Supporting Information

Flow Synthesis of Ethyl Isocyanoacetate Enabling the Telescoped Synthesis of 1,2,4-Triazoles and Pyrrolo[1,2-*c*]pyrimidines

Marcus Baumann, Antonio Manuel Rodriquez Garcia and Ian R. Baxendale

Department of Chemistry, Durham University, South Road, DH1 3LE, Durham, United Kingdom

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1. Materials and methods:

Unless otherwise stated, all solvents were purchased from Fisher Scientific and used without further purification. Substrates and reagents were purchased from Alfa Aesar or Sigma Aldrich and used as received.

^{1}H-NMR spectra were recorded on either Bruker Avance-400, Varian VNMRS-600 or Varian VNMRS-700 instruments and are reported relative to residual solvent: $CHCl_3$ (δ 7.26 ppm) or DMSO (δ 2.50 ppm). ^{13}C-NMR spectra were recorded on the same instruments and are reported relative to $CHCl_3$ (δ 77.16 ppm) or DMSO (δ 39.52 ppm). Data for ^{1}H-NMR are reported as follows: chemical shift (δ/ ppm) (integration, multiplicity, coupling constant (Hz)). Multiplicities are reported as follows: s = singlet, d = doublet, t = triplet, q = quartet, p = pentet, m = multiplet, br. s = broad singlet, app = apparent. Data for ^{13}C-NMR are reported in terms of chemical shift (δ/ ppm) and multiplicity (C, CH, CH_2 or CH_3). Data for ^{19}F-NMR were recorded on the above instruments at a frequency of 376 MHz using $CFCl_3$ as external standard. DEPT-135, COSY, HSQC, HMBC and NOESY experiments were used in the structural assignment. IR spectra were obtained by use of a Perkin Elmer RX1 spectrometer (neat, ATR sampling) with the intensities of the characteristic signals being reported as weak (w, <20% of tallest signal), medium (m, 21-70% of tallest signal) or strong (s, >71% of tallest signal). Low and high resolution mass spectrometry was performed using the indicated techniques on either Waters LCT Premier XE or Waters TQD instruments equipped with Acquity UPLC and a lock-mass electrospray ion source. For accurate mass measurements the deviation from the calculated formula is reported in ppm. Melting points were recorded on an Optimelt automated melting point system with a heating rate of 1 °C/min and are uncorrected. HPLC purification was accomplished using a PerkinElmer Series-200 instrument equipped with a Waters XBridge™ preparative C18 column (5 μm, 19x100 mm, 7 mL/min) with a gradient of MeCN/water (start 40:60 to 95/5 over 10 min, remaining at 95/5 for 5 min and returning to 60/40 over 2 min). Single crystal X-ray data were collected at 120.0K on a Bruker SMART 6000 (sealed tube, graphite monochromator) (compounds **7h** and **SI12f'**) and Bruker D8 Venture (Photon 100 CMOS detector, IμS microsource, focusing mirrors) (compounds **12a, 12f** and **12i**) diffractometers (λMoKα, λ=0.71073Å) equipped with Cryostream (Oxford Cryosystems) open flow nitrogen cryostates. The structures were solved by direct methods and refined by full-matrix least squares on F^2 for all data using SHELX [G.M. Sheldrick, *Acta Cryst*. (2008), A64, 112-122] and OLEX2 [O. V. Dolomanov, L. J. Bourhis, R. J. Gildea, J. A. K. Howard and H. Puschmann, *J. Appl. Cryst*. (2009), 42, 339-341] software. All non-hydrogen atoms were refined with anisotropic displacement parameters, the H-atoms in the structures **12a**, **12f** and **12i** were placed in calculated positions and refined in "riding" mode. The H atoms in the other structures were found in the difference Fourier maps and refined isotropically. Crystallographic data and parameters of the refinement are given in **Table 1.** Crystallographic data for the structures have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication CCDC-1039437-1039441.

2. Experimental procedure for the synthesis of ethyl isocyanoacetate 3:

Small scale procedure: A solution containing *N*-formyl glycine ethyl ester (**1**, 1.31 g, 10 mmol), DIPEA (2.62 g, 20 mmol) and DMAP (0.45 g, 3 mmol) in dry DCM (10 mL) was loaded in a sample loop and combined with a second stream containing triphosgene (**2**, 0.98 g, 3.3 mmol) also dissolved in dry DCM (10 mL) at individual channel flow rates of 0.5 mL/min. The combined stream was directed into two linked 10 mL FEP reactor vessels to achieve a 20 minutes residence time at ambient temperature. The output was collect and the solvent was carefully evaporated to 80% of its total volume. The crude material was filtered through silica (5 g) and washed with DCM (2 × 10 mL) to obtain the salt-free product. The desired product **3** was obtained as dark yellow oil after evaporation of the organic phase (1.03 g, 91 % isolated yield, >97% purity by ^{1}H NMR).
In an analogous fashion this procedure was used in order to prepare compound **3** on 100 mmol run scale by using stock solutions of the starting materials and pumping them directly through the HPLC pump head rather than by delivery through the sample loops.

^{1}H NMR (400 MHz, $CDCl_3$) δ 4.28 (2H, q, *J* = 7.2 Hz), 4.22 (2H, s), 1.32 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (101 MHz, $CDCl_3$) δ 164.0 (C), 161.4 (C), 62.9 (CH_2), 43.6 (CH_2), 14.2 (CH_3). IR (neat): ν 2984.4 (w), 2162.3 (s), 1748.1 (s), 1424.0 (w), 1373.8 (s), 1204.2 (s), 1097.2 (w), 1028.3 (s), 991.9 (m). This data was consistent with published data [I. Ugi, U. Fetzer, U. Eholzer, H. Knupfer and K. Offermann, *Angew. Chem. Int. Ed.* **1965,** *4*, 472-484].

3. Experimental procedure for the synthesis of 1,2,4-triazoles 7a-h:

Stock solutions of starting materials were prepared as follows:
Solution 1; *N*-formyl glycine ethyl ester (**1**, 6.55 g, 50 mmol, 1 M), DIPEA (13.1 g, 100 mmol) and DMAP (2.25 g, 15 mmol) in dry DCM (50 mL). *Solution 2*; triphosgene (**2**, 4.91 g, 16.5 mmol, 0.165 M) dissolved in dry DCM (50 mL). *Solution 3*; tert-butyl nitrite (**5**, 6.19 g, ~54 mmol; 90% purity, 1.08 M) in MeCN (50 mL). *Solution 5*; Potassium carbonate (43.2 g, 313 mmol, 0.313 M) in water (1000 mL). Variable aniline starting material solution scale up (*Solution 4*); aniline (**4**, 50 mmol) in MeCN (50 mL).

For small scale reactions a Uniqsis FlowSyn with an ALF delivery and automated control system was used to fill sample loops and deriver the reagents from a sample rack to the reactor. For larger scale reactions reagents were pumped directly through the pump heads from stock bottles.

Solutions 1 and 2 were pumped (Vapourtec R2+) at 0.25 ml/min per channel to unite and enter a flow coil (10 mL, Vapourtec FEP, 20 min residence time) maintained at ambient temperature. Simultaneously, solutions 3 and 5 were pumped at 0.25 mL/min per channel (Uniqsis Flowsyn) and combined before entering a flow coil (5 mL, Vapourtec FEP, 10 min residence time) also maintained at ambient temperature. The outputs from these two flow streams were similarly combined to enter a short residence coil (2.5 mL FEP, 2.5 min residence time) and then in succession diluted with an addition stream of pure ethanol (1 mL/min flow rate) followed by an aqueous feed of potassium carbonate (2 mL/min flow rate). A static mixer (316 Stainless Steel - Series 70 Rockingham systems Part No. 070-327) was placed in-line to thoroughly blend the flow stream before it passed into a heated reaction coil (2 x 52 mL polar bear plus units, 26 min residence time) maintained at 75 °C. The total reactor output for was collected and worked up by evaporation of the solvent followed by neutralisation with dilute hydrochloric acid (1 M) and partitioning into ethyl acetate. The products were isolated in high yield and purity after solvent evaporation and trituration of the crude product with a mixture of diethyl ether/ethanol 15:1.

4. Experimental procedure for the functionalisation of 1,2,4-triazole 7h:

Synthesis of ethyl 5-bromo-1-(4-chlorophenyl)-1*H*-1,2,4-triazole-3-carboxylate (8):

To a 50 mL round bottom flask containing dry THF (10 mL) were added **7h** (1.25 g, 5.0 mmol), NBS (4.0 g, 22.5 mmol) and NaH (0.6 g, 15.0 mol, 60% in paraffin oil). The resulting thick suspension was stirred for 10 h at room temperature at which point complete consumption of starting material was indicated by thin layer chromatography. After quenching the reaction mixture by careful addition of saturated ammonium chloride solution and extractive workup (DCM/water, 3x10 mL) the crude reaction product was obtained which was further purified by column chromatography on silica gel (hexane/EtOAc 0-25%) giving the title compound as colourless crystalline solid after removal of solvents under reduced pressure (1.37 g, 83%). ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.49 (2H, d, *J* = 8.0 Hz), 7.45 (2H, d, *J* = 8.0 Hz), 4.43 (2H, q, *J* = 7.2 Hz), 1.36 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 158.6 (C), 155.7 (C), 136.3 (C), 134.4 (C), 130.3 (C), 129.7 (2CH), 126.7 (2CH), 62.4 (CH_2), 14.2 (CH_3). IR (neat) ν 2987.4 (w), 1724.9 (s), 1485.0 (s), 1428.1 (s), 1341.4 (s), 1217.3 (s), 1089.8 (s), 995.5 (s), 839.0 (s), 685.1 (s), 517.8 (s) cm^{-1}. LC-MS (ESI) 329.9 m/z (M+H). HR-MS (ESI) calculated for $C_{11}H_{10}N_3O_2ClBr$ 329.9645, found 329.9645 (M+H, Δ = 0.0 ppm). Melting range: 107.1-109.6 °C.

Synthesis of Suzuki cross coupling products 9a-9e from 8:

Exemplary procedure for preparing Suzuki product **9e**: In a microwave vial containing dry toluene (2 ml) were combined **8** (165 mg, 0.5 mmol), 3,4-dimethoxyphenyl boronic acid (137 mg, 0.75 mmol), K_2CO_3 (173 mg, 1.25 mmol) and $Pd(PPh_3)_4$ (20 mg, 0.017 mmol). Using a Biotage Initiator microwave this reaction mixture was heated at 120 °C for 10h. After cooling to ambient temperature the reaction mixture was extracted with DCM/water (3x10 mL) yielding the crude product after drying of the combined organic layers over Na_2SO_4, filtration and removal of the volatiles under reduced pressure. Final purification was accomplished by either silica column chromatography (10-30% EtOAc/hexanes) or HPLC (40/60 MeCN/water to 95/5 MeCN/water) to yield **9e** (white solid, yield 63%). In analogy compounds **9a-9d** were prepared and isolated.

Ethyl 1-(4-chlorophenyl)-5-(4'propoxy-[1,1'-biphenyl]-4-yl)-1*H*-1,2,4-triazole-3-carboxylate 9a: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.55-7.58 (4H, m), 7.52 (2H, d, *J* = 8.0 Hz), 7.44 (2H, d, *J* = 8.0 Hz), 7.38 (2H, d, *J* = 8.0 Hz), 6.96 (2H, d, *J* = 8.0 Hz), 4.54 (2H, q, *J* = 7.2 Hz), 3.96 (2H, t, *J* = 8.0 Hz), 1.83 (2H, sextet, *J* = 8.0 Hz), 1.46 (3H, t, *J* = 7.2 Hz), 1.05 (3H, t, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.9 (C), 159.4 (C), 155.6 (C), 154.8 (C), 143.1 (C), 136.2 (C), 135.6 (C), 131.7 (C), 129.8 (2CH), 129.5 (2CH), 128.1 (2CH), 126.9 (2CH), 126.7 (2CH), 124.5 (C), 115.0 (2CH), 69.6 (CH$_2$), 62.2 (CH$_2$), 22.6 (CH$_2$), 14.4 (CH$_3$), 10.5 (CH$_3$). IR (neat) ν/cm^{-1} 2966 (w), 1736 (s), 1606 (m), 1498 (m), 1468 (s), 1198 (s), 1086 (m), 989 (m), 824 (s), 732 (s). LC-MS (ESI) m/z 462.0 (M+H). HR-MS (ESI) calculated for $C_{26}H_{25}N_3O_3Cl$ 462.1584, found 462.1580 (M+H, Δ = -0.9 ppm).

Ethyl 1-(4-chlorophenyl)-5-(3-(trifluoromethyl)phenyl)-1*H*-1,2,4-triazole-3-carboxylate 9b:^{1}H NMR (400 MHz, CDCl$_3$) δ 7.94 (1H, s), 7.71 (1H, d, *J* = 8.0 Hz), 7.60 (1H, d, *J* = 8.0 Hz), 7.50 (1H, d, *J* = 8.0 Hz), 7.46 (2H, d, *J* = 8.4 Hz), 7.34 (2H, d, *J* = 8.4 Hz), 4.55 (2H, q, *J* = 7.2 Hz), 1.47 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.6 (C), 154.9 (C), 154.2 (C), 136.1 (C), 135.6 (C), 132.0 (CH), 131.6 (C-CF$_3$, q, *J* = 32 Hz), 130.0 (2CH), 129.3 (CH), 127.5 (CH, q, *J* = 4 Hz), 127.4 (C), 126.8 (2CH), 126.3 (CH, q, *J* = 4 Hz), 123.4 (CF$_3$, q, *J* = 272 Hz), 62.4 (CH$_2$), 14.3 (CH$_3$). ^{19}F NMR (376 MHz, CDCl$_3$) δ -63.0 (s). IR (neat) ν/cm^{-1} 2984 (w), 1737 (s), 1499 (m), 1325 (s), 1205 (s), 1167 (s), 1126 (s), 1073 (s), 999 (s), 836 (s), 704 (s). LC-MS (ESI) m/z 396.5 (M+H). HR-MS (ESI) calculated for $C_{19}H_{14}N_3O_2ClF_3$ 396.0727, found 396.0721(M+H, Δ = -0.3 ppm).

Ethyl 1-(4-chlorophenyl)-5-(2-isopropylphenyl)-1*H*-1,2,4-triazole-3-carboxylate 9c: ^{1}H NMR (400 MHz, CDCl$_3$) δ 7.44-7.50 (1H, m), 7.35 (1H, d, *J* = 8.0 Hz), 7.29 (2H, d, *J* = 8.0 Hz), 7.20-7.30 (4H, m), 4.54 (2H, q, *J* = 7.2 Hz), 2.63 (1H, septet, *J* = 8.0 Hz), 1.47 (3H, t, *J* = 7.2 Hz), 0.96 (6H, d, *J* = 8.0 Hz). ^{13}C NMR (100 MHz, CDCl$_3$) δ 159.9 (C), 155.6 (C), 154.6 (C), 148.1 (C), 135.6 (C), 134.8 (C), 131.2 (CH), 130.3 (CH), 129.4 (2CH), 126.2 (CH), 126.1 (CH), 126.0 (C), 125.0 (2CH), 62.2 (CH$_2$), 30.5 (CH), 23.6 (2CH$_3$), 14.4 (CH$_3$). IR (neat) ν/cm^{-1} 2965 (w), 1737, 1498 (s), 1472 (s), 1383 (m), 1198 (s), 1166 (s), 1090 (s), 990 (s), 833 (s), 730 (s). LC-MS (ESI) m/z 370.1 (M+H). HR-MS (ESI) calculated for $C_{20}H_{21}N_3O_2Cl$ 370.1322, found 370.1318 (M+H, Δ = -1.1 ppm).

Ethyl 1-(4-chlorophenyl)-5-(2-methoxypyridin-3-yl)-1*H*-1,2,4-triazole-3-carboxylate 9d: ^{1}H NMR (400 MHz, CDCl$_3$) δ 8.29 (1H, dd, *J* = 1.6, 5.2 Hz), 7.99 (1H, dd, *J* = 2.0, 8.0 Hz), 7.35 (2H, d, *J* = 8.0 Hz), 7.26 (2H, d, *J* = 8.0 Hz), 7.03 (1H, dd, *J* = 4.8, 8.0 Hz), 4.53 (2H, q, *J* = 7.2 Hz), 3.51 (3H, s), 1.45 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, CDCl$_3$) δ 160.1 (C), 159.7 (C), 154.8 (C), 152.3 (C), 150.0 (CH), 140.8 (CH), 136.7 (C), 134.9 (C), 129.3 (2CH), 124.8 (2CH), 116.9 (CH), 111.1 (C), 62.2 (CH$_2$), 53.2 (CH$_3$), 14.4 (CH$_3$). IR (neat) ν/cm^{-1} 2965 (w), 1737 (m), 1579 (m), 1499 (s), 1469 (s), 1402 (s), 1204 (s), 1095 (m), 1017 (s), 989 (s), 909 (s), 727 (s). LC-MS (ESI) m/z 359.0 (M+H). HR-MS (ESI) calculated for $C_{17}H_{16}N_4O_3Cl$ 359.0911, found 359.0910 (M+H, Δ = -0.3 ppm).

Ethyl 1-(4-chlorophenyl)-5-(3,4-dimethoxyphenyl)-1*H*-1,2,4-triazole-3-carboxylate 9e: ^{1}H NMR (400 MHz, $CDCl_3$) δ 7.42 (2H, d, *J* = 8.0 Hz), 7.35 (2H, d, *J* = 8.0 Hz), 7.15 (1H, d, *J* = 2.4 Hz), 6.93 (1H, dd, *J* = 2.4, 8.4 Hz), 6.77 (1H, d, *J* = 8.4 Hz), 4.50 (2H, q, *J* = 7.2 Hz), 3.87 (3H, s), 3.78 (3H, s), 1.44 (3H, t, *J* = 7.2 Hz). ^{13}C NMR (100 MHz, $CDCl_3$) δ 160.0 (C), 155.6 (C), 154.5 (C), 151.0 (C), 149.0 (C), 136.4 (C), 135.5 (C), 129.7 (2CH), 127.0 (2CH), 122.3 (CH), 118.8 (C), 112.0 (CH), 110.8 (CH), 62.2 (CH_2), 56.0 (CH_3), 55.9 (CH_3), 14.3 (CH_3). IR (neat) ν/cm^{-1} 2928 (w), 1737 (s), 1498 (s), 1257 (m), 1204 (s), 1087 (m), 1024 (s), 729 (s). LC-MS (ESI) 388.0 m/z (M+H). HR-MS (ESI) calculated for $C_{19}H_{19}N_3O_4Cl$ 388.1064, found 388.1073 (M+H, Δ = 2.3 ppm).

5. Experimental procedure for the synthesis ethyl pyrrolo[1,2-*c*]pyrimidine-3-carboxylate 11:

Representative flow procedure: Solution **A** was prepared by dissolving *N*-formyl glycine ethyl ester (**1**, 1 equiv., 1 M), DIPEA (2 equiv.) and DMAP (0.3 equiv.) in dry DCM. Solution **B** consisted of triphosgene (**2**, 0.33 equiv., 0.33 M) dissolved in dry DCM and solution **C** was prepared by dissolving 2-pyrrolecarbaldehyde (1 equiv., 0.5 M) and piperidine (6 equiv.) in dry DCM. In order to prepare ethyl isocyanoacetate *in situ*, solutions **A** and **B** were pumped at 0.5 mL/min each and directed into a flow reactor (10 mL and 5 mL coil reactors in series) held at ambient temperature providing a residence time of 15 minutes. Upon exiting this section the ethyl isocyanoacetate reagent stream was combined with solution **C** (pumped at 1 mL/min) via a T-mixing piece leading into a subsequent flow reactor maintained at 85 °C (52 mL Polar Bear plus reactor; residence time 26 minutes). Using a fourth pump (0.5 mL/min) a stream of water was combined with the crude reaction stream in order to dissolve salts that formed during the course of the reaction sequence. After collecting the reaction product, extractive work-up (DCM/water, crude yield 85%) followed by chromatography using a ISOLERA chromatography system with a gradient sequence (Hex:EA 20:80 or a stepwise ISOLERA gradient: 0; 0-10%; 10-35%; 35-50%; 50-70%) delivers the target compound after evaporation of the volatiles with an isolated yield of 78%. Compound description: yellow waxy solid. Mp 68.5-69.7 °C. ^{1}H NMR (700 MHz, $CDCl_3$) δ 8.74 (s, 1H), 8.08 (s, 1H), 7.42 (d, *J* = 2.8 Hz, 1H), 6.85 (dd, *J* = 3.9, 2.8 Hz), 6.62 (d, *J* = 3.9 Hz, 1H), 4.32 (q, *J* = 7.2 Hz, 2H), 1.31 (t, *J* = 7.2 Hz, 3H). ^{13}C NMR (176 MHz, $CDCl_3$) δ 165.0 (C), 137.8 (CH), 130.5 (C), 130.4 (C), 117.67 (CH), 117.66 (CH), 113.5 (CH), 105.0 (CH), 61.3 (CH_2), 14.3 (CH_3). IR (neat): 2985.2 (w), 1703.5 (s), 1537.9 (m), 1453.8 (s), 1434.6 (s), 1351.8 (s), 1270.5 (s), 1204.4 (s), 1083.6 (s), 1020.3 (s), 936.2 (s), 894.0 (s), 795.8 (s), 775.4 (s), 733.5 (s), 613.1 (s) cm^{-1}. LC-MS (ESI): 213.0 (M+Na); HRMS (ESI): calculated for $C_{10}H_{11}N_2O_2$ 191.0821, found 191.0813 (M+H, Δ = -4.2 ppm).

6. Experimental procedures for difunctionalisation reactions of ethyl pyrrolo[1,2-*c*]pyrimidine-3-carboxylate 11 towards compounds 12a-i

Halogenation reactions of substrate **11**:

Ethyl pyrrolo[1,2-*c*]pyrimidine-3-carboxylate **11** (190 mg, 1.0 mmol) was dissolved in $CHCl_3$ (4 mL, 0.25 M) at ambient temperature. To this solution was added the appropriate halogenating agent (NCS, NBS or NIS) in stoichiometric amounts (1.0 mmol). The reaction mixture was stirred at ambient temperature and monitored by tlc to reach complete consumption of starting material in typically 2-3 hours. After aqueous extraction the organic layers were combined, dried over anhydrous sodium sulfate, filtered and evaporated under reduced pressure to yield monohalo-derivatives of **11**. For the synthesis of **12e** 2.0 equiv. of NBS (0.5 M in $CHCl_3$) were used. ^{1}H NMR spectroscopy was used to verify the presence of monofunctionalised products as well as the high purity of the sample (>90%). These materials were used directly in the subsequent step without further purification.

Nitration of substrate **11**:

A solution of **11** (190 mg, 1.0 mmol) in CH_2Cl_2 (0.5 M) was slowly added to a mixture containing KNO_3 (1.2 mmol) in CH_2Cl_2 (2 mL) and conc. H_2SO_4 (0.2 mL) maintained at 0 °C. This mixture was stirred under cooling for 30 min followed by a further 60 min at ambient temperature. Upon complete consumption of substrate **11** the reaction mixture was extracted with CH_2Cl_2 and water (3x15 mL). The combined organic layers were dried over anhydrous Na_2SO_4, filtered and evaporated under reduced pressure to yield the crude nitration product as a yellow solid. ^{1}H NMR revealed a mixture of two mono-nitration products (~1:1 ratio) that could be separated by silica gel chromatography (15% EtOAc/hexane). In order to prepare the dinitro product **12d** the same procedure can be used utilizing employing 2.2 equiv. KNO_3.

Trifluoroacetylisation of substrate **11**:

At ambient temperature trifluoroacetic anhydride (1.0 mmol) was added to a solution of **11** (190 mg, 1.0 mmol) in $CHCl_3$ (0.25 M) and DMAP (25 mg). The reaction mixture was then warmed to 50°C and stirred at this temperature for 12h. After aqueous extraction the desired product was obtained after evaporation of the volatiles as a light yellow solid. Residual sm can be easily separated by column chromatography (15% EtOAc/hexane). The resulting ethyl 7-(2,2,2-trifluoroacetyl)pyrrolo[1,2-*c*]pyrimidine-3-carboxylate was crystalised and single crystal X-ray diffraction experiments were used to confirm the connectivity of this product **SI12f'** and this structure has been deposited as CCDC 1039437.

Formylation of substrate **11**:

A solution of substrate **11** was prepared in $CHCl_3$ (0.3M, 3.3 mL) at ambient temperature. To this was added Vilsmeyer reagent (1.1 equiv.). After 2 h a second portion of Vilsmeier reagent was added (1.1 equiv.) that was needed as the quality of this commercial reagent was found to only lead to 50% conversion of **11** initially. After a total of 4 h tlc confirmed complete consumption of **11**. Clean mono-formylated product was isolated after aqueous extraction (3 × 10 mL) and removal of the solvents under reduced pressure. Using ^{1}H NMR spectroscopy revealed the presence of a single formylated product that did not require any further purification.

Synthesis of **12a**:

To a solution of ethyl 7-chloropyrrolo[1,2-*c*]pyrimidine-3-carboxylate (1 mmol) in DCM (2 mL) was added conc. H_2SO_4 (0.2 mL) and conc. HNO_3 (0.2 mL). This mixture was stirred at room temperature until all starting material was consumed (~4 h). The resulting mixture was neutralised with aqueous K_2CO_3 and subsequently extracted (DCM/water, 3 × 10 mL) to yield the crude product as a brown solid after evaporation of the solvent. Final purification was accomplished by silica gel chromatography using EtOAc/hexanes (10-20% EtOAc) as eluent. The connectivity of this structure was confirmed by X-ray crystallography (CCDC 1039441).

Synthesis of **12b**:

To a solution of ethyl 7-chloropyrrolo[1,2-*c*]pyrimidine-3-carboxylate (1 mmol) in $CHCl_3$ (2 mL) was added NBS (1.1 equiv.) and the resulting mixture was stirred at 45 °C for 10 h to reach full consumption of the starting material (monitored by tlc). The crude reaction product was directly extracted with water (3 × 10 mL) delivering the crude product after removal of the volatiles as light brown solid that was further purified by passing over a plug of silica (3 g, 20% EtOAc/hexanes as eluent).

Synthesis of **12c**:

To a solution of ethyl 7-bromopyrrolo[1,2-*c*]pyrimidine-3-carboxylate (1 mmol) in $CHCl_3$ (2 mL) was added NCS (1.1 equiv.) and the resulting mixture was stirred at 45 °C for 14 h to reach full consumption of the starting material (monitored by tlc). The crude reaction product was directly extracted with water (3 × 10 mL) delivering the crude product after removal of the volatiles as light brown solid that was further purified by passing over a plug of silica (3 g, 20% EtOAc/hexanes as eluent).

Synthesis of **12d** and **12e**: see sections on nitration and bromination of **11** above.

Synthesis of **12f**:

To a solution of ethyl 7-(2,2,2-trifluoroacetyl)pyrrolo[1,2-*c*]pyrimidine-3-carboxylate (0.5 mmol) prepared in $CHCl_3$ (2 mL) was added NBS (1.5 equiv.). The resulting mixture was stirred at 50 °C for 24 h to reach full conversion of the starting material. Direct extraction with DCM/water (3 × 10 mL) and removal of the solvents at reduced pressure yielded the crude product which was further purified by silica column chromatography (10-30% EtOAc/hexanes) whose structure was unambiguously confirmed by single crystal X-ray diffraction (CCDC 1039439).

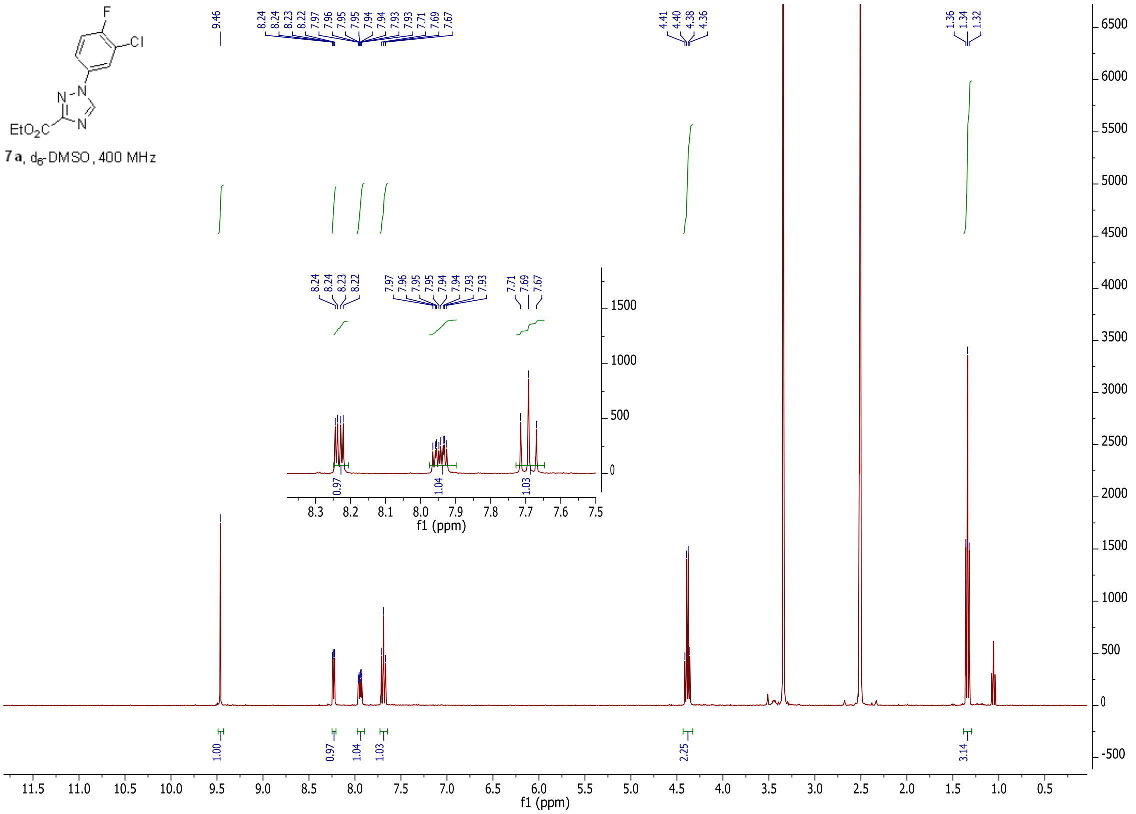
Synthesis of **12g**:

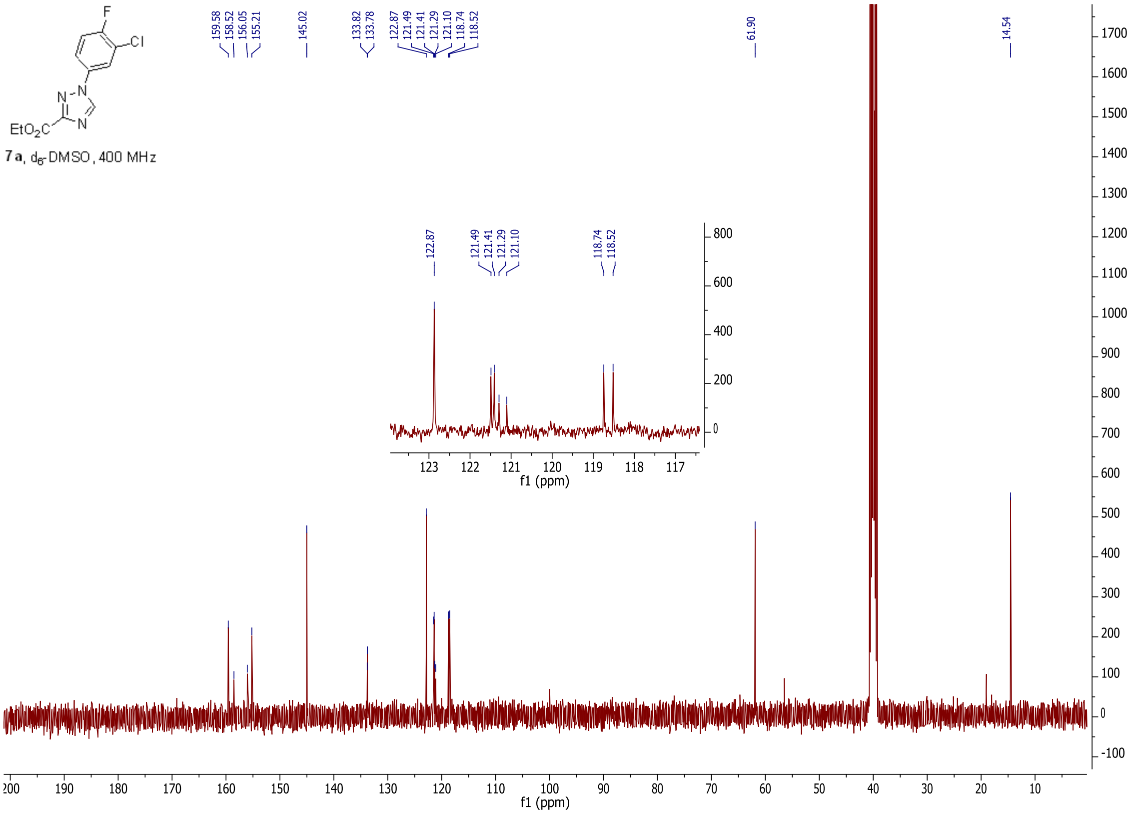
To a solution of ethyl 7-formylpyrrolo[1,2-*c*]pyrimidine-3-carboxylate (0.5 mmol) in $CHCl_3$ (2 mL) was added NIS (1.0 equiv.) in one portion. The resulting mixture was stirred at 40 °C for 12 h at which point tlc analysis indicated full conversion of the starting material. Direct extractive workup (DCM/water, 3 × 10 mL) furnished the crude product, which was further purified by silica column chromatography (10-25% EtOAc/hexanes).

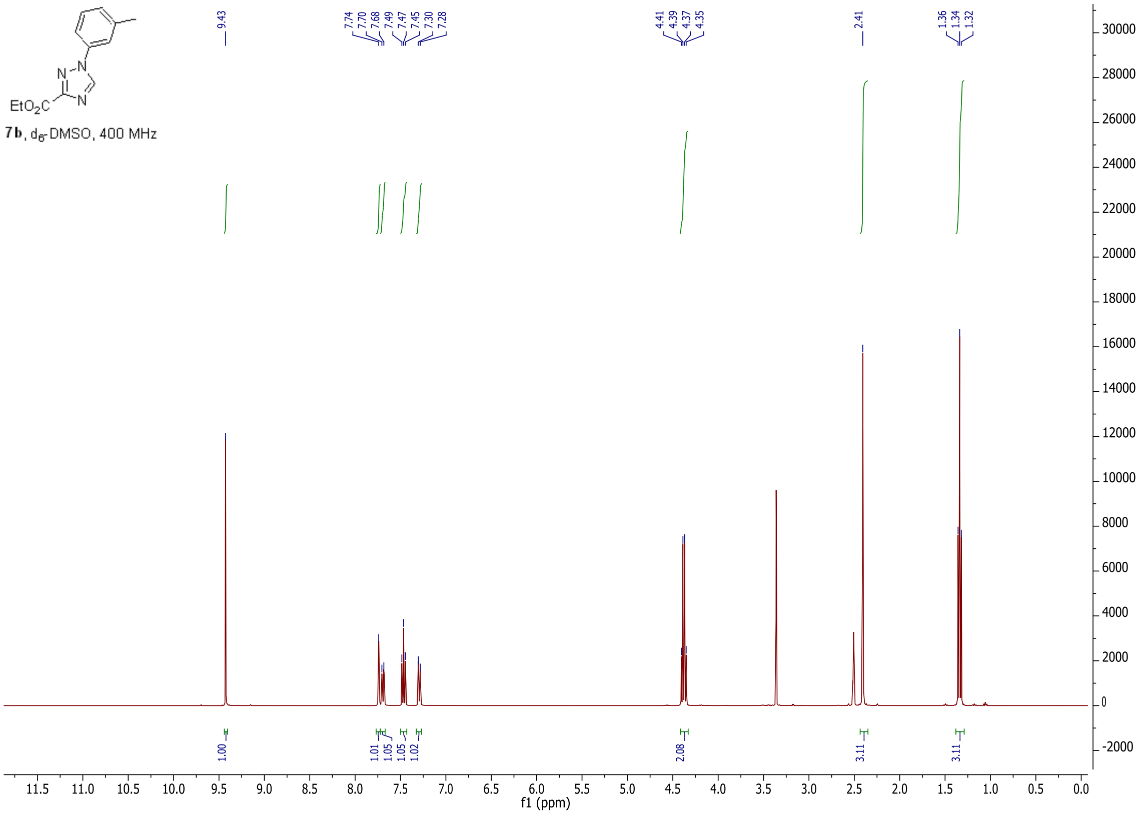
Synthesis of **12h** and **12i**:

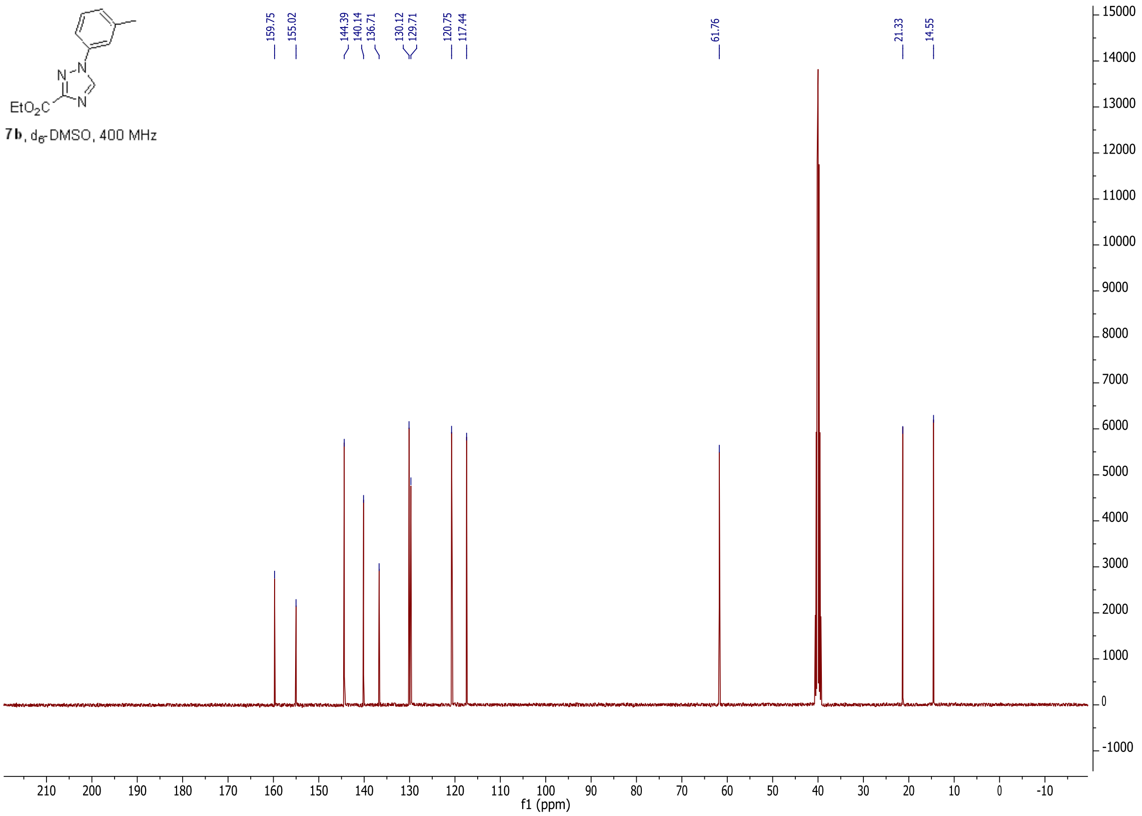
To a solution of ethyl 7-iodopyrrolo[1,2-*c*]pyrimidine-3-carboxylate (1 mmol) in $CHCl_3$ (2 mL) was added conc. H_2SO_4 (0.2 mL) and conc. HNO_3 (0.2 mL). The resulting mixture was stirred at room temperature for 4 h at which point tlc analysis indicated full conversion of starting material and the presence of two new products. After neutralization with aq. K_2CO_3 and extractive workup the crude product was dry-loaded onto silica gel (0.3 g) and placed on top of a silica column (6 g). Elution with 10-30% EtOAc/hexanes delivered both **12h** and **12i** as individual products. The connectivity of **12i** was further confirmed by single crystal X-ray diffraction (CCDC1039440).

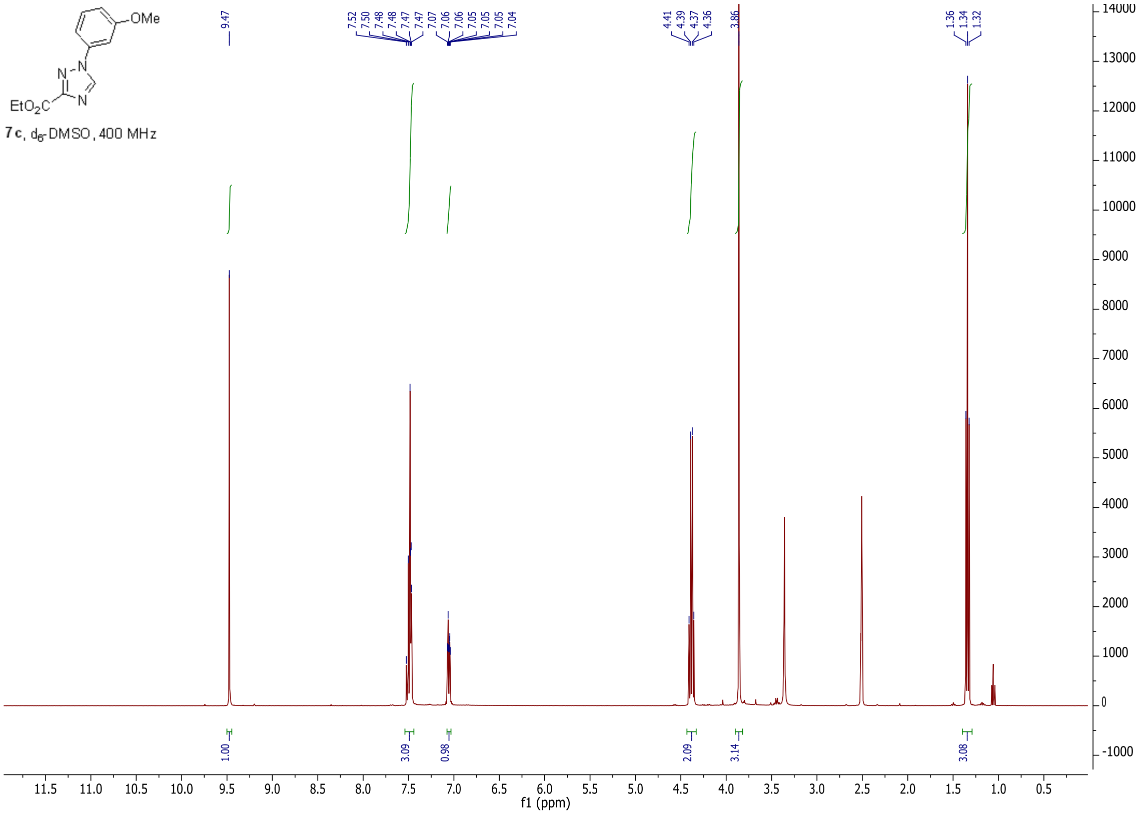
7. NMR-Spectra of compounds 7a-h:

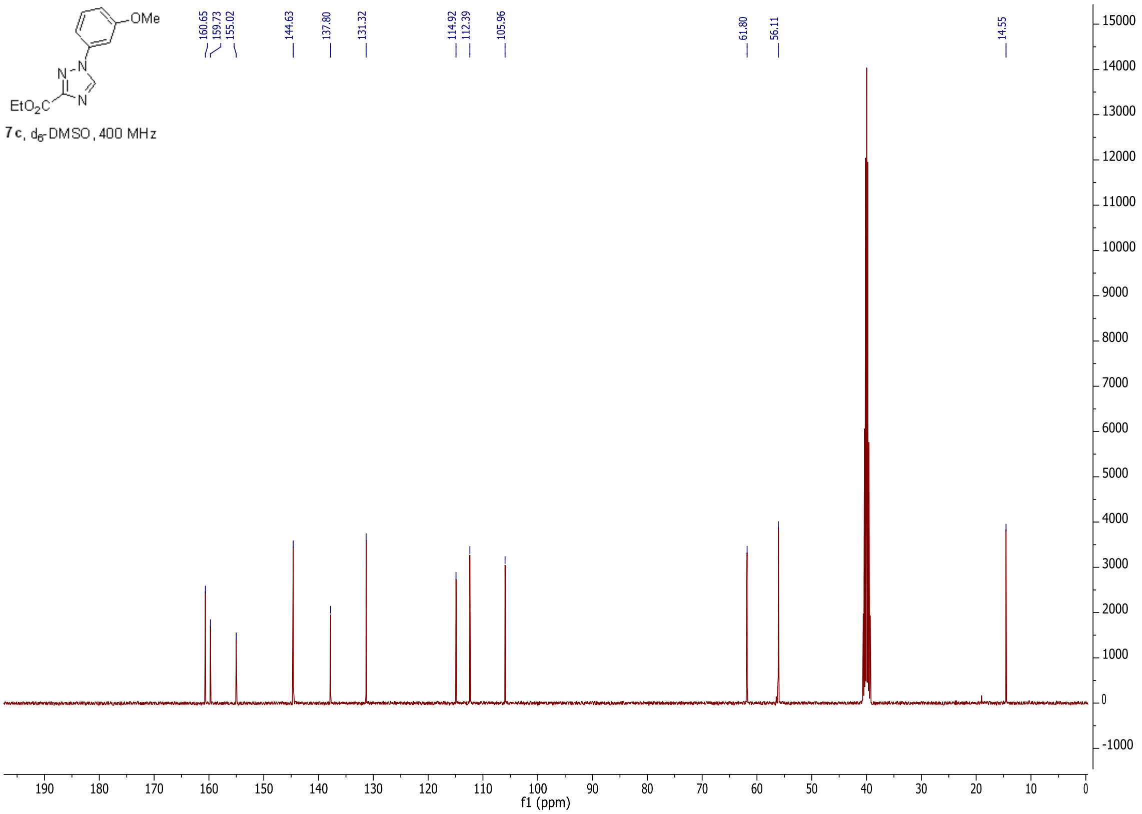


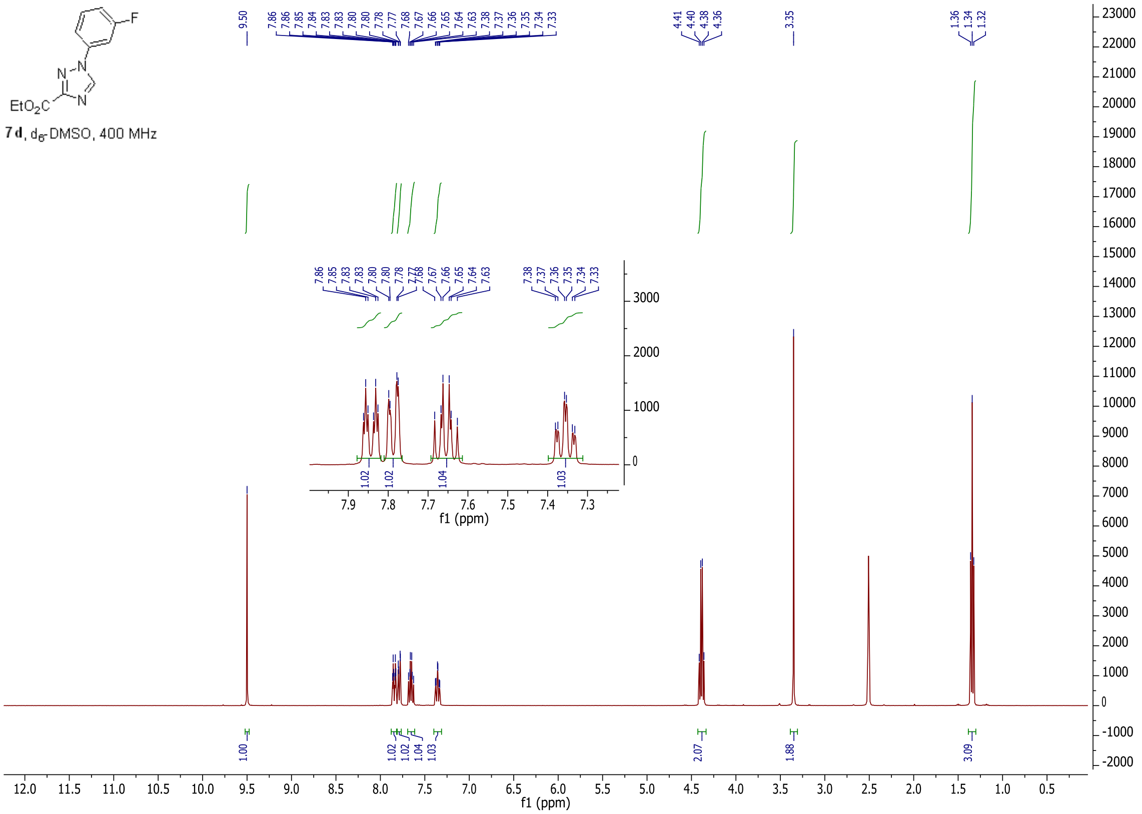



N
N
N
EtO$_2$C
7b, d$_6$-DMSO, 400 MHz
9.43
7.74
7.70
7.68
7.49
7.47
7.45
7.30
7.28
4.41
4.39
4.37
4.35
2.41
1.36
1.34
1.32
1.00
1.01
1.05
1.05
1.02
2.08
3.11
3.11
30000
28000
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

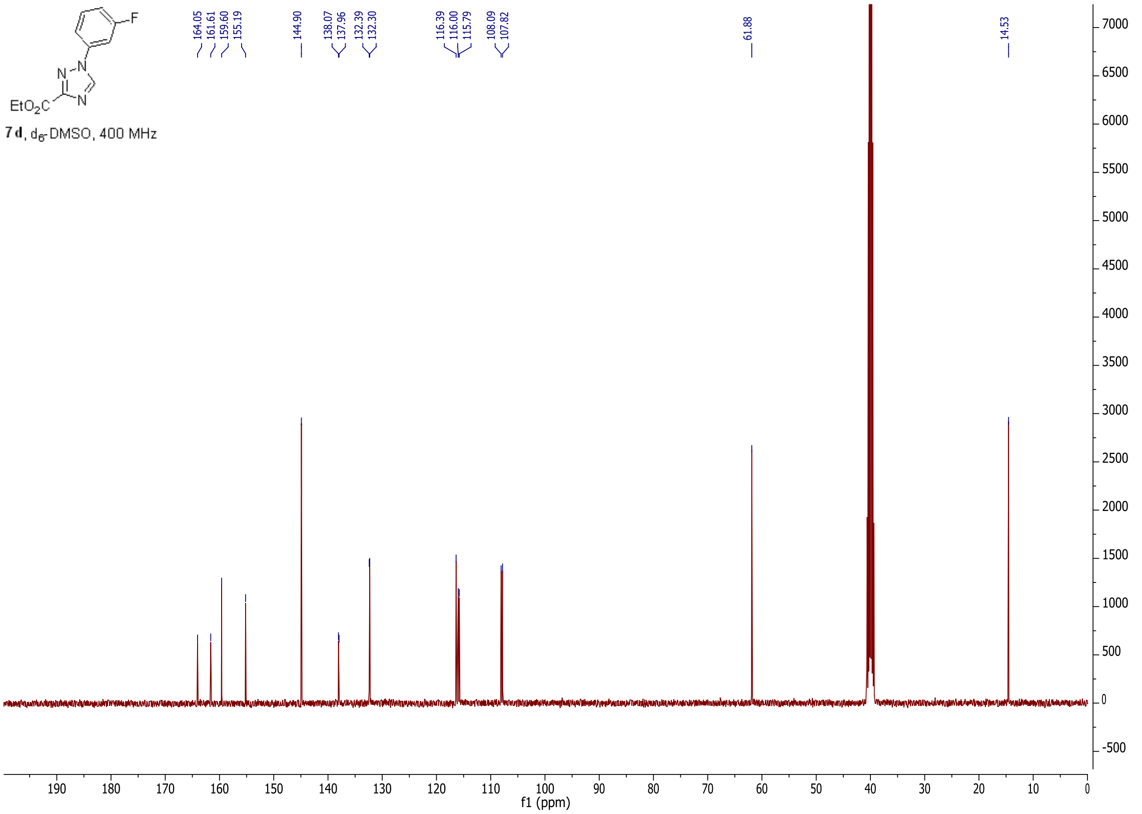

N
N
N
EtO$_2$C
7b, d$_6$-DMSO, 400 MHz
159.75
155.02
144.39
140.14
136.71
130.12
129.71
120.75
117.44
61.76
21.33
14.55
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


OMe
N
N
N
EtO$_2$C
7c, d$_6$-DMSO, 400 MHz
9.47
7.52
7.50
7.48
7.48
7.47
7.47
7.47
7.07
7.06
7.06
7.05
7.05
7.05
7.04
4.41
4.39
4.37
4.36
3.86
1.36
1.34
1.32
1.00
3.09
0.98
2.09
3.14
3.08
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

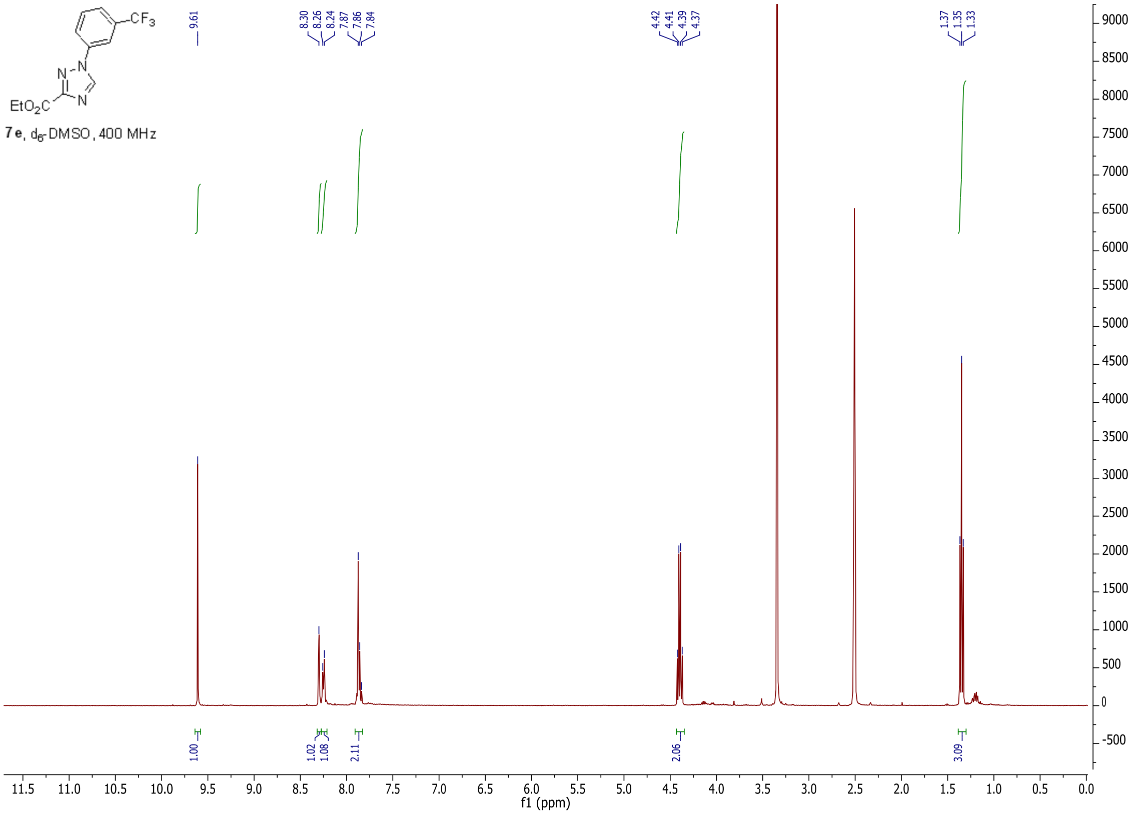

OMe
N
N
N
EtO$_2$C
7c, d$_6$-DMSO, 400 MHz
160.65
159.73
155.02
144.63
137.80
131.32
114.92
112.39
105.96
61.80
56.11
14.55
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)

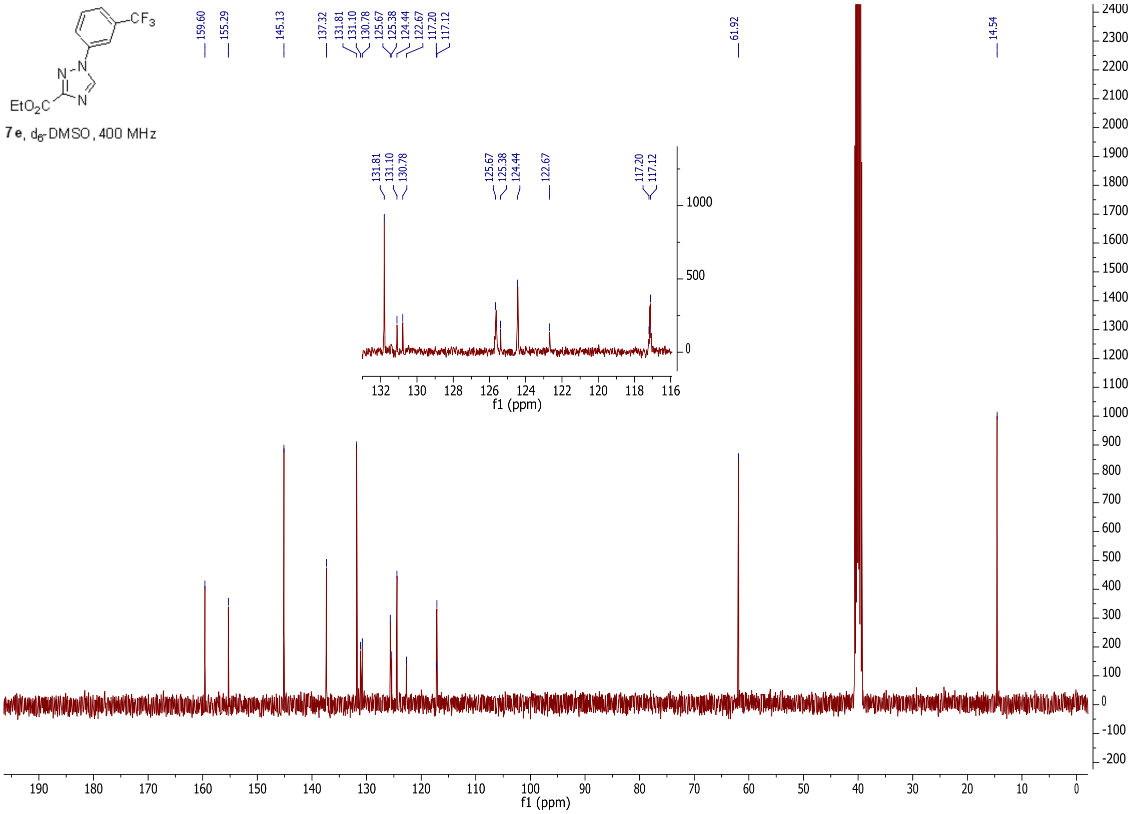


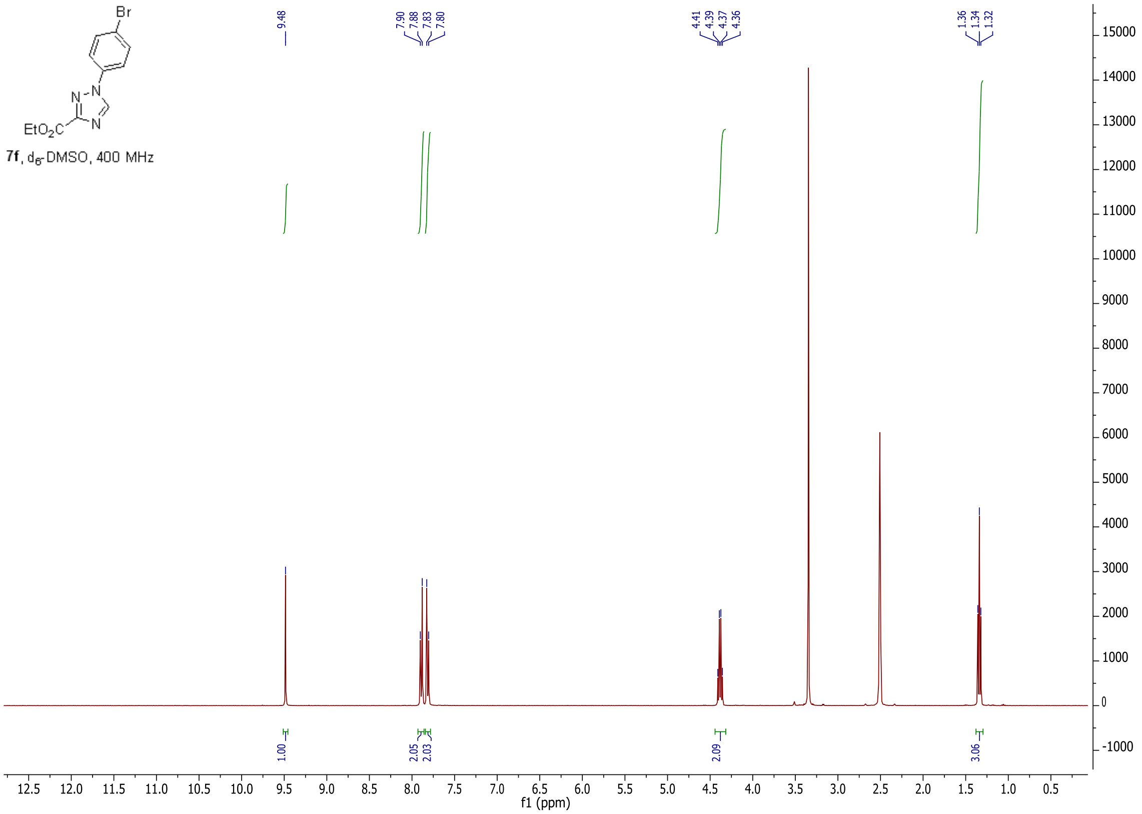
7d, d_6-DMSO, 400 MHz

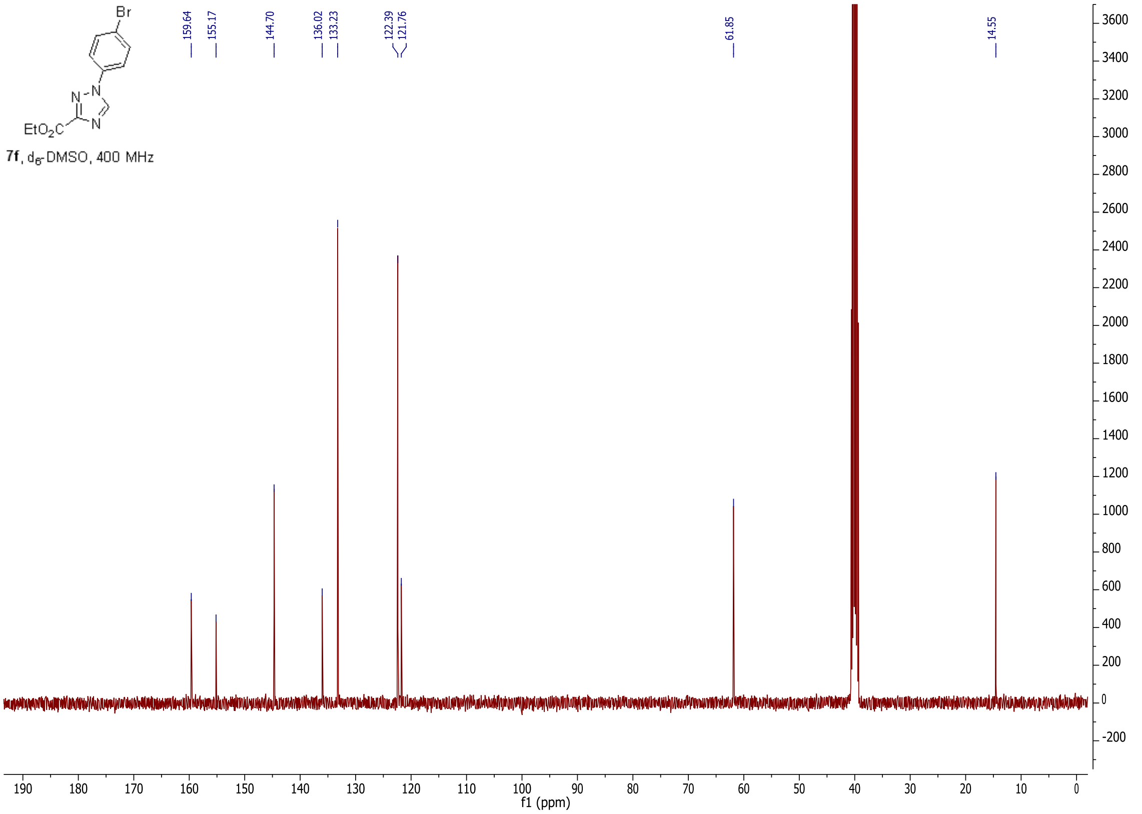


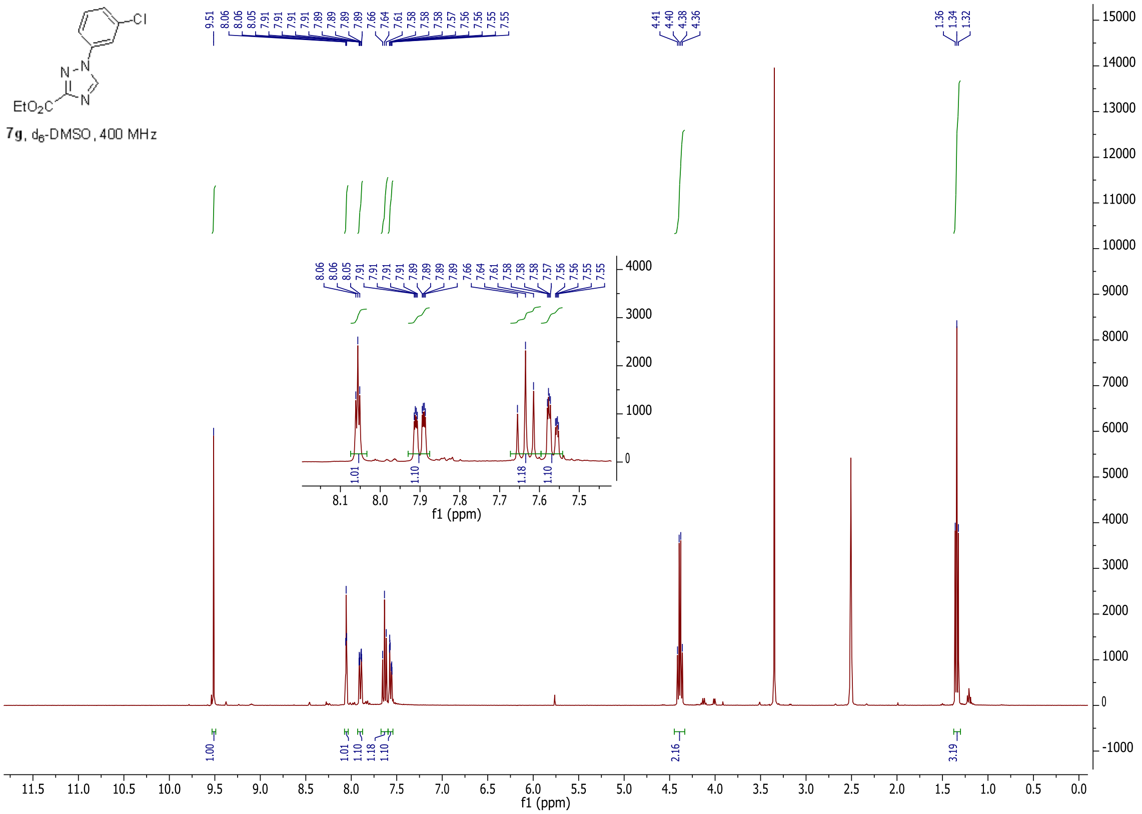
7d, d_6-DMSO, 400 MHz

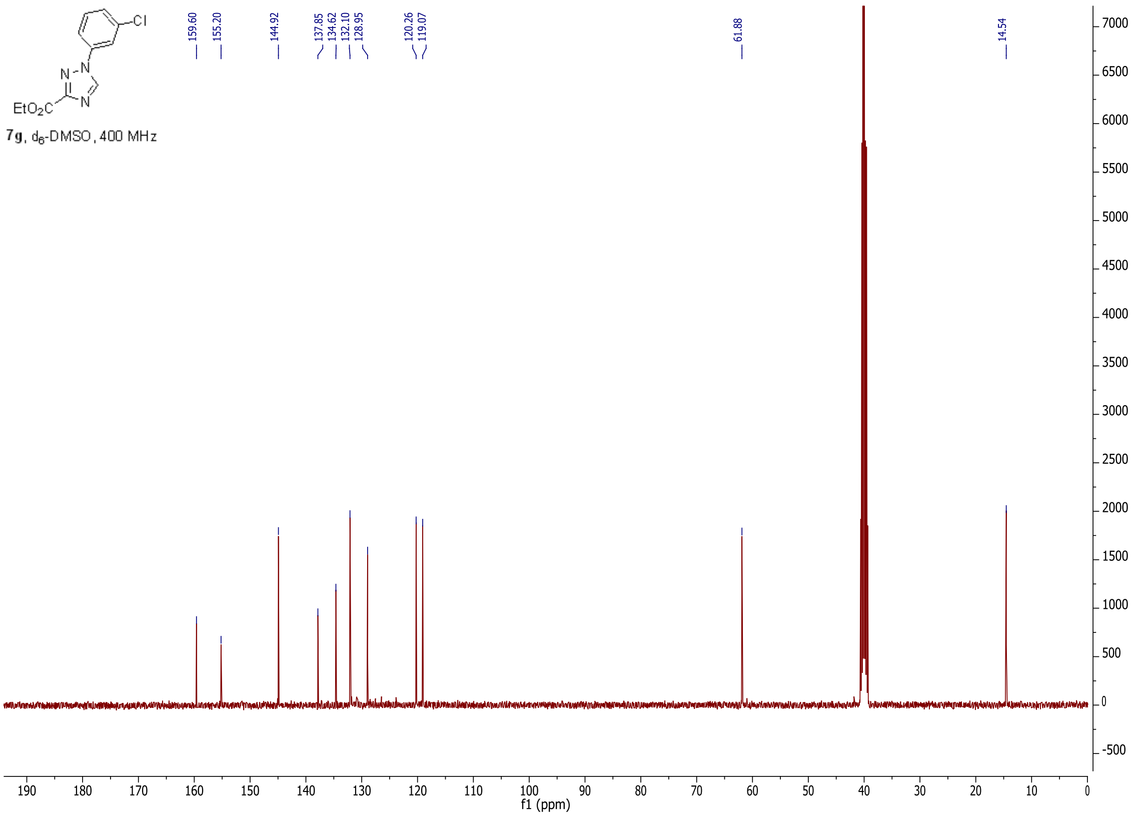

CF$_3$
N
N
N
EtO$_2$C
7e, d$_6$-DMSO, 400 MHz
9.61
8.30
8.26
8.24
7.87
7.86
7.84
4.42
4.41
4.39
4.37
1.37
1.35
1.33
1.00
1.02
1.08
2.11
2.06
3.09
f1 (ppm)

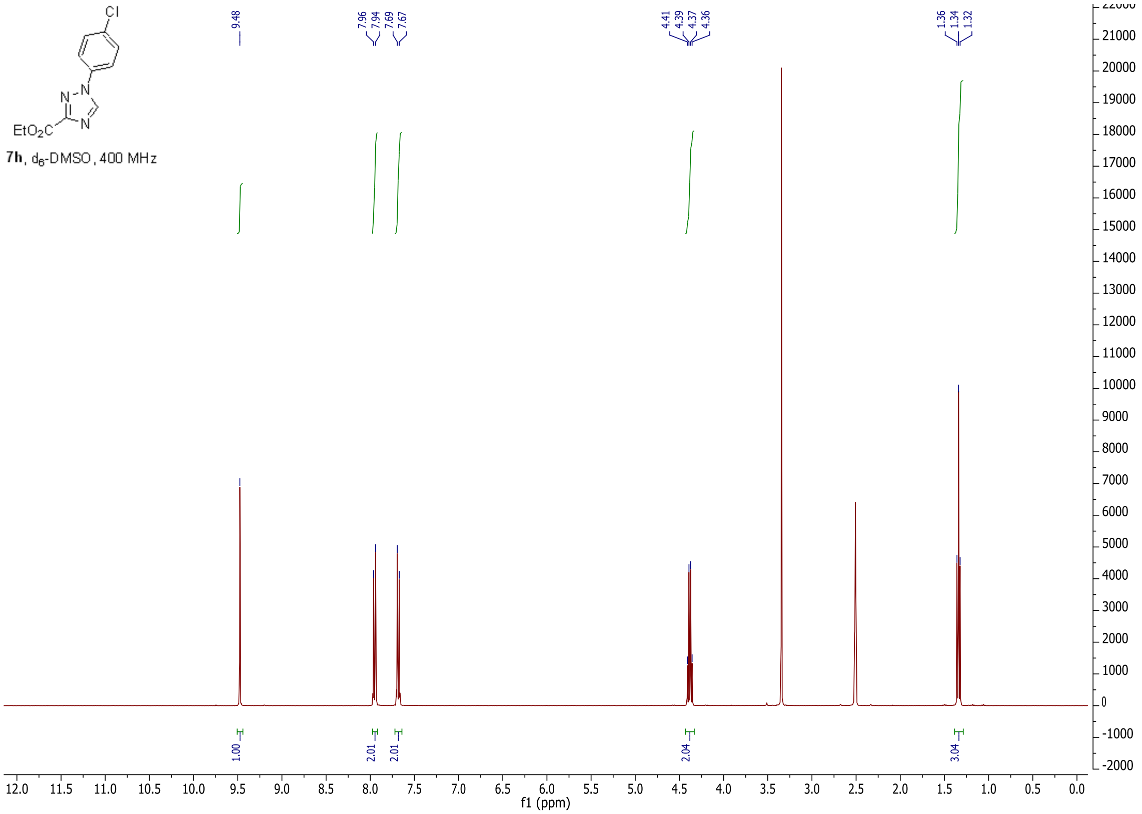

CF$_3$
N
N
N
EtO$_2$C
7e, d$_6$-DMSO, 400 MHz
159.60
155.29
145.13
137.32
131.81
131.10
130.78
125.67
125.38
124.44
122.67
117.20
117.12
61.92
14.54
f1 (ppm)


Br
N
N
N
EtO2C
7f, d6-DMSO, 400 MHz
9.48
7.90
7.88
7.83
7.80
4.41
4.39
4.37
4.36
1.36
1.34
1.32
1.00
2.05
2.03
2.09
3.06
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
f1 (ppm)

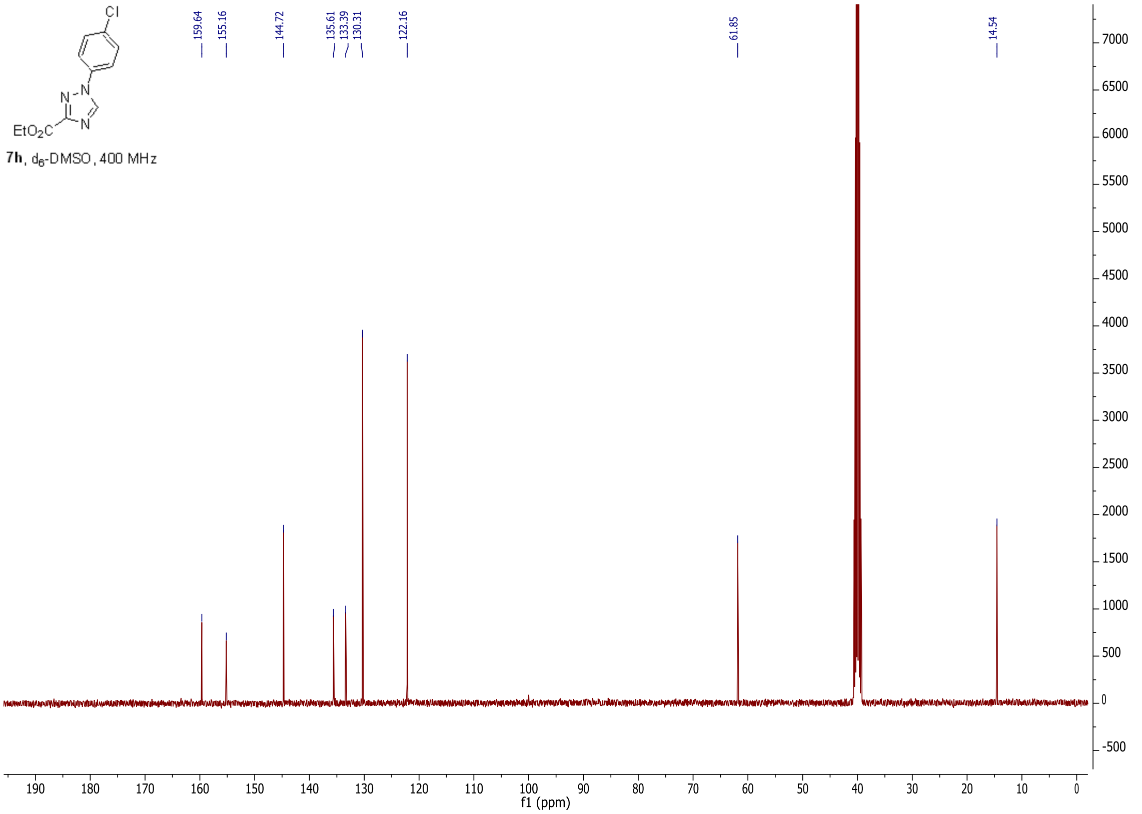

Br
N
N
N
EtO2C
7f, d6-DMSO, 400 MHz
159.64
155.17
144.70
136.02
133.23
122.39
121.76
61.85
14.55
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
f1 (ppm)


Cl
N
N
N
EtO2C
7g, d6-DMSO, 400 MHz
9.51
8.06
8.06
8.05
7.91
7.91
7.91
7.91
7.89
7.89
7.89
7.89
7.66
7.64
7.61
7.58
7.58
7.58
7.57
7.56
7.56
7.55
7.55
4.41
4.40
4.38
4.36
1.36
1.34
1.32
1.00
1.01
1.10
1.18
1.10
2.16
3.19
f1 (ppm)
8.1
8.0
7.9
7.8
7.7
7.6
7.5
4000
3000
2000
1000
0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000


Cl
N
N
N
EtO2C
7g, d6-DMSO, 400 MHz
159.60
155.20
144.92
137.85
134.62
132.10
128.95
120.26
119.07
61.88
14.54
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

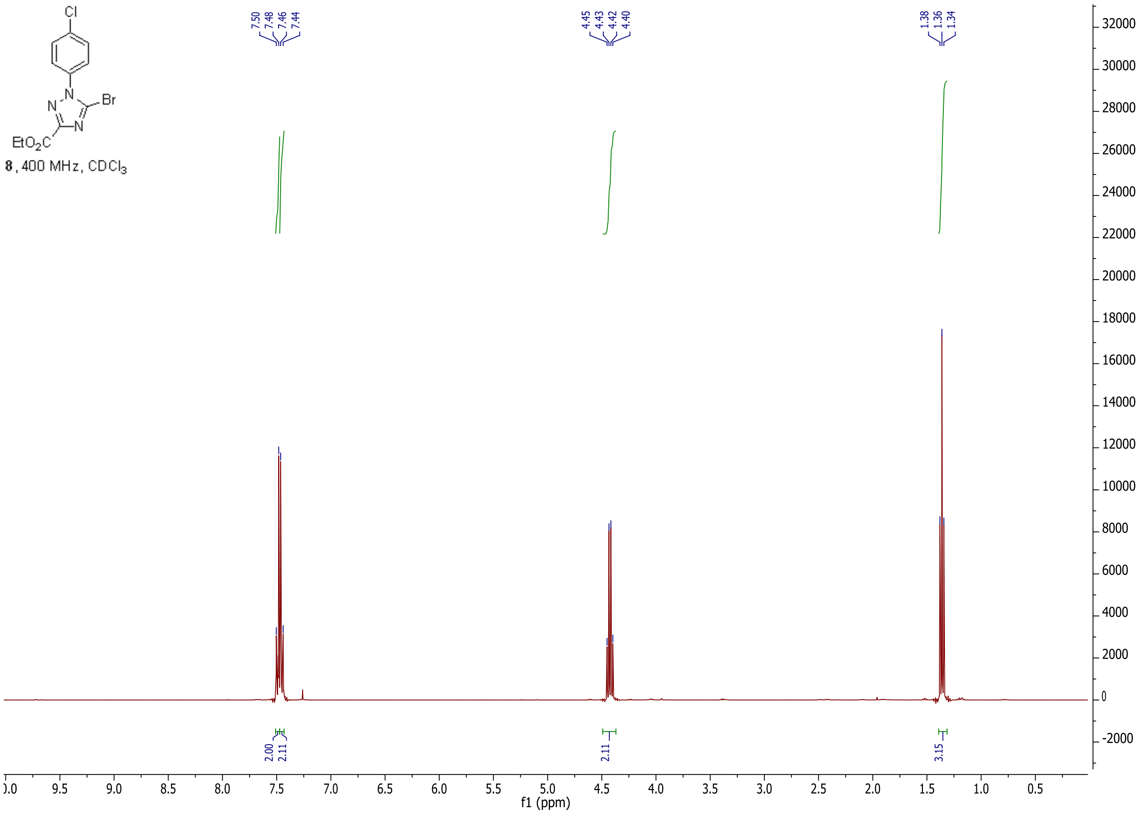


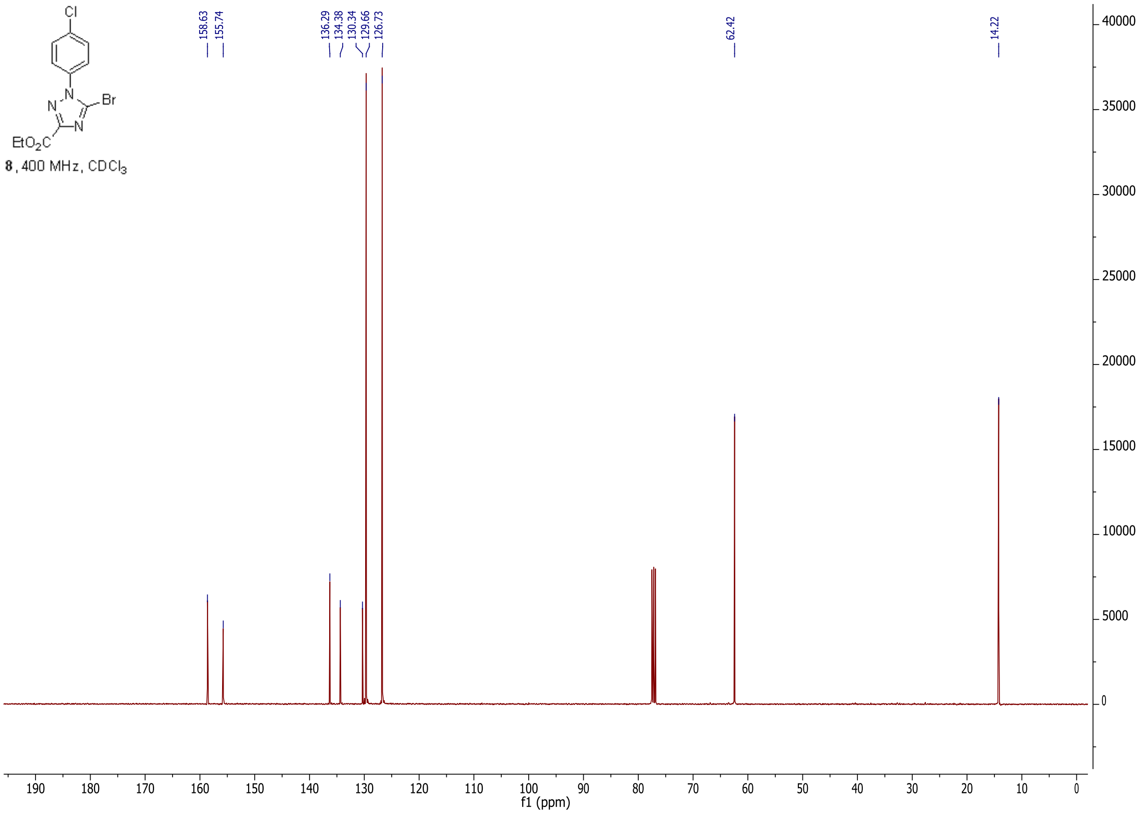
Cl
N
N
N
EtO2C
7h, d6-DMSO, 400 MHz
9.48
7.96
7.94
7.69
7.67
4.41
4.39
4.37
4.36
1.36
1.34
1.32
1.00
2.01
2.01
2.04
3.04
f1 (ppm)
12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
22000 21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000 -2000

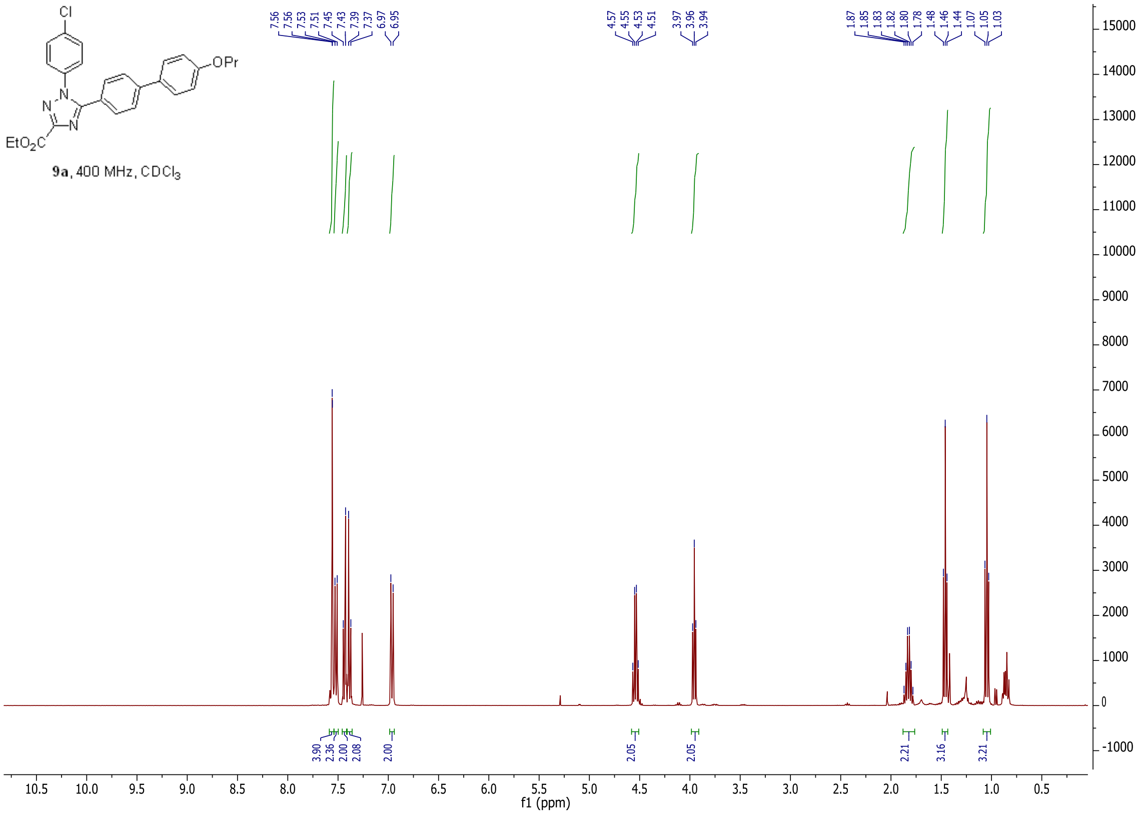


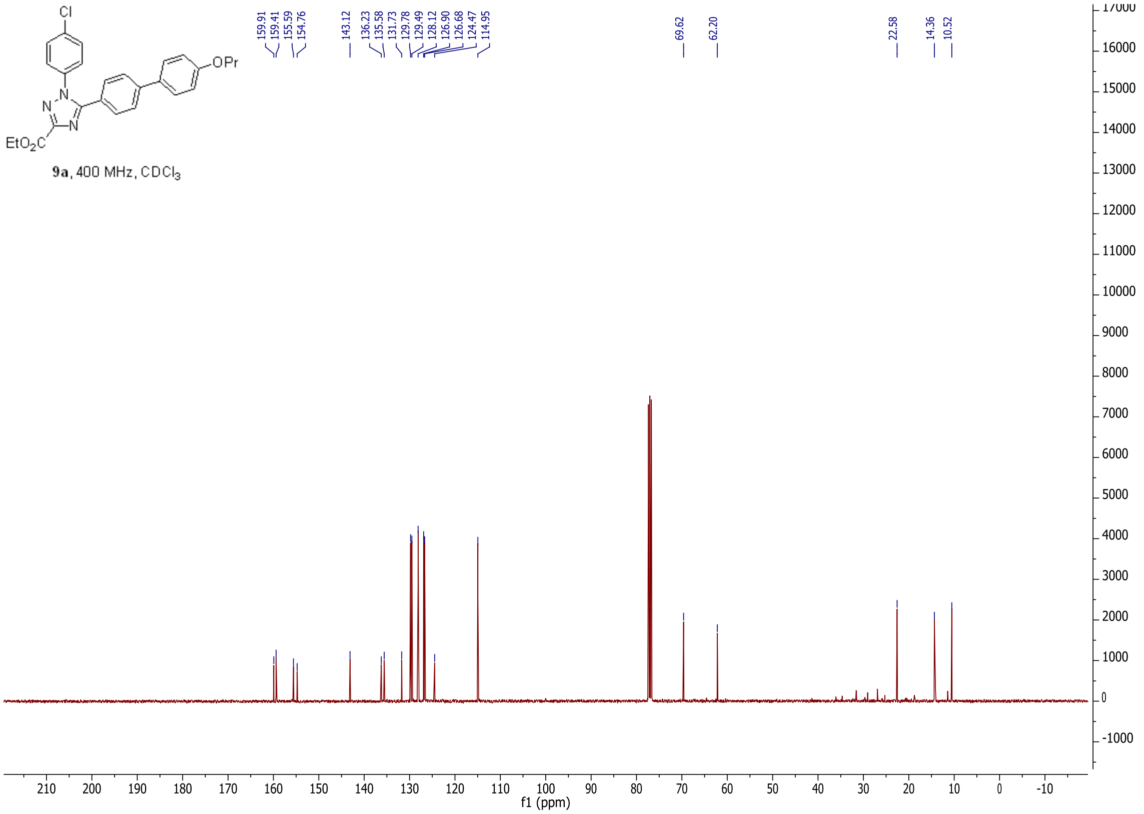
Cl
N
N
N
EtO2C
7h, d6-DMSO, 400 MHz
159.64
155.16
144.72
135.61
133.39
130.31
122.16
61.85
14.54
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
7000 6500 6000 5500 5000 4500 4000 3500 3000 2500 2000 1500 1000 500 0 -500

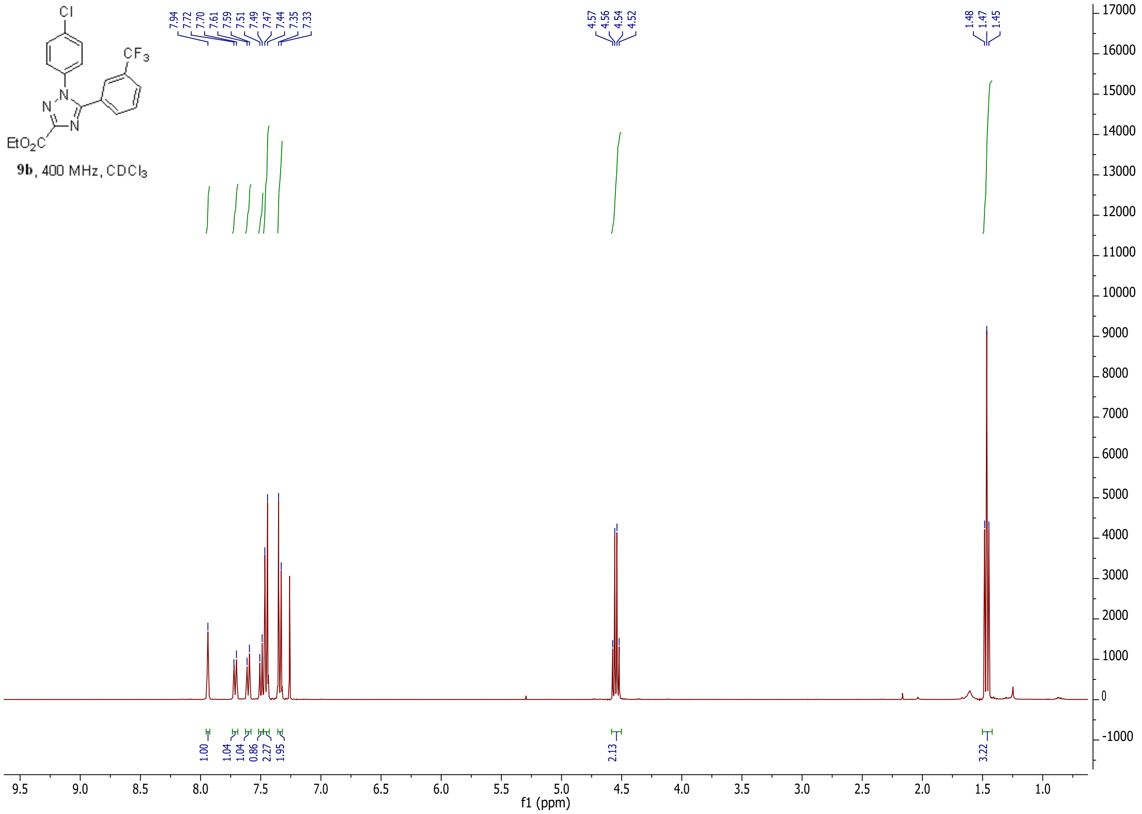
8. NMR-Spectra of compounds **8,** and **9a-e:**

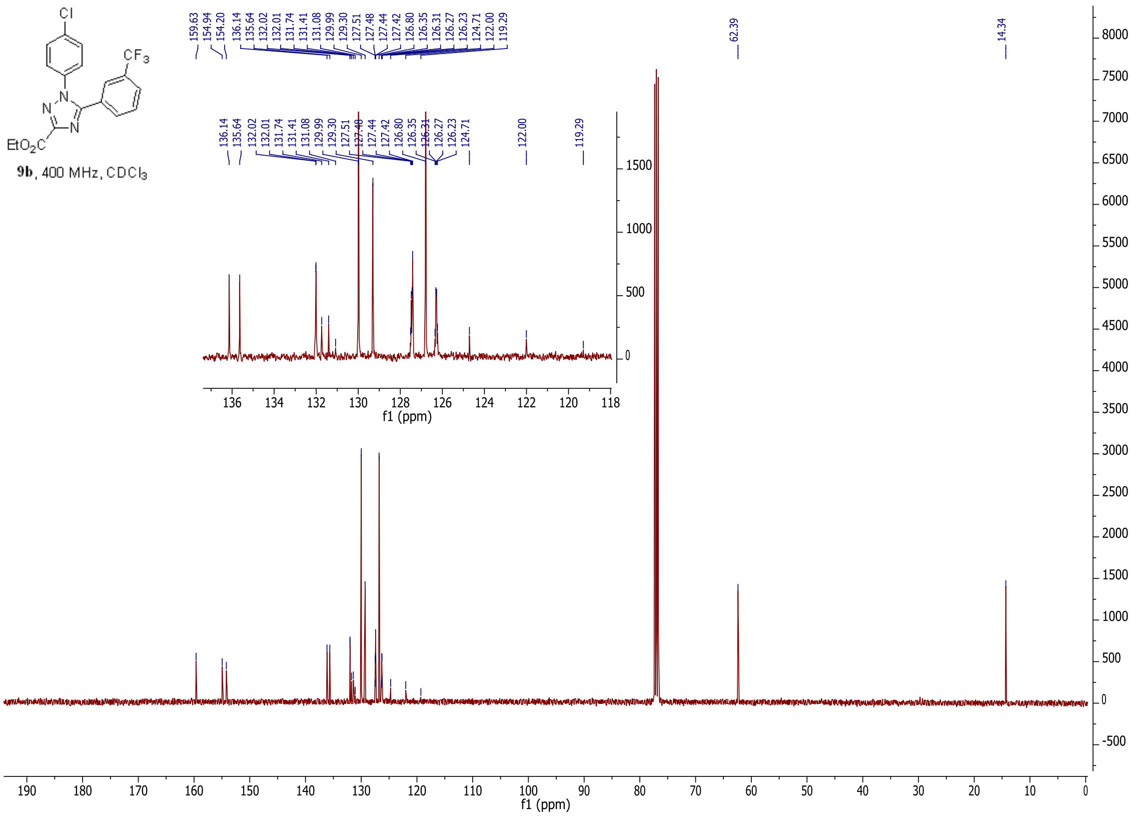


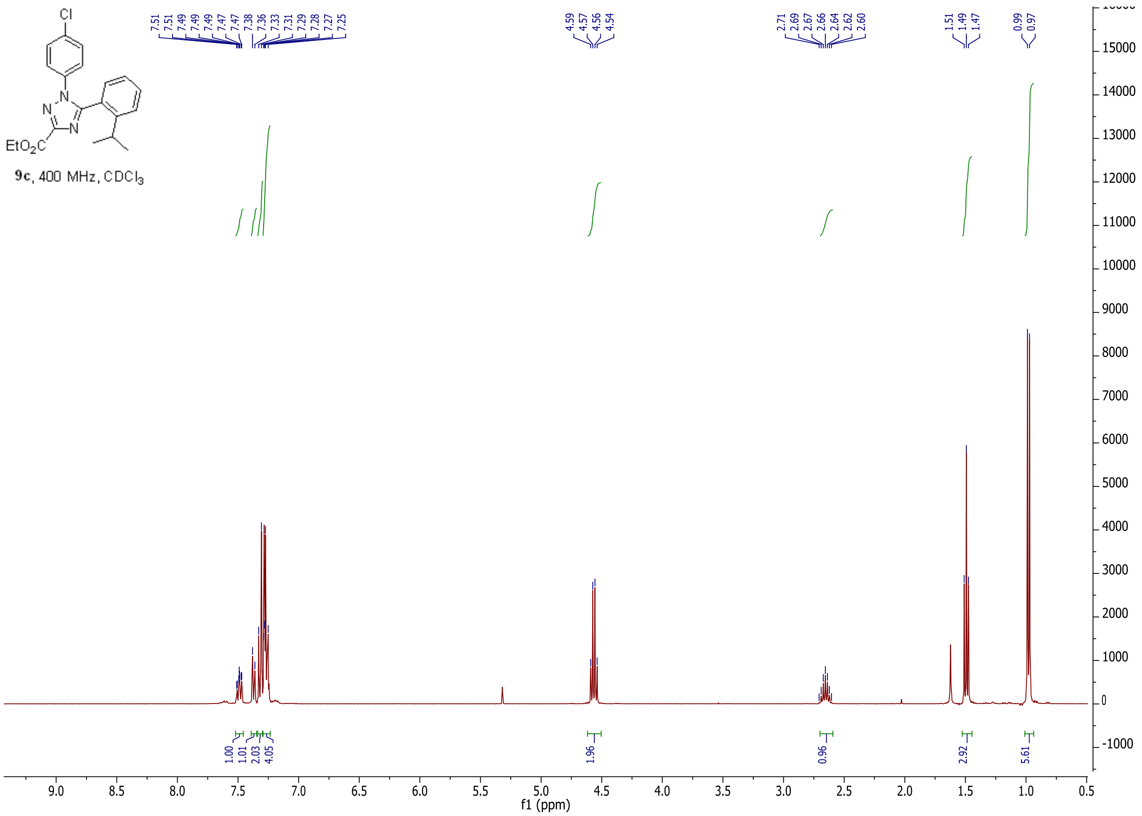


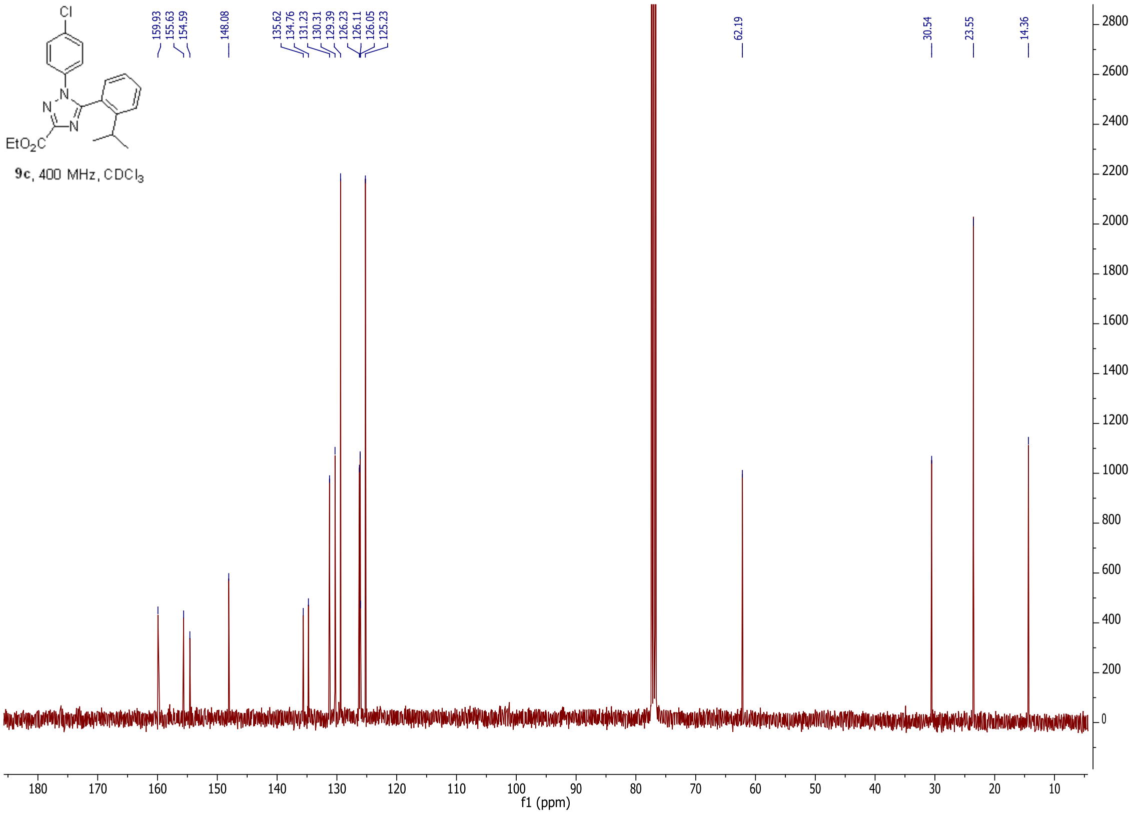

Cl
N
N
N
OPr
EtO2C
9a, 400 MHz, CDCl3
7.56
7.56
7.53
7.51
7.45
7.43
7.39
7.37
6.97
6.95
4.57
4.55
4.53
4.51
3.97
3.96
3.94
1.87
1.85
1.83
1.82
1.80
1.78
1.48
1.46
1.44
1.07
1.05
1.03
3.90
2.36
2.00
2.08
2.00
2.05
2.05
2.21
3.16
3.21
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

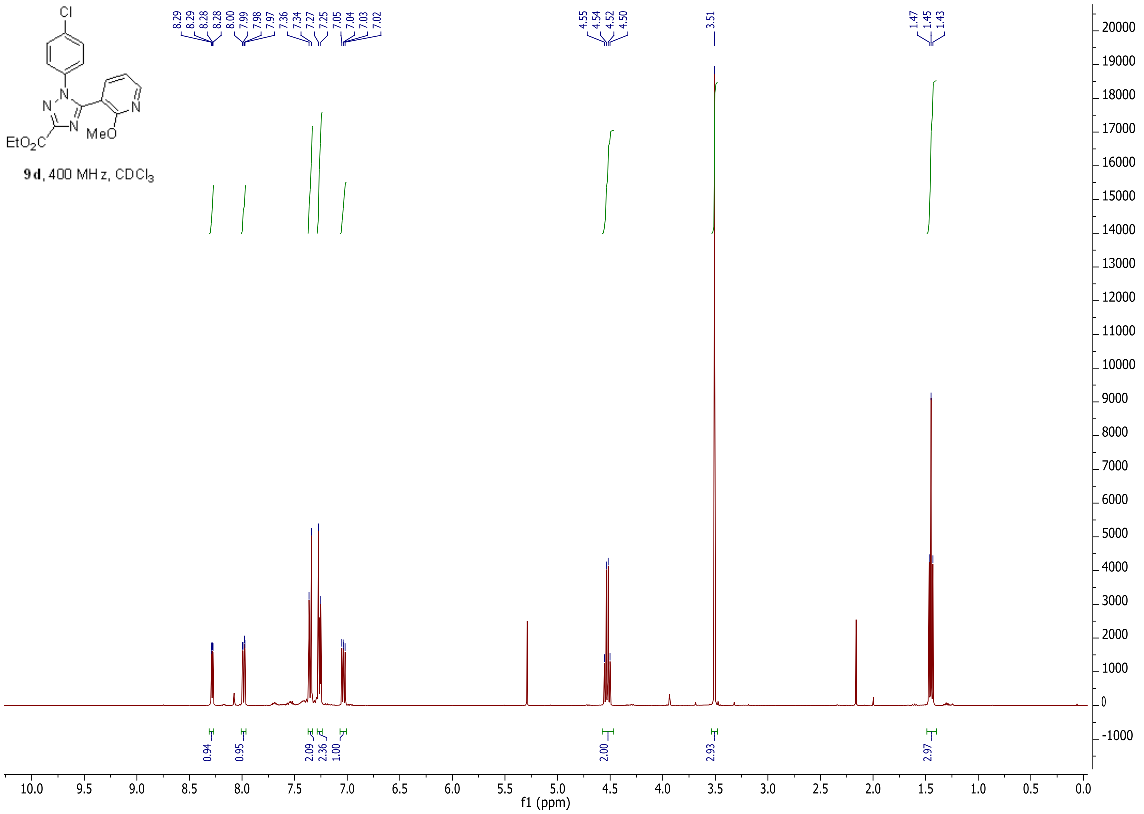

Cl
N
N
N
OPr
EtO2C
9a, 400 MHz, CDCl3
159.91
159.41
155.59
154.76
143.12
136.23
135.58
131.73
129.78
129.49
128.12
126.90
126.68
124.47
114.95
69.62
62.20
22.58
14.36
10.52
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)


Cl
CF3
N
N
N
EtO2C
9b, 400 MHz, CDCl3
7.94
7.72
7.70
7.61
7.59
7.51
7.49
7.47
7.44
7.35
7.33
4.57
4.56
4.54
4.52
1.48
1.47
1.45
1.00
1.04
1.04
0.86
2.27
1.95
2.13
3.22
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f1 (ppm)

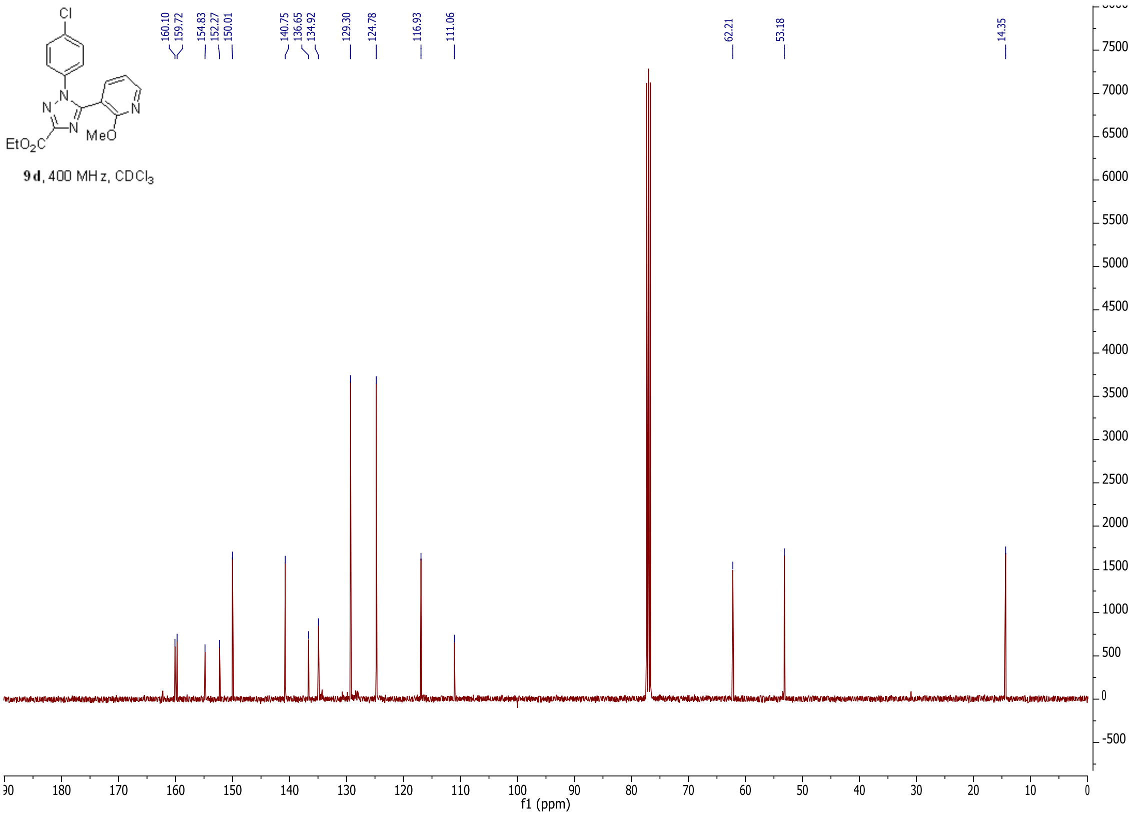

Cl
CF3
N
N
N
EtO2C
9b, 400 MHz, CDCl3
159.63
154.94
154.20
136.14
135.64
132.02
132.01
131.74
131.41
131.08
129.99
129.30
127.51
127.48
127.44
127.42
126.80
126.35
126.31
126.27
126.23
124.71
122.00
119.29
62.39
14.34
1500
1000
500
0
136
134
132
130
128
126
124
122
120
118
f1 (ppm)
8000
7500
7000
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


9c, 400 MHz, $CDCl_3$

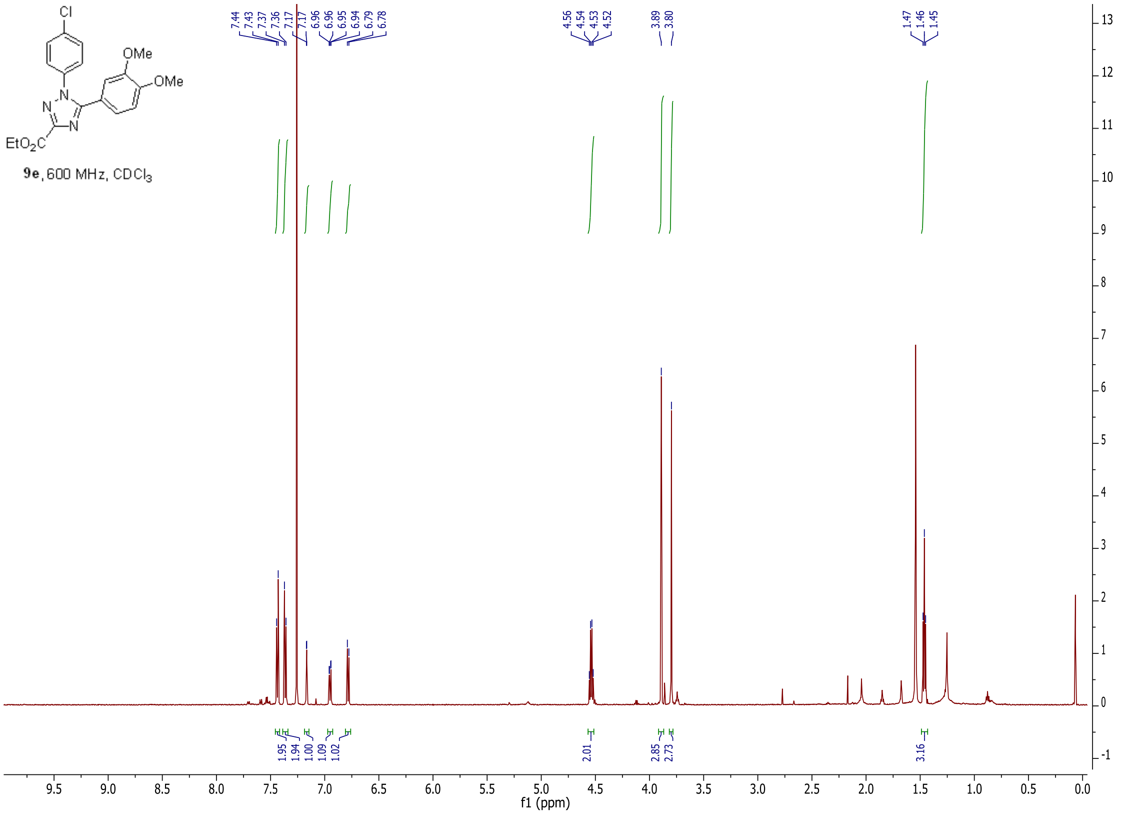

9c, 400 MHz, $CDCl_3$

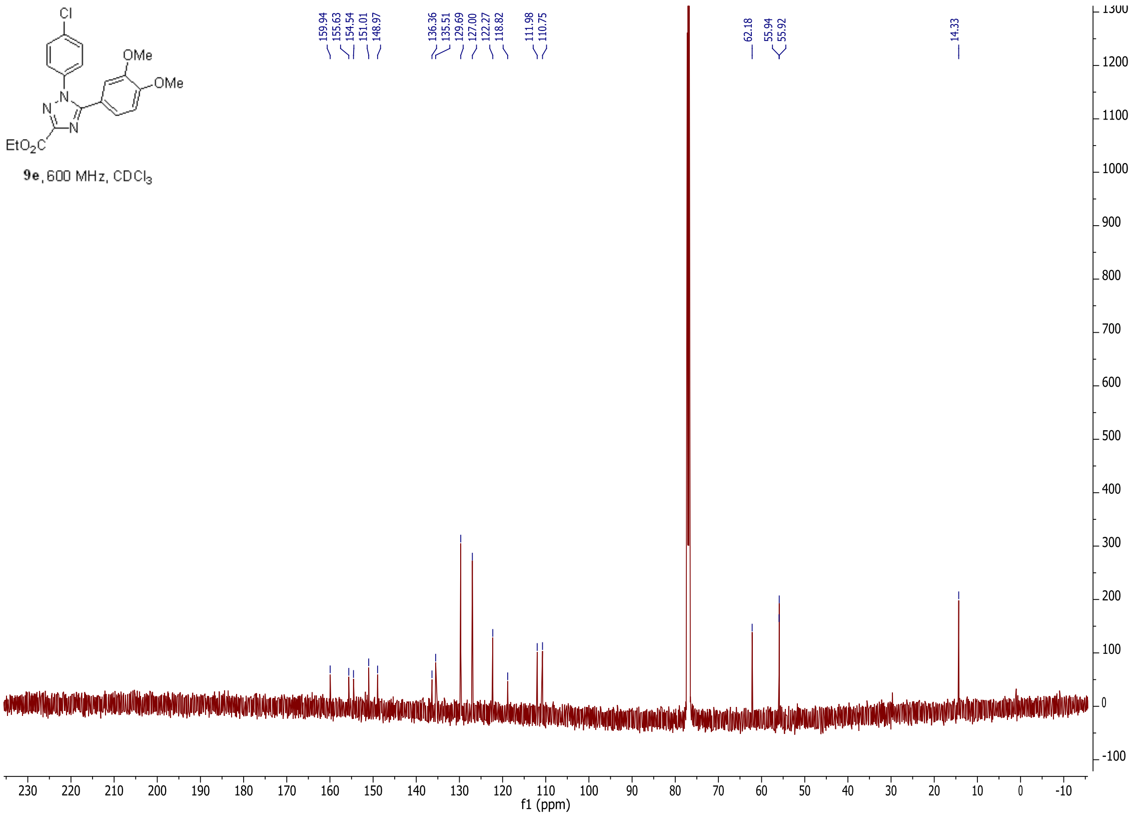


9d, 400 MHz, CDCl$_3$

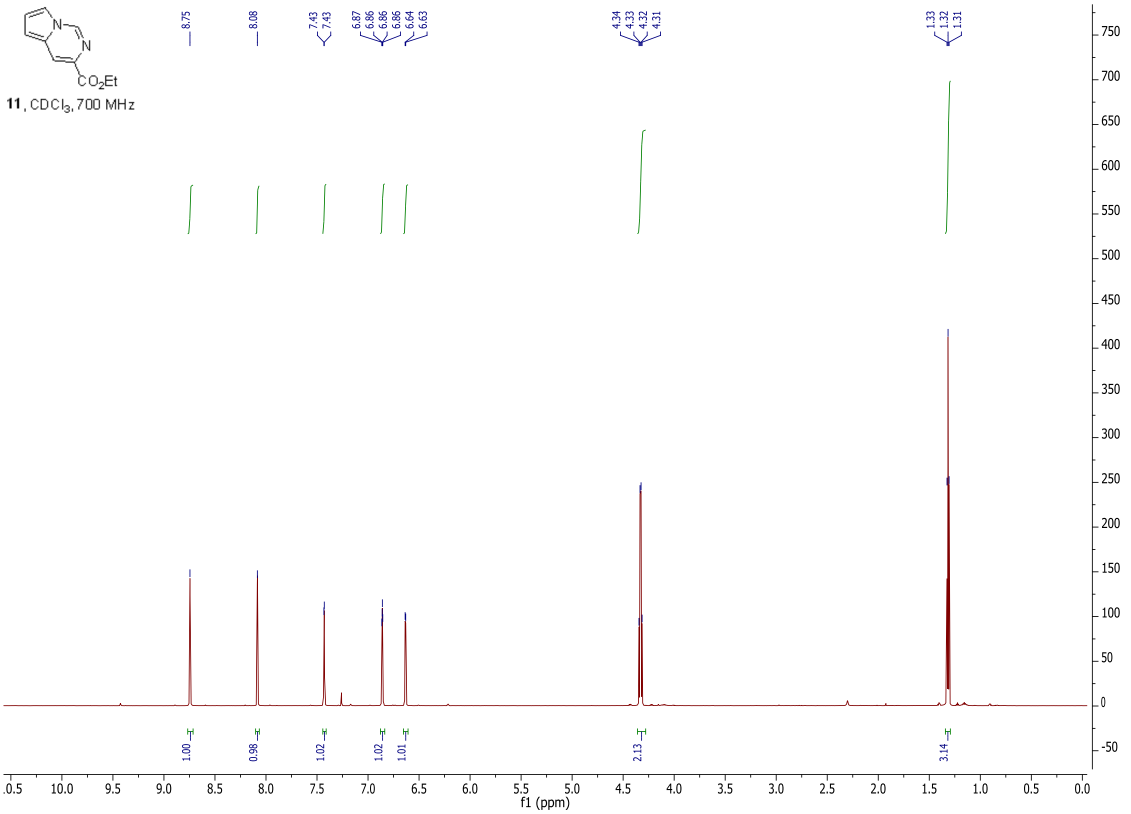


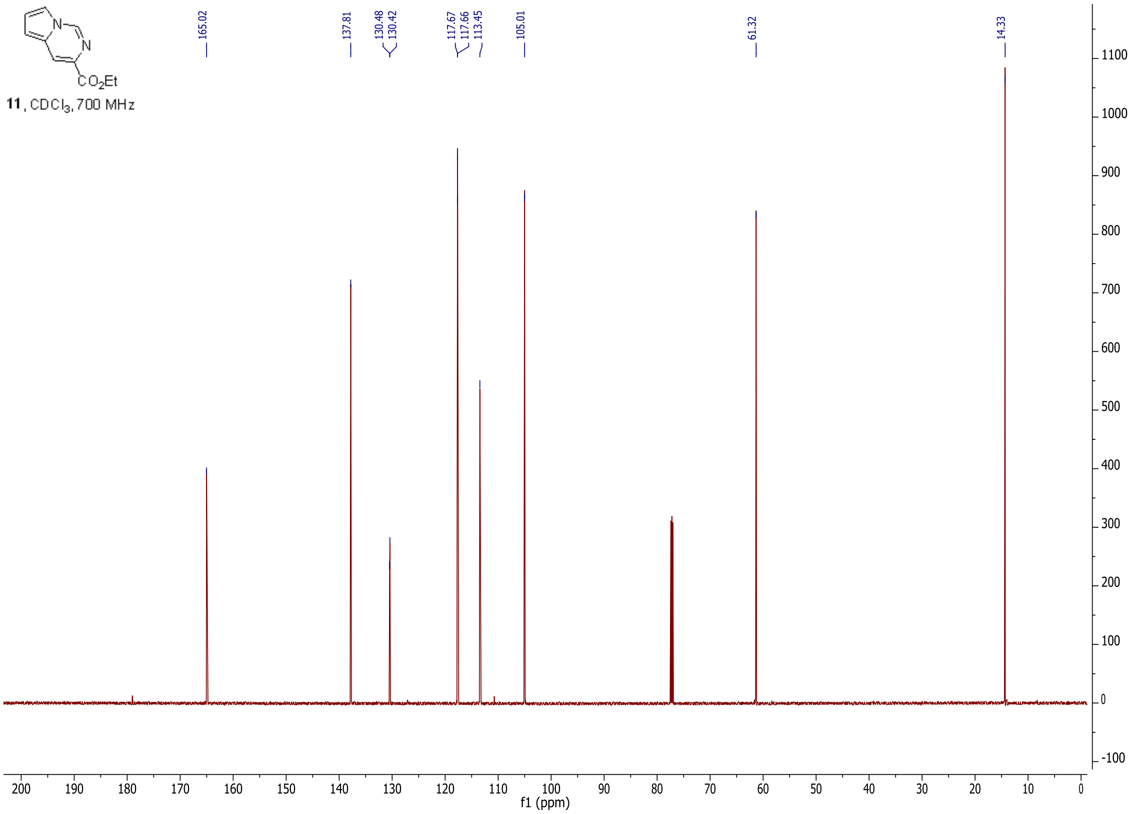
9d, 400 MHz, CDCl$_3$

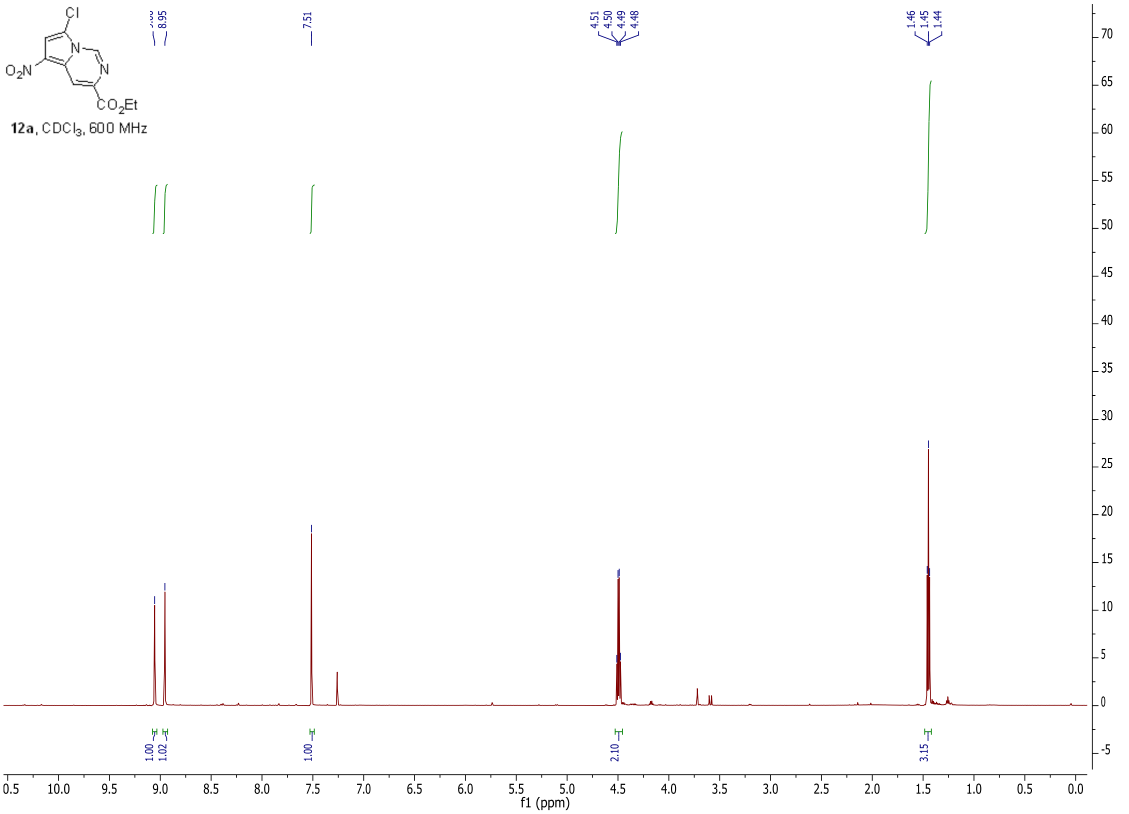

Cl
OMe
OMe
N
N
N
EtO$_2$C
9e, 600 MHz, CDCl$_3$
7.44
7.43
7.37
7.36
7.17
7.17
6.96
6.96
6.95
6.94
6.79
6.78
4.56
4.54
4.53
4.52
3.89
3.80
1.47
1.46
1.45
1.95
1.94
1.00
1.09
1.02
2.01
2.85
2.73
3.16
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
13
12
11
10
9
8
7
6
5
4
3
2
1
0
-1

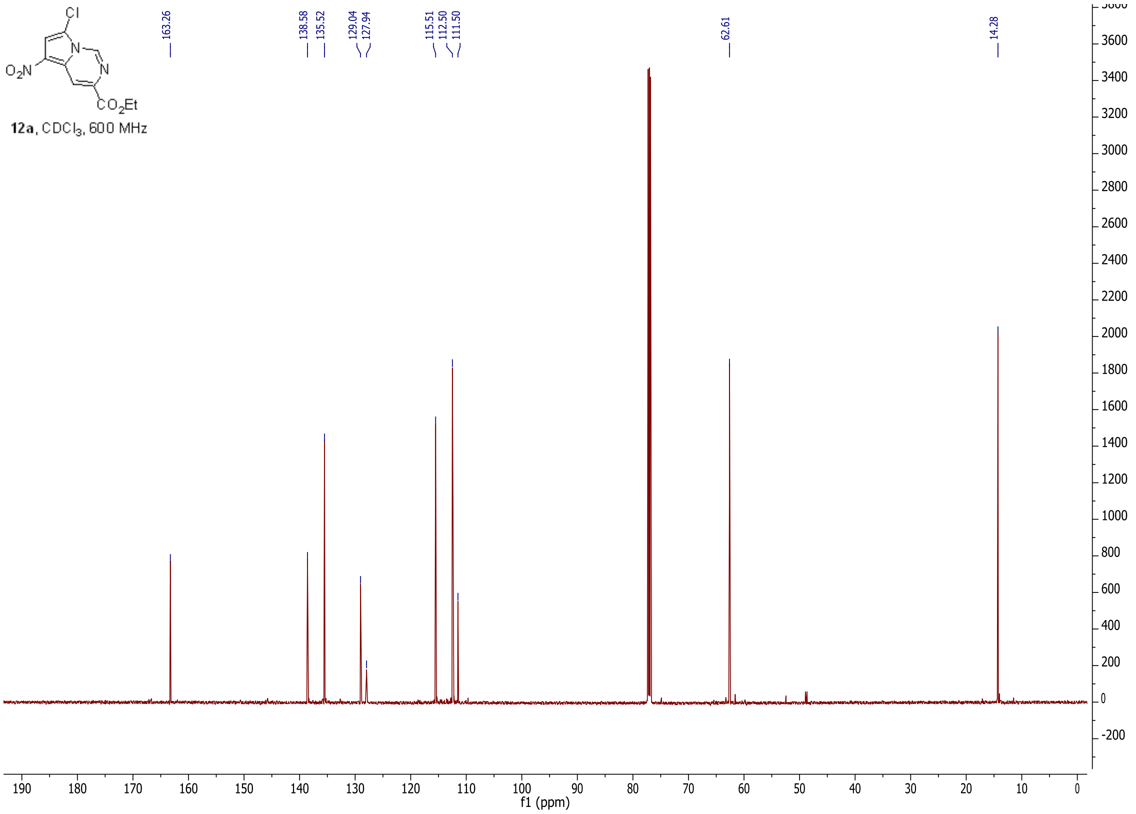

Cl
OMe
OMe
N
N
N
EtO$_2$C
9e, 600 MHz, CDCl$_3$
159.94
155.63
154.54
151.01
148.97
136.36
135.51
129.69
127.00
122.27
118.82
111.98
110.75
62.18
55.94
55.92
14.33
230
220
210
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
-10
f1 (ppm)
1300
1200
1100
1000
900
800
700
600
500
400
300
200
100
0
-100

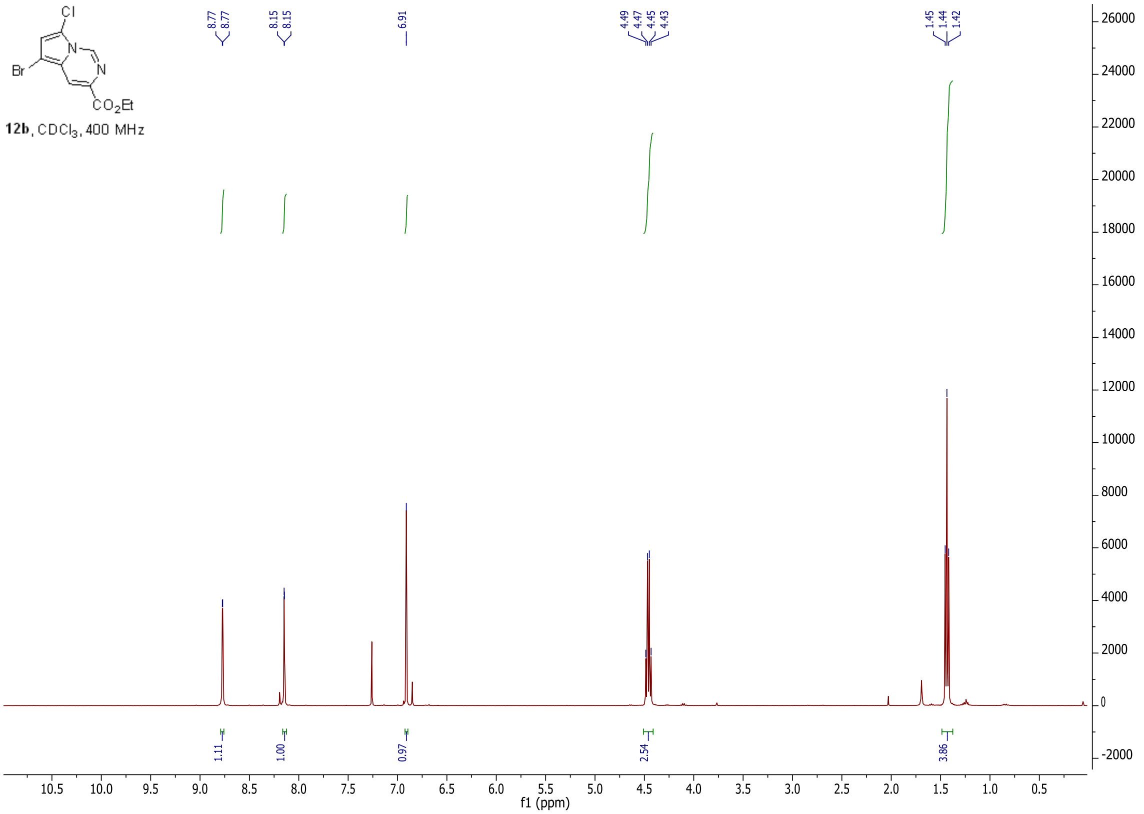
9. NMR-Spectra of compounds **11,** and **12a-i:**

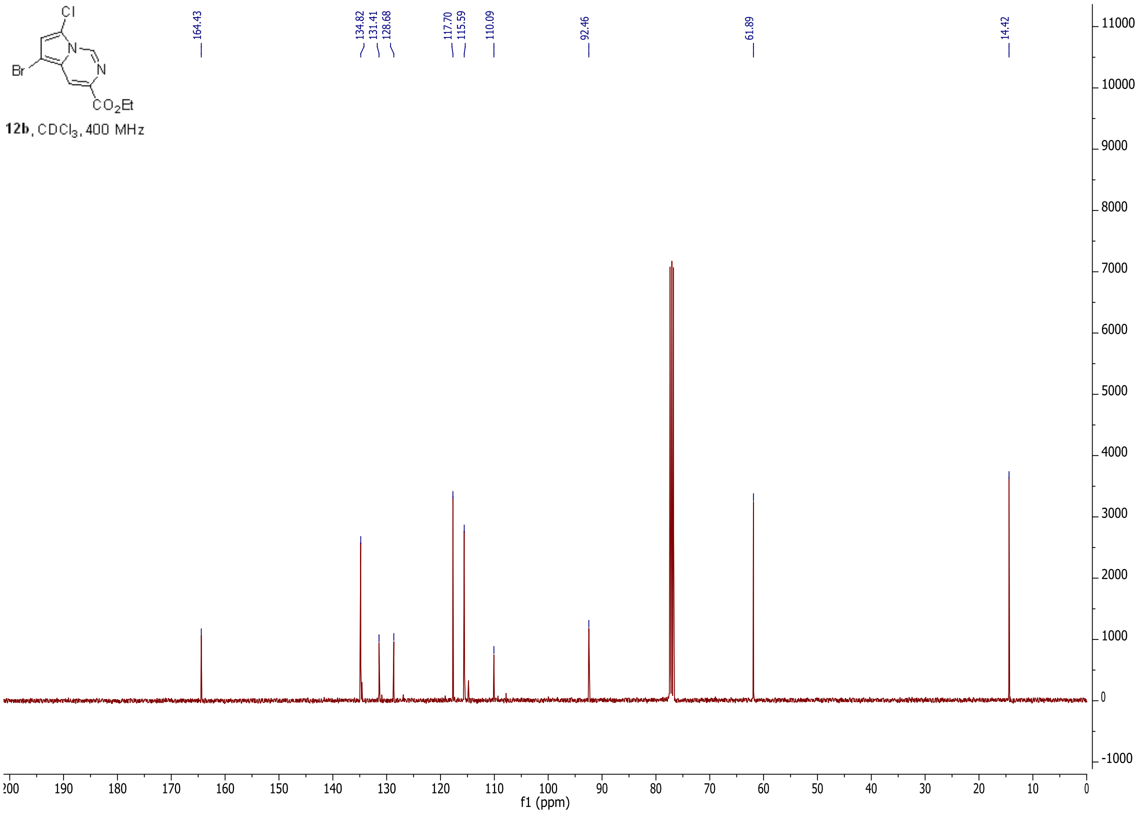


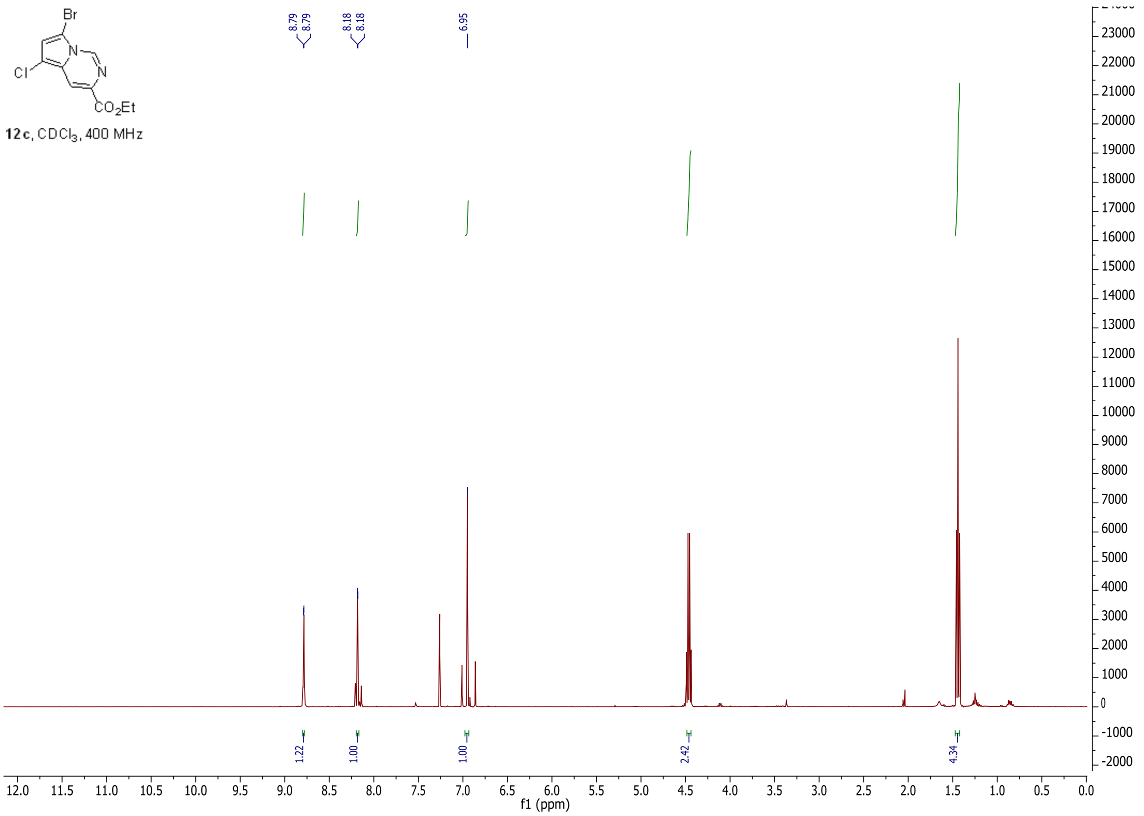



Cl
O_2N
N
CO_2Et
12a, $CDCl_3$, 600 MHz
8.95
7.51
4.51
4.50
4.49
4.48
1.46
1.45
1.44
1.00
1.02
1.00
2.10
3.15
70
65
60
55
50
45
40
35
30
25
20
15
10
5
0
-5
0.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)

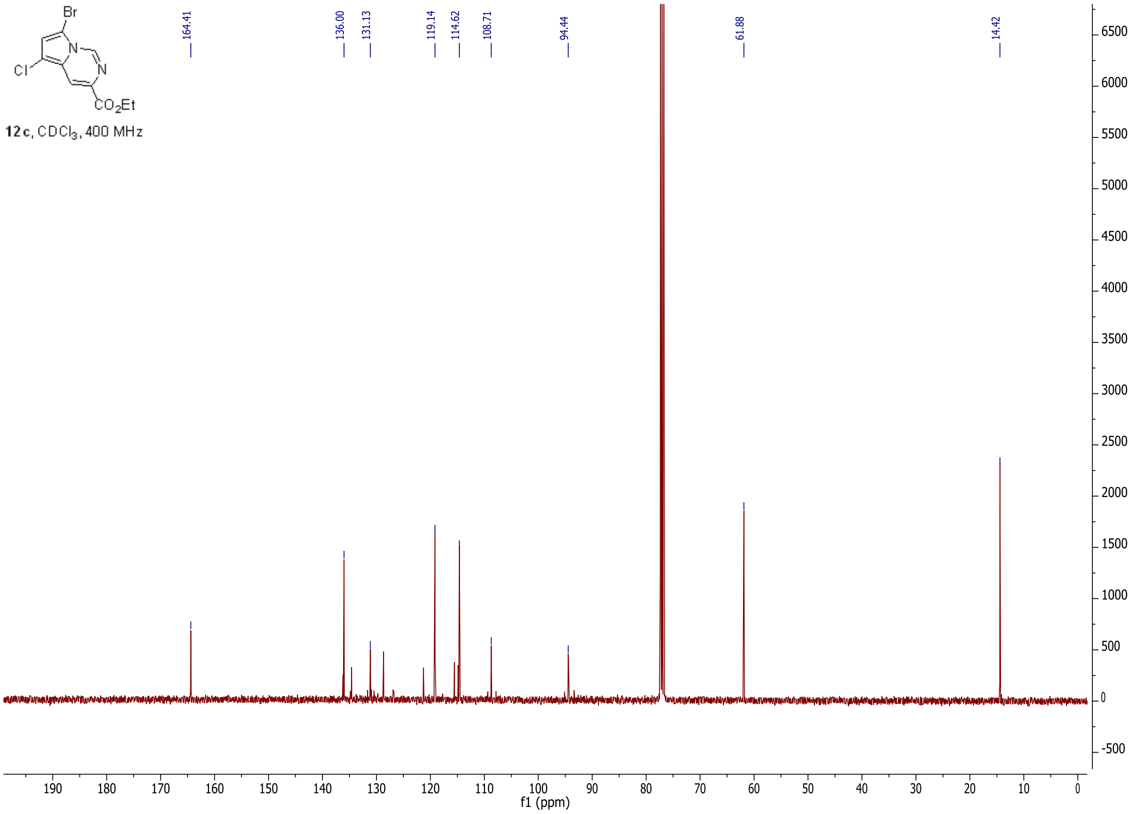

Cl
O_2N
N
CO_2Et
12a, $CDCl_3$, 600 MHz
163.26
138.58
135.52
129.04
127.94
115.51
112.50
111.50
62.61
14.28
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)


Cl
N
N
Br
CO2Et
12b, CDCl3, 400 MHz
8.77
8.77
8.15
8.15
6.91
4.49
4.47
4.45
4.43
1.45
1.44
1.42
1.11
1.00
0.97
2.54
3.86
26000
24000
22000
20000
18000
16000
14000
12000
10000
8000
6000
4000
2000
0
-2000
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
f1 (ppm)

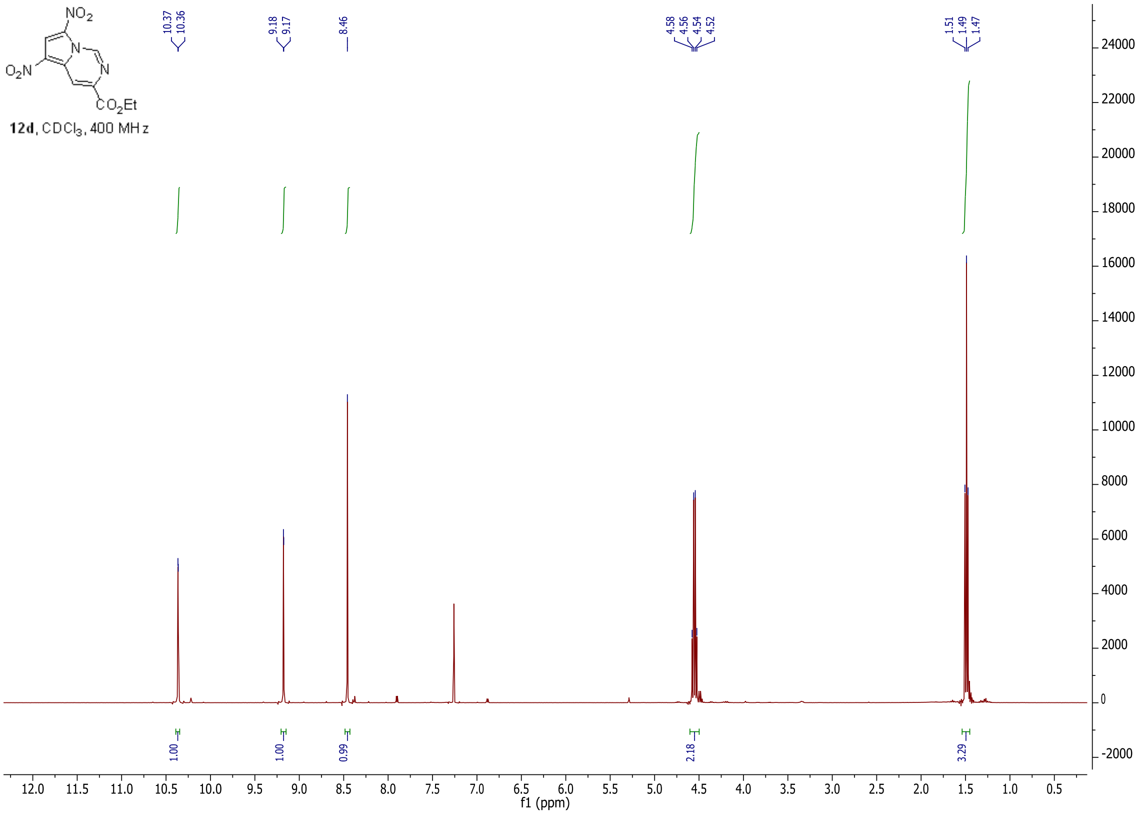

Cl
N
N
Br
CO2Et
12b, CDCl3, 400 MHz
164.43
134.82
131.41
128.68
117.70
115.59
110.09
92.46
61.89
14.42
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)



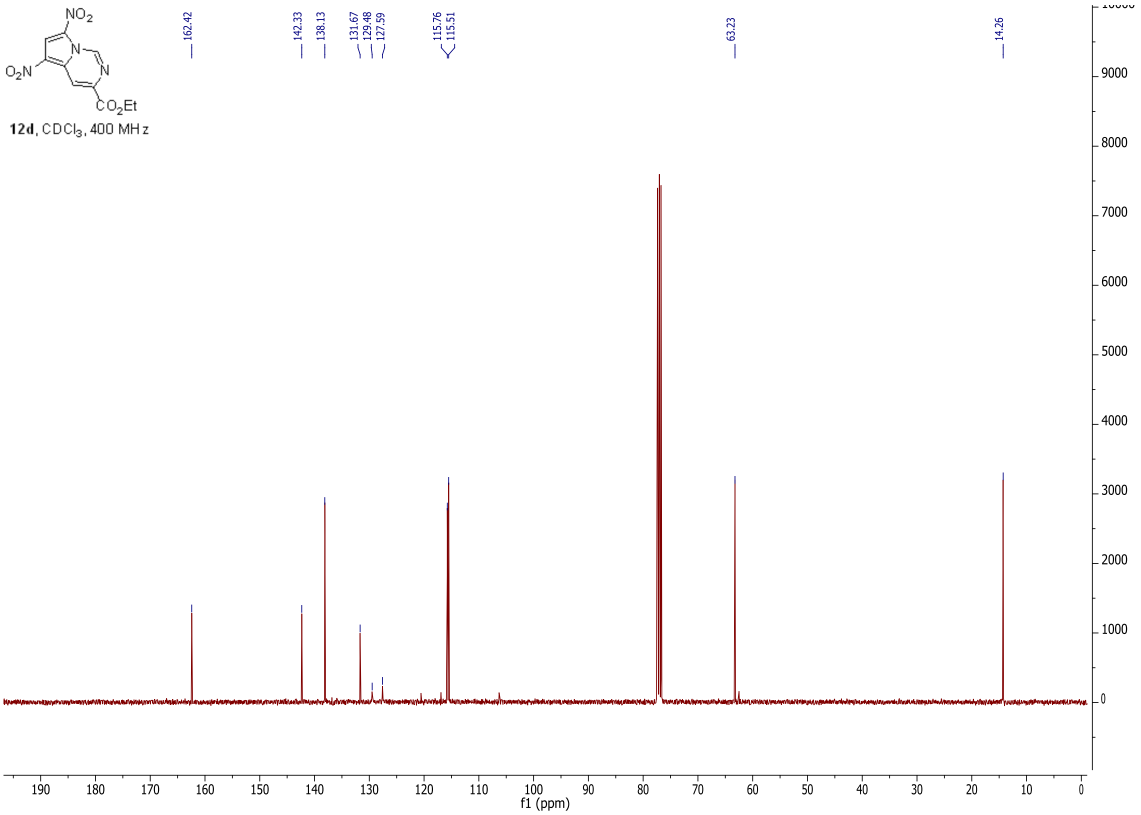
Br
Cl
N
N
CO$_2$Et
12c, CDCl$_3$, 400 MHz
8.79
8.79
8.18
8.18
6.95
1.22
1.00
1.00
2.42
4.34
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
0.0
f1 (ppm)
23000
22000
21000
20000
19000
18000
17000
16000
15000
14000
13000
12000
11000
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
-1000
-2000



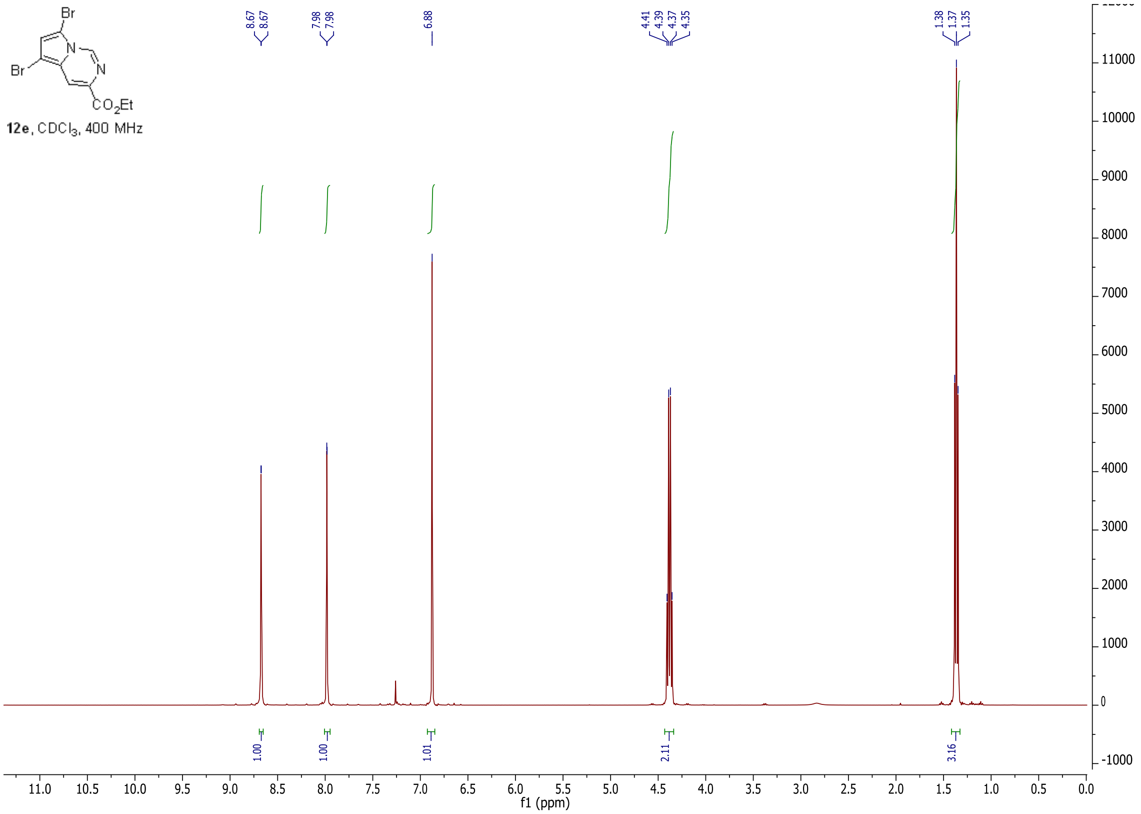
Br
Cl
N
N
CO$_2$Et
12c, CDCl$_3$, 400 MHz
164.41
136.00
131.13
119.14
114.62
108.71
94.44
61.88
14.42
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
0
f1 (ppm)
6500
6000
5500
5000
4500
4000
3500
3000
2500
2000
1500
1000
500
0
-500

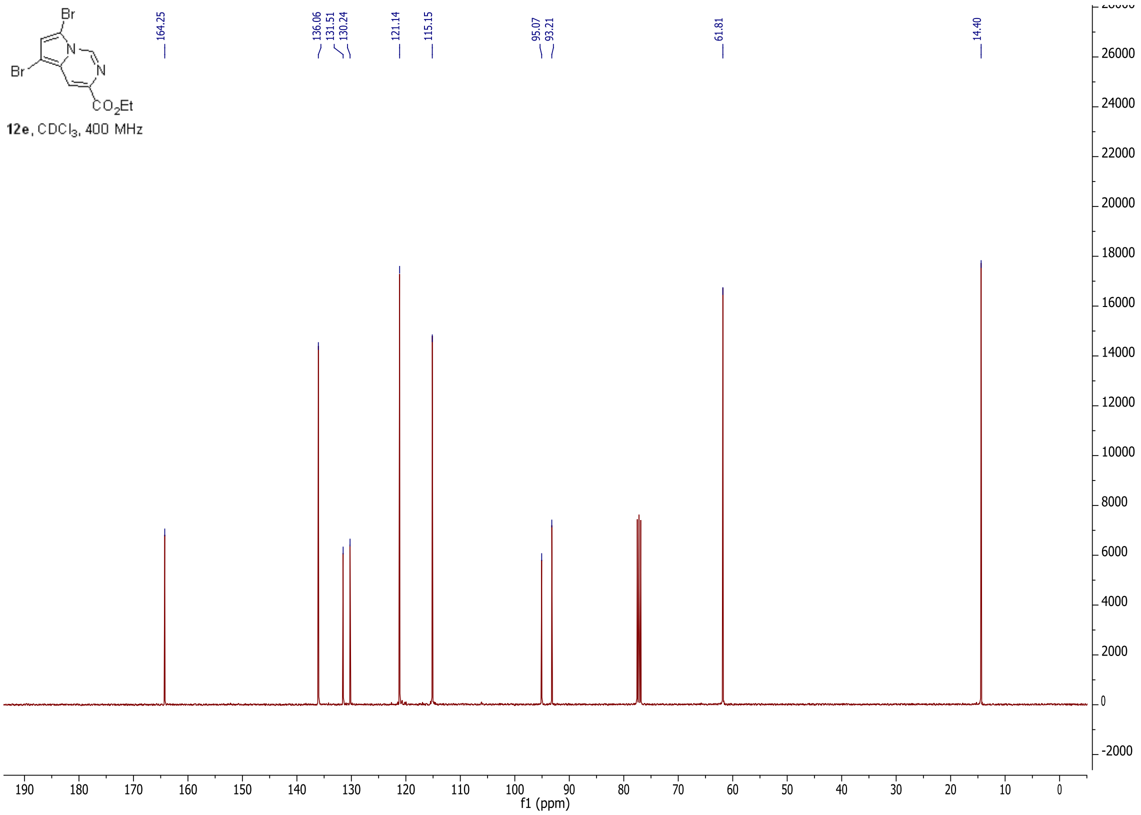


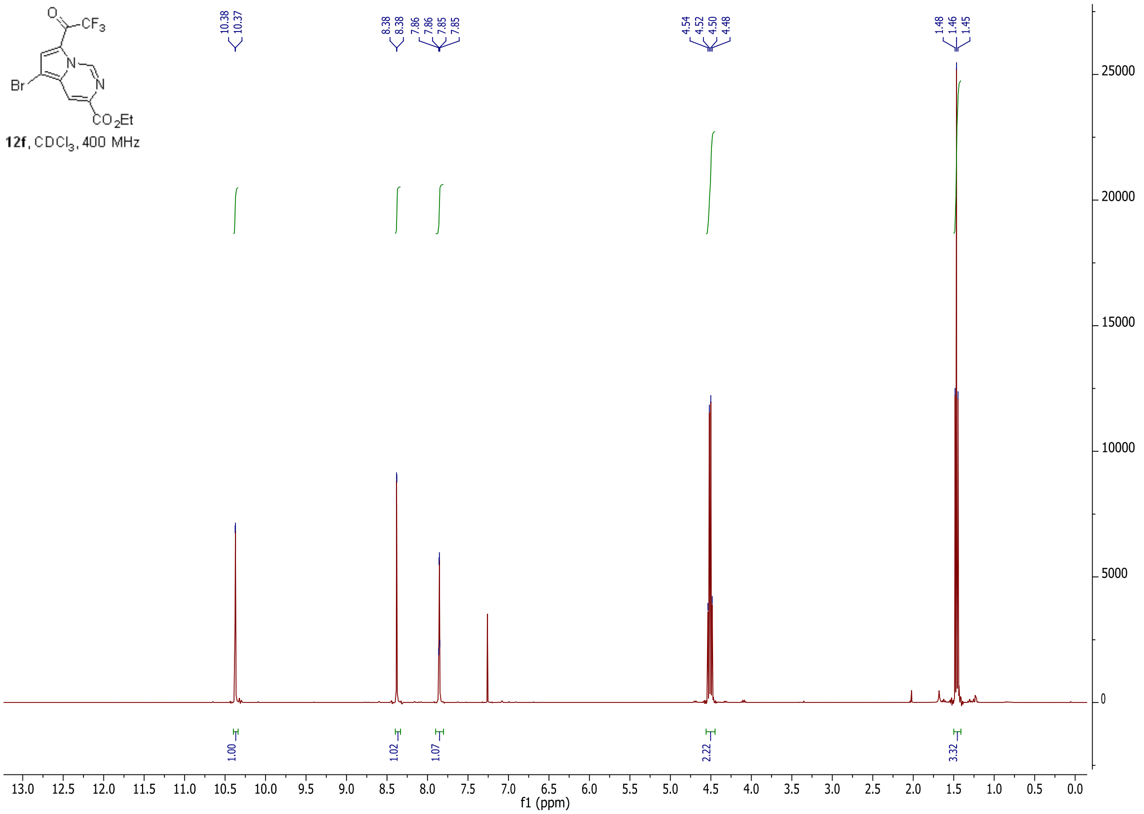
12d, $CDCl_3$, 400 MHz

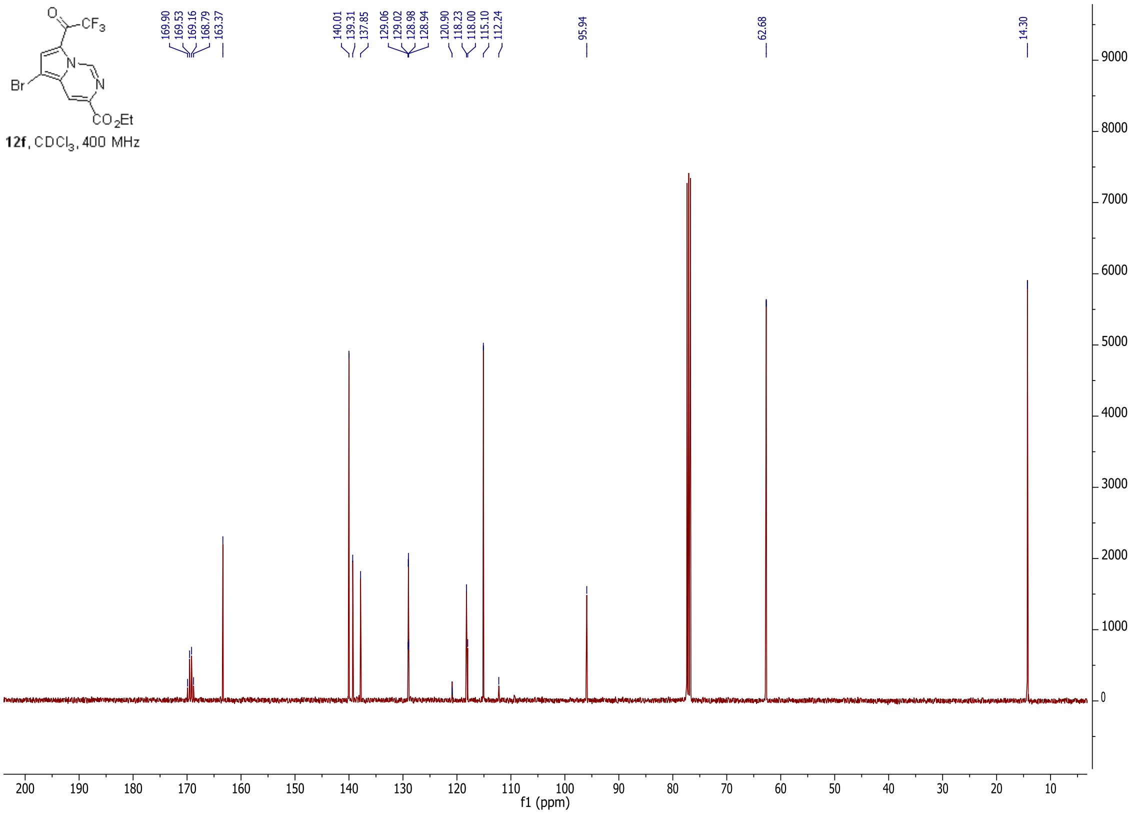


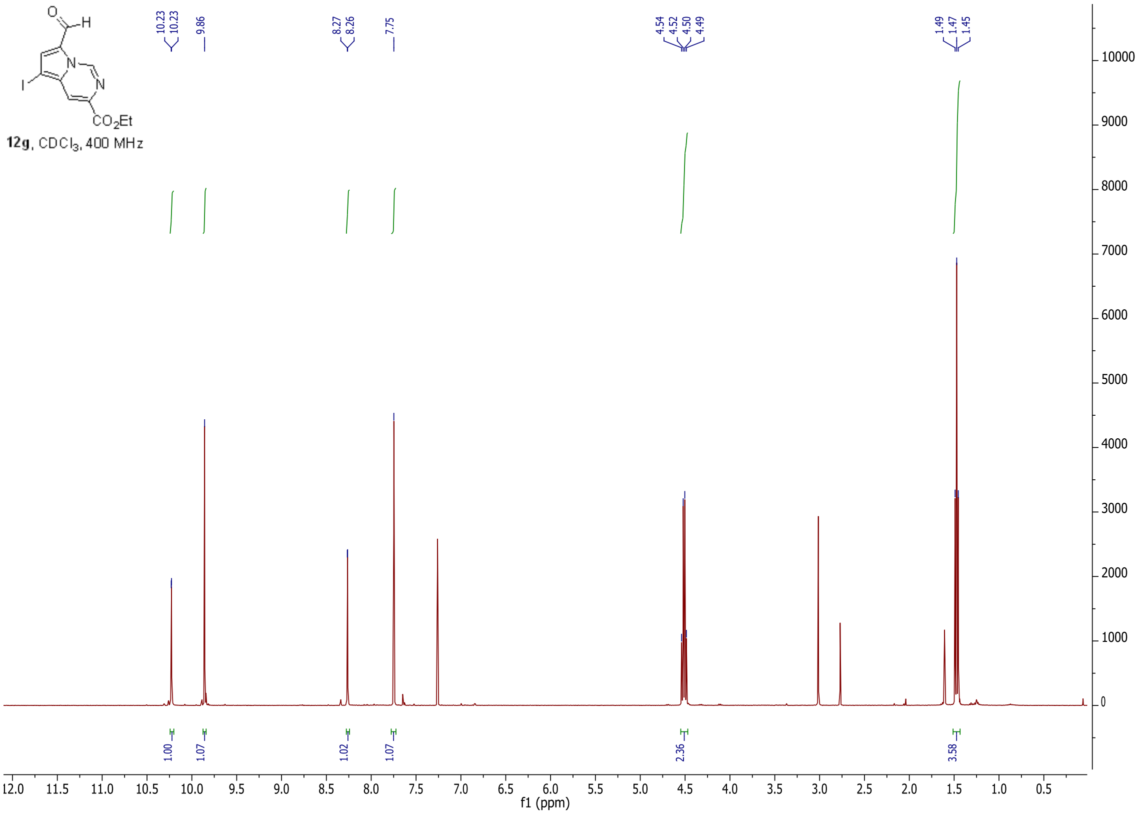
12d, $CDCl_3$, 400 MHz

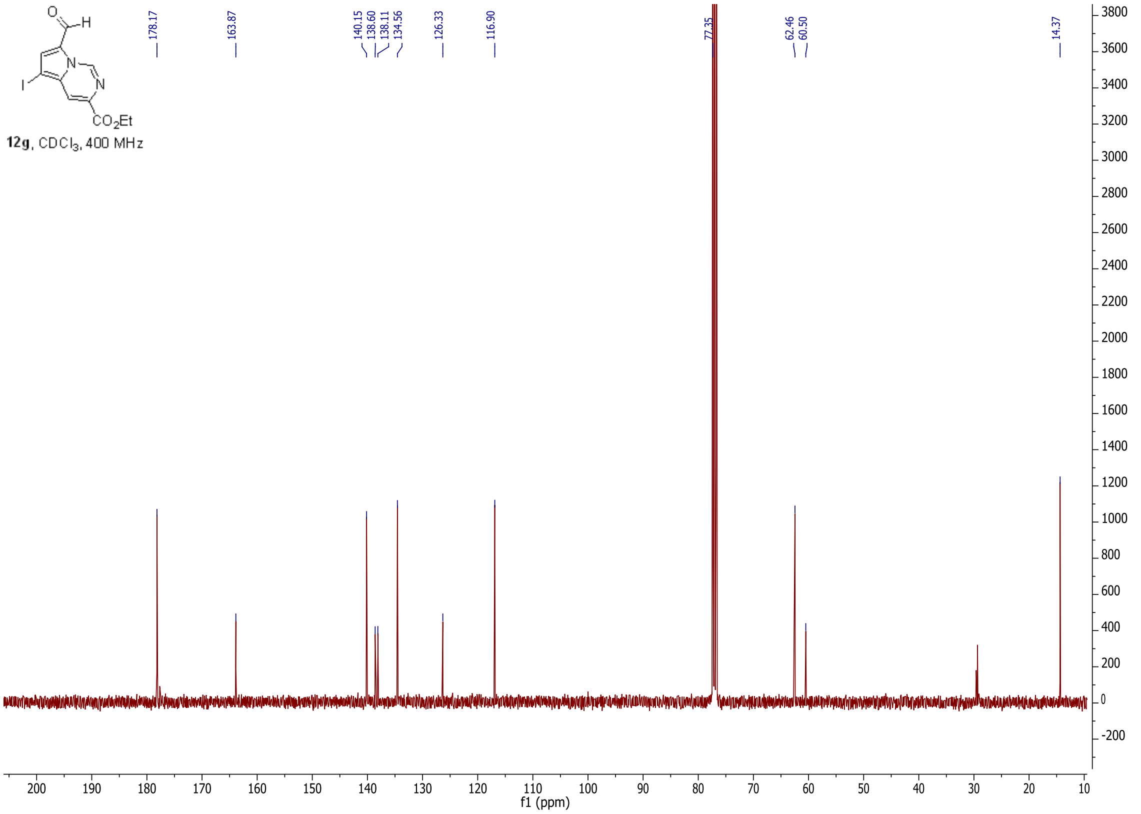

Br
Br
N
N
CO2Et
12e, CDCl3, 400 MHz
8.67
8.67
7.98
7.98
6.88
4.41
4.39
4.37
4.35
1.38
1.37
1.35
1.00
1.00
1.01
2.11
3.16
f1 (ppm)

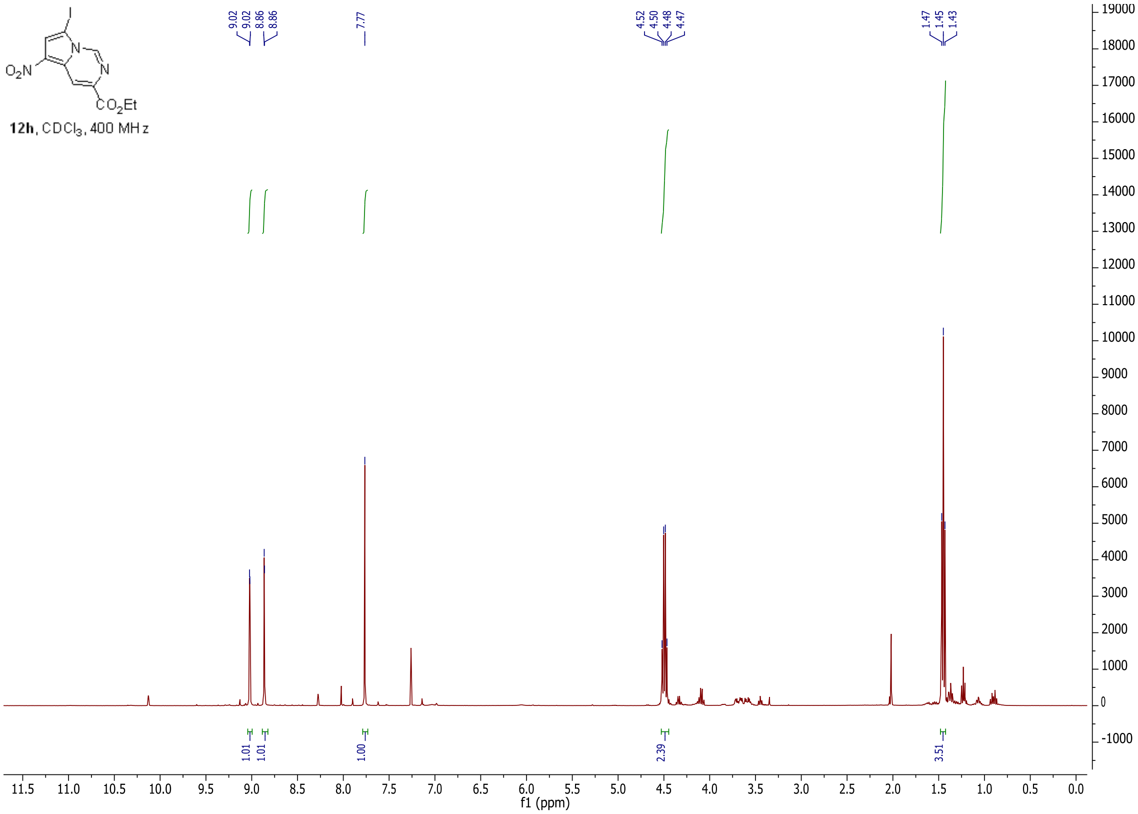

Br
Br
N
N
CO2Et
12e, CDCl3, 400 MHz
164.25
136.06
131.51
130.24
121.14
115.15
95.07
93.21
61.81
14.40
f1 (ppm)

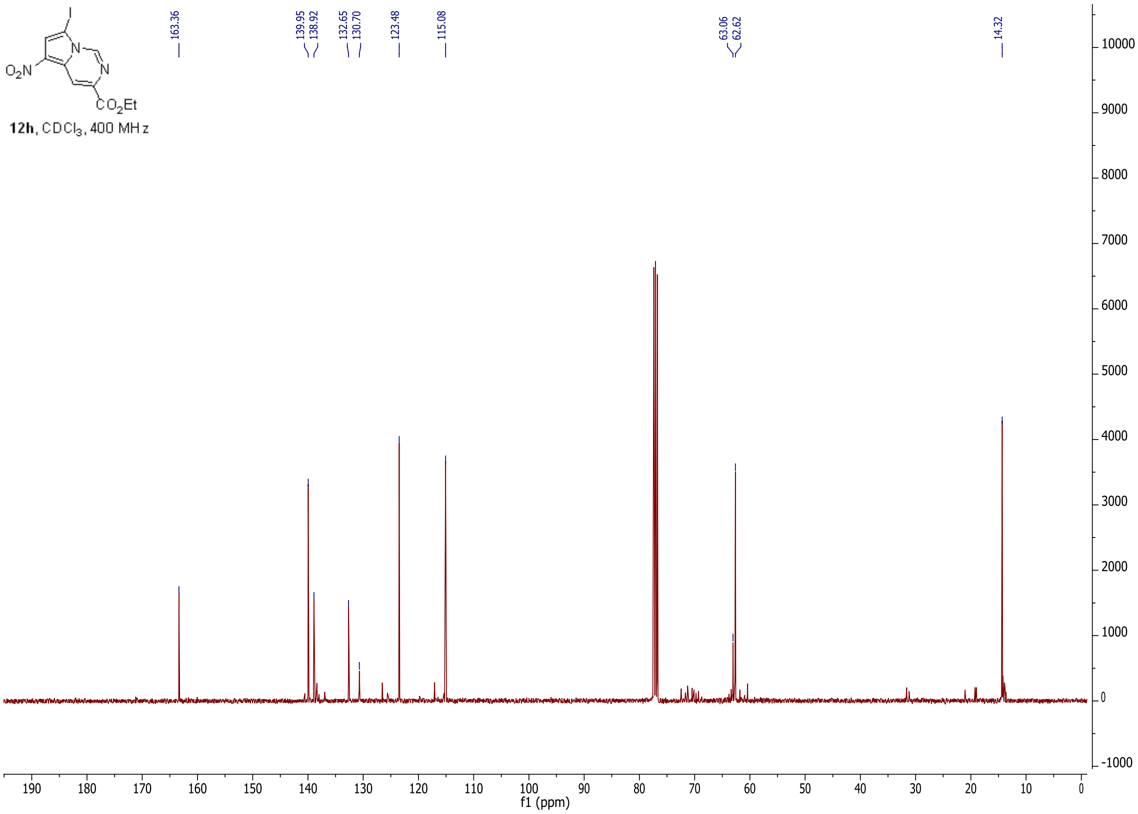

O
CF3
N
N
Br
CO2Et
12f, CDCl3, 400 MHz
10.38
10.37
8.38
8.38
7.86
7.86
7.85
7.85
4.54
4.52
4.50
4.48
1.48
1.46
1.45
1.00
1.02
1.07
2.22
3.32
25000
20000
15000
10000
5000
0
13.0 12.5 12.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5 0.0
f1 (ppm)

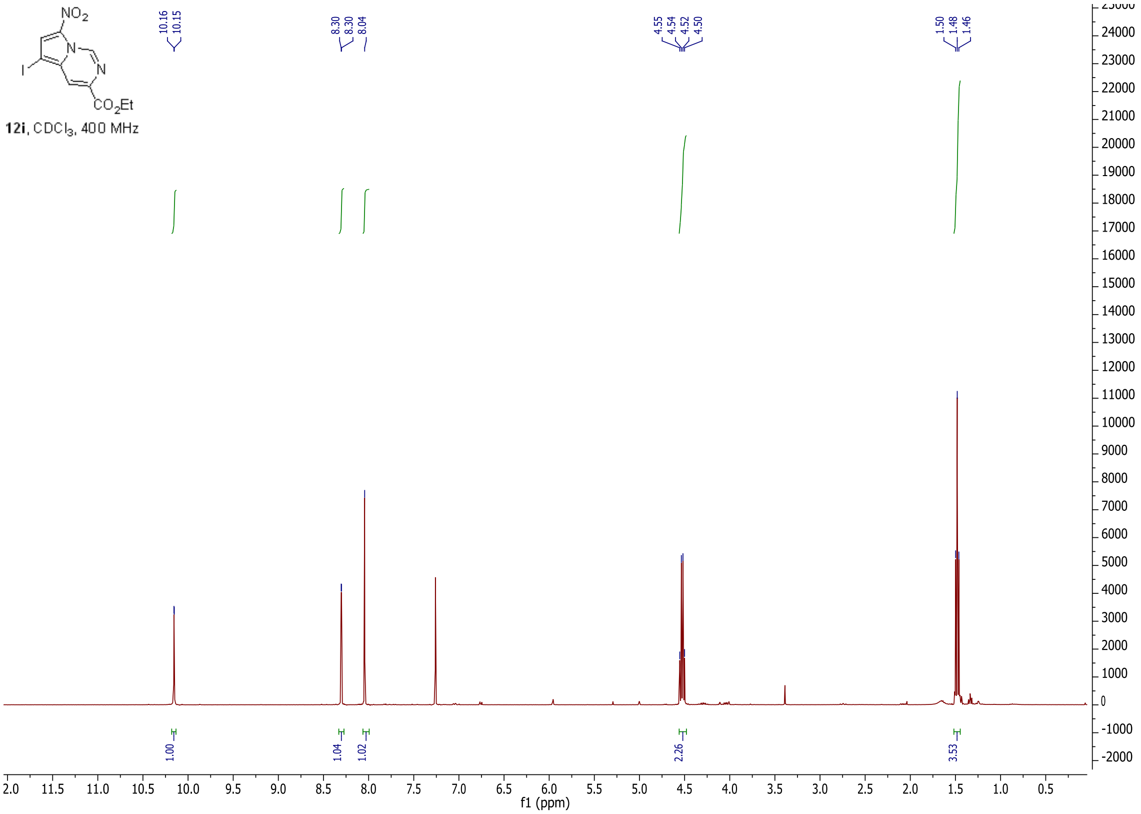

O
CF3
N
N
Br
CO2Et
12f, CDCl3, 400 MHz
169.90
169.53
169.16
168.79
163.37
140.01
139.31
137.85
129.06
129.02
128.98
128.94
120.90
118.23
118.00
115.10
112.24
95.94
62.68
14.30
9000
8000
7000
6000
5000
4000
3000
2000
1000
0
200 190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10
f1 (ppm)

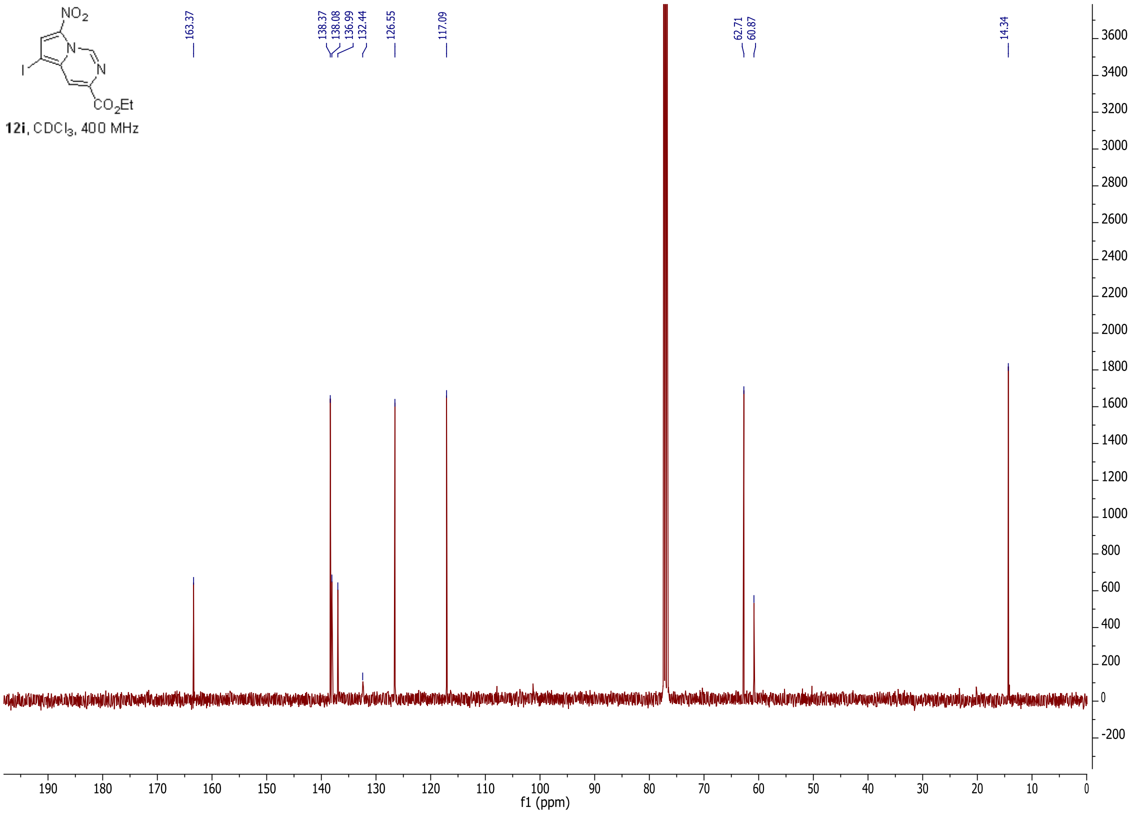

12g, CDCl3, 400 MHz
CO2Et
I
N
O
H
10.23
10.23
9.86
8.27
8.26
7.75
4.54
4.52
4.50
4.49
1.49
1.47
1.45
1.00
1.07
1.02
1.07
2.36
3.58
f1 (ppm)
12.0
11.5
11.0
10.5
10.0
9.5
9.0
8.5
8.0
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
0.5
10000
9000
8000
7000
6000
5000
4000
3000
2000
1000
0


12g, CDCl3, 400 MHz
CO2Et
I
N
O
H
178.17
163.87
140.15
138.60
138.11
134.56
126.33
116.90
77.35
62.46
60.50
14.37
f1 (ppm)
200
190
180
170
160
150
140
130
120
110
100
90
80
70
60
50
40
30
20
10
3800
3600
3400
3200
3000
2800
2600
2400
2200
2000
1800
1600
1400
1200
1000
800
600
400
200
0
-200


12h, $CDCl_3$, 400 MHz


12h, $CDCl_3$, 400 MHz


NO2
I
N
N
CO2Et
12i, CDCl3, 400 MHz
10.16
10.15
8.30
8.30
8.04
4.55
4.54
4.52
4.50
1.50
1.48
1.46
1.00
1.04
1.02
2.26
3.53
f1 (ppm)
2.0 11.5 11.0 10.5 10.0 9.5 9.0 8.5 8.0 7.5 7.0 6.5 6.0 5.5 5.0 4.5 4.0 3.5 3.0 2.5 2.0 1.5 1.0 0.5
25000 24000 23000 22000 21000 20000 19000 18000 17000 16000 15000 14000 13000 12000 11000 10000 9000 8000 7000 6000 5000 4000 3000 2000 1000 0 -1000 -2000


NO2
I
N
N
CO2Et
12i, CDCl3, 400 MHz
163.37
138.37
138.08
136.99
132.44
126.55
117.09
62.71
60.87
14.34
f1 (ppm)
190 180 170 160 150 140 130 120 110 100 90 80 70 60 50 40 30 20 10 0
3600 3400 3200 3000 2800 2600 2400 2200 2000 1800 1600 1400 1200 1000 800 600 400 200 0 -200

10. Experimental details for single crystal X-ray analysis:

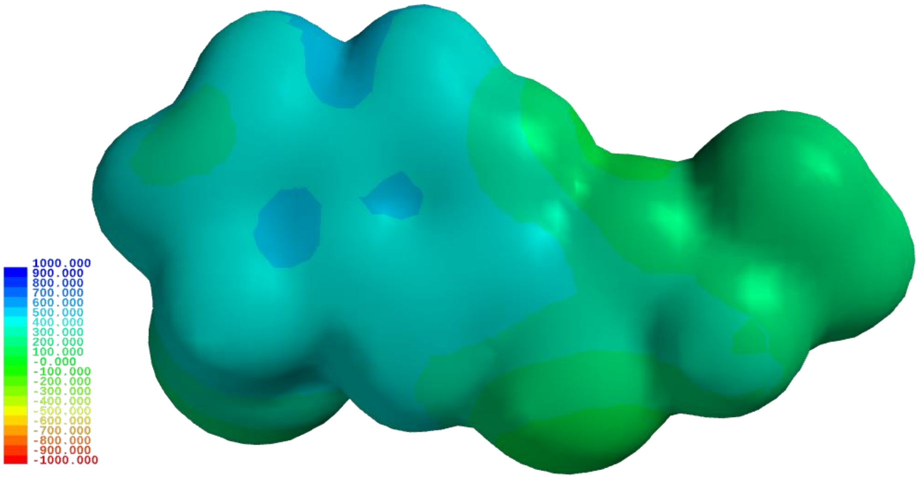
Table 1 Crystal data and structure refinement

Identification code	14srv265; **12i**	14srv235; **12f**	192B; **12a**	14srv167; **7h**	13srv320; **SI12f'**
Empirical formula	$C_{10}H_8IN_3O_4$	$C_{12}H_8N_2O_3F_3Br$	$C_{10}H_8ClN_3O_4$	$C_{11}H_{10}N_3O_2Cl$	$C_{12}H_9F_3N_2O_3$
Formula weight	361.09	377.12	269.64	251.67	286.21
Temperature/K	120.0	120.0	120.0	120.0	120
Crystal system	monoclinic	triclinic	triclinic	monoclinic	orthorhombic
Space group	$P2_1/c$	P-1	P-1	$P2_1$	Pbca
a/Å	14.7611(3)	6.79290(10)	6.3391(12)	8.0883(3)	12.5161(10)
b/Å	4.6408(3)	9.5186(2)	7.7064(15)	7.0136(3)	14.0082(11)
c/Å	17.1279(3)	10.3220(2)	12.819(2)	10.3616(4)	27.051(2)
α/°	90.00	102.643(3)	93.164(6)	90.00	90
β/°	90.424(2)	91.759(3)	102.778(6)	107.9650(10)	90
γ/°	90.00	104.107(3)	113.261(6)	90.00	90
Volume/Å^3	1173.29(8)	629.09(2)	553.93(18)	559.14(4)	4742.7(7)
Z	4	2	2	2	16
ρ_{calc}g/cm^3	2.044	1.928	1.617	1.495	1.603
μ/mm^{-1}	2.741	3.317	0.356	0.334	0.147
F(000)	696.0	360.0	276.0	260.0	2336.0
Crystal size/mm^3	0.56 × 0.14 × 0.07	0.424 × 0.249 × 0.187	0.28 × 0.22 × 0.02	0.4 × 0.22 × 0.14	0.63 × 0.46 × 0.33
2Θ range for data collection/°	4.76 to 60	4.54 to 56	7.14 to 58	4.14 to 58	3.012 to 49.998°
Index ranges	-20 ≤ h ≤ 20, -6 ≤ k ≤ 6, -24 ≤ l ≤ 24	-8 ≤ h ≤ 8, -12 ≤ k ≤ 12, -13 ≤ l ≤ 13	-8 ≤ h ≤ 8, -10 ≤ k ≤ 10, -17 ≤ l ≤ 17	-11 ≤ h ≤ 11, -9 ≤ k ≤ 9, -14 ≤ l ≤ 14	-14 ≤ h ≤ 14, -16 ≤ k ≤ 16, -32 ≤ l ≤ 32
Reflections collected	17049	10397	9387	6930	37987
Independent reflections, R_{int}, R_{sigma}	3436, 0.0632, 0.0474	3027, 0.0641, 0.0558	2696, 0.0929, 0.0912	2957, 0.0399, 0.0402	4178, 0.0371, 0.0214

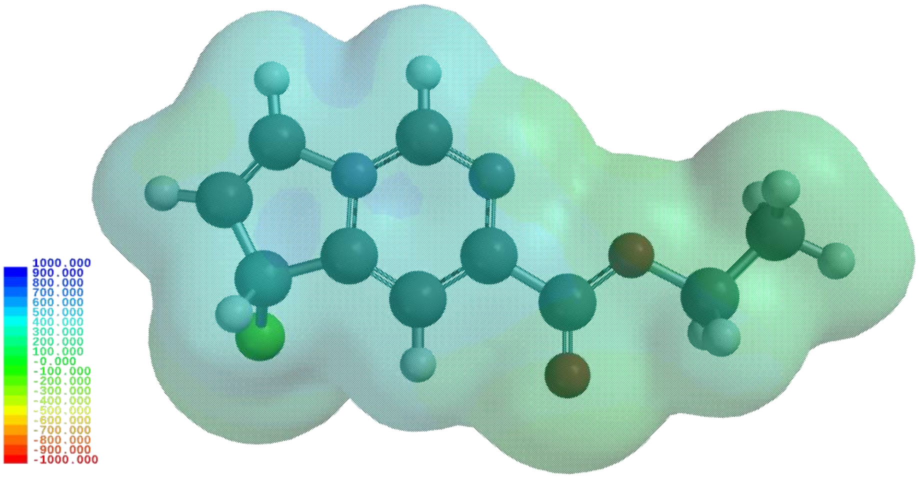
Data/restraints/parameters	3436/0/164	3027/0/191	2696/0/164	2957/1/194	4178/0/365
Goodness-of-fit on F^2	1.036	1.101	1.024	1.088	1.209
Final R_1/wR_2 indexes [I≥2σ (I)]	0.0320, 0.0742	0.0507, 0.1256	0.0889, 0.2074	0.0404, 0.1009	0.0665, 0.1543
Final R_1/wR_2 indexes [all data]	0.0384, 0.0774	0.0528, 0.1275	0.1213, 0.2298	0.0453, 0.1052	0.0778, 0.1646
Diff. peak/hole/ e Å^{-3}	2.01/-0.66	1.84/-0.99	1.90/-1.31	0.51/-0.31	0.49/-0.31

11. DFT calculations:

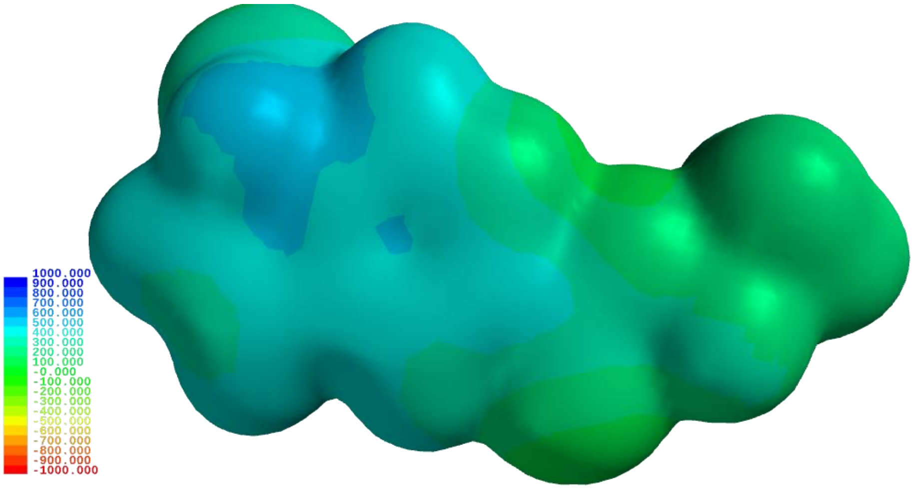
Electronic Surface Potentials attained from DFT calculations



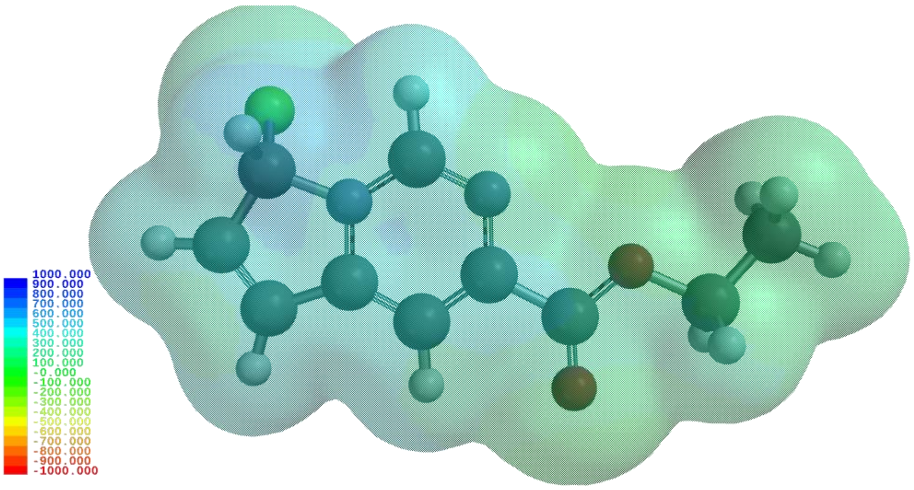
5ClH_py_py_PCM_fukui_ESP_solid (**5-Cl INT**)



5ClH_py_py_PCM_fukui_ESP (**5-Cl INT**)



7ClH_py_py_PCM_fukui_ESP_solid (**7-Cl INT**)



7ClH_py_py_PCM_fukui_ESP (**7-Cl INT**)

12. DFT calculations energy Table 2:

Table 2. Total Electronic Energies[a] (E, in a.u.) of all stationary points discussed in the main text for the compounds.

Structure	E	ΔZPE	G	NIMAG (ν)
Pyrrolopyrimidine	-647.004044411	0.190079	-646.853104	0
7-ClH*	-1107.00500394	0.193520	-1106.853212	0
7-Cl	-1106.60290081	0.180933	-1106.462740	0
5-ClH*	-1106.99936544	0.193153	-1106.848067	0
5-Cl	-1106.60471320	0.180405	-1106.465793	0
7-BrH*	-3220.97406844	0.193305	-3220.823035	0
7-Br	-3220.57004760	0.179910	-3220.432131	0
5-BrH*	-3220.96961194	0.192286	-3220.820449	0
5-Br	-3220.57253380	0.180675	-3220.433498	0
7-IH*	-942.431970713	0.192938	-942.281993	0
7-I	-942.024503083	0.179430	-941.888531	0
5-IH*	-942.429091879	0.192162	-942.280774	0
5-I	-942.027288745	0.179947	-941.890743	0

13. DFT calculations Z-matrix of all the stationary points of the reaction profiles:

Cartesian coordinates optimized at the M062x/6-311++G(2df,2pd) of all the stationary points discussed in the main text.

Pyrrolopyrimidine

```
 ---------------------------------------------------------------------
                         Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -1.166452   -1.587171    0.000060
      2          1           0       -0.581139    2.171410   -0.000084
      3          6           0        0.238368    0.211684   -0.000024
      4          6           0       -0.782491    1.110773   -0.000042
      5          6           0       -3.372830    1.184251   -0.000007
      6          6           0       -4.292545    0.115061    0.000043
      7          6           0       -3.594039   -1.070194    0.000074
      8          6           0       -2.107951    0.631382   -0.000005
      9          1           0       -1.374978   -2.649958    0.000100
     10          1           0       -3.926732   -2.093279    0.000113
     11          1           0       -5.366203    0.196642    0.000055
     12          1           0       -3.593706    2.237304   -0.000041
     13          7           0        0.040161   -1.151691    0.000029
     14          7           0       -2.262354   -0.763997    0.000046
     15          6           0        1.637715    0.724460   -0.000066
     16          8           0        1.907852    1.902437   -0.000135
     17          8           0        2.548756   -0.239694   -0.000004
     18          6           0        3.921067    0.186933   -0.000046
     19          6           0        4.779514   -1.053478    0.000071
     20          1           0        4.093389    0.802960    0.882031
     21          1           0        4.093384    0.802788   -0.882245
     22          1           0        5.830666   -0.769692    0.000030
     23          1           0        4.582847   -1.656165    0.885089
     24          1           0        4.582825   -1.656348   -0.884818
 ---------------------------------------------------------------------
```

7-ClH*

```
 ---------------------------------------------------------------------
                         Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        1.334857    1.126753    0.052636
      2          6           0       -0.002796    1.433263   -0.096784
      3          6           0       -0.897065    0.390864    0.078338
```

```
      4          6           0        0.737932   -1.106641    0.531974
      5          6           0        3.120765   -0.284917    0.514409
      6          6           0        3.589432    1.100699    0.204955
      7          6           0        2.557602    1.904144   -0.052722
      8          1           0       -0.339127    2.428710   -0.340078
      9          1           0        1.089787   -2.098722    0.784284
     10          1           0        4.638398    1.348747    0.208390
     11          1           0        2.576590    2.951721   -0.300542
     12          7           0       -0.535945   -0.860459    0.386833
     13          7           0        1.661546   -0.148759    0.370409
     14          6           0       -2.372473    0.696283   -0.092860
     15          8           0       -2.746573    1.815875   -0.316068
     16          8           0       -3.126728   -0.367956    0.024739
     17          6           0       -4.549028   -0.159618   -0.143292
     18          6           0       -5.220843   -1.501087   -0.011844
     19          1           0       -4.708087    0.290230   -1.122160
     20          1           0       -4.876971    0.546319    0.618337
     21          1           0       -6.294315   -1.377708   -0.142936
     22          1           0       -4.856652   -2.190451   -0.771223
     23          1           0       -5.039462   -1.930473    0.971627
     24         17           0        3.751287   -1.498852   -0.606632
     25          1           0        3.354861   -0.605167    1.528113
 ---------------------------------------------------------------------
```

7-Cl

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -1.335385    1.254789   -0.000151
      2          6           0        0.051971    1.495193   -0.000135
      3          6           0        0.901505    0.432504    0.000024
      4          6           0       -0.791366   -1.101773    0.000155
      5          6           0       -3.091032   -0.144294   -0.000040
      6          6           0       -3.581082    1.139292   -0.000208
      7          6           0       -2.482841    2.021596   -0.000280
      8          1           0        0.432244    2.505646   -0.000244
      9          1           0       -1.179923   -2.111496    0.000266
     10          1           0       -4.626353    1.396453   -0.000272
     11          1           0       -2.515024    3.096747   -0.000411
     12          7           0        0.470301   -0.874590    0.000169
     13          7           0       -1.728047   -0.095998    0.000002
     14          6           0        2.369951    0.693087    0.000038
     15          8           0        2.839425    1.806093   -0.000117
     16          8           0        3.097163   -0.415377    0.000104
     17          6           0        4.522878   -0.235101    0.000022
     18          6           0        5.154067   -1.604847    0.000090
     19          1           0        4.799087    0.342257    0.881842
```

```
     20          1           0        4.798995    0.342126   -0.881911
     21          1           0        6.238168   -1.504899    0.000018
     22          1           0        4.858437   -2.165791    0.885112
     23          1           0        4.858332   -2.165926   -0.884811
     24         17           0       -3.921437   -1.633494    0.000131
 ---------------------------------------------------------------------
```

5-ClH*

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -1.537521    0.022225    0.316472
      2          6           0       -0.360799   -0.672069    0.370177
      3          6           0        0.796727    0.062331    0.123433
      4          6           0       -0.354748    1.988715   -0.195552
      5          6           0       -2.841162    1.878943    0.004991
      6          6           0       -3.700325    0.908225    0.272707
      7          6           0       -2.968693   -0.375594    0.523599
      8          1           0       -0.323540   -1.728806    0.586592
      9          1           0       -0.405112    3.046317   -0.414776
     10          1           0       -2.979036    2.923971   -0.212462
     11          1           0       -4.771864    0.999342    0.322267
     12          7           0        0.795195    1.364013   -0.151781
     13          7           0       -1.510011    1.344681    0.029256
     14          6           0        2.120454   -0.673089    0.177842
     15          8           0        2.159220   -1.847102    0.430032
     16          8           0        3.143131    0.105652   -0.072036
     17          6           0        4.445621   -0.525207   -0.035747
     18          6           0        5.470320    0.537924   -0.332164
     19          1           0        4.451187   -1.325798   -0.774001
     20          1           0        4.577341   -0.964897    0.951701
     21          1           0        6.464079    0.095013   -0.302616
     22          1           0        5.310596    0.964724   -1.320516
     23          1           0        5.424059    1.333953    0.408556
     24         17           0       -3.438824   -1.678596   -0.596521
     25          1           0       -3.122062   -0.751364    1.535267
 ---------------------------------------------------------------------
```

5-Cl

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        1.601138    0.058465    0.000028
```

```
      2          6           0        0.390444   -0.659323    0.000132
      3          6           0       -0.773202    0.043998    0.000224
      4          6           0        0.284701    2.069104    0.000112
      5          6           0        2.767377    1.996164   -0.000087
      6          6           0        3.673102    0.961871   -0.000146
      7          6           0        2.947070   -0.243453   -0.000078
      8          1           0        0.388925   -1.739116    0.000147
      9          1           0        0.300961    3.151955    0.000101
     10          1           0        2.912949    3.061553   -0.000110
     11          1           0        4.744963    1.058571   -0.000229
     12          7           0       -0.821272    1.421564    0.000209
     13          7           0        1.512862    1.456058    0.000020
     14          6           0       -2.060499   -0.710115    0.000356
     15          8           0       -2.113585   -1.916772    0.000119
     16          8           0       -3.126902    0.076895    0.000110
     17          6           0       -4.401510   -0.588119   -0.000130
     18          6           0       -5.469826    0.476141   -0.000389
     19          1           0       -4.458686   -1.225461    0.881821
     20          1           0       -4.458325   -1.225527   -0.882056
     21          1           0       -6.451310    0.004889   -0.000586
     22          1           0       -5.388711    1.104965    0.884712
     23          1           0       -5.388331    1.104912   -0.885493
     24         17           0        3.595739   -1.832322   -0.000111
 ---------------------------------------------------------------------
```

7-BrH*

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.685229    1.422993    0.065934
      2          6           0       -0.666414    1.585255   -0.169173
      3          6           0       -1.470433    0.485020    0.068128
      4          6           0        0.269799   -0.808419    0.717890
      5          6           0        2.563244    0.233677    0.721791
      6          6           0        2.918343    1.627047    0.330427
      7          6           0        1.831965    2.304526   -0.046279
      8          1           0       -1.077745    2.519038   -0.518431
      9          1           0        0.698258   -1.739095    1.067138
     10          1           0        3.936218    1.978808    0.369169
     11          1           0        1.769025    3.326194   -0.379455
     12          7           0       -1.012174   -0.695397    0.505051
     13          7           0        1.111873    0.215053    0.508114
     14          6           0       -2.958785    0.635935   -0.178174
     15          8           0       -3.421765    1.689285   -0.523924
     16          8           0       -3.621133   -0.475405    0.026889
     17          6           0       -5.051473   -0.408741   -0.183653
     18          6           0       -5.610863   -1.783475    0.072272
```

```
     19          1           0       -5.225509   -0.072677   -1.204675
     20          1           0       -5.455079    0.337427    0.499172
     21          1           0       -6.689666   -1.762816   -0.070416
     22          1           0       -5.184592   -2.508491   -0.618489
     23          1           0       -5.402515   -2.101163    1.092133
     24          1           0        2.791240   -0.012382    1.755797
     25         35           0        3.440628   -1.087897   -0.385794
 ---------------------------------------------------------------------
```

7-Br

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.617555    1.577758   -0.000066
      2          6           0        0.787038    1.668859   -0.000157
      3          6           0        1.517963    0.521856   -0.000161
      4          6           0       -0.329394   -0.821630   -0.000001
      5          6           0       -2.516016    0.377983    0.000064
      6          6           0       -2.861240    1.708283    0.000044
      7          6           0       -1.673891    2.465634   -0.000032
      8          1           0        1.273015    2.632984   -0.000230
      9          1           0       -0.823633   -1.784308    0.000068
     10          1           0       -3.871295    2.079971    0.000074
     11          1           0       -1.588494    3.537979   -0.000070
     12          7           0        0.949698   -0.731279   -0.000077
     13          7           0       -1.154812    0.277419    0.000003
     14          6           0        3.005527    0.626228   -0.000260
     15          8           0        3.588997    1.684025   -0.000261
     16          8           0        3.612479   -0.551975   -0.000040
     17          6           0        5.049851   -0.519390    0.000056
     18          6           0        5.538005   -1.946282    0.000331
     19          1           0        5.383028    0.027149    0.881894
     20          1           0        5.383154    0.026855   -0.881915
     21          1           0        6.626626   -1.957571    0.000417
     22          1           0        5.186571   -2.473659    0.885515
     23          1           0        5.186708   -2.473956   -0.884730
     24         35           0       -3.609526   -1.127160    0.000085
 ---------------------------------------------------------------------
```

5-BrH*

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -1.018685    0.404393    0.449953
      2          6           0        0.088913   -0.396139    0.537131
```

```
      3          6           0        1.296413    0.183049    0.160684
      4          6           0        0.324092    2.167261   -0.341608
      5          6           0       -2.140692    2.349265    0.005928
      6          6           0       -3.074955    1.509601    0.427935
      7          6           0       -2.465843    0.183577    0.749694
      8          1           0        0.036161   -1.420738    0.872772
      9          1           0        0.362508    3.192219   -0.683203
     10          1           0       -2.184849    3.375123   -0.316681
     11          1           0       -4.125462    1.722090    0.529105
     12          7           0        1.407138    1.437208   -0.272990
     13          7           0       -0.875101    1.677886    0.013609
     14          6           0        2.545808   -0.669035    0.251249
     15          8           0        2.486134   -1.810448    0.621494
     16          8           0        3.626315   -0.020105   -0.105009
     17          6           0        4.865908   -0.764313   -0.039090
     18          6           0        5.973942    0.166682   -0.456029
     19          1           0        4.775703   -1.624734   -0.700473
     20          1           0        4.987206   -1.124268    0.981408
     21          1           0        6.922657   -0.365223   -0.415596
     22          1           0        5.818718    0.520951   -1.473243
     23          1           0        6.029044    1.023873    0.212304
     24          1           0       -2.627593   -0.144858    1.773901
     25         35           0       -3.171067   -1.232049   -0.387760
 ---------------------------------------------------------------------
```

5-Br

```
 ---------------------------------------------------------------------
                          Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        1.053021    0.469360   -0.000035
      2          6           0       -0.061820   -0.390355   -0.000065
      3          6           0       -1.302692    0.165892    0.000075
      4          6           0       -0.500549    2.304010    0.000269
      5          6           0        1.971560    2.536797    0.000149
      6          6           0        2.997227    1.621620   -0.000028
      7          6           0        2.425955    0.335364   -0.000136
      8          1           0        0.068365   -1.462347   -0.000197
      9          1           0       -0.617308    3.380581    0.000399
     10          1           0        1.983705    3.612097    0.000274
     11          1           0        4.048900    1.850498   -0.000069
     12          7           0       -1.519070    1.526146    0.000244
     13          7           0        0.792993    1.845665    0.000137
     14          6           0       -2.489857   -0.737981    0.000040
     15          8           0       -2.398483   -1.942251   -0.000096
     16          8           0       -3.642064   -0.083431    0.000245
     17          6           0       -4.829450   -0.893911    0.000259
     18          6           0       -6.014976    0.038348    0.000556
     19          1           0       -4.812214   -1.533279    0.882240
```

```
     20          1           0       -4.812431   -1.532993   -0.881934
     21          1           0       -6.934838   -0.544012    0.000582
     22          1           0       -6.006615    0.672132    0.885695
     23          1           0       -6.006843    0.672412   -0.884384
     24         35           0        3.343020   -1.291633   -0.000370
 ---------------------------------------------------------------------
```

7-IH*

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.144371    1.600045    0.090895
      2          6           0       -1.202647    1.659293   -0.222144
      3          6           0       -1.949043    0.528259    0.043429
      4          6           0       -0.167823   -0.616660    0.845188
      5          6           0        2.056027    0.565325    0.882981
      6          6           0        2.338482    1.960288    0.463402
      7          6           0        1.232233    2.547372   -0.007436
      8          1           0       -1.650372    2.543847   -0.646751
      9          1           0        0.297945   -1.500847    1.260792
     10          1           0        3.325666    2.385991    0.542722
     11          1           0        1.123570    3.545594   -0.395466
     12          7           0       -1.441014   -0.594502    0.573245
     13          7           0        0.624136    0.445513    0.617216
     14          6           0       -3.427958    0.562768   -0.285030
     15          8           0       -3.926617    1.531036   -0.792502
     16          8           0       -4.043777   -0.546159    0.044636
     17          6           0       -5.461004   -0.596694   -0.240044
     18          6           0       -5.967529   -1.935677    0.228836
     19          1           0       -5.593001   -0.454702   -1.311702
     20          1           0       -5.939179    0.232434    0.279195
     21          1           0       -7.034764   -2.006108    0.027340
     22          1           0       -5.462042   -2.744785   -0.295030
     23          1           0       -5.808726   -2.054598    1.299003
     24          1           0        2.279340    0.335809    1.921392
     25         53           0        3.176834   -0.844616   -0.298722
 ---------------------------------------------------------------------
```

7-I

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.010826    1.768489   -0.000106
      2          6           0        1.397075    1.761228   -0.000140
      3          6           0        2.046094    0.565899   -0.000102
```

```
      4          6           0        0.107723   -0.641770   -0.000006
      5          6           0       -1.994930    0.703843   -0.000011
      6          6           0       -2.237066    2.059168   -0.000064
      7          6           0       -1.000026    2.730535   -0.000121
      8          1           0        1.948650    2.689366   -0.000194
      9          1           0       -0.450810   -1.568673    0.000044
     10          1           0       -3.216533    2.505803   -0.000060
     11          1           0       -0.837054    3.793964   -0.000168
     12          7           0        1.390104   -0.643008   -0.000036
     13          7           0       -0.641449    0.510176   -0.000037
     14          6           0        3.537335    0.562731   -0.000138
     15          8           0        4.197003    1.574963   -0.000217
     16          8           0        4.055295   -0.657049   -0.000011
     17          6           0        5.490416   -0.736772    0.000009
     18          6           0        5.861605   -2.198793    0.000249
     19          1           0        5.866422   -0.219343    0.882111
     20          1           0        5.866431   -0.219632   -0.882259
     21          1           0        6.945571   -2.299786    0.000268
     22          1           0        5.467403   -2.695183    0.885299
     23          1           0        5.467409   -2.695472   -0.884643
     24         53           0       -3.349073   -0.851922    0.000085
 ---------------------------------------------------------------------
```

5-IH*

```
 ---------------------------------------------------------------------
Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0       -0.558668    0.661132    0.535505
      2          6           0        0.503210   -0.200648    0.660736
      3          6           0        1.729626    0.260000    0.201537
      4          6           0        0.872621    2.254204   -0.450561
      5          6           0       -1.550782    2.645080   -0.020618
      6          6           0       -2.521020    1.913067    0.514119
      7          6           0       -1.998082    0.572442    0.893668
      8          1           0        0.397267   -1.186665    1.087746
      9          1           0        0.962849    3.239480   -0.886565
     10          1           0       -1.537004    3.642730   -0.423715
     11          1           0       -3.544612    2.216925    0.649898
     12          7           0        1.905674    1.462645   -0.350613
     13          7           0       -0.344354    1.882546   -0.012986
     14          6           0        2.923932   -0.660393    0.336524
     15          8           0        2.808934   -1.752105    0.825647
     16          8           0        4.028545   -0.127554   -0.125461
     17          6           0        5.217845   -0.945872   -0.027256
     18          6           0        6.354860   -0.162168   -0.628483
     19          1           0        5.029206   -1.877840   -0.557919
     20          1           0        5.381778   -1.174557    1.024787
     21          1           0        7.267549   -0.752455   -0.571499
```

```
     22          1           0        6.155049    0.065321   -1.673896
     23          1           0        6.510816    0.769478   -0.088012
     24          1           0       -2.172093    0.273237    1.923423
     25         53           0       -2.941908   -0.973883   -0.294935
 ---------------------------------------------------------------------
```

5-I

```
 ---------------------------------------------------------------------
                          Standard orientation:
 ---------------------------------------------------------------------
 Center     Atomic      Atomic             Coordinates (Angstroms)
 Number     Number       Type             X           Y           Z
 ---------------------------------------------------------------------
      1          6           0        0.562045    0.734608    0.000017
      2          6           0       -0.476285   -0.216677   -0.000013
      3          6           0       -1.761282    0.228236    0.000120
      4          6           0       -1.148236    2.427441    0.000312
      5          6           0        1.293094    2.875002    0.000194
      6          6           0        2.394343    2.052555    0.000024
      7          6           0        1.942486    0.717204   -0.000076
      8          1           0       -0.256513   -1.274263   -0.000145
      9          1           0       -1.357349    3.489907    0.000438
     10          1           0        1.210229    3.947462    0.000312
     11          1           0        3.420200    2.379190   -0.000017
     12          7           0       -2.096111    1.564146    0.000286
     13          7           0        0.179633    2.082827    0.000184
     14          6           0       -2.864768   -0.776036    0.000084
     15          8           0       -2.668689   -1.967699   -0.000068
     16          8           0       -4.069796   -0.224390    0.000302
     17          6           0       -5.183007   -1.133620    0.000322
     18          6           0       -6.443048   -0.304222    0.000588
     19          1           0       -5.112255   -1.769316    0.882425
     20          1           0       -5.112477   -1.769081   -0.881970
     21          1           0       -7.311669   -0.960455    0.000607
     22          1           0       -6.486331    0.328305    0.885638
     23          1           0       -6.486548    0.328538   -0.884285
     24         53           0        3.111771   -0.987157   -0.000332
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