Electronic Supplementary Material (ESI) for Organic & Biomolecular Chemistry.


# Supporting Information

# Radical fluorination powered expedient synthesis of 3-fluorobicyclo[1.1.1]pentan-1-amine

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## Table of contents

General Information

Materials S2

Instrumentation S2

Experimental Procedures

General procedure for the decarboxylative fluorination of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid **(3)** to 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid **(4)** S3

Scale-up synthesis of 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid **(3)** S4

Procedure of bicyclo[1.1.1]pentane derivatives S5

$^{1}$H NMR, $^{13}$C NMR, $^{19}$F NMR spectra, Single X-ray crystal structures S9

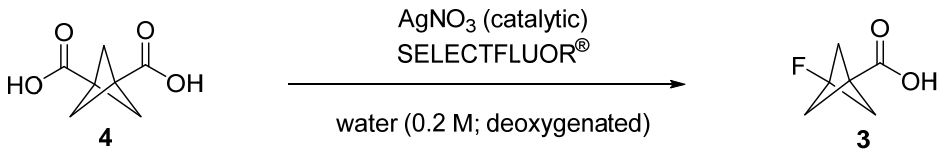
**General Information**

**Materials.** All chemicals were purchased from Sigma-Aldrich, Alfa Aesar and Merck were used as received. Anhydrous *t*-BuOH was taken from Sure/Seal™ bottle (Sigma-Aldrich). Deionised water was degassed with the sonicator followed by bubbling nitrogen. All reactions requiring anhydrous conditions were carried out under argon atmosphere using oven-dried glassware unless otherwise stated. Reaction progress was monitored using Merck 60 F254, 0.25 µm silica gel plates (TLC plates) and spots were visualized by UV and/or potassium permanganate, or ceric ammonium molybdate stain, and/or ninhydrin stain. Flash column chromatography was carried out using Merck 60 F254, 0.040-0.063 µm silica gel. Preparative TLC chromatography was carried out using Merck 60 F254, 0.25 µm silica gel plates. Names of structures were generated using ChemBioDraw ultra 14.0.0.

**Instrumentation.** Proton nuclear magnetic resonance ($^{1}$H NMR) spectra, carbon nuclear magnetic resonance ($^{13}$C NMR) and fluorine ($^{19}$F NMR) spectra were recorded on Bruker 400 MHz with CryoProbe. Chemical shifts for protons were reported in parts per million (ppm) that are referenced to residual protium in the NMR solvent ($CDCl_3$: 7.26 ppm; $CD_3OD$: 3.31 ppm). Chemical shifts for carbon were reported in ppm referenced to the carbon resonances of the NMR solvent ($CDCl_3$: 77.16 ppm; $CD_3OD$: 49.0 ppm). NMR Spectra were processed using MestReNova 10.0.1. Data is presented as follows: chemical shift, multiplicity (s = singlet, d = doublet), integration and coupling constants (*J*) in Hertz (Hz). Electron impact mass spectra (EIMS) were measured using a Finnigan MAT95XP double-focusing mass spectrometer. High resolution electrospray ionization (HRMS ESI) mass spectra were recorded using Agilent 6210 Time-of-Flight LC/MS. Infrared (IR) spectra were measured on a PerkinElmer Spectrum100 FT-IR spectrophotometer. Differential scanning calorimetry and melting point (uncorrected) were measured on Mettler Toledo DSC 1 and the data processed using STARe Default DB V10.00 software. Melting point (uncorrected) was also measured by BÜCHI B-540.

**Experimental Procedures**

**General procedure for the optimization studies of decarboxylative fluorination of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (4) to 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3).**




**4** **3**

To a RBF containing bicyclo[1.1.1]pentane-1,3-dicarboxylic acid **(4)*** (100 mg, 0.425 mmol) was added $AgNO_3$ (5, 7.5, 10 or 20 mol%) and SELECTFLUOR® (1.3, 1.8 or 2.5 eq.), was thoroughly flushed with argon under a condenser. To this mixture was added deoxygenated water (3.2 mL, 0.2 M) and stirred at 50, 65 or 90 °C for 16 h. The reaction was allowed to cool to rt and extracted with diethyl ether. This ether extract was dried over sodium sulphate, filtered and evaporated to dryness. This solid was re-dissolved in pentane and filtered slowly. The filtrate was concentrated *in vacuo* to afford **3** as a white solid.

To recover starting material **4** (if any), the remaining residue above was washed with DCM, dissolved with diethyl ether and filtered. The ether filtrate was concentrated *in vacuo* to recover **4** as a pale yellow solid.

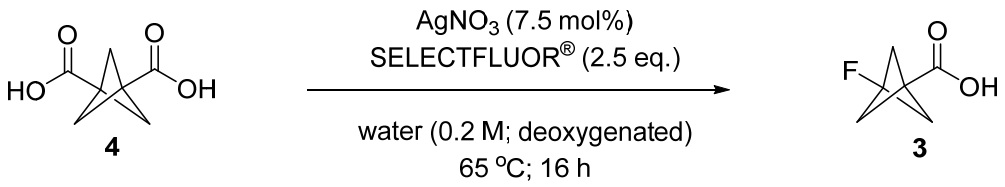
*The bicyclo[1.1.1]pentane-1,3-dicarboxylic acid **(4)** was obtained from TCG Lifesciences (~$150/gram).

**Table 1 Optimization studies for the decarboxylative fluorination of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (4) to 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3).**

| Entry | $AgNO_3$ (mol%) | SELECTFLUOR® (eq.) | Temp (°C) | 3 (%) | Recovered 4 (%) |
|---|---|---|---|---|---|
| 1 | 10 | 1.8 | 65 | 50% | ~2% |
| 2 | 10 | 1.8 | 90 | 47% | 0% |
| 3 | 10 | 1.8 | 50 | 56% | 4% |
| 4 | 10 | 1.3 | 65 | 49% | 18% |
| 5 | 20 | 1.8 | 65 | 50% | 4% |
| 6 | 10 | 2.5 | 65 | 63% | 4% |
| 7 | 7.5 | 2.5 | 65 | 67% | 8% |
| 8 | 5[a] | 2.5 | 65 | 50%[a] | 27% |

[a] Inconsistent yields were observed when $AgNO_3$ is 5 mol% or lower.

**Scale-up of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (4) to 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3).**




To a RBF containing bicyclo[1.1.1]pentane-1,3-dicarboxylic acid **(4)** (3.0 g, 19.2 mmol) was added $AgNO_3$ (245 mg, 1.44 mmol, 7.5 mol%) and SELECTFLUOR® (17.02 g, 48.0 mmol, 2.5 eq.), was thoroughly flushed with argon under a condenser. To this mixture was added deoxygenated water (96 mL) and stirred at 65 °C for 16 h. The reaction was allowed to cool to rt and extracted with diethyl ether. This ether extract was dried over sodium sulphate, filtered and evaporated to dryness. This solid was re-dissolved in pentane and filtered slowly. The filtrate was concentrated *in vacuo* to afford **3** (1.62 g, 65%) as a white solid.

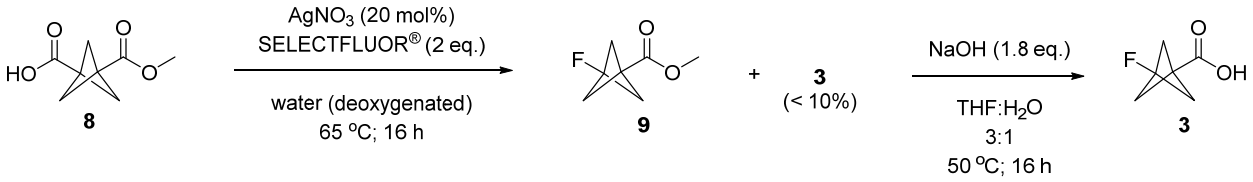
The remaining residue above was washed with DCM, dissolved with diethyl ether and filtered. The ether filtrate was concentrated *in vacuo* to recover **4** (271 mg, 9%) as a pale yellow solid.

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 2.40 (d, J (H,F) = 2.4 Hz, 6H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 174.5 (d, J (C,F) = 36.7 Hz), 74.8 (d, J (C,F) = 328.9 Hz), 55.7 (d, J (C,F) = 22.1 Hz), 28.1 (d, J (C,F) = 47.9 Hz). $^{19}$F NMR (376 MHz, $CDCl_3$) δ -149.8. HRMS: (ESI TOF) *m/z*: $[M-H]^-$ Calcd for $C_6H_6FO_2$ *m/z* 129.0357; Found 129.0352. IR: 2933.5, 1686.9, 1521.5, 1430.7, 1325.8, 1260.0, 1219.0, 1055.4, 945.1, 747.6, 614.2 $cm^{-1}$. Differential scanning calorimetry (DSC): thermal potential of – 699 J/g with an onset temperature of 203 °C. mp: 123 °C. Single X-ray crystal: slow evaporation of **4** in pentane in the refrigerator.

**Table 2 Scale-up studies for the decarboxylative fluorination of bicyclo[1.1.1]pentane-1,3-dicarboxylic acid (4) to 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3).**

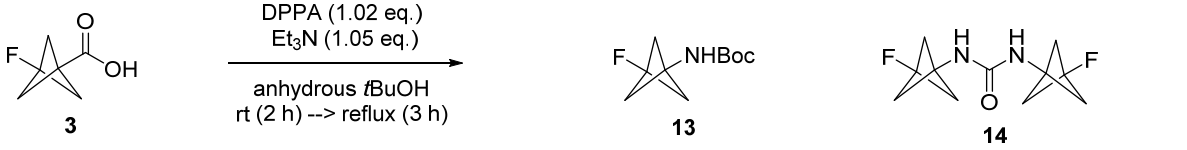
| Entry | SM | AgNO3 (mol %) | SELECTFLUOR® (eq.) | 4 (%) | Recovered 3 (%) |
|---|---|---|---|---|---|
| 1 | 0.5 g | 7.5 | 1.8 | 59% | 8% |
| **2** | **1 g** | **7.5** | **2.5** | **68%** | **2%** |
| 3 | 1 g | 5 | 2.5 | 43% | 28% |
| 4 | 1 g | 10 | 2.5 | 63% | 0% |
| **5** | **3 g** | **7.5** | **2.5** | **65%** | **9%** |
| 6 | 3 g | 10 | 2.5 | 64% | 0% |

**3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3) from 3-(methoxycarbonyl)bicyclo[1.1.1]pentane-1-carboxylic acid (8).**




To a RBF containing 3-(methoxycarbonyl)bicyclo[1.1.1]pentane-1-carboxylic acid **(8)** (100 mg; 0.588 mmol) was added $AgNO_3$ (20.0 mg, 0.188 mmol, 20 mol%) and SELECTFLUOR® (416 mg, 1.18 mmol, 2 eq), was thoroughly flushed with argon under a condenser. To this mixture was added deoxygenated water (2.9 mL) and stirred at 65 °C for 16 h. The reaction was allowed to cool to rt and extracted with diethyl ether. To this ether extract was added NaOH (42.3 mg, 1.058 mmol, 1.8 eq.) dissolved in 3:1 THF:$H_2O$ (2.9 mL), forming a biphasic reaction mixture. This mixture was stirred at 50 °C for 16 h. The reaction was allowed to cool to rt, and the organic layer separated. The aqueous layer was acidified with 2 N HCl and extracted with diethyl ether, dried over sodium sulphate, filtered and evaporated to dryness. This solid was re-dissolved in pentane and filtered slowly. The filtrate was concentrated *in vacuo* to afford **3** (24.3 mg, 32%) as a white solid.

**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13) and 1,3-bis(3-fluorobicyclo[1.1.1]pentan-1-yl)urea (14).**




Formation of side product **14** increases with decreasing scale of reaction.

To a dried 2-necked RBF (heatgun dried under vacuum) was added 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid **(3)** (2.33 g, 17.9 mmol), was thoroughly flushed with argon under a condenser. Anhydrous *t*-BuOH (24 mL) followed by $Et_3N$ (2.62 mL, 18.8 mmol, 1.05 eq.) were added. DPPA (3.93 mL, 18.3 mmol, 1.02 eq.) was added dropwise into the reaction mixture within 15 min and stirred at rt for 2 h, followed by refluxing for another 3 h. The reaction mixture was evaporated under reduced pressure and diluted with diethyl ether. This ether extract was washed with saturated bicarbonate, dried over sodium sulphate, filtered and concentrated *in vacuo*. The residue was purified by silica gel flash chromatography (gradient elution from 0:100 to 100:0 with product **13** eluting from 10:90 to 15:85 and urea side product **14** eluting from 70:30 to 90:10 diethyl ether-pentane) to afford **13** (3.0 g, 83%) as a white solid. The isolated urea side product was further purified by trituration with diethyl ether:DCM mixture (10:0.5) to afford **14** (52 mg, 2.6%) a white solid.

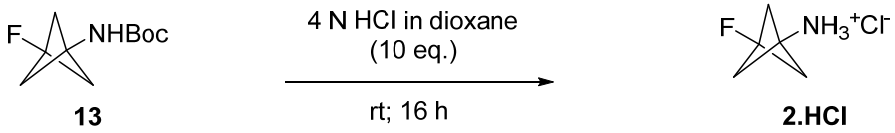
Note: **13** can also be carried to the next step without purification by eluting the reaction mixture through a short pad of silica with 20% diethyl ether in pentane.

**13**: $^{1}$H NMR (400 MHz, $CDCl_3$) δ 2.32 (br d, J (H,F) = 1.8 Hz, 6H)*, 1.45 (s, 9H). $^{1}$H NMR (400 MHz, $CD_3OD$) δ 2.25 (d, J (H,F) = 2.1 Hz, 6H), 1.44 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 154.9, 80.3, 76.9 (d, J (C,F) = 315.6 Hz), 55.4 (d, J (C,F) = 20.4 Hz), 40.0 (d, J (C,F) = 71.5 Hz), 28.5. $^{13}$C NMR (101 MHz, $CD_3OD$) δ 157.4, 80.5, 77.8 (d, J (C,F) = 314.3 Hz), 55.8 (d, J (C,F) = 20.3 Hz), 40.4 (d, J (C,F) = 70.6 Hz), 28.7. $^{19}$F NMR (376 MHz, $CDCl_3$) δ -169.1. IR: 3347.3, 2996.1, 1688.7, 1508.0, 1252.2, 1164.5, 1017.8, 613.5 $cm^{-1}$. DSC: thermal potential of –431 J/g with an onset temperature of 233 °C. mp : 137 °C. Single X-ray crystal: slow evaporation of **13** in pentane at rt.

*Doublet is a broad peak. Depending on the concentration, coupling constant could range from 1.7 to 2.1 ppm.

**14:** $^{1}$H NMR (400 MHz, $CD_3OD$) δ 2.27 (d, J (H, F) = 2.1 Hz, 6H). $^{13}$C NMR (101 MHz, $CD_3OD$) δ159.5, 77.7 (d, J (C, F) = 314.4 Hz), 56.0 (d, J (C, F) = 20.3 Hz), 40.6 (d, J (C, F) = 70.9 Hz). $^{19}$F NMR (376 MHz, $CD_3OD$) δ -169.9. HRMS: (ESI TOF) *m/z*: $[M+H]^+$ Calcd for $C_{11}H_{15}F_2N_2O$ *m/z* 229.1147; Found 229.1145. (ESI TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{11}H_{14}F_2N_2NaO$ m/z 251.0966 ; Found 251.0963. IR: 3550.1, 3016.1, 1641.2, 1562.3, 1244.8, 1086.9, 588.2 $cm^{-1}$. DSC: thermal potential of - 1777 J/g with an onset temperature of 247 °C. mp: 235 - 238 °C (decomposition). Single X-ray crystal: Layering technique with **14** dissolved in DCM layered with diethyl ether on top.

**3-fluorobicyclo[1.1.1]pentan-1-aminium chloride (2.HCl).**

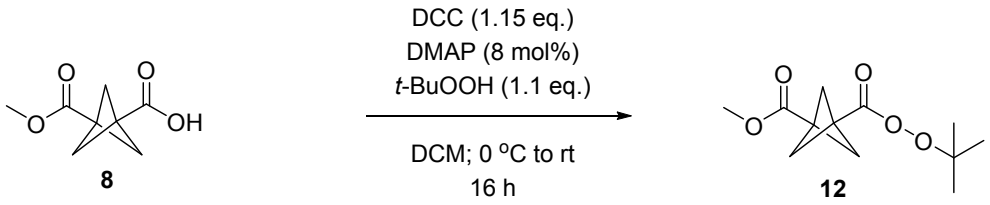



**13** **2.HCl**

To tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate **(13)** (3.0 g, 14.9 mmol) was added 4 N HCl in dioxane (37 mL, 149 mmol, 10 eq.) and stirred overnight at rt. Reaction mixture was then evaporated to dryness to furnish the crude product as a pale yellow solid. This residue was then washed with diethyl ether followed by DCM, to afford **2.HCl** (1.97 g, 96%) as a white solid.

$^{1}$H NMR (400 MHz, $CD_3OD$) δ 2.43 (d, J (H,F) = 2.0 Hz, 6H). $^{13}$C NMR (101 MHz, $CD_3OD$) δ 76.1 (d, J (C,F) = 321.7 Hz), 55.5 (d, J (C,F) = 21.2 Hz), 39.4 (d, J (C,F) = 71.3 Hz). $^{19}$F NMR (376 MHz, $CD_3OD$) δ -171.3. HRMS: (ESI TOF) *m/z*: $[M+H-HCl]^+$ Calcd for $C_5H_9FN$ *m/z* 102.0714; Found 102.0718. IR: 3021.4.2, 2774.1, 1477.3, 1335.9, 1249.9, 1085.3, 589.4 $cm^{-1}$. DSC: thermal potential of -1260 J/g with an onset temperature of 224 °C. mp: 160 °C

**methyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate (12).**

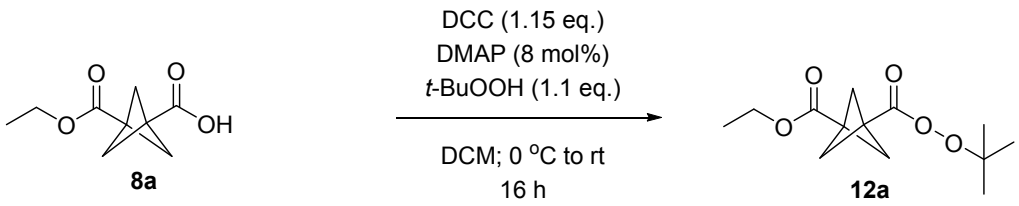



To a solution of 3-(methoxycarbonyl)bicyclo[1.1.1]pentane-1-carboxylic acid **(8)** (100 mg, 0.588 mmol) in DCM (2 mL), was added DMAP (5.74 mg, 0.047 mmol, 8 mol%), followed by a 70% w/w solution of *tert*-butylhydroperoxide in water (83.3 µL, 0.646 mmol, 1.1 eq.), and stirred at 0 °C for 5 min. To this reaction mixture was added a solution of DCC (139 mg, 0.676 mmol, 1.15 eq.) in DCM (1 mL), and the resulting mixture was stirred at 0 °C for 30 min. The reaction mixture was then allowed to warm to rt and stir for 16 h. The reaction mixture was evaporated and filtered through a short pad of silica gel with 20% diethyl ether in petroleum ether, followed by purification with silica gel flash chromatography (gradient elution from 0:100 to 20:80 with product **12** eluting from 10:90 to 15:85 diethyl ether-petroleum ether) to afford **12** (102 mg, 72%) as a colourless solid.*

*We have observed that the compound turns yellow on standing overnight in the refrigerator; however, no significant decomposition of the product was observed after prolonged storage (>30 days) under cold conditions (-20 °C). We have employed both freshly prepared and stored **12** as starting material in our experiments and have observed similar outcomes.

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 3.70 (s, 3H), 2.38 (s, 6H), 1.32 (s, 9H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 169.3, 166.4, 84.0, 53.4, 52.0, 38.6, 35.9, 26.2. HRMS: (ESI TOF) *m/z*: $[M+H]^+$ Calcd for $C_{12}H_{19}O_5$ *m/z* 243.1227; Found 243.1227. (ESI TOF) *m/z*: $[M+Na]^+$ Calcd for $C_{12}H_{18}NaO_5$ *m/z* 265.1046; Found 265.1058. IR: 2991.2, 1766.9, 1724.6, 1367.9, 1343.2, 1263.7, 1207.2, 1104.8, 1004.2 $cm^{-1}$.

**ethyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate (12a).**



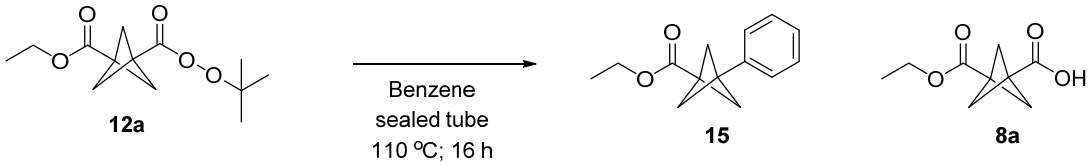

To a solution of 3-(ethoxycarbonyl)bicyclo[1.1.1]pentane-1-carboxylic acid **(8a)** (500 mg, 2.72 mmol) in DCM (7 mL), was added DMAP (26.5 mg, 0.217 mmol, 8 mol%), followed by a 70% w/w solution of *tert*-butylhydroperoxide in water (384 µL, 2.98 mmol, 1.1 eq.), and stirred at 0 °C for 5 min. To this reaction mixture was added a solution of DCC (644 mg, 3.12 mmol, 1.15 eq.) in DCM (6.5 mL), and the resulting mixture was stirred at 0 °C for 30 min. The reaction mixture was then allowed to warm to rt and then stir for 16 h. The reaction mixture was evaporated and filtered through a short pad of silica gel with 20% diethyl ether in petroleum ether, followed by purification with

silica gel flash chromatography (gradient elution from 0:100 to 20:80 with product **12a** eluting from 10:90 to 20:80 diethyl ether-petroleum ether) to afford **12a** (490 mg, 70%) as a pale yellow oil.*

*No significant decomposition of the product was observed after prolonged storage (>20 days) under cold conditions (-20 °C). We have employed both freshly prepared and stored **12a** as starting material in our experiments and have observed similar outcomes.

$^{1}$H NMR (400 MHz, $CDCl_3$) δ 4.14 (q, J = 7.1 Hz, 2H), 2.37 (s, 6H), 1.31 (s, 9H), 1.26 (t, J = 7.1 Hz, 4H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 168.8, 166.2, 83.8, 60.8, 53.2, 38.6, 35.6, 26.1, 14.1. IR: 2981.8, 1773.1, 1733.7, 1369.2, 1269.1, 1204.8, 1022.5 $cm^{-1}$.

**ethyl 3-phenylbicyclo[1.1.1]pentane-1-carboxylate (15).**

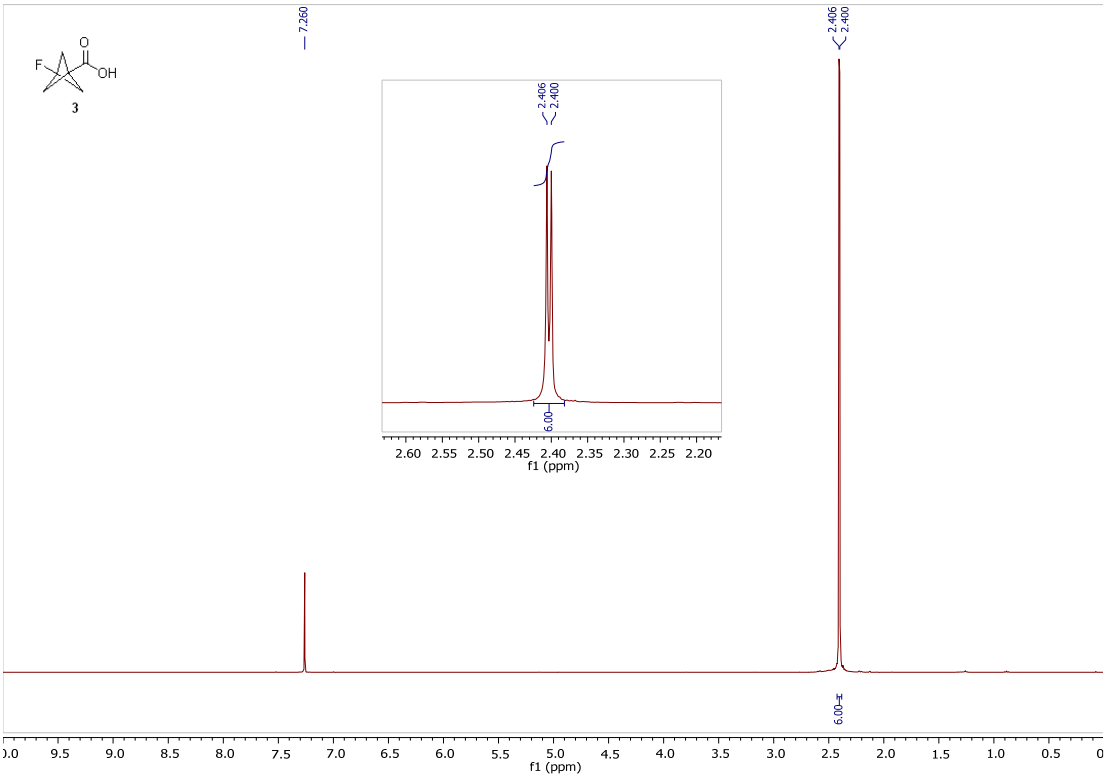



To ethyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate **(12a)** (50 mg, 0.195 mmol) was added to a sealed tube, was thoroughly flushed with argon. Benzene (1 mL) was added and the reaction mixture stirred at 110 °C for 16 h. The reaction mixture was evaporated under reduced pressure and diluted with diethyl ether. The organics was washed with saturated bicarbonate, dried over sodium sulphate, filtered and concentrated *in vacuo*. The residue was purified by preparative TLC chromatography (8% diethyl ether in petroleum ether) to afford **15** (7 mg, 17%) as a colourless oil. The remaining aqueous layer was acidified with 6 N HCl and extracted with diethyl ether, dried over sodium sulphate, filtered and concentrated *in vacuo* to afford **8a** (10 mg, 28%) as a white solid.

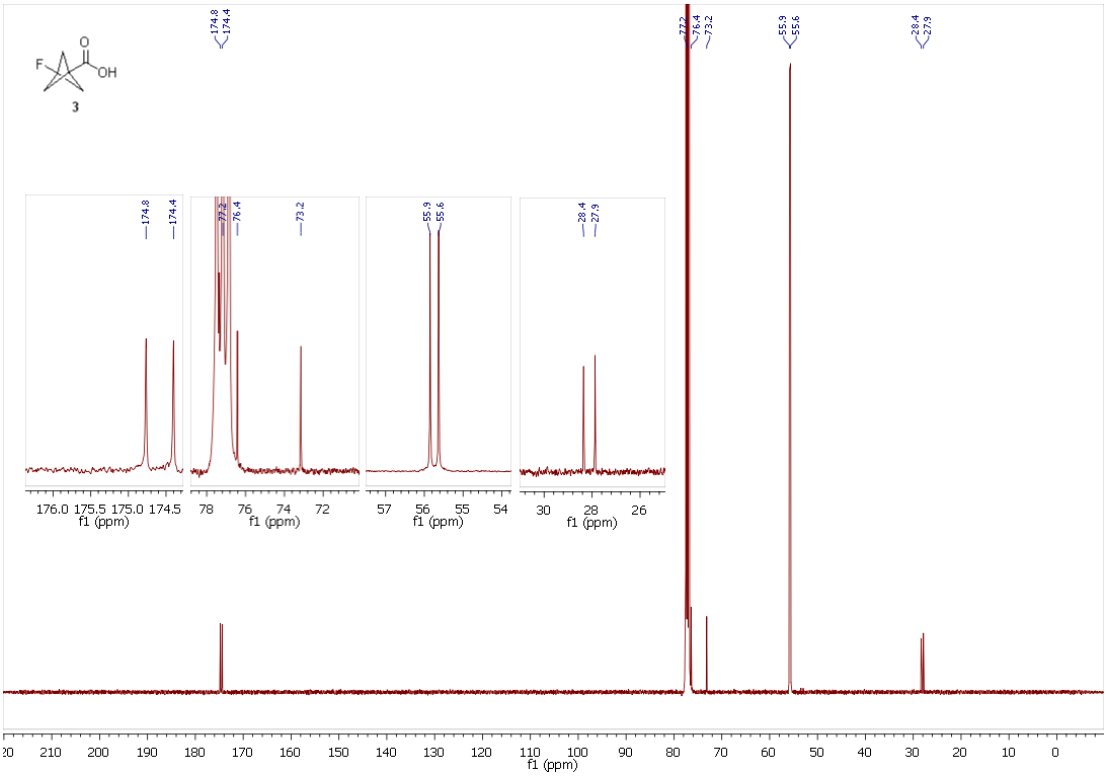
$^{1}$H NMR (400 MHz, $CDCl_3$) δ 7.35 – 7.28 (m, 2H), 7.26 – 7.20 (m, 3H), 4.17 (q, J = 7.1 Hz, 2H), 2.32 (s, 6H), 1.29 (t, J = 7.1 Hz, 3H). $^{13}$C NMR (101 MHz, $CDCl_3$) δ 170.5, 139.9, 128.4, 127.0, 126.2, 60.7, 53.5, 41.8, 37.3, 14.4. IR: 2978.6, 1729.2, 1371.2, 1296.4, 1200.2, 1112.9, 1016.7, 749.5, 697.9 $cm^{-1}$.

**$^{1}$H NMR, $^{13}$C NMR, $^{19}$F NMR Spectra and X-ray crystal structures**

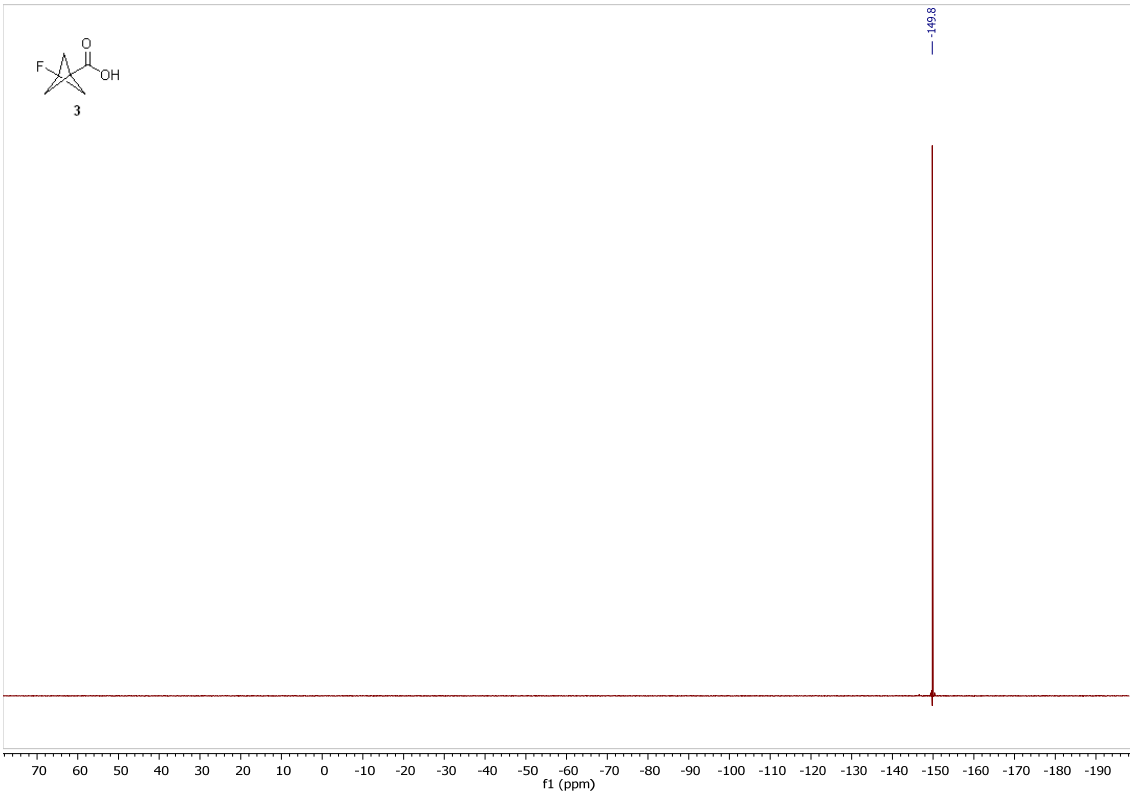
**3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3), $^{1}$H NMR (400 MHz, $CDCl_3$)**



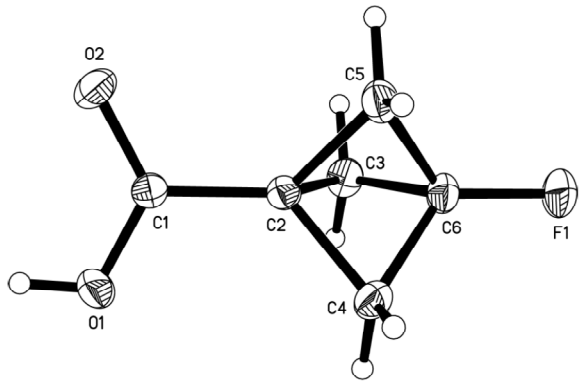

**3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3), $^{13}$C NMR (101 MHz, $CDCl_3$)**

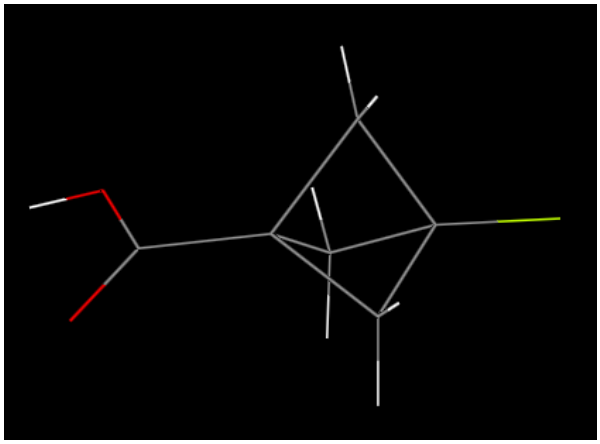


**3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3), $^{19}$F NMR (376 MHz, $CDCl_3$)**



**Single X-ray crystal structure of 3-fluorobicyclo[1.1.1]pentane-1-carboxylic acid (3).**



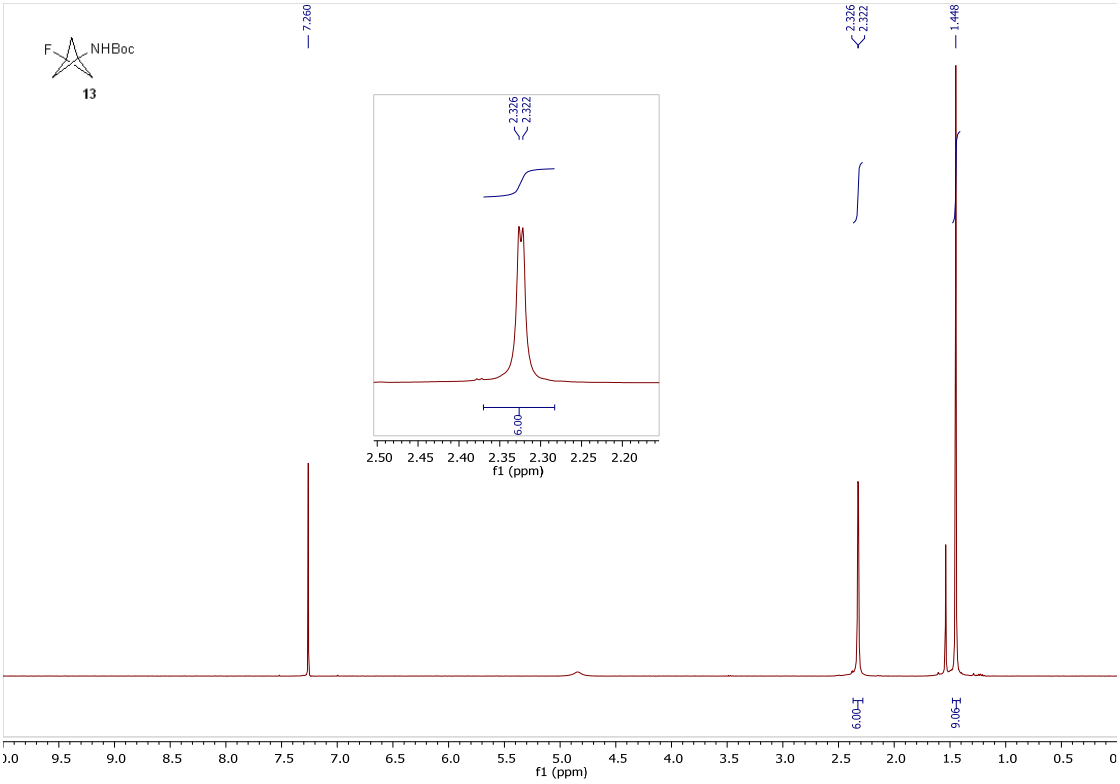
**Bond lengths (Å).**

| | | | |
|---|---|---|---|
| C1-O2 | 1.2611(19) | C1-O1 | 1.2674(19) |
| C1-C2 | 1.482(2) | C2-C5 | 1.550(2) |
| C2-C4 | 1.555(2) | C2-C3 | 1.567(2) |
| C2-C6 | 1.815(2) | C3-C6 | 1.531(2) |
| C4-C6 | 1.536(2) | C5-C6 | 1.537(2) |
| C6-F1 | 1.3678(18) | | |

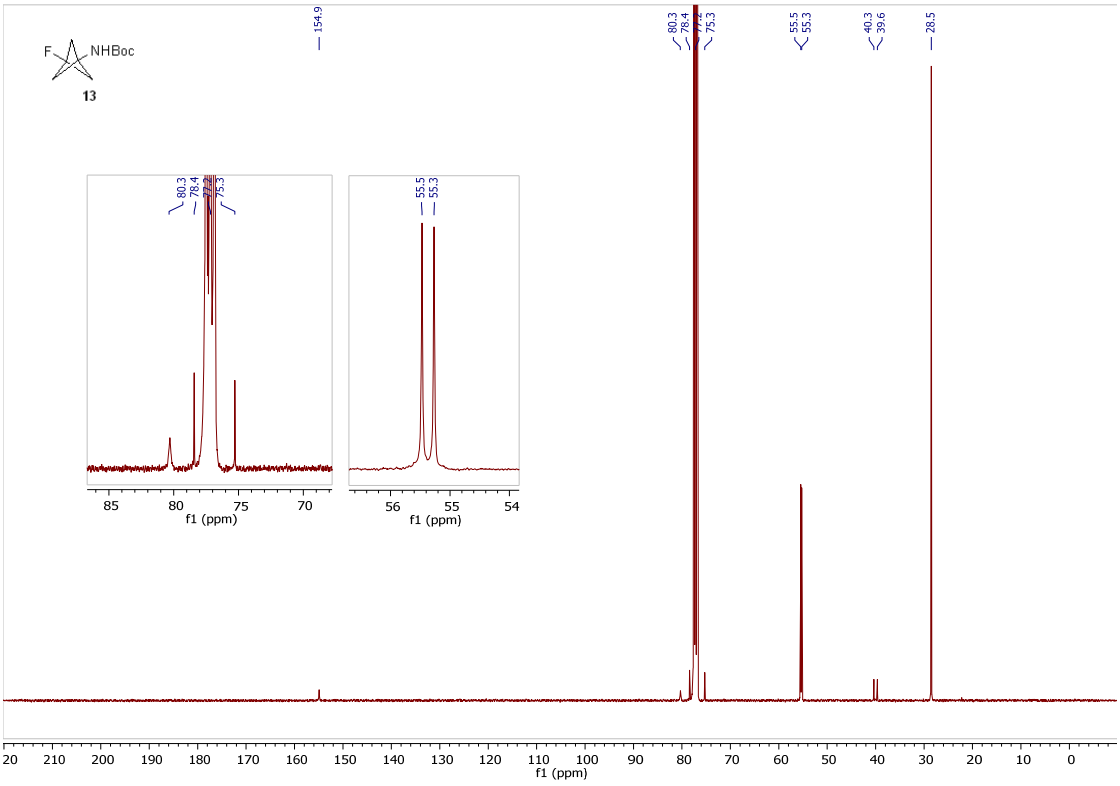
**Bond angles (°)**

| | | | |
|---|---|---|---|
| O2-C1-O1 | 124.32(14) | O2-C1-C2 | 118.51(14) |
| O1-C1-C2 | 117.11(14) | C1-C2-C5 | 128.26(15) |
| C1-C2-C4 | 128.34(13) | C5-C2-C4 | 88.81(12) |
| C1-C2-C3 | 122.76(13) | C5-C2-C3 | 88.11(12) |
| C4-C2-C3 | 87.69(12) | C1-C2-C6 | 175.97(13) |
| C5-C2-C6 | 53.64(10) | C4-C2-C6 | 53.57(9) |
| C3-C2-C6 | 53.21(9) | C6-C3-C2 | 71.71(11) |
| C6-C4-C2 | 71.90(11) | C6-C5-C2 | 72.03(11) |
| F1-C6-C3 | 124.84(14) | F1-C6-C4 | 125.68(14) |
| C3-C6-C4 | 89.69(12) | F1-C6-C5 | 125.53(14) |
| C3-C6-C5 | 89.93(13) | C4-C6-C5 | 89.99(13) |
| F1-C6-C2 | 179.79(16) | C3-C6-C2 | 55.08(9) |
| C4-C6-C2 | 54.53(9) | C5-C6-C2 | 54.33(9) |

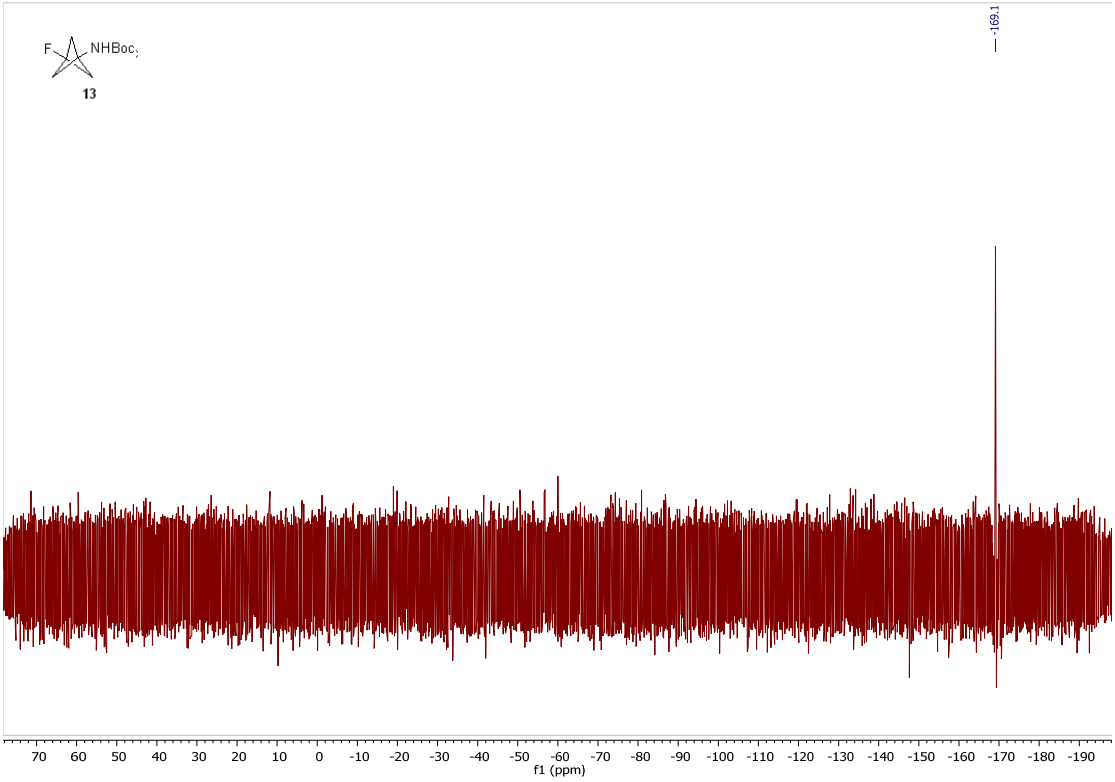
**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13), $^{1}$H NMR (400 MHz, $CDCl_3$)**



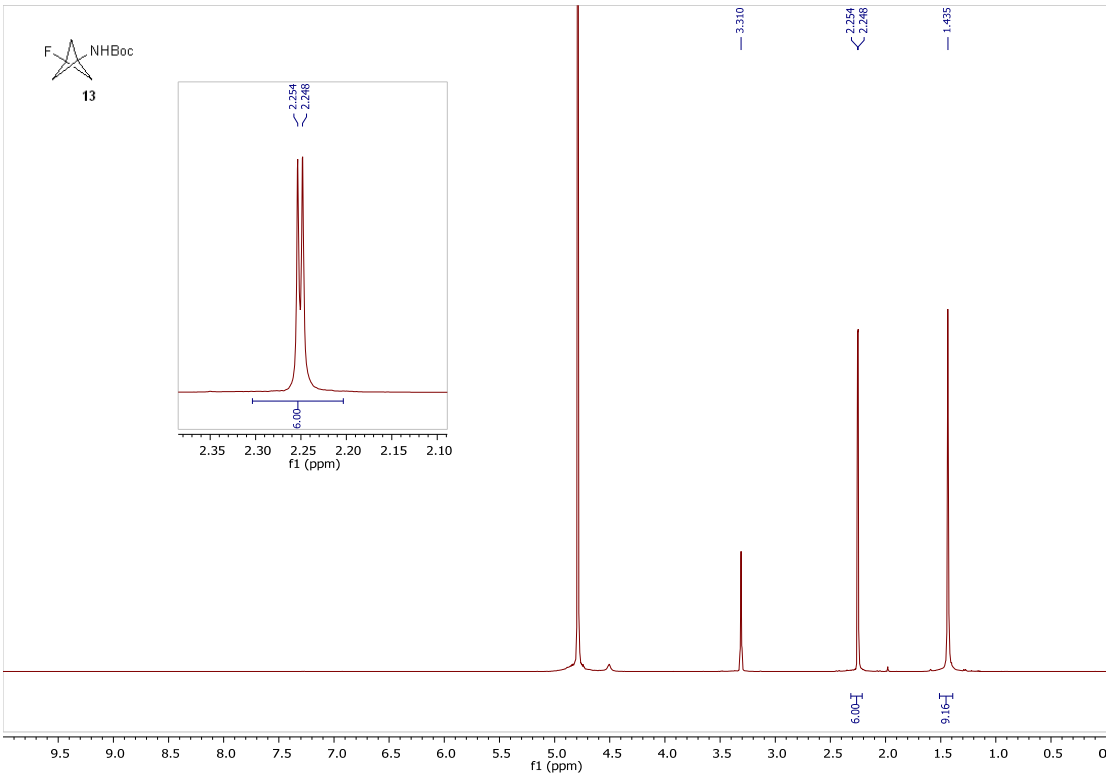

**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13), $^{13}$C NMR (101 MHz, $CDCl_3$)**



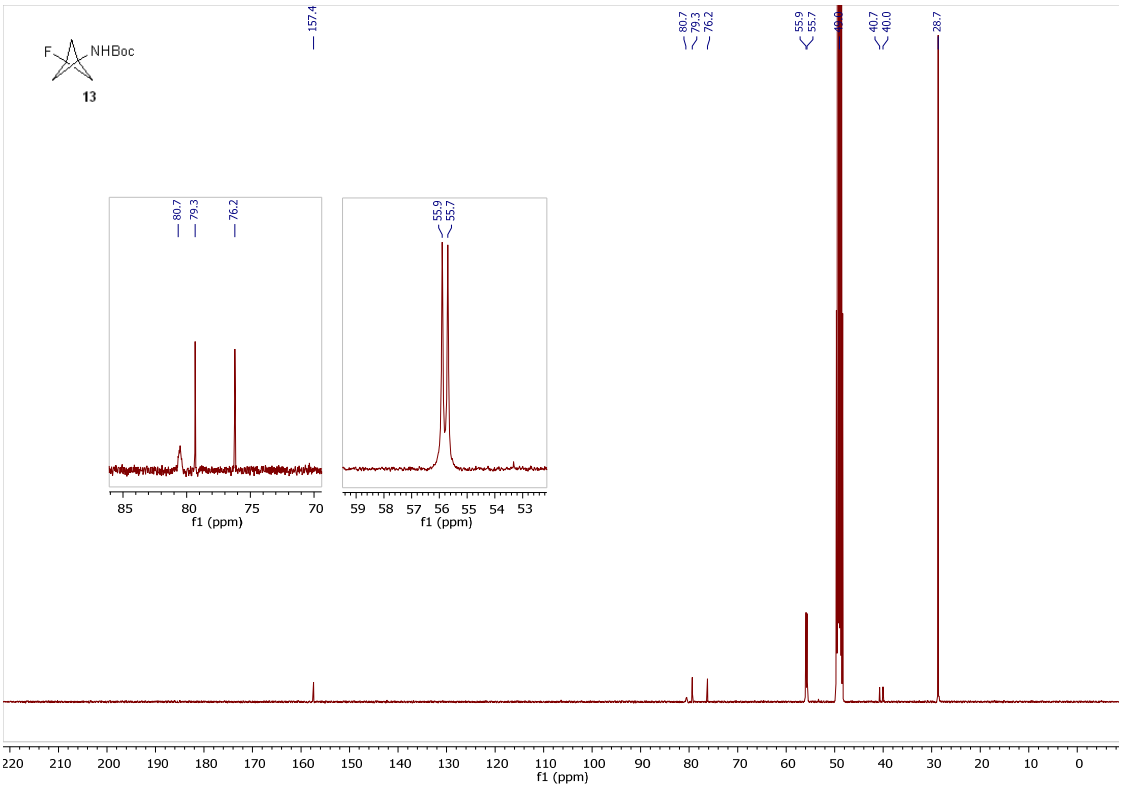
**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13), $^{19}$F NMR (376 MHz, $CDCl_3$)**



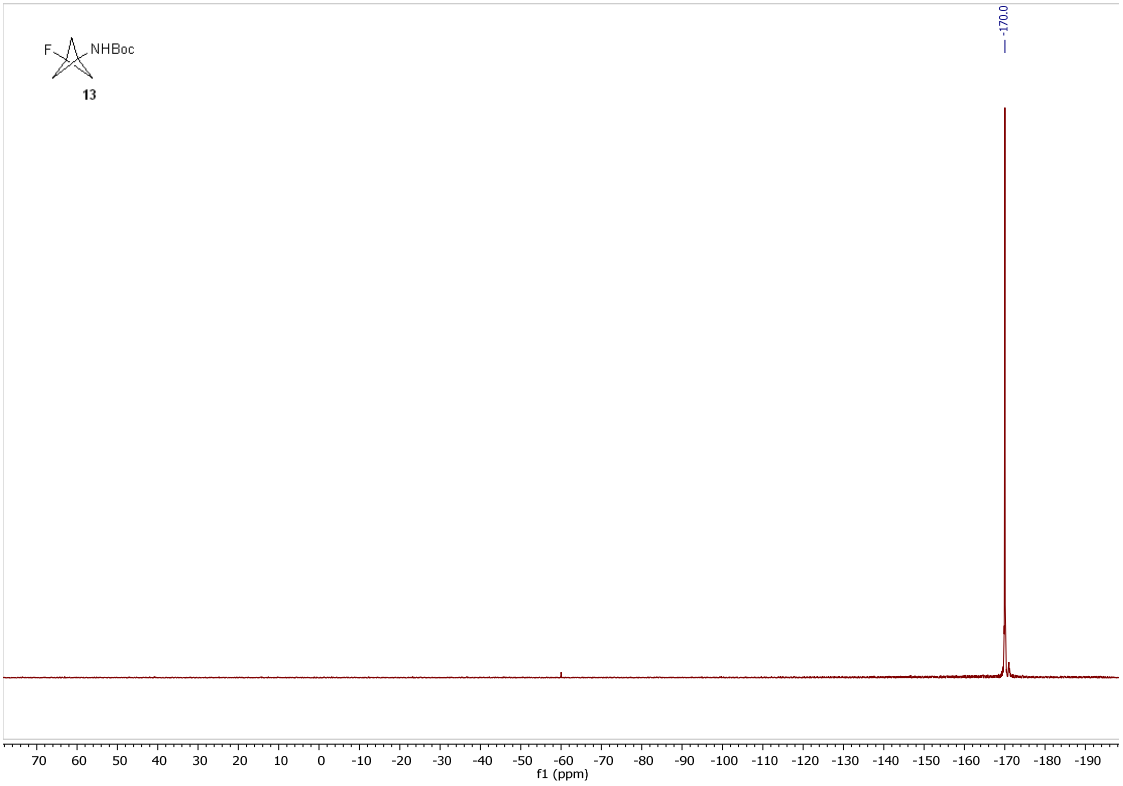

**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13), $^{1}$H NMR (400 MHz, $CD_3OD$)**



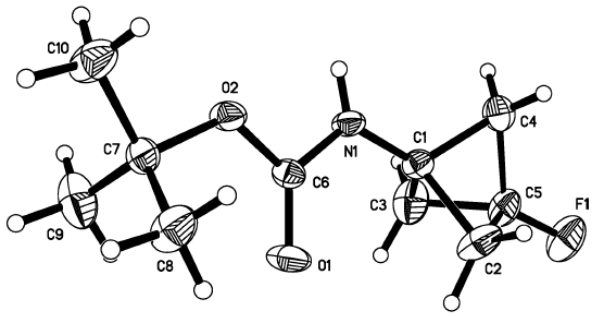
**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13), $^{13}$C NMR (101 MHz, $CD_3OD$)**

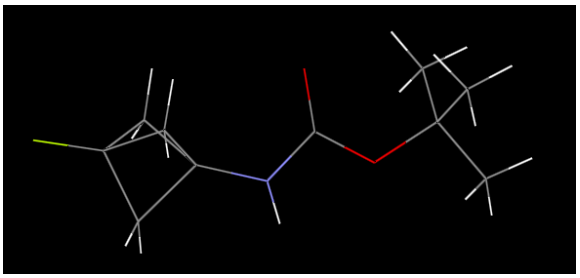



**tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13), $^{19}$F NMR (376 MHz, $CD_3OD$)**



**Single X-ray crystal structure of tert-butyl (3-fluorobicyclo[1.1.1]pentan-1-yl)carbamate (13).**



**Bond lengths (Å)**

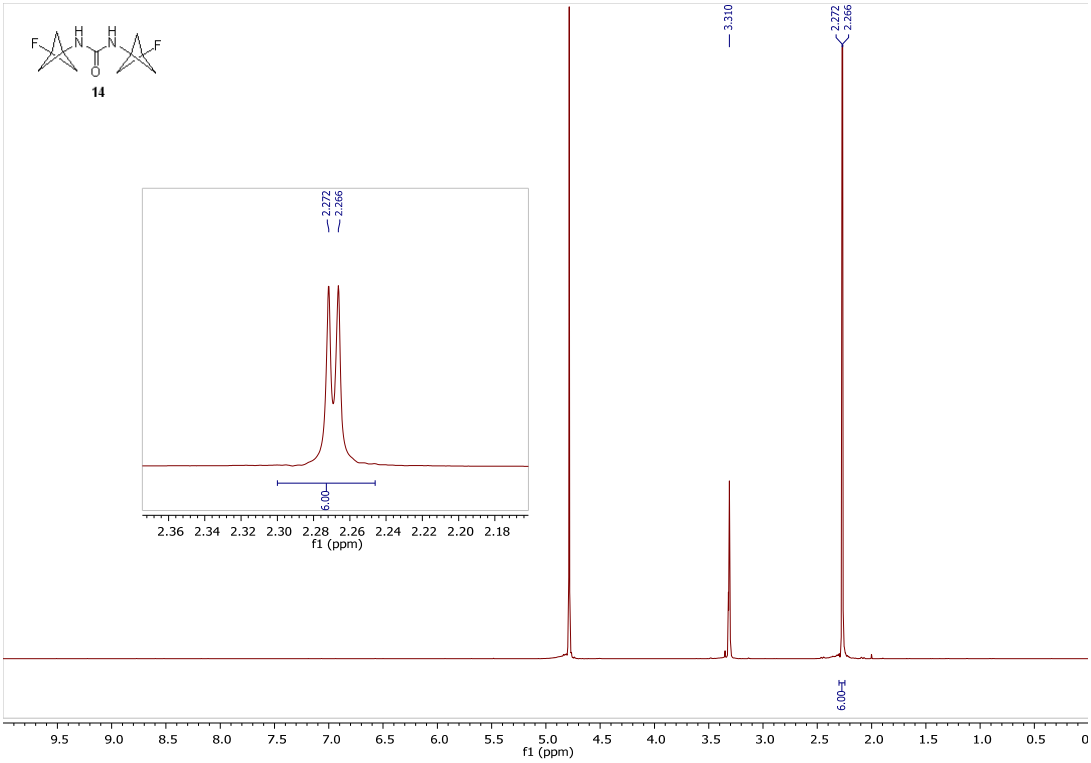
| | | | |
|---|---|---|---|
| C1-N1 | 1.4223(18) | C1-C4A | 1.532(7) |
| C1-C2 | 1.536(3) | C1-C3 | 1.540(3) |
| C1-C4 | 1.552(3) | C1-C2A | 1.570(8) |
| C1-C3A | 1.604(7) | C1-C5 | 1.812(2) |
| C2-C5 | 1.527(3) | C3-C5 | 1.542(3) |
| C4-C5 | 1.546(3) | C2A-C5 | 1.506(8) |
| C3A-C5 | 1.531(7) | C4A-C5 | 1.460(8) |
| C5-F1 | 1.3714(17) | C6-O1 | 1.2121(17) |
| C6-O2 | 1.3431(17) | C6-N1 | 1.3485(18) |
| C7-O2 | 1.4785(17) | C7-C9 | 1.508(2) |
| C7-C8 | 1.514(2) | C7-C10 | 1.520(2) |
| C11-N2 | 1.4166(18) | C11-C14 | 1.541(2) |
| C11-C15 | 1.553(2) | C11-C13 | 1.556(2) |
| C11-C12 | 1.812(2) | C12-F2 | 1.3724(17) |
| C12-C14 | 1.518(2) | C12-C15 | 1.530(2) |
| C12-C13 | 1.530(2) | C16-O3 | 1.2143(17) |
| C16-O4 | 1.3456(17) | C16-N2 | 1.3469(19) |
| C17-O4 | 1.4767(17) | C17-C18 | 1.507(2) |
| C17-C19 | 1.507(2) | C17-C20 | 1.520(2) |

**Bond angles (°)**

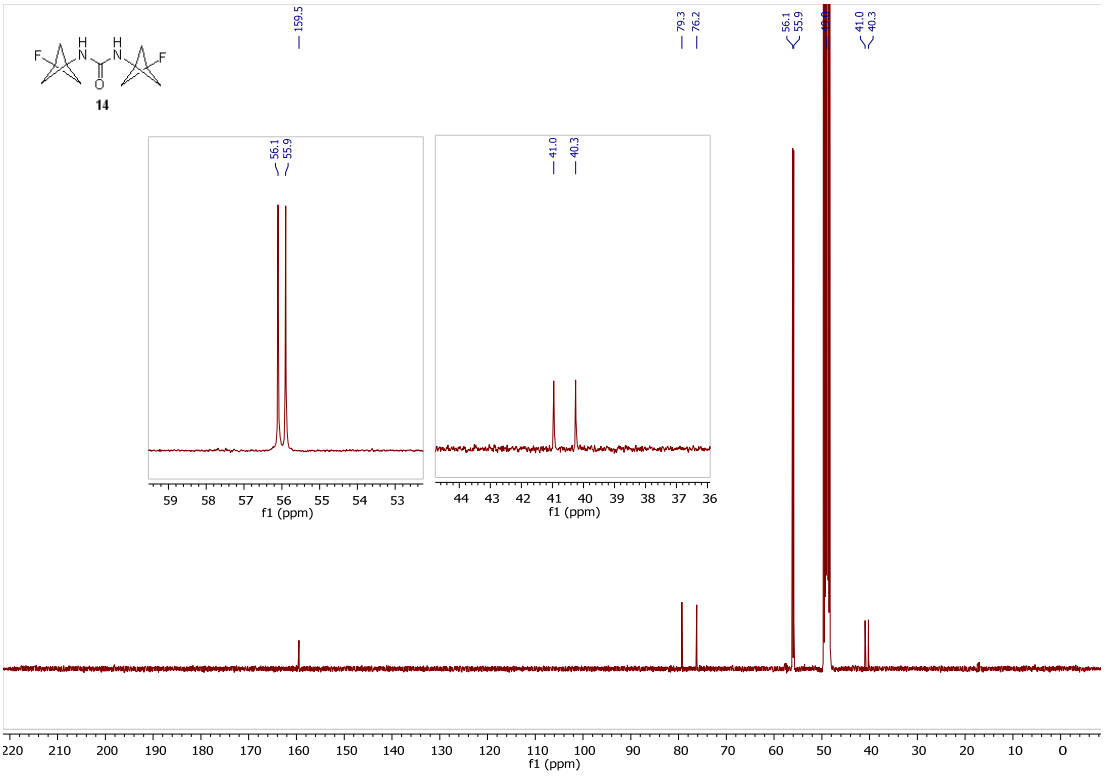
| | | | |
|---|---|---|---|
| N1-C1-C4A | 127.1(3) | N1-C1-C2 | 127.25(16) |
| N1-C1-C3 | 128.18(15) | C2-C1-C3 | 89.29(19) |
| N1-C1-C4 | 122.84(15) | C2-C1-C4 | 88.80(18) |
| C3-C1-C4 | 88.17(17) | N1-C1-C2A | 126.6(3) |
| C4A-C1-C2A | 87.5(4) | N1-C1-C3A | 130.4(3) |
| C4A-C1-C3A | 85.6(4) | C2A-C1-C3A | 85.2(4) |
| N1-C1-C5 | 176.77(13) | C4A-C1-C5 | 50.9(3) |
| C2-C1-C5 | 53.51(13) | C3-C1-C5 | 54.03(12) |

| | | | |
|---|---|---|---|
| C4-C1-C5 | 54.04(13) | C2A-C1-C5 | 52.3(3) |
| C3A-C1-C5 | 52.8(3) | C5-C2-C1 | 72.52(15) |
| C1-C3-C5 | 72.01(14) | C5-C4-C1 | 71.60(14) |
| C5-C2A-C1 | 72.1(4) | C5-C3A-C1 | 70.5(3) |
| C5-C4A-C1 | 74.5(3) | F1-C5-C4A | 125.3(3) |
| F1-C5-C2A | 124.5(3) | C4A-C5-C2A | 92.6(4) |
| F1-C5-C2 | 126.11(17) | F1-C5-C3A | 123.5(3) |
| C4A-C5-C3A | 90.8(4) | C2A-C5-C3A | 90.0(4) |
| F1-C5-C3 | 126.06(16) | C2-C5-C3 | 89.57(19) |
| F1-C5-C4 | 125.55(16) | C2-C5-C4 | 89.36(18) |
| C3-C5-C4 | 88.33(18) | F1-C5-C1 | 179.90(17) |
| C4A-C5-C1 | 54.6(3) | C2A-C5-C1 | 55.6(3) |
| C2-C5-C1 | 53.97(13) | C3A-C5-C1 | 56.6(3) |
| C3-C5-C1 | 53.95(12) | C4-C5-C1 | 54.36(12) |
| O1-C6-O2 | 125.93(13) | O1-C6-N1 | 123.90(13) |
| O2-C6-N1 | 110.15(12) | O2-C7-C9 | 108.76(12) |
| O2-C7-C8 | 111.85(12) | C9-C7-C8 | 113.87(15) |
| O2-C7-C10 | 102.64(12) | C9-C7-C10 | 110.36(14) |
| C8-C7-C10 | 108.78(13) | N2-C11-C14 | 122.94(13) |
| N2-C11-C15 | 127.65(13) | C14-C11-C15 | 88.18(12) |
| N2-C11-C13 | 129.43(13) | C14-C11-C13 | 87.80(12) |
| C15-C11-C13 | 87.79(12) | N2-C11-C12 | 175.88(13) |
| C14-C11-C12 | 53.07(9) | C15-C11-C12 | 53.39(9) |
| C13-C11-C12 | 53.38(9) | F2-C12-C14 | 125.47(14) |
| F2-C12-C15 | 125.16(13) | C14-C12-C15 | 89.90(13) |
| F2-C12-C13 | 125.80(14) | C14-C12-C13 | 89.61(13) |
| C15-C12-C13 | 89.58(12) | F2-C12-C11 | 179.49(15) |
| C14-C12-C11 | 54.27(9) | C15-C12-C11 | 54.59(9) |
| C13-C12-C11 | 54.70(9) | C12-C13-C11 | 71.91(11) |
| C12-C14-C11 | 72.66(11) | C12-C15-C11 | 72.02(10) |
| O3-C16-O4 | 126.01(13) | O3-C16-N2 | 124.63(13) |
| O4-C16-N2 | 109.35(12) | O4-C17-C18 | 112.23(12) |
| O4-C17-C19 | 108.51(13) | C18-C17-C19 | 112.92(16) |
| O4-C17-C20 | 101.82(12) | C18-C17-C20 | 110.04(14) |
| C19-C17-C20 | 110.77(15) | C6-N1-C1 | 121.96(12) |
| C16-N2-C11 | 122.58(12) | C6-O2-C7 | 120.81(11) |
| C16-O4-C17 | 121.99(11) | | |

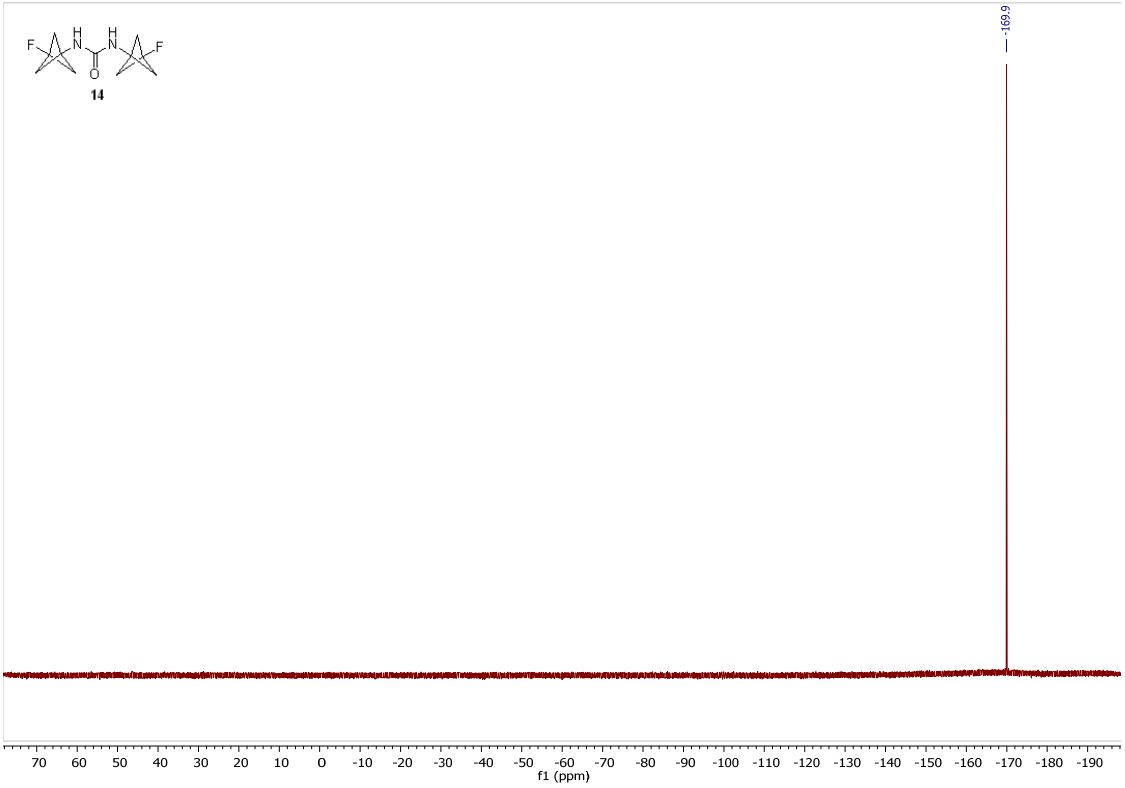
**1,3-bis(3-fluorobicyclo[1.1.1]pentan-1-yl)urea (14), $^{1}$H NMR (400 MHz, $CD_3OD$)**



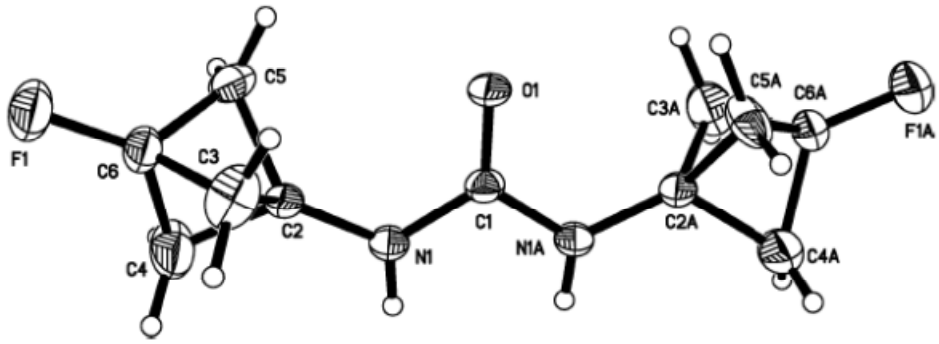

**1,3-bis(3-fluorobicyclo[1.1.1]pentan-1-yl)urea (14), $^{13}$C NMR (101 MHz, $CD_3OD$)**

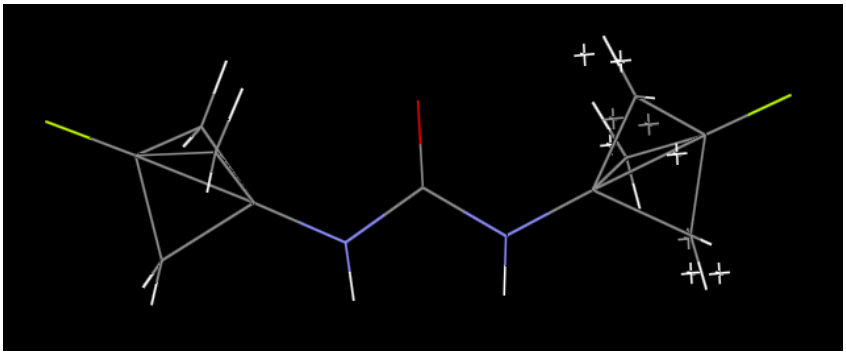


**1,3-bis(3-fluorobicyclo[1.1.1]pentan-1-yl)urea (14), $^{19}$F NMR (376 MHz, $CD_3OD$)**



**1,3-bis(3-fluorobicyclo[1.1.1]pentan-1-yl)urea (14).**



**Bond lengths (Å)**

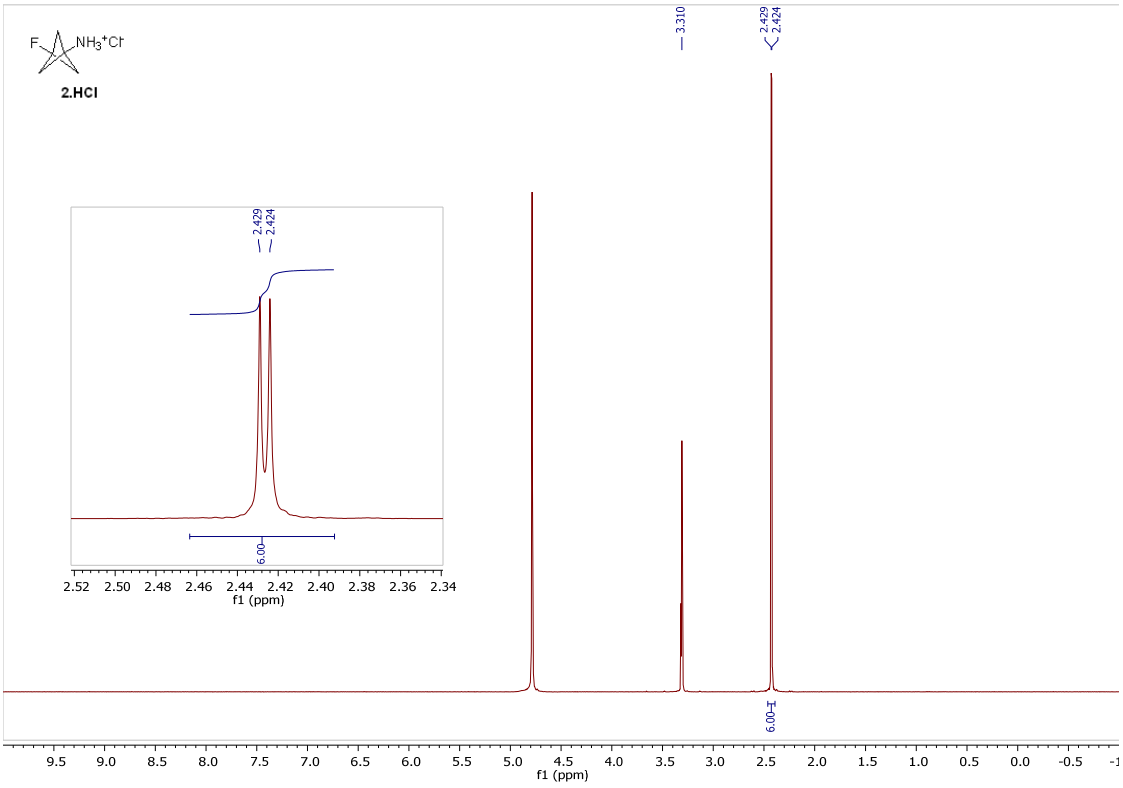
| | | | |
|---|---|---|---|
| C1-O1 | 1.235(2) | C1-N1 | 1.3568(16) |
| C1-N1 | 1.3569(16) | C2-N1 | 1.4186(19) |
| C2-C5A | 1.525(10) | C2-C4 | 1.533(10) |
| C2-C3 | 1.536(6) | C2-C4A | 1.549(11) |
| C2-C3A | 1.561(7) | C2-C5 | 1.566(8) |
| C2-C6 | 1.810(2) | C3-C6 | 1.526(7) |
| C4-C6 | 1.543(11) | C5-C6 | 1.490(9) |
| C3A-C6 | 1.526(7) | C4A-C6 | 1.480(12) |
| C5A-C6 | 1.544(10) | C6-F1 | 1.3654(18) |

**Bond angles (°)**

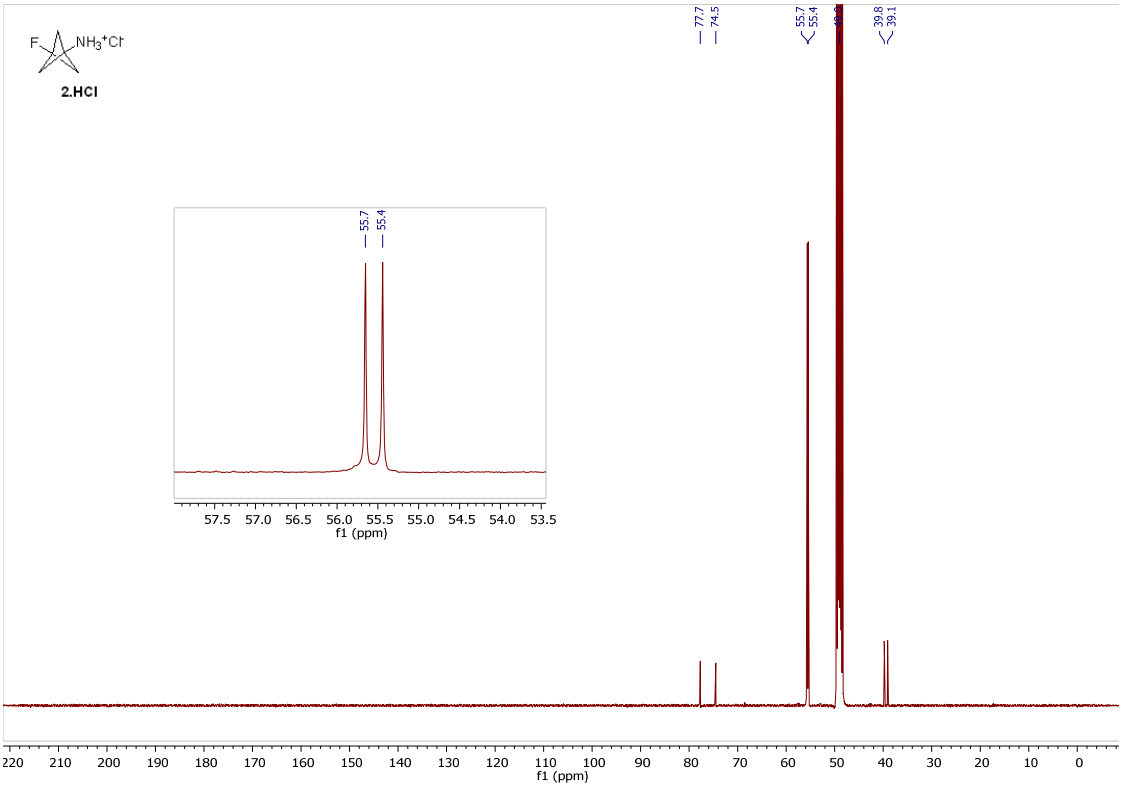
| | | | |
|---|---|---|---|
| O1-C1-N1 | 122.70(9) | O1-C1-N1 | 122.69(9) |
| N1-C1-N1 | 114.61(17) | N1-C2-C5A | 126.3(4) |
| N1-C2-C4 | 124.1(4) | N1-C2-C3 | 126.8(3) |
| C4-C2-C3 | 87.8(4) | N1-C2-C4A | 126.7(5) |
| C5A-C2-C4A | 86.9(5) | N1-C2-C3A | 127.9(3) |
| C5A-C2-C3A | 88.0(4) | C4A-C2-C3A | 87.8(4) |
| N1-C2-C5 | 129.6(3) | C4-C2-C5 | 87.1(5) |

| | | | |
|---|---|---|---|
| C3-C2-C5 | 88.2(4) | N1-C2-C6 | 178.20(12) |
| C5A-C2-C6 | 54.3(4) | C4-C2-C6 | 54.2(4) |
| C3-C2-C6 | 53.5(3) | C4A-C2-C6 | 51.6(4) |
| C3A-C2-C6 | 53.2(3) | C5-C2-C6 | 51.8(3) |
| C6-C3-C2 | 72.5(3) | C2-C4-C6 | 72.1(5) |
| C6-C5-C2 | 72.6(4) | C6-C3A-C2 | 71.8(3) |
| C6-C4A-C2 | 73.4(5) | C2-C5A-C6 | 72.3(4) |
| F1-C6-C4A | 123.9(4) | F1-C6-C5 | 125.1(3) |
| F1-C6-C3A | 125.5(3) | C4A-C6-C3A | 91.7(5) |
| F1-C6-C3 | 126.1(3) | C5-C6-C3 | 91.5(4) |
| F1-C6-C4 | 125.4(4) | C5-C6-C4 | 89.6(4) |
| C3-C6-C4 | 87.8(4) | F1-C6-C5A | 127.1(4) |
| C4A-C6-C5A | 88.7(4) | C3A-C6-C5A | 88.6(4) |
| F1-C6-C2 | 179.02(14) | C4A-C6-C2 | 55.1(4) |
| C5-C6-C2 | 55.6(3) | C3A-C6-C2 | 55.0(3) |
| C3-C6-C2 | 54.0(2) | C4-C6-C2 | 53.7(4) |
| C5A-C6-C2 | 53.4(4) | C1-N1-C2 | 121.83(12) |

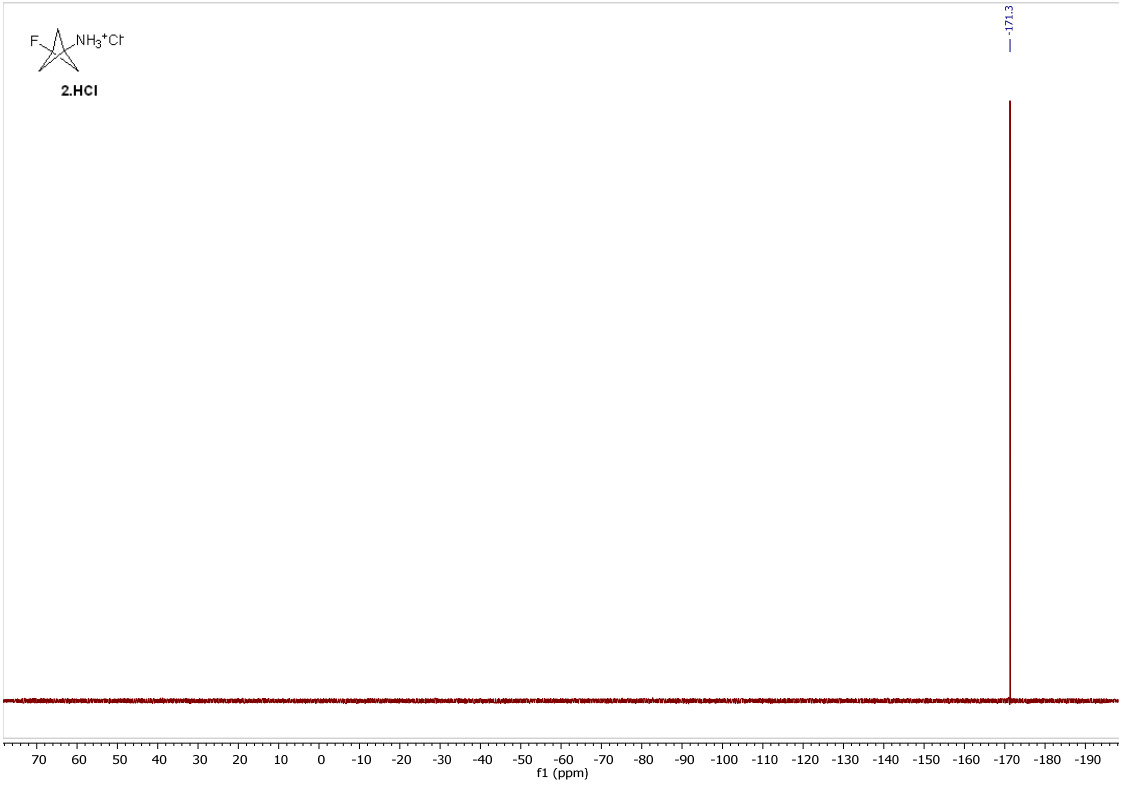
**3-fluorobicyclo[1.1.1]pentan-1-aminium chloride (2.HCl), $^{1}$H NMR (400 MHz, $CD_3OD$)**



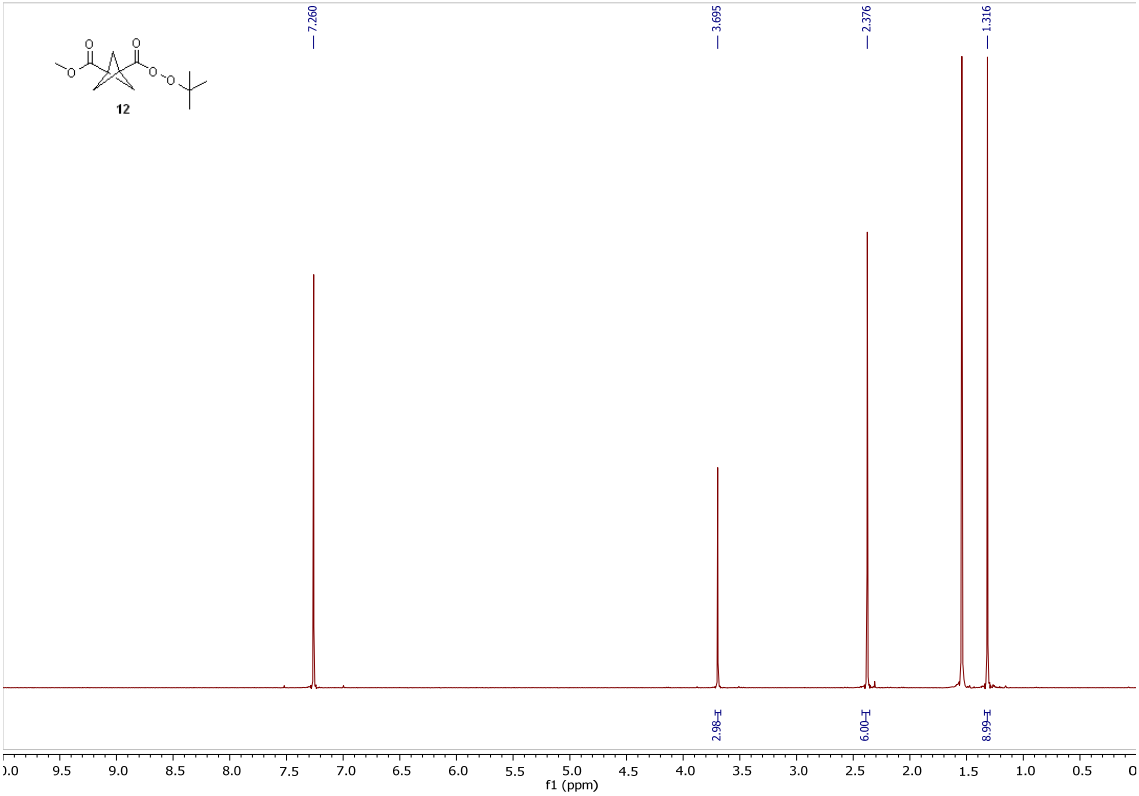

**3-fluorobicyclo[1.1.1]pentan-1-aminium chloride (2.HCl), $^{13}$C NMR (101 MHz, $CD_3OD$)**



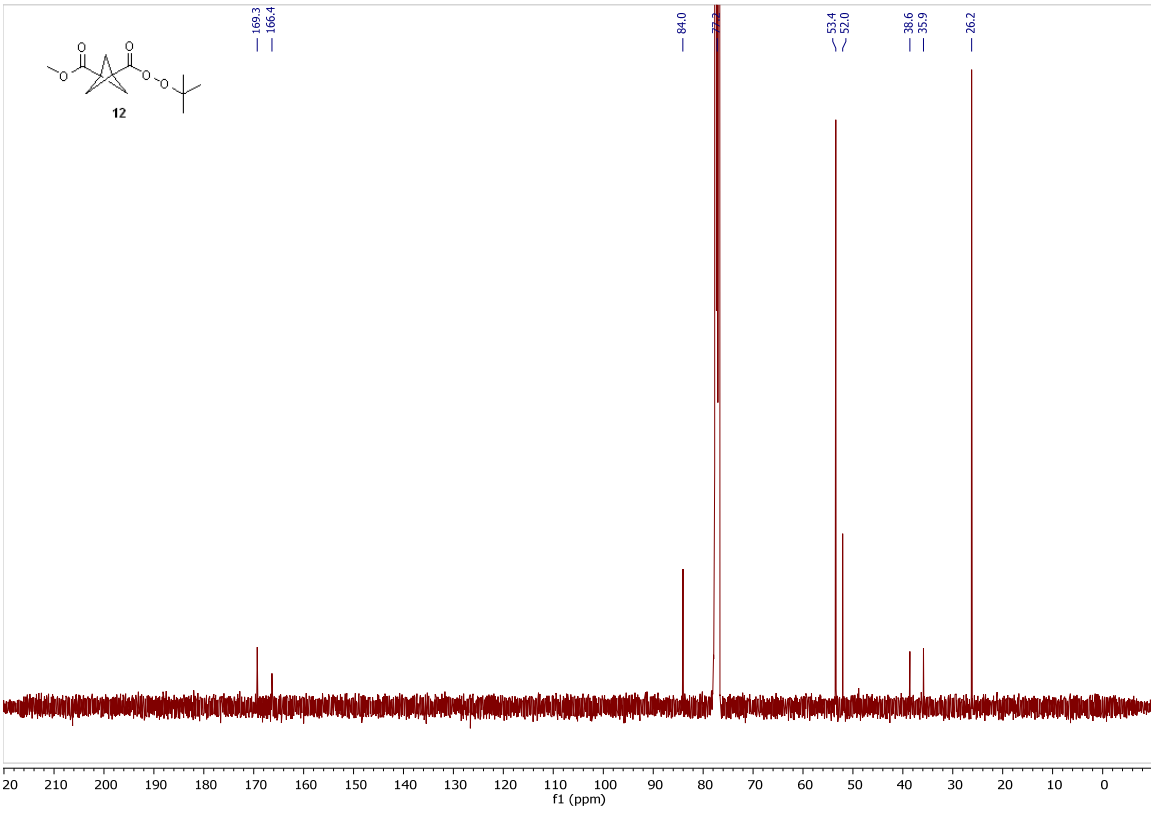
**3-fluorobicyclo[1.1.1]pentan-1-aminium chloride (2.HCl), $^{19}$F NMR (376 MHz, $CD_3OD$)**



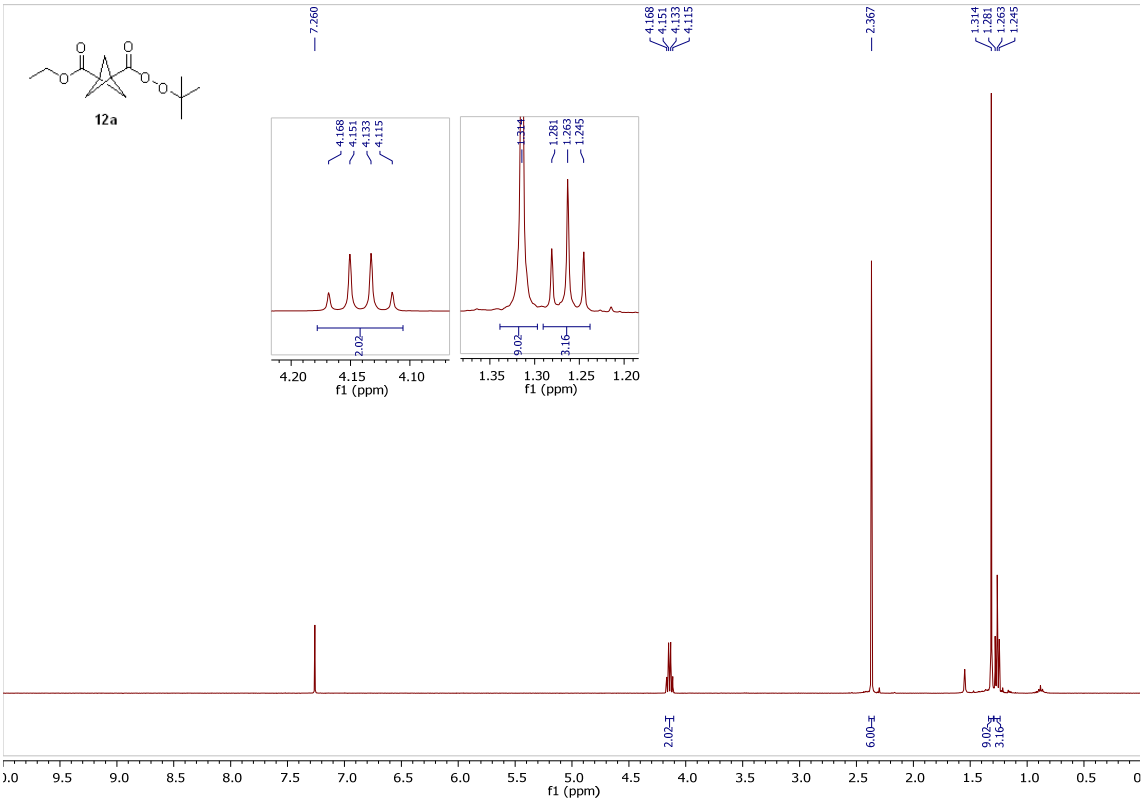
**methyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate (12), $^{1}$H NMR (400 MHz, $CDCl_3$)**



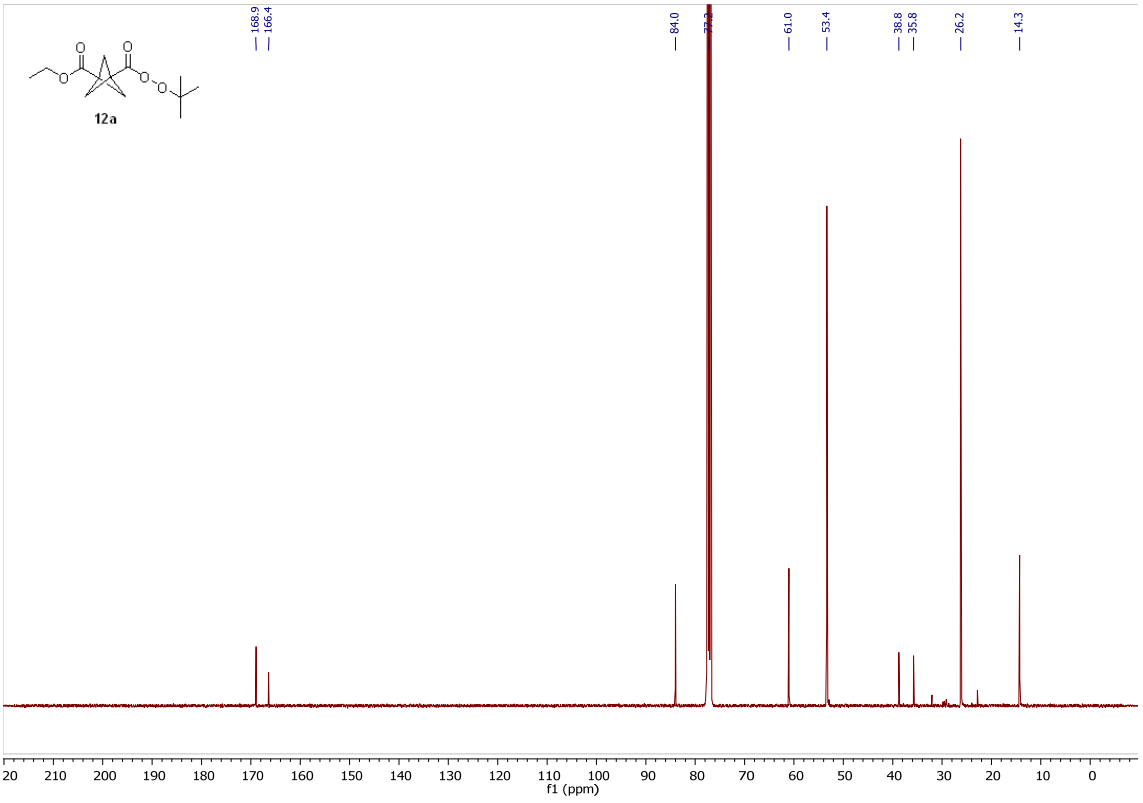

**methyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate (12), $^{13}$C NMR (101 MHz, $CDCl_3$)**



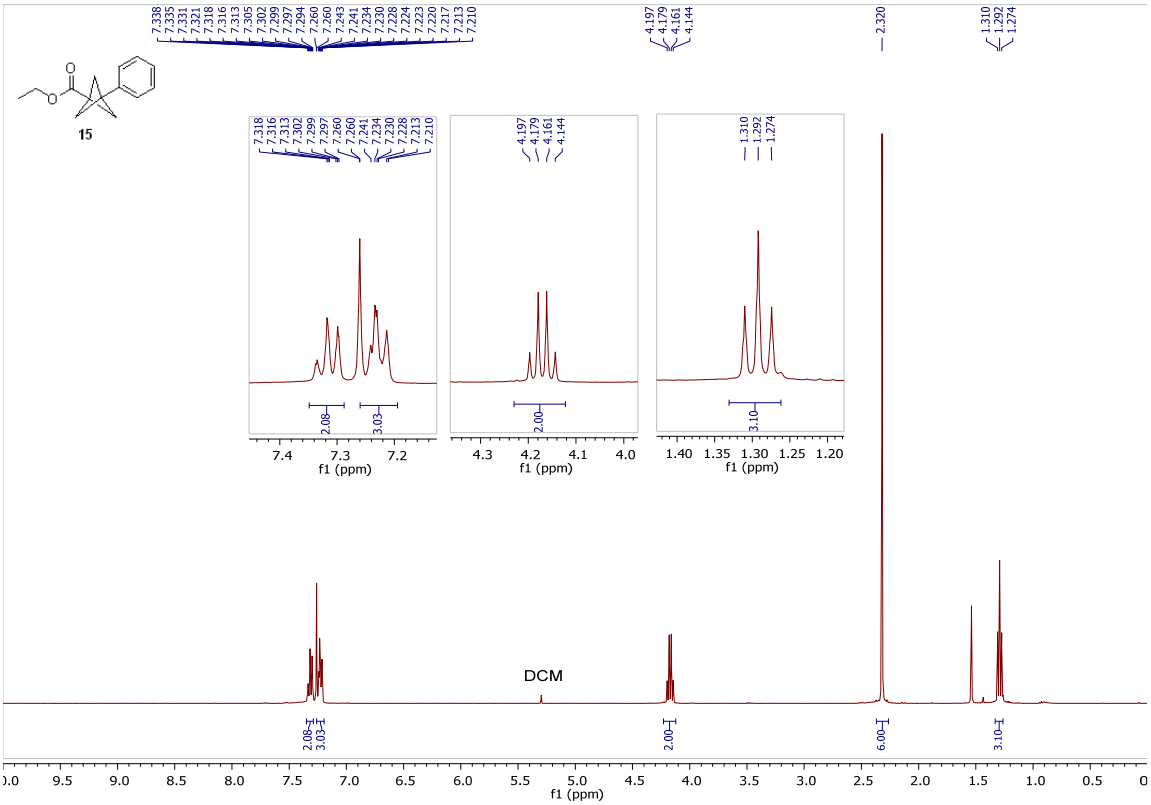
**ethyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate (12a), $^{1}$H NMR (400 MHz, $CDCl_3$)**




**ethyl 3-((tert-butylperoxy)carbonyl)bicyclo[1.1.1]pentane-1-carboxylate (12a), $^{13}$C NMR (101 MHz, $CDCl_3$)**



**ethyl 3-phenylbicyclo[1.1.1]pentane-1-carboxylate (15), $^{1}$H NMR (400 MHz, $CDCl_3$)**




**ethyl 3-phenylbicyclo[1.1.1]pentane-1-carboxylate (15), $^{13}$C NMR (101 MHz, $CDCl_3$)**