydrogen atoms were included in calculated positions and were refined using the riding mode. Isotropic atomic displacement parameters for these hydrogens were used as appropriate multiples of Ueq for the attached carbon atom.

MDAP (Mass directed auto-purification). The HPLC analysis was conducted on X-SELECT CSH C18 column (150 mm x 30 mm i.d. 5µ packing diameter) at ambient temperature. The solvent system in the high pH prep was 10 mM ammonium bicarbonate in H_2O adjusted to pH 10 with ammonia (A) and acetonitrile (B). Alternatively, the acidic method employed 0.1% v/v trifluoroacetic acid in water (A) to 0.1% v/v trifluoroacetic acid in acetonitrile (B). The UV detection was an averaged signal from wavelength 210 – 350 nm. MS analysis was conducted on Waters Acquity Qda mass detector with Atlernate-scan Positive and Negative Electrospray (scan range 160 – 1250 Daltons).

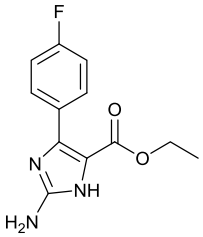
General procedure for 2-aminoimidazole synthesis (Method A). To a solution of vinyl azide (1 eq) in the solvent indicated (200 mM solution) in a microwave reactor vial with stir bar was added cyanamide (3 eq), and base as indicated. The vial was then sealed before being placed in a heat block at the indicated temperature and time. The reaction was then concentrated and the product purified using the method specified for each example.

General procedure for 2-aminoimidazole synthesis (Method B). To a solution of vinyl azide (1 eq) in *tert*-butanol (200 mM solution) in a microwave reactor vial with stir bar was added cyanamide (3 eq), and potassium acetate (0.2 eq). The vial was then sealed before subjecting to microwave radiation at 125 °C for 20 minutes. The pressure typically reached 2.0 to 3.5 Bar. The reaction was then concentrate, and the product purified using the method specified for each example.

General procedure for 2-aminoimidazole synthesis (Method C). To a solution of vinyl-azide (1 eq) in ethanol (200 mM solution) in a 2-dram vial with stir bar was added cyanamide (3 eq), and potassium acetate (0.2 eq). The vial was suspended between 2 Kessil lamps over a stirplate. The reaction was stirred and irradiated with blue light (456 nm) for 2 hours. The reaction was concentrated under a stream of nitrogen before dissolving in DMSO. The product was purified using reverse phase mass directed auto purification (MDAP) using an acidic method.

General procedure for vinyl azide synthesis (Method D).[1,2] To a cold (-10 °C) solution of aldehyde (1 eq) and 25% ethyl azido acetate solution in ethanol (2 eq) was added dropwise a 21% sodium ethoxide solution in ethanol (2 eq). The solution was stirred at -10 °C over 16 hours before quenching with NH_4Cl(aq) and extracting with EtOAc. The product was purified using silica gel flash chromatography.

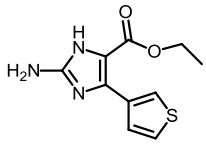
General procedure for vinyl azide synthesis (Method E).[3] To a 300 mM solution of vinyl boronic acid (1eq) in methanol was added copper (II) sulfate (0.1 eq) and sodium azide (1.2 eq). The suspension was stirred for 4 hours at which point full consumption of vinyl boronic acid was observed by LCMS. The reaction was filtered over a silica pad and concentrated in a vial using a stream of nitrogen.



Ethyl 2-amino-4-(4-fluorophenyl)-1H-imidazole-5-carboxylate (4a).

Ethyl 2-azido-3-(4-fluorophenyl)acrylate (1.15 mmol) was subjected to Method A. The product was purified on silica gel chromatography with 10% methanol / dichloromethane as eluant giving product as a white solid (192 mg, 67% yield). ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 7.80 (dd, *J*=8.31, 5.62 Hz, 2H), 7.05-7.16 (m, 2H), 5.50 (s, 1H), 4.25 (q, *J*=7.09 Hz, 2H), 1.30 (t, *J*=7.09 Hz, 3H). LCMS AUC shows 100% purity, m/z = 250 (MH+).

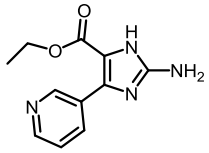
Ethyl 2-azido-3-(4-fluorophenyl)acrylate (0.2 mmol) was subjected to Method B. The product was purified on silica gel chromatography with 10% methanol / dichloromethane as eluant giving product as a white solid (48 mg, 96% yield). LCMS AUC shows 100% purity, m/z = 250 (MH) ^{1}H NMR (400 MHz, DMSO-d_6) δ 10.84 (br. s., 1H), 7.99 (dd, *J*=5.87, 8.56 Hz, 2H), 7.18 (t, *J*=9.05 Hz, 2H), 6.22 (br. s., 2H), 4.18 (q, *J*=7.09 Hz, 2H), 1.25 (t, *J*=7.09 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ 163.3, 160.9, 160.0, 152.0, 131.2, 131.1, 116.9, 114.8, 114.6, 59.8, 14.7. HRMS calcd for $C_{12}H_{13}FN_3O_2$ (M+H) 250.0992, found 250.0996.



Ethyl 2-amino-4-(thiophen-3-yl)-1H-imidazole-5-carboxylate (4b)

Ethyl 2-azido-3-(thiophen-3-yl)acrylate (0.154 mmol) was subjected to Method B, giving pure ethyl 2-amino-4-(thiophen-3-yl)-1H-imidazole-5-carboxylate (36 mg, 98%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.73 (s, 1 H) 8.22 (dd, *J*=2.93, 0.98 Hz, 1 H) 7.74 (dd, *J*=4.89, 0.98 Hz, 1 H) 7.49 (dd, *J*=4.89, 2.93 Hz, 1 H) 6.58 (br s, 2 H) 4.10 - 4.34 (m, 3 H) 1.29 (t, *J*=7.09 Hz, 3 H); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 163.31, 160.12,151.86, 135.72, 128.86, 125.08, 124.75, 59.79, 14.89; HRMS (ESI+) m/z [M+H]+ Calcd for Chemical Formula: $C_{10}H_{12}N_3O_2S$ 238.0654, found 238.0654; LCMS AUC gave 100%, m/z = 238.1 [M+H].

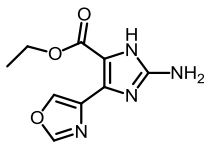
Ethyl 2-azido-3-(thiophen-3-yl)acrylate (.106mmol) was subjected to Method C without purification, giving ethyl 2-amino-4-(thiophen-3-yl)-1H-imidazole-5-carboxylate (79% AUC, 100% conversion, m/z = 238.1 [M+H]).



Ethyl 2-amino-4-(pyridin-3-yl)-1H-imidazole-5-carboxylate (4c).

Ethyl 2-azido-3-(pyridin-3-yl)acrylate (.117mmol) was subjected to Method B, giving pure ethyl 2-amino-4-(pyridin-3-yl)-1H-imidazole-5-carboxylate (25mg, 92%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.54 (s, 1 H) 8.03 (d, *J*=8.78 Hz, 2 H) 7.80 (s, 1 H) 6.62 (d, *J*=8.78 Hz, 1 H) 4.77 (t, *J*=5.27 Hz, 2 H) 4.33 (q, *J*=7.03 Hz, 3 H) 4.13 - 4.27 (m, 3 H) 3.51 - 3.73 (m, 3 H) 3.39 - 3.51 (m, 3 H) 1.23 - 1.38 (m, 6 H); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 159.88, 152.52, 149.90, 148.69, 143.24, 136.25, 130.39, 123.14, 112.98, 60.01, 14.62,; HRMS (ESI+) m/z [M+H]+ Calcd for Chemical Formula: $C_{11}H_{13}N_4O_2$+ 233.104, 233.104 found. LCMS AUC gave 100% purity, m/z = 233.1 [M+H].

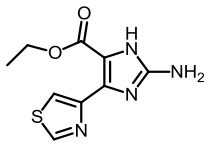
Ethyl-2-azido-3-(pyridin-3-yl)acrylate (.115mmol) was subjected to Method C, giving pure ethyl 2-amino-4-(pyridin-3-yl)-1H-imidazole-5-carboxylate confirmed via LCMS (81% AUC, 100% conversion, m/z = 233.1 [M+H]).



Ethyl 2-amino-4-(oxazol-4-yl)-1H-imidazole-5-carboxylate (4d).

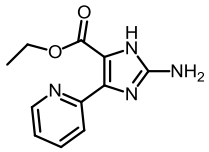
Ethyl 2-azido-3-(oxazol-4-yl)acrylate (0.066mmol) was subjected to Method B, giving pure ethyl 2-amino-4-(oxazol-4-yl)-1H-imidazole-5-carboxylate (12.8mg, 88% yield). 1H NMR (400 MHz, DMSO-d6) δ ppm 1.28 - 1.39 (m, 4 H) 4.36 (q, J=7.34 Hz, 3 H) 7.34 (br s, 3 H) 8.70 (d, J=0.98 Hz, 1 H) 8.81 (d, J=0.98 Hz, 1 H). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 165.28, 161.61, 152.00, 151.66, 138.41, 132.47, 132.44, 59.81, 14.85. HRMS Calcd for $C_9H_{11}N_4O_3^+$ 223.0831, found 223.0835. LCMS AUC gave 84% purity, m/z = 166.0 [M+H].

Ethyl 2-azido-3-(oxazol-4-yl)acrylate was subjected to Method C, ethyl 2-amino-4-(oxazol-4-yl)-1H-imidazole-5-carboxylate was identified via crude LCMS (81% AUC, 100% conversion, m/z = 166.0 [M+H].



ethyl 2-amino-5-(thiazol-4-yl)-4H-imidazole-4-carboxylate (4e).

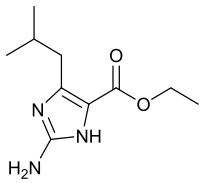
Ethyl-2-azido-3-(thiazol-4-yl)acrylate (0.107mmol) was subjected to Method B, giving pure ethyl 2-amino-5-(thiazol-4-yl)-4H-imidazole-4-carboxylate (23.9mg, 94%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.14 (d, *J*=1.96 Hz, 2 H) 8.46 (d, *J*=1.96 Hz, 2 H) 8.18 (br s, 2 H) 5.67 (br s, 3 H) 4.20 (q, *J*=7.34 Hz, 3 H) 1.23 - 1.29 (m, 3 H); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 162.12, 153.67, 150.68, 147.11, 133.00, 119.60, 118.44, 59.93, 14.74. HRMS Calcd for Chemical Formula: $C_9H_{11}N_4O_2S^+$ 239.0604, found 239.0604; LCMS AUC gave 100% purity, m/z = 239.1 [M+H].



ethyl 2-amino-4-(pyridin-2-yl)-1H-imidazole-5-carboxylate (4f).

Ethyl 2-azido-3-(pyridin-2-yl)acrylate (0.181mmol) was subjected to Method B, giving pure ethyl 2-amino-4-(pyridin-2-yl)-1H-imidazole-5-carboxylate (35 mg, 83%). ^{1}H NMR (400 MHz, DMSO-d6) δ ppm 1.29 (t, J=7.34 Hz, 3 H) 4.33 (q, J=6.85 Hz, 2 H) 7.31 (br s, 2 H) 7.43 - 7.58 (m, 1 H) 8.02 (td, J=7.82, 1.47 Hz, 1 H) 8.41 (d, J=8.31 Hz, 1 H) 8.74 (d, J=4.40 Hz, 1 H) 13.04 (s, 1 H); ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 159.25, 149.54, 148.27, 145.80, 137.81, 132.46, 125.12, 125.07, 115.87, 61.85, 14.36,; HRMS for Chemical Formula: $C_{11}H_{13}N_4O_2^+$ 233.1039, found 233.1041; LCMS AUC gave 100% purity, m/z = 233.1 [M+H].

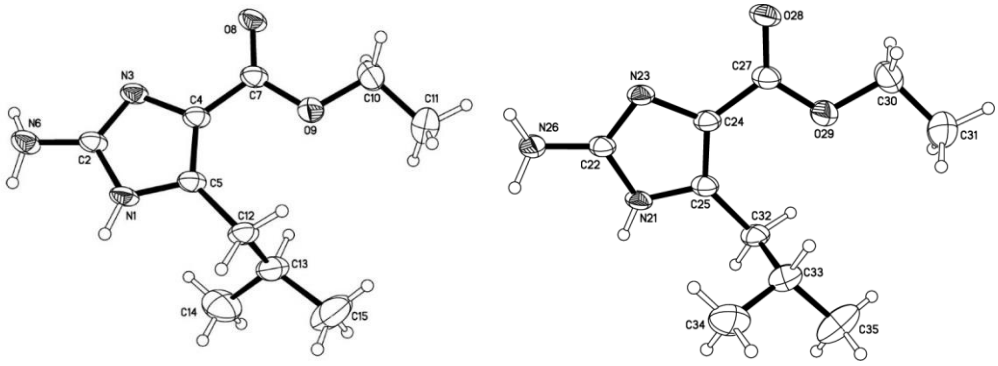
Ethyl 2-azido-3-(pyridin-2-yl)acrylate (.197mmol) was subjected to Method C. Ethyl 2-amino-4-(pyridin-2-yl)-1H-imidazole-5-carboxylate was identified via crude LCMS (70% AUC, 100% conversion m/z = 233.1 [M+H]).

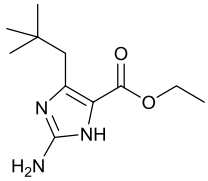


Ethyl 2-amino-5-isobutyl-1H-imidazole-4-carboxylate (4g).
Ethyl-2-azido-5-methylhex-2-enoate (**3g**, 0.2 mmol) was subjected to Method B. The product was purified on silica gel chromatography with 6% methanol / dichloromethane as eluant giving product as a white solid (41 mg, 97% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.58 (br. s., 2H), 5.63 (br. s., 1H), 4.14 (q, *J*=7.09 Hz, 2H), 2.54 (s, 1H), 1.89-1.93 (m, 2H), 1.24 (t, *J*=7.09 Hz, 3H), 0.86 (d, *J*=6.60 Hz, 6H). ^{13}C NMR (101 MHz, DMSO-d6) δ ppm 160.9, 151.4, 59.2, 48.9, 40.3, 36.8, 28.7, 22.6, 14.6. HRMS calcd for $C_{10}H_{18}N_3O_2$ (M+H) 212.1399, found 212.1403. LCMS AUC shows 100% purity, m/z = 212 (MH+).

Ethyl-2-azido-5-methylhex-2-enoate (**3g**, 0.151mmol) was subjected to Method C, giving pure ethyl 2-amino-5-isobutyl-1H-imidazole-4-carboxylate (11.1mg, 34.7%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.20 (s, 2 H) 5.89 (s, 1 H) 4.15 (q, *J*=6.85 Hz, 2 H) 2.53 - 2.56 (m, 2 H) 1.91 (dt, *J*=13.33, 6.79 Hz, 1 H) 1.20 - 1.28 (m, 5 H) 0.86 (d, *J*=6.36 Hz, 8 H. LCMS AUC gave 99% purity, m/z = 212.1 [M+H].

The product **4g** was crystallized from ethanol and water using vapour diffusion techniques and the X-ray crystal structure was solved and refined as outlined in the General Methods section above. Full details of this specific data collection and refinement result can be found in the crystallographic information file (CIF) deposited as ESI, together with the checkCIF output. The CIF was also deposited with the Cambridge Crystallographic Data Centre (CCDC 1911715). The asymmetric unit contains two independent molecules, shown below using 50% probability ellipsoids for the non-hydrogen atoms.





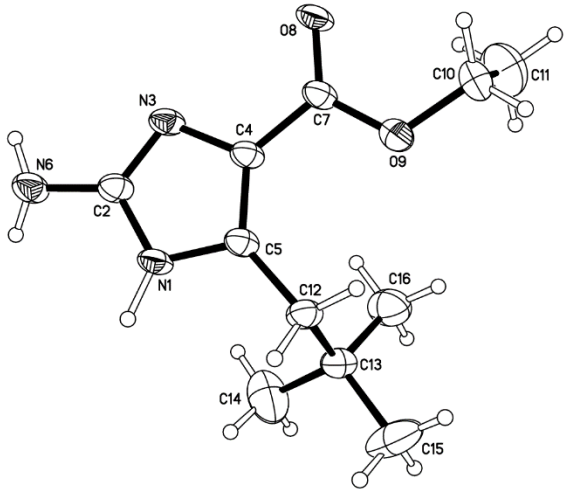
Ethyl 2-amino-5-neopentyl-1H-imidazole-4-carboxylate (4h).

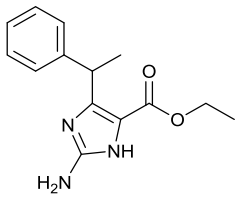
Ethyl-2-azido-5,5-dimethylhex-2-enoate (0.2 mmol) was subjected to Method B. The product was purified on silica gel column chromatography with 8% methanol / dichloromethane as eluant giving

product as a white solid (43 mg, 95% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.58 (br. s., 2H), 5.57 (br s, 2H), 4.13 (q, *J*=7.09 Hz, 2H), 2.59 (s, 2H), 1.24 (t, *J*=7.09 Hz, 3H), 0.91 (s, 9H). ^{13}C NMR (101 MHz, DMSO-d6) δ ppm 163.3, 161.0, 151.2, 118.8, 59.2, 32.4, 30.1, 21.5, 14.9. HRMS calcd for $C_{11}H_{20}N_3O_2$ (M+H) 226.1556, found 226.1559. LCMS AUC shows 100% purity, m/z = 226 (MH+).

Ethyl-2-azido-5,5-dimethylhex-2-enoate (**3h**, 37.4mg, 0.176 mmol) was subjected to Method C, giving ethyl 2-amino-5-neopentyl-1H-imidazole-4-carboxylate (51% AUC, 53% conversion, m/z = 226.2).

The product **4h** was crystallized from ethanol and water using vapour diffusion techniques and the X-ray crystal structure was solved and refined as outlined in the General Methods section above. The experiment was initially complicated by the presence of a second, weaker diffraction pattern that appeared to result from a different unit cell. It was not possible to pinpoint the exact origin or identity of the second (possibly intergrown) component but its presence has not affected the reported **4h** structure unduly, presumably because of a lack of reflection overlap. Full details of this specific data collection and refinement result can be found in the crystallographic information file (CIF) submitted as ESI, together with the checkCIF output. The CIF was also deposited with the Cambridge Crystallographic Data Centre (CCDC 1911716). The asymmetric unit contains one independent molecule, shown below using 50% probability ellipsoids for the non-hydrogen atoms.

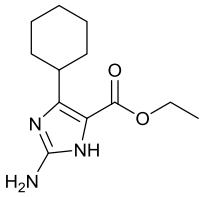




Ethyl 2-amino-5-(1-phenylethyl)-1H-imidazole-4-carboxylate (4i).
Ethyl-2-azido-4-phenylpent-2-enoate (**3i**, 0.2 mmol) was subjected to Method B. The product was purified on silica gel column chromatography with 6% methanol / dichloromethane as eluant giving product as a colorless oil (41 mg, 79% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.28-7.39 (m, 2H), 7.24 (t, *J*=7.58 Hz, 2H), 7.07-7.18 (m, 1H), 6.22 (br. s., 1H), 5.69 (br. s., 2H), 4.70 (d, *J*=6.60 Hz, 1H), 4.08-4.25 (m, 2H), 1.48 (d, *J*=7.09 Hz, 3H), 1.25 (t, *J*=7.09 Hz, 3H). ^{13}C NMR (101 MHz, DMSO-d6) δ

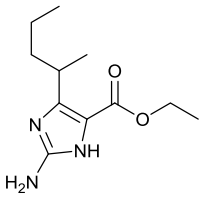
ppm 174.6, 138.3, 134.3, 132.7, 130.5, 129.1, 127.9, 52.3, 49.0, 41.9, 17.4. HRMS calcd for $C_{14}H_{18}FN_3O_2$ (M+H) 260.1399, found 260.1401. LCMS AUC shows 100% purity, m/z = 260 (MH+).

Ethyl-2-azido-4-phenylpent-2-enoate (**3i**, 0.2 mmol) was subjected to Method C giving ethyl 2-amino-5-(1-phenylethyl)-1H-imidazole-4-carboxylate (38% AUC, 44% conversion, m/z =260.2).



Ethyl 2-amino-5-cyclohexyl-1H-imidazole-4-carboxylate (4j).
Ethyl-2-azido-3-cyclohexylacrylate (**3j**, 0.2 mmol) was subjected to Method A. The product was purified on silica gel column chromatography with 6% methanol / dichloromethane as eluant giving product as a pale yellow oil (40 mg, 84% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.57 (br. s., 3H), 5.60 (s, 2H), 4.14 (q, *J*=7.09 Hz, 2H), 3.10 (tt, *J*=3.24, 11.68 Hz, 1H), 1.59-1.82 (m, 5H), 1.37-1.55 (m, 2H), 1.09-1.36 (m, 6H). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 163.3, 160.6, 151.5, 118.8, 59.2, 49.0, 36.6, 32.4, 26.7, 26.2, 21.5, 14.8. HRMS calcd for $C_{12}H_{20}N_3O_2$ (M+H) 238.1556, found 238.1559. LCMS AUC shows 100% purity, m/z = 238 (MH+).

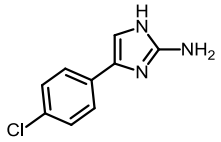
Ethyl 2-azido-3-cyclohexylacrylate was subjected to Method C for 7 hours, giving ethyl 2-amino-5-cyclohexyl-1H-imidazole-4-carboxylate (79% AUC, 92.9% Conversion, m/z = 238.2).



Ethyl 2-amino-5-(pentan-2-yl)-1H-imidazole-4-carboxylate (4k).

Ethyl-2-azido-4-methylhept-2-enoate (**3k**, 0.156 mmol) was subjected to Method B. The product was purified on silica gel column chromatography with 8% methanol / dichloromethane as eluant giving product as a colorless oil (31 mg, 88% yield). ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 6.59 (br. s., 1H), 5.60 (br. s., 2H), 4.03-4.23 (m, 2H), 3.32-3.38 (m, 1H), 1.49-1.66 (m, 1H), 1.31-1.45 (m, 1H), 1.20-1.29 (t, 3H), 1.11-1.20 (m, 2H), 1.09 (d, *J*=6.85 Hz, 3H), 0.75-0.87 (t, 3H). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 163.3, 160.7, 151.8, 118.9, 67.4, 59.2, 31.7, 20.9, 20.6, 14.9, 14.3. HRMS calcd for $C_{11}H_{20}N_3O_2$ (M+H) 226.1556, found 226.1559. LCMS AUC shows 100% purity, m/z = 226 (MH+).

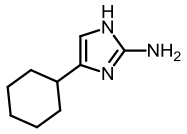
Ethyl-2-azido-4-methylhept-2-enoate (.079 mmol) was subjected to Method C. The product was purified via MDAP, giving ethyl 2-amino-5-(pentan-2-yl)-4H-imidazole-4-carboxylate (.022 mmol, 28.0% yield). LCMS AUC gave 100% AUC, m/z = 226.2 [M+H].



4-(4-chlorophenyl)-1H-imidazol-2-amine (4l).

1-(2-Azidovinyl)-4-chlorobenzene (**3l**, 0.194mmol) was subjected to Method B, followed by purification using MDAP giving the formic acid salt of 4-(4-chlorophenyl)-1H-imidazol-2-amine (24 mg, 88%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.34 (s, 2 H) 7.61 - 7.69 (m, 3 H) 7.33 - 7.51 (m, 3 H) 7.24 (s, 2 H). ^{13}C NMR (101 MHz, DMSO-d_6) δ ppm 150.53, 132.14, 131.22, 130.44, 128.90, 125.64, 110.64. HRMS Calcd for $C_9H_9ClN_3$+ 194.0485, found 194.0486. LCMS AUC gave 100% purity, m/z = 194 [M+H].

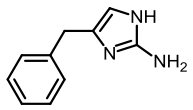
1-(2-Azidovinyl)-4-chlorobenzene (**3l**, 0.194mmol) was subjected to Method C giving 4-(4-chlorophenyl)-1H-imidazol-2-amine identified via LCMS (79% AUC, 100% conversion, m/z = 194 [M+H]).



4-Cyclohexyl-1H-imidazol-2-amine (4m).

2-Azidovinyl)cyclohexane (**3m**, 0.147 mmol) was subjected to Method B, giving pure 4-cyclohexyl-1H-imidazol-2-amine (20 mg, 82%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.42 (s, 1 H) 7.44 - 7.71 (m, 2 H) 6.29 - 6.43 (m, 1 H) 2.25 - 2.48 (m, 1 H) 1.79 - 1.93 (m, 2 H) 1.60 - 1.76 (m, 3 H) 1.10 - 1.35 (m, 6 H). HRMS Calcd for Chemical Formula $C_9H_{16}N_3^+$ 166.1344, found 166.1346. LCMS AUC gave 84% purity, m/z = 166 [M+H].

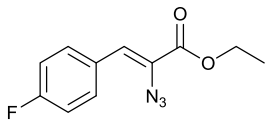
2-Azidovinyl)cyclohexane (**3m**, 0.213 mmol) was subjected to Method C without purification giving 4-cyclohexyl-1H-imidazol-2-amine confirmed via LCMS (62% AUC, 94% conversion, m/z = 166 [M+H]).



4-Benzyl-1H-imidazol-2-amine (4n).

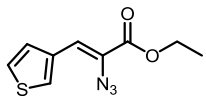
3-Azidoallyl)benzene (**3n**, 0.19 mmol) was subjected to Method B, giving pure (E)-(3-azidoallyl)benzene (17mg, 64%). ^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 8.37 - 8.55 (m, 1 H) 7.21 - 7.40 (m, 5 H) 6.44 - 6.52 (m, 1 H) 3.85 (s, 2 H); HRMS (ESI+) m/z [M+H]+ Calcd for Chemical Formula: $C_{10}H_{12}N_3^+$ 174.1031 found 174.1033.

3-Azidoallyl)benzene (0.19 mmol) was subjected to Method C giving ethyl 2-amino-4-(thiophen-3-yl)-1H-imidazole-5-carboxylate (71% AUC, 96% conversion).



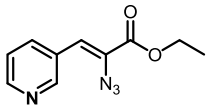
Ethyl-2-azido-3-(4-fluorophenyl)acrylate[4] (3a).

4-Fluorobenzaldehyde was subjected to method D giving product as a colorless oil in 58% yield. LCMS showed 100% purity and no molecular ion. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.77-7.92 (m, 2H), 7.02-7.17 (m, 2H), 6.89 (s, 1H), 4.32-4.46 (m, 2H), 1.37-1.48 (m, 3H). ^{13}C NMR (101 MHz, CHLOROFORM-d) δ 164.2, 163.5, 161.7, 132.6, 132.5, 129.5, 129.5, 125.2, 124.0, 115.7, 115.5, 62.3, 14.2, 14.1.



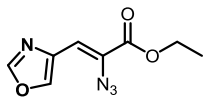
Ethyl 2-azido-3-(thiophen-3-yl)acrylate[5] (3b).

Thiophene-3-carbaldehyde (1.338 mmol) was subjected to method D giving ethyl 2-azido-3-(thiophen-3-yl)acrylate (94.3mg, 31.6%); ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.92 (d, *J*=2.45 Hz, 1 H) 7.54 (dd, *J*=5.14, 1.22 Hz, 1 H) 7.32 - 7.40 (m, 1 H) 7.00 (s, 1 H) 4.40 (q, *J*=7.34 Hz, 2 H) 1.40 - 1.47 (m, 3 H). LCMS AUC gave 100%, no molecular ion.



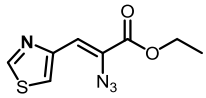
Ethyl 2-azido-3-(pyridin-3-yl)acrylate[6] (3c).

Nicotinaldehyde (9.34mmol) was subjected to Method D giving ethyl 2-azido-3-(pyridin-3-yl)acrylate (418mg, 20.52%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.93 (d, *J*=1.96 Hz, 2 H) 8.53 (dd, *J*=4.65, 1.71 Hz, 2 H) 8.35 - 8.39 (m, 4 H) 7.46 (dd, *J*=8.07, 4.65 Hz, 2 H) 6.95 (s, 2 H) 4.34 (q, *J*=6.85 Hz, 3 H) 1.34 (t, *J*=7.09 Hz, 5 H); HRMS (ESI+) m/z [M+H]+ LCMS 100% AUC, no molecular ion.



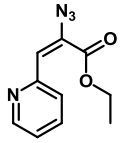
Ethyl 2-azido-3-(oxazol-4-yl)acrylate (3d)

Oxazole-4-carbaldehyde (2.66 mmol) was subjected to Method D, giving ethyl 2-azido-3-(oxazol-4-yl)acrylate (170mg, 30.7%). ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.32 - 8.40 (m, 2 H) 7.92 (s, 2 H) 6.91 (s, 2 H) 4.38 (q, *J*=7.34 Hz, 4 H) 1.34 - 1.47 (m, 5 H). LCMS 100% AUC, no molecular ion.



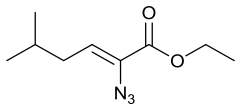
Ethyl 2-azido-3-(thiazol-4-yl)acrylate[7] (3e).

Thiazole-4-carbaldehyde (2.274 mmol) was subjected to Method D, giving pure ethyl 2-azido-3-(thiazol-4-yl)acrylate (189.2mg, 37.1%); ^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.16 (d, *J*=1.96 Hz, 1 H) 8.45 (d, *J*=1.47 Hz, 1 H) 7.07 (s, 1 H) 4.32 (q, *J*=6.85 Hz, 3 H) 1.29 - 1.36 (m, 4 H). LCMS AUC 100% purity, no molecular ion.



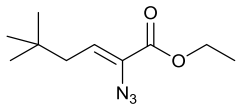
(E)-ethyl 2-azido-3-(pyridin-2-yl)acrylate[8] (3f).

Picolinaldehyde was subjected to Method D, giving pure (E)-ethyl 2-azido-3-(pyridin-2-yl)acrylate (217.6mg, 42.7%); ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.66 - 8.69 (m, 1 H) 8.24 (dt, *J*=8.19, 1.04 Hz, 1 H) 7.76 (td, *J*=7.70, 1.71 Hz, 1 H) 7.23 (ddd, *J*=7.34, 4.89, 0.98 Hz, 1 H) 7.12 (s, 1 H) 4.37 - 4.44 (m, 3 H) 1.39 - 1.44 (m, 3 H). LCMS AUC 100% purity, no molecular ion.



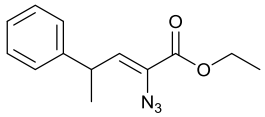
Ethyl-2-azido-5-methylhex-2-enoate (3g).

3-Methylbutanal was subjected to method D giving product as a colorless oil in 63% yield. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ ppm 6.23 (t, *J*=7.70 Hz, 1H), 4.31 (q, *J*=7.09 Hz, 2H), 2.13 (dd, *J*=6.85, 7.58 Hz, 2H), 1.75 (td, *J*=6.72, 13.45 Hz, 1H), 1.31-1.42 (m, 3H), 0.88-0.99 (m, 6H). LCMS AUC 94% purity, no molecular ion.



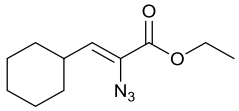
Ethyl-2-azido-5,5-dimethylhex-2-enoate (3h).

3,3-Dimethylbutanal was subjected to method D giving product as a colorless oil in 60% yield. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 6.28 (t, *J*=7.95 Hz, 1H), 4.32 (q, *J*=7.09 Hz, 2H), 2.15 (d, *J*=8.07 Hz, 2H), 1.37 (t, *J*=7.09 Hz, 3H), 0.96 (s, 9H). LCMS AUC 96% purity, no molecular ion.



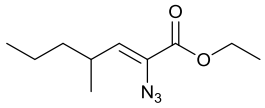
Ethyl-2-azido-4-phenylpent-2-enoate (3i).

2-Phenylpropanal was subjected to method D giving product as a colorless oil in 20% yield. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 7.31-7.44 (m, 3H), 7.18-7.31 (m, 3H), 6.28 (d, *J*=9.78 Hz, 1H), 4.22-4.37 (m, 2H), 4.02 (qd, *J*=6.98, 9.87 Hz, 1H), 1.38-1.46 (d, 3H), 1.32-1.38 (m, 3H). LCMS AUC 94% purity, no molecular ion.



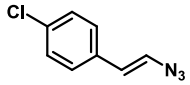
Ethyl-2-azido-3-cyclohexylacrylate[9] (3j).

Cyclohexanecarbaldehyde was subjected to method D giving product as a colorless oil in 49% yield. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 6.05 (d, *J*=9.54 Hz, 1H), 4.30 (q, *J*=7.17 Hz, 2H), 2.45-2.60 (m, 1H), 1.62-1.80 (m, 4H), 1.36 (t, *J*=7.21 Hz, 3H), 1.03-1.32 (m, 5H), 0.86-0.95 (m, 1H). LCMS AUC 99% purity, no molecular ion.



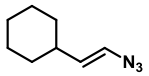
Ethyl-2-azido-4-methylhept-2-enoate (3k).

2-methylpentanal was subjected to method D giving product as a colorless oil in 24% yield. ^{1}H NMR (400 MHz, CHLOROFORM-d) δ 6.01 (d, *J*=10.03 Hz, 1H), 4.20-4.38 (m, 2H), 2.60-2.80 (m, 1H), 1.19-1.44 (m, 7H), 0.97-1.07 (m, 3H), 0.81-0.97 (m, 3H). LCMS AUC 92% purity, no molecular ion.



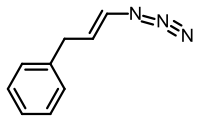
1-(2-azidovinyl)-4-chlorobenzene[10] (3l)

4-chlorostyryl)boronic acid (1.332mmol) was subjected to Method E, giving 1-(2-azidovinyl)-4-chlorobenzene (123mg, 51.4%); ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.27 - 7.31 (m, 3 H) 7.21 - 7.25 (m, 3 H) 6.63 (d, *J*=14.18 Hz, 1 H) 6.26 (s, 1 H). LCMS AUC 100% purity, no molecular ion.



(E)-(2-azidovinyl)cyclohexane (3m).

2-cyclohexylvinyl)boronic acid (1.061mmol was subjected to Method E, giving 2-azidovinyl)cyclohexane (165mg, 99%); ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.84 (dd, *J*=13.69, 0.98 Hz, 1 H) 5.34 (dd, *J*=13.69, 7.34 Hz, 1 H) 1.89 - 2.06 (m, 1 H) 1.63 - 1.81 (m, 7 H) 1.04 - 1.34 (m, 7 H). LCMS AUC 100% purity, no molecular ion.



3-azidoallyl)benzene[11] (3n).

Phenylboronic acid (5.55mmol), was subjected to Method E, giving 3-azidoallyl)benzene (176, 79%); ^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.30 - 7.37 (m, 4 H) 7.19 - 7.27 (m, 3 H) 5.96 (d, *J*=13.69 Hz, 1 H) 5.52 - 5.61 (m, 1 H) 3.39 (dd, *J*=7.34, 0.98 Hz, 2 H). LCMS AUC 99% purity, no molecular ion.

Notes and References

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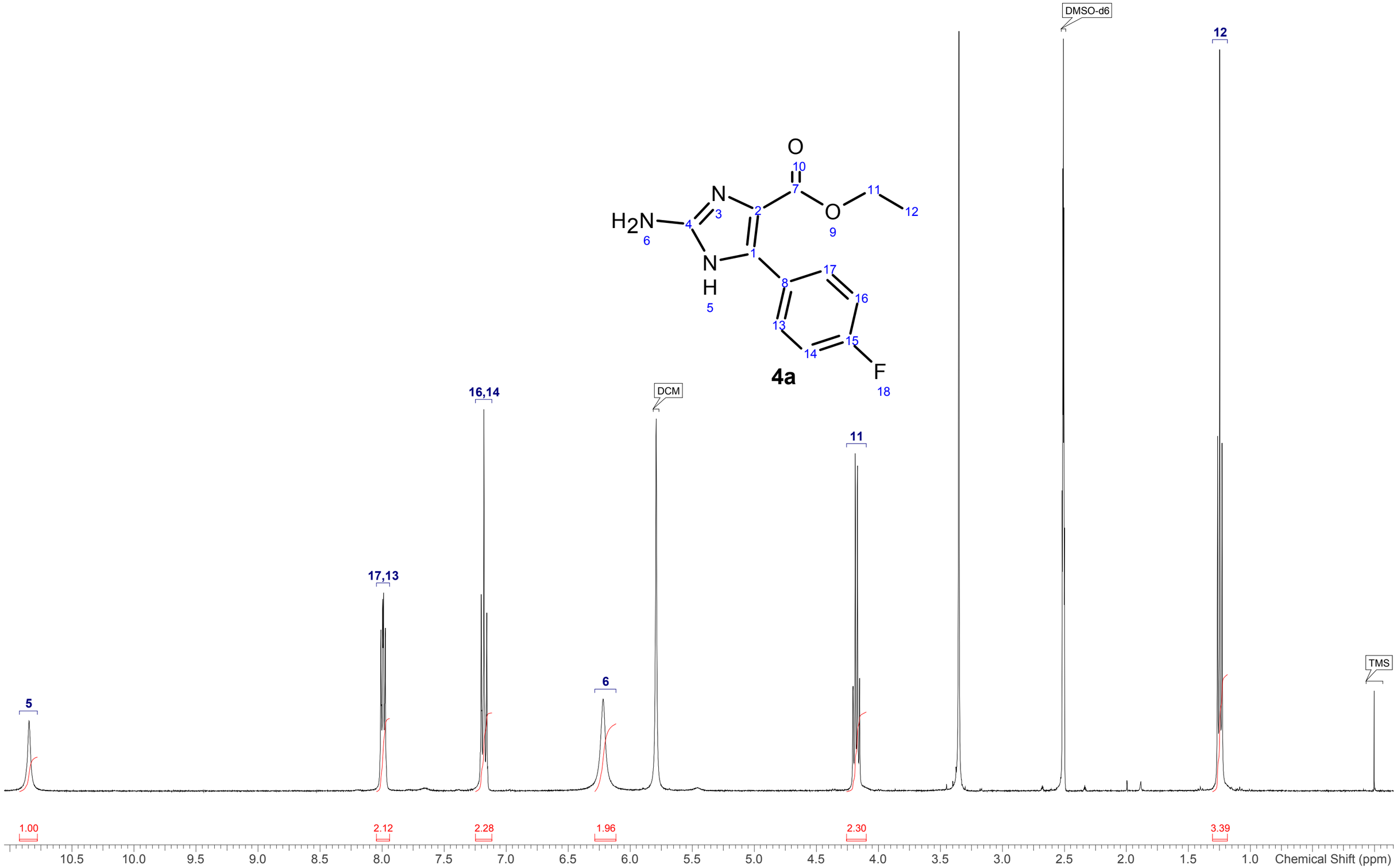
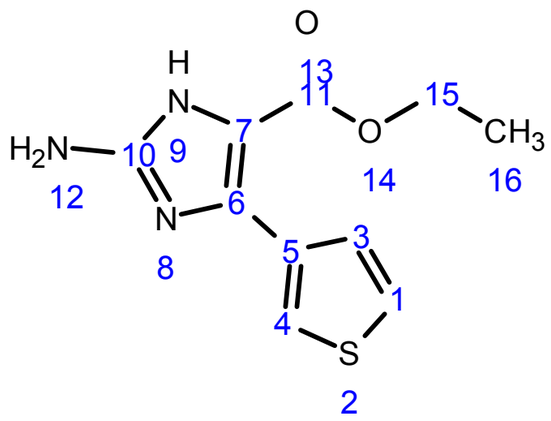
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.84 (br s, 1 H) 7.94 - 8.04 (m, 2 H) 7.11 - 7.25 (m, 2 H) 6.22 (br s, 2 H) 4.18 (q, *J*=6.85 Hz, 2 H) 1.25 (t, *J*=7.09 Hz, 3 H)

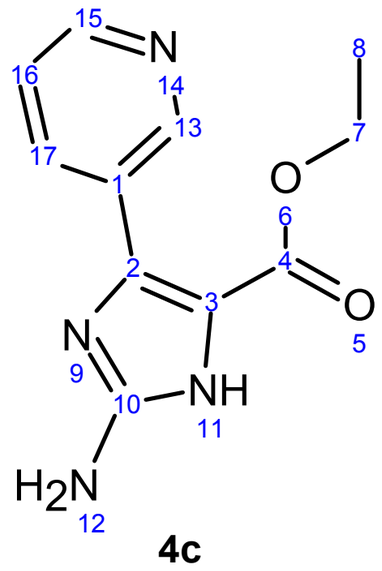


^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.29 (t, *J*=7.09 Hz, 4 H) 4.22 (q, *J*=7.34 Hz, 2 H) 5.76 (s, 3 H) 7.49 (dd, *J*=5.14, 3.18 Hz, 1 H) 7.70 - 7.77 (m, 1 H) 8.21 (d, *J*=2.45 Hz, 1 H) 10.75 (br s, 1 H)



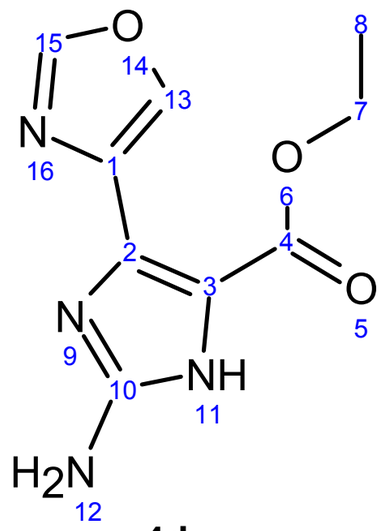
4b

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.23 (t, *J*=7.09 Hz, 3 H) 4.18 (q, *J*=6.85 Hz, 2 H) 5.88 (br s, 2 H) 7.34 - 7.44 (m, 1 H) 8.23 (dt, *J*=7.83, 1.96 Hz, 1 H) 8.48 (dd, *J*=4.89, 1.47 Hz, 1 H) 9.02 (d, *J*=1.96 Hz, 1 H)



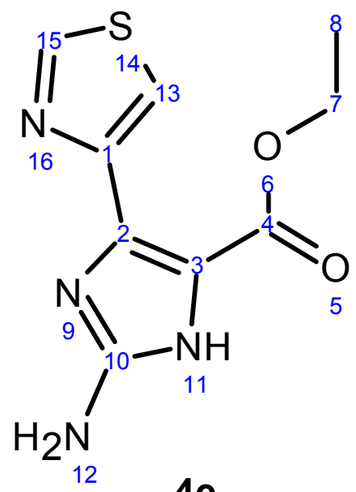
4c

[1]H NMR (400 MHz, DMSO-d_6) δ ppm 1.28 - 1.39 (m, 4 H) 4.36 (q, *J*=7.34 Hz, 3 H) 7.34 (br s, 3 H) 8.70 (d, *J*=0.98 Hz, 1 H) 8.81 (d, *J*=0.98 Hz, 1 H)



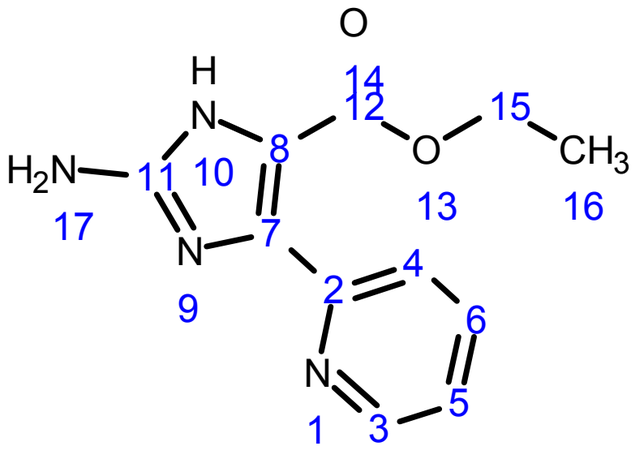
4d

[1]H NMR (400 MHz, DMSO-d_6) δ ppm 1.23 - 1.29 (m, 3 H) 4.20 (q, *J*=7.34 Hz, 3 H) 5.67 (br s, 3 H) 8.18 (br s, 2 H) 8.46 (d, *J*=1.96 Hz, 2 H) 9.14 (d, *J*=1.96 Hz, 2 H)



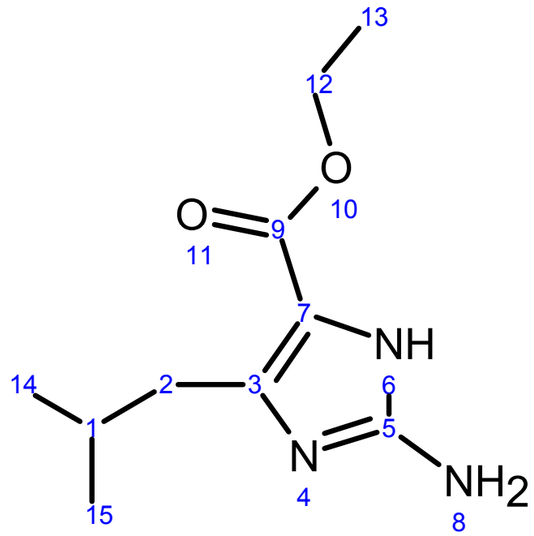
4e

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 1.29 (t, *J*=7.34 Hz, 3 H) 4.33 (q, *J*=6.85 Hz, 2 H) 7.31 (br s, 2 H) 7.43 - 7.58 (m, 1 H) 8.02 (td, *J*=7.82, 1.47 Hz, 1 H) 8.41 (d, *J*=8.31 Hz, 1 H) 8.74 (d, *J*=4.40 Hz, 1 H) 13.04 (s, 1 H)



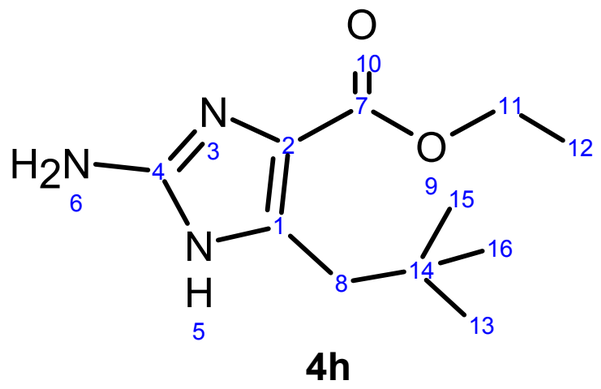
4f

[1]H NMR (400 MHz, DMSO-d_6) δ ppm 0.86 (d, *J*=6.85 Hz, 6 H) 1.24 (t, *J*=7.09 Hz, 3 H) 1.91 (dt, *J*=13.33, 6.79 Hz, 1 H) 2.50 - 2.57 (m, 3 H) 4.16 (q, *J*=7.34 Hz, 2 H) 8.21 (s, 1 H)



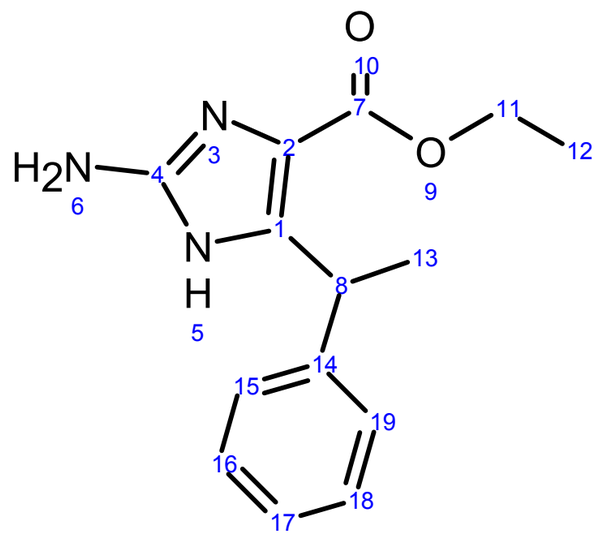
4g

[1]H NMR (400 MHz, DMSO-d_6) δ ppm 10.41 - 10.80 (m, 1 H) 6.58 (br s, 3 H) 5.46 - 5.67 (m, 2 H) 4.13 (q, *J*=6.85 Hz, 2 H) 2.59 (s, 2 H) 1.25 (t, *J*=7.09 Hz, 3 H) 0.87 - 0.98 (m, 9 H)



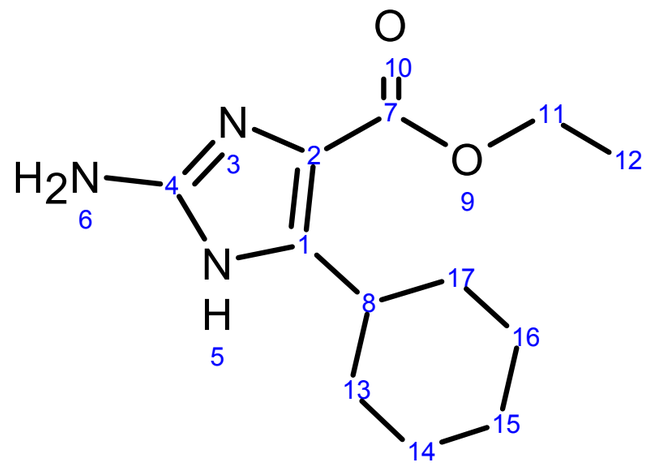
4h

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.56 (br s, 1 H) 7.29 - 7.38 (m, 2 H) 7.19 - 7.28 (m, 2 H) 7.05 - 7.17 (m, 1 H) 6.16 - 6.28 (m, 1 H) 5.69 (br s, 2 H) 4.64 - 4.77 (m, 1 H) 4.06 - 4.26 (m, 2 H) 1.48 (d, *J*=7.34 Hz, 3 H) 1.25 (t, *J*=7.09 Hz, 3 H)



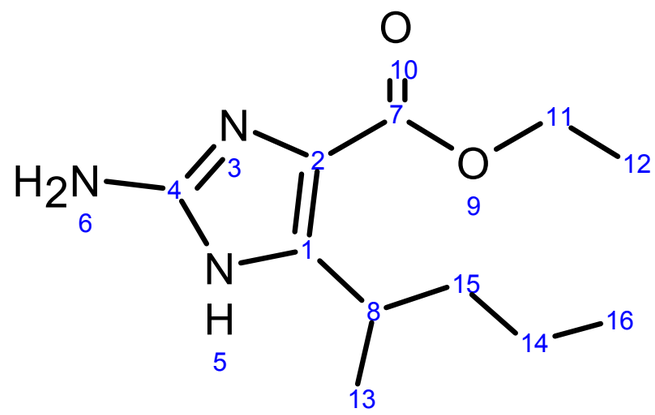
4i

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 10.32 - 10.92 (m, 1 H) 6.57 (br s, 3 H) 5.49 - 5.66 (m, 2 H) 4.06 - 4.21 (m, 2 H) 3.03 - 3.15 (m, 1 H) 1.61 - 1.82 (m, 5 H) 1.39 - 1.55 (m, 2 H) 1.10 - 1.35 (m, 6 H)



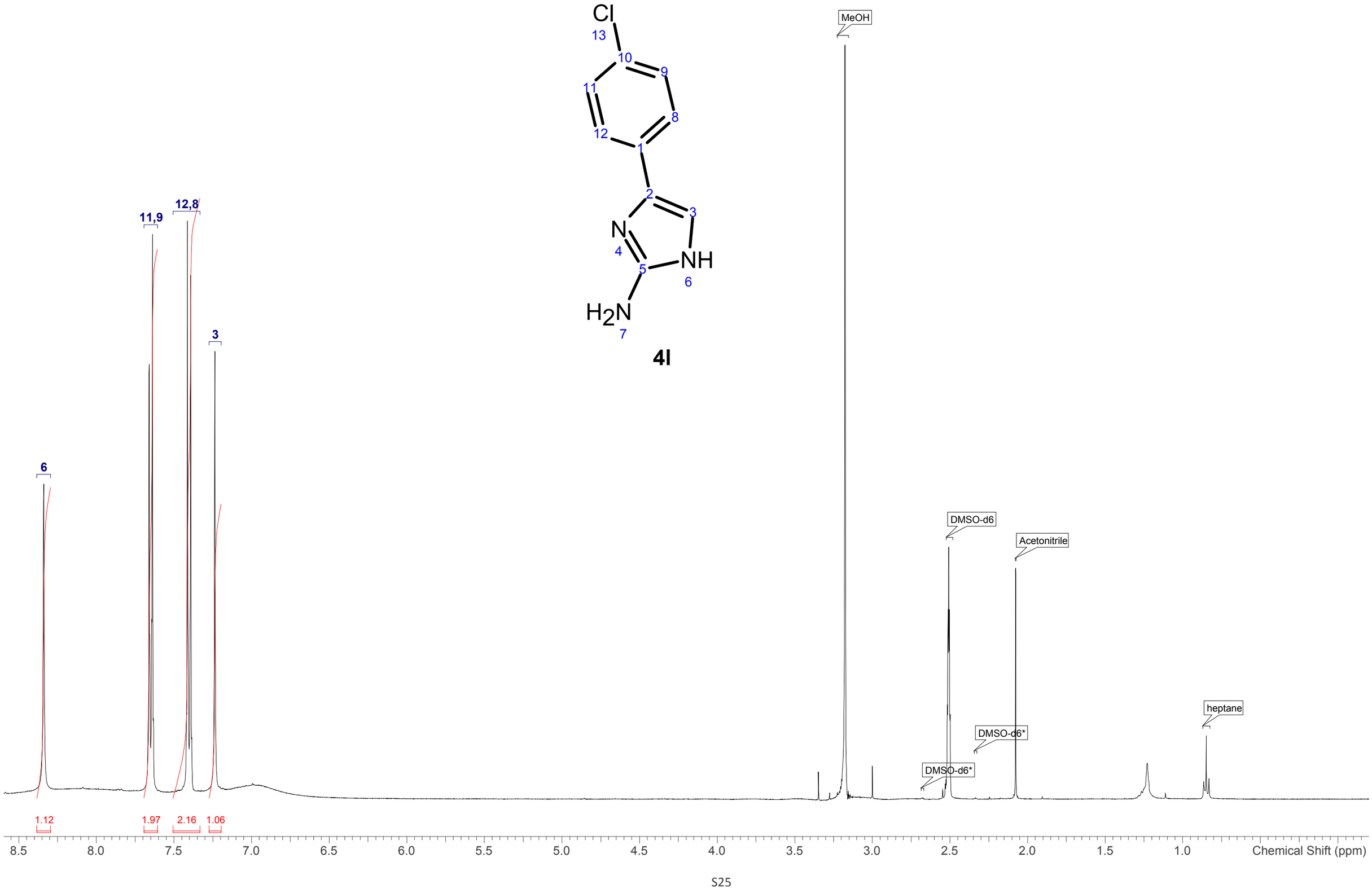
4j

[1]H NMR (400 MHz, DMSO-d_6) δ ppm 10.32 - 10.67 (m, 1 H) 6.59 (br s, 1 H) 5.60 (br s, 2 H) 4.09 - 4.20 (m, 1 H) 4.05 - 4.21 (m, 1 H) 3.30 - 3.42 (m, 2 H) 1.90 - 1.93 (m, 1 H) 1.32 - 1.62 (m, 2 H) 1.21 - 1.26 (m, 3 H) 1.12 - 1.20 (m, 2 H) 1.07 - 1.11 (m, 3 H) 0.78 - 0.86 (m, 3 H)

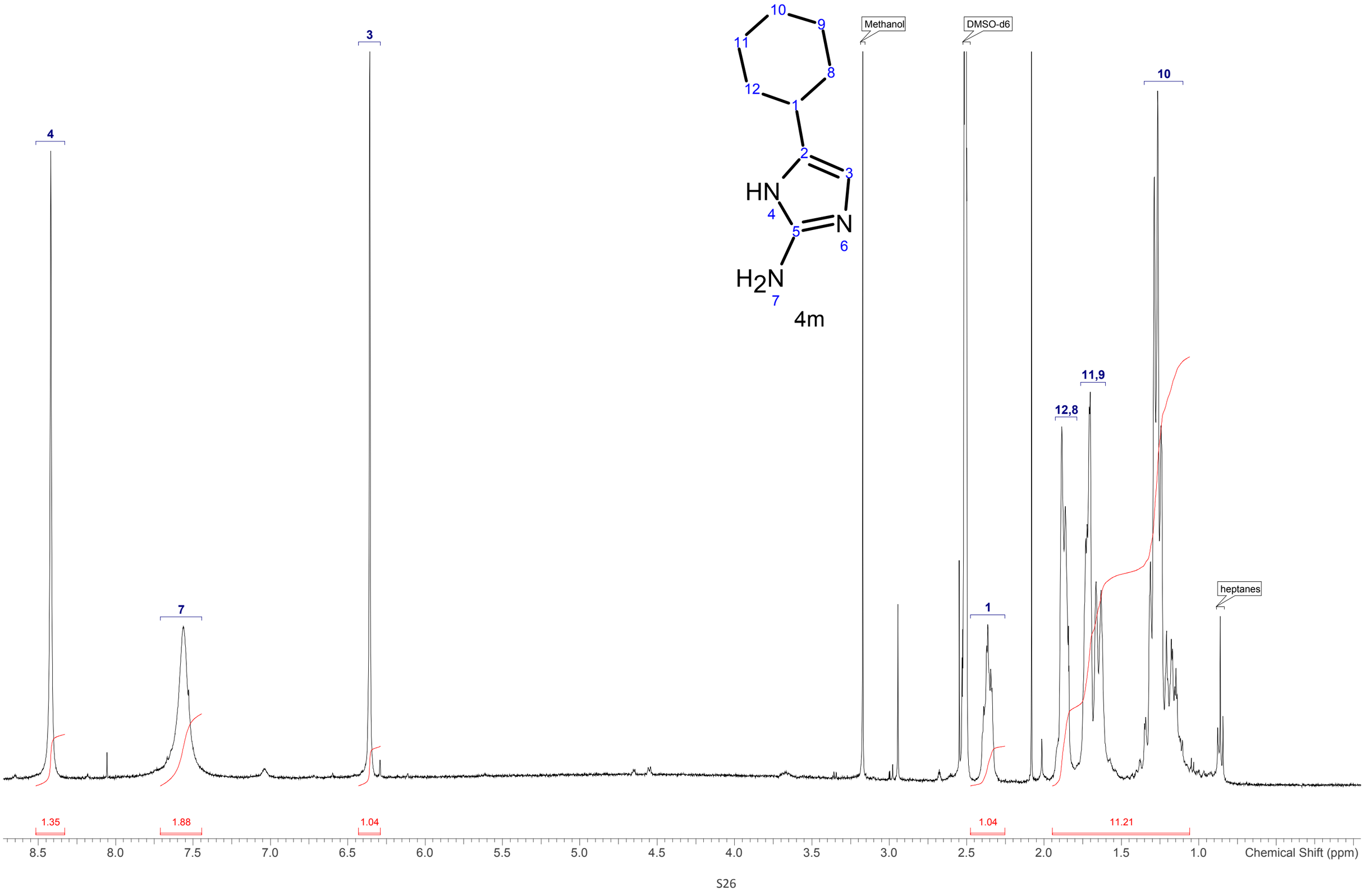


4k

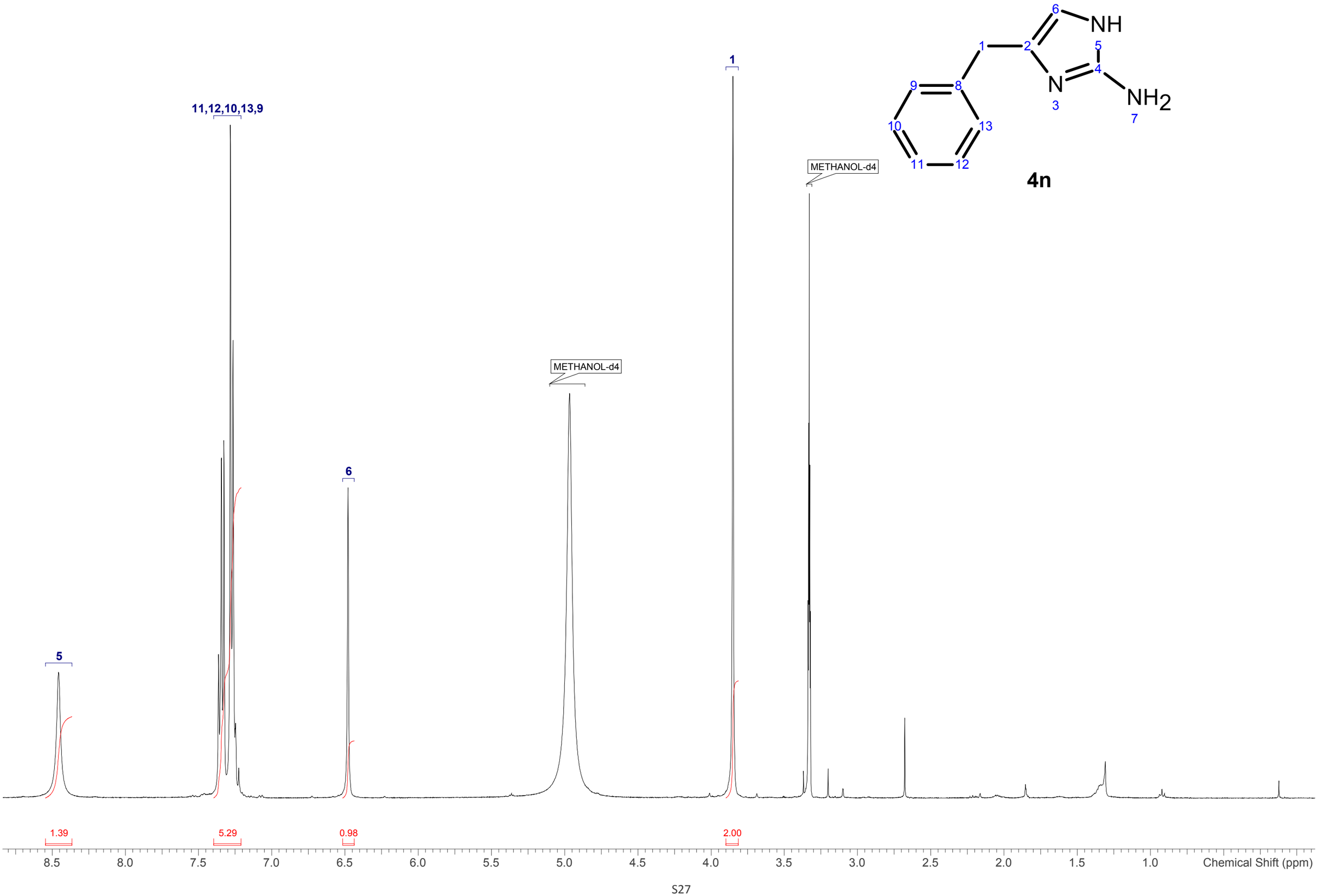
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 7.24 (s, 2 H) 7.33 - 7.51 (m, 3 H) 7.61 - 7.69 (m, 3 H) 8.34 (s, 2 H)



[1]H NMR (400 MHz, DMSO-d_6) δ ppm 1.10 - 1.35 (m, 6 H) 1.60 - 1.76 (m, 3 H) 1.79 - 1.93 (m, 2 H) 2.25 - 2.48 (m, 1 H) 6.29 - 6.43 (m, 1 H) 7.44 - 7.71 (m, 2 H) 8.42 (s, 1 H)

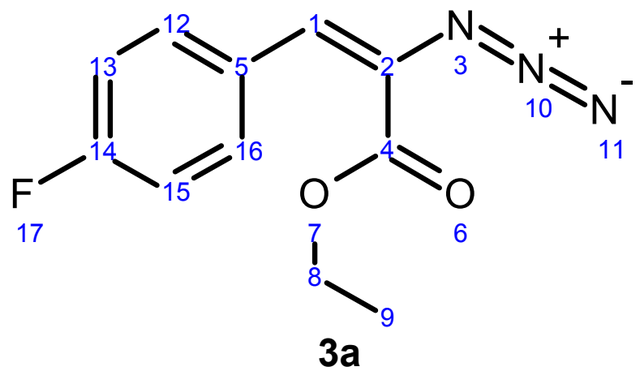


^{1}H NMR (400 MHz, METHANOL-d_4) δ ppm 8.37 - 8.55 (m, 1 H) 7.21 - 7.40 (m, 5 H) 6.44 - 6.52 (m, 1 H) 3.85 (s, 2 H)



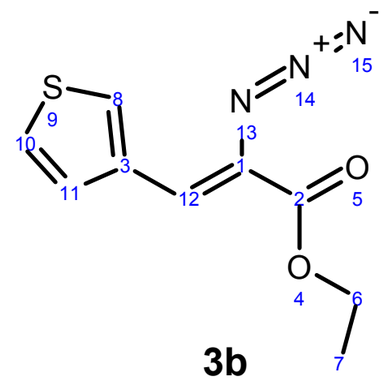
4n

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.78 - 7.93 (m, 2 H) 7.04 - 7.14 (m, 2 H) 6.89 (s, 1 H) 4.39 (q, *J*=7.19 Hz, 2 H) 1.42 (t, *J*=7.15 Hz, 3 H)



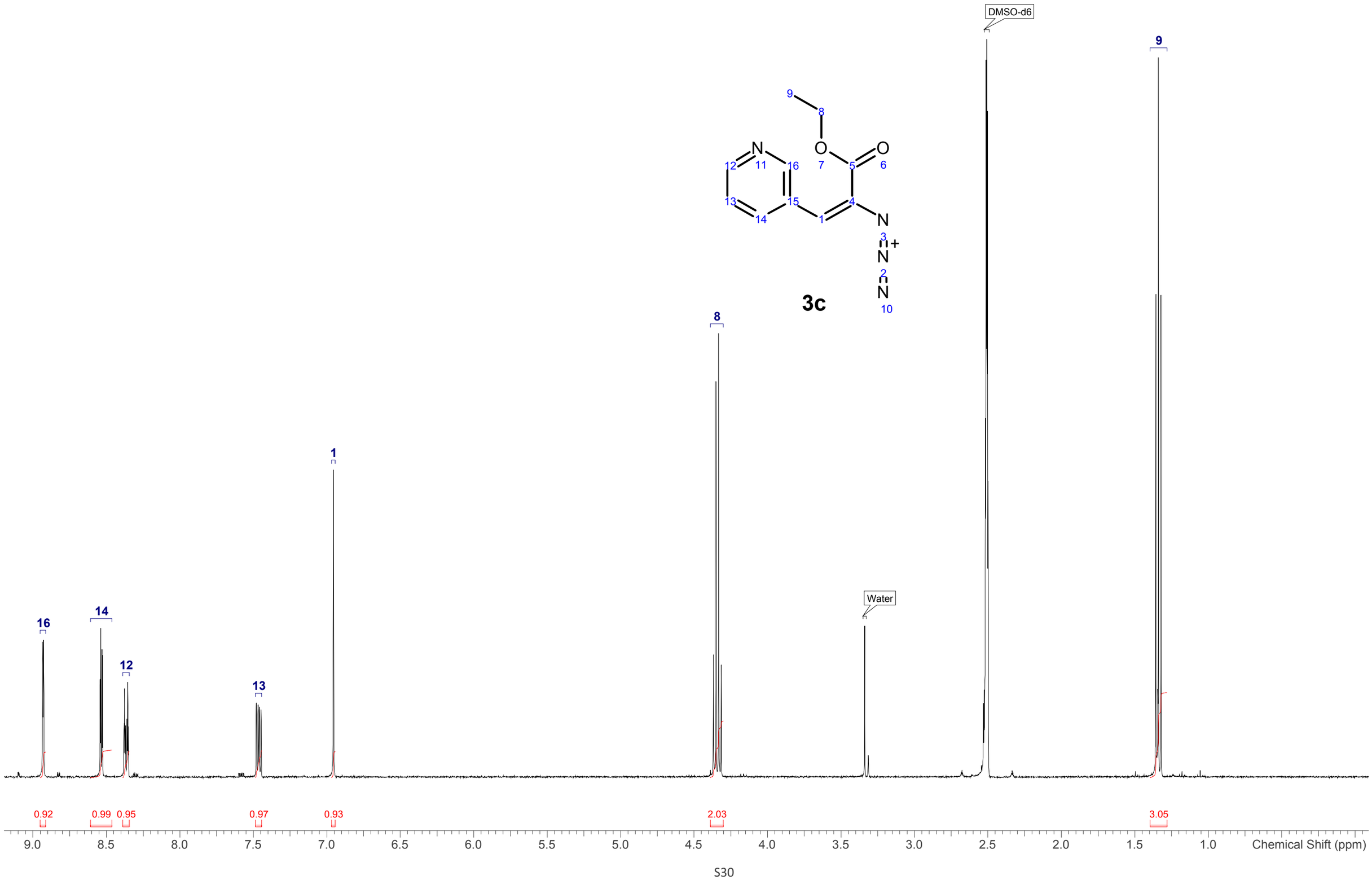
3a

[1]H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.92 (d, *J*=2.45 Hz, 1 H) 7.54 (dd, *J*=5.14, 1.22 Hz, 1 H) 7.32 - 7.40 (m, 1 H) 7.00 (s, 1 H) 4.40 (q, *J*=7.34 Hz, 2 H) 1.40 - 1.47 (m, 3 H)

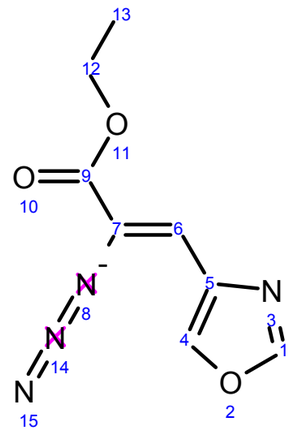


3b

^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 8.93 (d, *J*=1.96 Hz, 2 H) 8.53 (dd, *J*=4.65, 1.71 Hz, 2 H) 8.35 - 8.39 (m, 4 H) 7.46 (dd, *J*=8.07, 4.65 Hz, 2 H) 6.95 (s, 2 H) 4.34 (q, *J*=6.85 Hz, 3 H) 1.34 (t, *J*=7.09 Hz, 5 H)



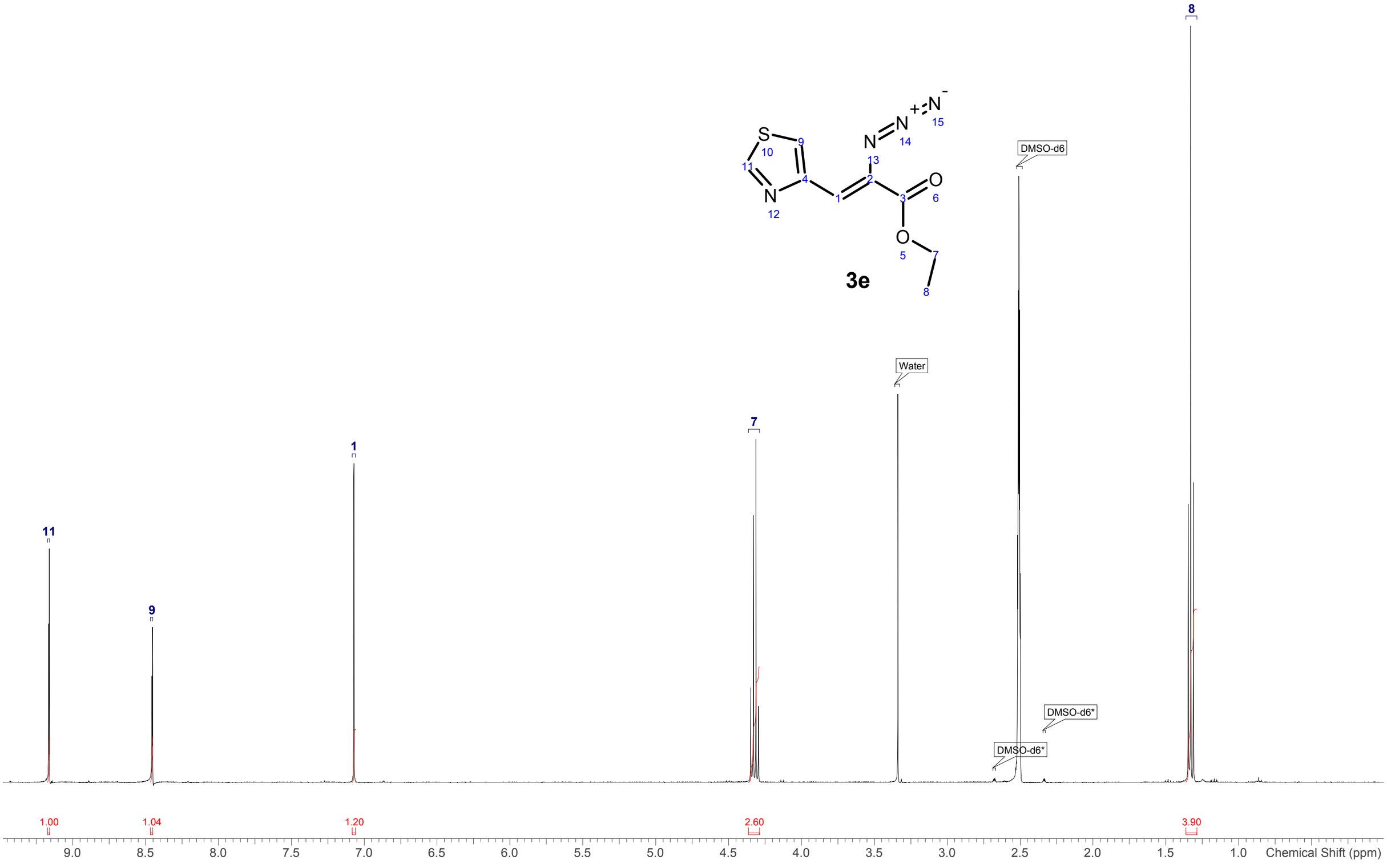
^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.32 - 8.40 (m, 2 H) 7.92 (s, 2 H) 6.91 (s, 2 H) 4.38 (q, *J*=7.34 Hz, 4 H) 1.34 - 1.47 (m, 5 H)



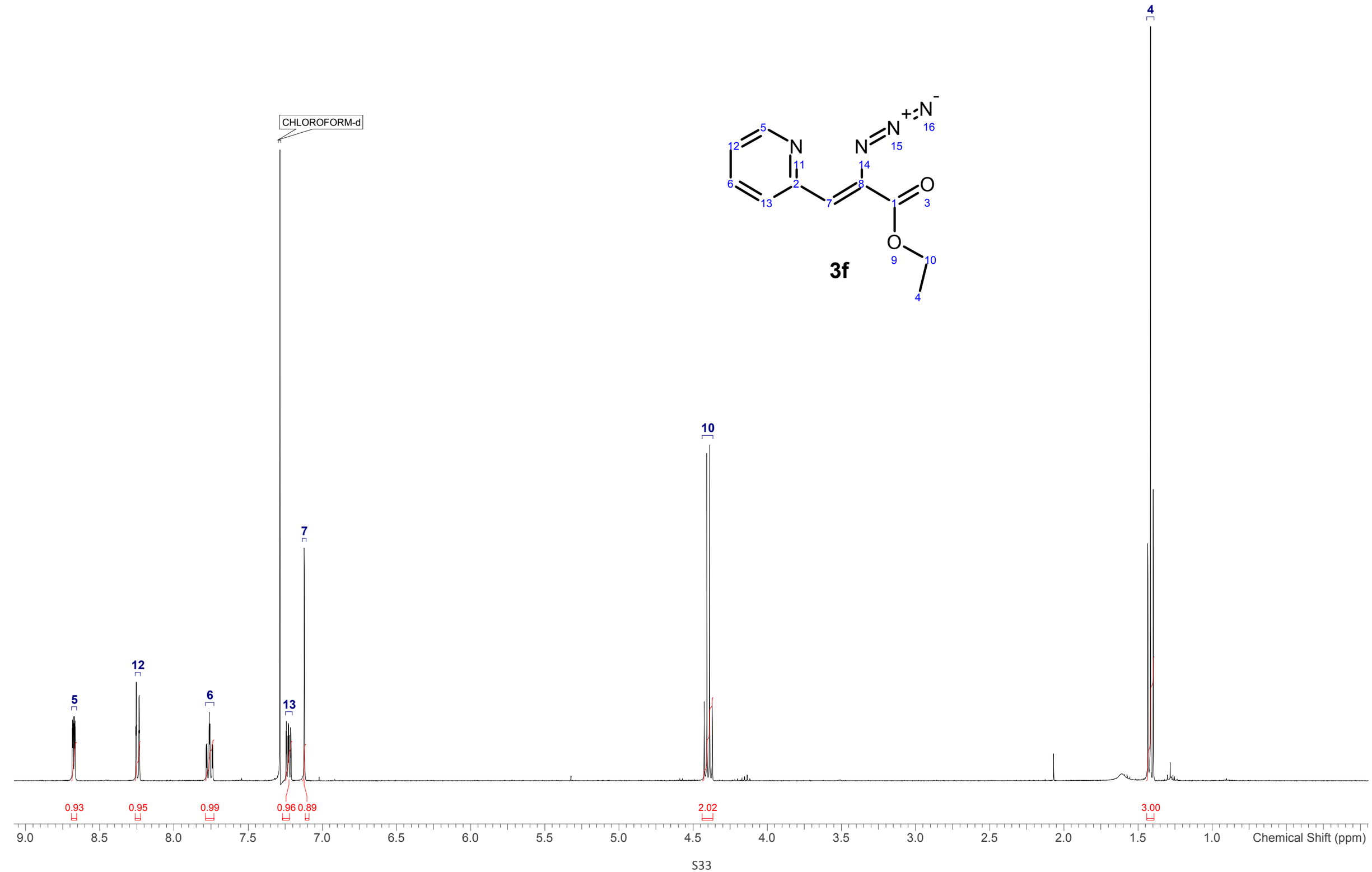
3d

+

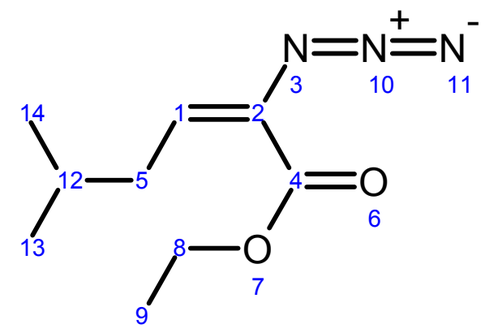
^{1}H NMR (400 MHz, DMSO-d_6) δ ppm 9.16 (d, *J*=1.96 Hz, 1 H) 8.45 (d, *J*=1.47 Hz, 1 H) 7.07 (s, 1 H) 4.32 (q, *J*=6.85 Hz, 3 H) 1.29 - 1.36 (m, 4 H)



^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 8.66 - 8.69 (m, 1 H) 8.24 (dt, *J*=8.19, 1.04 Hz, 1 H) 7.76 (td, *J*=7.70, 1.71 Hz, 1 H) 7.23 (ddd, *J*=7.34, 4.89, 0.98 Hz, 1 H) 7.12 (s, 1 H) 4.37 - 4.44 (m, 3 H) 1.39 - 1.44 (m, 3 H)

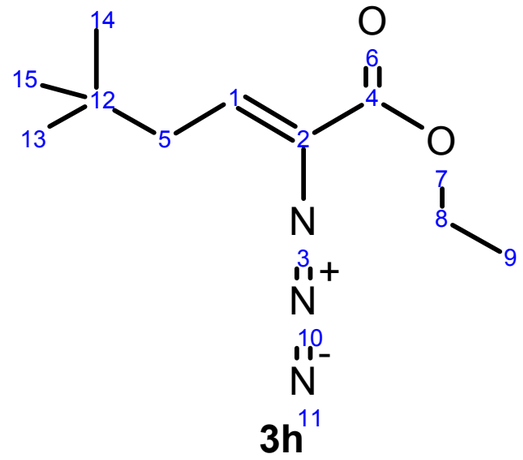


^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.23 (t, *J*=7.58 Hz, 1 H) 4.24 - 4.36 (m, 2 H) 2.06 - 2.18 (m, 2 H) 1.66 - 1.82 (m, 1 H) 1.27 - 1.41 (m, 3 H) 0.94 (d, *J*=6.85 Hz, 6 H)



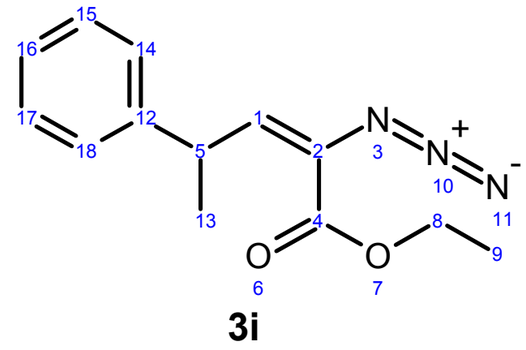
3g

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.21 - 6.33 (m, 1 H) 4.24 - 4.39 (m, 2 H) 2.12 - 2.21 (m, 2 H) 1.33 - 1.42 (m, 3 H) 0.92 - 1.01 (m, 9 H)

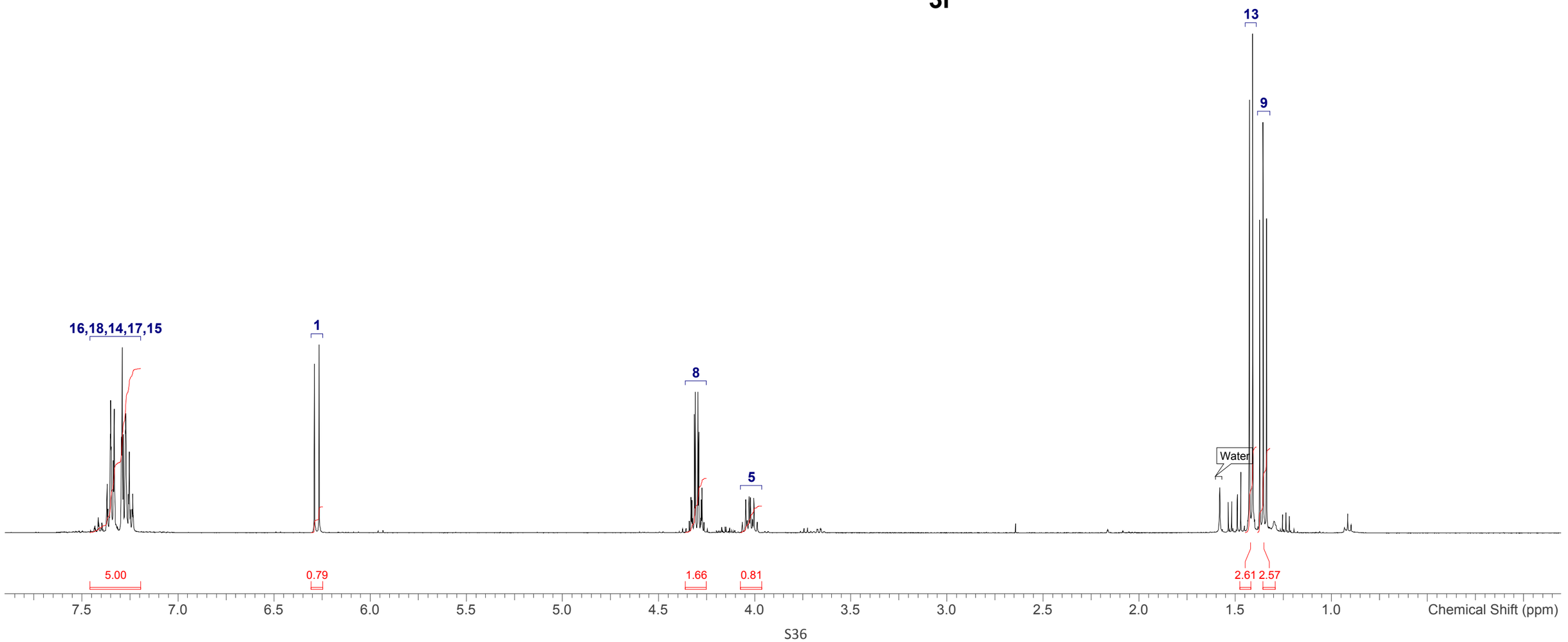


3h

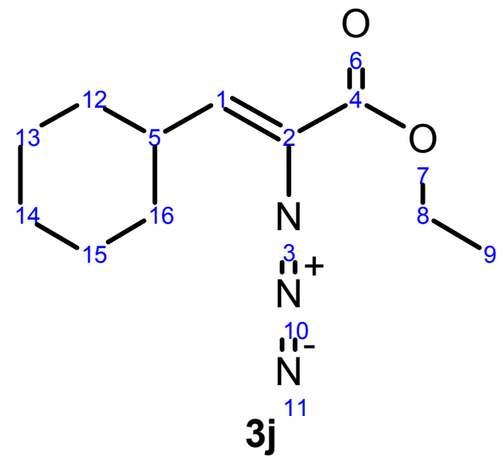
^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.19 - 7.46 (m, 5 H) 6.28 (d, *J*=9.78 Hz, 1 H) 4.25 - 4.36 (m, 2 H) 4.03 (dd, *J*=9.78, 6.85 Hz, 1 H) 1.39 - 1.45 (m, 3 H) 1.32 - 1.38 (m, 3 H)



3i

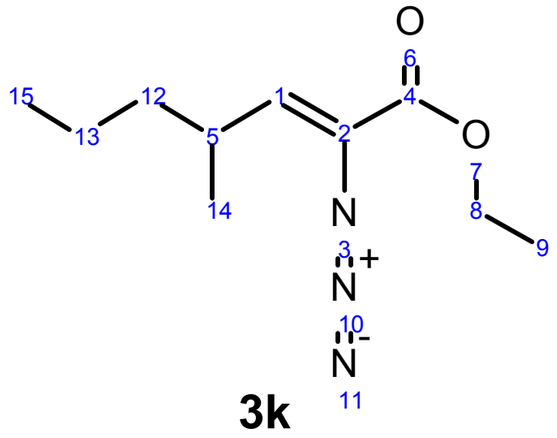


^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.05 (d, *J*=9.29 Hz, 1 H) 4.30 (q, *J*=7.17 Hz, 2 H) 2.47 - 2.58 (m, 1 H) 1.65 - 1.79 (m, 6 H) 1.36 (t, *J*=7.09 Hz, 4 H) 1.05 - 1.34 (m, 6 H)



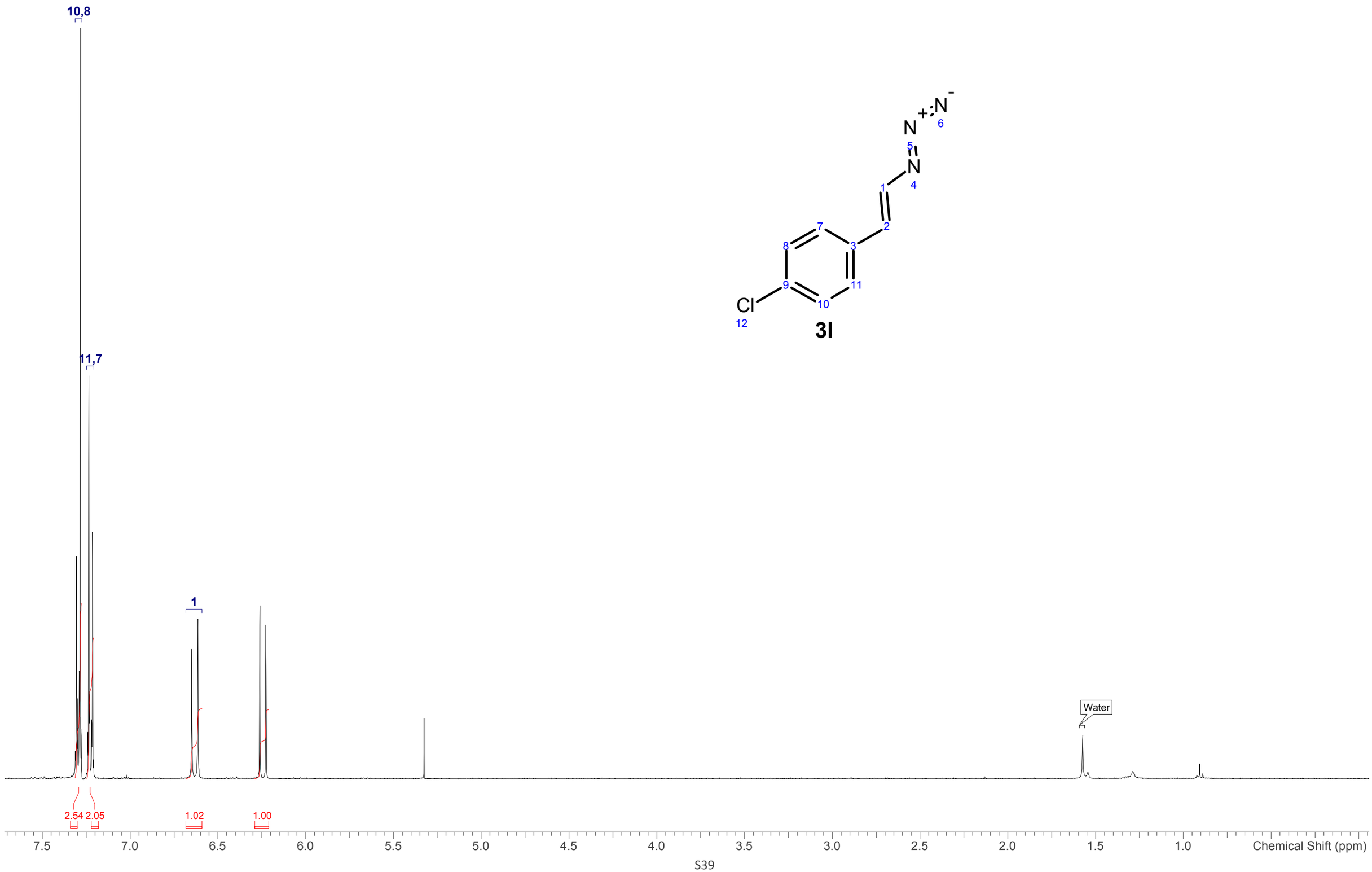
3j

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 6.01 (d, *J*=9.78 Hz, 1 H) 4.25 - 4.35 (m, 2 H) 2.63 - 2.78 (m, 1 H) 1.37 (t, *J*=7.09 Hz, 4 H) 1.23 - 1.34 (m, 4 H) 1.01 (d, *J*=6.85 Hz, 3 H) 0.88 - 0.95 (m, 3 H)



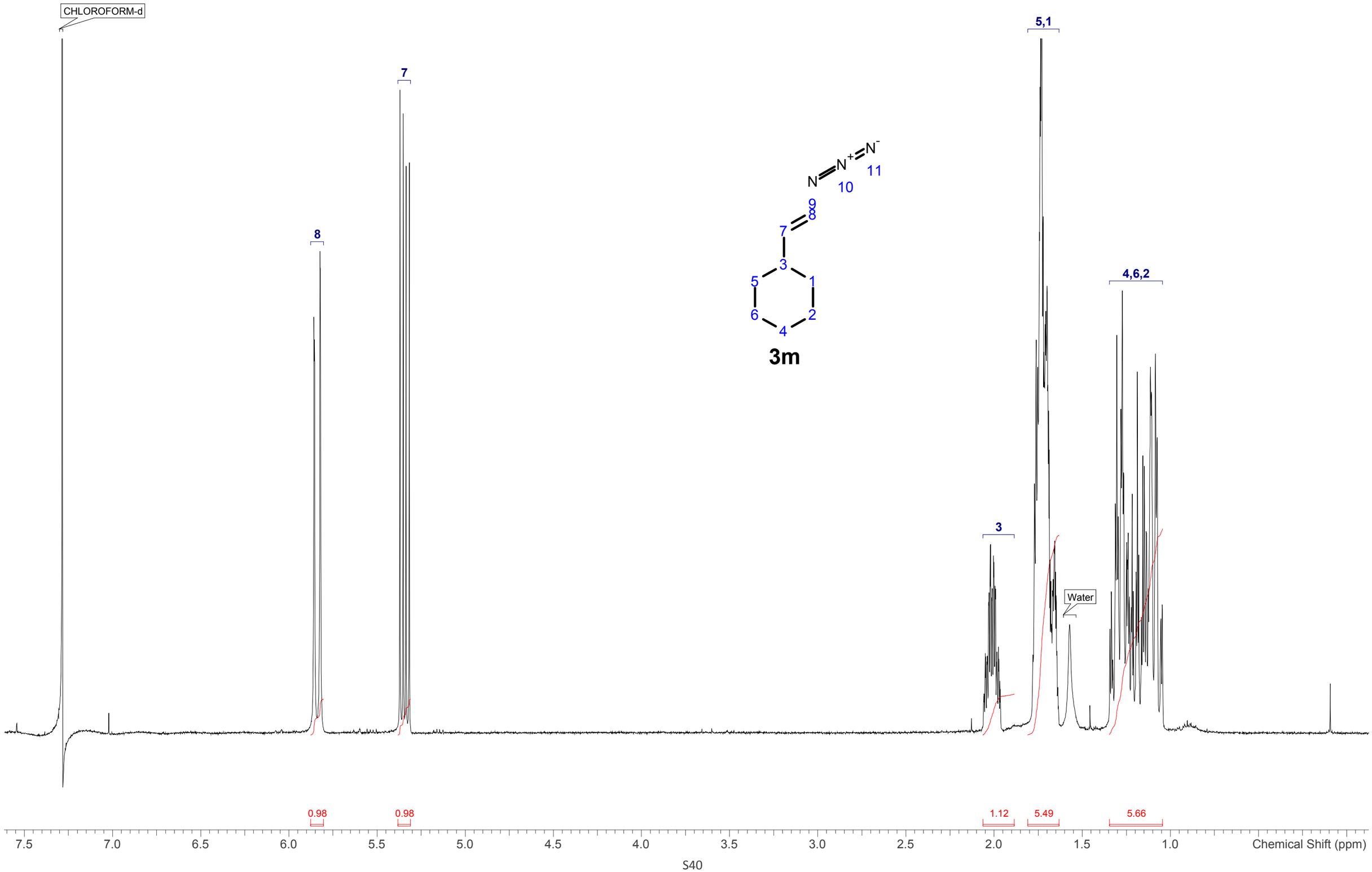
3k

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.27 - 7.31 (m, 3 H) 7.21 - 7.25 (m, 3 H) 6.63 (d, *J*=14.18 Hz, 1 H) 6.26 (s, 1 H)



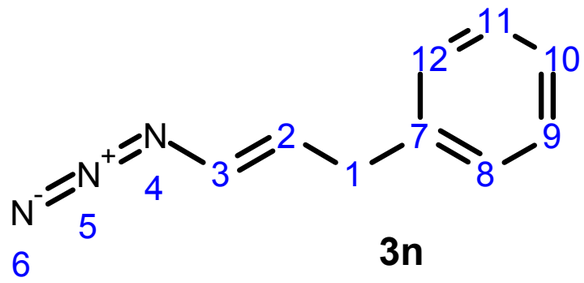
3l

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 5.84 (dd, *J*=13.69, 0.98 Hz, 1 H) 5.34 (dd, *J*=13.69, 7.34 Hz, 1 H) 1.89 - 2.06 (m, 1 H) 1.63 - 1.81 (m, 7 H) 1.04 - 1.34 (m, 7 H)



3m

^{1}H NMR (400 MHz, CHLOROFORM-*d*) δ ppm 7.30 - 7.37 (m, 2 H) 7.19 - 7.27 (m, 3 H) 5.96 (d, *J*=13.69 Hz, 1 H) 5.52 - 5.61 (m, 1 H) 3.39 (dd, *J*=7.34, 0.98 Hz, 2 H)



3n