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*Electronic Supplementary Information (ESI)*

# IBX-Mediated Oxidation of Unactivated Cyclic Amines: Application in Highly Diastereoselective Oxidative Ugi-type and aza-Friedel-Crafts Reactions

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## General information

Starting materials were purchased from Sigma Aldrich, Fisher Scientific and Acros Organics and were used without purification, unless stated otherwise. (3a*R*,6a*S*)-Octahydrocyclopenta[*c*]pyrrole hydrochloride was purchased from AK Scientific and dissolved in $CH_2Cl_2$, washed with sat. aq. $Na_2CO_3$, extracted with $CH_2Cl_2$, dried ($Na_2SO_4$) and concentrated *in vacuo* before use. Unless stated otherwise, the solvents were purchased from VWR Chemicals and were used without further treatment. Cyclohexane (*c*Hex) was purified by distillation before use. Celite® 512 medium was purchased from Sigma Aldrich. Column Chromatography was performed on Silica-P Flash Silica Gel (particle size 40-63 µm, pore diameter 60 Å) from Silicycle. Preparative thin layer chromatography was performed on Silica Gel plates $F_{254}$ (20 x 20 cm, 2000 µm, pore diameter 60 Å) from Silicycle. Thin Layer Chromatography (TLC) was performed using TLC plates $F_{254}$ (silica gel 60 on aluminium) from Merck Serono KGaA (Darmstadt) and compounds were visualized by UV detection (254 or 366 nm) and stained with basic aq. $KMnO_4$ or ninhydrin/ethanol.

$^1H$, $^{13}C$, COSY, HSQC, HMBC and NOESY nuclear magnetic resonance (NMR) spectra were recorded on a Bruker Avance 500 (500.23 MHz for $^1H$ and 125.78 MHz for $^{13}C$) in $CDCl_3$ or DMSO-$d_6$ using the residual solvent as internal standard ($CDCl_3$: $\delta$ = 7.26 for $^1H$ NMR and $\delta$ = 77.16 for $^{13}C$ NMR, DMSO-$d_6$: $\delta$ = 2.50 for $^1H$ NMR and $\delta$ = 39.52 for $^{13}C$ NMR) or Bruker Avance 400 (400.13 MHz for $^1H$ and 100.62 MHz for $^{13}C$) using the residual solvent as internal standard ($CDCl_3$: $\delta$ = 7.26 for $^1H$ NMR and $\delta$ = 77.16 for $^{13}C$ NMR, DMSO-$d_6$: $\delta$ = 2.50 for $^1H$ NMR and $\delta$ = 39.52 for $^{13}C$ NMR). Chemical shifts (δ) are given in ppm and coupling constants (*J*) are quoted in hertz (Hz). Resonances are described as s (singlet), d (doublet), t (triplet), q (quartet), bs (broad singlet) and m (multiplet) or combinations thereof. The COSY-, HMBC- and HSQC-NMR spectra were used for the assignment of the proton signals and the NOESY-NMR spectra were used for the assignment of the relative stereochemistry. The APT-NMR spectra were used for the assignment of the carbons. Names of chemical structures were deduced from generic names and/or important functionalities.

Electrospray Ionization (ESI) high resolution mass spectrometry was carried out using a Bruker micrOTOF-Q instrument in positive ion mode (capillary potential of 4500 V). Infrared (IR) spectra were recorded neat using a FTIR-8400s from Shimadzu. Signal intensities are described as strong (s), medium (m), weak (w) or broad (br). Melting points were determined on a Büchi M-565 and are not corrected.

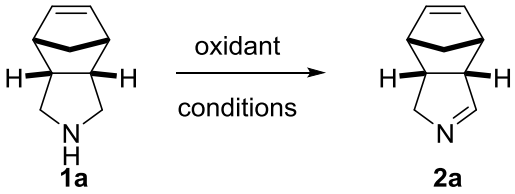
X-ray single crystal data were collected at 100Kon a Bruker X8 Prospector with Cu microsource and focusing optics, and Apex II detector. Data were integrated and corrected for absorption with SAINT V8.34A and SADABS 2012/1, and the structure was solved and refined with SHELX 2014 and shelXle. Hydrogen atoms were detected in the Fourier difference maps, those on C were refined with constraints on bond lengths and angles, those on N were refined freely.

## Optimization data

*General procedure for optimization of the reaction conditions for the oxidation of meso-pyrrolidine **1a** with IBX in Supplementary table S1:*

To a solution of pyrrolidine **1a** (0.25 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.2 M) was added IBX (70 mg, 0.25 mmol, 1.0 eq.). The reaction mixture was stirred for 0.5 - 1 h at rt or 60 °C (oil bath, closed vessel). The reaction mixture was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (1 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 10 mL), extracted with $CH_2Cl_2$ (2 x 10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Subsequently, the yield of **2a** was determined with $^1$H-NMR spectroscopy after dissolving the crude product in $CDCl_3$ and adding 2,5-dimethylfuran (0.125 mmol, 0.5 eq.) as standard for NMR spectroscopy.

*Supplementary table S1: Optimization of reaction conditions for IBX-mediated oxidation.*




| Entry | Oxidant | Solvent | *T* [°C] | *t* | Yield |
|---|---|---|---|---|---|
| 1 | $NaIO_3$ | DMSO | rt | 30 min | –[a] |
| 2 | $PhI(OAc)_2$ | DMSO | rt | 30 min | 38% |
| 3 | $PhI(CO_2CF_3)_2$ | DMSO | rt | 30 min | 33% |
| 4 | DMP | DMSO | rt | 30 min | 55% |
| 5 | IBX | DMSO | rt | 30 min | 90% |
| 6 | IBX | DMF | rt | 30 min | 92% |
| 7 | IBX | MeCN | rt | 1 h | 19% |
| 8 | IBX | MeCN | 60 | 1 h | 78% |
| 9 | IBX | MeOH | 60 | 1 h | 81% |
| 10 | IBX | $CH_2Cl_2$ | 60 | 1 h | 95% |
| 11 | IBX | THF:DMSO (9:1) | 60 | 1 h | 94% |
| 12 | IBX | THF | 60 | 1 h | 58% |
| 13 | IBX | DMC | 60 | 1 h | 31% |
| 14 | IBX | TFE | 60 | 1 h | 47% |
| 15 | IBX | EtOAc | 60 | 1 h | 19% |
| 16 | IBX | toluene | 60 | 1 h | 10% |

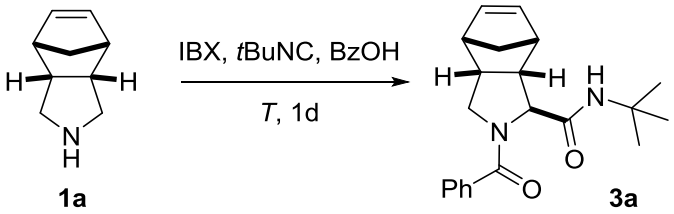
[a] used with and without preactivation[1]

[1] Nicolaou, K. C.; Montagnon, T.; Baran, P. S. *Angew. Chem. Int. Ed.*, **2002**, *41*, 1386.

*General procedure for optimization of the reaction conditions for the oxidative Ugi-type reaction in Table 3 and Supplementary table S2:*

To a solution of pyrrolidine **1a** (0.25 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.5 M) were added IBX (70 mg, 0.25 mmol, 1.0 eq.), benzoic acid (0.375 mmol, 1.5 eq.) and *tert*-butyl isocyanide (0.375 mmol, 1.5 eq.). The reaction mixture was stirred for 24 h at rt or 60 °C (oil bath, closed vessel). The suspension was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (1 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 10 mL), extracted with $CH_2Cl_2$ (2 x 10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Subsequently, the yield of **3a** was determined with $^1$H-NMR spectroscopy after dissolving the crude product in $CDCl_3$ and adding 2,5-dimethylfuran (0.125 mmol, 0.5 eq.) as standard for NMR spectroscopy.

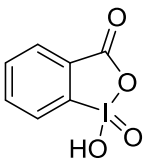
*Supplementary table S2: Optimization of reaction conditions for oxidative Ugi-type reaction.*




**1a** **3a**

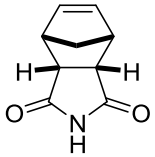
| Entry | Solvent [0.5 M] | T [°C] | Yield |
|---|---|---|---|
| 1 | DMSO [0.2 m] | rt | 26% |
| 2 | DMSO | rt | 37% |
| 3 | TFE | 60 | 19% |
| 4 | MeOH | 60 | 25% |
| 5 | MeCN | 60 | 50% |
| 6 | $CH_2Cl_2$ | 60 | 54% |

## Synthetic procedures

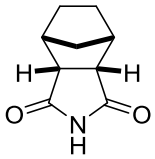


***o*-iodoxybenzoic acid[2] (IBX, S1):** To a solution of Oxone® (74.3 g, 242 mmol, 6.0 eq.) in $H_2O$ (0.2 M) was added 2-iodobenzoic acid (10.0 g, 40.3 mmol, 1.0 eq.). The reaction mixture was stirred for 3 h at 70 °C and then cooled to rt. The solid was filtered off, washed with cold $H_2O$ (500 mL) and cold acetone (300 mL) and dried *in vacuo* (60 °C, 18 h). Compound **S1** (7.17 g, 25.5 mmol, 63%) was obtained without the need of purification as an off-white solid. **$^1$H NMR** (500 MHz, DMSO-$d_6$): $\delta$ 8.15 (d, $J$ = 8.0 Hz, 1H), 8.06 – 7.97 (m, 2H), 7.84 (t, $J$ = 7.3 Hz, 1H) ppm. **$^{13}$C NMR** (126 MHz, DMSO-$d_6$): $\delta$ 167.6 (C*), 146.6 (C*), 133.5 (CH), 133.1 (CH), 131.5 (C*), 130.1 (CH), 125.1 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3097 (w), 1636 (m), 1560 (w), 1331 (m), 1294 (s), 1246 (m), 1138 (m), 831 (m), 773 (m), 748 (s), 692 (s), 673 (s), 648 (m), 592 (s), 577 (s).

## *Substrate synthesis*



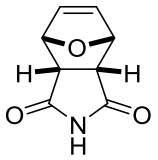
**imid S2a:** To a solution of maleimide (7.28 g, 75.0 mmol, 1.0 eq.) in diethyl ether (0.68 M) was added cyclopentadiene (7.0 mL, 80.0 mmol, 1.06 eq.) dropwise. The reaction mixture was stirred for 2 h at rt. The product was filtered off and washed with diethyl ether. Compound **S2a** (12.0 g, 73.5 mmol, 98%) was obtained without the need of purification as an off-white solid. **$R_f$** = 0.30 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 184.4 – 188.6 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.47 (bs, 1H, N*H*), 6.17 (d, $J$ = 2.0 Hz, 2H, C*H*=C*H*), 3.36 (s, 2H, C(O)CHC*H*$CH_2$), 3.31 – 3.22 (m, 2H, C(O)C*H*), 1.72 (d, $J$ = 8.8 Hz, 1H, C$H_2$), 1.51 (d, $J$ = 8.8 Hz, 1H, C$H_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 178.5 (C*), 134.7 (CH), 52.4 ($CH_2$), 47.4 (CH), 45.0 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3159 (m), 2991 (m), 1753.17 (m), 1697 (s), 1352 (m), 1294 (m), 1186 (s), 1120 (s), 991 (m), 839 (s), 829 (s), 729 (s), 660 (s), 604 (s). **HRMS** (ESI): *m/z* calulated for $C_9H_{10}NO_2$ $[M+H]^+$:164.0706, found: 164.0711.



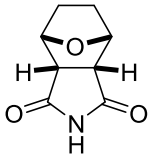
**imid S2b:** To a solution of palladium on carbon 10% (15 mg, 0.04 mol%) in $CH_2Cl_2$ (0.1 mL) and methanol (27 mL) was added imid **S2a** (6.56 g, 4.0 mmol). The reaction mixture was stirred for 63 h at rt under $H_2$ atmosphere (1 atm.). The reaction mixture was filtered over Celite®, washed with methanol and concentrated *in vacuo*. Compound **S2b** (5.86 g, 36.3 mmol, 90%) was obtained without the need of purification as an off-white solid. **$R_f$** = 0.21 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 175 – 177 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 9.01 (bs, 1H, N*H*), 3.10 (s, 2H, C(O)C*H*), 2.72 (s, 2H, C(O)CHC*H*$CH_2$), 1.76 – 1.48 (m, 4H, C$H_2$CHC$H_2$C$H_2$), 1.46 – 1.25 (m, 2H, C$H_2$C$H_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 179.6 (C*), 50.3 (CH), 42.2 ($CH_2$), 39.3 (CH), 24.8 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3173 (w), 1695 (s), 1350 (m),

[2] Adapted procedure from: Frigerio, M.; Santagostino M.; Sputore, S. *J. Org. Chem.*, **1999**, *64*, 4537.

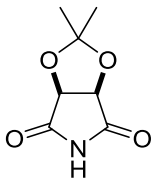
1177 (s), 995 (m), 822 (m), 588 (s), 459 (s). **HRMS** (ESI): *m/z* calulated for $C_9H_{11}NNaO_2$ $[M+Na]^+$:188.0682, found: 188.0689.



**imid S2c:** To a solution of maleimide (1.46 g, 15 mmol, 1.0 eq.) in $H_2O$ (1.07 M) was added furan (1.34 mL, 18 mmol, 1.2 eq.) dropwise. The reaction mixture was stirred for 1 h at 90 °C under microwave irradiation and then cooled to rt. The product was filtered off and washed with $H_2O$ (100 mL) and diethyl ether (20 mL). Compound **S2c** (1.38 g, 0.84 mmol, 54%) was obtained without the need of purification as an off-white solid. $\mathbf{R_f}$ = 0.23 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 168.6 - 171.3 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.15 (bs, 1H, N*H*), 6.52 (s, 2H, C*H*=C*H*), 5.32 (s, 2H, OC*H*), 2.89 (s, 2H, C(O)C*H*) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 176.1 (C*), 136.7 (CH), 81.1 (CH), 48.9 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3148 (w), 1772 (m), 1701 (s), 1352 (m), 1287 (m), 1204 (m), 1186 (s), 897 (m), 820 (s), 733 (s), 633 (s), 582 (s). **HRMS** (ESI): *m/z* calulated for $C_8H_7NNaO_3$ $[M+Na]^+$: 188.0318, found: 188.0320.



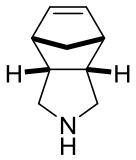
**imid S2d:** To a solution of palladium on carbon 10% (0.10 g, 0.04 mol%) in $CH_2Cl_2$ (0.1 mL) and methanol (100 mL) was added imid **S2c** (10.19 g, 62.0 mmol). The reaction mixture was stirred for 48 h at rt under $H_2$ atmosphere (1 atm.). The reaction mixture was filtered over Celite®, washed with methanol and concentrated *in vacuo*. Compound **S2d** (9.9 g, 59.0 mmol, 96%) was obtained without the need of purification as an off-white solid. $\mathbf{R_f}$ = 0.21 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 184 - 186 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.76 (bs, 1H, N*H*), 4.94 – 4.86 (m, 2H, OC*H*), 2.91 (s, 2H, NC(O)C*H*), 1.90 – 1.83 (m, 2H, C$H_2$C$H_2$), 1.62 – 1.54 (m, 2H, C$H_2$C$H_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 177.8 (C*), 79.2 (CH), 51.4 (CH), 28.6 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3004 (w), 1672 (s), 1306 (m), 1182 (s), 899 (m), 839 (m), 815 (s), 559 (m), 455 (s).



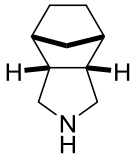
**imid S2f:**[3] To a solution of $Mn(ClO_4)_2$·6 $H_2O$ (15 mg, 0.3 mol%) in acetone (100 mL) was added picolic acid (44 mg, 1.8 mol%) and maleimide (1.94 g, 20.0 mmol, 1.0 eq.). The reaction mixture was cooled to 0 °C and an aq. sodiumacetate solution (1.0 mL, 0.6 M) and hydrogen peroxide (2.58 mL, 30.0 mmol, 1.5 eq.) were added. The solution was stirred for 29 h at rt, after which it was quenched with solid sodium thiosulfate. The suspension was filtered, washed with acetone, dried ($Na_2SO_4$) and concentrated *in vacuo*. The resulting oil was diluted in acetone (100 mL) and 2,2-dimethoxypropane (9.2 mL, 74.9 mmol, 4.0 eq.) and *p*-toluenesulfonic acid monohydrate (356 mg, 1.9 mmol, 0.1 eq.) were added. The solution was stirred 144 h at rt (until conversion was complete according to TLC). The reaction was quenched with sat. aq. $NaHCO_3$ (20 mL), extracted with $CH_2Cl_2$ (3 x 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. The crude product was purified by flash chromatography ($SiO_2$) with an eluent gradient (10:1 → 1:1 v/v *c*Hex:EtOAc) to obtain compound **S2f** (740 mg, 4.30 mmol, 22%) as a colourless oil. $\mathbf{R_f}$ = 0.31 (cHex:EtOAc 1:1 v/v). **mp**: 143.4 – 146.4 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.13 (bs, 1H, N*H*), 4.88 (s, 2H, C*H*), 1.51 (s, 3H, C$H_3$), 1.44 (s, 3H, C$H_3$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 172.2 (C*), 116.5 (C*), 76.1 (CH), 26.8

[3] First part of procedure adapted from P. Saisaha, D. Pijper, R. P. van Summeren, R. Hoen, C. Smit, J. W. de Boer, R. Hage, P. L. Alsters, B. L. Feringa, W. R. Browne, *Org. Biomol. Chem.* **2010**, *8*, 4444.

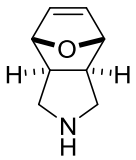
($CH_3$), 25.7 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3205 (m), 3094 (w), 1717 (s), 1375 (m), 1354 (m), 1192 (s), 1153 (m), 1097 (s), 987 (m), 849 (m), 756 (s), 712(m), 633 (w), 575 (s).



**pyrrolidine 1a:** To a solution of $LiAlH_4$ (3.5 g, 92.0 mmol, 1.5 eq.) in THF[4] (500 mL, anh.) was slowly added imid **S2a** (10.0 g, 61.0 mmol, 1.0 eq.) under $N_2$ atmosphere at 0 °C. The reaction mixture was stirred for 18 h at 45 °C, after which the reaction was quenched with $H_2O$ (5 mL) to remove the excess of $LiAlH_4$. The suspension was filtered over Celite®, washed with THF and concentrated *in vacuo* to give compound **1a** (3.0 g, 22.0 mmol, 36%) as a yellow solid. $\mathbf{R_f}$ = 0.09 ($CH_2Cl_2$:MeOH:$NEt_3$ 100:1:0.5 v/v). **mp**: 100.5 – 109.4 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 6.24 – 6.15 (m, 2H, C*H*=C*H*), 2.84 – 2.78 (m, 2H, NHC$H_2$CHC*H*C$H_2$), 2.76 – 2.64 (m, 3H, NHC*$H_2$*C*H*), 2.57 (d, *J* = 12.2 Hz, 2H, NHC*$H_2$*), 1.78 (bs, 1H, N*H*), 1.47 – 1.36 (m, 2H, CHC*$H_2$*CH) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 135.8 (CH), 53.1 ($CH_2$), 50.1 ($CH_2$), 48.2 (CH), 46.5 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3051 (w), 2957 (m), 2930 (s), 1344 (m), 1250 (m), 1092 (m), 895 (m), 870 (m), 800 (s), 743 (s), 689 (m). **HRMS** (ESI): *m/z* calculated for $C_9H_{14}N$ $[M+H]^+$: 136.1121, found: 136.1126.



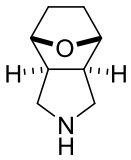
**pyrrolidine 1b:** To a solution of $LiAlH_4$ (2.0 g, 54.0 mmol, 1.5 eq.) in THF[4] (300 mL, anh.) was slowly added imid **S2b** (5.8 g, 36.0 mmol, 1.0 eq.) under $N_2$ atmosphere at 0 °C. The reaction mixture was stirred for 18 h at 70 °C, after which the reaction was quenched with $H_2O$ (4 mL) to remove the excess of $LiAlH_4$. The suspension was filtered over Celite®, washed with THF and concentrated *in vacuo* to give compound **1b** (3.6 g, 26.0 mmol, 72%) as a yellow solid. $\mathbf{R_f}$ = 0.66 ($CH_2Cl_2$:MeOH:$NEt_3$ 100:1:0.5 v/v). **mp**: 96.8 – 103.3 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 2.91 (d, *J* = 12.0 Hz, 2H, NHC*$H_2$*), 2.64 – 2.55 (m, 2H, NHC*$H_2$*), 2.41 – 2.35 (m, 2H, NHC$H_2$C*H*), 2.13 (s, 2H, NHC$H_2$CHC*H*C$H_2$), 1.88 (bs, 1H, N*H*), 1.54 – 1.26 (m, 6H, C*$H_2$*CHC*$H_2$*C*$H_2$*) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 48.3 ($CH_2$), 45.8 (CH), 43.0 ($CH_2$), 41.1 (CH), 23.3 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2937 (s), 2864 (m), 1290 (m), 1250 (m), 1221 (w), 1184 (w), 1111 (m), 1005 (m), 961 (w), 910 (m), 843 (s), 797 (m), 598 (s). **HRMS** (ESI): *m/z* calculated for $C_9H_{16}N$ $[M+H]^+$: 138.1277, found: 138.1291.



**pyrrolidine 1c:** To a solution of $LiAlH_4$ (1.7 g, 45.0 mmol, 1.5 eq.) in THF[5] (250 mL, anh.) was slowly added imid **S2c** (5.0 g, 30.0 mmol, 1.0 eq.) under $N_2$ atmosphere at 0 °C. The reaction mixture was stirred for 18 h at 40 °C, after which the reaction was quenched with $H_2O$ (4 mL) to remove the excess of $LiAlH_4$. The suspension was filtered over Celite®, washed with THF and concentrated *in vacuo* to give compound **1c** (3.1 g, 20.0 mmol, 65%) as a red oil. $\mathbf{R_f}$ = 0.07 ($CH_2Cl_2$:MeOH:$NEt_3$ 100:1:0.5 v/v). **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 6.36 (s, 2H, C*H*=C*H*), 4.70 (s, 2H, OC*H*), 2.92 – 2.83 (m, 4H, C*$H_2$*), 2.45 (bs, 1H, N*H*), 2.30 – 2.22 (m, 2H, $CH_2$C*H*) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 137.1 (CH), 83.9 (CH), 51.6 ($CH_2$), 46.8 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3258 (w), 2991 (w), 2926 (w), 1308 (w), 1067 (w), 949 (m), 891 (s),

[4] Distilled under nitrogen from sodium/benzophenone before use
[5] Distilled under nitrogen from sodium/benzophenone before use

964 (s), 843 (s), 810 (s), 712 (s), 692 (s), 590 (s). **HRMS** (ESI): *m/z* calculated for $C_8H_{12}NO$ $[M+H]^+$: 138.0913, found: 138.0920.



**pyrrolidine 1d:** To a solution of $LiAlH_4$ (3.4 g, 86.0 mmol, 1.5 eq.) in THF[5] (500 mL, anh.) was slowly added imid **S2d** (9.6 g, 58.0 mmol, 1.0 eq.) under $N_2$ atmosphere at 0 °C. The reaction mixture was stirred for 19 h at 45 °C, after which the reaction was quenched with $H_2O$ (5 mL) to remove the excess of $LiAlH_4$. The suspension was filtered over Celite®, washed with THF and concentrated *in vacuo* to give compound **1d** (6.0 g, 43.0 mmol, 75%) as a yellow oil. $\mathbf{R_f}$ = 0.07 ($CH_2Cl_2$:MeOH:$NEt_3$ 100:1:0.5 v/v). **$^1$H NMR** (400 MHz, $CDCl_3$): $\delta$ 4.30 – 4.23 (m, 2H, OC*H*), 2.92 (dd, *J* = 11.3 Hz, 6.4 Hz, 2H, NC*H*$_2$), 2.69 (dd, *J* = 11.3, 2.4 Hz, 2H, NC*H*$_2$), 2.40 (bs, 1H, N*H*), 2.24 – 2.20 (m, 2H, $NCH_2CH$), 1.64 – 1.56 (m, 2H, $CH_2CH_2$), 1.42 – 1.35 (m, 2H, $CH_2CH_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 81.3 (CH), 53.3 ($CH_2$), 49.9 (CH), 28.9 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3173 (m), 2945 (s), 2909 (m), 2853 (s), 1221 (m), 1182 (s), 1082 (s), 1024 (s), 1005 (s), 989 (s), 959 (s), 912 (s), 901 (s), 795 (s), 629 (s), 584 (s). **HRMS** (ESI): *m/z* calculated for $C_8H_{14}NO$ $[M+H]^+$:140.1070, found: 140.1069.

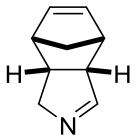
**pyrrolidine 1f:** To a solution of $LiAlH_4$ (230 mg, 6.1 mmol, 1.5 eq.) in THF[6] (35 mL, anh.) was slowly added imid **S2f** (700 mg, 4.1 mmol, 1.0 eq.) under $N_2$ atmosphere at 0 °C. The reaction mixture was stirred for 18 h at 55 °C, after which the reaction was quenched with $H_2O$ (2 mL) to remove the excess of $LiAlH_4$. The suspension was filtered over Celite®, washed with THF and concentrated *in vacuo* to give compound **1f** (444 mg, 3.1 mmol, 51%) as a colourless oil. $\mathbf{R_f}$ = 0.16 ($CH_2Cl_2$:MeOH:$NEt_3$ 100:1:0.5 v/v). **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 4.65 (s, 2H, $NHCH_2CH$), 3.11 (d, *J* = 14.0 Hz, 2H NHC*H*$_2$), 2.51 (d, *J* = 13.3 Hz, 2H, NHC*H*$_2$), 1.75 (bs, 1H, N*H*), 1.45 (s, 3H, C*H*$_3$), 1.31 (s, 3H, C*H*$_3$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 110.3 (C*), 81.7 (CH), 54.4 ($CH_2$), 26.1 ($CH_3$), 23.9 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2980 (m), 2928 (s), 1373 (m), 1207 (s), 1150 (m), 1080 (m), 1034 (s), 897 (m), 851 (s), 822 (m), 625 (m). **HRMS** (ESI): *m/z* calculated for $C_7H_{14}NO_2$ $[M+H]^+$: 144.1019, found: 144.1025.

[6] Distilled under nitrogen from sodium/benzophenone before use

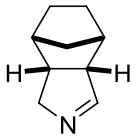
## *Oxidation of meso-pyrrolidines*

**General procedure 1:**

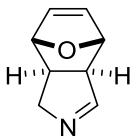
To a solution of the pyrrolidine (0.5 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.2 M) was added IBX (140 mg, 0.5 mmol, 1.0 eq.). The reaction mixture was stirred for 1 h at 60 °C (oil bath) in a closed vessel. The reaction was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (2 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 20 mL), extracted with $CH_2Cl_2$ (2 x 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. If necessary, the crude product was purified by flash chromatography.



**1-pyrroline 2a:** Prepared from pyrrolidine **1a** (69 mg, 0.50 mmol, 1 eq.) according to general procedure **1**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (1:1 → 1:2 v/v *c*Hex:EtOAc, 100:1 → 50:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **2a** (59 mg, 0.44 mmol, 88%) as a light yellow solid. $\mathbf{R_f}$ = 0.24 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 81.0 – 85.0 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.28 (s, 1H, N=C*H*), 6.11 – 5.94 (m, 2H, *H*C=C*H*), 3.72 – 3.62 (m, 1H, NC$H_2$), 3.55 – 3.41 (m, 1H, N=CHC*H*), 3.24 – 3.11 (m, 1H, NC$H_2$), 3.03 (s, 1H, N=CHCHC*H*CH$_2$), 2.92 (s, 1H, NCH$_2$CHC*H*CH$_2$), 2.83 – 2.73 (m, 1H, NCH$_2$C*H*), 1.52 (d, *J* = 8.1 Hz, 1H, CHC$H_2$CH), 1.36 (d, *J* = 8.2 Hz, 1H, CHC$H_2$CH) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 167.2 (CH), 135.5 (CH), 133.6 (CH), 62.9 ($CH_2$), 60.3 (CH), 51.1 ($CH_2$), 45.4 (CH), 44.2 (CH), 41.0 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2958 (m), 2918 (m), 2798 (m), 1339 (s), 1207 (m), 1182 (s), 1096 (m), 953 (m), 899 (m), 841 (m), 800 (m), 739 (s), 725 (s). **HRMS** (ESI): *m/z* calculated for $C_9H_{12}N$ $[M+H]^+$: 134.0964, found: 110.0966.

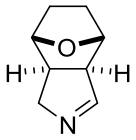


**1-pyrroline 2b:** Prepared from pyrrolidine **1b** (73 mg, 0.50 mmol, 1 eq.) according to general procedure **1**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (1:1 v/v *c*Hex:EtOAc, 100:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **2b** (65 mg, 0.48 mmol, 97%) as a light yellow solid. $\mathbf{R_f}$ = 0.24 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 81.0 – 88.1 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.41 (s, 1H, N=C*H*), 3.84 – 3.77 (m, 1H, NC$H_2$), 3.70 – 3.61 (m, 1H, NC$H_2$), 3.23 – 3.13 (m, 1H, N=CHC*H*), 2.64 – 2.53 (m, 1H, NCH$_2$C*H*), 2.50 (s, 1H, N=CHCHC*H*CH$_2$), 2.16 (s, 1H, NCH$_2$CHC*H*CH$_2$), 1.52 (d, *J* = 9.4 Hz, 1H, CHC$H_2$CH), 1.43 (d, *J* = 9.0 Hz, 1H, CHC$H_2$CH), 1.31 (d, *J* = 6.3 Hz, 2H, C$H_2$C$H_2$), 1.19 (d, *J* = 7.4 Hz, 2H, C$H_2$C$H_2$) ppm. **$^{13}$C-NMR** (126 MHz, $CDCl_3$): *δ* 169.2 (CH), 60.9 ($CH_2$), 58.3 (CH), 42.6 (CH), 42.1 ($CH_2$), 40.0 (CH), 38.5 (CH), 26.0 ($CH_2$), 22.1 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2945 (s), 2860 (m), 1670 (w), 1381 (w), 1298 (m), 1225 (m), 1177 (m), 1161 (m), 1119 (s), 1092 (s), 1018 (w), 995 (w), 889 (m), 822 (w), 656 (w). **HRMS** (ESI): *m/z* calculated for $C_9H_{14}N$ $[M+H]^+$: 136.1121, found: 136.1125.



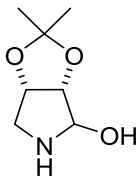
**1-pyrroline 2c:** Prepared from pyrrolidine **1c** (79 mg, 0.50 mmol, 1 eq.) according to general procedure **1**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (1:1 v/v cHex:EtOAc, 100:1 → 10:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **2c** (66 mg [3% *c*Hex], 0.47 mmol, 95%) as a reddish brown solid. $\mathbf{R_f}$ = 0.18 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 100.0 – 109.2 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.49 – 7.36 (m, 1H, N=C*H*), 6.46 – 6.29 (m, 2H, C*H*=C*H*), 4.95 (s, 1H, NCH$_2$CHC*H*O), 4.75 (s, 1H, N=CHCHC*H*O), 4.04 – 3.86 (m, 1H, NC$H_2$), 3.72 – 3.59 (m, 1H, NC$H_2$), 3.10 (dd, *J* = 7.1 Hz, *J* = 2.9 Hz, 1H, N=CHC*H*), 2.57 – 2.44 (m, 1H, NCH$_2$C*H*) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 164.1 (CH),

137.5 (CH), 136.2 (CH), 84.2 (CH), 79.7 (CH), 63.6 ($CH_2$), 59.7 (CH), 42.3 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2978 (m), 1458 (w), 1342 (m), 1229 (m), 1190 (m), 1157 (s), 1032 (s), 997 (m), 949 (s), 897 (s), 866 (m), 810 (s), 723 (s), 692 (s), 681 (s), 625 (s). **HRMS** (ESI): *m/z* calculated for $C_8H_{10}NO$ $[M+H]^+$: 136.0757, found: 136.0758.



**1-pyrroline 2d:** Prepared from pyrrolidine **1d** (72 mg, 0.50 mmol, 1 eq.) according to general procedure **1**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (1:1 cHex:EtOAc, 100:1 → 20:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **2d** (60 mg [17% $CH_2Cl_2$], 0.36 mmol, 71%) as a light yellow solid. $\mathbf{R_f}$ = 0.18 ($CH_2Cl_2$:MeOH 100:1 v/v).**mp**: 150.6 – 157.2 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.35 (d, *J* = 3.3 Hz, 1H, N=C*H*), 4.51 (d, *J* = 4.7 Hz, 1H, $NCH_2CHCHO$), 4.34 (d, *J* = 4.7 Hz, 1H, N=CHCHC*H*O), 4.10 – 4.00 (m, 1H, $NCH_2$), 3.74 – 3.65 (m, 1H, $NCH_2$), 3.03 (dd, *J* = 7.8 Hz, *J* = 2.9 Hz, 1H, N=CHC*H*), 2.42 – 2.34 (m, 1H, $NCH_2CH$), 1.79 – 1.64 (m, 2H, $CH_2CH_2$), 1.58 – 1.43 (m, 2H, $CH_2CH_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 165.1 (CH), 82.6 (CH), 77.4 (CH), 67.9 ($CH_2$), 61.1 (CH), 44.1 (CH), 29.3 ($CH_2$), 28.7 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2949 (m), 1655 (w), 1393 (m), 1315 (m), 1225 (s), 1215 (s), 1175 (s), 1047 (m), 972 (s), 924 (s), 805 (s), 623 (s). **HRMS** (ESI): *m/z* calculated for $C_8H_{12}NO$ $[M+H]^+$: 138.0913, found: 138.0916.

**1-pyrroline 2e:**[7] Prepared from pyrrolidine **1e** (56 mg, 0.50 mmol, 1 eq.) according to general procedure **1**. Compound **2e** (38 mg, 0.35 mmol, 70%) was obtained without the need of purification as a light yellow solid. $\mathbf{R_f}$ = 0.38 ($CH_2Cl_2$:MeOH 100:1 v/v). **mp**: 99.8 – 111.7 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.32 – 7.28 (m, 1H, NHC*H*), 4.11 – 3.98 (m, 1H, $NHCH_2$), 3.57 – 3.46 (m, 1H, $NHCH_2$), 3.27 (t, *J* = 8.9 Hz, 1H, NHCHC*H*), 2.72 – 2.57 (m, 1H, $NHCH_2CH$), 1.73 – 1.19 (m, 6H, $CH_2CH_2CH_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 169.6 (CH), 70.3 ($CH_2$), 55.2 (CH), 38.7 (CH), 34.8 ($CH_2$), 29.4 ($CH_2$), 25.0 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2931 (s), 2901 (m), 1466 (m), 1306 (m), 1204 (s), 1182 (s), 1157 (m), 1134 (s), 1070 (m), 932 (s),. **HRMS** (ESI): *m/z* calculated for $C_7H_{12}N$ $[M+H]^+$: 110.0964, found: 110.0973.



**α-hydroxypyrrolidine 2f**[8]**:** To a solution of pyrrolidine **1f** (0.25 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.2 M) was added IBX (70 mg, 0.25 mmol, 1.0 eq.). The reaction mixture was stirred for 1 h at 60 °C in an oil bath. The reaction was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (1 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 10 mL), extracted with $CH_2Cl_2$ (2 x 10 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Compound **2f** was obtained in 48% yield, as determined with $^1$H-NMR spectroscopy after dissolving the crude product in $CDCl_3$ and adding 2,5-dimethylfuran (0.125 mmol, 0.5 eq.) as standard for NMR spectroscopy. **$^1$H NMR** (500 MHz, $CDCl_3$) δ 4.72 – 4.66 (m, 1H, $NHCH_2CH$), 4.37 (dd, *J* = 7.1, 3.9 Hz, 1H, NHCHOC*H*), 3.33 (dd, *J* = 9.9, 6.1 Hz, 1H, $NHCH_2$), 3.26 (d, *J* = 4.1 Hz, 1H, NHC*H*O), 2.59 (dd, *J* = 9.8, 3.5 Hz, 1H, $NHCH_2$), 1.51 (s, 1H, $CH_3$), 1.32 (s, 1H, $CH_3$) ppm.**$^{13}$C NMR** (126 MHz, $CDCl_3$) δ 113.6 (C*), 85.4 (CH), 80.8 (CH), 77.4 (CH), 52.5 ($CH_2$), 27.0 ($CH_3$), 25.2 ($CH_3$).

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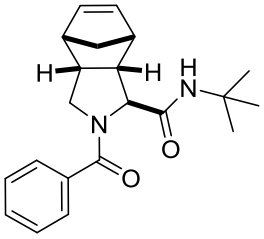
[7] Signals of the trimerized product are visible in the NMR spectrum.
[8] Full characterization was not possible due to instability of compound **2f** towards aqueous workup and silica gel chromatography. Proposed structure was determined with 2D-NMR spectroscopy.

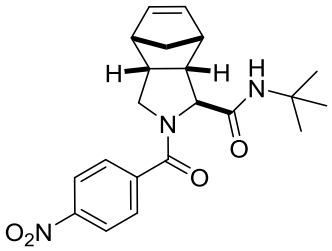
## *Oxidative Ugi-type three-component reaction*

**General procedure 2:**

To a solution of the pyrrolidine (0.5 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.5 M) were added IBX (140 mg, 0.5 mmol, 1.0 eq.), the carboxylic acid (0.75 mmol, 1.5 eq.) and the isocyanide (0.75 mmol, 1.5 eq.). The reaction mixture was stirred for 48 h at 60 °C (oil bath) in a closed vessel. The suspension was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (2 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 20 mL), extracted with $CH_2Cl_2$ (2 x 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. If necessary, the crude product was purified by flash chromatography or preparative thin layer chromatography. Note: Rotamers were observed in all NMR spectra.[9]



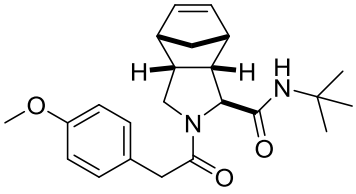
**prolyl peptide 3a:** Prepared from pyrrolidine **1a** (69 mg, 0.50 mmol, 1.0 eq.), benzoic acid (92 mg, 0.75 mmol, 1.5 eq.) and *t*-butyl isocyanide (87 µL, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (4:1 → 2:1 v/v *c*Hex:EtOAc), to obtain compound **3a** (99 mg, 0.29 mmol, 59%) as an off-white solid. $\mathbf{R_f}$ = 0.48 (*c*Hex:EtOAc 1:1 v/v). **mp**: 191.0 – 193.7 °C (decomposition).**$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 7.45 – 7.32 (m, 5H, *Ph*), 6.64 (s, 1H, N*H*), 6.20 (dd, *J* = 5.7 Hz, *J* = 3.0 Hz, 1 H, $NCH_2CHCHCH$=CH), 5.91 (dd, *J* = 5.7 Hz, *J* = 3.0 Hz, 1H, C(O)CHCHCHC*H*=CH), 4.43 (s, 1H, C(O)C*H*), 3.55 (dd, *J* = 11.7 Hz, *J* = 8.6 Hz, 1H, $NCH_2$), 3.45 – 3.38 (m, 1H, C(O)CHC*H*), 3.08 – 2.98 (m, 2H, $NCH_2CHCHCH_2CH$), 2.93 – 2.84 (m, 1H, $NCH_2CHCHCH_2$), 2.82 – 2.74 (m, 1H, $NCH_2CH$), 1.49 – 1.36 (m, 2H, $CHCH_2CH$), 1.32 (s, 9H $C(CH_3)_3$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 170.3 (C*), 169.7 (C*), 136.7 (C*), 134.9 (CH), 134.4 (CH), 130.1 (CH), 128.5 (CH), 126.6 (CH), 63.0 (CH), 52.1 ($CH_2$), 51.7 ($CH_2$), 47.1 (CH), 46.6 (CH), 45.6 (CH), 45.0 (CH), 28.8 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3300 (w), 2935 (w), 1670 (m), 1599 (s), 1566 (s), 1535 (s), 1410 (s), 1389 (m), 1317 (m), 1223 (m), 1205 (m), 731 (m), 716 (s), 621 (m). **HRMS** (ESI): *m/z* calculated for $C_{21}H_{27}N_2O_2$ $[M+H]^+$: 339.2067, found: 339.2056.



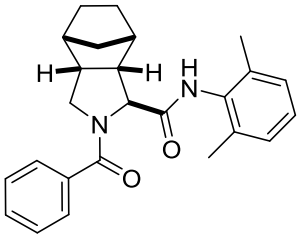
**prolyl peptide 3b:** Prepared from pyrrolidine **1a** (69 mg, 0.50 mmol, 1.0 eq.), 4-nitrobenzoic acid (125 mg, 0.75 mmol, 1.5 eq.) and *t*-butyl isocyanide (87 µL, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (4:1 → 2:1 v/v *c*Hex:EtOAc), to obtain compound **3b** (114 mg [12% $CH_2Cl_2$], 0.26 mmol, 52%) as an off-white solid. $\mathbf{R_f}$ = 0.40 (*c*Hex:EtOAc 1:1 v/v). **mp**: >150 °C decomposition. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.27 (d, *J* = 8.3 Hz, 2H, $C(NO_2)CH$), 7.59 – 7.51 (m, 2H, $C(NO_2)CHCH$), 6.40 (s, 1H, N*H*), 6.22 (dd, *J* = 5.7 Hz, *J* = 3.0 Hz, 1H, CH=C*H*), 5.93 (dd, *J* = 5.8 Hz, *J* = 3.0 Hz, 1H, C*H*=CH), 4.37 (d, *J* = 2.0 Hz, 1H, NC*H*), 3.60 (dd, *J* = 11.7 Hz, *J* = 8.9 Hz, 1H, $NCH_2$), 3.43 –3.31 (m, 1H, $NCH_2$), 3.04 (s, 1H, C*H*), 2.97 – 2.89 (m, 2H, C*H*), 2.81 (s, 1H, C*H*), 1.51 (d, *J* = 8.6 Hz, 1H, $CHCH_2CH$), 1.42 (d, *J* = 8.6 Hz, 1H, $CHCH_2CH$), 1.34 (s, 9H, $C(CH_3)_3$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 169.9 (C*), 167.4 (C*), 148.7 (C*), 142.6 (C*), 135.1 (CH), 134.5 (CH), 127.8 (CH), 124.0 (CH), 63.5 (CH), 52.2 ($CH_2$), 51.8 ($CH_2$), 51.4 (C*), 47.0 (CH), 46.7 (CH), 45.7 (CH), 28.9 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) =

[9] Two sets of resonances were observed in all $^1$H and $^{13}$C spectra, corresponding to different rotamers. Incomplete coalencence was observed at 100 °C, as depicted on S38.

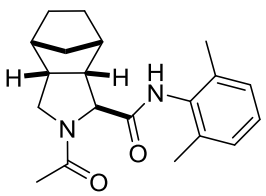
3308 (m), 2976 (m), 2932 (m), 1599 (m), 1520 (s), 1437 (m), 1340 (s), 1313 (m), 1227 (m), 1209 (m), 1016 (w), 854 (m), 831 (m), 602 (m). **HRMS** (ESI): *m/z* calculated for $C_{21}H_{26}N_3O_4$ $[M+H]^+$: 384.1918, found: 384.1908.



**prolyl peptide 3c:** Prepared from pyrrolidine **1a** (69 mg, 0.50 mmol, 1.0 eq.), 2-(4-methoxyphenyl)acetic acid (126 mg, 0.75 mmol, 1.5 eq.) and *t*-butyl isocyanide (87 µL, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (10:1 → 1:1 v/v *c*Hex:EtOAc), to obtain compound **3c** (103 mg, 0.28 mmol, 56%) as an off-white solid. $\mathbf{R_f}$ = 0.34 (*c*Hex:EtOAc 1:1 v/v). **mp**: 133.7 – 140.9 °C (decomposition). **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.12 (d, *J* = 9.0 Hz, 2H, C(OMe)CHC*H*), 6.84 (d, *J* = 8.0 Hz, 2H, C(OMe)C*H*), 6.10 – 6.03 (m, 1H, CH=C*H*), 5.74 – 5.63 (m, 1H, C*H*=CH), 4.14 (s, 1H, NC*H*), 3.78 (s, 3H, $H_3$CO), 3.52 – 3.45 (m, 2H, C*$CH_2$), 3.36 – 3.22 (m, 2H, NC$H_2$, C*H*), 3.24 – 3.15 (m, 1H, NC$H_2$), 2.94 (s, 1H, C*H*), 2.91 – 2.87 (m, 1H, C*H*), 2.83 (s, 1H, C*H*), 1.66 (s, 1H, N*H*), 1.39 – 1.34 (m, 1H, CHC$H_2$CH), 1.31 – 1.25 (m, 10H, C($CH_3$)$_3$, CHC$H_2$CH) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 170.5 (C*), 170.0 (C*), 158.7 (C*), 135.2 (CH), 134.5 (CH), 129.9 (CH), 126.3 (C*), 114.2 (CH), 63.2 (CH), 55.4 ($CH_3$), 51.7 ($CH_2$), 51.1 (C*), 50.0 ($CH_2$), 47.1 (CH), 46.6 (CH), 45.8 (CH), 45.2 (CH), 41.8 ($CH_2$), 28.8 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3283 (w), 2934 (w), 1647 (s), 1626 (s), 1516 (m), 1389 (w), 1290 (w), 1277 (w), 1250 (s), 1219 (m), 1024 (m), 856 (w), 820 (m), 735 (m). **HRMS** (ESI): *m/z* calculated for $C_{23}H_{31}N_2O_3$ $[M+H]^+$: 383.2329, found: 383.2331.

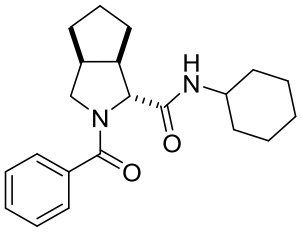


**prolyl peptide 3d:** Prepared from pyrrolidine **1b** (73 mg, 0.50 mmol, 1.0 eq.), benzoic acid (92 mg, 0.75 mmol, 1.5 eq.) and 1,3-dimethylbenzene isocyanide (98 mg, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:1 → 5:1 v/v *c*Hex:EtOAc), to obtain compound **3d** (118 mg, 0.30 mmol, 61%) as an off-white solid. $\mathbf{R_f}$ = 0.64 (*c*Hex:EtOAc 1:1 v/v). **mp**: 77.7 – 91.8 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 8.09 (bs, 1H, N*H*), 7.59 – 7.37 (m, 5H, *Ph*), 7.12 – 7.01 (m, 3H, C($CH_3$)C*HCHCH*), 5.22 (s, 1H, NC*H*), 3.62 (dd, *J* = 11.9 Hz, *J* = 8.4 Hz, 1H, NC*$H_2$*), 3.49 (d, *J* = 12.0 Hz, 1H, NC*$H_2$*), 3.30 – 3.17 (m, 1H, NCHC*H*), 2.78 – 2.66 (m, 1H, NC$H_2$C*H*), 2.42 (s, 1H, NCHCHC*H*C$H_2$CH), 2.33 – 2.14 (m, 7H, C*$H_3$*, C*$H_3$*, NC$H_2$CHC*H*C$H_2$), 1.72 – 1.19 (m, 6H, C*$H_2$*CHC*$H_2$*C*$H_2$*) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 169.57 (C*), 169.58 (C*), 136.1 (C*), 135.2 (C*), 133.9 (C*), 130.5 (CH), 128.6 (CH), 128.3 (CH), 127.3 (CH), 126.8 (CH), 60.6 (CH), 50.3 ($CH_2$), 44.4 (CH), 44.3 (CH), 42.0 ($CH_2$), 41.5 (CH), 41.0 (CH), 23.3 ($CH_2$), 22.9 ($CH_2$), 18.6 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3263 (br), 2953 (w), 1684 (s), 1609 (s), 1516 (s), 1447 (s), 1420 (s), 1398 (s), 1375 (s), 1296 (w), 1175 (m), 881 (m), 766 (s), 721 (s), 698 (s). **HRMS** (ESI): *m/z* calculated for $C_{25}H_{29}N_2O_2$ $[M+H]^+$: 389.2224, found: 389.2221.

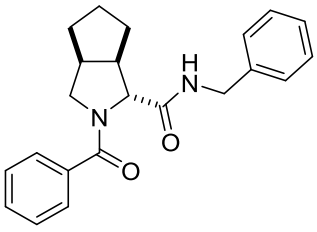


**prolyl peptide 3e:** Prepared from pyrrolidine **1b** (73 mg, 0.50 mmol, 1.0 eq.), acetic acid (43 µL, 0.75 mmol, 1.5 eq.) and 1,3-dimethylbenzene isocyanide (98 mg, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by preparative thin layer chromatography ($SiO_2$, *c*Hex:EtOAc 1:1 v/v), to obtain compound **3e** (70 mg, 0.22 mmol, 43%) as an off-white solid. Two-step procedure: To a solution of pyrrolidine **1b** (72 mg, 0.5 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.2 M) were added IBX (140 mg, 0.5 mmol,

1.0 eq.). The reaction mixture was stirred for 1 h at 60 °C (oil bath) in a closed vessel. The suspension was cooled to rt and acetic acid (43 µL, 0.75 mmol, 1.5 eq.) and 1,3-dimethylbenzene isocyanide (98 mg, 0.75 mmol, 1 eq.) were added, after which stirring was proceeded for 23 h at 60 °C (oil bath) in a closed vessel. The suspension was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (2 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 20 mL), extracted with $CH_2Cl_2$ (2 x 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification was achieved by preparative thin layer chromatography ($SiO_2$, *c*Hex:EtOAc 1:1 v/v), to obtain compound **3e** (88 mg, 0.27 mmol, 54%) as an off-white solid. $\mathbf{R_f}$ = 0.73 (*c*Hex:EtOAc 1:1 v/v). **mp**: 171.6 – 179.5 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.18 (bs, 1H, N*H*), 7.16 – 7.00 (m, 3H, *Ar*), 4.89 (s, 1H, NC*H*), 3.62 (d, *J* = 11.5 Hz, 1H, NC$H_2$), 3.47 (dd, *J* = 11.7 Hz, *J* = 8.3 Hz, 1H, NC$H_2$), 3.18 (dd, *J* = 10.9 Hz, *J* = 4.9 Hz, 1H, NCHC*H*), 2.81 – 2.68 (m, 1H, $NCH_2CH$), 2.44 – 2.34 (m, 1H, NCHCHC*H*$CH_2$), 2.34 – 2.30 (m, 1H, $NCH_2CHCHCH_2$), 2.18 (d, *J* = 5.1 Hz, 6H, C$H_3$), 1.60 – 1.58 (m, 1H, CHC$H_2$CH), 1.54 – 1.49 (m, 1H, CHC$H_2$CH), 1.45 – 1.39 (m, 2H, C$H_2$C$H_2$), 1.35 – 1.27 (m, 2H, C$H_2$C$H_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 169.8 (C*), 169.6 (C*), 135.2 (C*), 134.0 (C*), 128.2 (CH), 127.1 (CH), 77.4 (CH), 60.2 (CH), 48.4 ($CH_2$), 44.6 (CH), 43.8 (CH), 42.0 ($CH_2$), 41.5 (CH), 40.9 (CH), 23.3 ($CH_2$), 22.9 ($CH_2$), 22.6 ($CH_3$), 18.5 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3309 (w), 1647 (s), 1506 (m), 1471 (m), 1406 (s), 1375 (m), 1192 (m), 1034 (w), 847 (w), 773 (m), 640 (m). **HRMS** (ESI): *m/z* calculated for $C_{20}H_{26}N_2NaO_2$ $[M+Na]^+$: 349.1886, found: 349.1879.



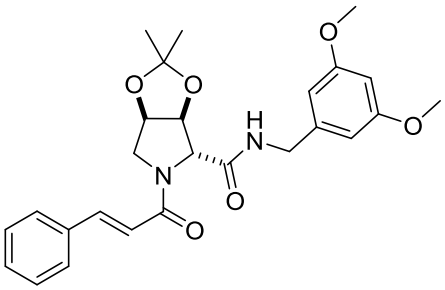
**prolyl peptide 3f:** Prepared from pyrrolidine **1e** (56 mg, 0.50 mmol, 1.0 eq.), benzoic acid (92 mg, 0.75 mmol, 1.5 eq.) and cyclohexyl isocyanide (95 µL, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:1 → 8:1 v/v *c*Hex:EtOAc), to obtain compound **3f** (96 mg, 0.27 mmol, 54%) as a yellow oil. $\mathbf{R_f}$ = 0.45 (*c*Hex:EtOAc 1:1 v/v). **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 7.52 – 7.32 (m, 5H, *Ph*), 6.73 (d, *J* = 8.3 Hz, 1H N*H*), 4.65 – 4.54 (m, 1H, C*H*C(O)), 3.85 – 3.67 (m, 2H, NC$H_2$, NCHC*H*), 3.29 (d, *J* = 11.3 Hz, 1H, NC$H_2$), 3.24 – 3.13 (m, 1H, $NCH_2CH$), 2.75 – 2.68 (m, 1H, C(O)NHC*H*), 2.02 – 1.51 (m, 10H, C$H_2$)[10], 1.42 – 1.03 (m, 6H, C$H_2$)[10] ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 170.6 (C*), 170.1 (C*), 136.3 (C*), 130.3 (CH), 128.6 (CH), 127.0 (CH), 66.6 (CH), 56.0 ($CH_2$), 48.3 (CH), 44.3 (CH), 43.4 (CH), 33.1 ($CH_2$), 32.8 ($CH_2$), 26.3 ($CH_2$), 25.6 ($CH_2$), 24.7 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3302 (br), 2928 (s), 1616 (s), 1541 (s), 1522 (m), 1418 (s), 1225 (w), 891 (w), 725 (m), 698 (s). **HRMS** (ESI): *m/z* calculated for $C_{21}H_{29}N_2O_2$ $[M+H]^+$: 341.2224, found: 341.2207.



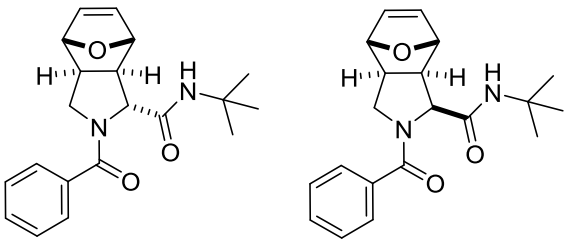
**prolyl peptide 3g:** Prepared from pyrrolidine **1e** (56 mg, 0.50 mmol, 1.0 eq.), benzoic acid (92 mg, 0.75 mmol, 1.5 eq.) and benzyl isocyanide (86 µL, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:1 → 2:1 v/v *c*Hex:EtOAc) and by preparative thin layer chromatography ($SiO_2$, *c*Hex:EtOAc 1:1 v/v), to obtain compound **3g** (72 mg, 0.21 mmol, 41%) as a yellow oil.

[10] Signals are overlapped with the signals of the rotamers.

**$R_f$** = 0.35 (*c*Hex:EtOAc 1:1 v/v). **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.46 – 7.09 (m, 10H, *Ph*)[11], 4.63 (s, 1H, C*H*C(O)), 4.47 – 4.31 (m, 2H, NHC*H*$_2$)[10], 3.67 (dd, *J* = 11.3Hz, *J* = 7.4 Hz, 1H, NC*H*$_2$), 3.26 (dd, *J* = 11.2 Hz, *J* = 2.8 Hz, 1H, NC*H*$_2$), 3.22 – 3.12 (m, 1H, NCHC*H*), 2.78 – 2.58 (m, 1H, NCH$_2$C*H*), 1.97 – 1.16 (m, 6H, C*H*$_2$C*H*$_2$C*H*$_2$)[10] ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 171.1 (C*), 170.7 (C*), 138.5 (C*), 136.1 (C*), 128.5 (CH), 128.4 (CH), 127.6 (CH), 127.4 (CH), 127.2 (CH), 127.1 (CH), 66.5 (CH), 56.0 ($CH_2$), 44.6 (CH), 43.6 ($CH_2$), 43.5 (CH), 33.1 ($CH_2$), 32.7 ($CH_2$), 31.1 ($CH_2$), 26.3 ($CH_2$), 25.7 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3290 (br), 2945 (w), 1616 (s), 1541 (m), 1497 (m), 1447 (m), 1418 (s), 1361 (w), 1228 (m), 721 (m), 696 (s), 677 (m), 663 (m). **HRMS** (ESI): *m/z* calculated for $C_{22}H_{25}N_2O_2$ $[M+H]^+$: 349.1911, found: 349.1895.



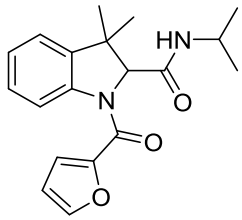
**prolyl peptide 3h:** Prepared from pyrrolidine **1f** (72 mg, 0.50 mmol, 1.0 eq.), cinnamic acid (109 mg, 0.75 mmol, 1.5 eq.) and 1-(isocyanomethyl)-3,5-dimethoxybenzyl (117 µL, 0.75 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (20:1 → 1:2 v/v *c*Hex:EtOAc) and by preparative thin layer chromatography ($SiO_2$, *c*Hex:EtOAc 1:1 v/v), to obtain compound **3h** (110 mg [3% $CH_2Cl_2$], 0.23 mmol, 45%) as a yellow solid. **$R_f$** = 0.34 (*c*Hex:EtOAc 1:1 v/v). **mp**: 52.1 – 61.5 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.71 (d, *J* = 15.4 Hz, 1H, C(O)C*H*=C*H*), 7.53 (dd, *J* = 6.5 Hz, *J* = 3.0 Hz, 2H, *Ph*), 7.43 – 7.35 (m, 3H, *Ph*), 7.12 (d, *J* = 8.0 Hz, 1H, CH$_2$C*C*H*), 6.72 (d, *J* = 15.5 Hz, 1H, C(O)C*H*=C*H*), 6.43 – 6.37 (m, 2H, CH$_2$C*C*HC(OMe)C*H*), 5.13 (d, *J* = 5.7 Hz, 1H, NC*H*), 4.95 – 4.89 (m, 2H, C*H*O), 4.41 – 4.33 (m, 1H, NHC*H*$_2$), 4.31 – 4.23 (m, 1H, NHC*H*$_2$), 4.00 (d, *J* = 11.9 Hz, 1H, NC*H*$_2$), 3.81 (s, 3H, OC*H*$_3$), 3.77 (s, 3H, OC*H*$_3$), 3.72 – 3.66 (m, 1H, NC*H*$_2$), 1.75 (bs, 1H, N*H*), 1.41 (s, 3H, C*C*H*$_3$), 1.32 (s, 3H, C*C*H*$_3$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): *δ* 168.7 (C*), 165.8 (C*), 160.6 (C*), 158.6 (C*), 143.7 (CH), 134.9 (C*), 130.2 (CH), 129.0 (CH), 128.1 (CH), 118.6 (C*), 117.2 (CH), 112.0 (C*), 103.9 (CH), 98.6 (CH), 80.6 (CH), 79.8 (CH), 65.7 (CH), 55.5 ($CH_3$), 53.2 ($CH_2$), 39.1 ($CH_2$), 26.9 ($CH_3$), 24.9 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3294 (br), 2935 (w), 1647 (s), 1610 (m), 1578 (w), 1508 (s), 1418 (s), 1373 (m), 1261 (m), 1205 (s), 1155 (s), (m), 1034 (m), 974 (m), 764 (m), 702 (m), 565 (w). **HRMS** (ESI): *m/z* calculated for $C_{26}H_{31}N_2O_6$ $[M+H]^+$: 467.2177, found: 467.2167.



**prolyl peptide 3i (major) and prolyl peptide 3i' (minor):** Prepared from pyrrolidine **1c** (40 mg [87% pure], 0.25 mmol, 1.0 eq.), benzoic acid (46 mg, 0.38 mmol, 1.5 eq.) and *t*-butyl isocyanide (44 µL, 0.38 mmol, 1.5 eq.) according to general procedure **2**. Purification was achieved by preparative thin layer chromatography ($SiO_2$, *c*Hex:EtOAc 1:3, v/v), to obtain the compound **3i** (32 mg, 0.09 mmol, 38%) as an off-white solid and the diastereoisomer **3i'** (16 mg, 0.05 mmol, 19%) as an off-white solid in a 2:1 diastereoisomeric ratio. **3i**: **$R_f$** = 0.14 (*c*Hex:EtOAc 1:1 v/v). **mp**: 176.8 – 185.3 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): *δ* 7.49 – 7.38 (m, 5H, *Ph*), 6.93 (s, 1H, N*H*), 6.42 (dd, *J* = 6.1 Hz, *J* = 1.9 Hz, 1H, NCH$_2$CHCHC*H*=CH), 6.35 (dd, *J* = 1.5 Hz, *J* = 1.5 Hz, 1H,

[11] Signals are overlapped with the signals of the rotamers and $CHCl_3$.

$NCH_2CHCHCH{=}CH$), 4.95 – 4.84 (m, 2H, $NCH_2CHCHO$, $NCH$), 4.65 (s, 1H, $NCHCHCHO$), 3.73 (dd, $J$ = 11.9 Hz, $J$ = 8.3 Hz, 1H, $NCH_2$), 3.52 (dd, $J$ = 12.0 Hz, $J$ = 1.9 Hz, 1H, $NCH_2$), 2.98 (d, $J$ = 7.1 Hz, 1H, $NCHCH$), 2.42 (t, $J$ = 7.8 Hz, 1H, $NCH_2CH$), 1.35 (s, 9H, $C(CH_3)_3$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 170.1 (C*), 169.8 (C*), 137.1 (CH), 136.6 (CH), 136.2 (CH), 130.3 (CH), 128.6 (CH), 127.0 (C*), 84.0 (CH), 83.7 (CH), 64.1 (CH), 52.9 ($CH_2$), 51.4 (C*), 44.7 (CH), 44.3 (CH), 28.8 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3292 (w), 2966 (w), 1676 (s), 1601 (s), 1570 (s), 1541 (s), 1447 (m), 1425 (s), 1356 (m), 1281 (w), 1259 (w), 1223 (m), 1030 (w), 941 (w), 903 (s), 868 (w), 847 (w), 719 (s), 692 (s), 665 (s), 619 (m). **HRMS** (ESI): *m/z* calculated for $C_{20}H_{25}N_2O_3$ $[M+H]^+$: 341.1860, found: 341.1849. **3i'**: **$R_f$** = 0.10 (*c*Hex:EtOAc 1:1 v/v). **mp**: 184.0 – 190.0 °C (decomposition). **$^1$H NMR** (500 MHz, DMSO-$d_6$): $\delta$ 7.59 – 7.19 (m, 5H, *Ph*), 6.50 – 6.31 (m, 2H, $HC{=}CH$), 4.86 (s, 1H, $CHO$), 4.78 – 4.59 (m, 2H, $NCH$, $CHO$), 3.53 (t, $J$ = 9.7 Hz, 1H), 3.40 – 3.30 (m, 1H, $NCH_2$),[12] 2.68 – 2.56 (m, 1H, $NHCH_2CH$), 2.54 – 2.40 (m, 1H, $NCHCH$),[13] 1.30 (s, 9H, $C(CH_3)_3$,) ppm.[14] **$^{13}$C NMR** (126 MHz, DMSO-$d_6$): $\delta$ 168.4 (C*), 168.0 (C*), 137.2 (CH), 137.1 (C*), 136.7 (CH), 130.3 (CH), 128.7 (CH), 127.6 (CH), 79.4 (CH, CH), 60.5 (CH), 53.0 ($CH_2$), 50.7 (C*), 47.2 (CH), 45.4 (CH), 29.1 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2974 (w), 1670 (s), 1624 (s), 1418 (s), 1313 (w), 1223 (m), 1142 (m), 986 (m), 951 (m), 906 (m), 822 (w), 661 (m). **HRMS** (ESI): *m/z* calculated for $C_{20}H_{25}N_2O_3$ $[M+H]^+$: 341.1860, found: 341.1850.



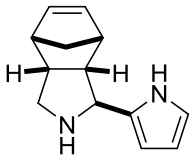

**prolyl peptide 3j:** To a solution of 3,3-dimethylindoline (37 mg, 0.25 mmol, 1.0 eq.) in DMSO (0.5 M) were added IBX (70 mg, 0.25 mmol, 1.0 eq.), furoic acid (43 mg, 0.38 mmol, 1.5 eq.) and *i*-propyl isocyanide (35 µL, 0.38 mmol, 1.5 eq.). The reaction mixture was stirred for 48 h at rt. The suspension was quenched with sat. aq. $Na_2S_2O_4$ (2 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 20 mL), extracted with $CH_2Cl_2$ (2 x 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:1 → 5:1 v/v *c*Hex:EtOAc) and by preparative thin layer chromatography ($SiO_2$, *c*Hex:EtOAc 1:1, v/v), to obtain compound **3j** (32 mg [13% $CH_2Cl_2$], 0.09 mmol, 35%) as a yellow solid. **$R_f$** = 0.32 (*c*Hex:EtOAc 1:1 v/v). **mp:** 63.2 – 73.8 °C. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 8.17 (d, $J$ = 8.2 Hz, 1H, $NC^*CH$), 7.59 – 7.55 (m, 1H, $OCHCHCH$), 7.31 – 7.27 (m, 2H, $OCHCHCH$, $NC^*CHCH$), 7.20 – 7.13 (m, 2H, $NC^*C^*CHCH$), 6.54 (dd, $J$ = 3.5 Hz, $J$ = 1.8 Hz, 1H, $OCHCH$), 5.43 – 5.35 (m, 1H, $NH$) 4.95 (s, 1H, $NCH$), 4.07 – 3.93 (m, 1H, $NHCH$), 1.43 (s, 3H, $C^*CH_3$), 1.40 (s, 3H, $C^*CH_3$), 0.94 (dd, $J$ = 13.5 Hz, $J$ = 6.5 Hz, 6H, $CH(CH_3)_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 168.6 (C*), 158.1 (C*), 147.5 (C*), 145.3 (CH), 141.1 (C*), 139.9 (C*), 128.3 (CH), 125.5 (CH), 122.5 (CH), 118.4 (CH), 118.0 (CH), 112.2 (CH), 75.0 (CH), 45.0 (C*), 41.4 (CH), 32.7 ($CH_3$), 29.8 (C*), 22.9 ($CH_3$), 22.6 ($CH_3$), 22.4 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3285 (br), 2966 (w), 1653 (s), 1558 (m), 1477 (s), 1456 (s), 1394 (s), 1366 (s), 1283 (m), 1171 (w), 885 (w), 750 (s), 594 (w). **HRMS** (ESI): *m/z* calculated for $C_{19}H_{23}N_2O_3$ $[M+H]^+$: 327.1703, found: 327.1707.

[12] Signal overlaps with $H_2O$ peak. The $H_2O$ was an impurity in the solvent MeOD-$d_4$.
[13] Signal overlaps with residual solvent peak of MeOD-$d_4$.
[14] Signals are overlapped with the signals of the rotamers.

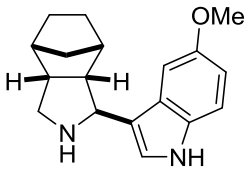
## *Oxidative aza-Friedel-Crafts reaction*

**General procedure 3:**

To a solution of the pyrrolidine (0.25 mmol, 1.0 eq.) in $CH_2Cl_2$ (0.25 M) were added IBX (70 mg, 0.25 mmol, 1.0 eq.). The reaction mixture was stirred for 1 h at 60 °C (oil bath) in a closed vessel. The suspension was cooled to rt and trifluoroacetic acid (38 µL, 0.5 mmol, 2.0 eq.) and the pyrrole or indole (0.5 mmol, 2.0 eq.) were added. The reaction mixture was stirred for 1 h at 60 °C (oil bath) in a closed vessel. The suspension was cooled to rt, quenched with sat. aq. $Na_2S_2O_4$ (2 mL), washed with sat. aq. $Na_2CO_3$/brine (3:1, 20 mL), extracted with $CH_2Cl_2$ (2 x 20 mL), dried ($Na_2SO_4$) and concentrated *in vacuo*. If necessary, the crude product was purified by flash chromatography.



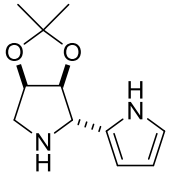
**pyrrolyl pyrrolidine 4a:** Prepared from pyrrolidine **1a** (33 mg, 0.25 mmol, 1.0 eq.) and pyrrole (35 µL, 0.50 mmol, 2.0 eq.) according to general procedure **3**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:0 → 20:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **4a** (24 mg, 0.12 mmol, 48%) as a grey solid. $\mathbf{R_f}$ = 0.32 ($CH_2Cl_2$:MeOH 20:1 v/v). **mp**: > 86.3 °C decomposition. **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 9.04 (bs, 1H, C*N*H*), 6.72 – 6.64 (m, 1H,C*NHC*H*), 6.32 – 6.21 (m, 2H, *H*C=C*H*), 6.20 – 6.14 (m, 1H, C*NHCHC*H*), 6.05 – 5.95 (m, 1H, C*NHCHCHC*H*), 3.82 (d, *J* = 4.5 Hz, 1H, C*C*H*NH), 3.06 (dt, *J* = 9.0 Hz, *J* = 4.4 Hz, 1H, NHCHC*H*), 3.00 – 2.95 (m, 1H, $CHCH_2CH$), 2.93 – 2.78 (m, 3H, $CHCH_2CH$, $NHCH_2CH$), 2.50 (dd, *J* = 11.8 Hz, *J* = 4.6 Hz, 1H, $NHCH_2$), 2.29 – 2.06 (bs, 1H, $CH_2NH$), 1.60 (dt, *J* = 8.2 Hz, *J* = 1.8 Hz, 1H, $CHCH_2CH$), 1.52 (dt, *J* = 8.2 Hz, *J* = 1.5 Hz, 1H, $CHCH_2CH$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 155.5 (C*), 136.5 (CH), 116.7 (CH), 108.5 (CH), 104.4 (CH), 58.7 (CH), 54.7 (CH), 53.6 ($CH_2$), 49.0 ($CH_2$), 48.7 (CH), 46.0 (CH), 45.8 (CH) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3072 (w), 2934 (m), 2862 (m), 1448 (w), 1414 (w), 1028 (w), 918 (m), 879 (m), 833 (m), 725 (s), 563 (w). **HRMS** (ESI): *m/z* calculated for $C_{13}H_{17}N_2$ $[M+H]^+$: 201.1386, found: 201.1394.



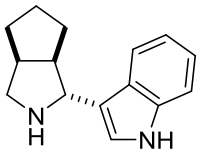
**pyrrolyl pyrrolidine 4b:** Prepared from pyrrolidine **1b** (38 mg, 0.26 mmol, 1.0 eq.) and 5-methoxy-1*H*-indole (77 µL, 0.52 mmol, 2.0 eq.) according to general procedure **3**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:0 → 20:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **4b** (44 mg, 0.16 mmol, 60%) as a dark yellow oil. $\mathbf{R_f}$ = 0.66 ($CH_2Cl_2$:MeOH 50:1 v/v). **$^1$H NMR** (500 MHz, $CDCl_3$): $\delta$ 7.94 (bs, 1H, C*N*H*), 7.23 (d, *J* = 8.7 Hz, 1H, NHC*C*H*), 7.09 (s, 1H, C*C*HC*(OMe)), 6.98 (s, 1H, C*NHC*HC*), 6.85 (d, *J* = 9.0 Hz, 1H, C(OMe)C*H*), 4.45 (s, 1H, $CH_2NHCH$), 3.86 (s, 3H, $OCH_3$), 3.03 – 2.91 (m, 2H, $NHCH_2$), 2.78 – 2.54 (m, 2H, $NHCH_2CH$, NHCHC*H*), 2.46 – 2.36 (m, 1H, $NHCH_2CHCHCH_2CH$), 2.27 – 2.19 (m, 1H, $NHCH_2CHCHCH_2$), 2.01 (bs, 1H, $CH_2NH$), 1.80 (t, *J* = 9.4 Hz, 1H, $CH_2$), 1.71 – 1.36 (m, 5H, $CH_2CHCH_2CH_2$) ppm. **$^{13}$C NMR** (126 MHz, $CDCl_3$): $\delta$ 154.0 (C*), 131.9 (C*), 126.8 (C*), 121.4 (CH), 119.9 (C*),[15] 112.3 (CH), 112.0 (CH), 101.0 (CH), 56.1 (CH), 55.0 ($CH_3$), 52.0 (CH), 46.4 ($CH_2$), 45.9 (CH), 43.4 ($CH_2$), 40.9 (CH), 40.8 (CH), 23.6 ($CH_2$), 23.1 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2941 (w), 1481 (m), 1437 (m), 1290 (w),

[15] Very weak signal assigned with HMBC.

1209 (s), 1171 (m), 1101 (w), 1051 (w), 1028 (m), 924 (m), 795 (m), 733 (m), 640 (m), 606 (m). **HRMS** (ESI): *m/z* calculated for $C_{18}H_{23}N_2O$ $[M+H]^+$: 283.1805, found: 283.1801.

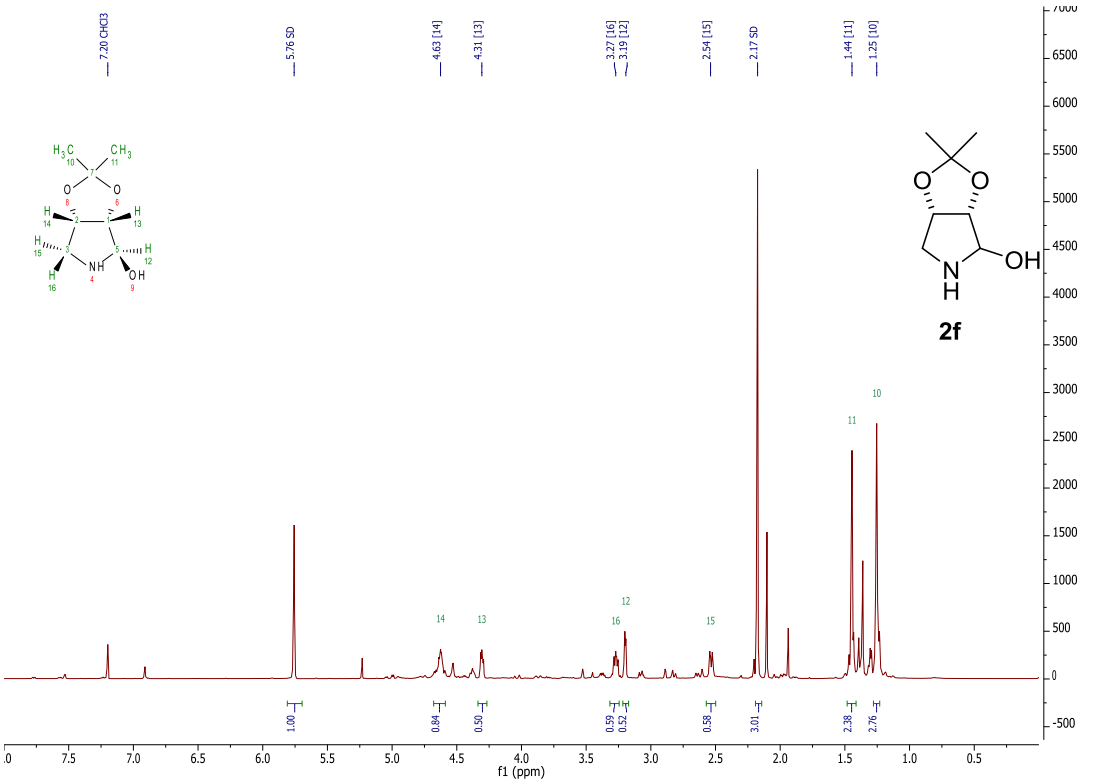


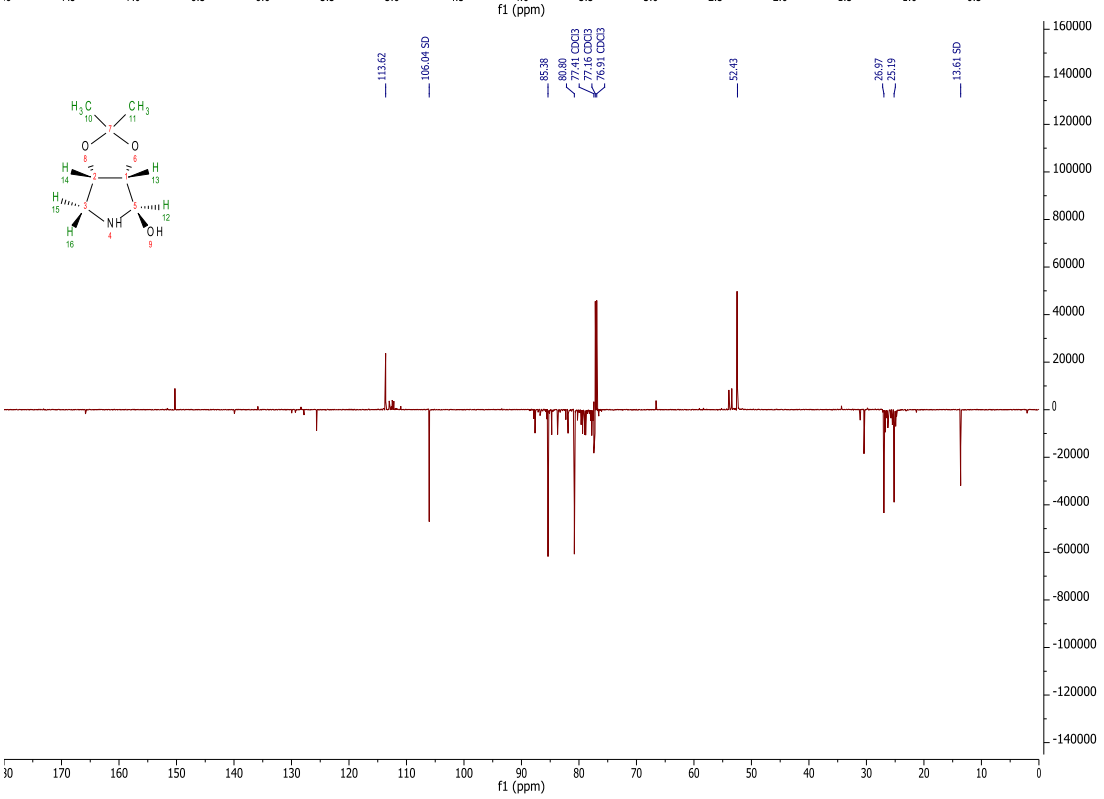
**pyrrolyl pyrrolidine 4c:** Prepared from pyrrolidine **1f** (36 mg, 0.25 mmol, 1.0 eq.) and pyrrole (35 µL, 0.50 mmol, 2.0 eq.) according to general procedure **3**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:0 → 20:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **4c** (27 mg, 0.13 mmol, 52%, *dr* > 13:1) as a brown solid. $\mathbf{R_f}$ = 0.92 ($CH_2Cl_2$:MeOH 50:1 v/v). **mp**: 112.0 – 124.2 °C. $^{1}$**H NMR** (500 MHz, $CDCl_3$): *δ* 8.80 (bs, 1H, N*H*C*), 6.77 – 6.65 (m, *J* = 3.1 Hz, *J* = 1.7 Hz, 1H, C*NHC*H*), 6.16 (q, *J* = 2.9 Hz, 1H, C*NHCHC*H*), 6.05 – 6.00 (m, 1H, C*NHCHCHC*H*), 4.95 (d, *J* = 5.4 Hz, 1H, NHCHC*H*), 4.67 (dd, *J* = 5.4 Hz, *J* = 3.7 Hz, 1H, NHCH$_2$C*H*), 4.34 (s, 1H, NHC*H*C*), 3.03 (d, *J* = 13.6, 1H, NHC*H*$_2$), 2.63 (dd, *J* = 13.6, 3.9 Hz, 1H, NHC*H*$_2$), 2.47 (bs, 1H, CH$_2$N*H*), 1.50 (s, 3H, C*C*H*$_3$), 1.36 (s, 3H, C*C*H*$_3$) ppm. $^{13}$**C NMR** (126 MHz, $CDCl_3$): *δ* 129.3 (C*), 116.7 (CH), 110.6 (C*), 108.8 (CH), 105.1 (CH), 86.0 (CH), 82.3 (CH), 62.5 (CH), 52.6 ($CH_2$), 26.1 ($CH_3$), 23.9 ($CH_3$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 3265 (w), 1381 (w), 1367 (w), 1204 (m), 1090 (m), 1045 (m), 1030 (s), 947 (w), 891 (m), 881 (m), 866 (m), 851 (m), 710 (s), 604 (s). **HRMS** (ESI): *m/z* calculated for $C_{18}H_{23}N_2O$ $[M+H]^+$: 209.1285, found: 209.1279.



**pyrrolyl pyrrolidine 4d:** Prepared from pyrrolidine **1e** (29 mg, 0.25 mmol, 1.0 eq.) and indole (60 mg, 0.50 mmol, 2.0 eq.) according to general procedure **3**. Purification was achieved by flash chromatography ($SiO_2$) with an eluent gradient (100:0 – 20:1 v/v $CH_2Cl_2$:MeOH), to obtain compound **4d** (43 mg, 0.19 mmol, 75%) as a brown solid. $\mathbf{R_f}$ = 0.10 ($CH_2Cl_2$:MeOH 20:1 v/v). **mp**: > 69.8 °C decomposition.$^{1}$**H NMR** (500 MHz, $CDCl_3$) δ 8.22 (bs, 1H, N*H*C*), 7.74 (d, *J* = 7.9 Hz, 1H, NHC*C*C*H*), 7.35 (d, *J* = 8.0 Hz, 1H, NHC*C*H*), 7.23 – 7.06 (m, 3H, C*H*NHC*CHC*H*C*H*), 3.92 (d, *J* = 7.1 Hz, 1H, NHC*H*CH), 3.40 (dd, *J* = 10.7, 8.0 Hz, 1H, NHC*H*$_2$), 2.89 – 2.73 (m, 2H, NHCH$_2$C*H*C*H*), 2.55 (dd, *J* = 10.7, 7.1 Hz, 1H, NHC*H*$_2$), 2.40 (bs, 1H, N*H*CH$_2$), 1.74 – 1.43 (m, 6H, C*H*$_2$C*H*$_2$C*H*$_2$) ppm. $^{13}$**C NMR** (126 MHz, $CDCl_3$) δ 136.7 (C*), 126.6 (C*), 122.2 (CH), 122.0 (CH), 119.6 (CH), 119.6 (CH), 117.1 (C*), 111.5 (CH), 63.1 (CH), 53.7 ($CH_2$), 50.8 (CH), 44.3 (CH), 32.1 ($CH_2$), 31.4 ($CH_2$), 25.5 ($CH_2$) ppm. **IR** (neat): $\nu_{max}$ ($cm^{-1}$) = 2930 (w), 2860 (w), 1456 (w), 1448 (w), 1339 (w), 735 (s), 608 (m), 426 (m). **HRMS** (ESI): *m/z* calculated for $C_{15}H_{19}N_2$ $[M+H]^+$: 227.1543, found: 227.1542.

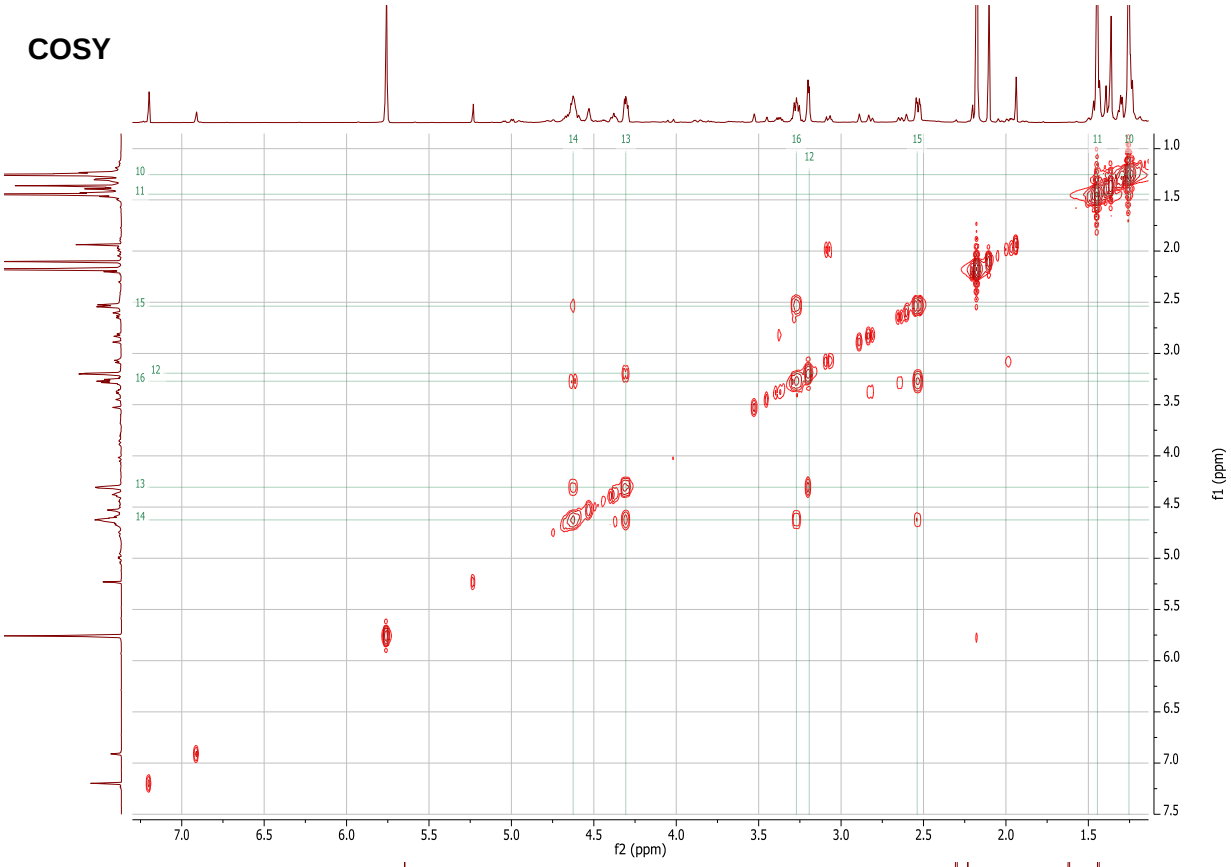
# Structural analysis of compound 2f[16]



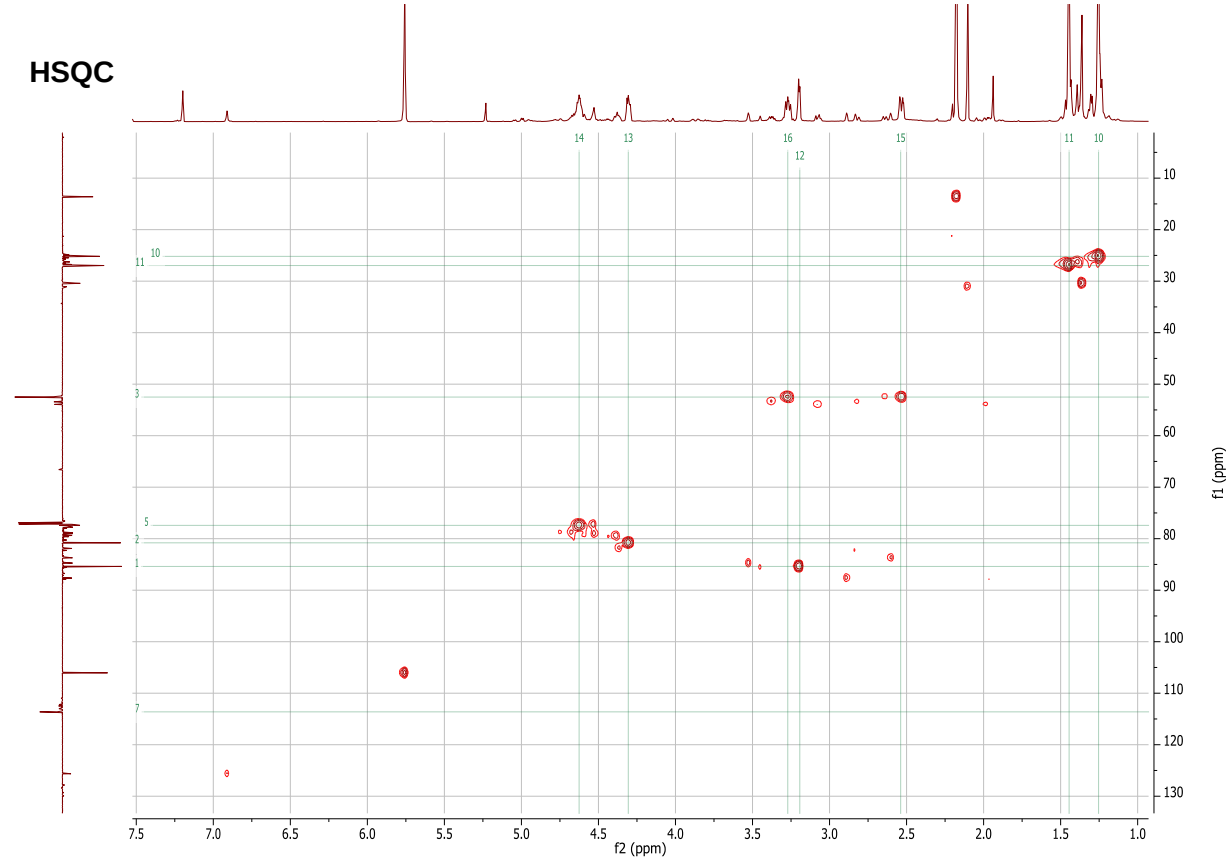




[16] Relative stereochemistry at the hemiaminal stereocenter undetermined

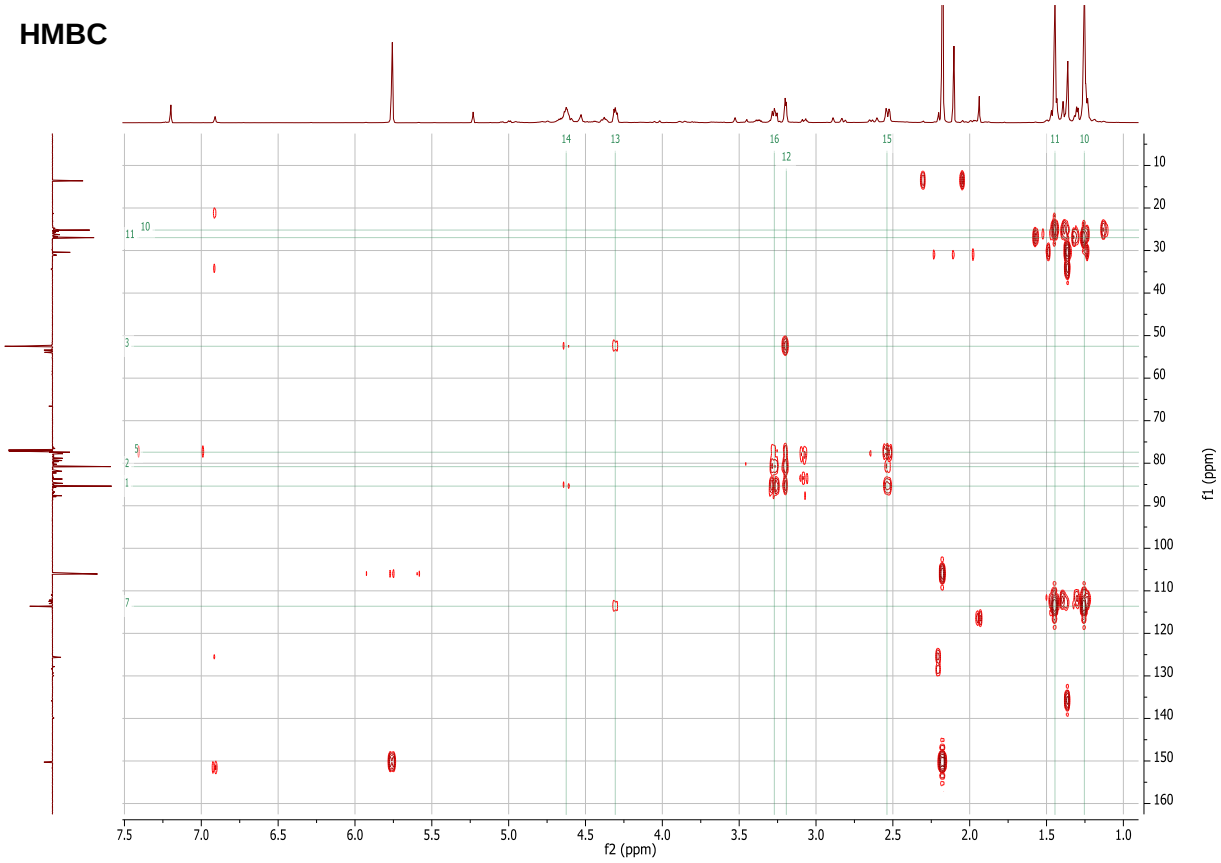
**COSY**




**HSQC**



**HMBC**


14
13
16
12
15
11
10
11
10
3
5
2
1
7
10
20
30
40
50
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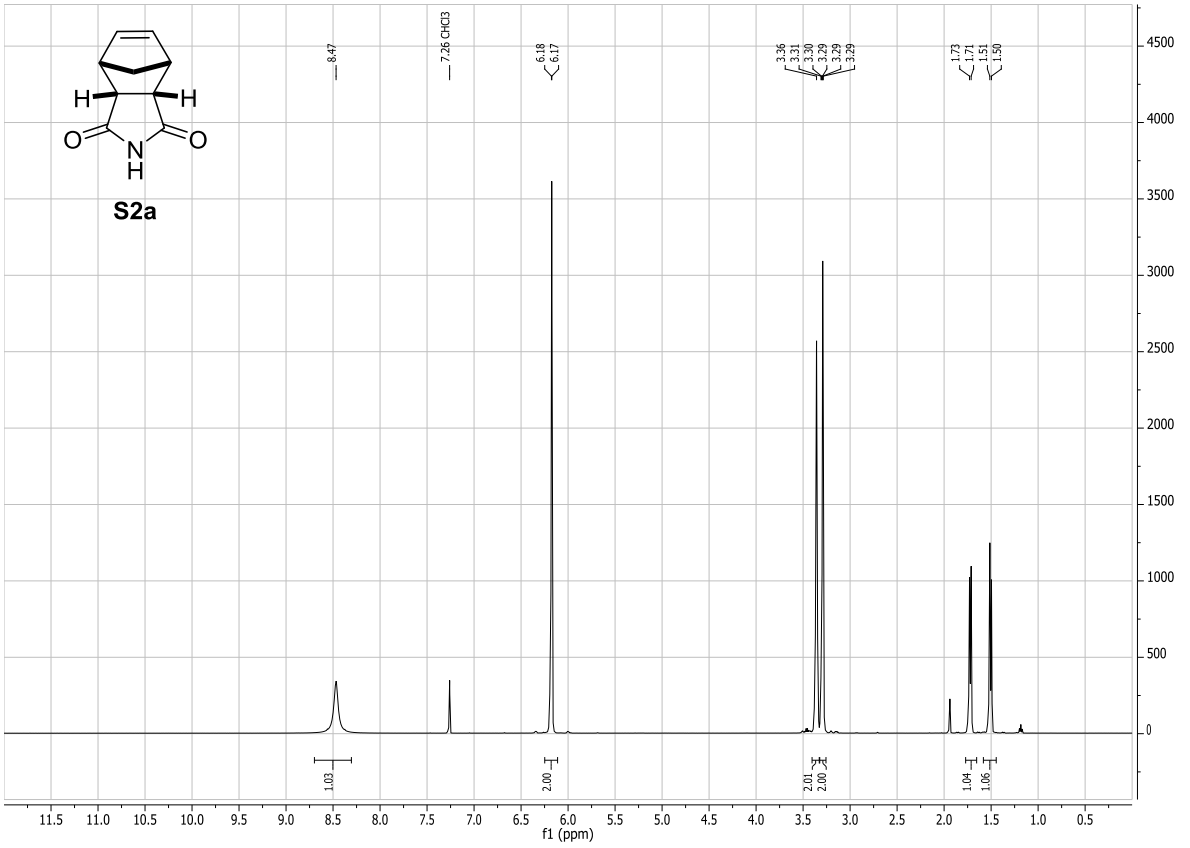
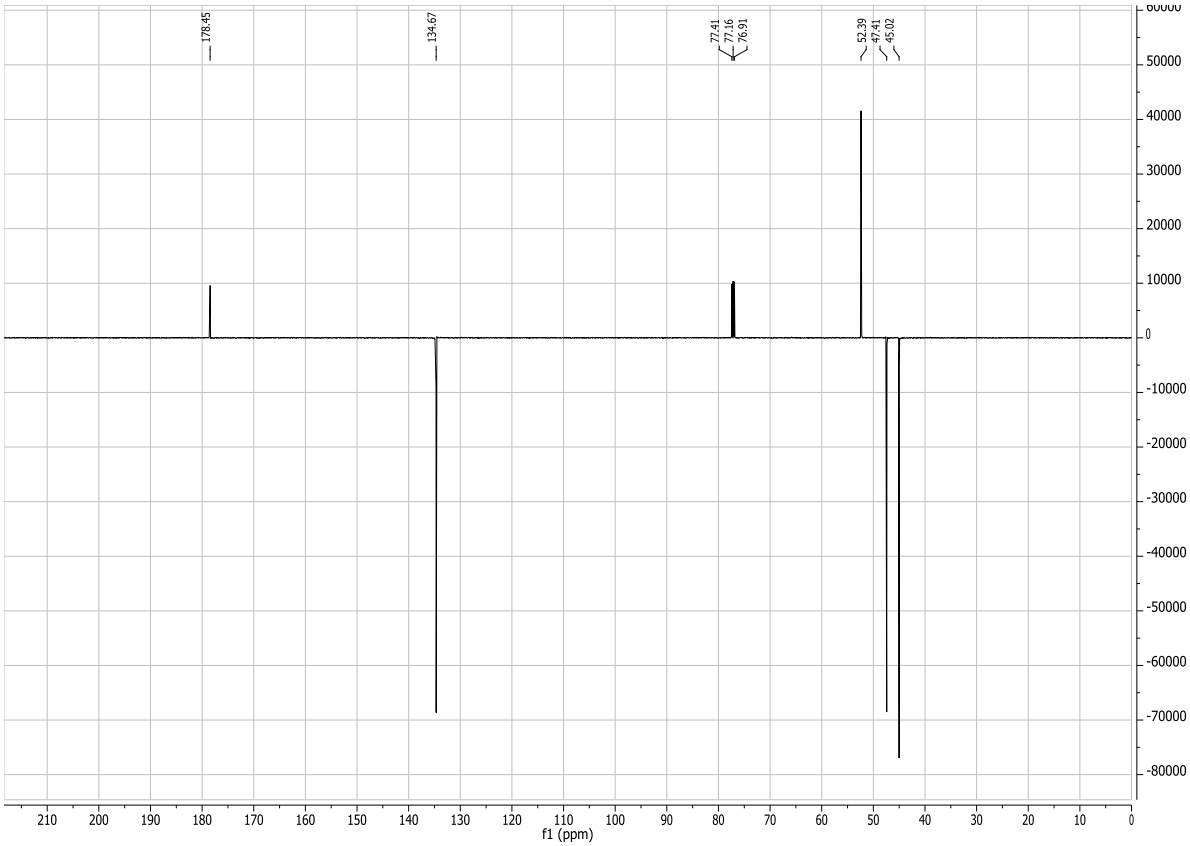
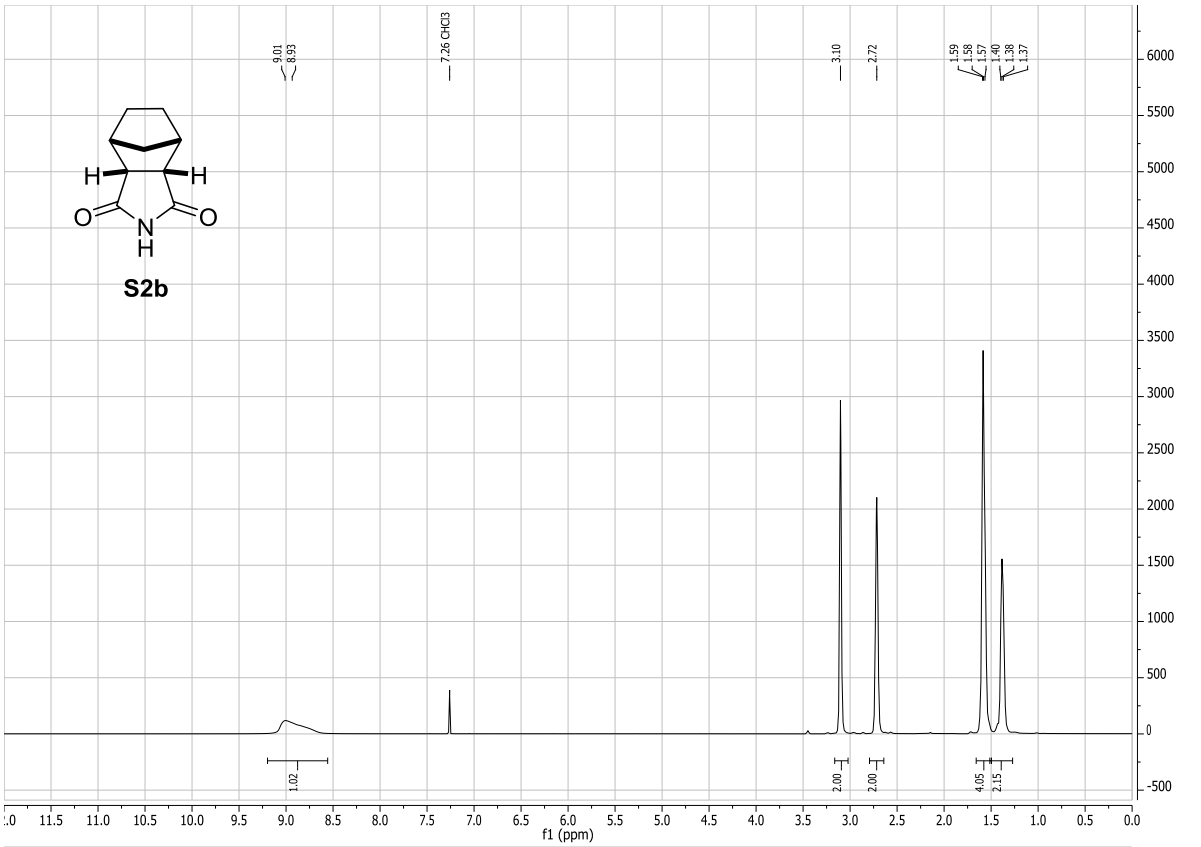
80
90
100
110
120
130
140
150
160
f1 (ppm)
7.5
7.0
6.5
6.0
5.5
5.0
4.5
4.0
3.5
3.0
2.5
2.0
1.5
1.0
f2 (ppm)

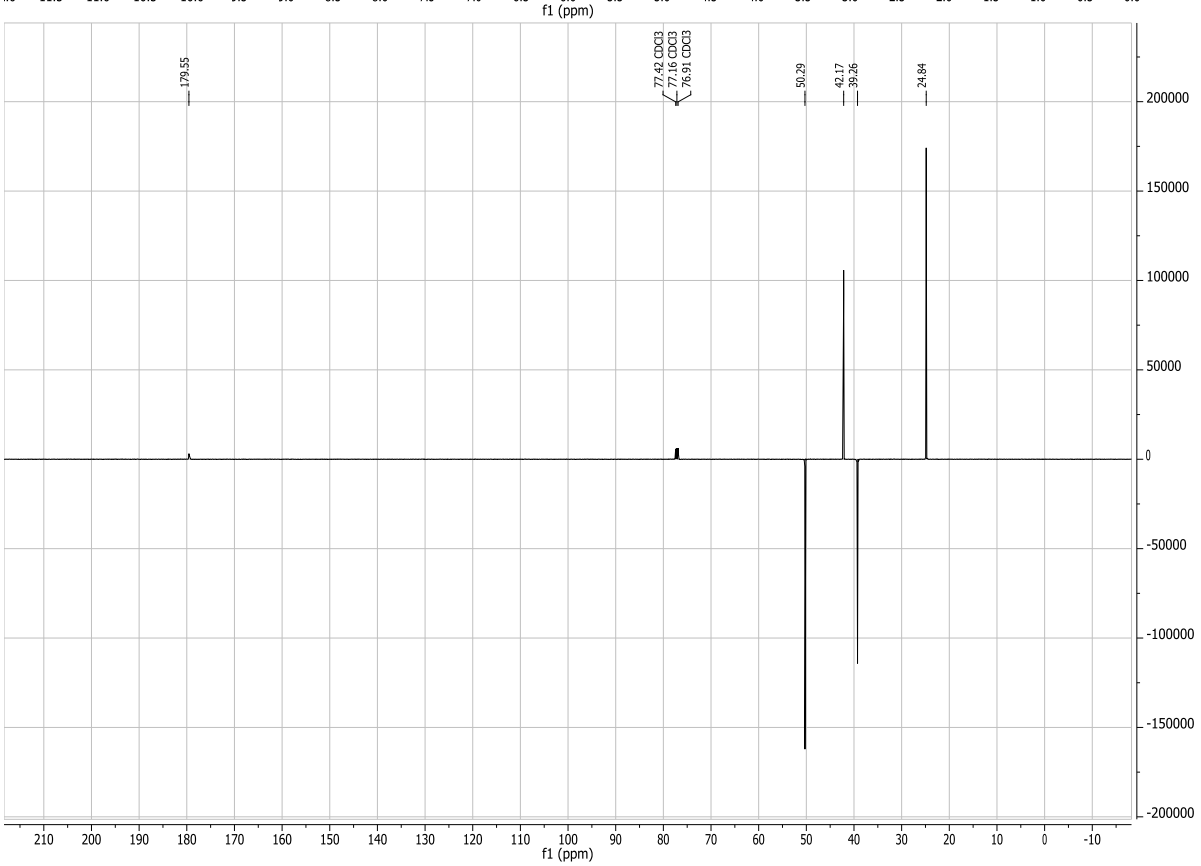
## Copies of NMRs

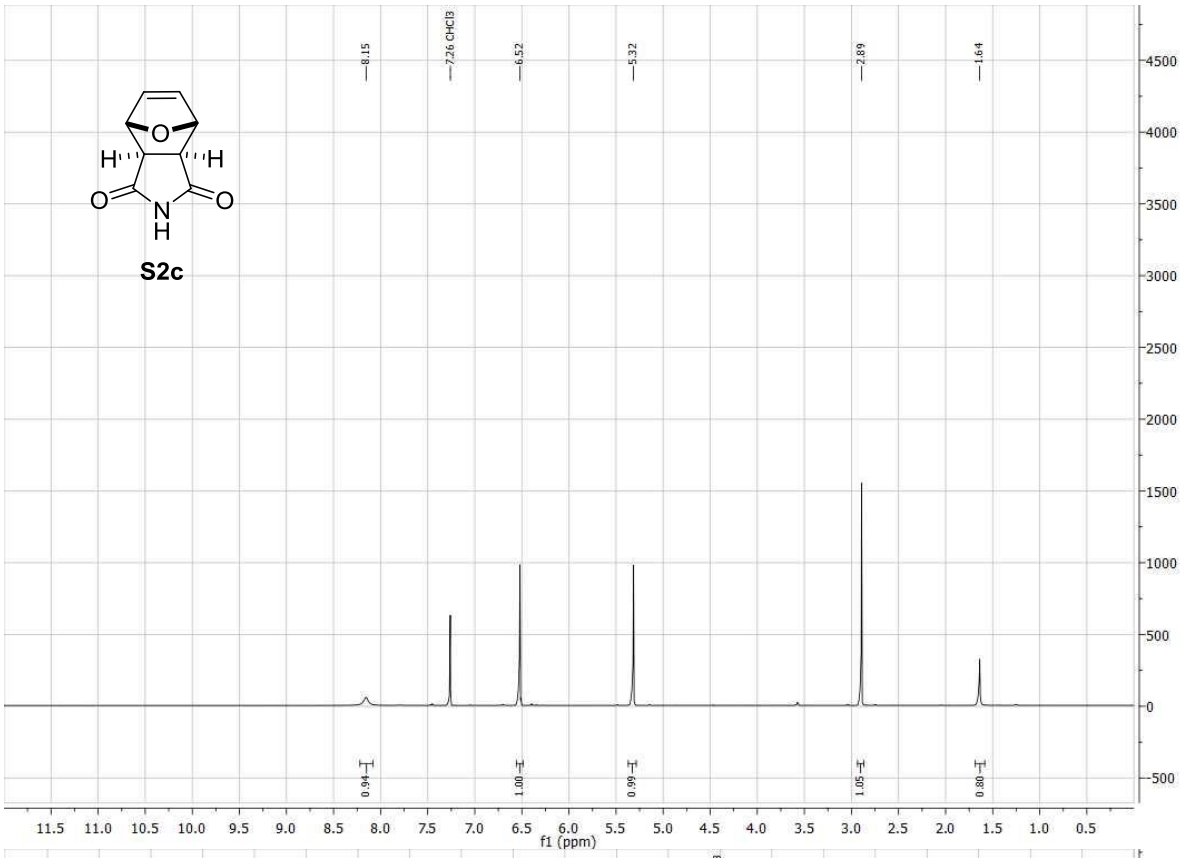


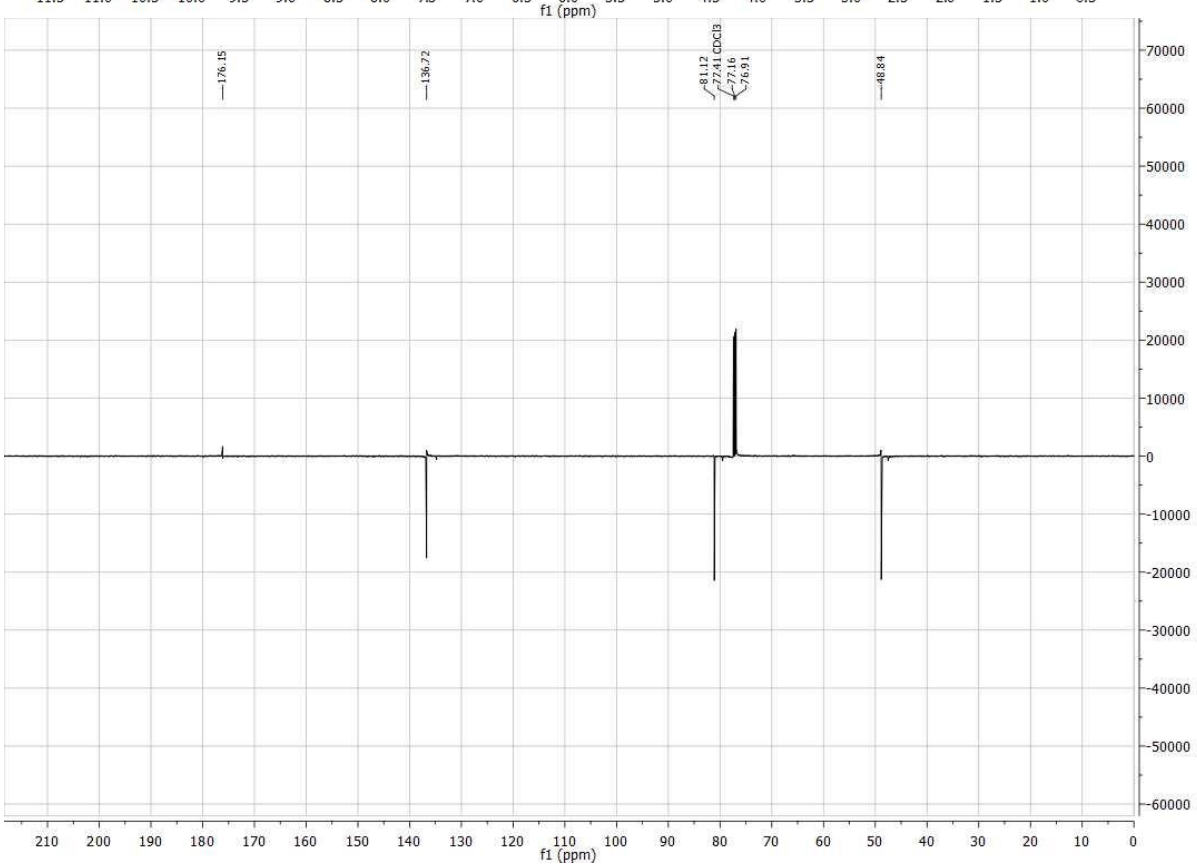

9.01
8.93
7.26 CHCl3
3.10
2.72
1.59
1.58
1.57
1.40
1.38
1.37
1.02
2.00
2.00
4.05
2.15
f1 (ppm)

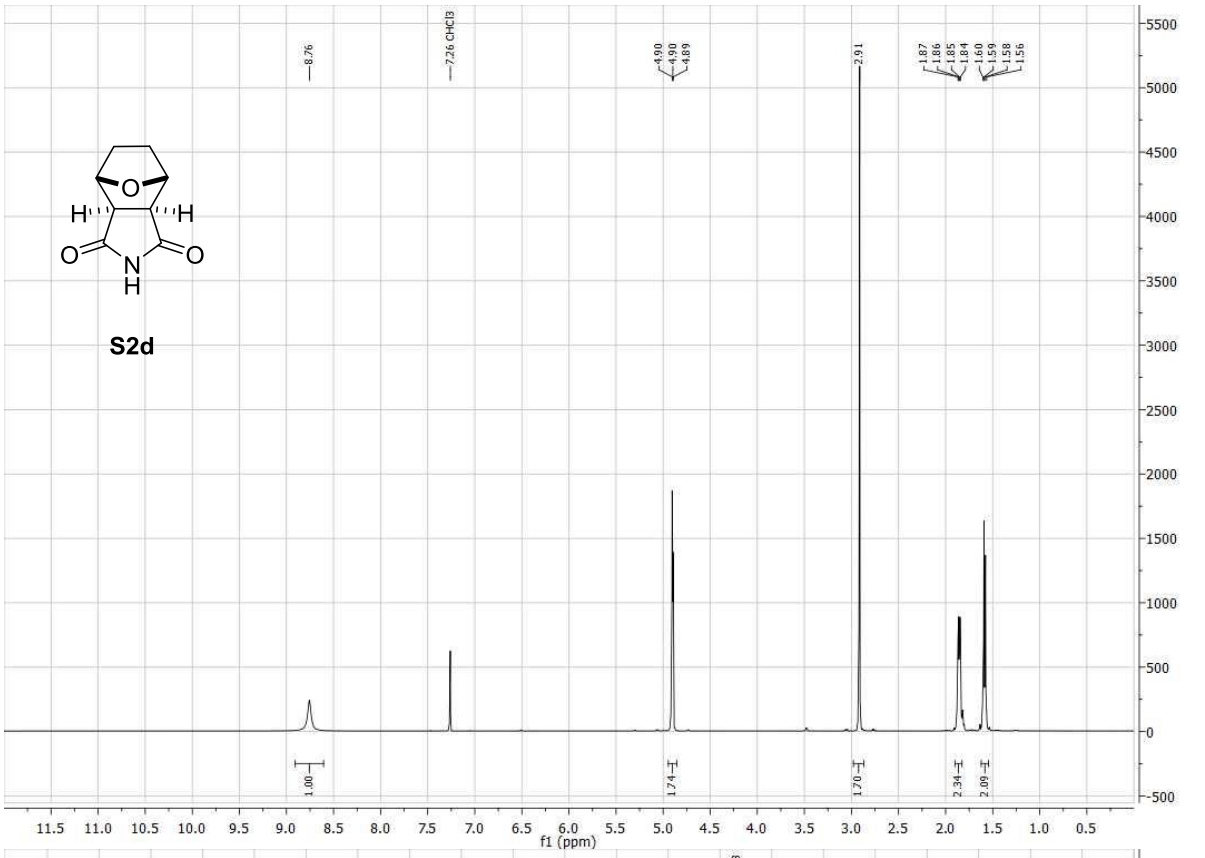
**S2b**


179.55
77.42 CDCl3
77.16 CDCl3
76.91 CDCl3
50.29
42.17
39.26
24.84
f1 (ppm)

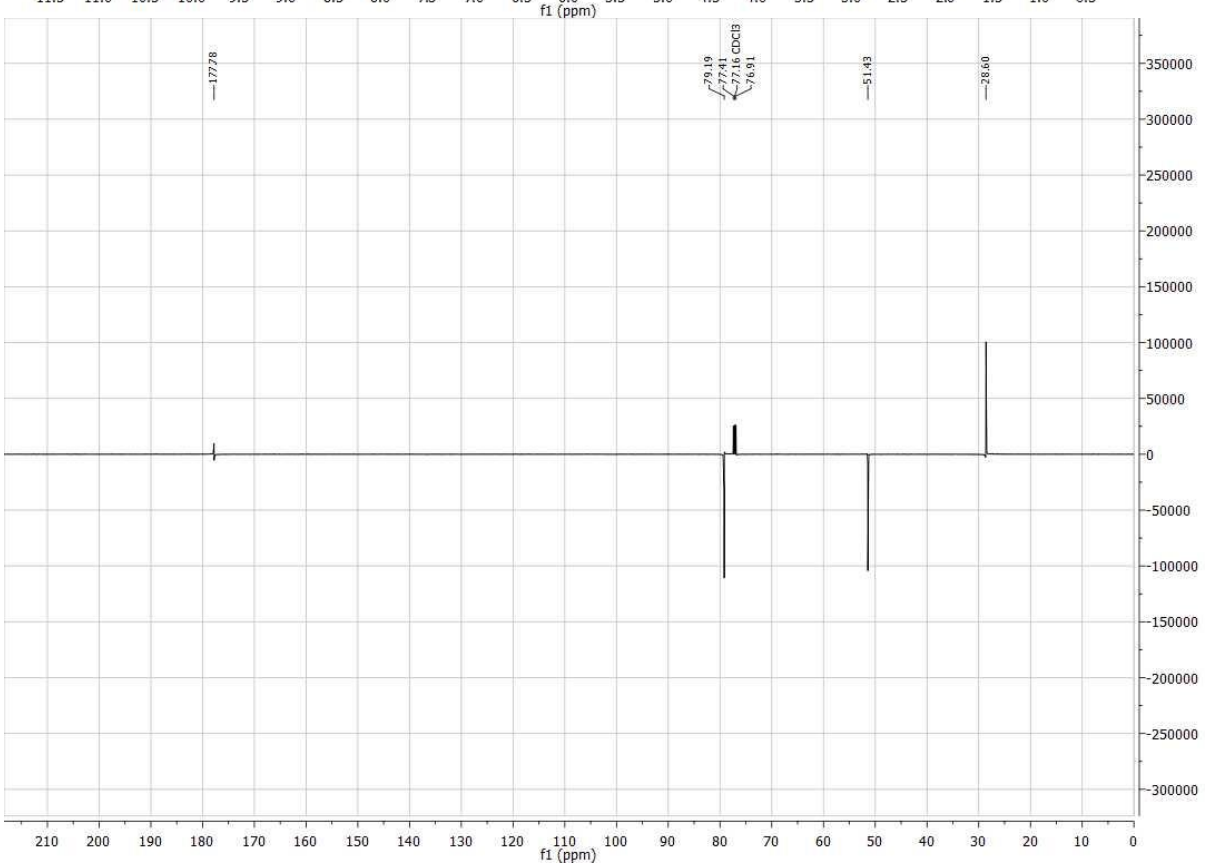

8.15
7.26 CHCl3
6.52
5.32
2.89
1.64
0.94
1.00
0.99
1.05
0.80
f1 (ppm)

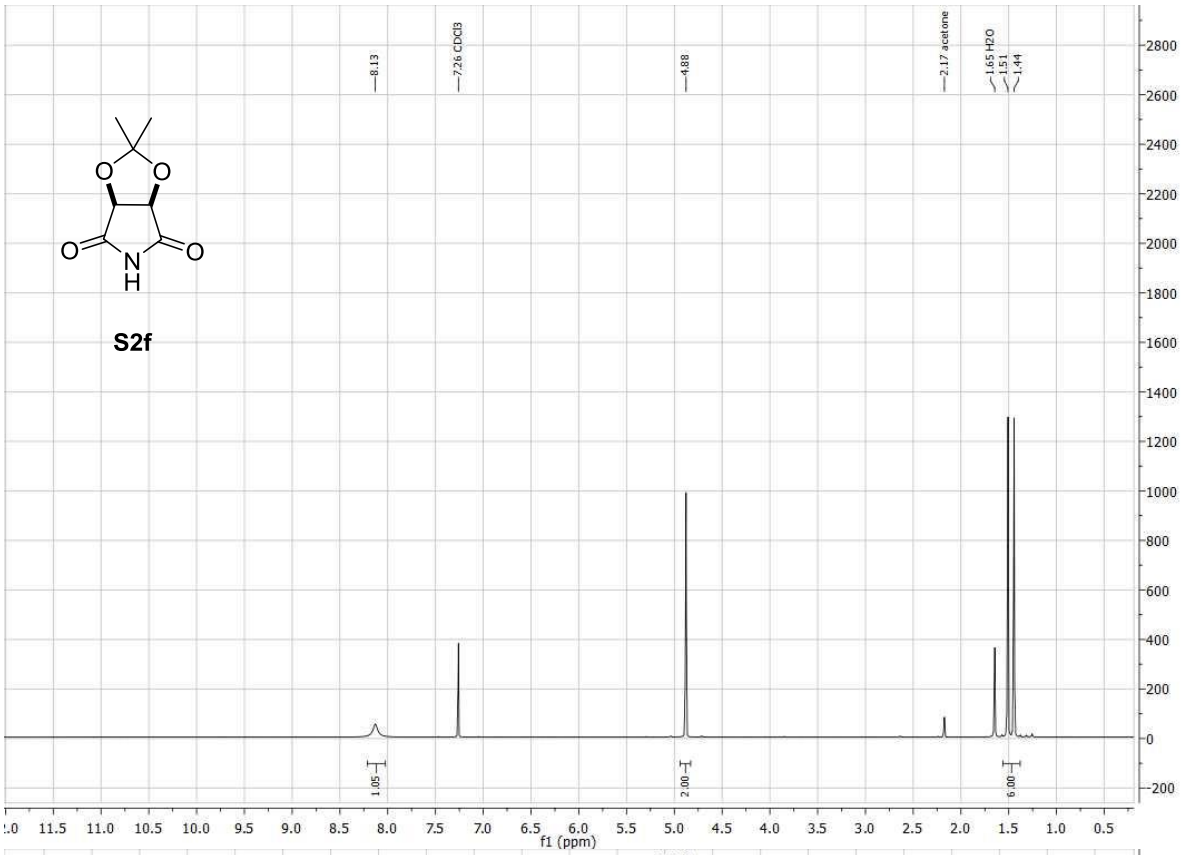
**S2c**


176.15
136.72
81.12
77.41 CDCl3
77.16
76.91
48.84
f1 (ppm)

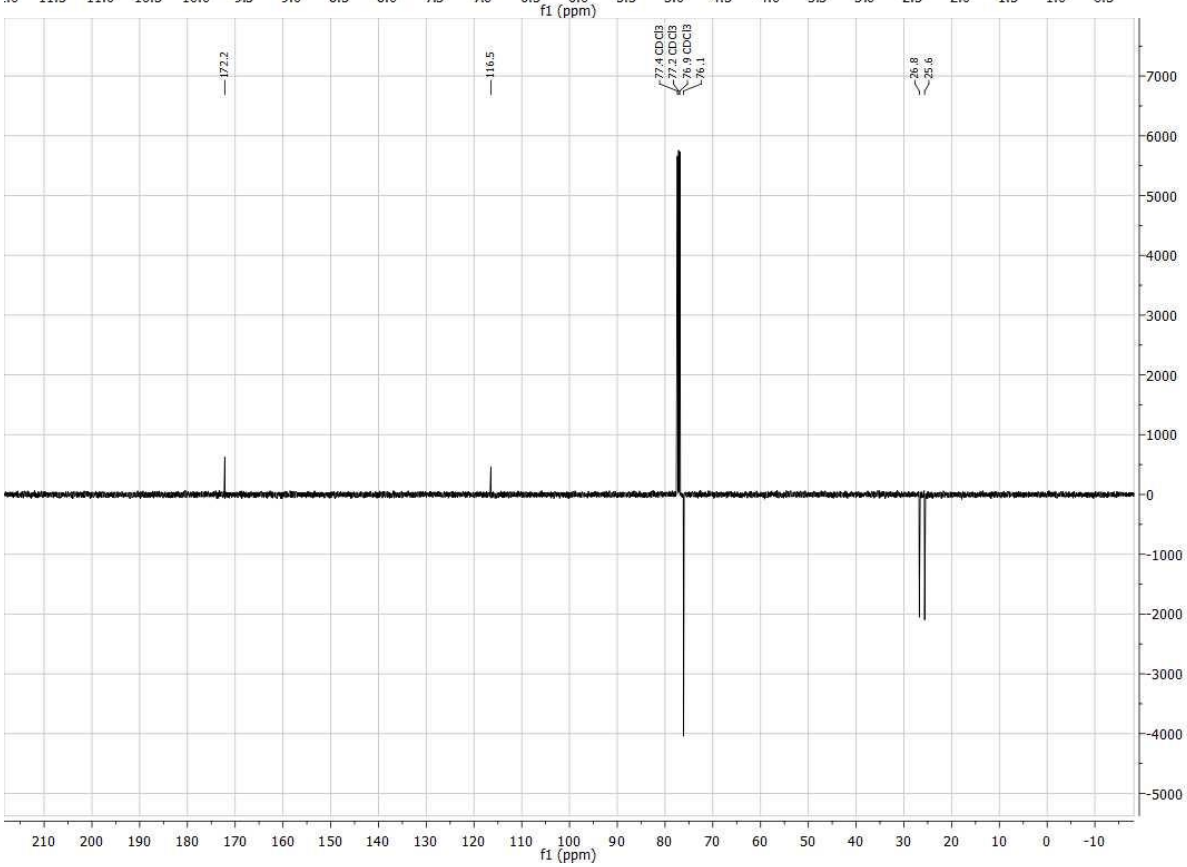

8.76
7.26 CHCl3
4.90
4.90
4.89
2.91
1.87
1.86
1.85
1.84
1.60
1.59
1.58
1.56
1.00
1.74
1.70
2.34
2.09
f1 (ppm)

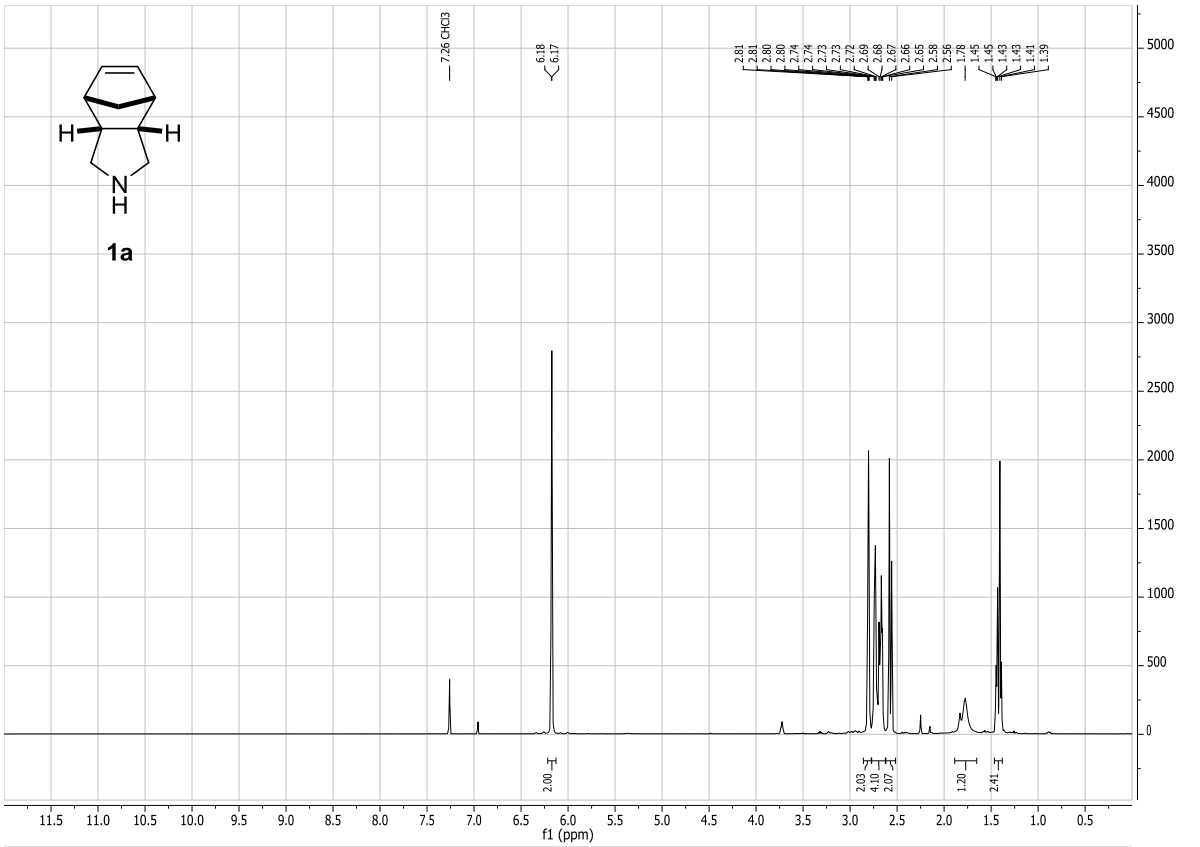
**S2d**


177.78
79.19
77.41
77.16 CDCl3
76.91
51.43
28.60
f1 (ppm)

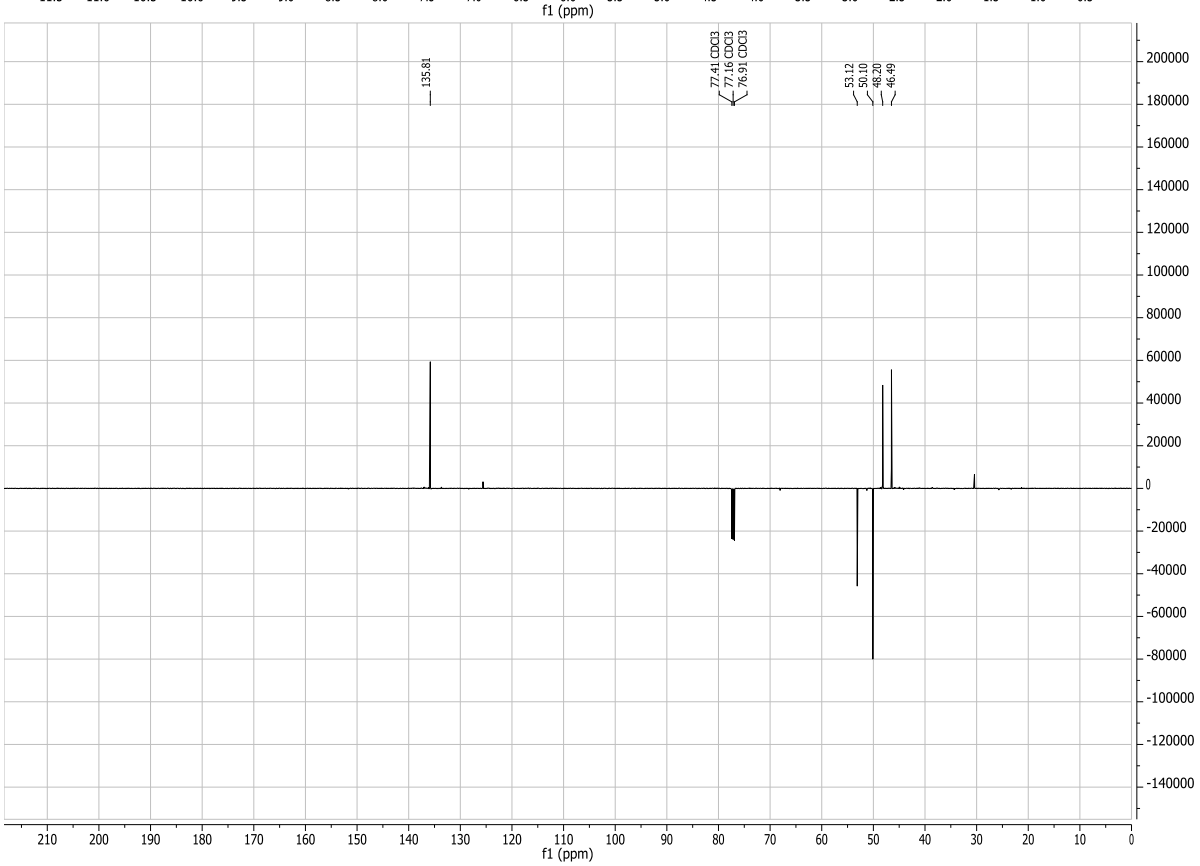

8.13
7.26 CDCl3
4.88
2.17 acetone
1.65 H2O
1.51
1.44
1.05
2.00
6.00
f1 (ppm)

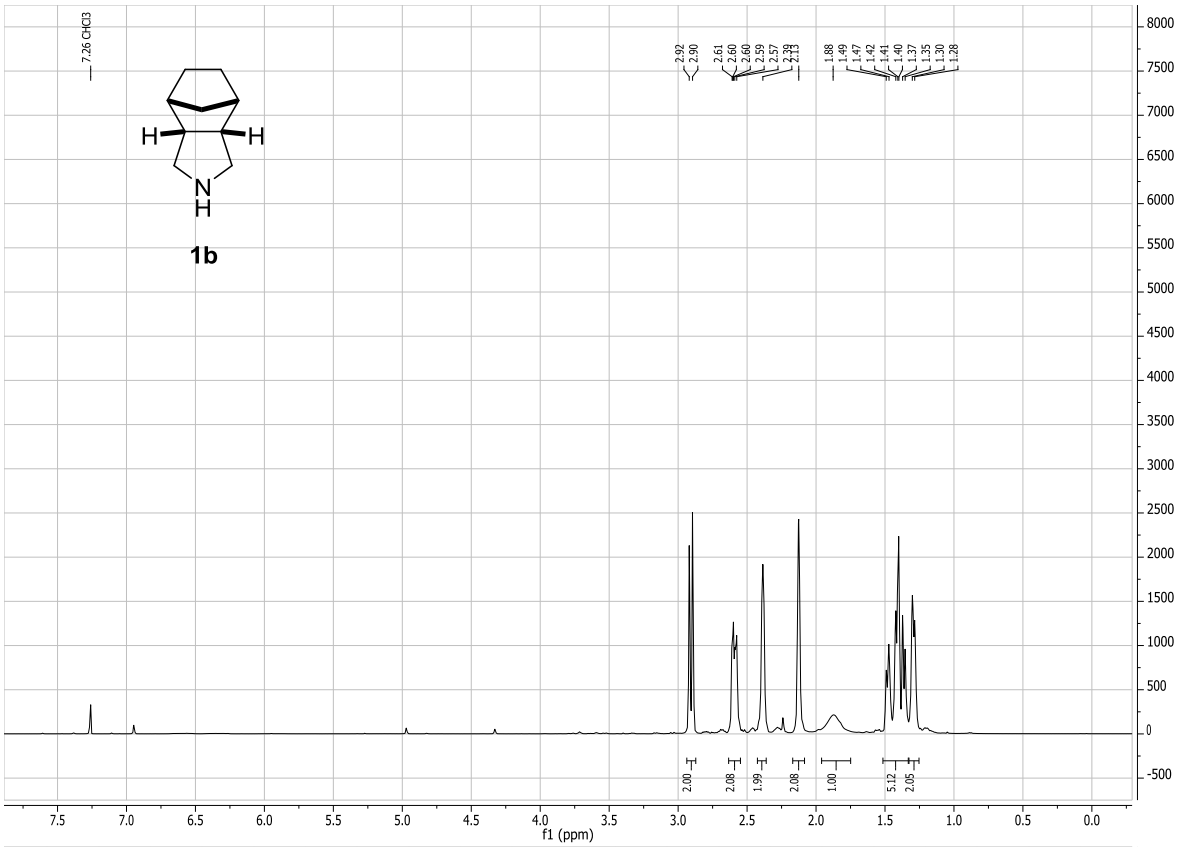
**S2f**


172.2
116.5
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
76.1
26.8
25.6
f1 (ppm)

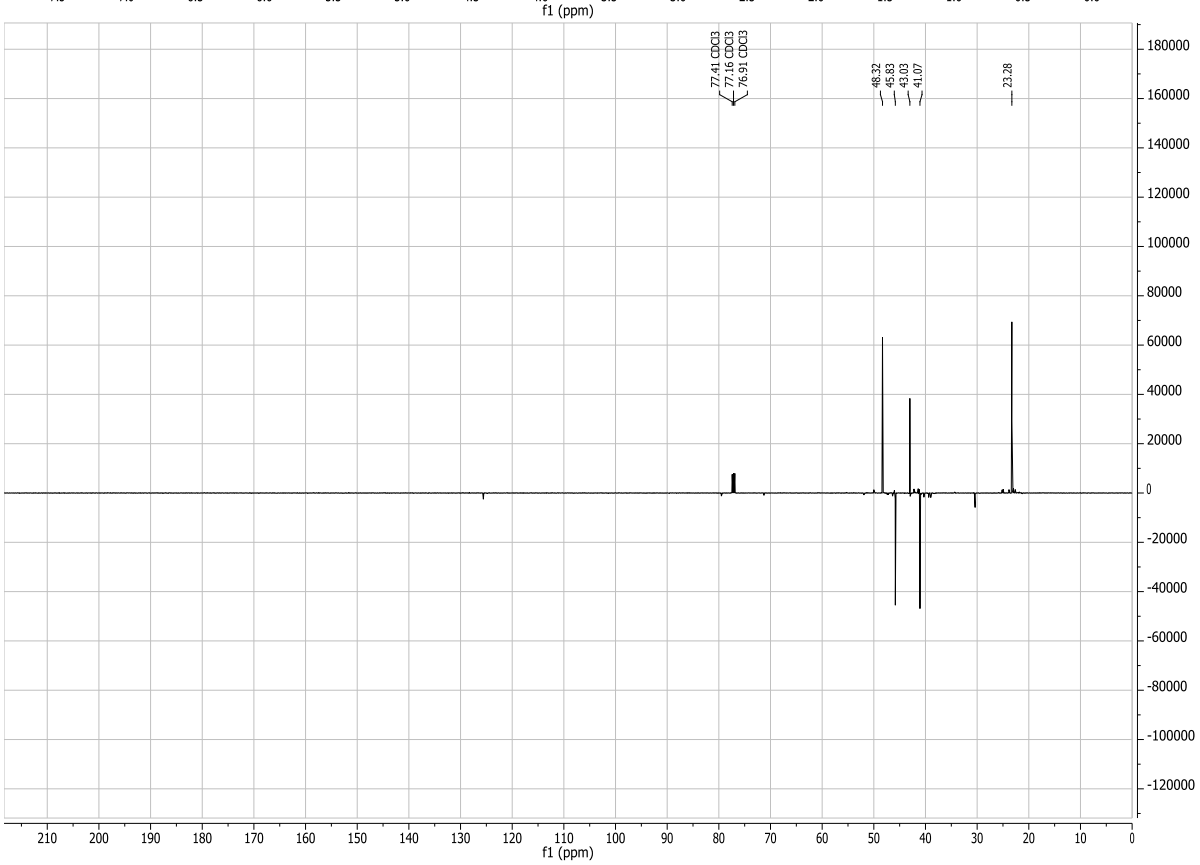

7.26 CHCl3
6.18
6.17
2.81
2.81
2.80
2.80
2.74
2.74
2.73
2.73
2.72
2.72
2.69
2.68
2.67
2.66
2.65
2.58
2.56
1.78
1.45
1.45
1.43
1.43
1.41
1.39
2.00
2.03
4.10
2.07
1.20
2.41
f1 (ppm)

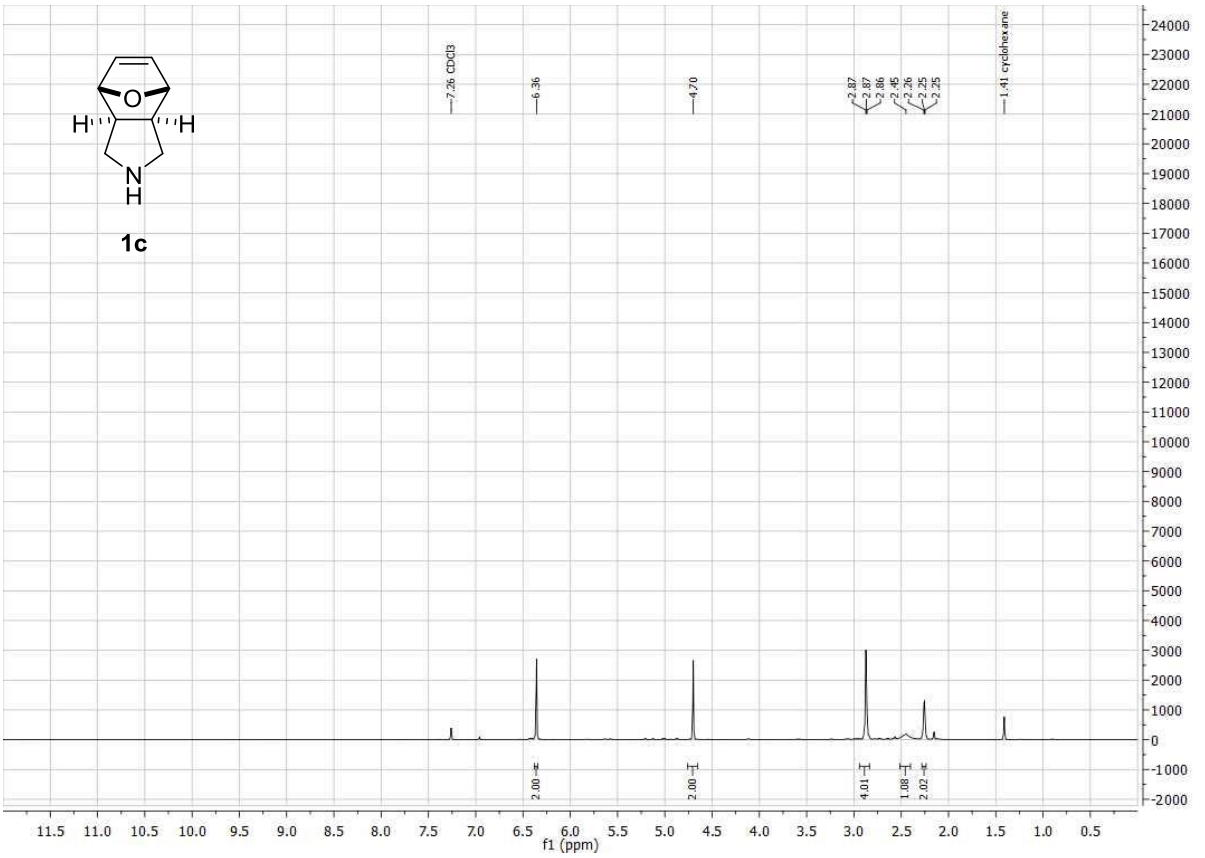
**1a**

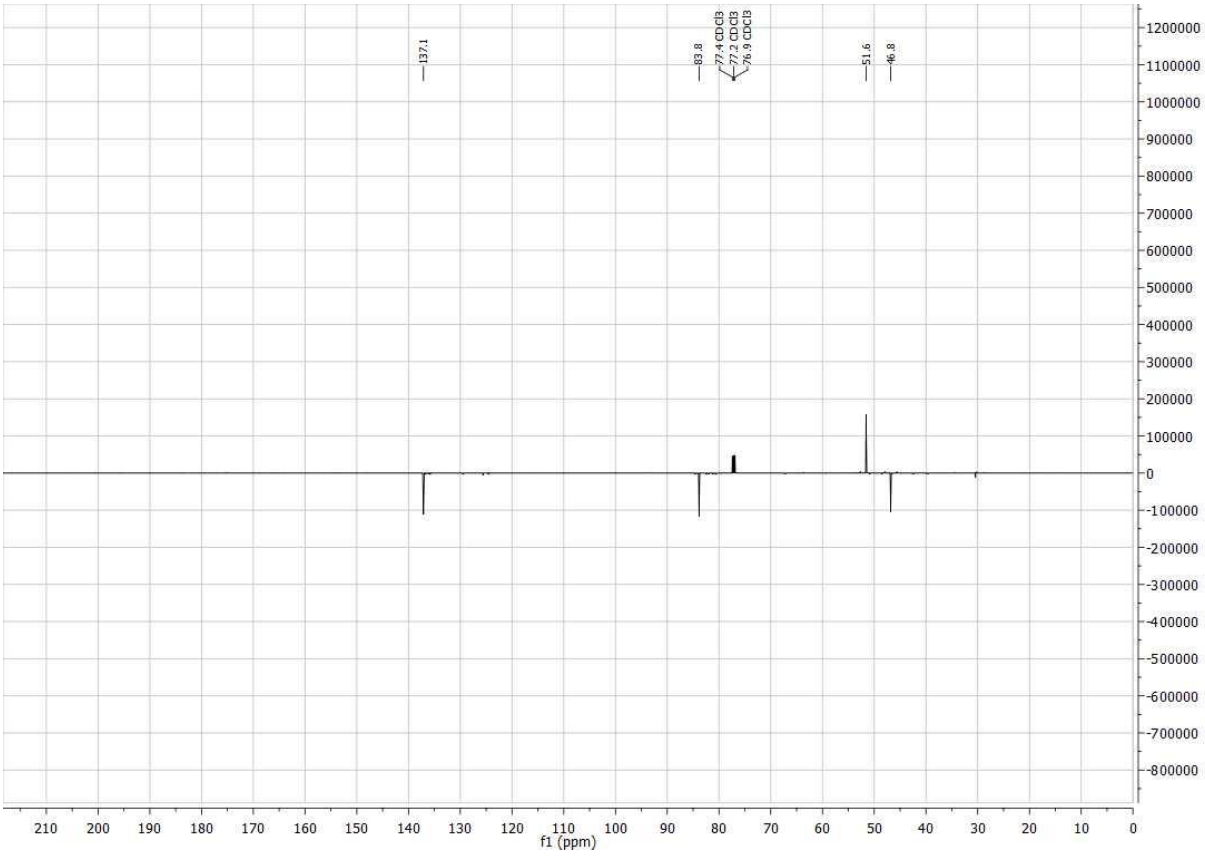

135.81
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
53.12
50.10
48.20
46.49
f1 (ppm)

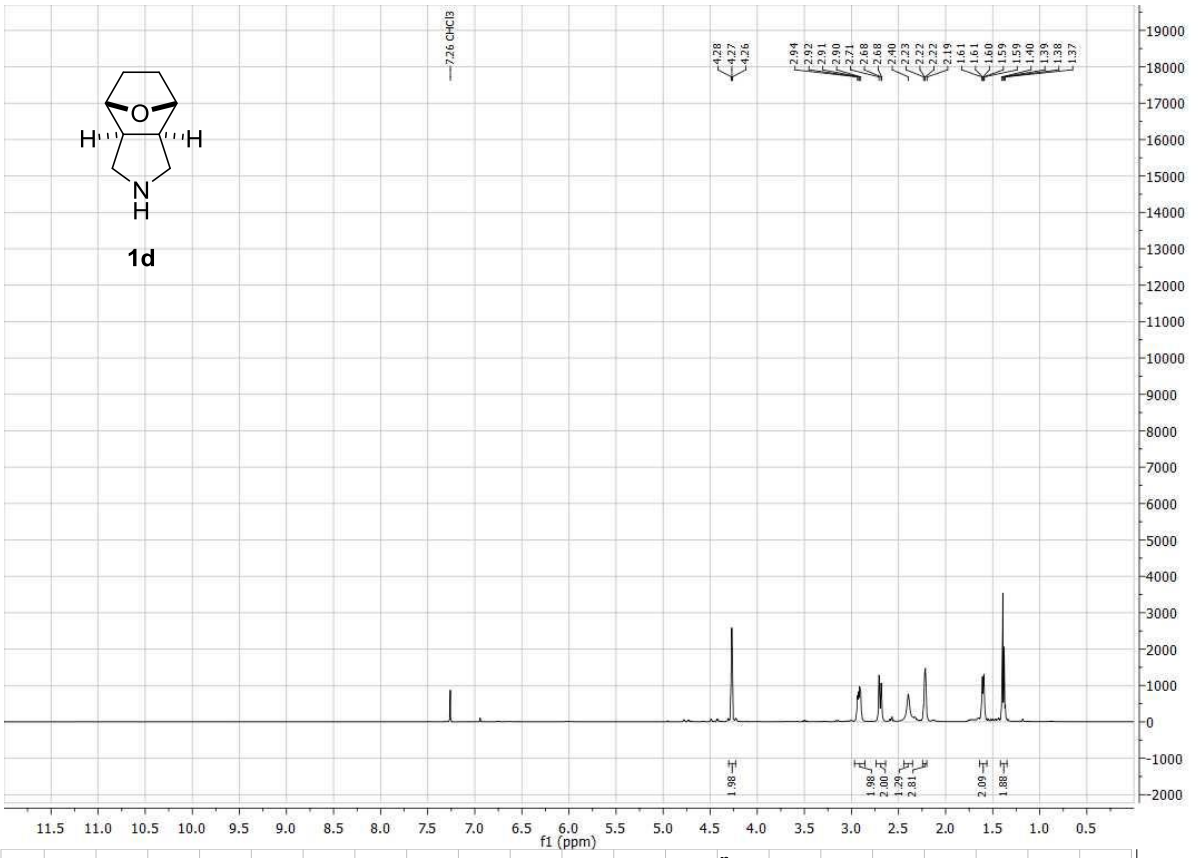

7.26 CHCl3
2.92
2.90
2.61
2.60
2.60
2.59
2.57
2.39
2.13
1.88
1.49
1.47
1.42
1.41
1.40
1.37
1.35
1.30
1.28
2.00
2.08
1.99
2.08
1.00
5.12
2.05
f1 (ppm)

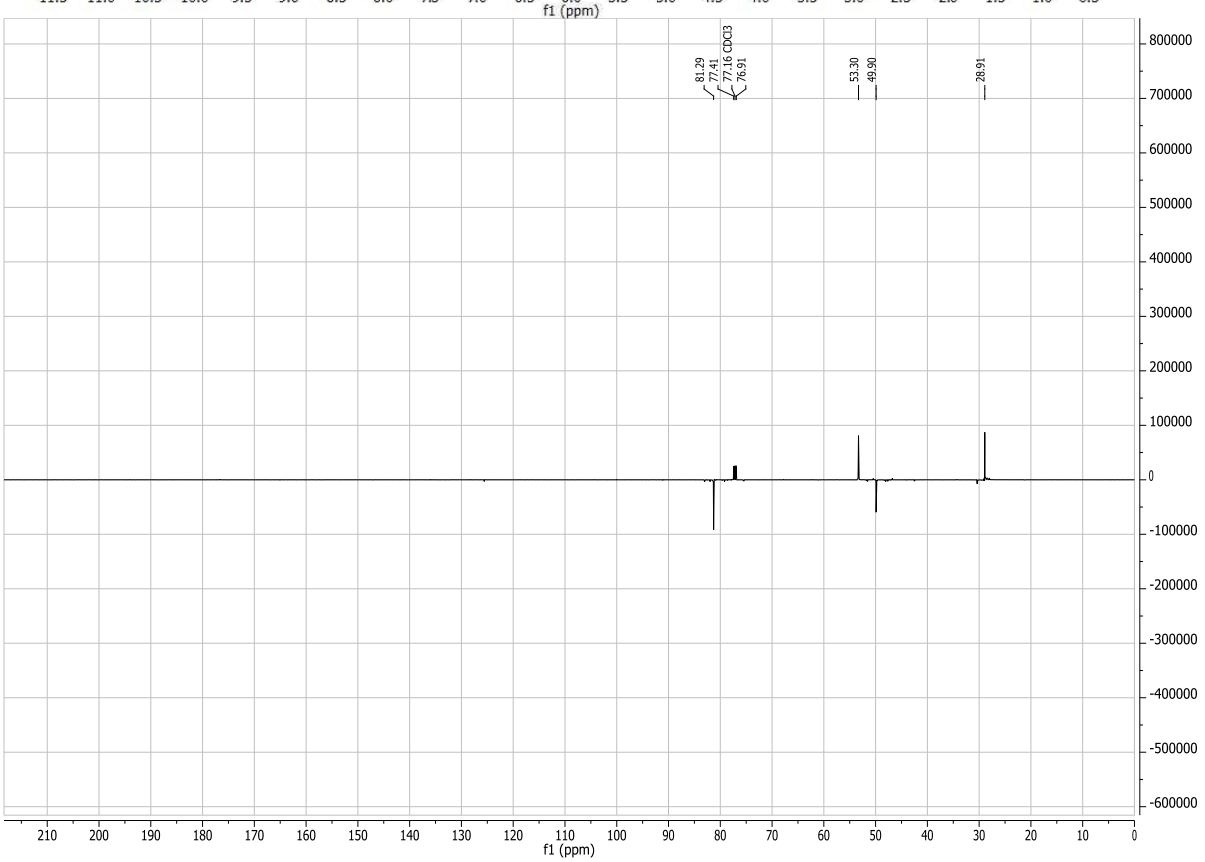
**1b**


77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
48.32
45.83
43.03
41.07
23.28
f1 (ppm)

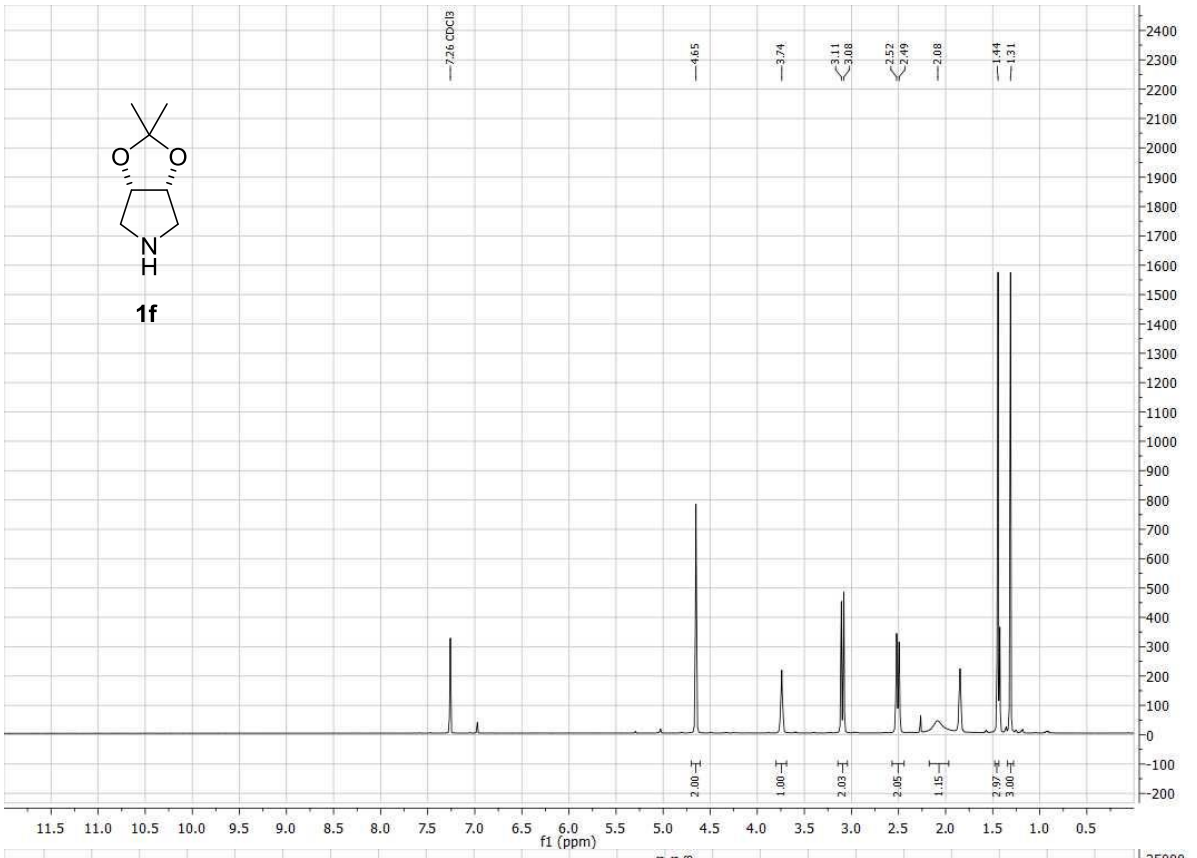

1c
7.26 CDCl3
6.36
4.70
2.87
2.87
2.86
2.46
2.26
2.25
2.25
1.41 cyclohexane
2.00
2.00
4.01
1.08
2.02
f1 (ppm)


137.1
83.8
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
51.6
46.8
f1 (ppm)

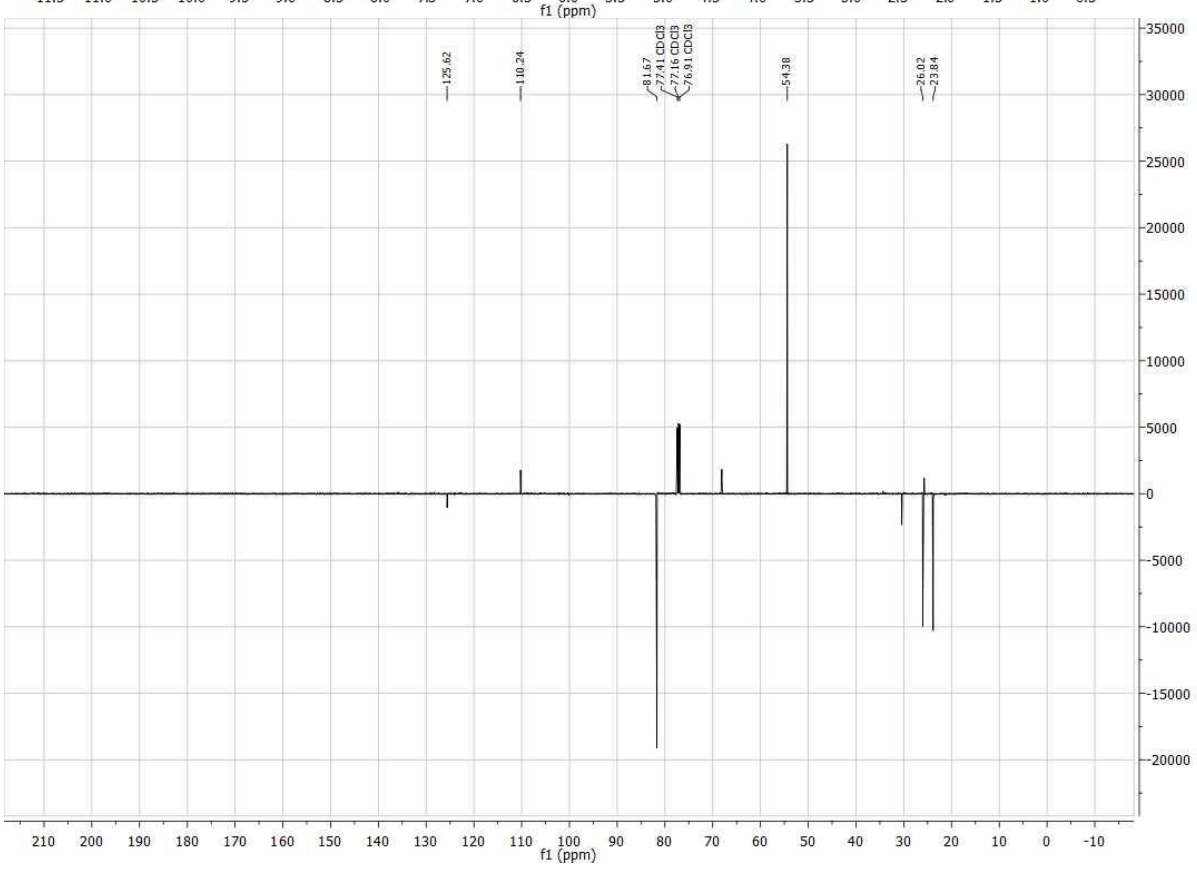

7.26 CHCl3
4.28
4.27
4.26
2.94
2.92
2.91
2.90
2.71
2.68
2.68
2.40
2.23
2.22
2.22
2.19
1.61
1.61
1.60
1.59
1.59
1.40
1.39
1.38
1.37
1.98
1.98
2.00
1.29
2.81
2.09
1.88
f1 (ppm)

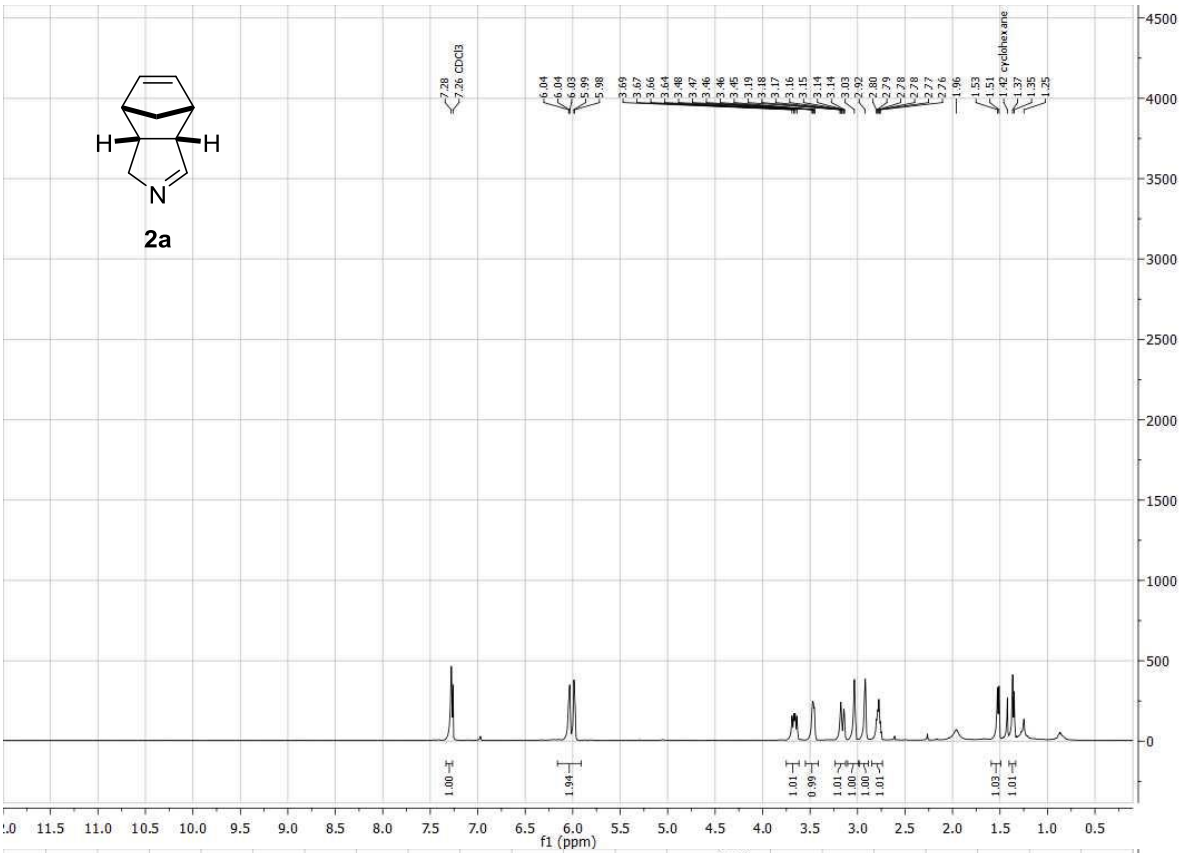

81.29
77.41
77.16 CDCl3
76.91
53.30
49.90
28.91
f1 (ppm)

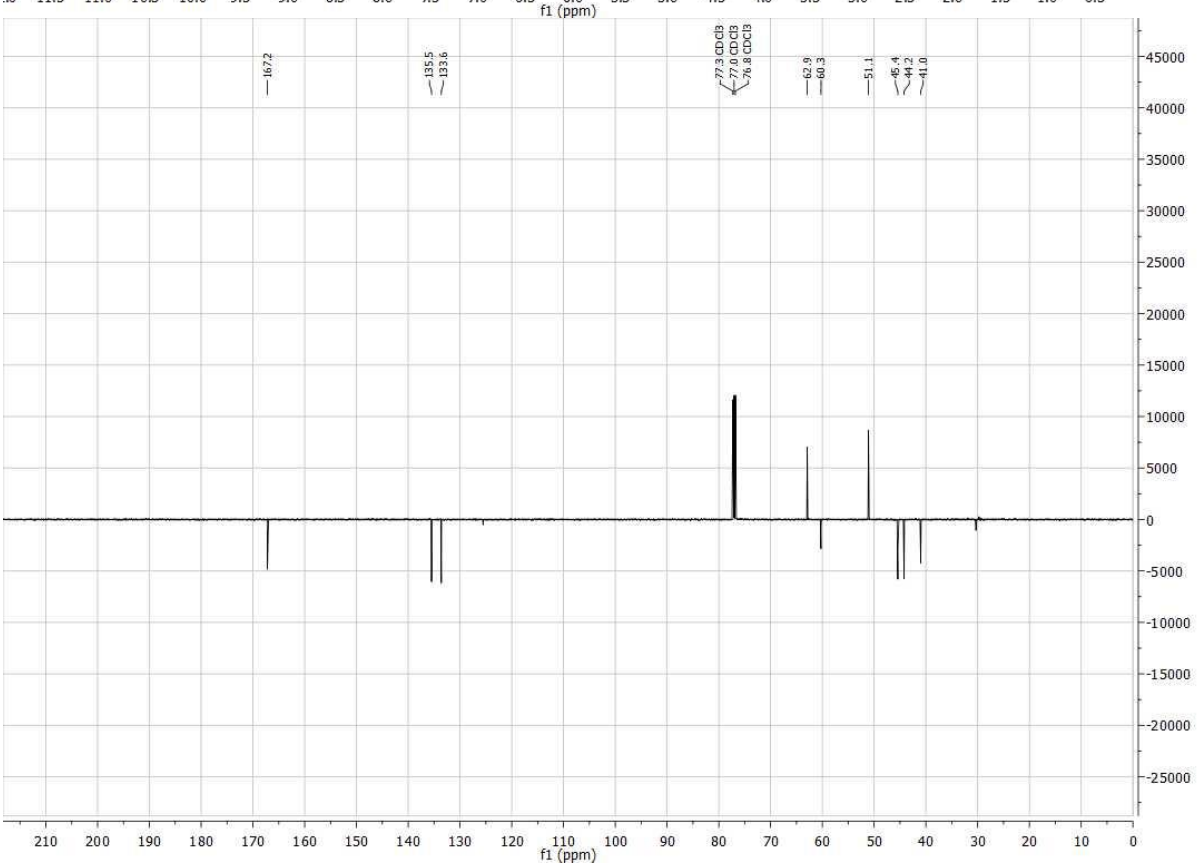
**1d**

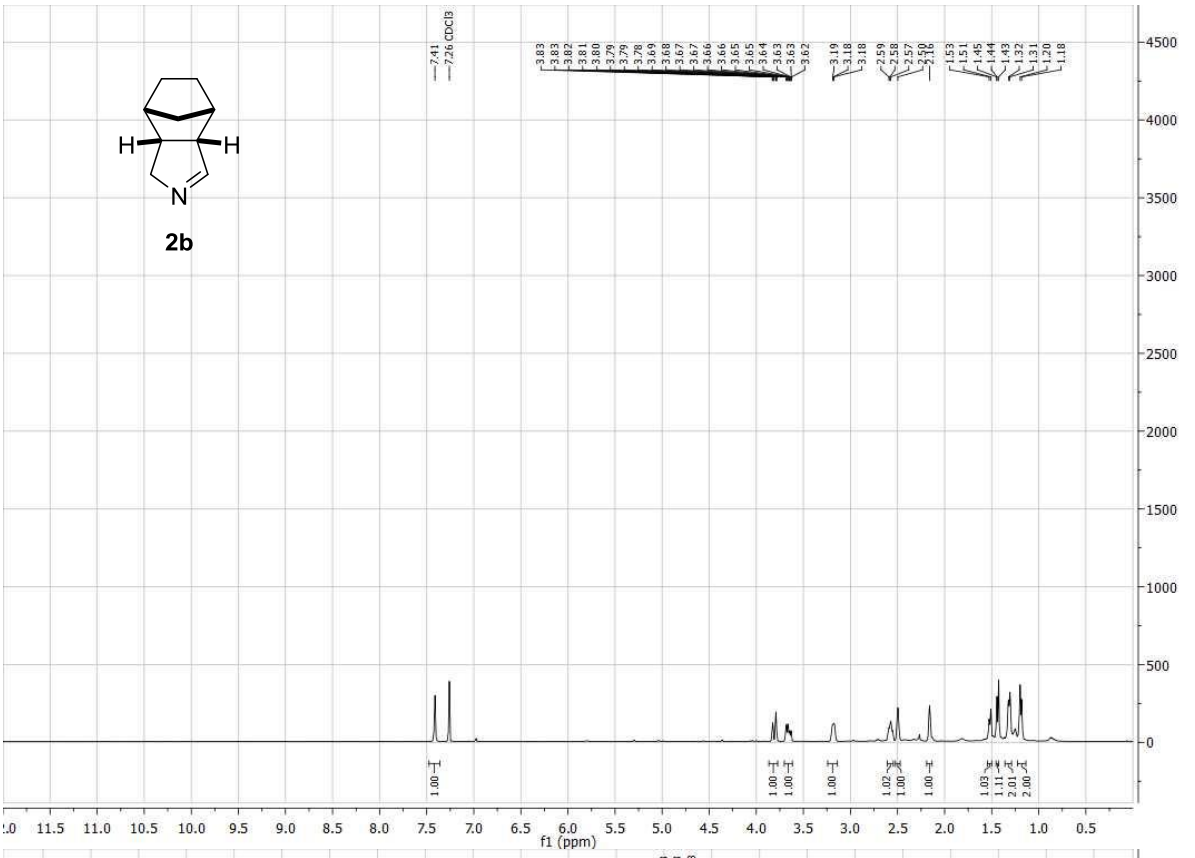

7.26 CDCl3
4.65
3.74
3.11
3.08
2.52
2.49
2.08
1.44
1.31
2.00
1.00
2.03
2.05
1.15
2.97
3.00
f1 (ppm)

**1f**

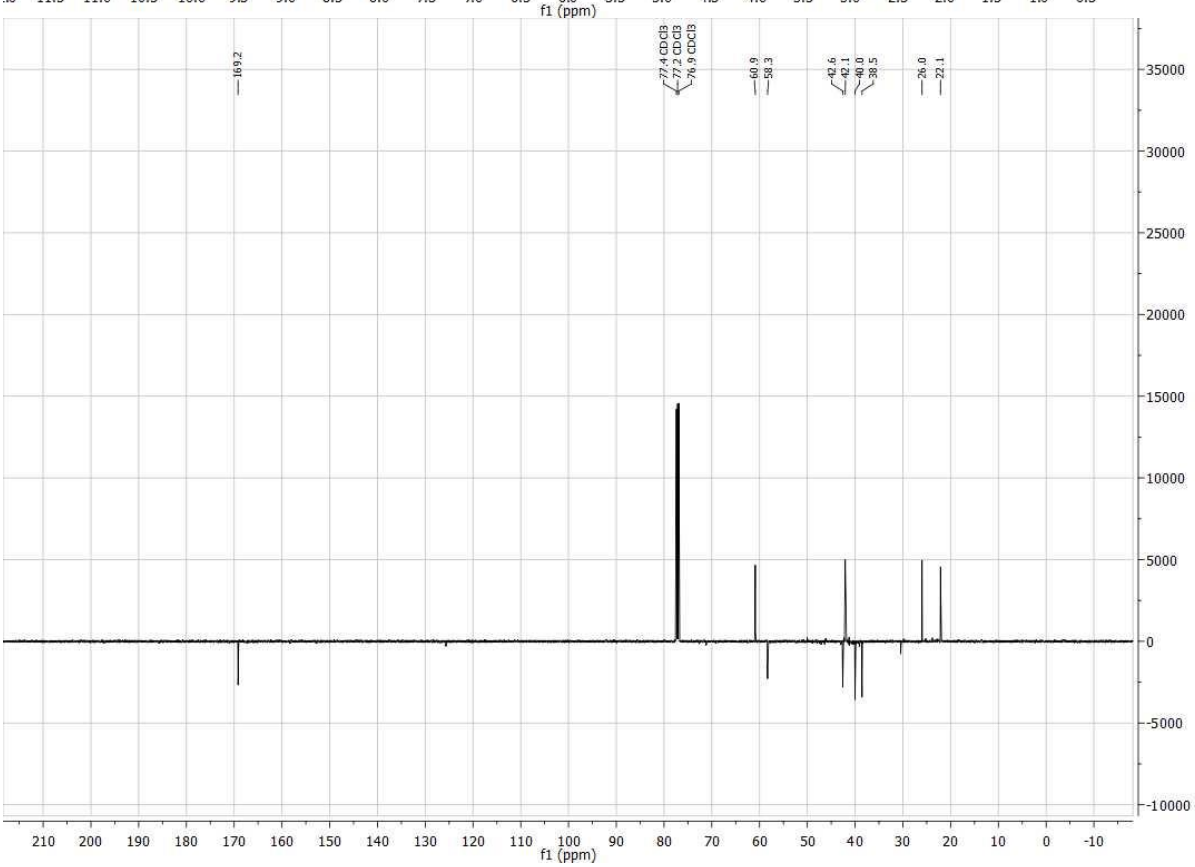

125.62
110.24
81.67
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
54.38
26.02
23.84
f1 (ppm)

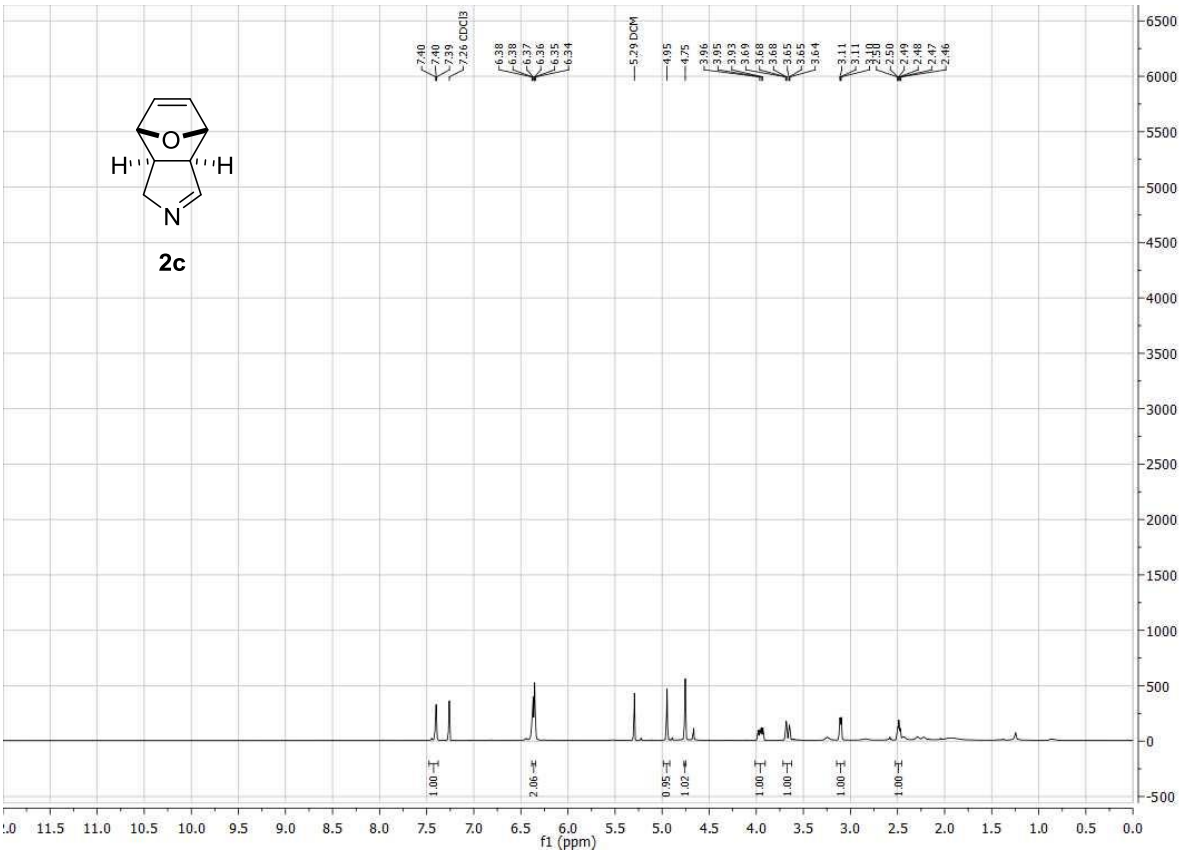

H
H
N
2a
7.28
7.26 CDCl3
6.04
6.04
6.03
5.99
5.98
3.69
3.67
3.66
3.64
3.48
3.47
3.46
3.46
3.45
3.19
3.18
3.17
3.16
3.15
3.14
3.03
2.92
2.80
2.79
2.78
2.78
2.77
2.76
1.96
1.53
1.51
1.42 cyclohex ane
1.37
1.35
1.25
1.00
1.94
1.01
0.99
1.01
1.00
1.00
1.01
1.03
1.01
f1 (ppm)

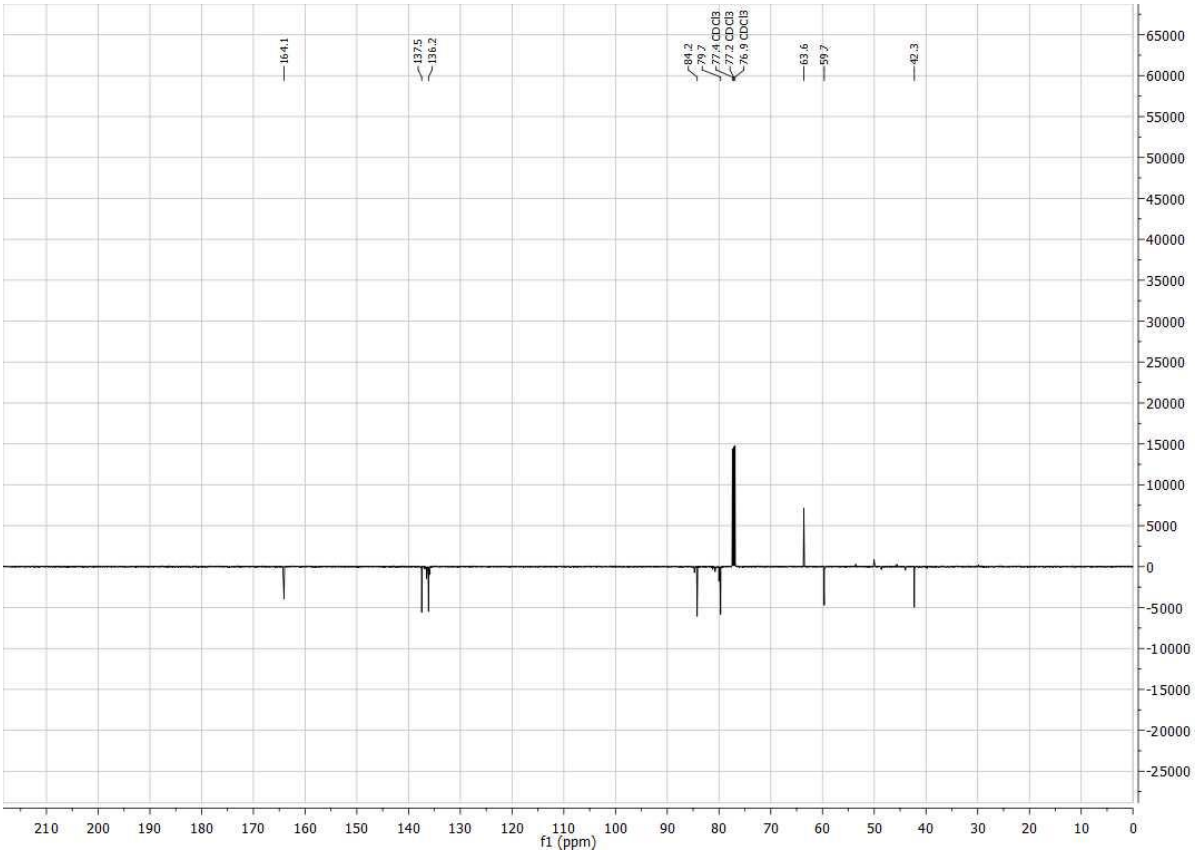

167.2
135.5
133.6
77.3 CDCl3
77.0 CDCl3
76.8 CDCl3
62.9
60.3
51.1
45.4
44.2
41.0
f1 (ppm)

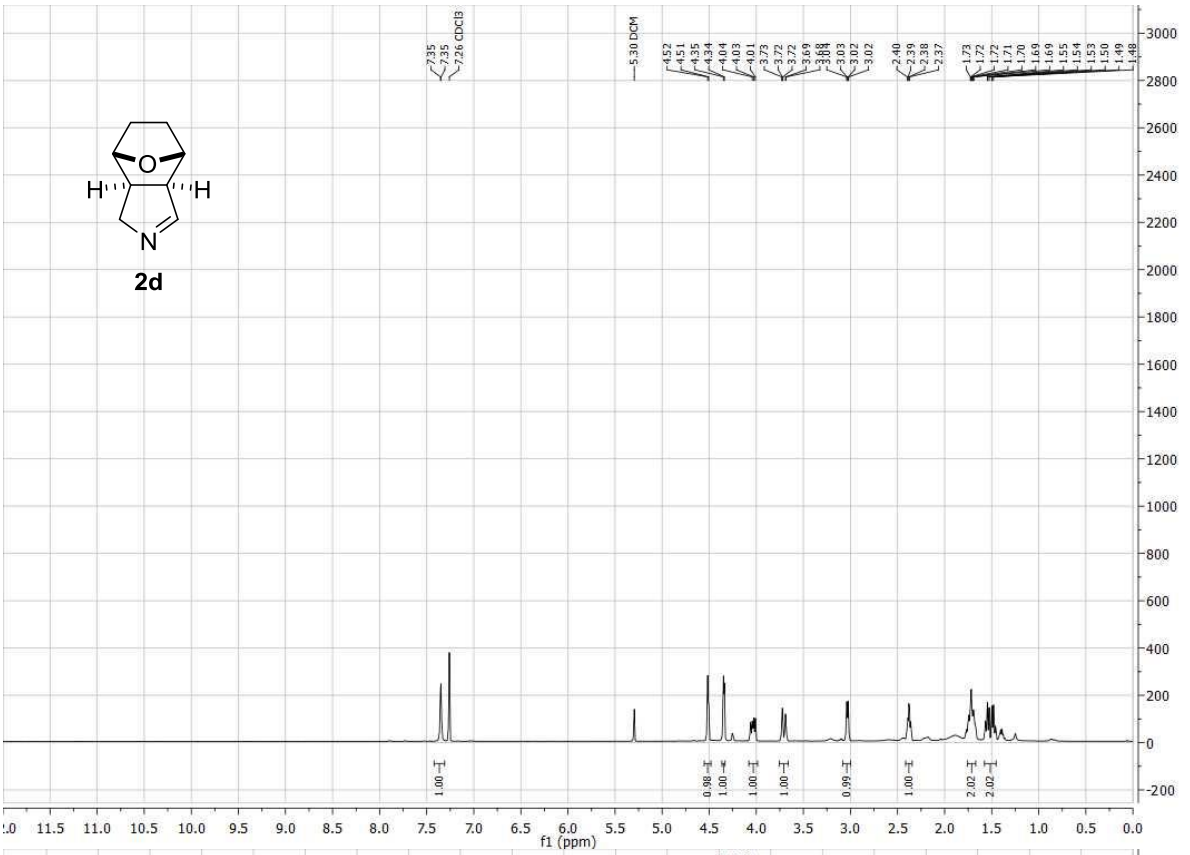

H
H
N
7.41
7.26 CDCl3
3.83
3.82
3.81
3.80
3.79
3.78
3.69
3.68
3.67
3.66
3.65
3.64
3.63
3.62
3.19
3.18
2.59
2.58
2.57
2.10
1.53
1.51
1.45
1.44
1.43
1.32
1.31
1.20
1.18
1.00
1.00
1.00
1.00
1.02
1.00
1.00
1.03
1.11
2.01
2.00
f1 (ppm)

**2b**

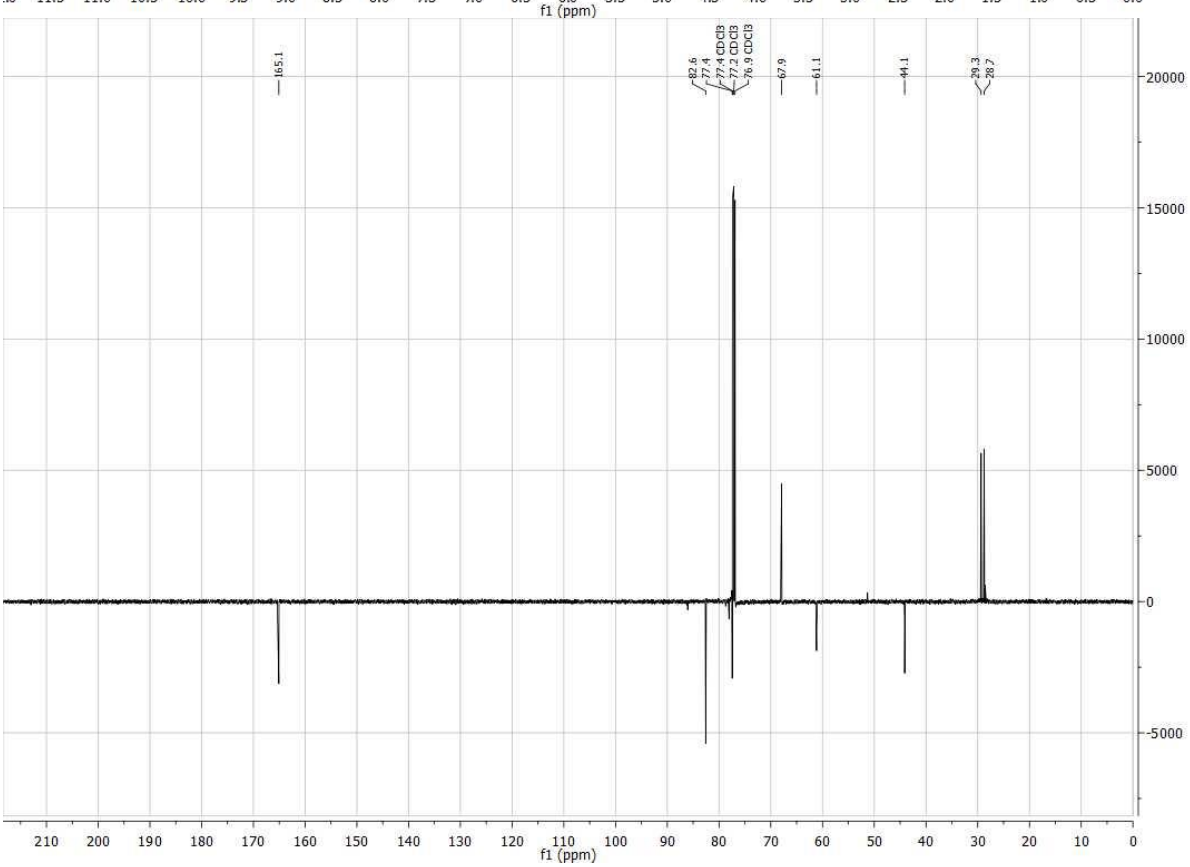

169.2
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
60.9
58.3
42.6
42.1
40.0
38.5
26.0
22.1
f1 (ppm)

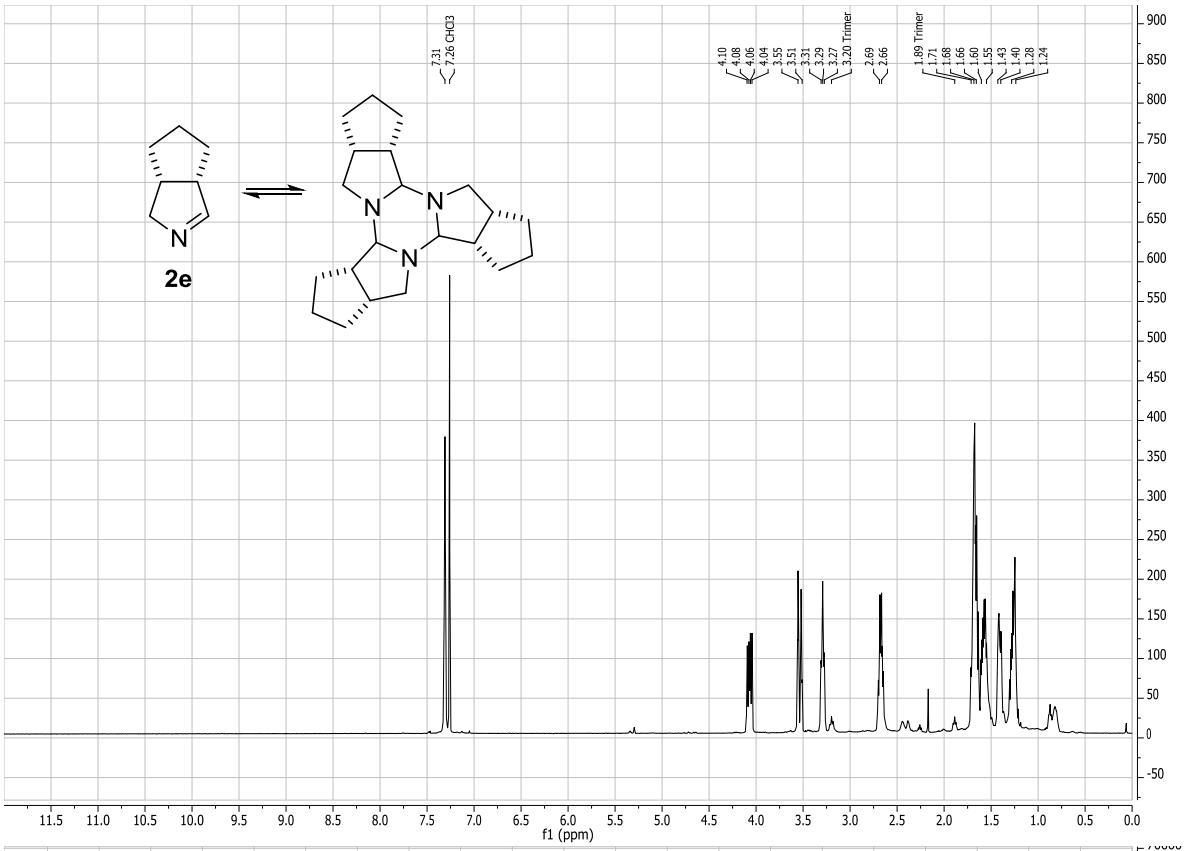

7.40
7.40
7.39
7.26 CDCl3
6.38
6.38
6.37
6.36
6.35
6.34
5.29 DCM
4.95
4.75
3.96
3.95
3.93
3.69
3.68
3.68
3.65
3.65
3.64
3.11
3.11
2.50
2.50
2.49
2.48
2.47
2.46
O
H
H
N
2c
1.00
2.06
0.95
1.02
1.00
1.00
1.00
1.00
f1 (ppm)

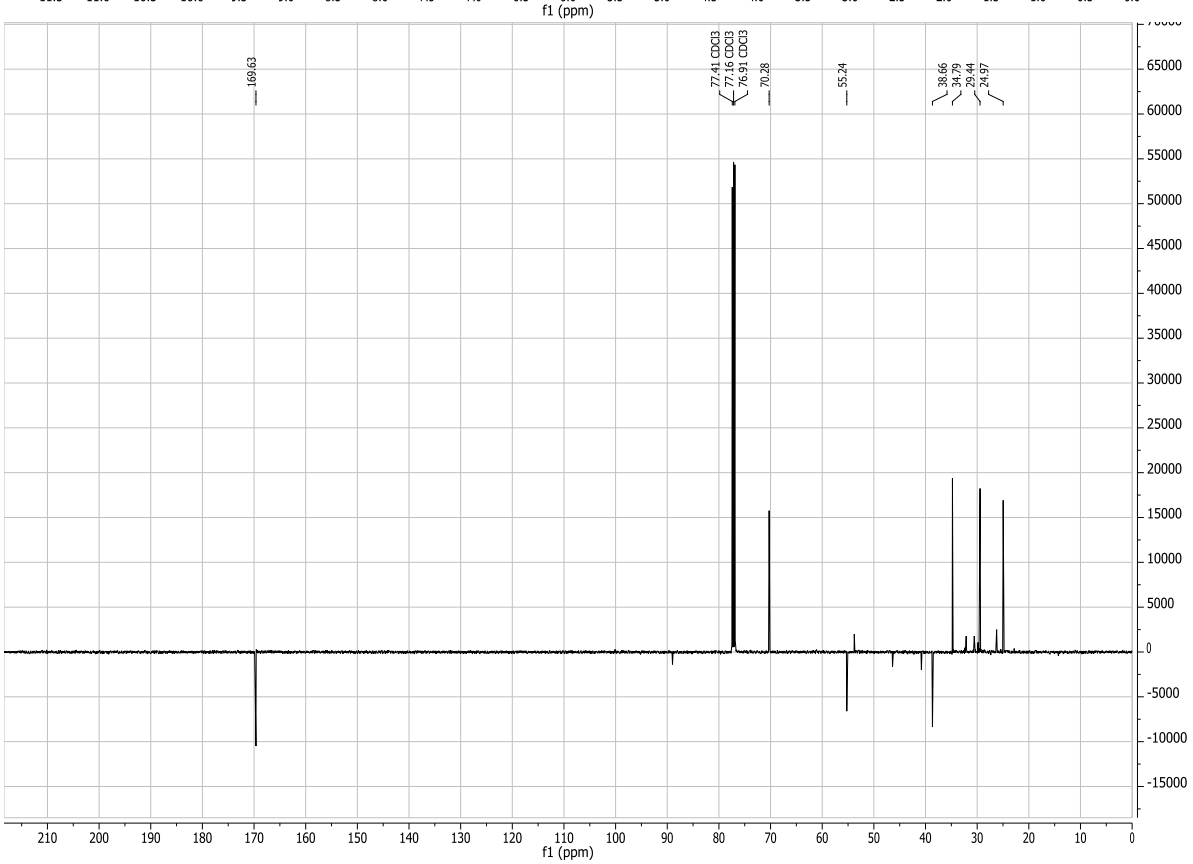

164.1
137.5
136.2
84.2
79.7
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
63.6
59.7
42.3
f1 (ppm)

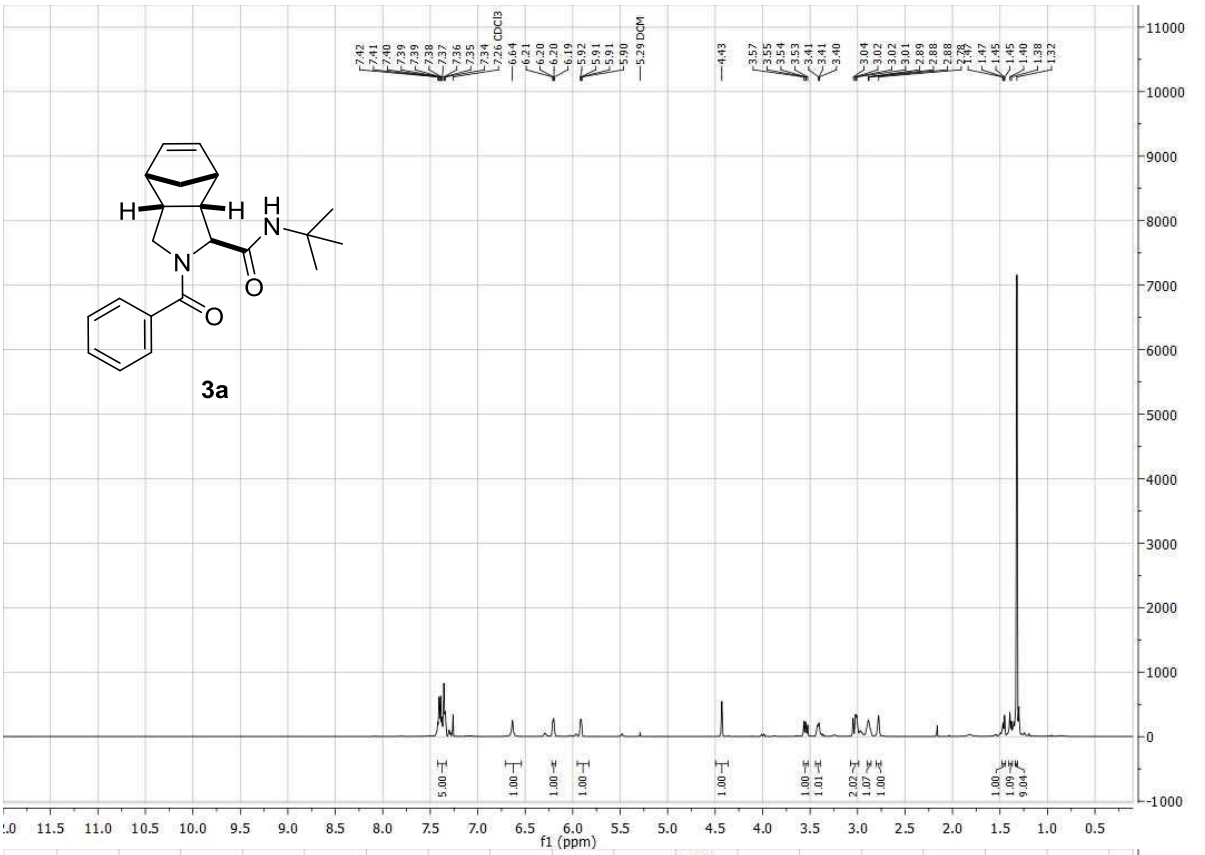

7.35
7.35
7.26 CDCl3
5.30 DCM
4.52
4.51
4.35
4.34
4.04
4.03
4.01
3.73
3.72
3.72
3.69
3.68
3.04
3.03
3.02
3.02
2.40
2.39
2.38
2.37
1.73
1.72
1.72
1.71
1.70
1.69
1.69
1.55
1.54
1.53
1.50
1.49
1.48
1.00
0.98
1.00
1.00
1.00
0.99
1.00
2.02
2.02
f1 (ppm)

**2d**

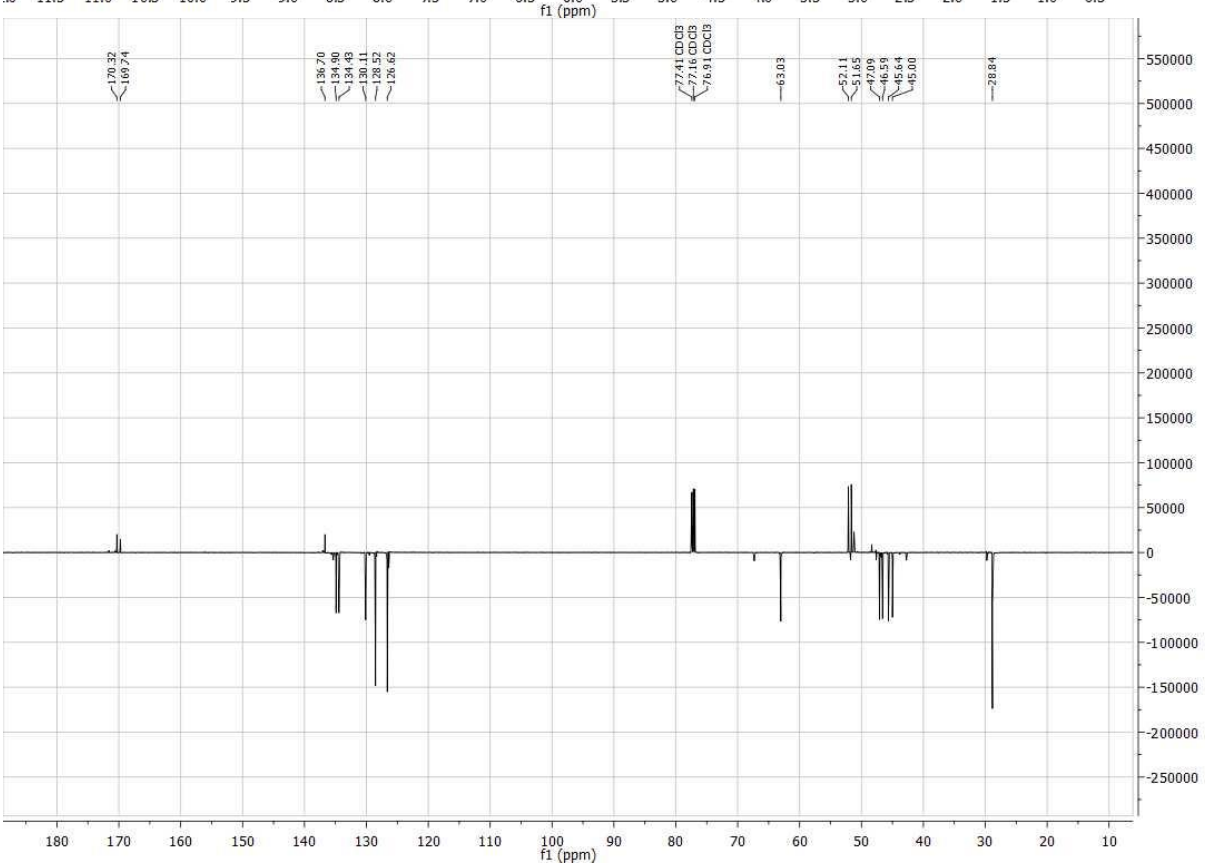

165.1
82.6
77.4
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
67.9
61.1
44.1
29.3
28.7
f1 (ppm)

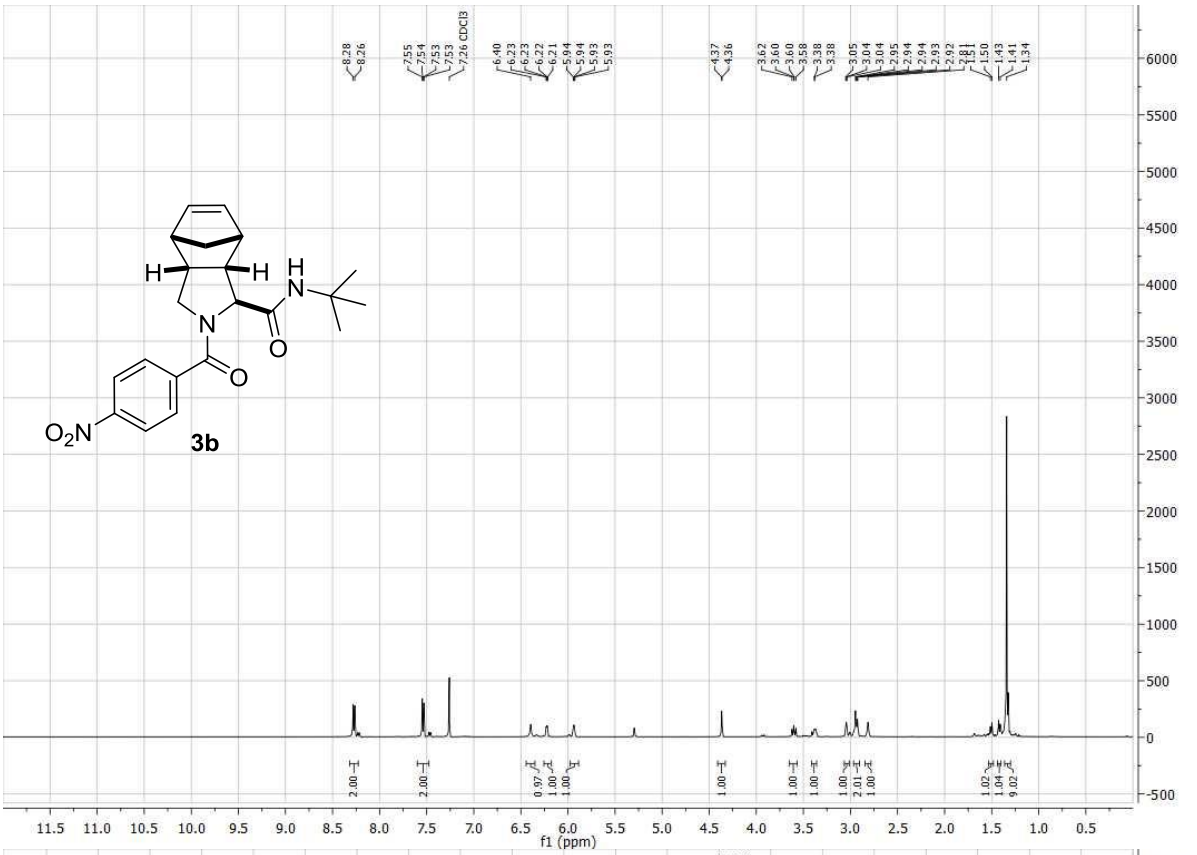

7.31
7.26 CHCl3
4.10
4.08
4.06
4.04
3.55
3.51
3.31
3.29
3.27
3.20 Trimer
2.69
2.66
1.89 Trimer
1.71
1.68
1.66
1.60
1.55
1.43
1.40
1.28
1.24
2e
f1 (ppm)

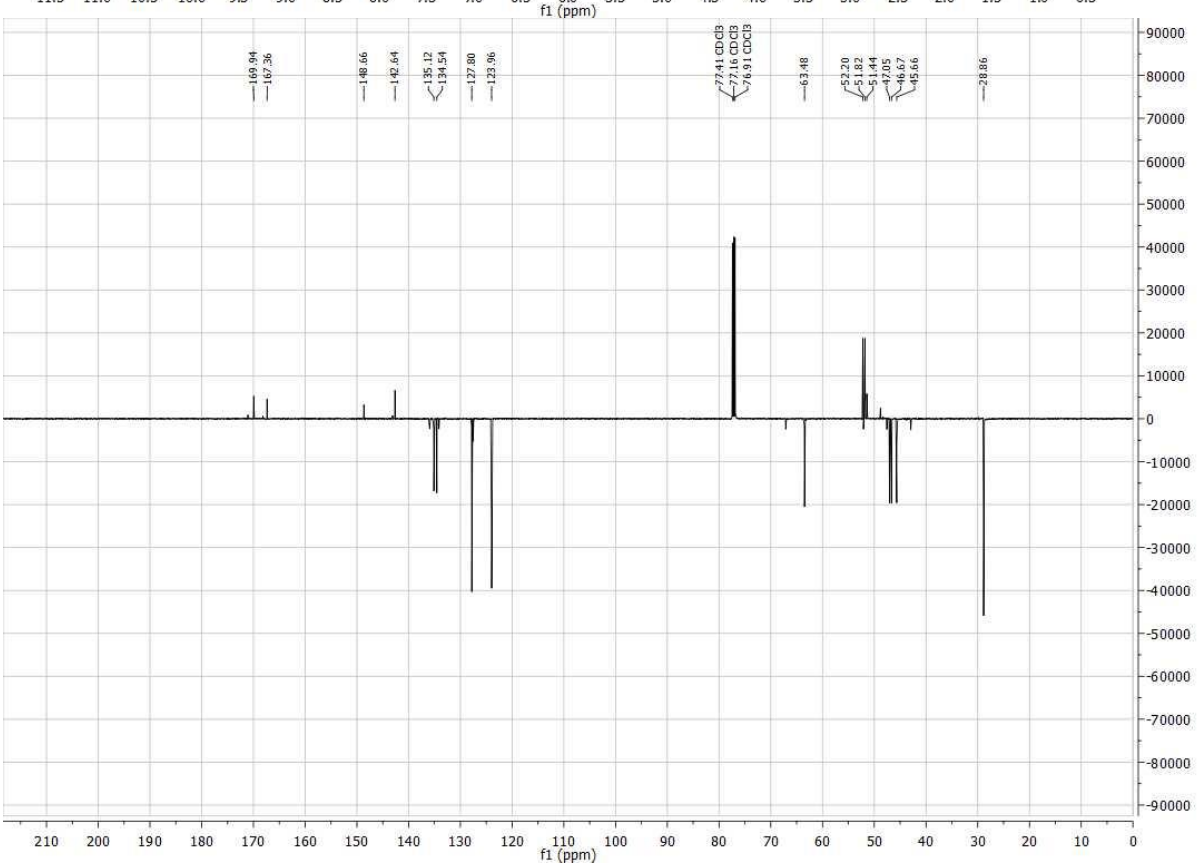

169.63
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
70.28
55.24
38.66
34.79
29.44
24.97
f1 (ppm)


7.42
7.41
7.40
7.39
7.39
7.38
7.37
7.36
7.35
7.34
7.26 CDCl3
6.64
6.21
6.20
6.20
6.19
5.92
5.91
5.91
5.90
5.29 DCM
4.43
3.57
3.55
3.54
3.53
3.41
3.41
3.40
3.04
3.02
3.02
3.01
2.89
2.88
2.88
2.78
1.47
1.45
1.45
1.40
1.38
1.32
5.00
1.00
1.00
1.00
1.00
1.00
1.01
2.02
1.07
1.00
1.00
1.09
9.04
f1 (ppm)

**3a**


170.32
169.74
136.70
134.90
134.43
130.11
128.52
126.62
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
63.03
52.11
51.65
47.09
46.59
45.64
45.00
28.84
f1 (ppm)


8.28
8.26
7.55
7.54
7.53
7.53
7.26 CDCl3
6.40
6.23
6.23
6.22
6.21
5.94
5.94
5.93
5.93
4.37
4.36
3.62
3.60
3.60
3.58
3.38
3.38
3.05
3.04
3.04
2.95
2.94
2.94
2.93
2.92
1.81
1.50
1.43
1.41
1.34
H
H
H
N
N
O
O
O2N
3b
2.00
2.00
0.97
1.00
1.00
1.00
1.00
1.00
2.01
1.00
1.02
1.04
9.02
f1 (ppm)


169.94
167.36
148.66
142.64
135.12
134.54
127.80
123.96
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
63.48
52.20
51.82
51.44
47.05
46.67
45.66
28.86
f1 (ppm)

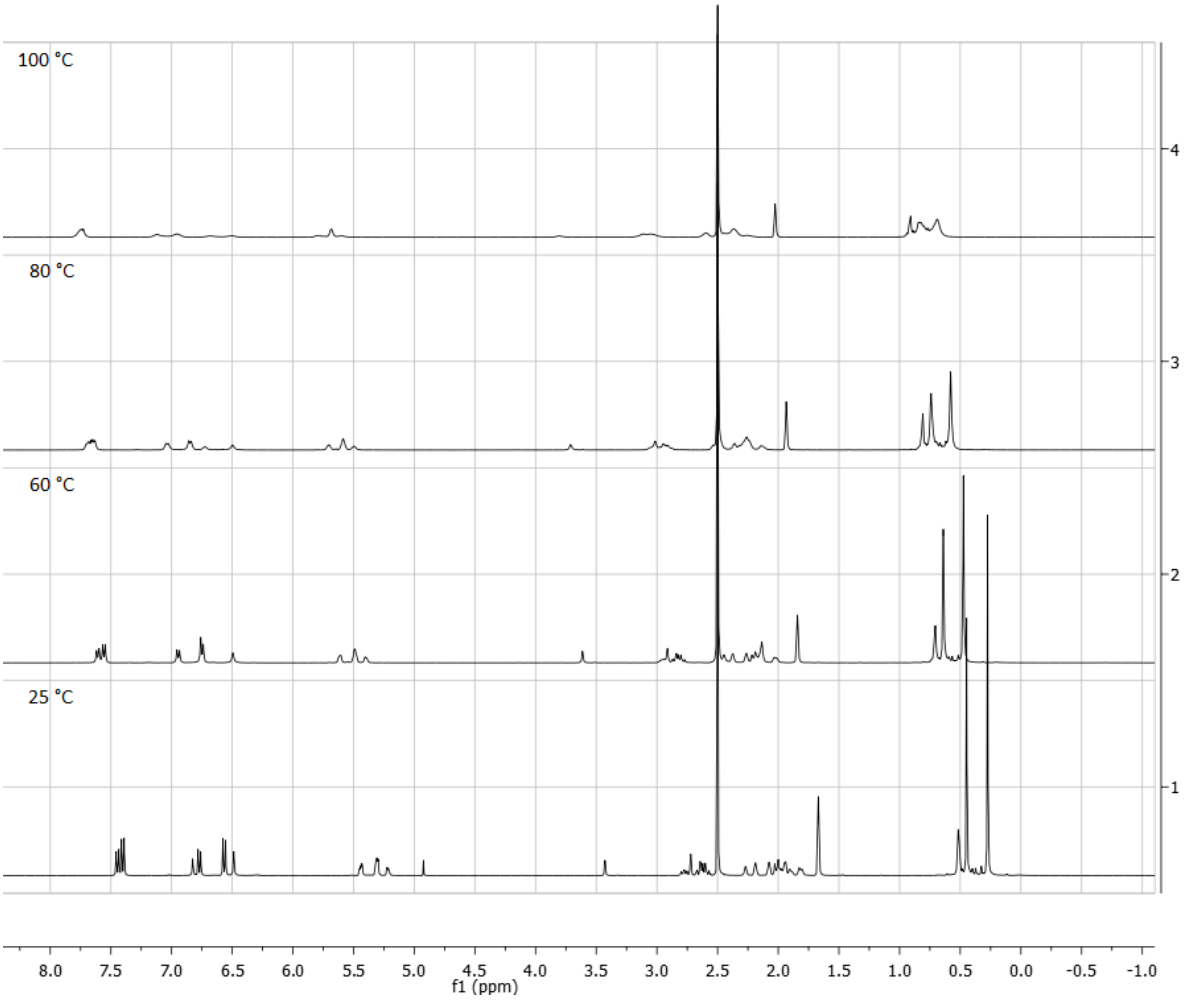
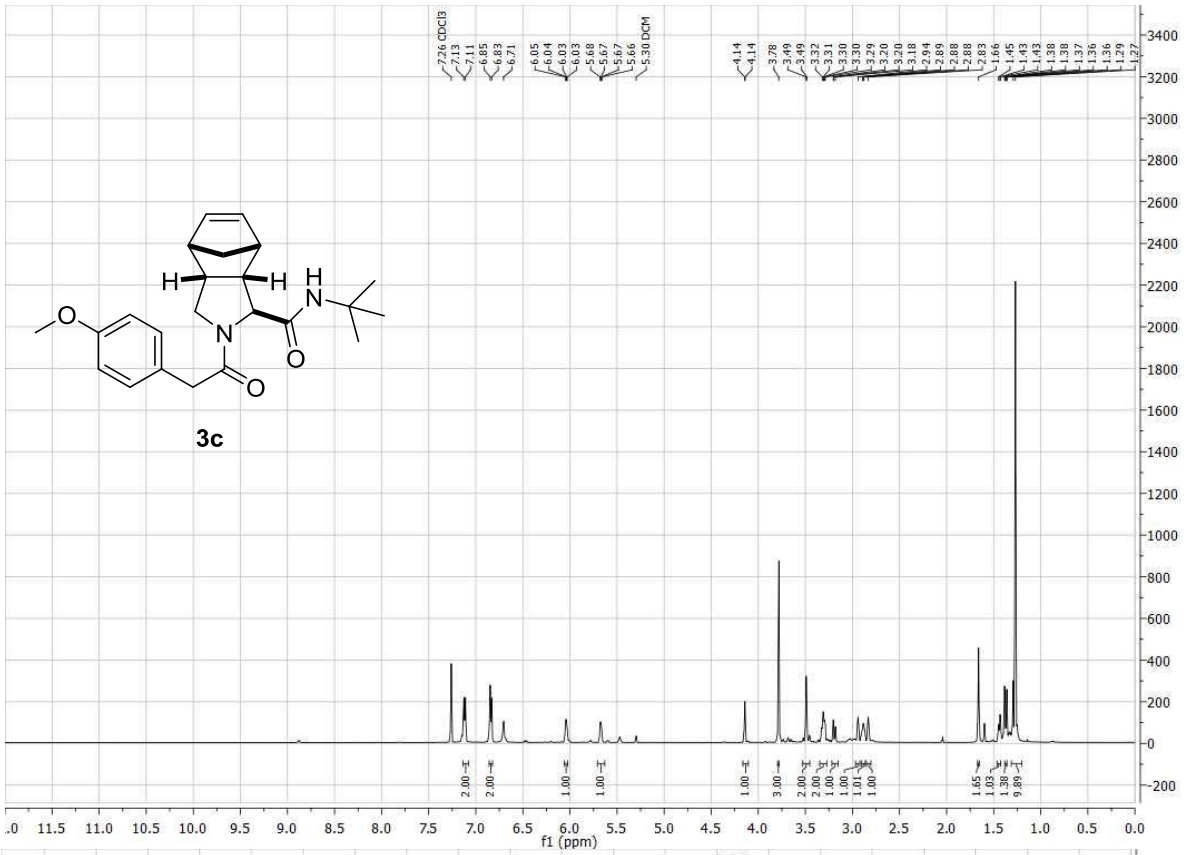
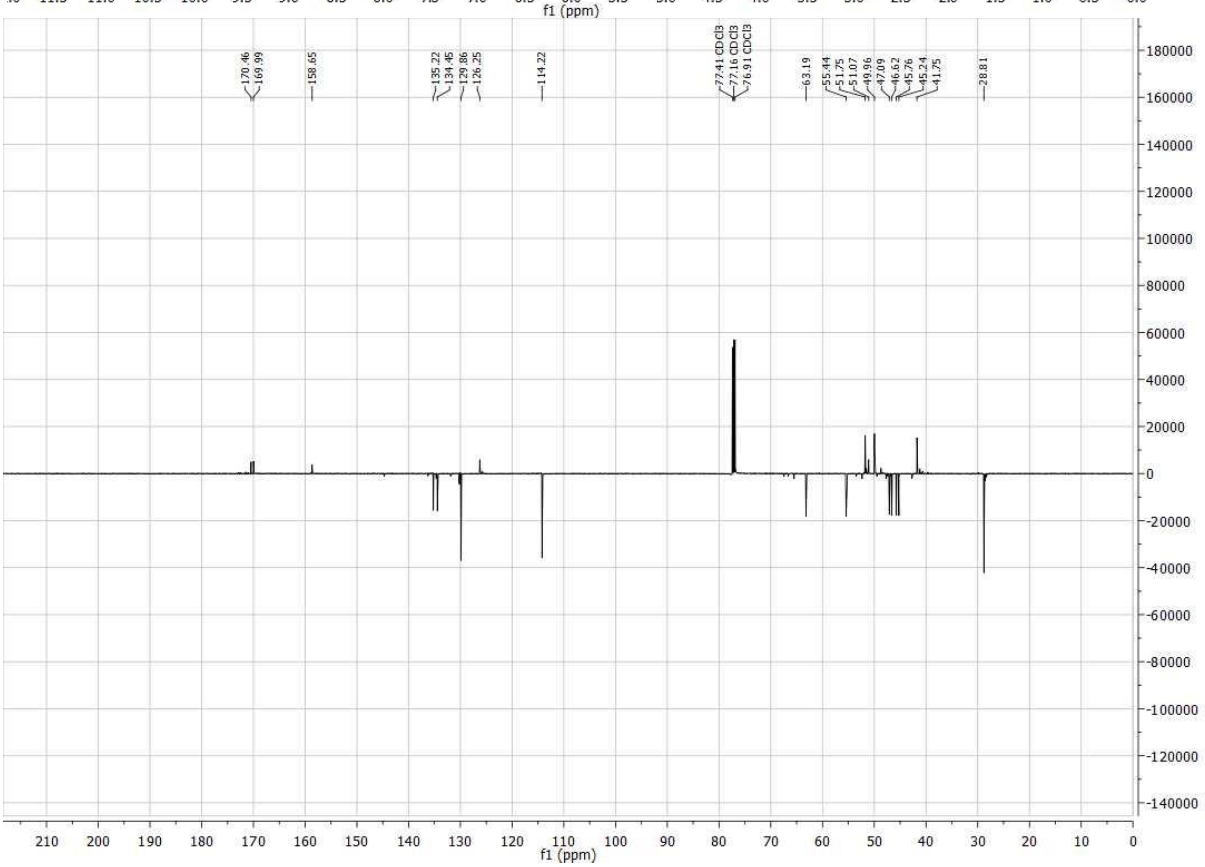


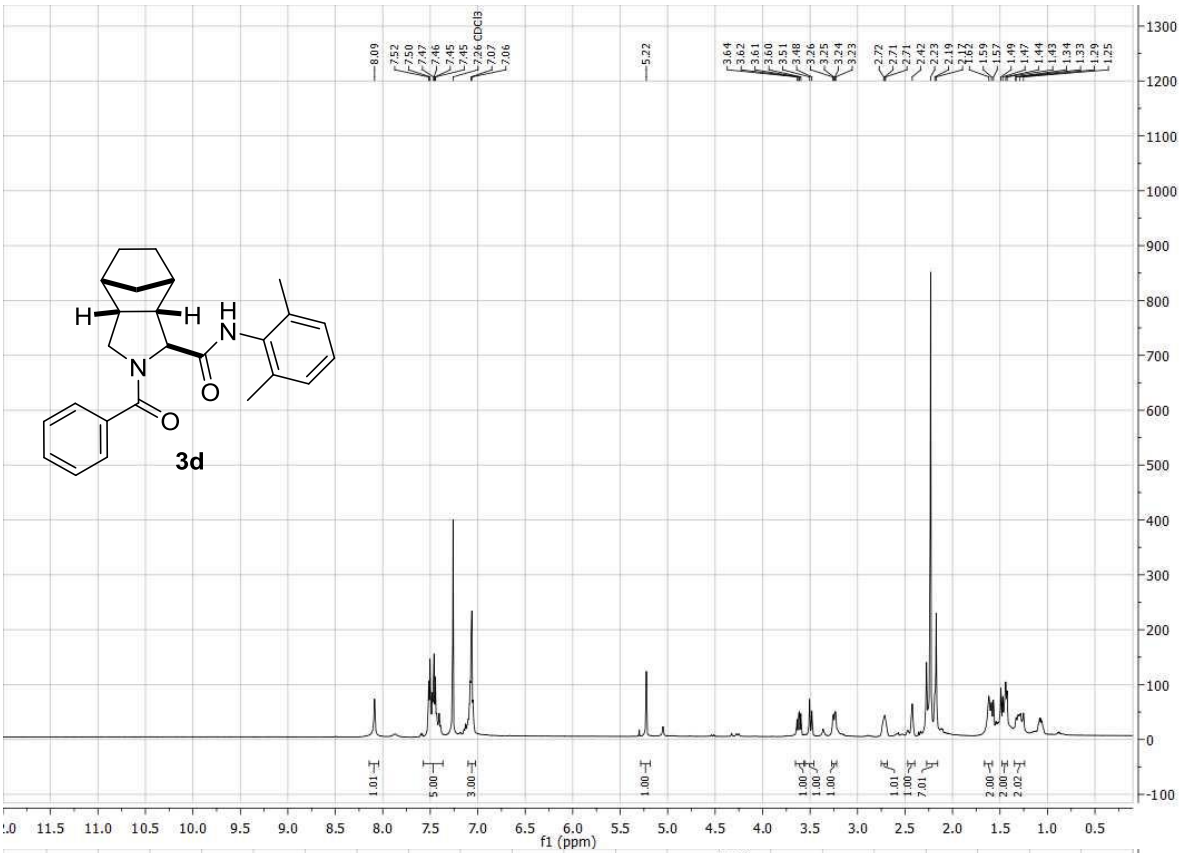

**Figure S1.** High temperature NMR spectra of **3b** in DMSO-$d_6$ showing incomplete coalencence of the rotameric signals.

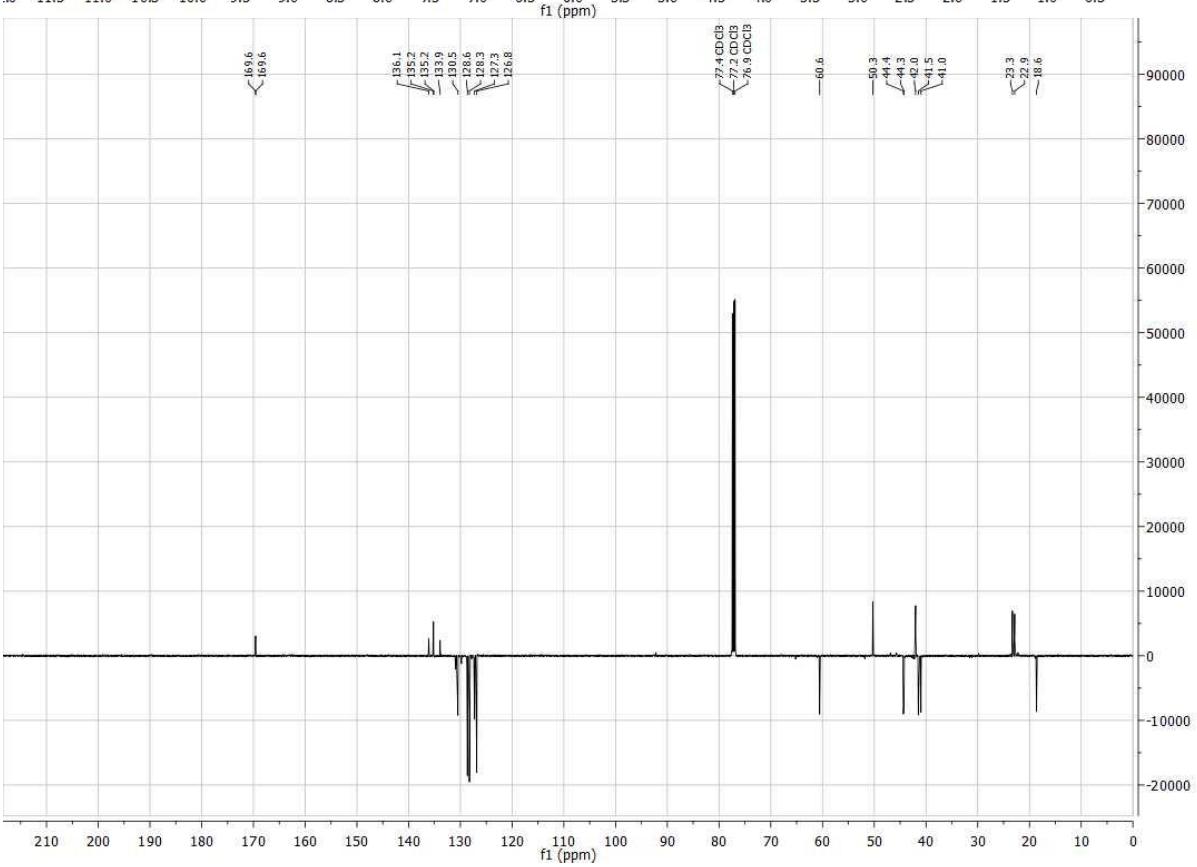

7.26 CDCl3
7.13
7.11
6.85
6.83
6.71
6.05
6.04
6.03
6.03
5.68
5.67
5.67
5.66
5.30 DCM
4.14
4.14
3.78
3.49
3.49
3.32
3.31
3.30
3.30
3.29
3.20
3.20
3.18
2.94
2.89
2.88
2.88
2.83
1.66
1.45
1.43
1.43
1.38
1.38
1.37
1.36
1.36
1.29
1.27
2.00
2.00
1.00
1.00
1.00
3.00
2.00
2.00
1.00
1.01
1.00
1.65
1.03
1.38
9.89
f1 (ppm)

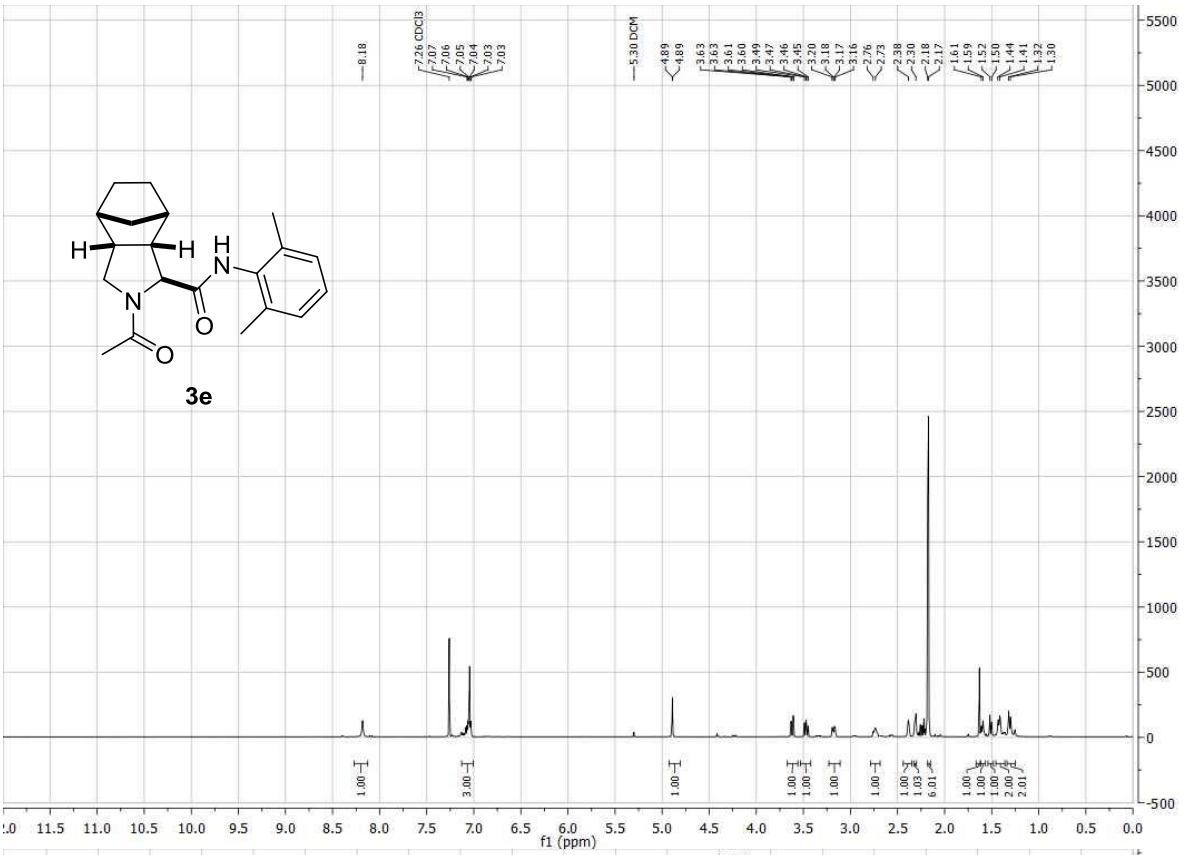

170.46
169.99
158.65
135.22
134.46
129.86
126.25
114.22
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
63.19
55.44
51.75
51.07
49.96
47.09
46.62
45.76
45.24
41.75
28.81
f1 (ppm)


H
H
H
N
O
N
O
O

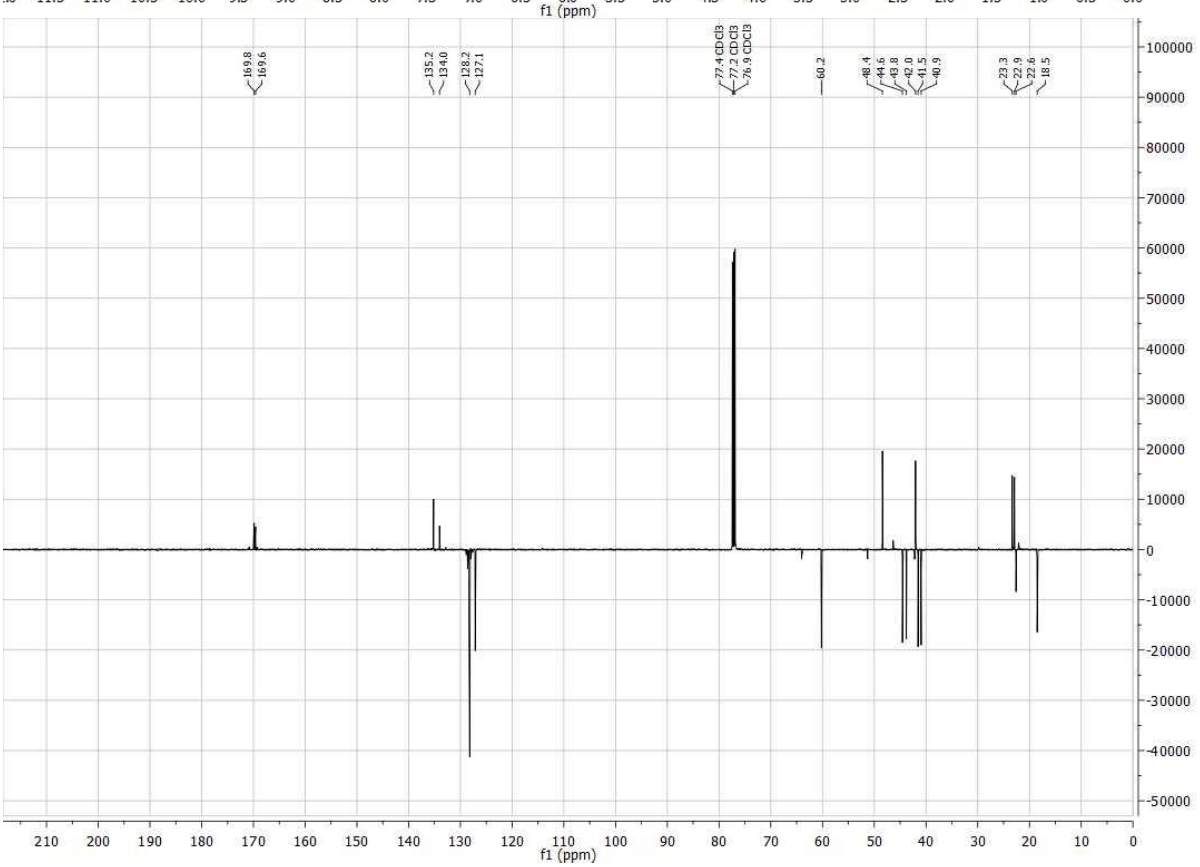
**3c**

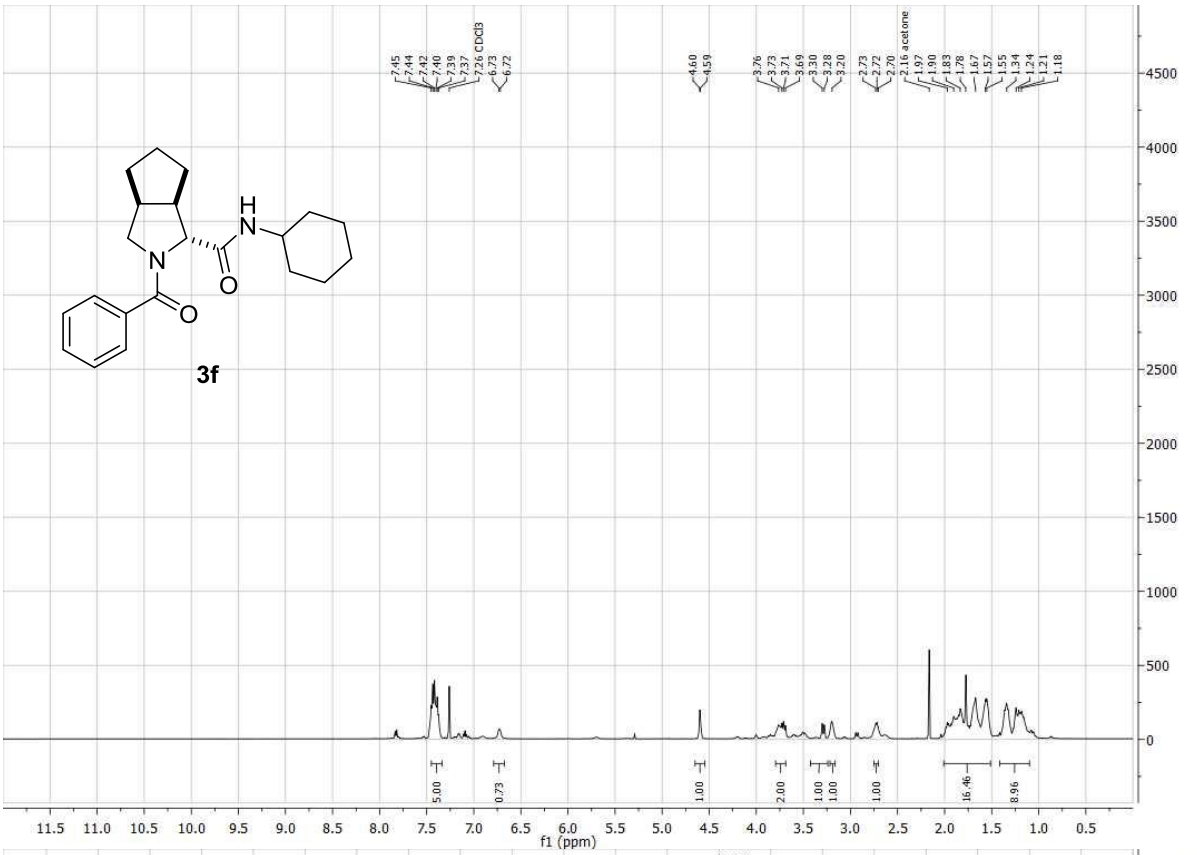

3d
f1 (ppm)


f1 (ppm)

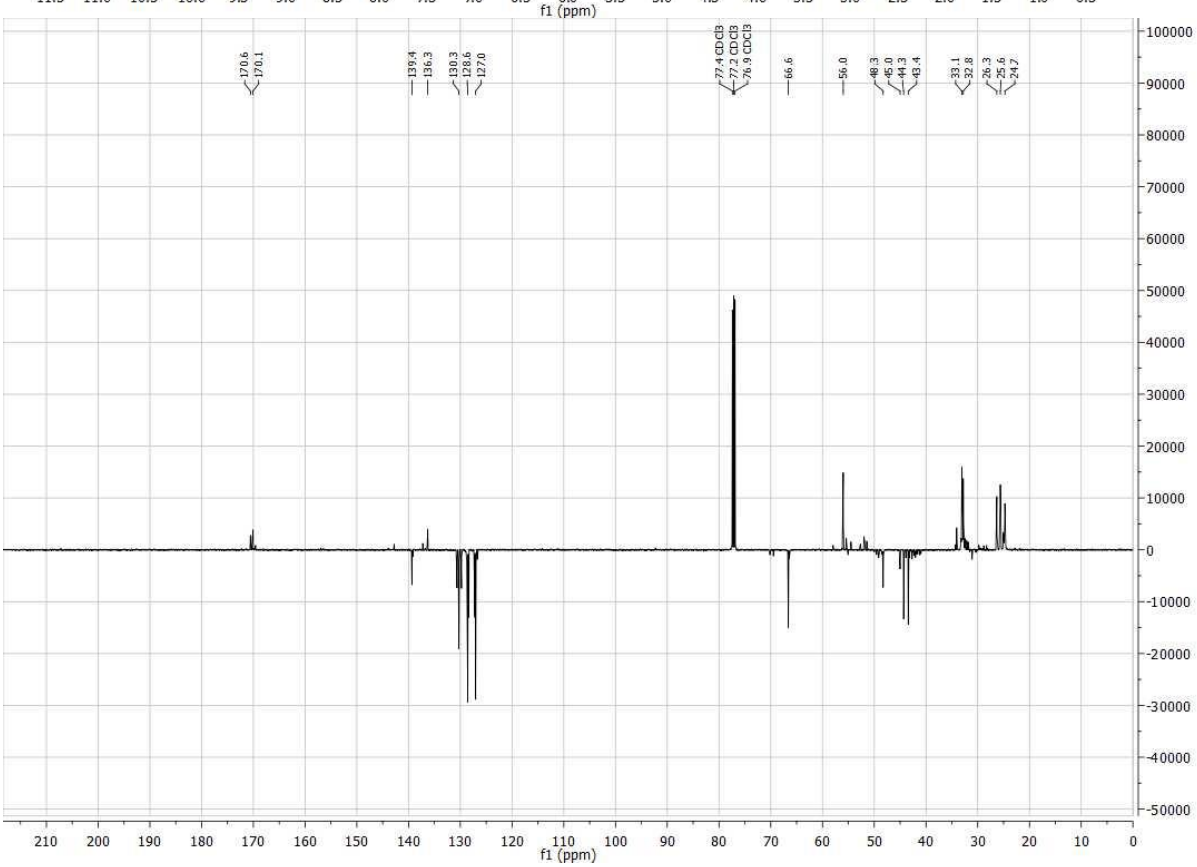

8.18
7.26 CDCl3
7.07
7.06
7.05
7.04
7.03
7.03
5.30 DCM
4.89
4.89
3.63
3.63
3.61
3.60
3.49
3.47
3.46
3.45
3.20
3.18
3.17
3.16
2.76
2.73
2.38
2.30
2.18
2.17
1.61
1.59
1.52
1.50
1.44
1.41
1.32
1.30
1.00
3.00
1.00
1.00
1.00
1.00
1.00
1.03
6.01
1.00
1.00
2.00
2.01
f1 (ppm)

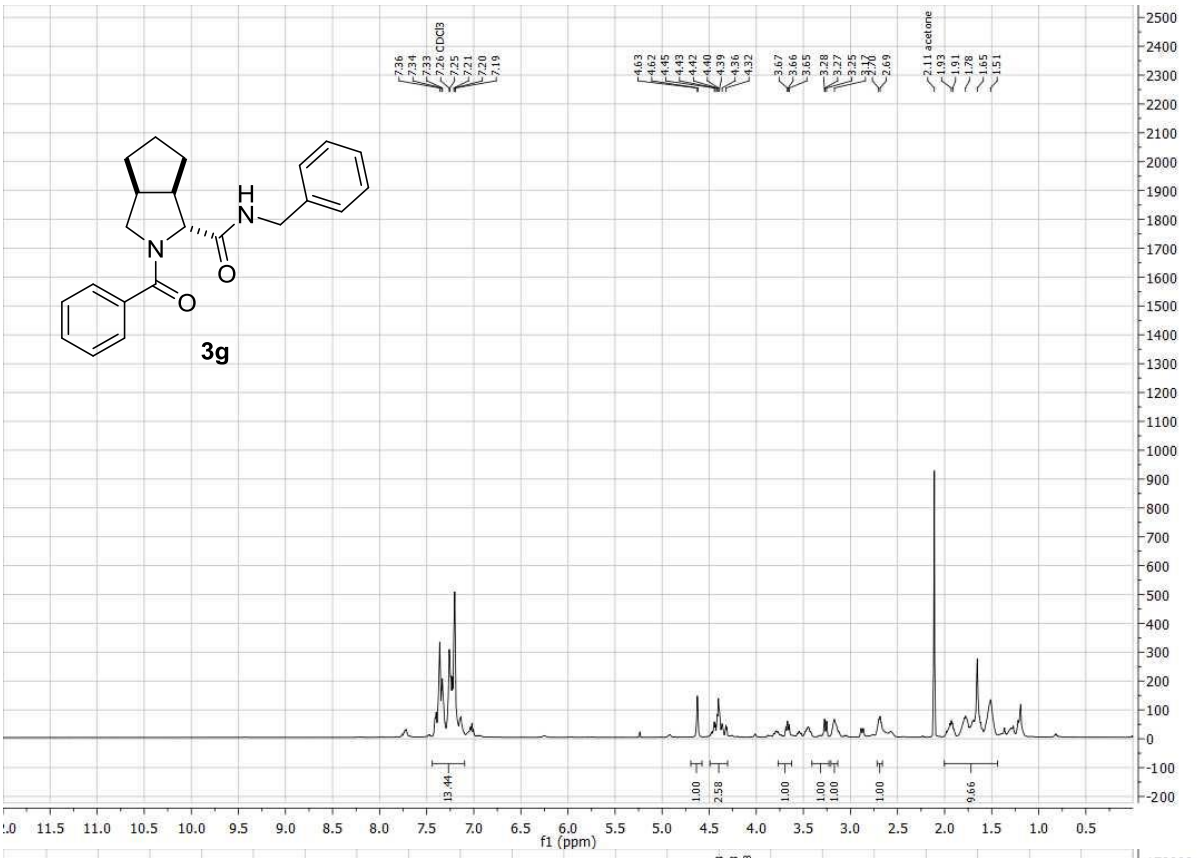
**3e**

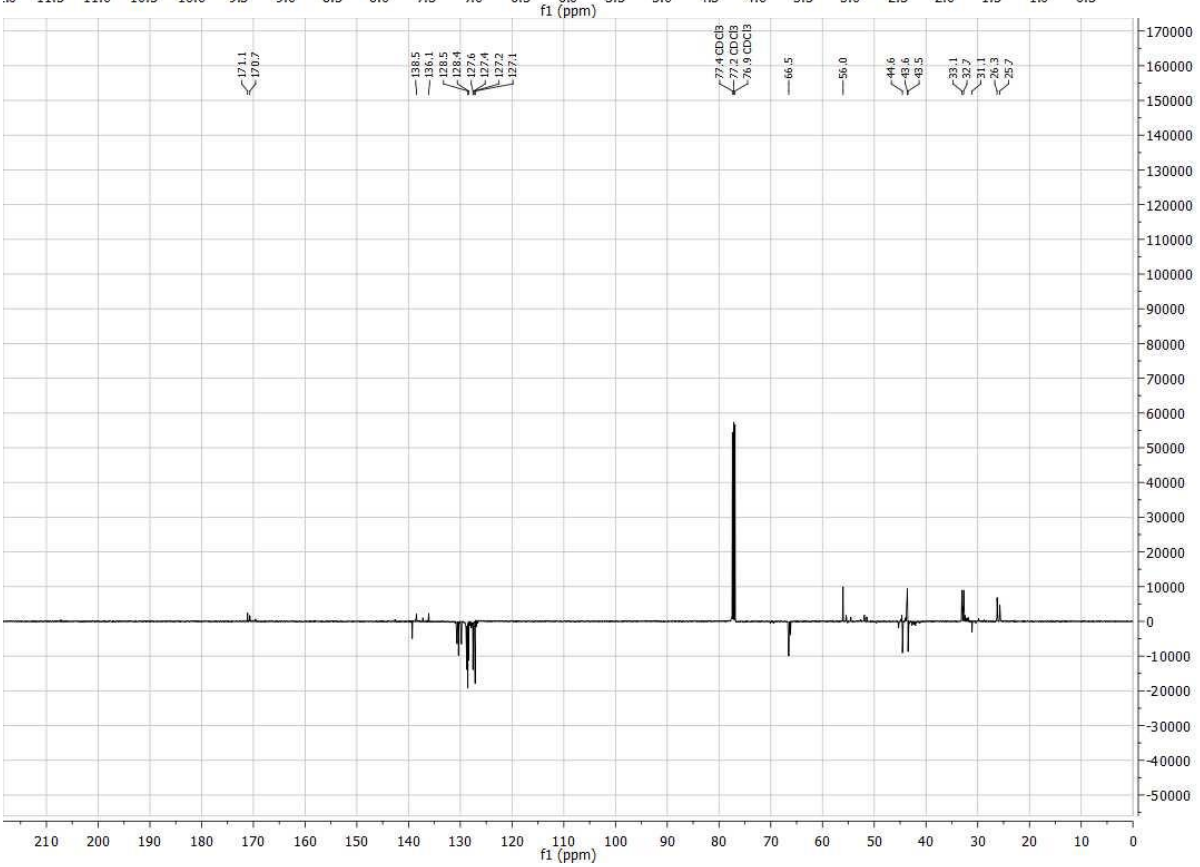

169.8
169.6
135.2
134.0
128.2
127.1
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
60.2
48.4
44.6
43.8
42.0
41.5
40.9
23.3
22.9
22.6
18.5
f1 (ppm)

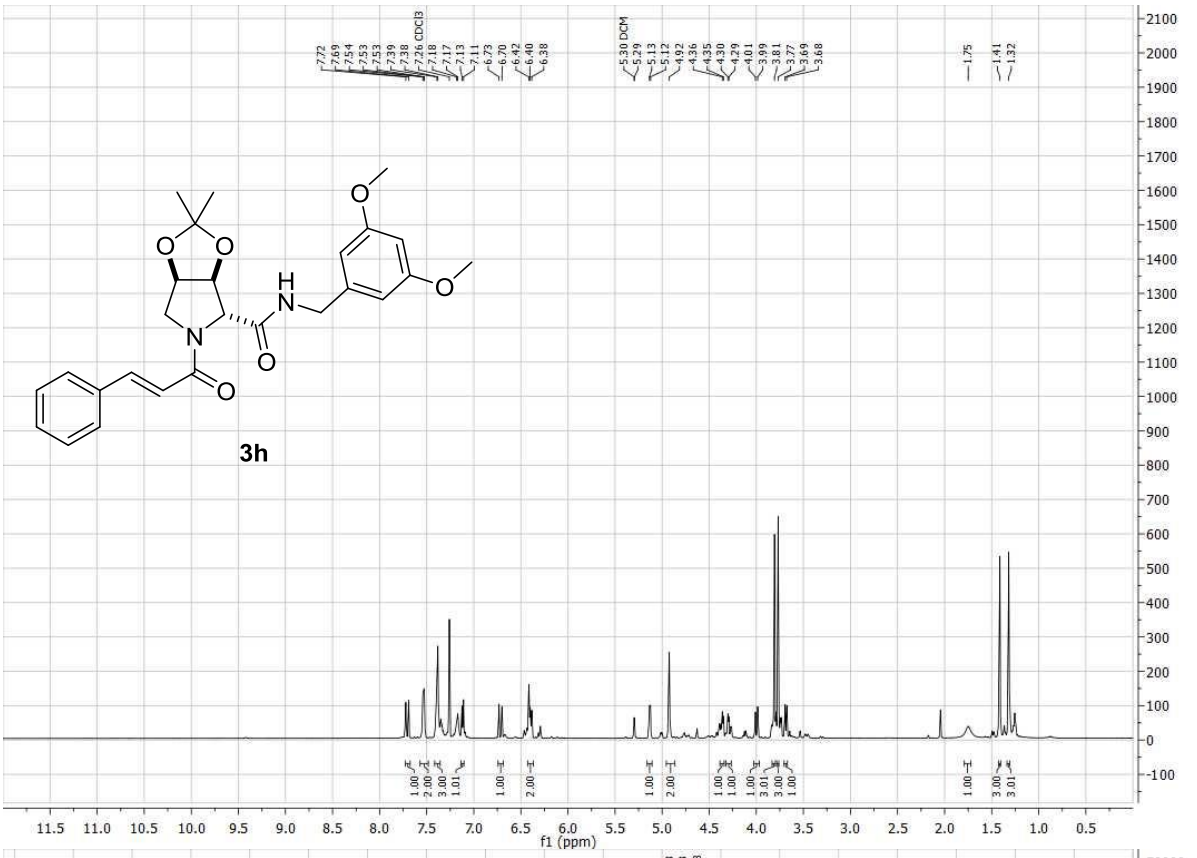

7.45
7.44
7.42
7.40
7.39
7.37
7.26 CDCl3
6.73
6.72
4.60
4.59
3.76
3.73
3.71
3.69
3.30
3.28
3.20
2.73
2.72
2.70
2.16 acetone
1.97
1.90
1.83
1.78
1.67
1.57
1.55
1.34
1.24
1.21
1.18
5.00
0.73
1.00
2.00
1.00
1.00
1.00
16.46
8.96
f1 (ppm)

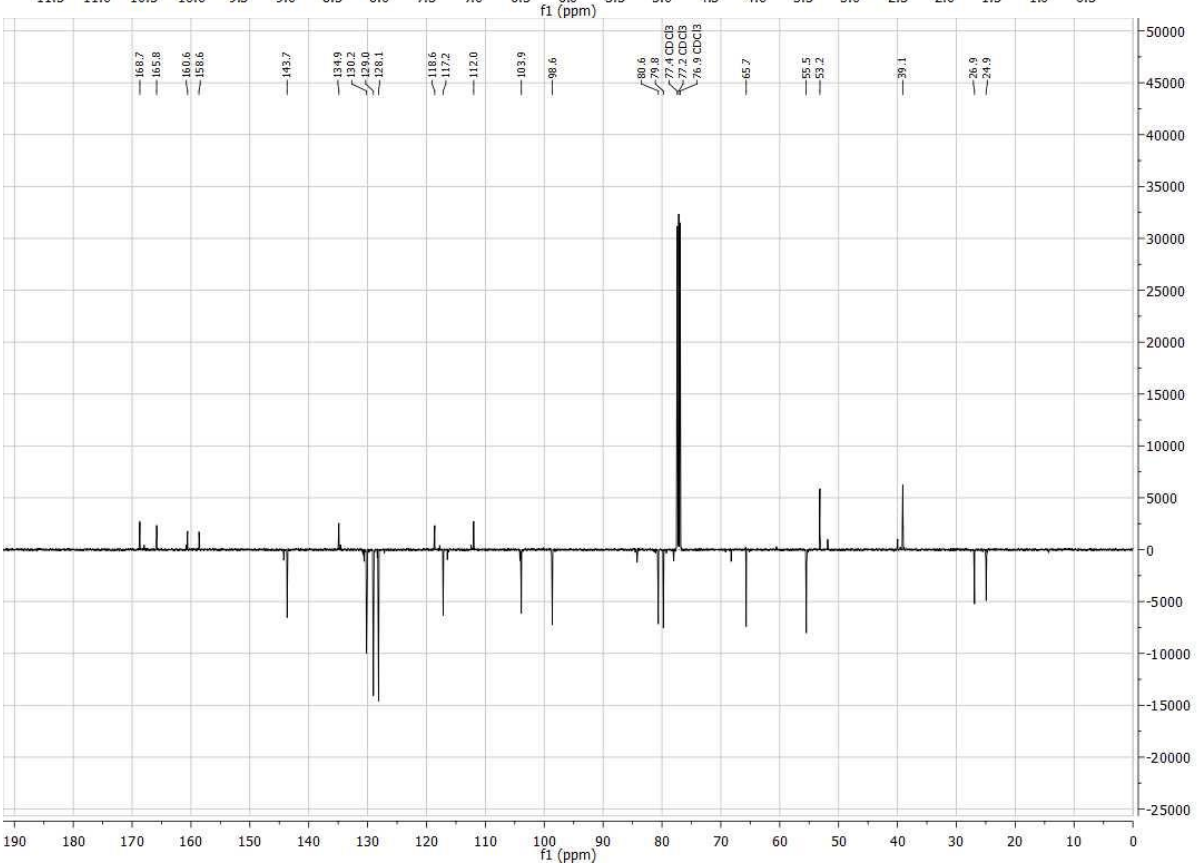
**3f**

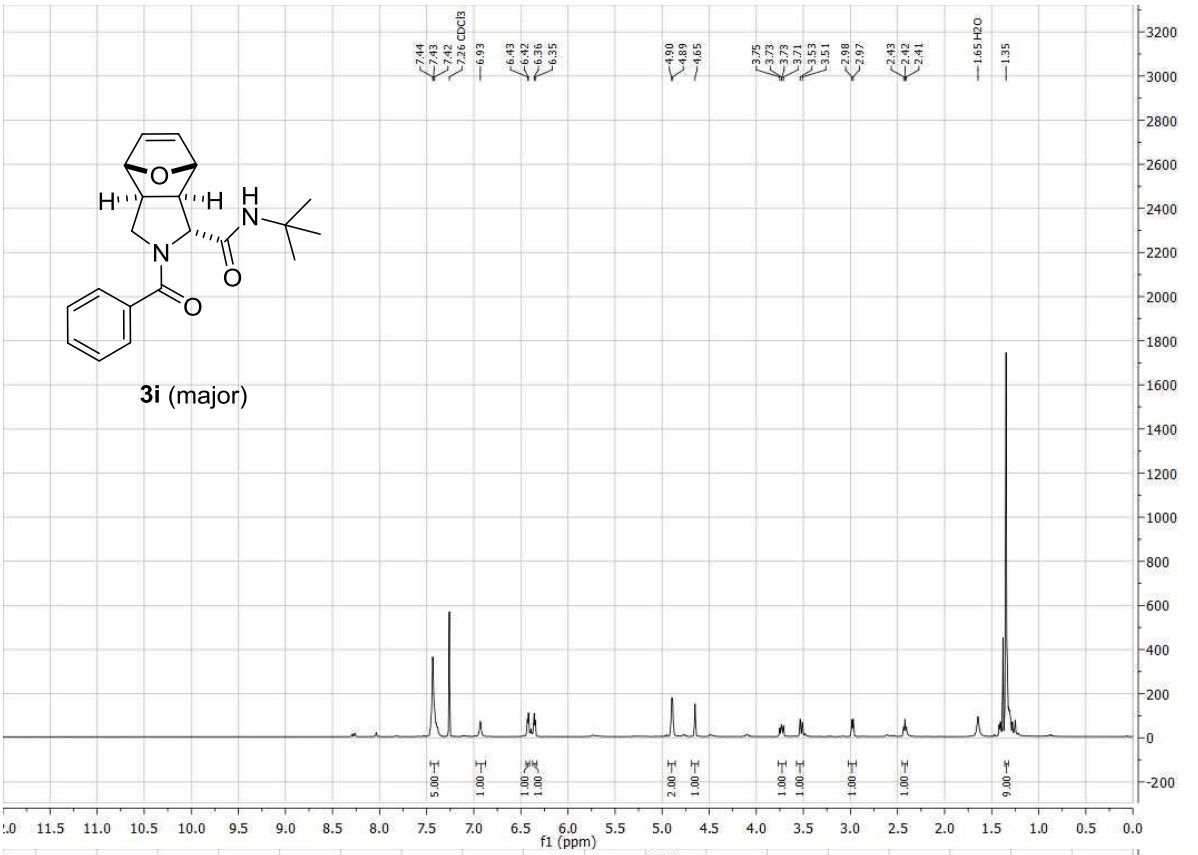

170.6
170.1
139.4
136.3
130.3
128.6
127.0
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
66.6
56.0
48.3
45.0
44.3
43.4
33.1
32.8
26.3
25.6
24.7
f1 (ppm)


7.36
7.34
7.33
7.26 CDCl3
7.25
7.21
7.20
7.19
4.63
4.62
4.45
4.43
4.42
4.40
4.39
4.36
4.32
3.67
3.66
3.65
3.28
3.27
3.25
3.17
3.16
2.69
2.11 acetone
1.93
1.91
1.78
1.65
1.51
13.44
1.00
2.58
1.00
1.00
1.00
1.00
9.66
f1 (ppm)

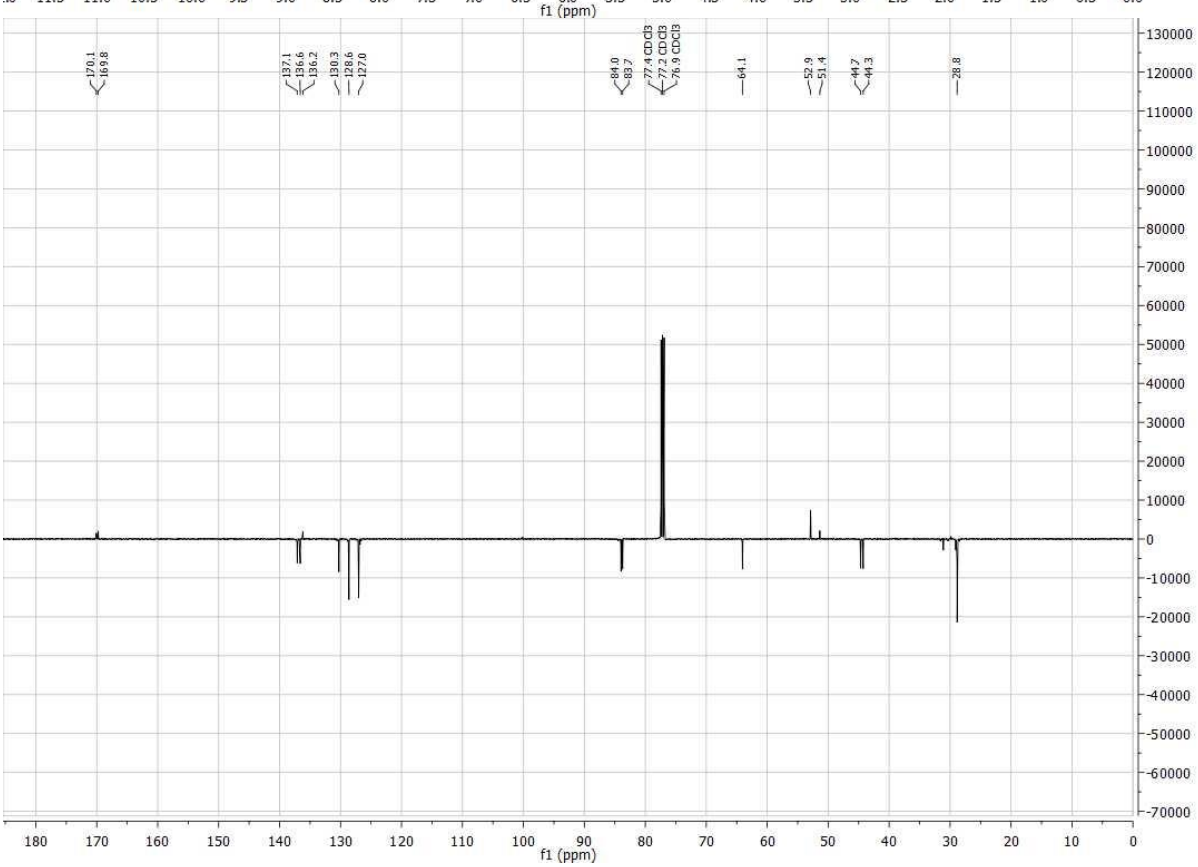

171.1
170.7
138.5
136.1
128.5
128.4
127.6
127.4
127.2
127.1
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
66.5
56.0
44.6
43.6
43.5
33.1
32.7
31.1
26.3
25.7
f1 (ppm)

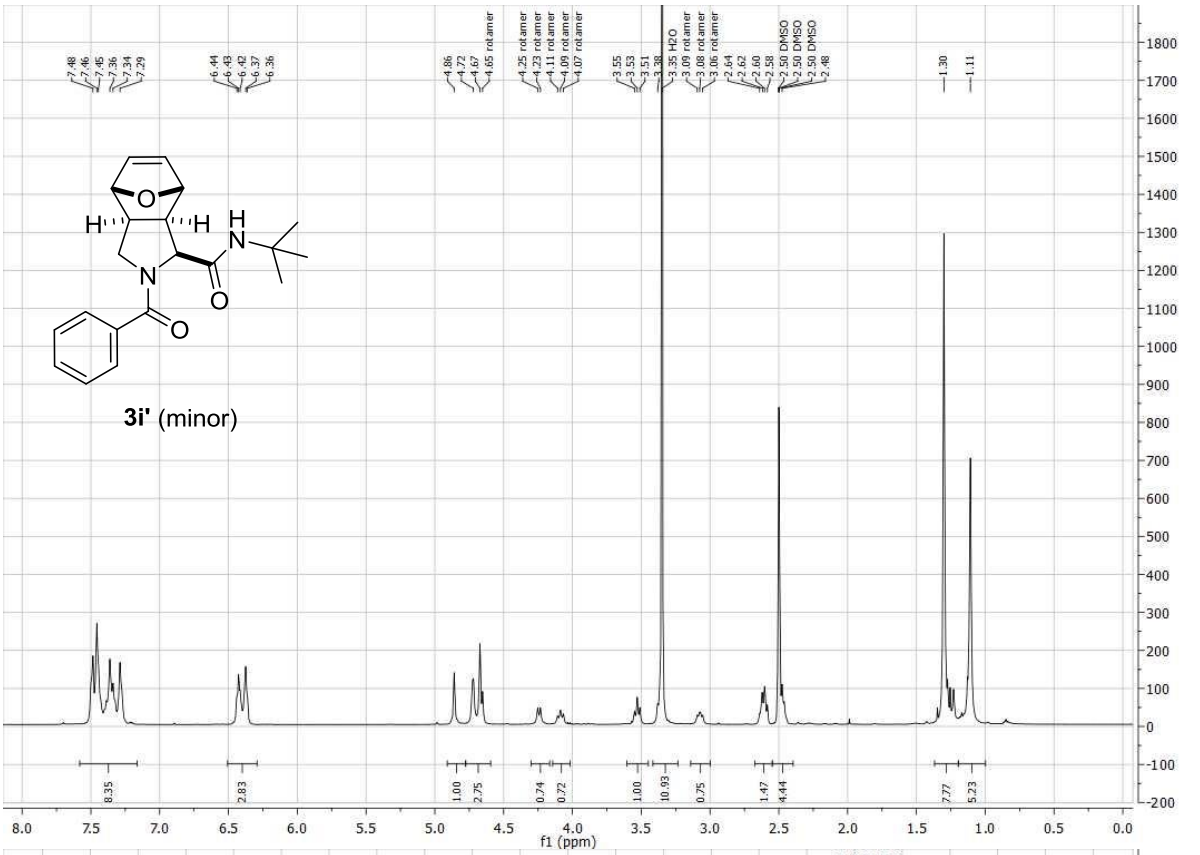

7.72
7.69
7.54
7.53
7.53
7.53
7.39
7.38
7.26 CDCl3
7.18
7.17
7.13
7.11
6.73
6.70
6.42
6.40
6.38
5.30 DCM
5.29
5.13
5.12
4.92
4.36
4.35
4.30
4.29
4.01
3.99
3.81
3.77
3.69
3.68
1.75
1.41
1.32
O
O
O
H
N
N
O
O
3h
f1 (ppm)


168.7
165.8
160.6
158.6
143.7
134.9
130.2
129.0
128.1
118.6
117.2
112.0
103.9
98.6
80.6
79.8
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
65.7
55.5
53.2
39.1
26.9
24.9
f1 (ppm)

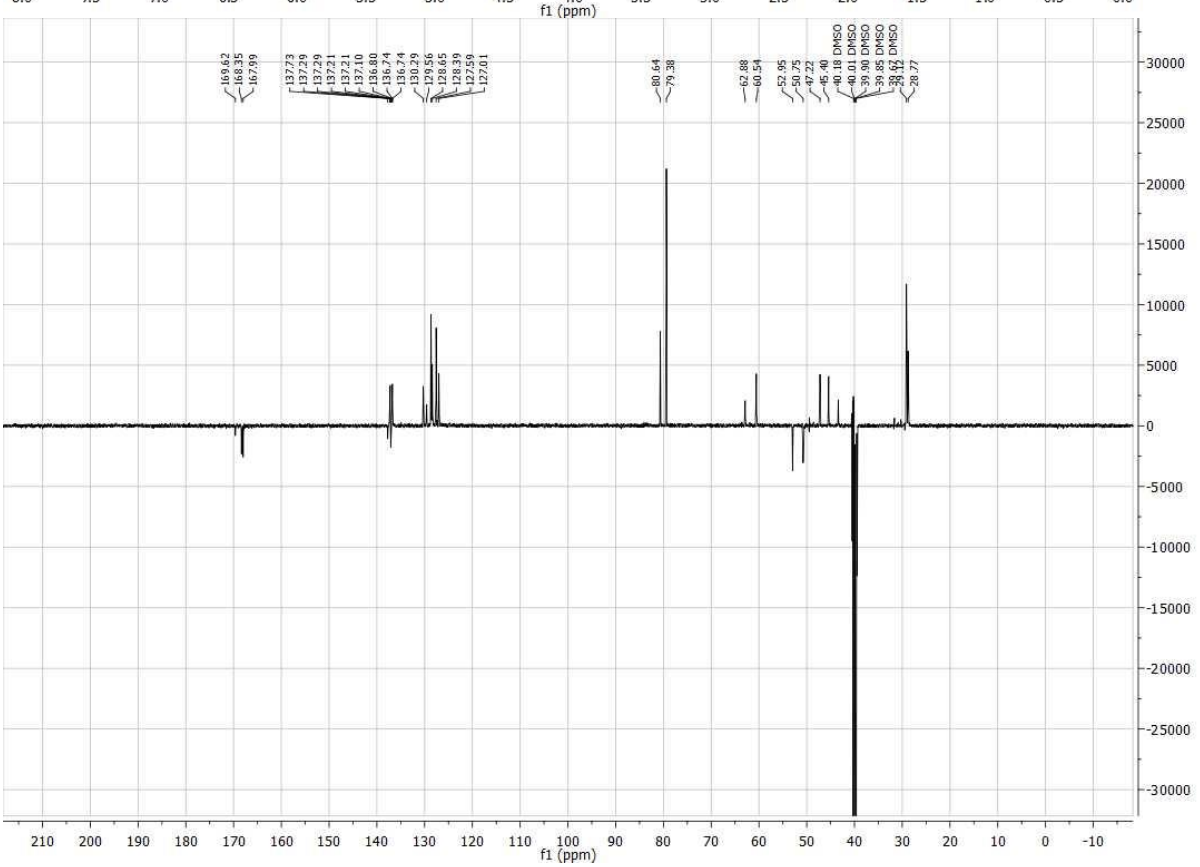

7.44
7.43
7.42
7.26 CDCl3
6.93
6.43
6.42
6.36
6.35
4.90
4.89
4.65
3.75
3.73
3.73
3.71
3.53
3.51
2.98
2.97
2.43
2.42
2.41
1.65 H2O
1.35
5.00
1.00
1.00
1.00
2.00
1.00
1.00
1.00
1.00
1.00
9.00
f1 (ppm)

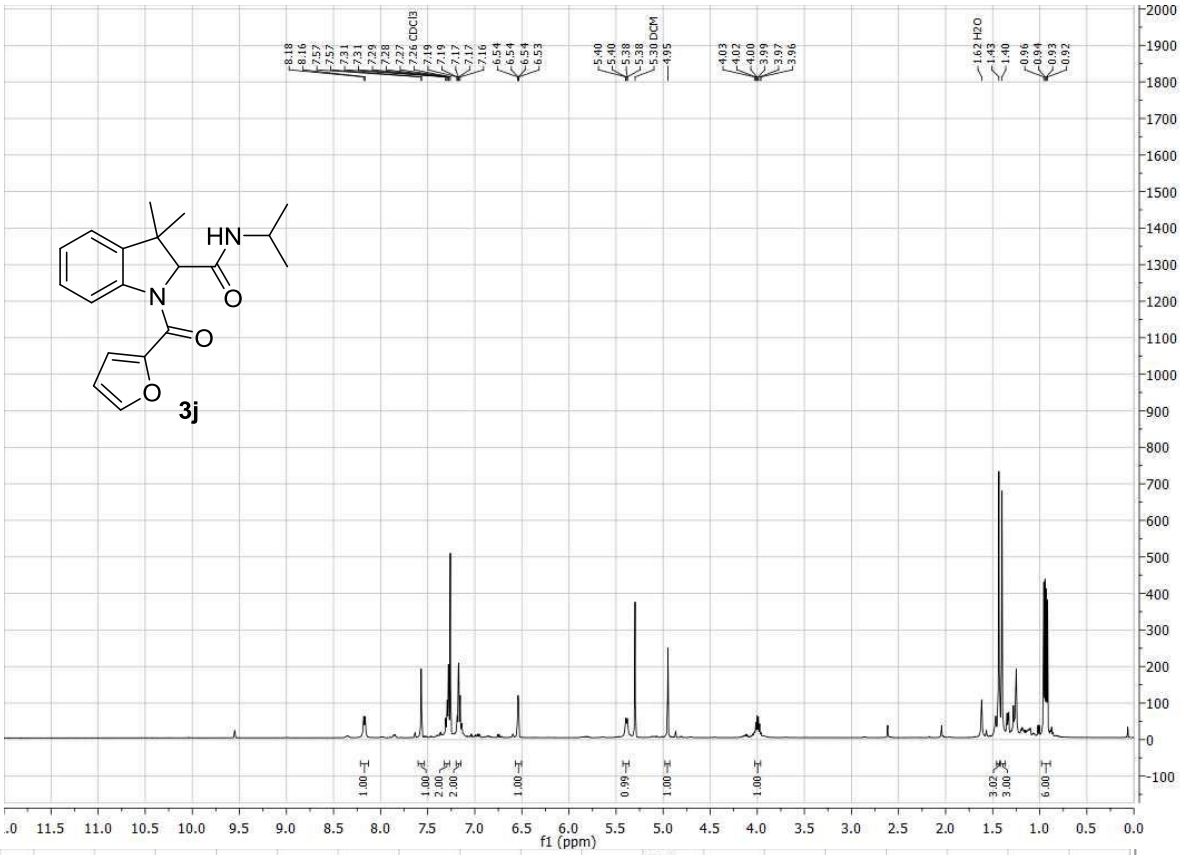
**3i** (major)

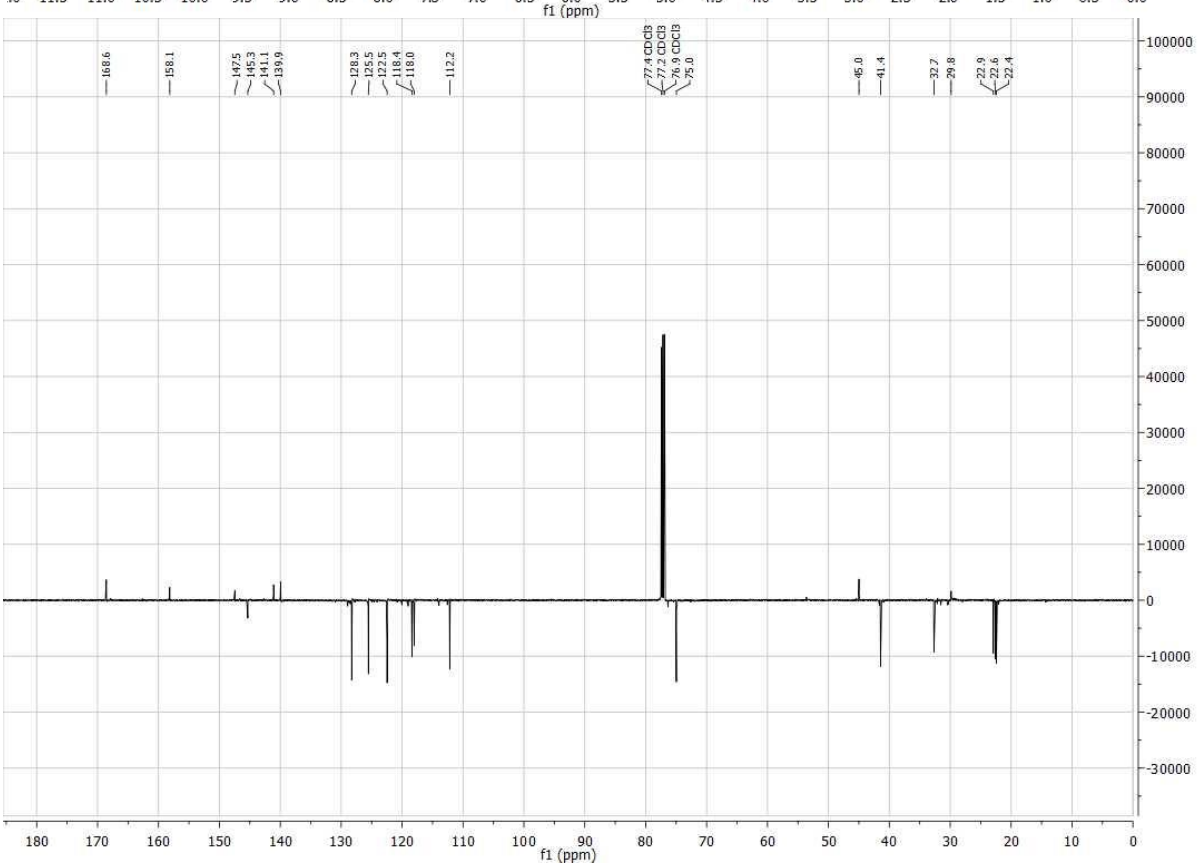

170.1
169.8
137.1
136.6
136.2
130.3
128.6
127.0
84.0
83.7
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
64.1
52.9
51.4
44.7
44.3
28.8
f1 (ppm)

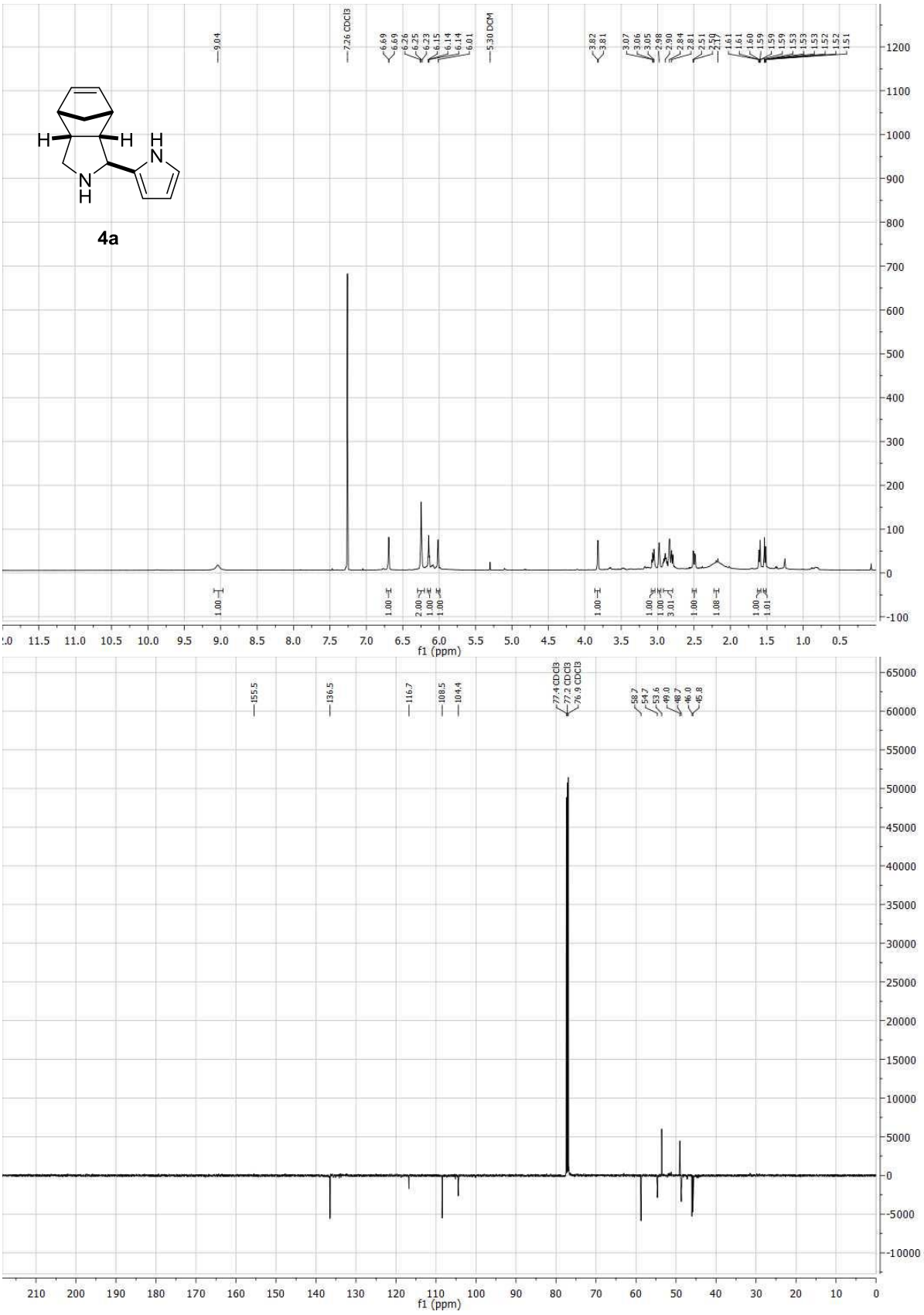

7.48
7.46
7.45
7.36
7.34
7.29
6.44
6.43
6.42
6.37
6.36
4.86
4.72
4.67
4.65 rotamer
4.25 rotamer
4.23 rotamer
4.11 rotamer
4.09 rotamer
4.07 rotamer
3.55
3.53
3.51
3.38
3.35 H2O
3.09 rotamer
3.08 rotamer
3.06 rotamer
2.64
2.62
2.60
2.58
2.50 DMSO
2.50 DMSO
2.50 DMSO
2.48
1.30
1.11
8.35
2.83
1.00
2.75
0.74
0.72
1.00
10.93
0.75
1.47
4.44
7.77
5.23
f1 (ppm)

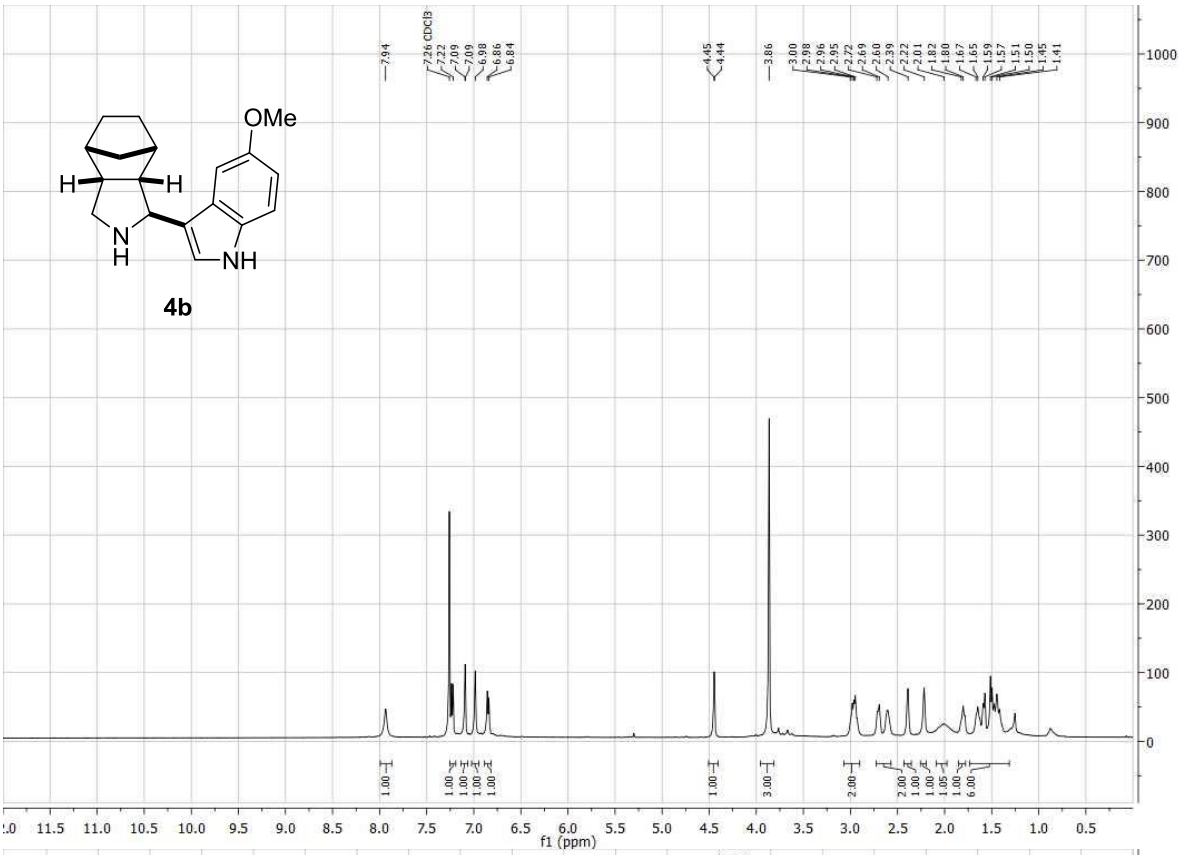
**3i'** (minor)


169.62
168.35
167.99
137.73
137.29
137.29
137.29
137.21
137.10
136.80
136.74
136.74
130.29
129.56
128.65
128.39
127.59
127.01
80.64
79.38
62.88
60.54
52.95
50.75
47.22
45.48
40.18 DMSO
40.01 DMSO
39.90 DMSO
39.85 DMSO
39.69 DMSO
28.77
f1 (ppm)

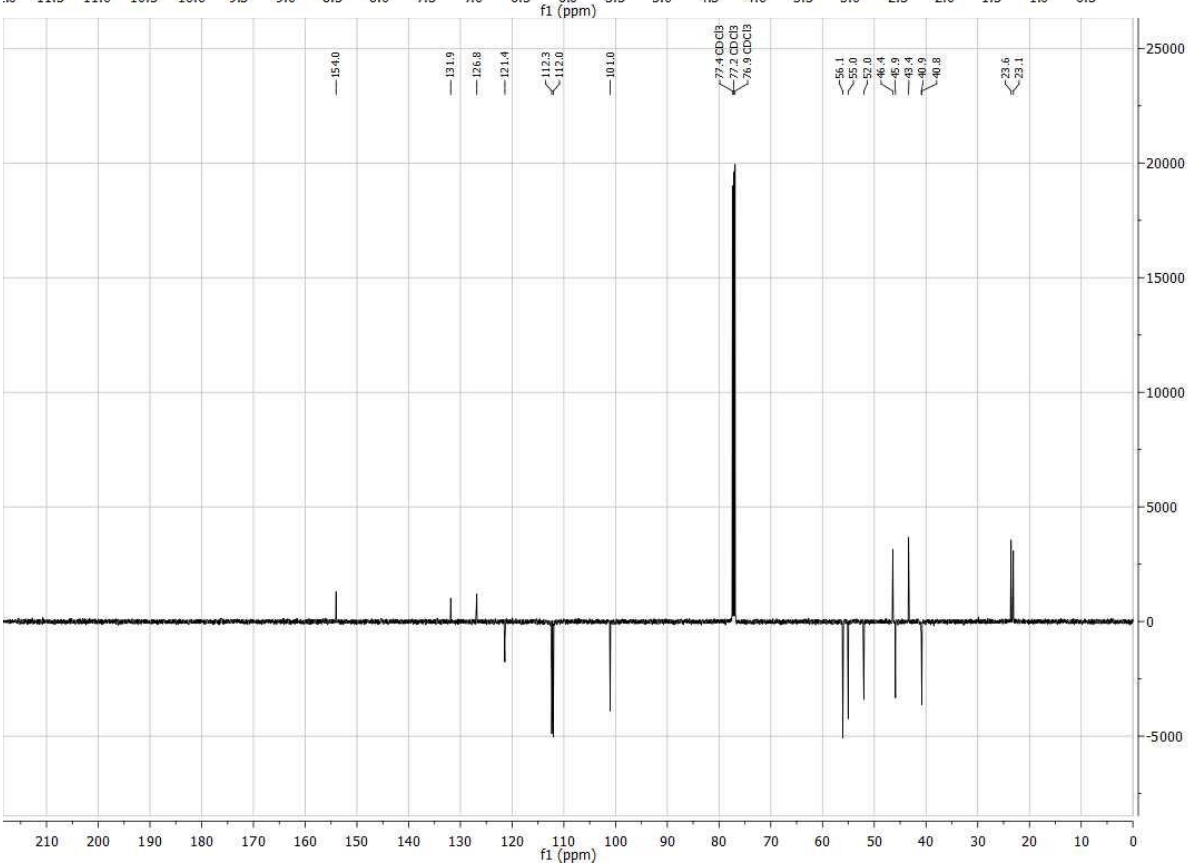

HN
O
N
O
O
3j
8.18
8.16
7.57
7.57
7.31
7.31
7.29
7.29
7.27
7.26 CDCl3
7.19
7.19
7.17
7.17
7.16
6.54
6.54
6.54
6.53
5.40
5.40
5.38
5.38
5.30 DCM
4.95
4.03
4.02
4.00
3.99
3.97
3.96
1.62 H2O
1.43
1.40
0.96
0.94
0.93
0.92
1.00
1.00
2.00
2.00
1.00
0.99
1.00
1.00
3.02
3.00
6.00
f1 (ppm)

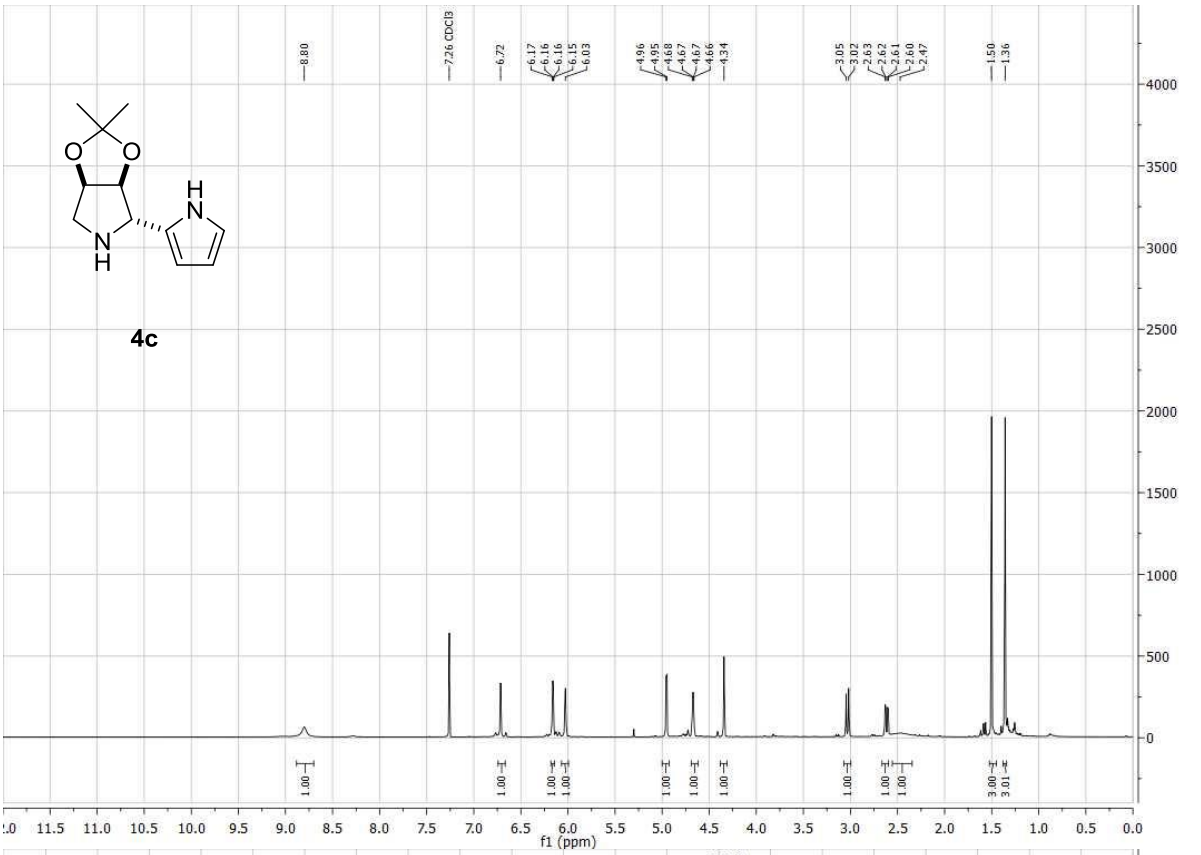

168.6
158.1
147.5
145.3
141.1
139.9
128.3
125.5
122.5
118.4
118.0
112.2
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
75.0
46.0
41.4
32.7
29.8
22.9
22.6
22.4
f1 (ppm)


4a
9.04
7.26 CDCl3
6.69
6.69
6.26
6.25
6.23
6.15
6.14
6.14
6.01
5.30 DCM
3.82
3.81
3.07
3.06
3.05
2.98
2.90
2.84
2.81
2.51
2.50
2.19
1.61
1.61
1.60
1.59
1.59
1.59
1.53
1.53
1.52
1.52
1.51
1.00
1.00
2.00
1.00
1.00
1.00
1.00
3.01
1.00
1.08
1.00
1.01
f1 (ppm)
155.5
136.5
116.7
108.5
104.4
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
58.2
54.7
53.6
49.0
48.7
46.0
45.8
f1 (ppm)

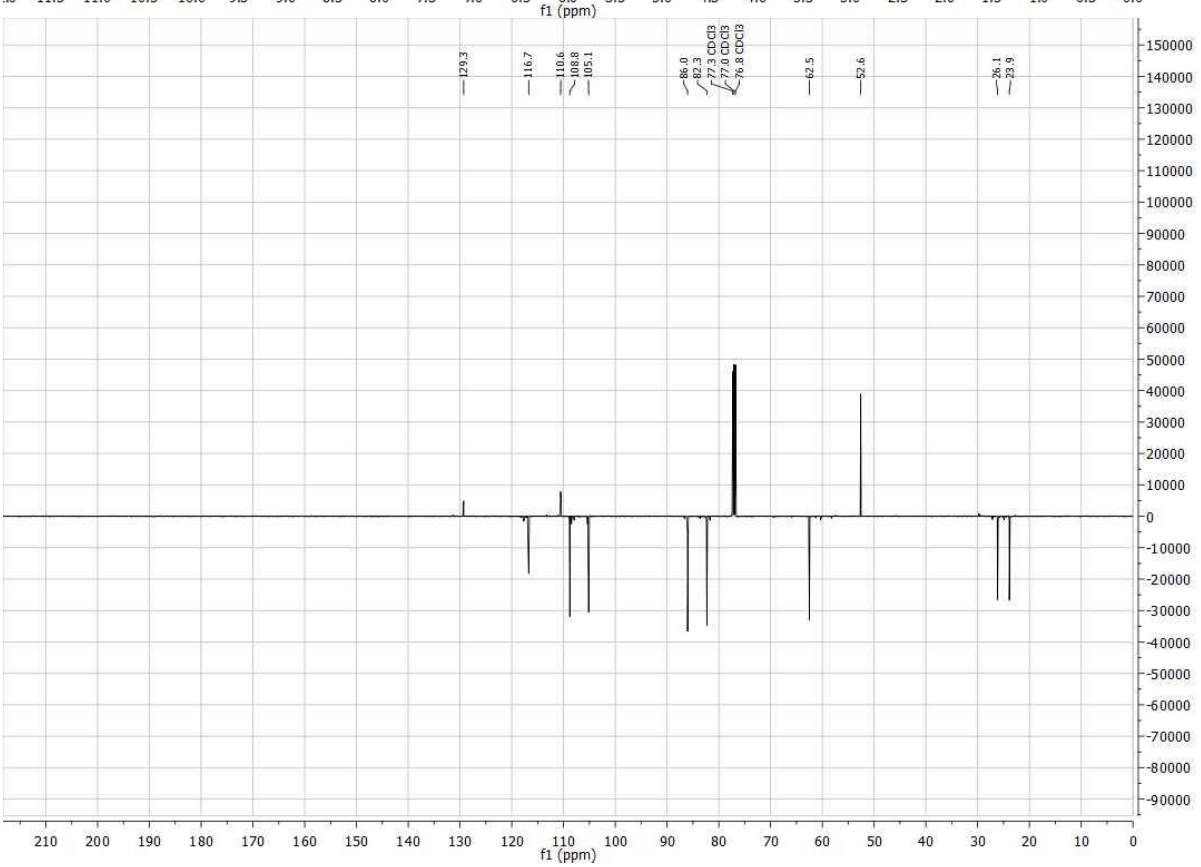

OMe
H
H
N
H
NH
7.94
7.26 CDCl3
7.22
7.09
7.09
6.98
6.86
6.84
4.45
4.44
3.86
3.00
2.98
2.96
2.95
2.72
2.69
2.60
2.39
2.22
2.01
1.82
1.80
1.67
1.65
1.59
1.57
1.51
1.50
1.45
1.41
1.00
1.00
1.00
1.00
1.00
3.00
2.00
2.00
1.00
1.05
1.00
6.00
f1 (ppm)

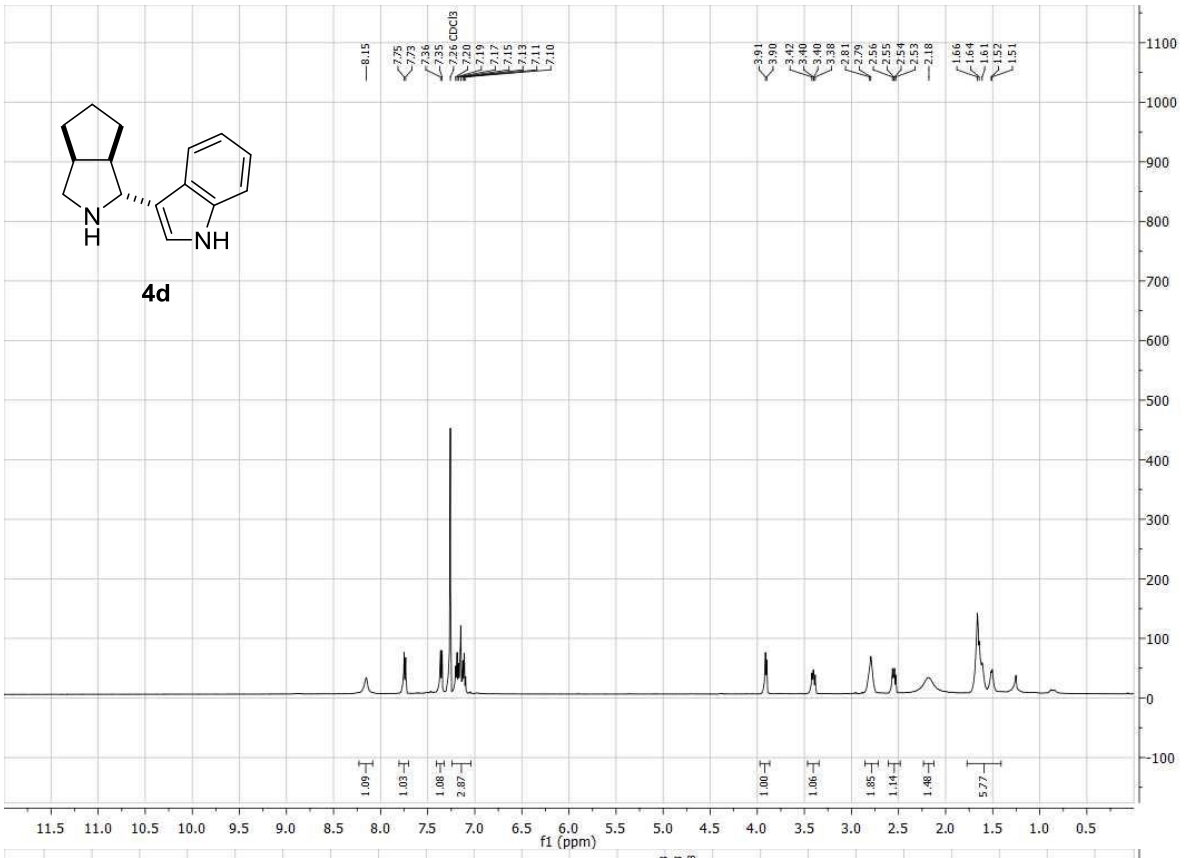
**4b**


154.0
131.9
126.8
121.4
112.3
112.0
101.0
77.4 CDCl3
77.2 CDCl3
76.9 CDCl3
56.1
55.0
52.0
46.4
45.9
43.4
40.9
40.8
23.6
23.1
f1 (ppm)

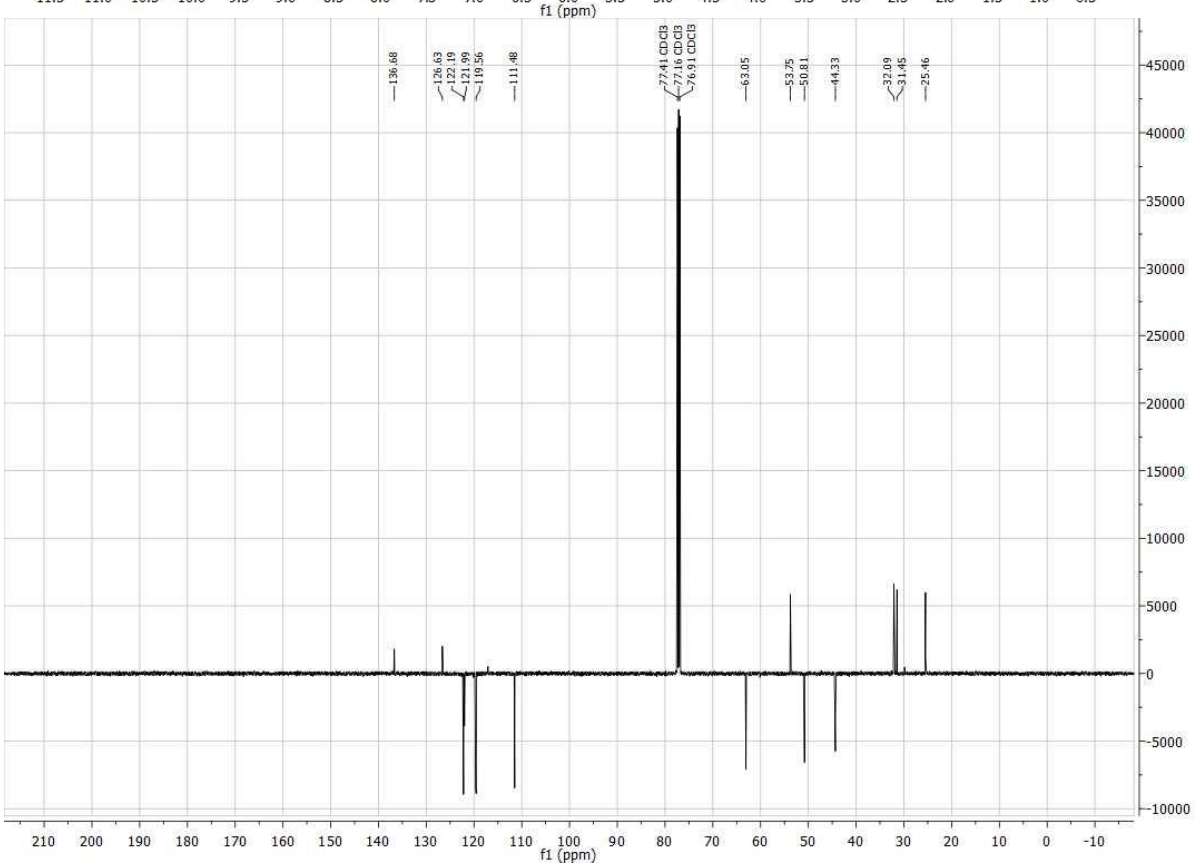

8.80
7.26 CDCl3
6.72
6.17
6.16
6.16
6.15
6.03
4.96
4.95
4.68
4.67
4.67
4.66
4.34
3.05
3.02
2.63
2.62
2.61
2.60
2.47
1.50
1.36
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
1.00
3.00
3.01
f1 (ppm)

**4c**


129.3
116.7
110.6
108.8
105.1
86.0
82.3
77.3 CDCl3
77.0 CDCl3
76.8 CDCl3
62.5
52.6
26.1
23.9
f1 (ppm)


8.15
7.75
7.73
7.36
7.35
7.26 CDCl3
7.20
7.19
7.17
7.15
7.13
7.11
7.10
3.91
3.90
3.42
3.40
3.40
3.38
2.81
2.79
2.56
2.55
2.54
2.53
2.18
1.66
1.64
1.61
1.52
1.51
1.09
1.03
1.08
2.87
1.00
1.06
1.85
1.14
1.48
5.77
f1 (ppm)

**4d**


136.68
126.63
122.19
121.99
119.56
111.48
77.41 CDCl3
77.16 CDCl3
76.91 CDCl3
63.05
53.75
50.81
44.33
32.09
31.46
25.46
f1 (ppm)