Synthesis of functionalised azepanes and piperidines from bicyclic halogenated aminocyclopropane derivatives

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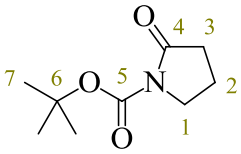
Characterisation data

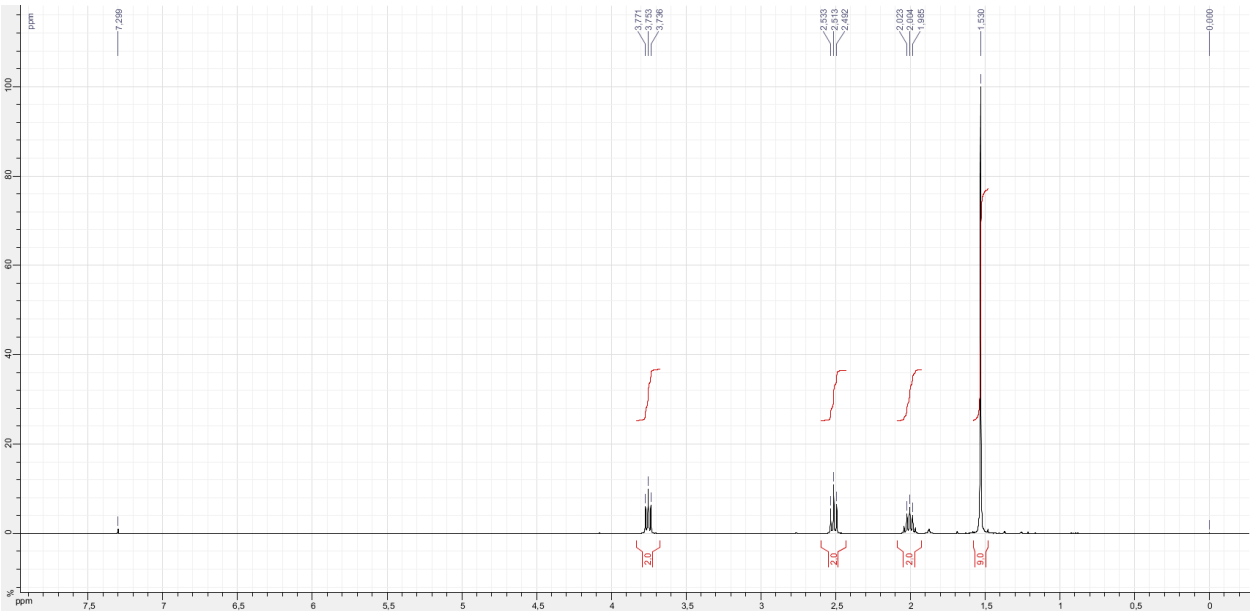
General information: NMR spectra were recorded with AM 400 or AVANCE 400 Bruker spectrometers (^{1}H at 400.2 MHz, ^{13}C at 100.6 MHz. Chemical shifts δ are given in ppm, referenced to the peak of tetramethylsilane, defined at δ = 0.00 (^{1}H NMR), or the solvent peak of $CDCl_3$, defined at δ = 77.0 (^{13}C NMR). Multiplicities are abbreviated as follows: s = singlet, d = doublet, t = triplet, q = quadruplet, quint = quintuplet, sext = sextuplet, sept = septuplet, m = multiplet, br = broad. Coupling constants *J* are given in Hz and are rounded to the closest multiple of 0.5. Infrared spectra were recorded with a Perkin-Elmer 2000 or a Perkin-Elmer Spectrum Two FT-IR spectrometer. Melting points were determined using a Büchi 535 apparatus and were not corrected. Low-resolution mass spectra were recorded on a Hewlett-Packard Quad GC-MS engine spectrometer *via* direct injection. High-resolution mass spectrometry was performed on a JEOL GC-mate II spectrometer. Underlined *m/z* values indicate the base peaks.

I. Cyclopropane substrates and intermediates

tert-Butyl 2-oxopyrrolidine-1-carboxylate[1]

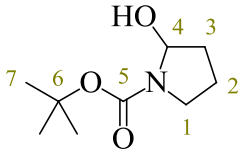


Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.53 (9 H, s, H7), 2.00 (2 H, tt, *J* 8.0, 7.0, H2), 2.51 (2 H, t, *J* 8.0, H3), 3.75 (2 H, t, *J* 7.0, H1).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

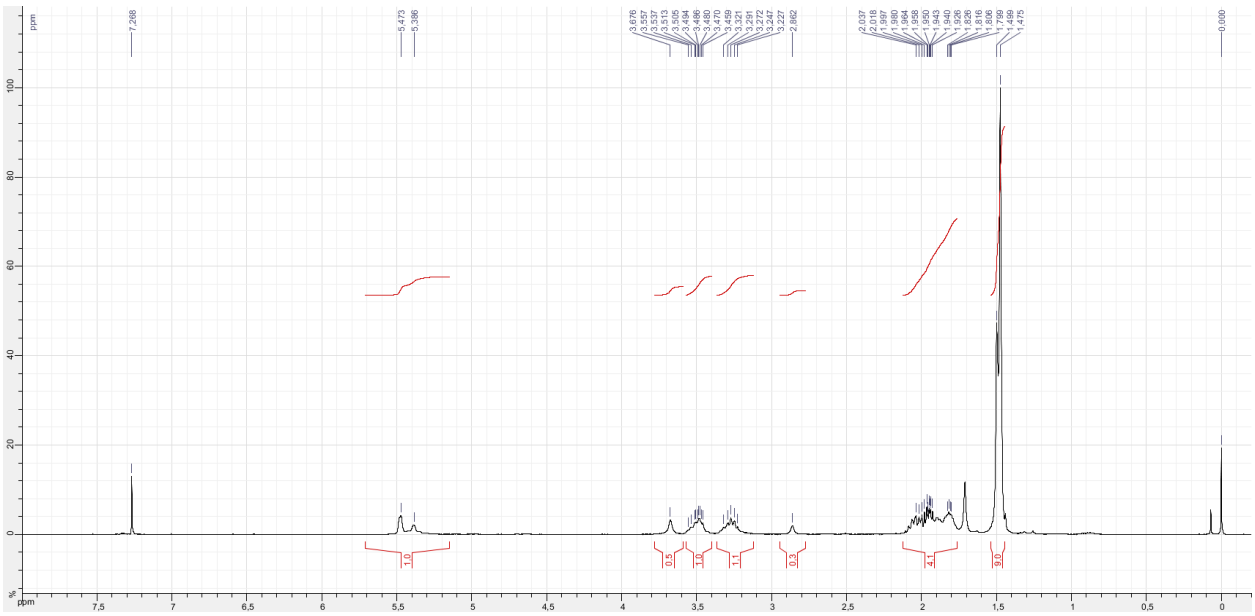
tert-Butyl 2-hydroxypyrrolidine-1-carboxylate[2]



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz), 65 : 35 mixture of two rotamers: δ 1.47 (5.85 H, s, H7), 1.50 (3.15 H, s, H7), 1.75-2.12 (4 H, m, H2, H2, H3, H3), 2.86 (0.35 H, br s, OH), 3.10−3.37 (1 H, m, H1a, H1a), 3.38−3.58 (1 H, m, H1b, H1b), 3.68 (0.65 H, br s, OH), 5.39 (0.35 H, m, H4), 5.47 (0.65 H, m, H4).

1− L. Banfi, A. Basso, V. Cerulli, G. Guanti, R. Riva, *J. Org. Chem.* **2008**, *73*, 1608−1611 (supporting information).

2− S. Peixoto, T. M. Nguyen, D. Crich, B. Delpech, C. Marazano, *Org. Lett.* **2010**, *12*, 4760−4763 (supporting information).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

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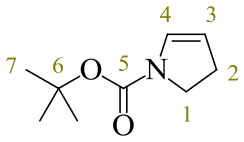
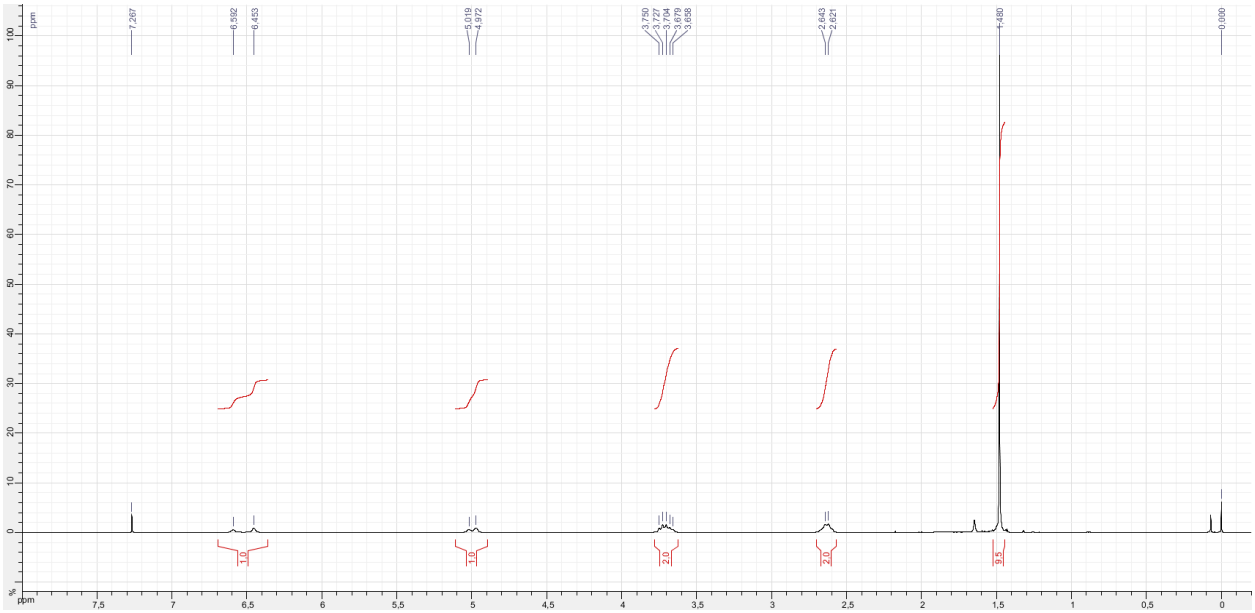
tert-Butyl 2,3-dihydropyrrole-1-carboxylate **1a**[3]



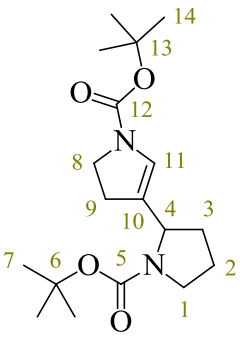
Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz), 58 : 42 mixture of two rotamers: δ 1.48 (9 H, s, H7, H7), 2.63 (2 H, m, H2, H2), 3.68 (0.84 H, t, *J* 9.0, H1), 3.73 (1.16 H, t, *J* 9.0, H1), 4.97 (0.58 H, br s, H3), 5.02 (0.42 H, br s, H3), 6.45 (0.58 H, br s, H4), 6.59 (0.42 H, br s, H4).



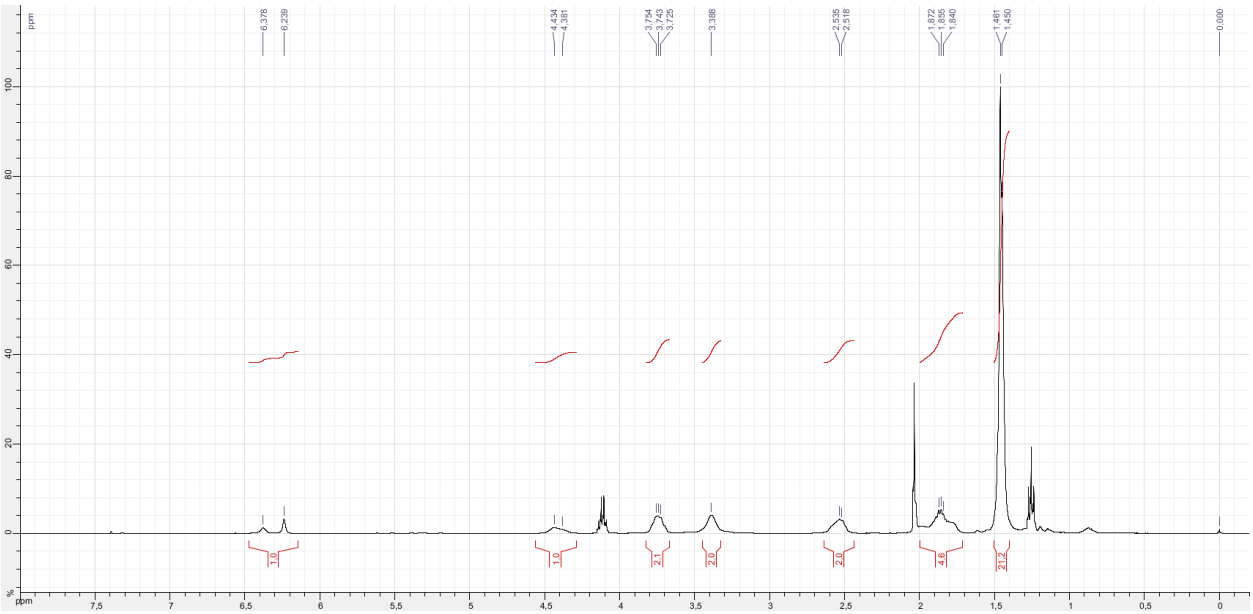
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

3– R. K. Dieter, R. R. Sharma, *J. Org. Chem.* **1996**, *61*, 4180–4184.

tert-Butyl 4-(1-*tert*-butoxycarbonylpyrrolidin-2-yl)-2,3-dihydropyrrole-1-carboxylate[4]



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz), mixture of four rotamers: δ 1.45 and 1.46 (18 H, two br s, H7, H14), 1.70−2.05 (4 H, m, H2−H3), 2.53 (2 H, m, H9), 3.39 (2 H, m, H1), 3.74 (2 H, m, H8), 4.38 (0.4 H, br s, H4), 4.43 (0.6 H, br s, H4), 6.24 (0.6 H, br s, H11), 6.38 (0.4 H, br s, H11).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).
Note: this sample contained some ethyl acetate.

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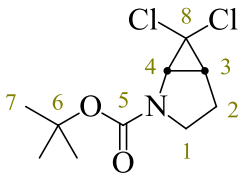
tert-Butyl 6,6-dichloro-2-azabicyclo[3.1.0]hexane-2-carboxylate **2a**

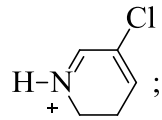
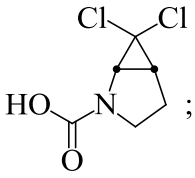
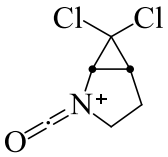


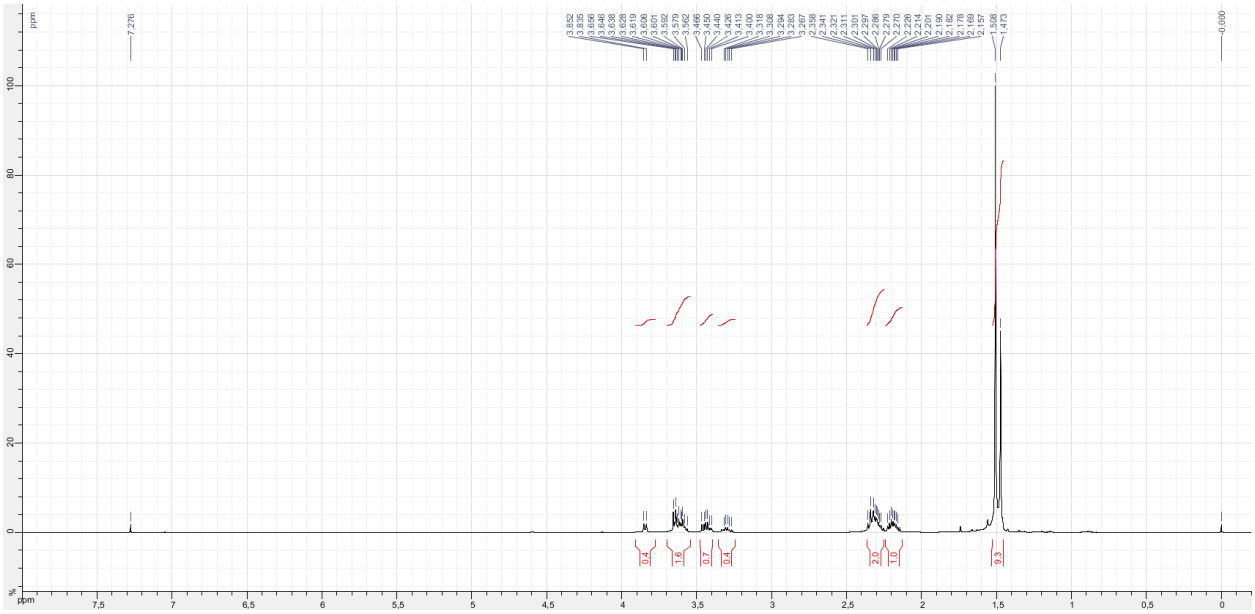
Pale yellow solid.[5] M.p. 54.3−55.9 °C. R_f 0.3 [EtOAc/petroleum ether 10%, $KMnO_4$, not UV-active]. IR (neat) ν 2978 (m), 2934 (w), 2904 (w), 1707 (s, C=O), 1478 (w), 1450 (w), 1393 (s), 1368 (m), 1356 (m), 1346 (m), 1288 (w), 1257 (m), 1173 (m), 1127 (m), 1052 (w), 877 (m), 860 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz), 63 : 37 mixture of two rotamers. Major rotamer: δ 1.50 (9 H, s, H7), 2.11−2.36 (3 H, m, H2, H3), 3.37−3.66 (2 H, m, H1), 3.63 (1 H, d, J 7.0, H4).

4− This compound does not appear to have been described yet. Its structure is consistent with the reported NMR data of a closely related derivative with Cbz groups at both nitrogen atoms: E. L. Myers, J. G. de Vries, V. K. Aggarwal, *Angew. Chem. Int. Ed.* **2007**, *46*, 1893–1896 (supporting information).

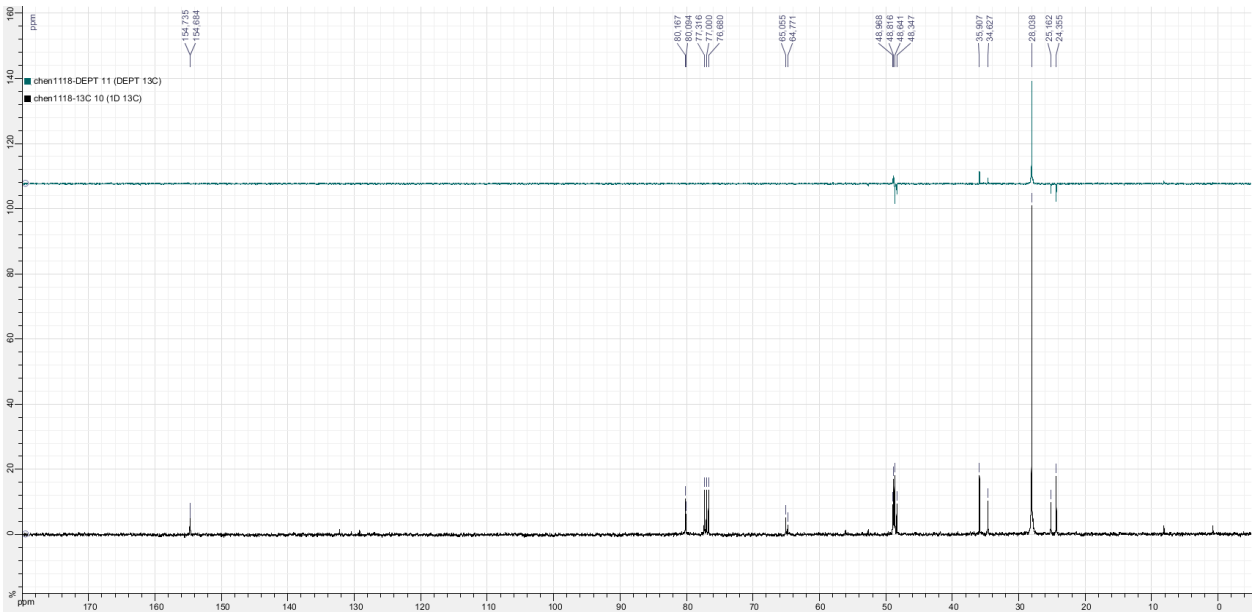
5− Typically, this compound was obtained as an oil after flash column chromatography but became a solid upon standing in the freezer and remained so when warmed back to room temperature.

Minor rotamer: δ 1.45 (9 H, s, H7), 2.11−2.36 (3 H, m, H2, H3), 3.28 (1 H, td, *J* 10.5, 5.5, H1a), 3.37−3.66 (1 H, m, H1b), 3.82 (1 H, d, *J* 7.0, H4). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 63 : 37 mixture of two rotamers. Major rotamer: δ 24.4 (C2), 28.0 (C7), 35.9 (C3), 48.6 (C1), 48.8 (C4), 65.1 (C8), 80.2 (C6), 154.7 (C5). Minor rotamer: δ 25.2 (C2), 28.0 (C7), 34.6 (C3), 48.3 (C1), 49.0 (C4), 64.8 (C8), 80.1 (C6), 154.7 (C5). MS (positive CI, NH_3): *m/z* 116 (M'^{+} with ^{35}Cl),[a] 118 (M'^{+} with ^{37}Cl),[a] 151, 160, 196 ($M''H^{+}$ with two ^{35}Cl),[a] 198 ($M''H^{+}$ with one ^{35}Cl and one ^{37}Cl),[a] 213 ($M''H^{+}..NH_3$ with two ^{35}Cl),[a] 214, 215 ($M''H^{+}..NH_3$ with one ^{35}Cl and one ^{37}Cl),[a] 216, 217, 252 (MH^{+} with two ^{35}Cl), 254 (MH^{+} with one ^{35}Cl and one ^{37}Cl), 269 ($MH^{+}..NH_3$ with two ^{35}Cl), 271 ($MH^{+}..NH_3$ with one ^{35}Cl and one ^{37}Cl). MS (EI): *m/z* 114, 116, 118, 132, 160, 162, 176, 178 ($[M-t\text{BuO}]^{+}$ with two ^{35}Cl),[a] 180 ($[M-t\text{BuO}]^{+}$ with one ^{35}Cl and one ^{37}Cl),[a] 195, 200, 201, 226, 251 ($M^{+\bullet}$ with two ^{35}Cl). HRMS (EI): *m/z* 251.0474 ($M^{+\bullet}$ $C_{10}H_{15}{}^{35}Cl_2NO_2{}^{+\bullet}$ requires 251.0475).

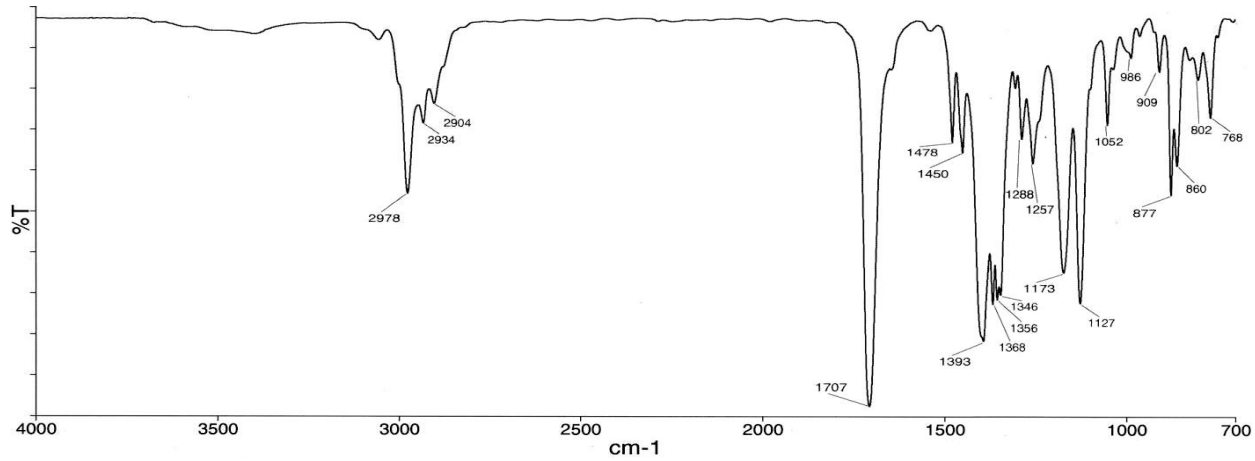
[a] M'^{+} =  ; M'' =  ; $[M-t\text{BuO}]^{+}$ =  (tentative assignments)



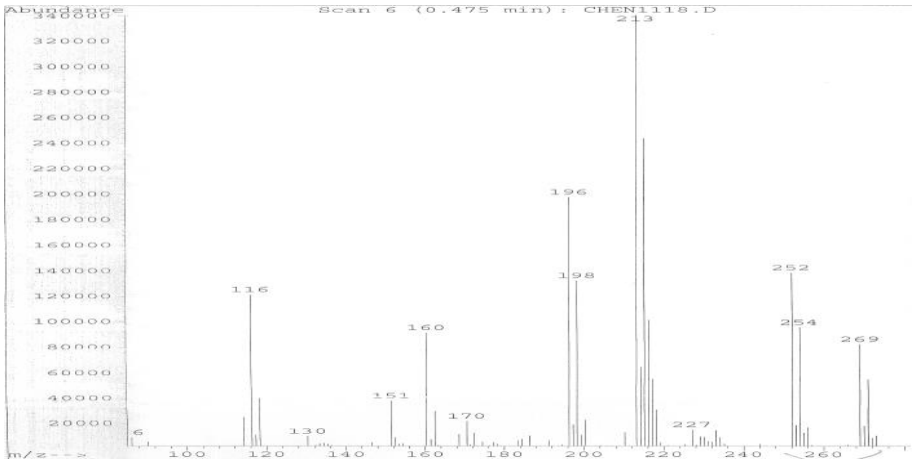
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



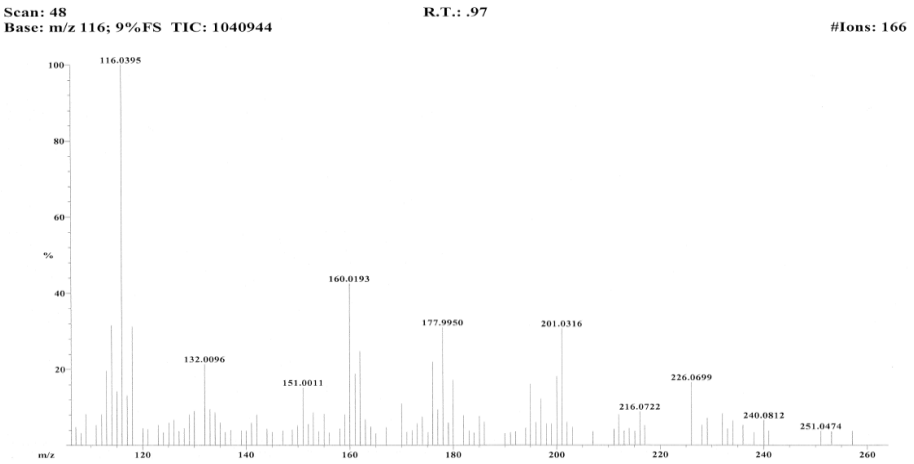
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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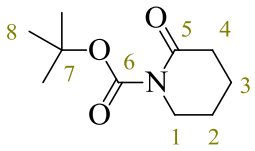
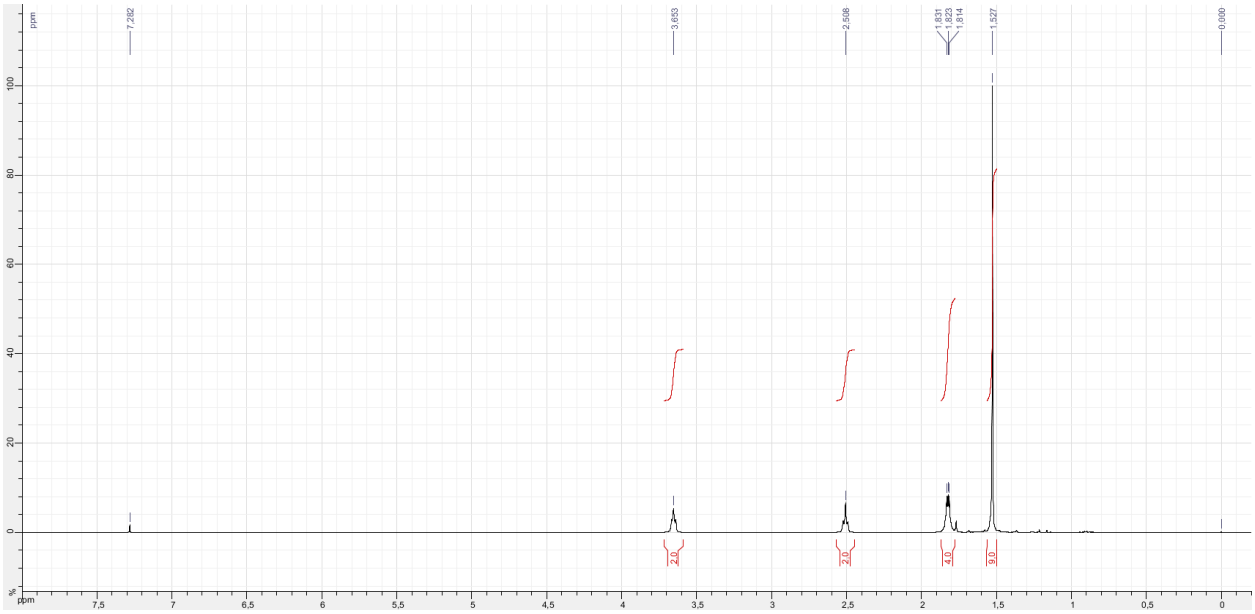
tert-Butyl 2-oxopiperidine-1-carboxylate[2]



Red oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.53 (9 H, s, H8), 1.77−1.87 (4 H, m, H2−H3), 2.51 (2 H, br t, *J* 6.5, H4), 3.65 (2 H, br t, *J* 6.0, H1).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

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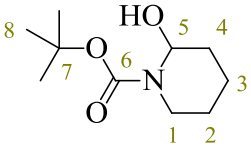
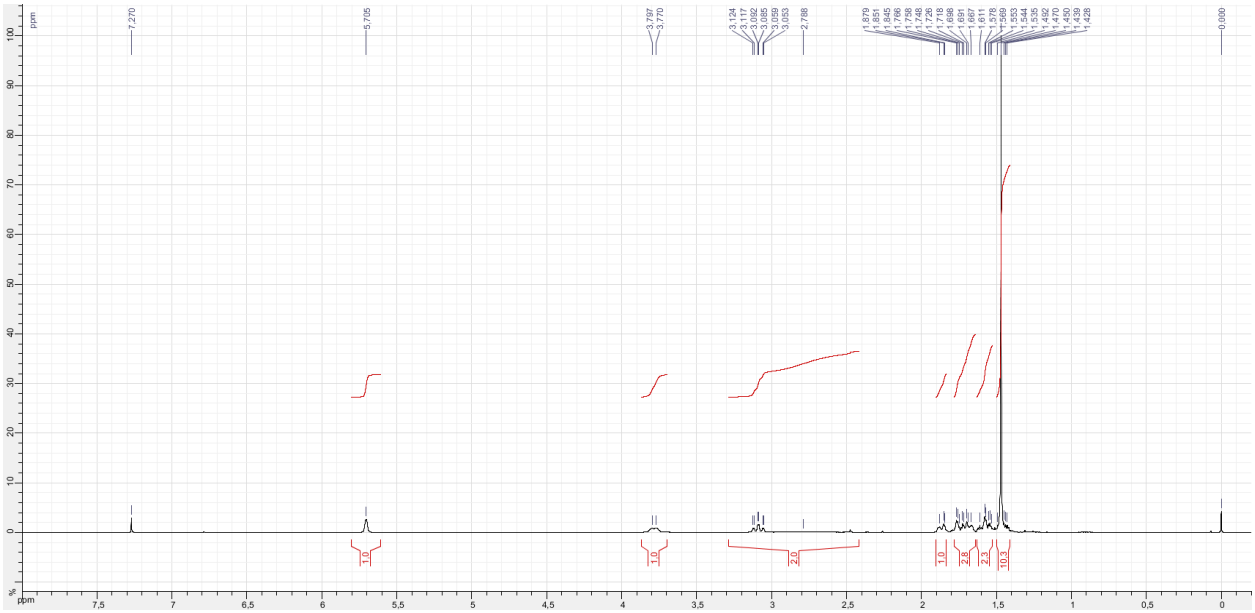
tert-Butyl 2-hydroxypiperidine-1-carboxylate[2]



Colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.38−1.92 (6 H, m, H2−H4), 1.47 (9 H, s, H8), 2.79 (1 H, br s, OH), 3.09 (1 H, ddd, *J* 13.5, 12.0, 3.0, H1a), 3.78 (1 H, br d, *J* 12.0, H1b), 5.70 (1 H, br s, H5).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

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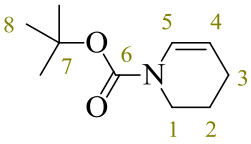
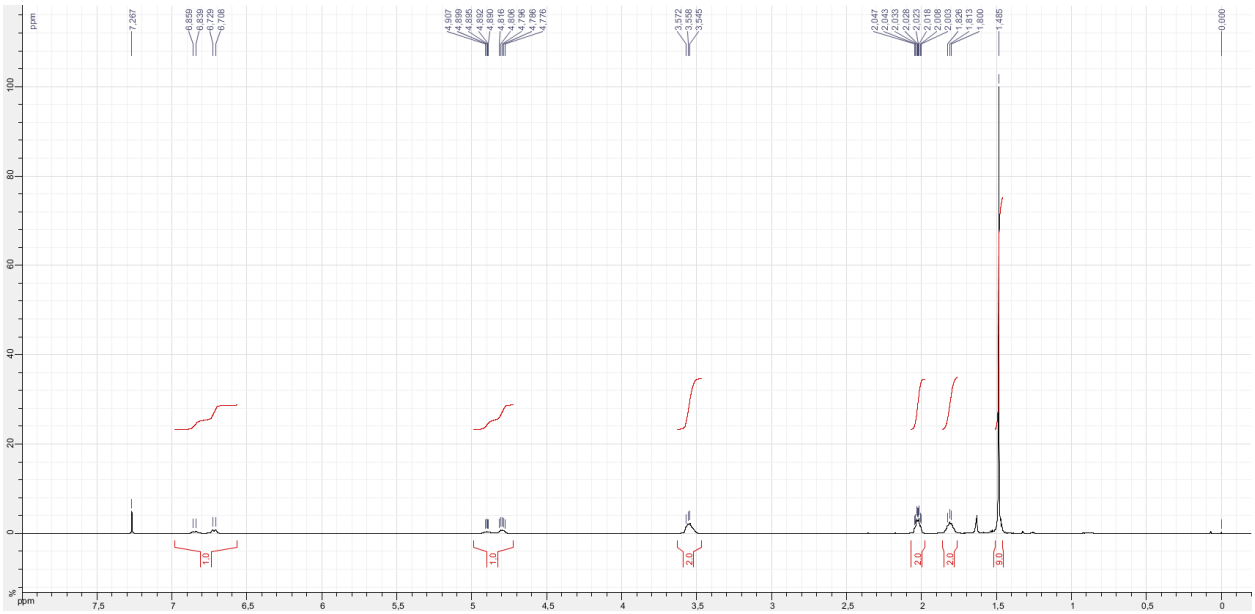
tert-Butyl 3,4-dihydro-2*H*-pyridine-1-carboxylate **1b**[6]



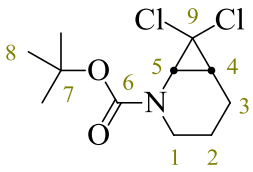
Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz), 60 : 40 mixture of two rotamers: δ 1.48 (9 H, s, H8, H8), 1.75−1.86 (2 H, m, H2, H2), 1.99−2.06 (2 H, m, H3, H3), 3.49−3.60 (2 H, m, H1, H1), 4.80 (0.6 H, ddd, *J* 8.5, 4.5, 3.0, H4), 4.90 (0.4 H, m, H4), 6.72 (0.6 H, d, *J* 8.5, H5), 6.85 (0.4 H, d, *J* 7.5, H5).



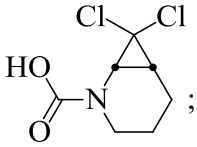
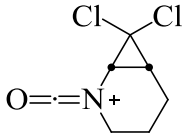
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

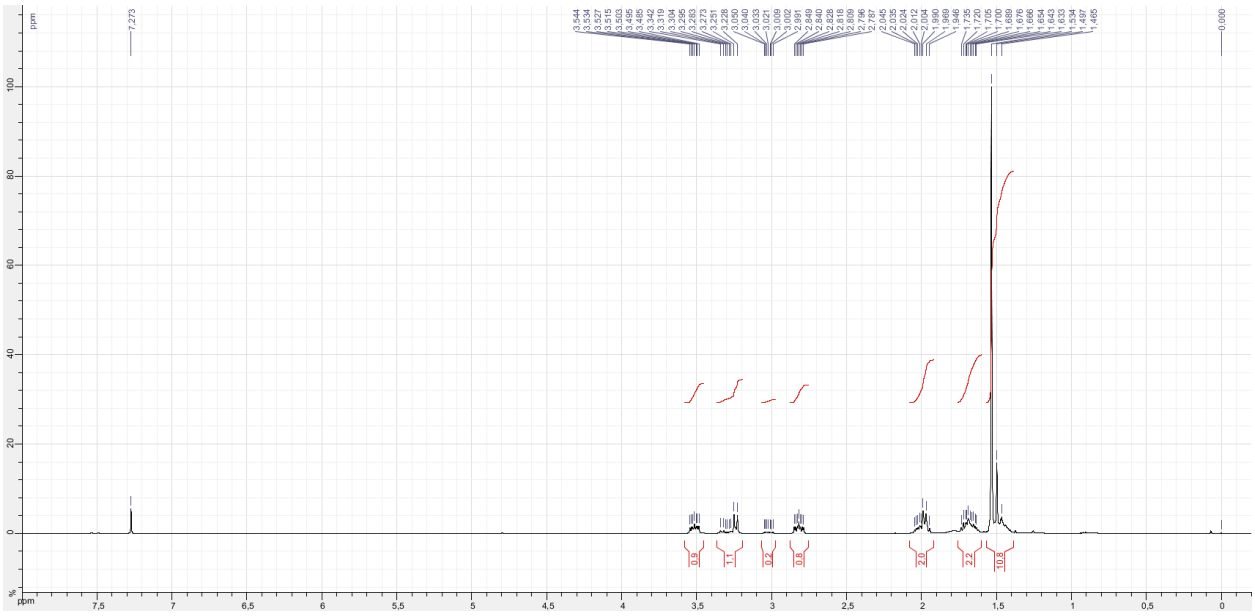
6− N. Gigant, G. Dequirez, P. Retailleau, I. Gillaizeau, P. Dauban, *Chem. Eur. J.* **2012**, *18*, 90−94 (supporting information).

tert-Butyl 7,7-dichloro-2-azabicyclo[4.1.0]heptane-2-carboxylate **2b**



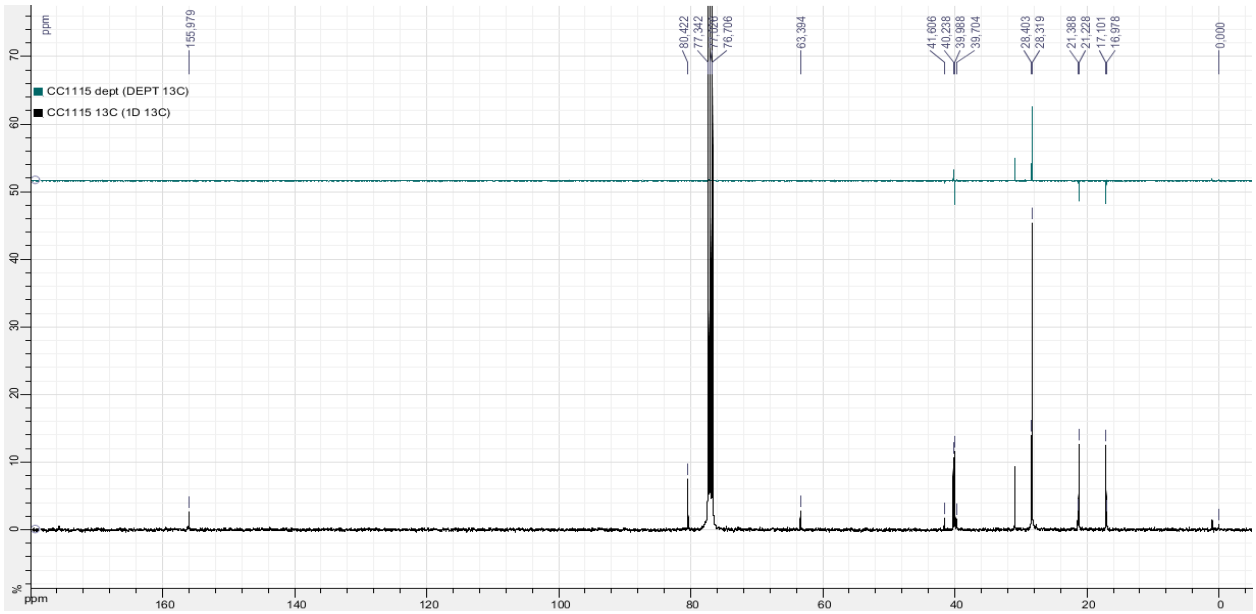
Pale yellow oil.[7] R_f 0.2 [EtOAc/petroleum ether 9%, PMA, UV-active]; 0.15 [EtOAc/petroleum ether 5% eluted two times]. IR (neat) *ν* 2976 (m), 2935 (m), 2873 (w), 2361 (w), 2342 (w), 1710 (s, C=O), 1476 (w), 1455 (m), 1403 (s), 1392 (m), 1368 (s), 1354 (m), 1308 (m), 1257 (m), 1168 (s), 1137 (m), 1093 (w), 1024 (w), 839 (w), 824 (w), 772 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz), 85 : 15 mixture of two rotamers. Major rotamer: *δ* 1.39−1.51 (1 H, m, H2a), 1.53 (9 H, s, H8), 1.61−1.75 (2 H, m, H2b, H3a), 1.93−2.06 (2 H, m, H3b, H4), 2.82 (1 H, ddd, *J* 12.5, 8.5, 3.5, H1a), 3.24 (1 H, d, *J* 9.0, H5), 3.51 (1 H, ddd, *J* 12.5, 7.0, 4.0, H1b). Minor rotamer, characteristic signals: *δ* 1.50 (9 H, s, H8), 3.02 (1 H, ddd, *J* 12.0, 7.5, 4.0, H1a), 3.27 (1 H, ddd, *J* 12.0, 9.5, 4.5, H1b), 3.33 (1 H, d, *J* 9.0, H5). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 85 : 15 mixture of two rotamers. Major rotamer: *δ* 17.1 (C3), 21.2 (C2), 28.3 (C8), 28.4 (C4), 40.0 (C1), 40.2 (C5), 63.4 (C9), 80.4 (C7), 156.0 (C6). Minor rotamer, characteristic signals: *δ* 17.0 (C3), 21.4 (C2), 39.7 (C5), 41.6 (C1). MS (positive CI, NH_3): *m/z* 210 ($M'H^+$ with two ^{35}Cl),[a] 212 ($M'H^+$ with one ^{35}Cl and one ^{37}Cl),[a] 227 ($M'H^+..NH_3$ with two ^{35}Cl),[a] 229 ($M'H^+..NH_3$ with one ^{35}Cl and one ^{37}Cl),[a] 266 (MH^+ with two ^{35}Cl), 268 (MH^+ with one ^{35}Cl and one ^{37}Cl), 270 (MH^+ with two ^{37}Cl), 283 ($MH^+..NH_3$ with two ^{35}Cl), 284, 285 ($MH^+..NH_3$ with one ^{35}Cl and one ^{37}Cl), 286, 287 ($MH^+..NH_3$ with two ^{37}Cl). MS (EI): *m/z* 128, 130, 132, 135, 174, 192 ([M−*t*BuO]$^+$ with two ^{35}Cl),[a] 194 ([M−*t*BuO]$^+$ with one ^{35}Cl and one ^{37}Cl),[a] 209, 211, 232, 234. HRMS (EI): *m/z* 265.0627 ($M^{+\bullet}$ $C_{11}H_{17}{}^{35}Cl_2NO_2{}^{+\bullet}$ requires 265.0631).

[a] M' =  ; [M−*t*BuO]$^+$ =  (tentative assignments)

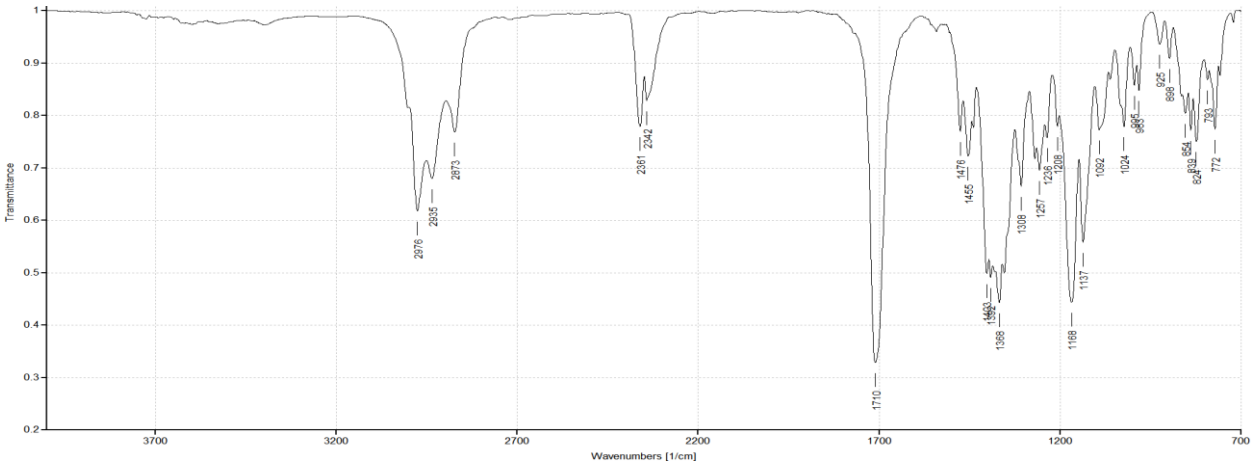


^1H NMR spectrum ($CDCl_3$, 400 MHz).

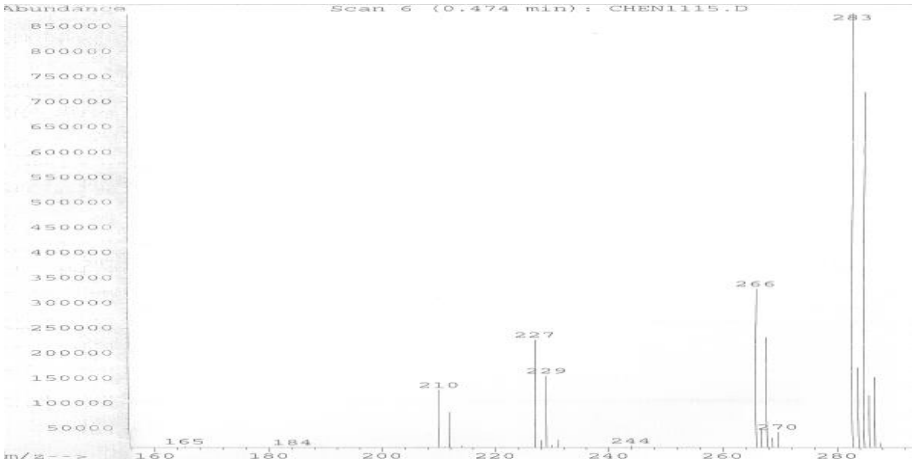
7− Upon standing in the freezer, a sample of this compound crystallised. It did not melt at room temperature (23 °C) but did melt when the flask was held in the chemist's hand for a moment.



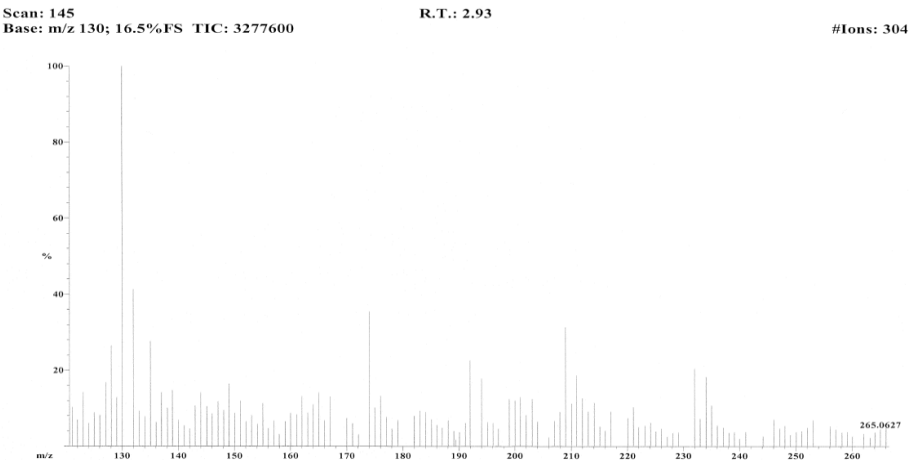
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).
The signal at 30.9 ppm is due to residual acetone contained in the NMR tube.



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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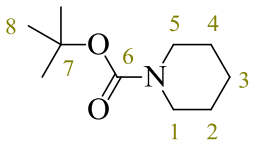
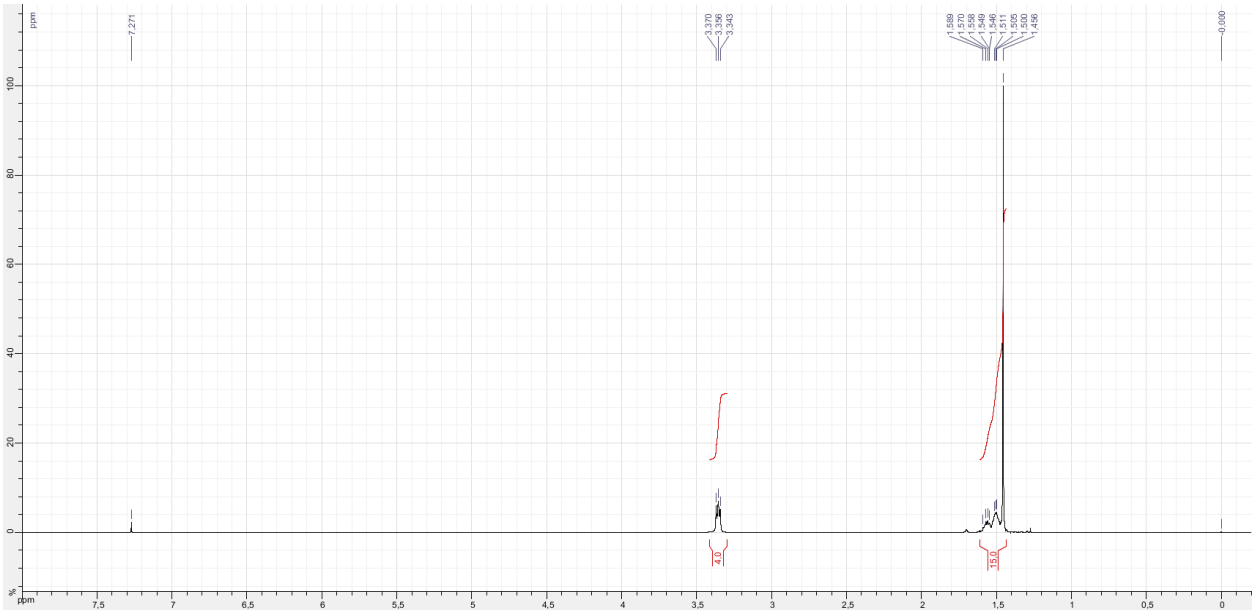
tert-Butyl piperidine-1-carboxylate[8]



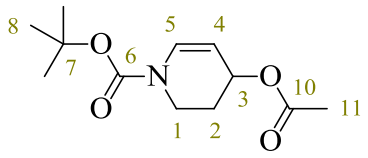
Colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.46 (9 H, s, H8), 1.47−1.60 (6 H, m, H2−H4), 3.36 (4 H, m looking like a br t, J 5.5, H1, H5).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

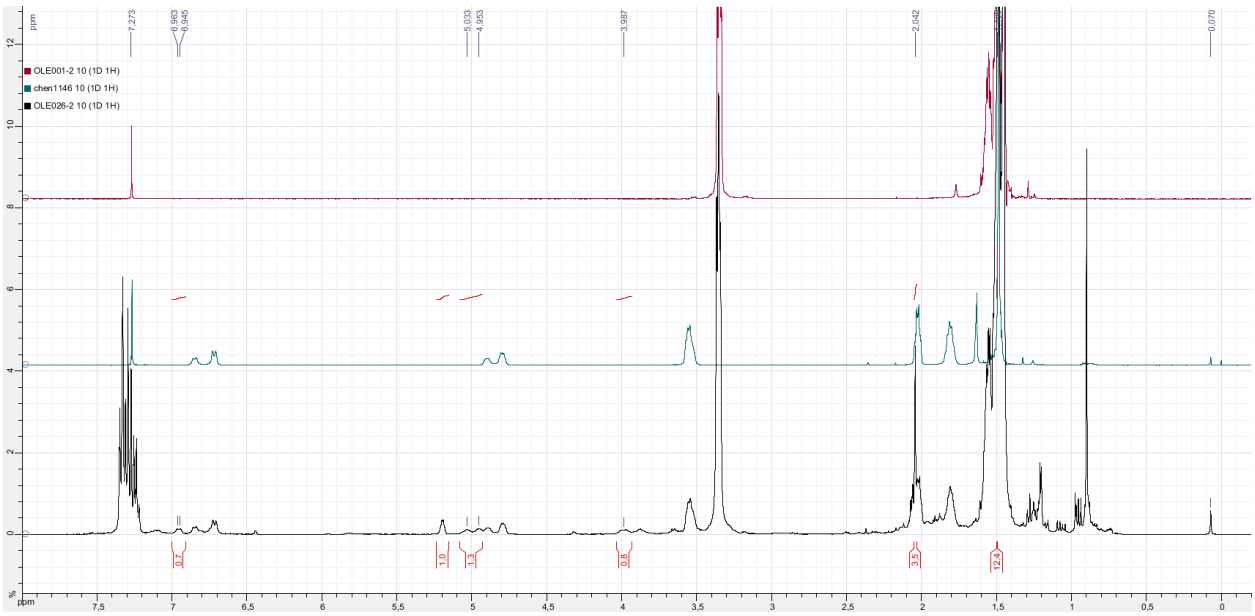
8− D. Stead, G. Carbone, P. O'Brien, K. R. Campos, I. Coldham, A. Sanderson, *J. Am. Chem. Soc.* **2010**, *132*, 7260−7261 (supporting information).

tert-Butyl 4-acetoxy-3,4-dihydro-2*H*-pyridine-1-carboxylate **1f**[9]



^{1}H NMR ($CDCl_3$, 400 MHz), mixture of two rotamers, characteristic signals: δ 1.50 (9 H, s, H8), 2.04 (3 H, s, H11), 3.99 (1 H, m, H1b), 4.95 and 5.03 (1 H, m, H4), 5.19 (1 H, m looking like q, *J* 4.0, H3), 6.95 (1 H, br d, *J* 7.5, H5).

Note: this compound was observed in the crude products of Kharasch-Sosnovsky reactions performed from *tert*-butyl piperidine-1-carboxylate but it was not isolated.



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product containing *tert*-butyl piperidine-1-carboxylate, **1b** and **1f** in a ratio of 73 : 18 : 09, approximately. Spectra of pure *tert*-butyl piperidine-1-carboxylate (in red) and **1b** (in green) are also displayed. The signals that are assigned to **1f** have been integrated.

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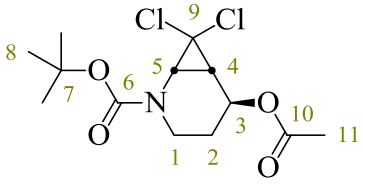
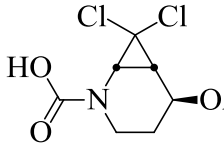
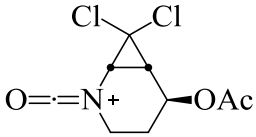
tert-Butyl (1*R**,5*R**,6*R**)-5-acetoxy-7,7-dichloro-2-azabicyclo[4.1.0]heptane-2-carboxylate **2f**

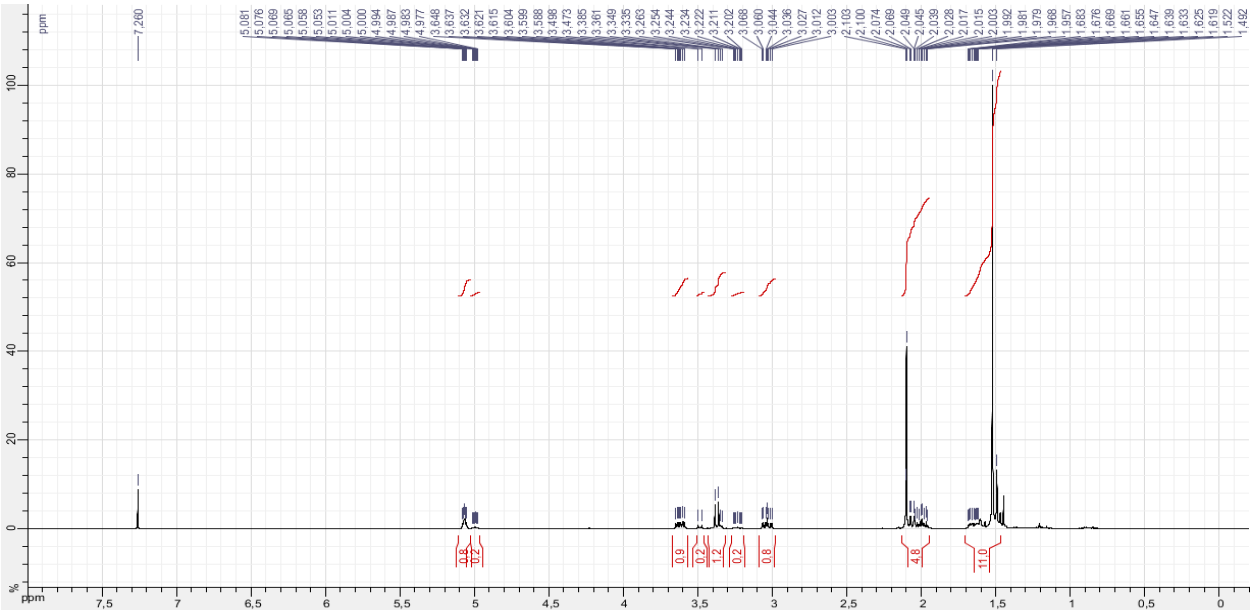


Viscous yellow oil. R_f 0.15 [EtOAc/petroleum ether 9%, PMA, UV-active]. IR (neat) ν 2978 (m), 2936 (m), 2884 (w), 1744 (s), 1712 (s), 1478 (m), 1456 (m), 1404 (m), 1392 (m), 1369 (s), 1338 (m), 1319 (m), 1236 (s), 1217 (m), 1167 (s), 1136 (m), 1073 (m), 1049 (m), 1021 (m), 858 (m), 827 (m), 773 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz), 82 : 18 mixture of two rotamers. Major rotamer: δ 1.52 (9 H, s, H8), 1.65 (1 H, dddd, *J* 14.5, 6.5, 5.0, 3.5, H2a), 2.00 (1 H, ddt, *J* 14.5, 9.5, 4.5, H2b), 2.06 (1 H, dd, *J* 9.5, 2.0, H4), 2.10 (3 H, s, H11), 3.04 (1 H, ddd, *J* 13.0, 9.5, 3.5, H1a), 3.37 (1 H, d, *J* 9.5, H5), 3.62 (1 H, ddd, *J* 13.0, 6.5, 4.5, H1b), 5.07 (1 H, ddd, *J* 5.0, 4.5, 2.0, H3). Minor rotamer, characteristic signals: δ 1.49 (9 H, s, H8), 2.10 (3 H, s, H11),

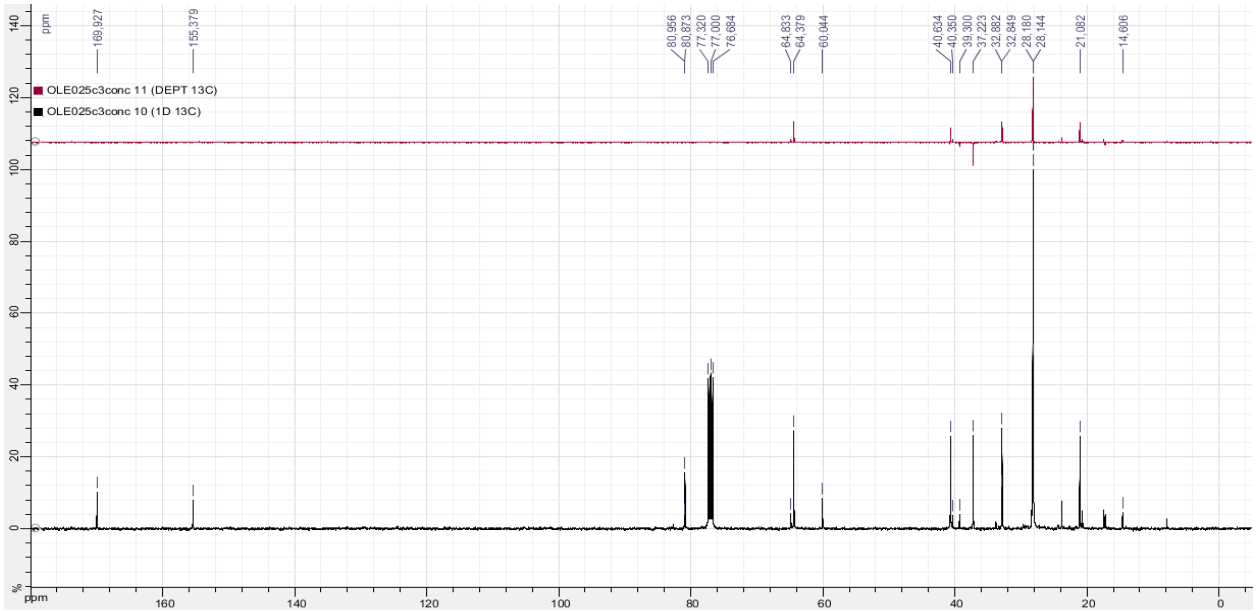
9– G. Caillot, J. Dufour, M.-C. Belhomme, T. Poisson, L. Grimaud, X. Pannecoucke, I. Gillaizeau, *Chem. Commun.* **2014**, *50*, 5887–5890 (supporting information).

3.23 (1 H, ddd, *J* 13.0, 8.0, 3.5, H1a), 3.33−3.42 (1 H, m, H1b), 3.49 (1 H, d, *J* 10.0, H5), 4.99 (1 H, ddd, *J* 7.0, 4.0, 2.5, H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 82 : 18 mixture of two rotamers. Major rotamer: δ 21.1 (C11), 28.1 (C2), 28.2 (C8), 32.8 (C4), 37.2 (C1), 40.6 (C5), 60.0 (C9), 64.4 (C3), 80.9 (C7), 155.4 (C6), 169.9 (C10). Minor rotamer, characteristic signals: δ 32.9 (C4), 39.3 (C1), 40.3 (C5), 64.8 (C3), 81.0 (C7). MS (positive CI, NH_3): *m/z* 164, 166, 268 ($M'H^+$ with two ^{35}Cl),[a] 270 ($M'H^+$ with one ^{35}Cl and one ^{37}Cl),[a] 285 ($M'H^+..NH_3$ with two ^{35}Cl),[a] 286, 287 ($M'H^+..NH_3$ with one ^{35}Cl and one ^{37}Cl),[a] 289 ($M'H^+..NH_3$ with two ^{37}Cl),[a] 324 (MH^+ with two ^{35}Cl), 325, 326 (MH^+ with one ^{35}Cl and one ^{37}Cl), 341 ($MH^+..NH_3$ with two ^{35}Cl), 342, 343($MH^+..NH_3$ with one ^{35}Cl and one ^{37}Cl). MS (EI): *m/z* 128, 163, 164, 165, 207, 209, 250 ($[M-t\text{BuO}]^+$ with two ^{35}Cl),[a] 252 ($[M-t\text{BuO}]^+$ with one ^{35}Cl and one ^{37}Cl).[a] HRMS (EI): *m/z* 250.0046 ($[M-t\text{BuO}]^+$ $C_9H_{10}{}^{35}Cl_2NO_3^+$ requires 250.0032).[a]

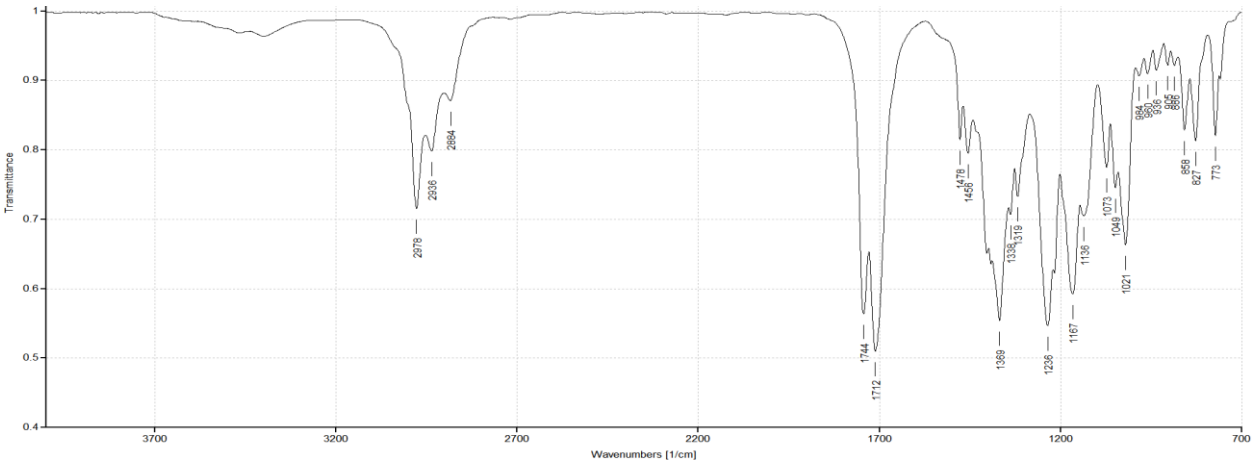
[a] M' =  ; $[M-t\text{BuO}]^+$ =  (tentative assignments)



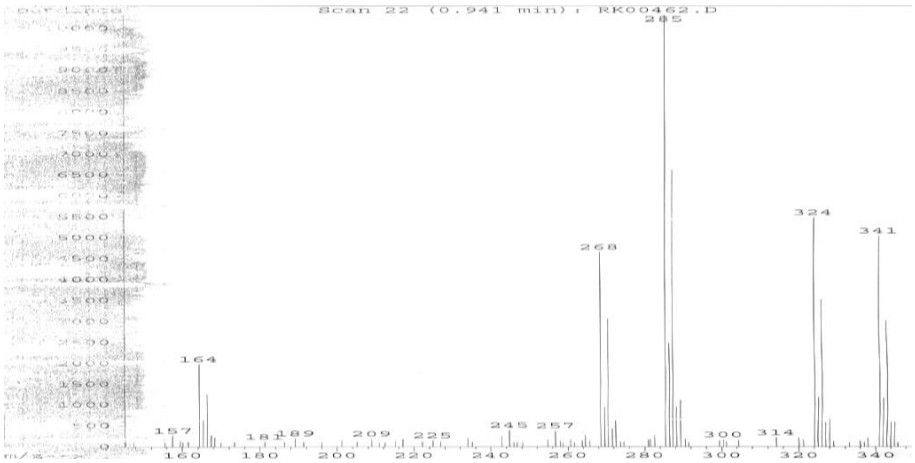
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



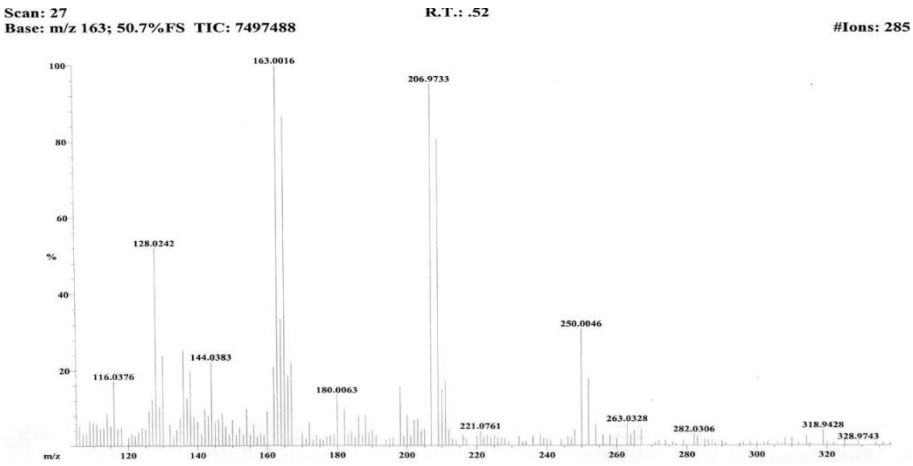
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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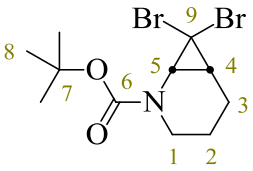
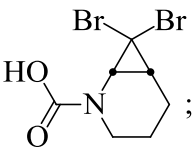
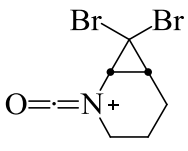
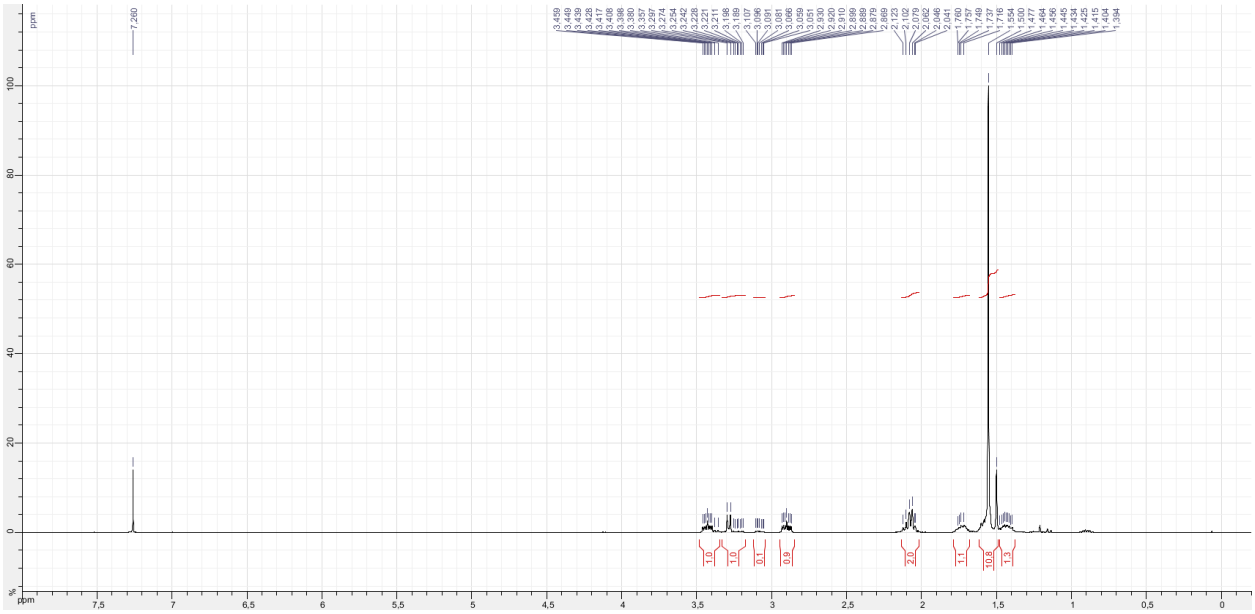
tert-Butyl 7,7-dibromo-2-azabicyclo[4.1.0]heptane-2-carboxylate **2c**

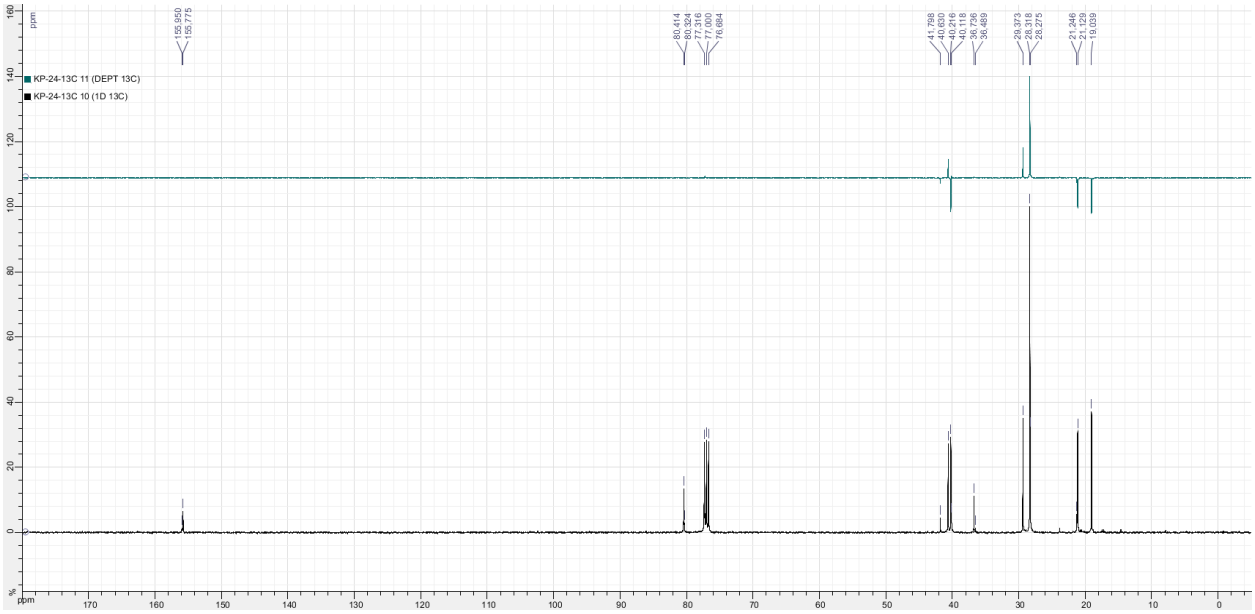


White solid. M.p. 46.8−48.0 °C. R_f 0.2 [EtOAc/petroleum ether 10%, PMA, UV-active]. IR (neat) ν 2971 (m), 2933 (w), 2872 (w), 1704 (s, C=O), 1451 (w), 1400 (m), 1392 (m), 1366 (m), 1348 (m), 1315 (w), 1255 (w), 1161 (m), 1135 (m), 1015 (w), 755 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz), 88 : 12 mixture of two rotamers. Major rotamer: δ 1.44 (1 H, m, H2a), 1.55 (9 H, s, H8), 1.52−1.62 (1 H, m, H2b or H3a), 1.74 (1 H, m, H2b or H3a), 2.02−2.13 (2 H, m, H3b, H4), 2.90 (1 H, ddd, J 12.5, 8.0, 4.0, H1a), 3.29 (1 H, d, J 9.0, H5), 3.43 (1 H, ddd, J 12.5, 8.0, 4.5, H1b). Minor rotamer, characteristic signals: δ 1.50 (9 H, s, H8), 3.08 (1 H, ddd, J 12.5, 6.5, 4.0, H1a), 3.22 (1 H, ddd, J 12.5, 9.5, 4.0, H1b), 3.37 (1 H, d, J 9.0, H5). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 88 : 12 mixture of two rotamers. Major rotamer: δ 19.0 (C3), 21.1 (C2), 28.3 (C8), 29.4 (C4), 36.7 (C9), 40.2 (C1), 40.6 (C5), 80.4 (C7), 155.8 (C6). Minor rotamer, characteristic signals: δ 21.2 (C2), 28.3 (C8), 36.5 (C9), 40.1 (C5), 41.8 (C1), 80.3 (C7), 155.9 (C6). MS (positive CI, NH_3): *m/z* 175, 177, 298 ($M'H^+$ with two ^{79}Br),[a] 300 ($M'H^+$ with one ^{79}Br and one ^{81}Br),[a] 302 ($M'H^+$ with two ^{81}Br),[a] 315 ($M'H^+$ with two ^{79}Br),[a] 317 ($M'H^+..NH_3$ with one ^{79}Br and one ^{81}Br),[a] 319 ($M'H^+..NH_3$ with two ^{81}Br),[a] 354 (MH^+ with two ^{79}Br), 356 (MH^+ with one ^{79}Br and one ^{81}Br), 358 (MH^+ with two ^{81}Br), 371 ($MH^+..NH_3$ with two ^{79}Br), 373 ($MH^+..NH_3$ with one ^{79}Br and one ^{81}Br), 375 ($MH^+..NH_3$ with two ^{81}Br). MS (EI): *m/z* 94, 95, 119, 146, 174, 175, 176, 199, 218, 220, 255, 280 ($[M-t\text{BuO}]^+$ with two ^{79}Br), 282 ($[M-t\text{BuO}]^+$ with one ^{79}Br and one ^{81}Br),[a] 284 ($[M-t\text{BuO}]^+$ with two ^{81}Br), 297, 299, 301, 353 ($M^{+\bullet}$ with two ^{79}Br), 355 ($M^{+\bullet}$ with one ^{79}Br and one ^{81}Br), 357 ($M^{+\bullet}$ with two ^{81}Br). HRMS (EI): *m/z* 352.9629 ($M^{+\bullet}$ $C_{11}H_{17}{}^{79}Br_2NO_2{}^{+\bullet}$ requires 352.9621).

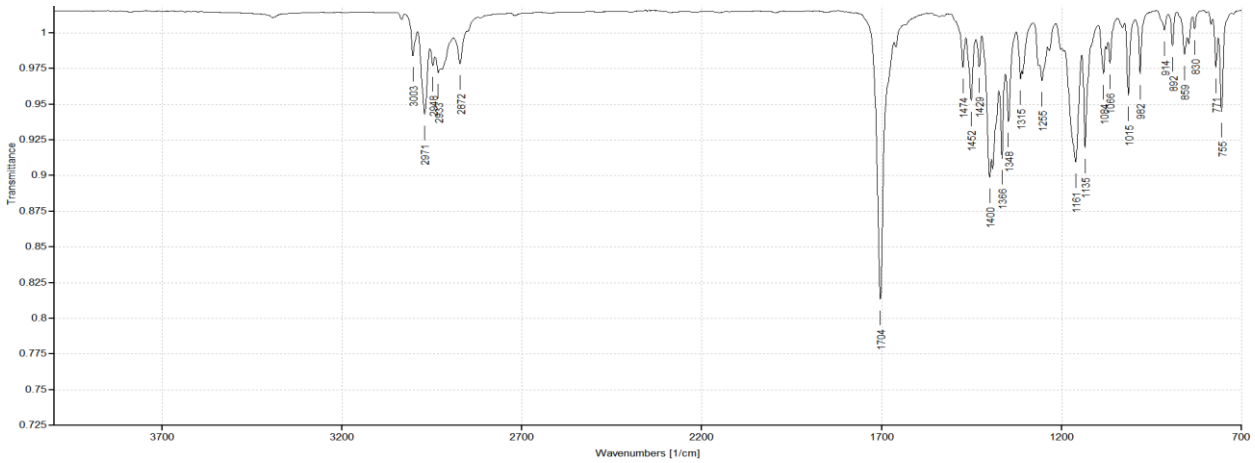
[a] M' =  ; $[M-t\text{BuO}]^+$ =  (tentative assignments)



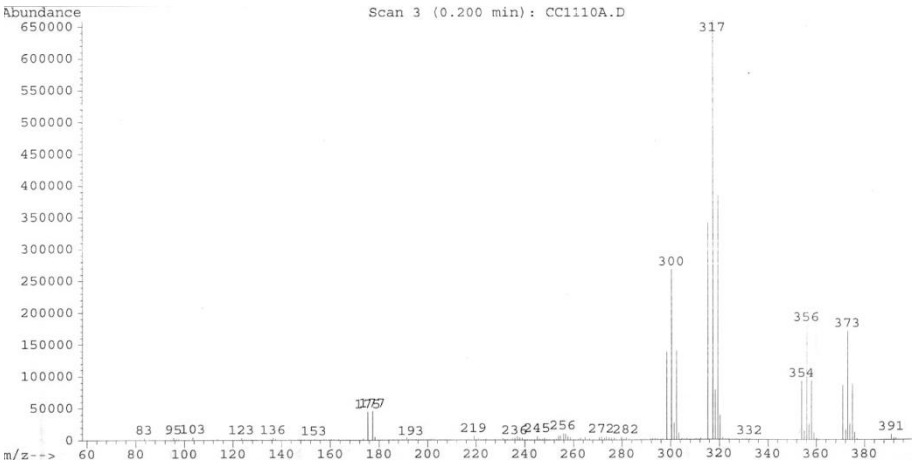
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



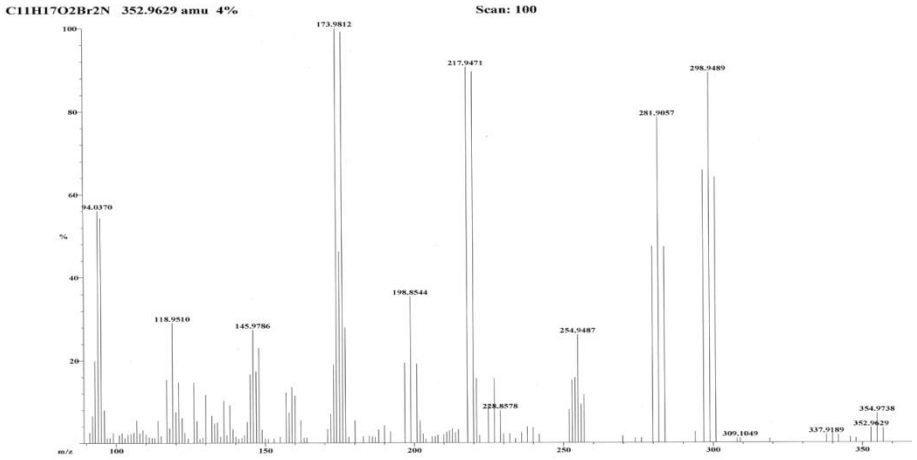
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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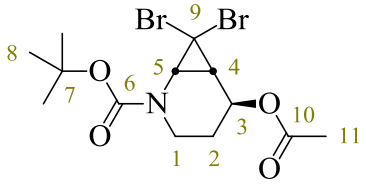
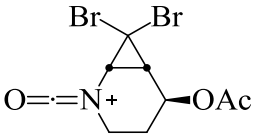
tert-Butyl (1*R**,5*S**,6*R**)-5-acetoxy-7,7-dibromo-2-azabicyclo[4.1.0]heptane-2-carboxylate **2g**

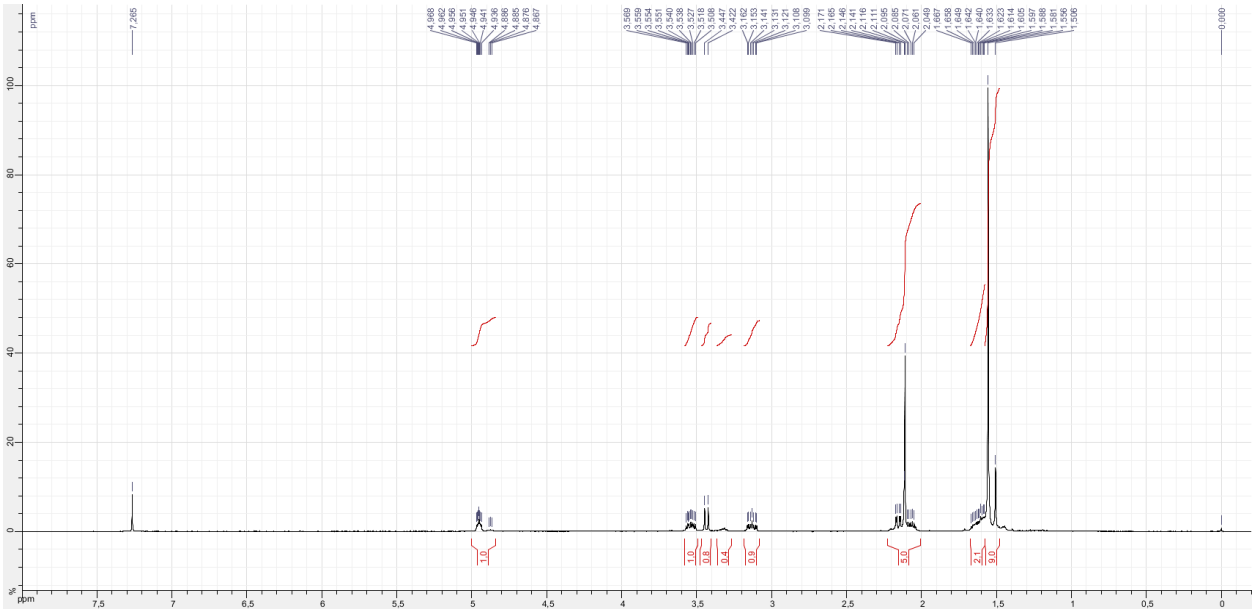


White solid, mp. 97.8-99.5°C. R_f 0.25 [EtOAc/petroleum ether 10%, PMA, UV-active]. IR (neat) *v* 2977 (m), 2935 (w), 2884 (w), 1742 (s), 1711 (s), 1477 (w), 1455 (w), 1402 (m), 1393 (m), 1368 (s), 1337 (m), 1317 (m), 1235 (s), 1216 (m), 1167 (m), 1139 (m), 1070 (w), 1046 (m), 1020 (m), 857 (w), 761 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz), 86 : 14 mixture of two rotamers. Major rotamer: δ 1.56 (9 H, s, H8), 1.63 (1 H, dddd, *J* 14.0, 7.5, 6.0, 3.5, H2a), 2.08 (1 H, ddt, *J* 14.0, 8.5, 4.5, H2b), 2.11 (3 H, s, H11), 2.16 (1 H, dd, *J* 9.5, 2.5, H4), 3.13 (1 H, ddd, *J* 13.0, 8.5, 3.5, H1a), 3.43 (1 H, d, *J* 9.5, H5), 3.54 (1 H, ddd, *J* 13.0, 7.5, 4.5, H1b), 4.95 (1 H, ddd, *J* 6.0, 4.5, 2.5, H3). Minor rotamer, characteristic signals: δ 1.51 (9 H, s, H8), 2.12 (3 H, s, H11), 2.19 (1 H, dd, *J* 10.0, 3.0, H4), 4.88 (1 H, ddd, *J* 8.0, 4.0, 3.0, H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 86 : 14 mixture of two rotamers. Major rotamer: δ 21.1 (C11), 28.2 (C2), 28.3 (C8), 31.5 (C9), 34.0 (C4), 38.1 (C1), 41.3 (C5), 66.4 (C3), 80.9 (C7), 155.2 (C6), 169.8 (C10). Minor rotamer, characteristic signals: δ 28.0 (C2), 31.4 (C9), 34.1 (C4), 40.1 (C1), 41.0 (C5), 67.0 (C3), 155.4 (C6). MS (EI): *m/z* 172, 173, 174, 226, 251, 253, 255, 295, 297, 299, 338 ($[M-tBuO]^+$

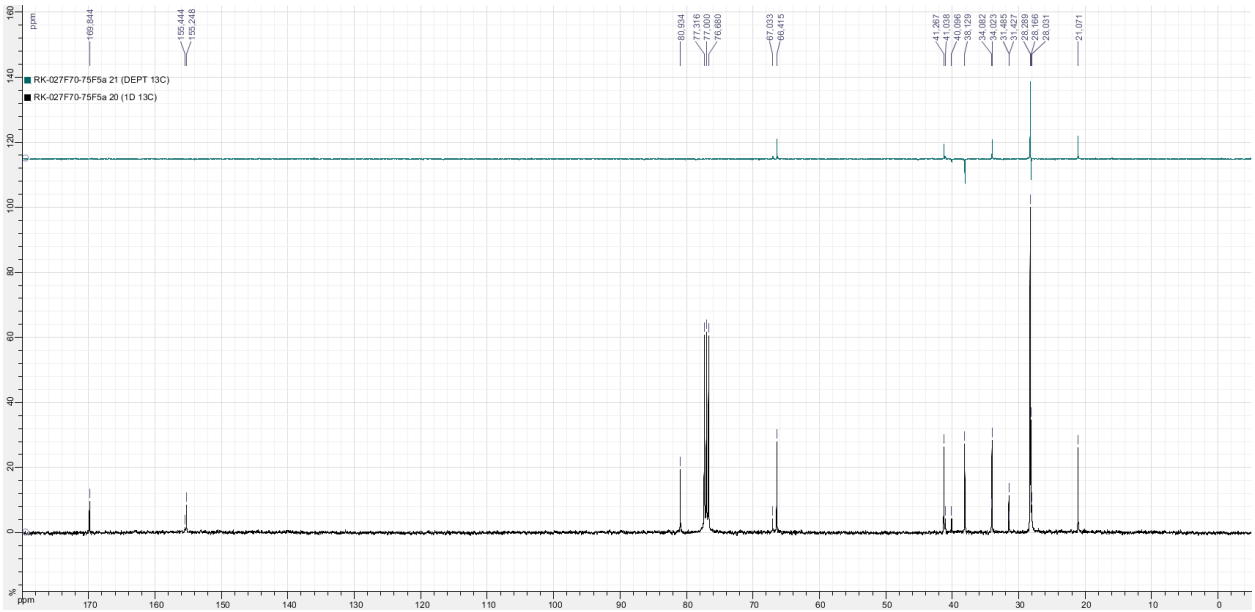
with two ^{79}Br),[a] 340 ([M−*t*BuO]$^+$ with one ^{79}Br and one ^{81}Br),[a] 342 ([M−*t*BuO]$^+$ with two ^{81}Br).[a] HRMS (EI): *m/z* 337.9032 ([M−*t*BuO]$^+$ $C_9H_{10}{}^{79}Br_2NO_3{}^+$ requires 337.9022).[a]

[a] [M−*t*BuO]$^+$ = 

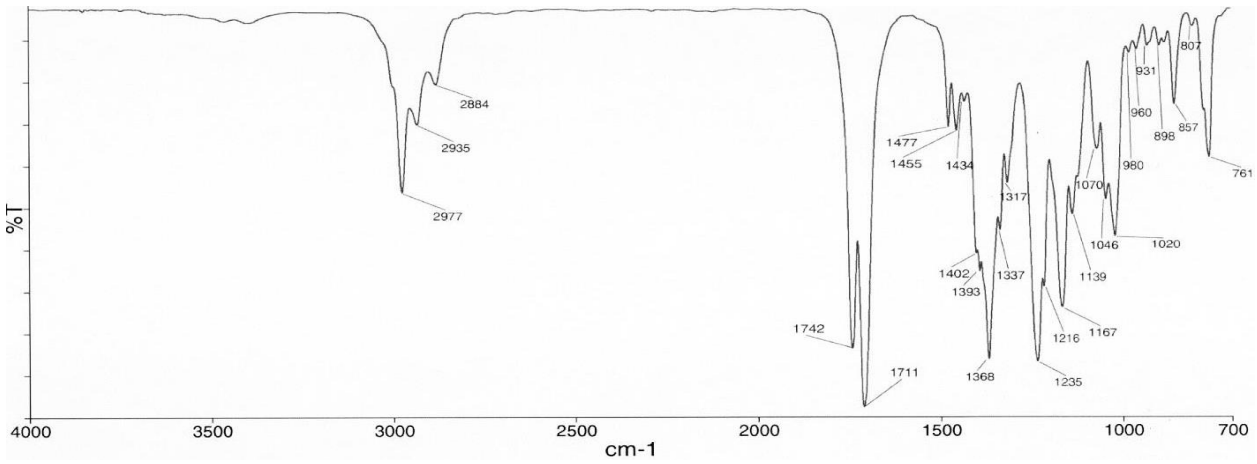
(tentative assignment)



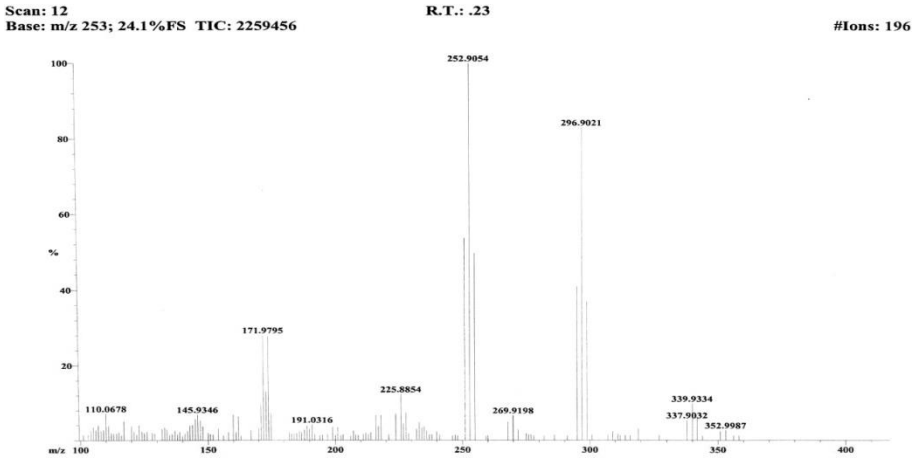
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (EI).

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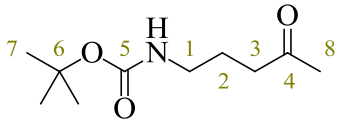
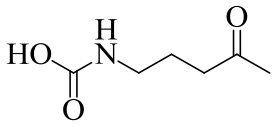
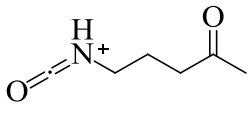
tert-Butyl *N*-(4-oxopentyl)carbamate[10]

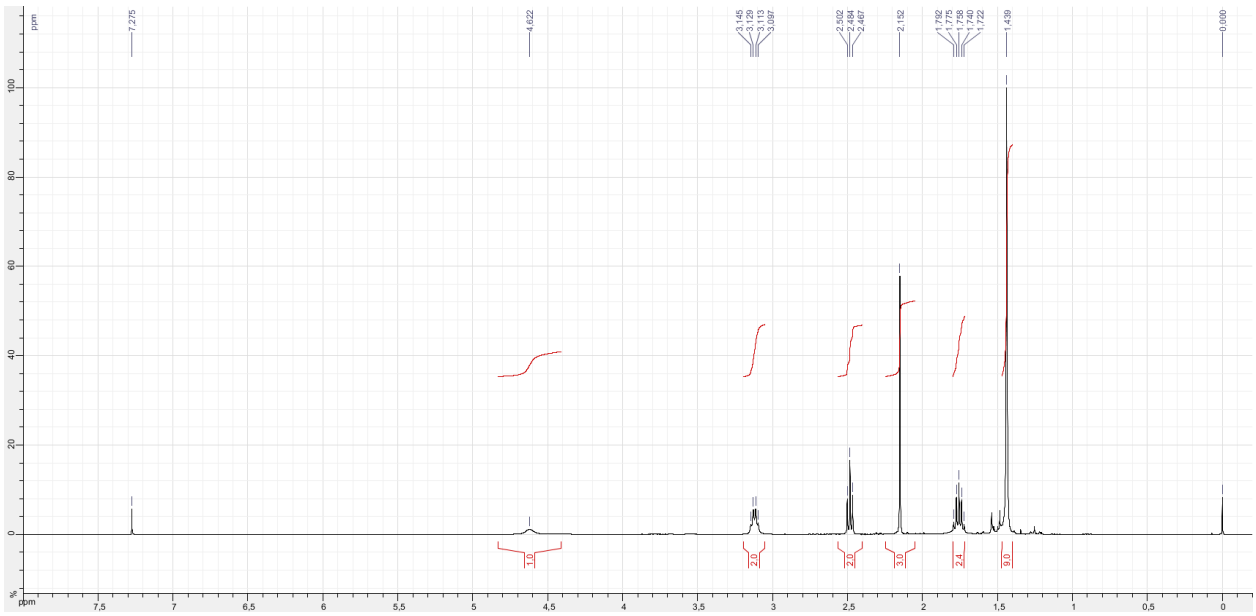


Pale yellow oil. IR (neat) *v* 3361 (br, m, NH), 2978 (m), 2934 (m), 1713 (s, C=O), 1521 (m), 1452 (w), 1393 (m), 1366 (m), 1271 (m), 1252 (m), 1169 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): *δ* 1.44 (9 H, s, H7), 1.76 (2 H, quint, *J* 7.0, H2), 2.15 (3 H, s, H8), 2.48 (2 H, t, *J* 7.0, H3), 3.07−3.17 (2 H, m looking like q, *J* 6.5, H1), 4.62 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 23.9 (C2), 28.3 (C7), 29.9 (C8), 39.8, 40.6 (C1, C3), 79.0 (C6), 156.0 (C5), 208.4 (C4). MS (positive CI, NH_3): *m/z* 85, 102, <u>146</u> ($M'H^+$),[a] 147, 163 ($M'H^+..NH_3$),[a] 202 (MH^+), 203, 219 ($MH^+..NH_3$). MS (EI): *m/z* 128 ($[M-tBuO]^+$),[a] 143, 144, <u>145</u>.

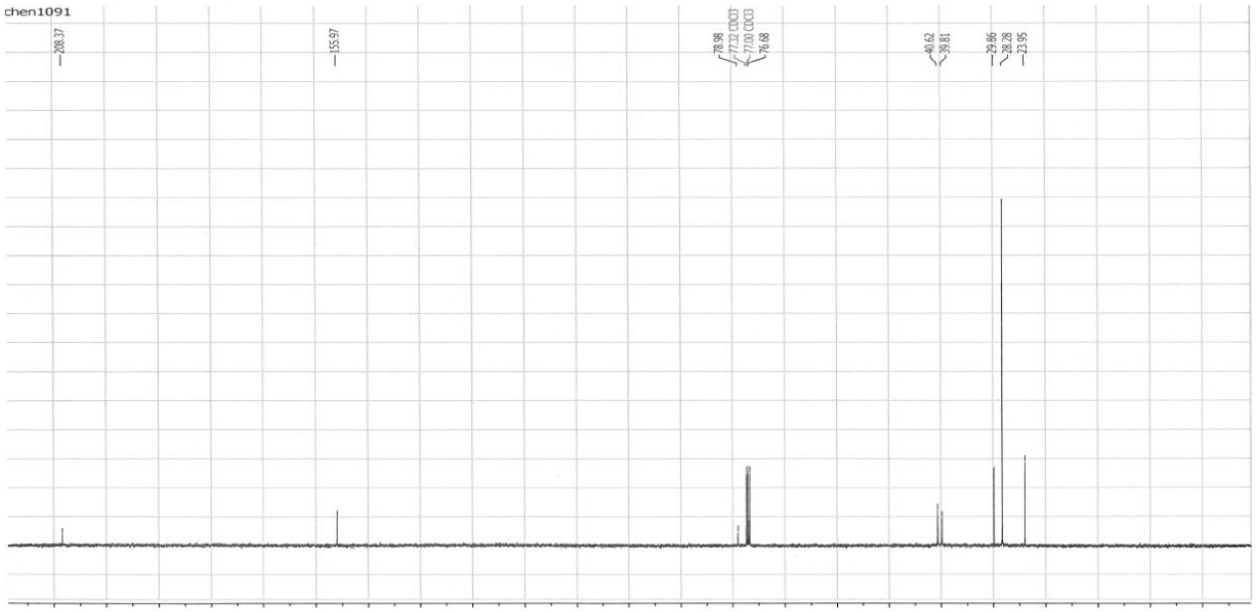
[a] M' =  ; $[M-tBuO]^+$ = 

(tentative assignments)

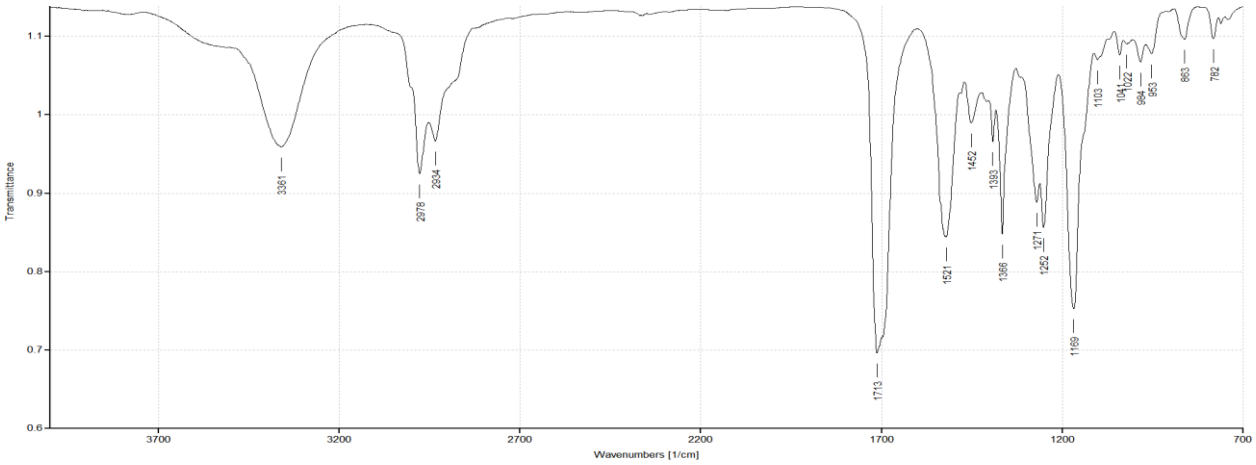
10− K. Miyazawa, T. Koike, M. Akita, *Adv. Synth. Catal.* **2014**, *356*, 2749−2755 (supporting information).



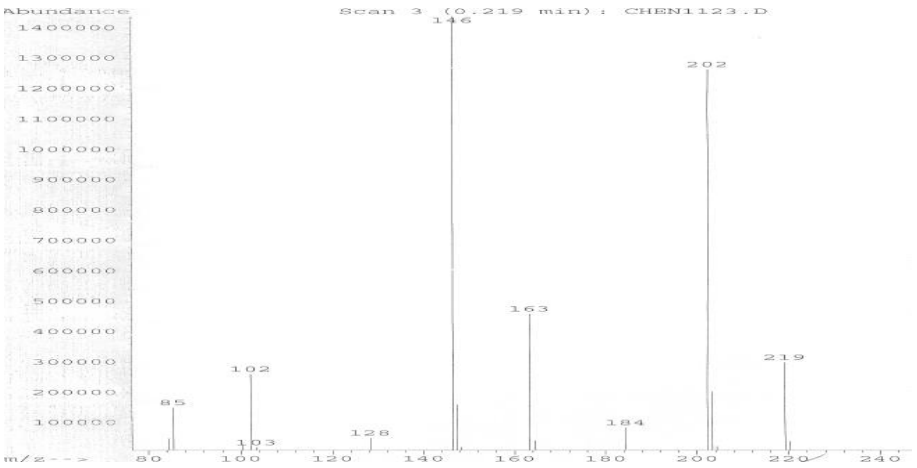
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



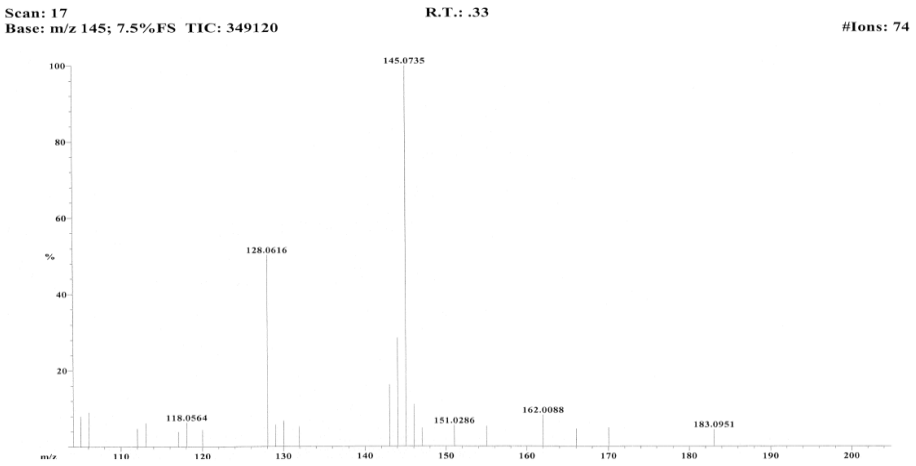
^{13}C NMR spectrum ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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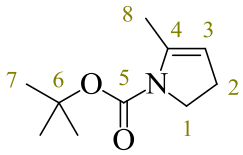
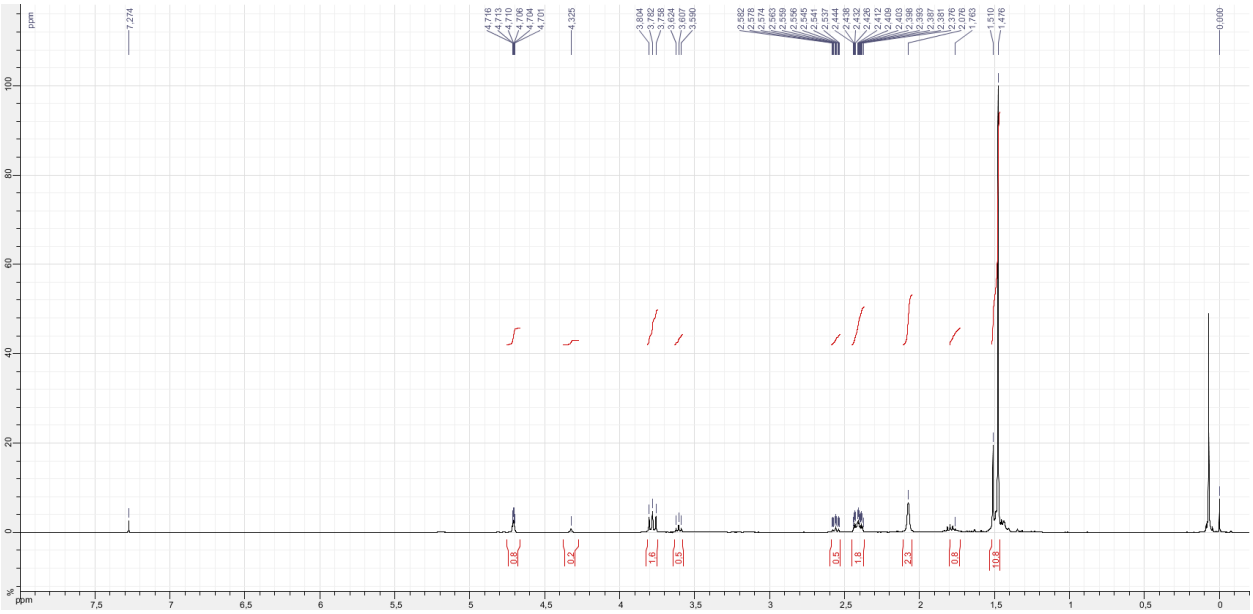
tert-Butyl 5-methyl-2,3-dihydropyrrole-1-carboxylate **1d**



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz), 77 : 23 mixture of two rotamers: δ 1.48 (6.93 H, s, H7), H7), 1.51 (2.07 H, s, H7), 1.76 (0.69 H, br s, H8), 2.08 (2.31 H, td, *J* 2.0, 1.5, H8), 2.56 (0.46 H, tt, J 7.0, 1.6, H2), 2.41 (2 H, tdq, *J* 9.0, 2.5, 2.0, H2), 3.61 (0.46 H, t, *J* 7.0, H1), 3.78 (1.54 H, t, *J* 9.0, H1), 4.32 (0.23 H, br s, H3), 4.71 (0.77 H, tq, *J* 2.5, 1.5, H3).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

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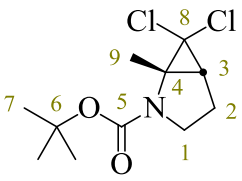
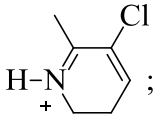
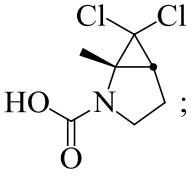
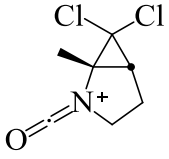
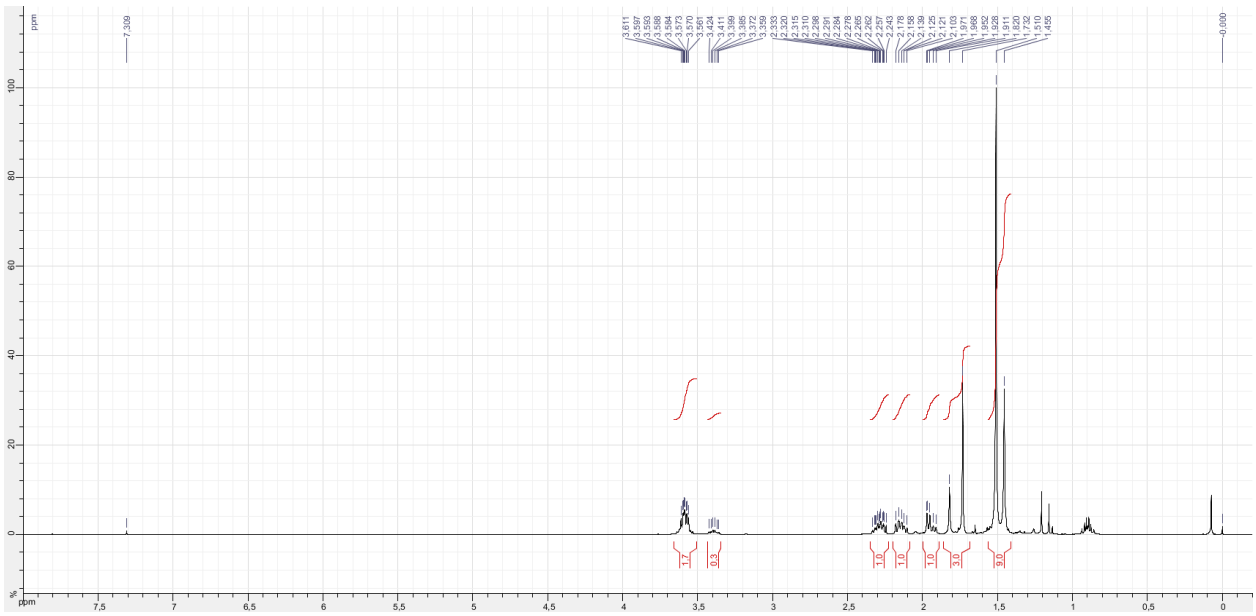
tert-Butyl 6,6-dichloro-1-methyl-2-azabicyclo[3.1.0]hexane-2-carboxylate **2d**



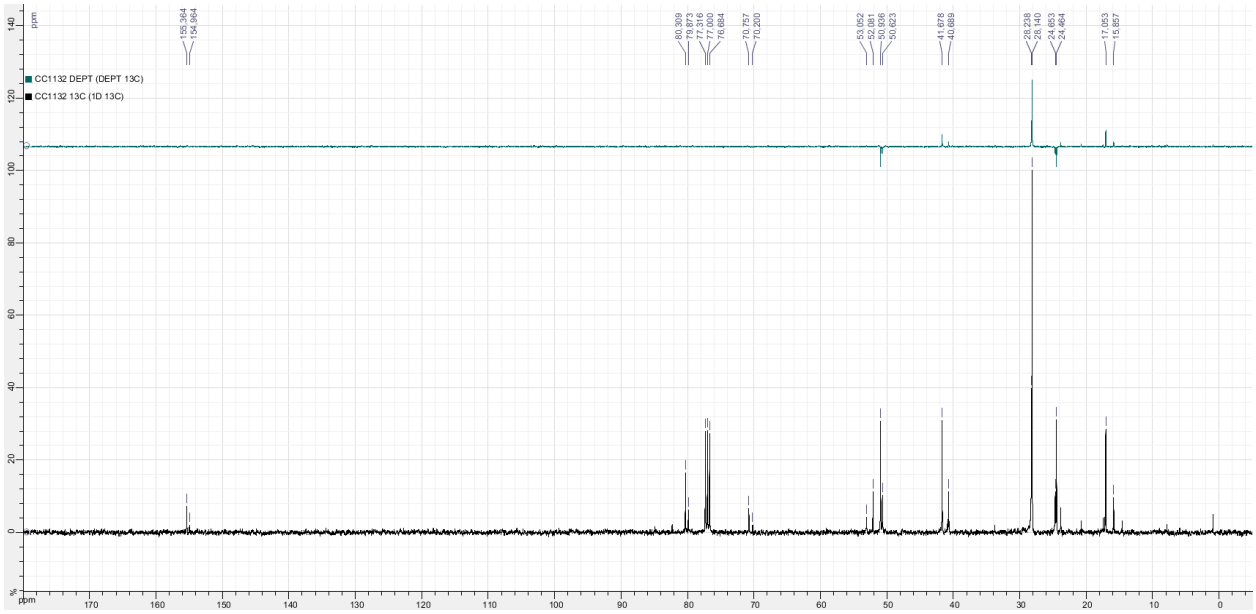
Pale yellow oil (solid in the freezer at −20 °C). R_f 0.1 [EtOAc/petroleum ether 10%, PMA, not UV-active]. IR (neat) ν 2978 (m), 2937 (w), 2901 (w), 1706 (s, C=O), 1479 (w), 1453 (w), 1392 (m), 1381 (m), 1367 (s), 1341 (m), 1258 (w), 1163 (m), 1110 (m), 1081 (w), 1066 (w), 1003 (w), 851 (w), 771 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz), 74 : 26 mixture of two rotamers. Major rotamer: δ 1.51 (9 H, s, H7), 1.73 (3 H, s, H9), 1.96 (1 H, dd, J 7.5, 1.0, H3), 2.09−2.20 (1 H, m, H2a), 2.23−2.35 (1 H, m, H2b), 3.52−3.65 (2 H, m, H1). Minor rotamer: δ 1.45 (9 H, s, H7), 1.82 (3 H, s, H9), 1.92 (1 H, br d, J 7.0, H3), 2.09−2.20 (1 H, m, H2a), 2.23−2.35 (1 H, m, H2b), 3.39 (1 H, td, J 10.5, 5.0, H1a), 3.52−3.65 (1 H, m, H1b). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 74 : 26 mixture of two rotamers. Major rotamer: δ 17.1 (C9), 24.5 (C2), 28.1 (C7), 41.7 (C3), 50.9 (C1), 52.1 (C4), 70.8 (C8), 80.3 (C6), 155.4 (C5). Minor rotamer: δ 15.9 (C9), 24.7 (C2), 28.2 (C7), 40.7 (C3), 50.6 (C1), 53.1 (C4), 70.2 (C8), 79.9 (C6), 155.0 (C5). MS (positive CI, NH_3): *m/z* 96, 130 (M'$^+$ with ^{35}Cl),[a] 157, 210 (M"H$^+$ with two ^{35}Cl),[a] 212 (M"H$^+$ with one ^{35}Cl and one ^{37}Cl),[a] 214 (M"H$^+$ with two ^{37}Cl),[a] 227 (M"H$^+$..NH_3 with two ^{35}Cl),[a] 229 (M"H$^+$..NH_3 with one ^{35}Cl and one ^{37}Cl),[a] 266 (MH$^+$ with two ^{35}Cl), 267, 268 (MH$^+$ with one ^{35}Cl and one ^{37}Cl), 270 (MH$^+$ with two ^{37}Cl), 283 (MH$^+$..NH_3 with two ^{35}Cl), 285 (MH$^+$..NH_3 with one ^{35}Cl and one ^{37}Cl). MS (EI): *m/z* 128, 130, 132, 165, 174, 192 ([M−*t*BuO]$^+$ with two ^{35}Cl),[a] 194 ([M−*t*BuO]$^+$ with one ^{35}Cl and one ^{37}Cl),[a] 209, 210, 246, 265 (M$^{+\bullet}$ with two ^{35}Cl). HRMS (EI): *m/z* 265.0641 (M$^{+\bullet}$ $C_{11}H_{17}{}^{35}Cl_2NO_2{}^{+\bullet}$ requires 265.0631).

[a] M'$^+$ =  ; M" =  ; [M−*t*BuO]$^+$ = 

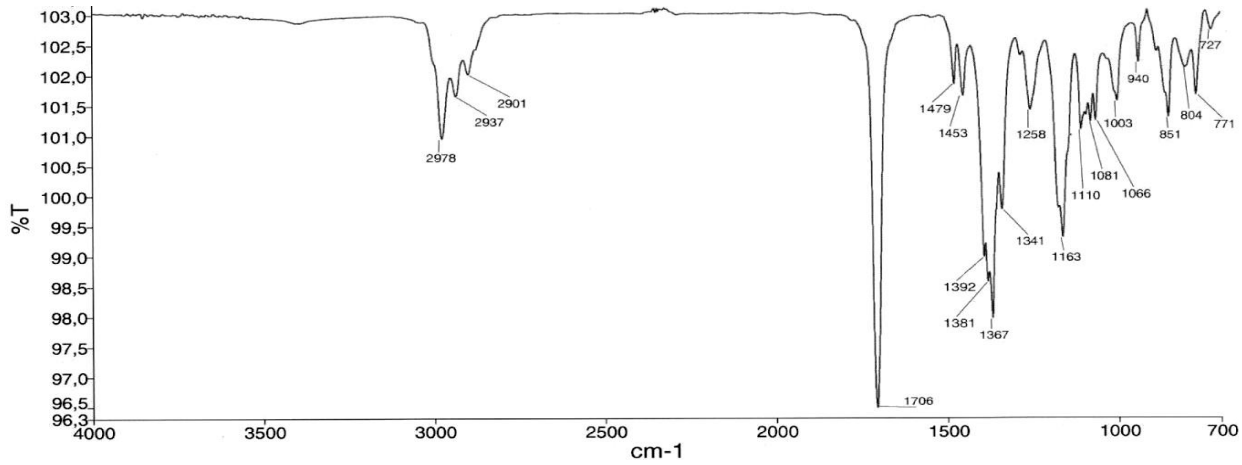
(tentative assignments)



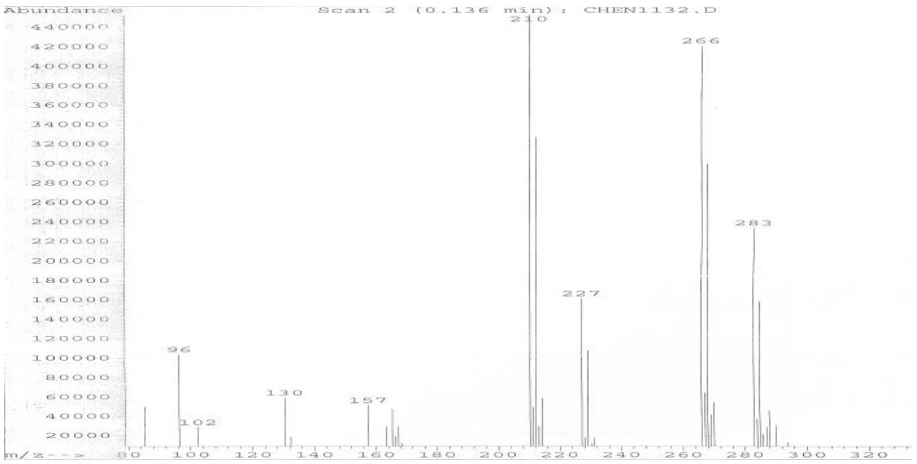
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



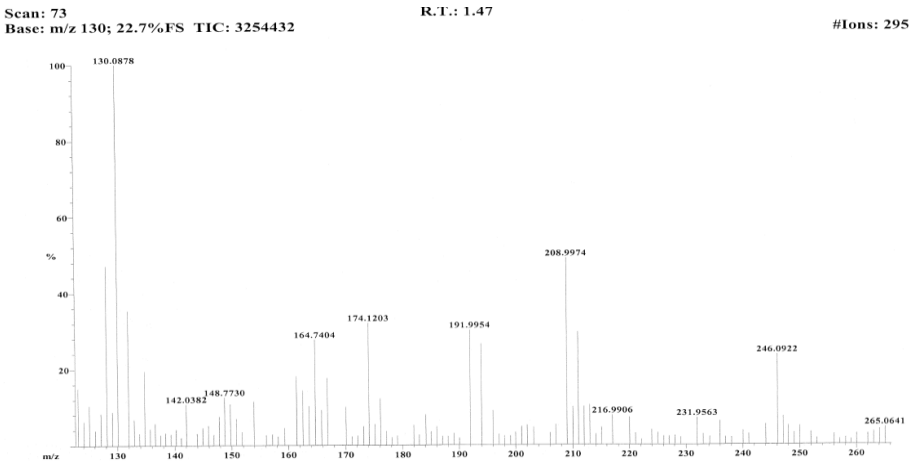
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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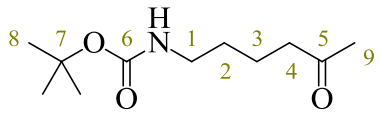
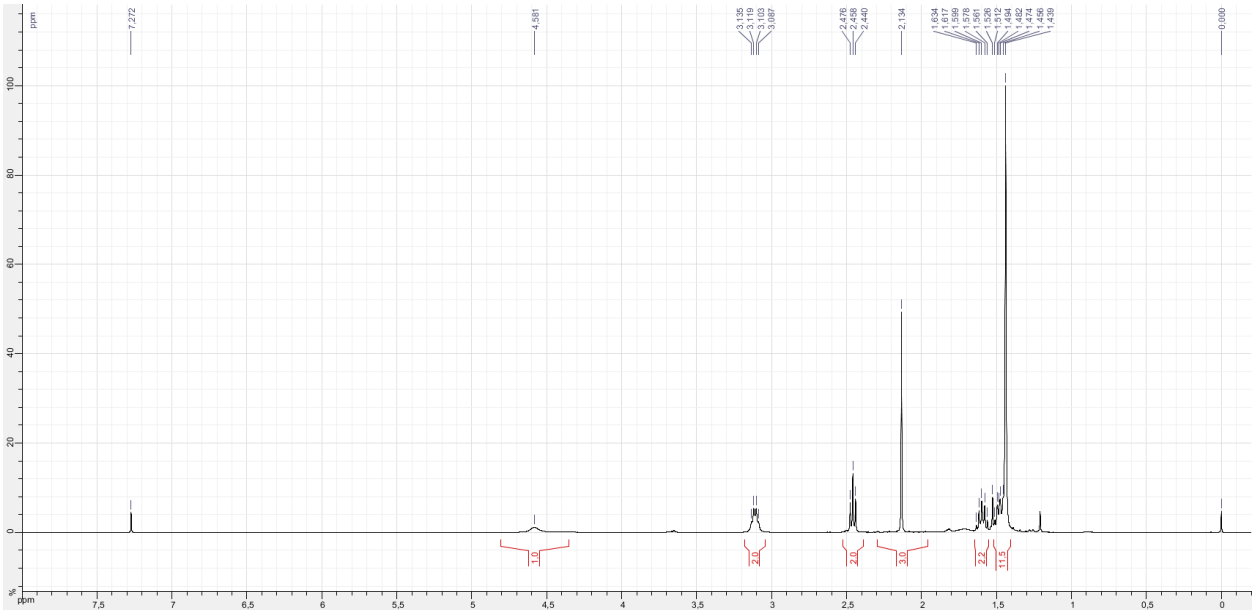
tert-Butyl *N*-(5-oxohexyl)carbamate[11]



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.44 (9 H, s, H8), 1.47 (2 H, m, H3), 1.60 (2 H, m, H2), 2.13 (3 H, s, H9), 2.46 (2 H, t, *J* 7.0, H4), 3.06−3.16 (2 H, m looking like q, *J* 6.5, H1), 4.58 (1 H, br s, NH).

11− X. Zheng, J. He, H.-H. Li, A. Wang, X.-J. Dai, A.-E Wang, P.-Q. Huang, *Angew. Chem. Int. Ed.* **2015**, *54*, 13739−13742 (supporting information).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

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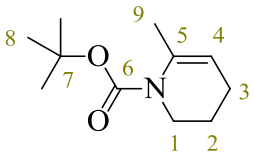
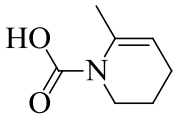
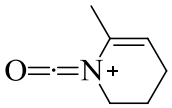
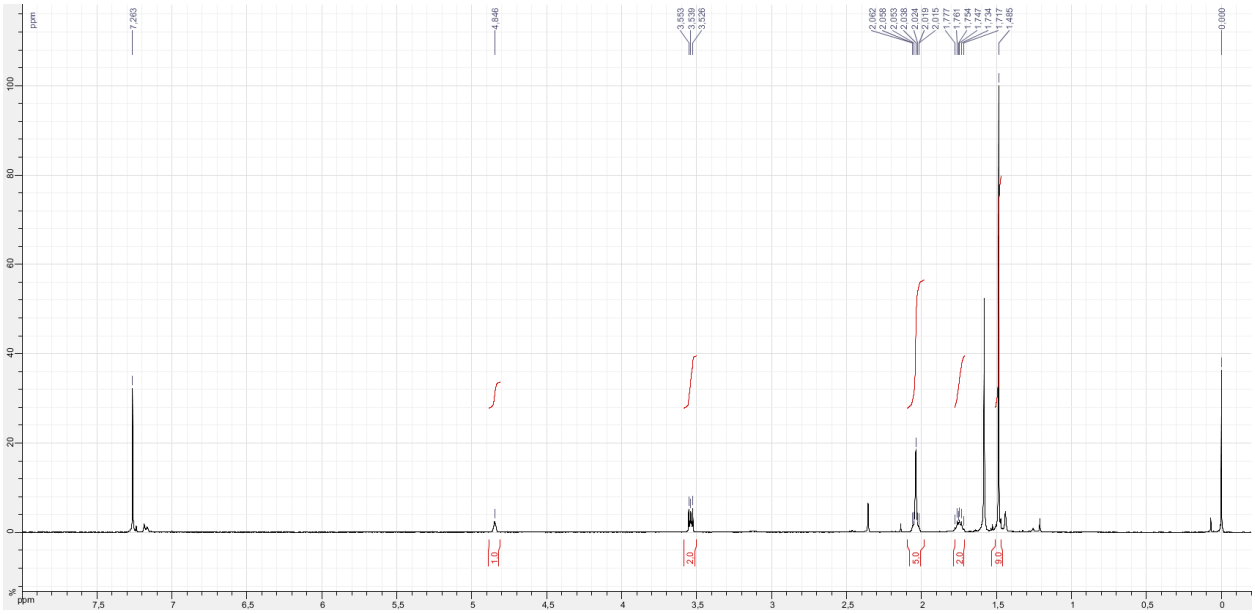
tert-Butyl 6-methyl-3,4-dihydro-2*H*-pyridine-1-carboxylate **1e**[12]



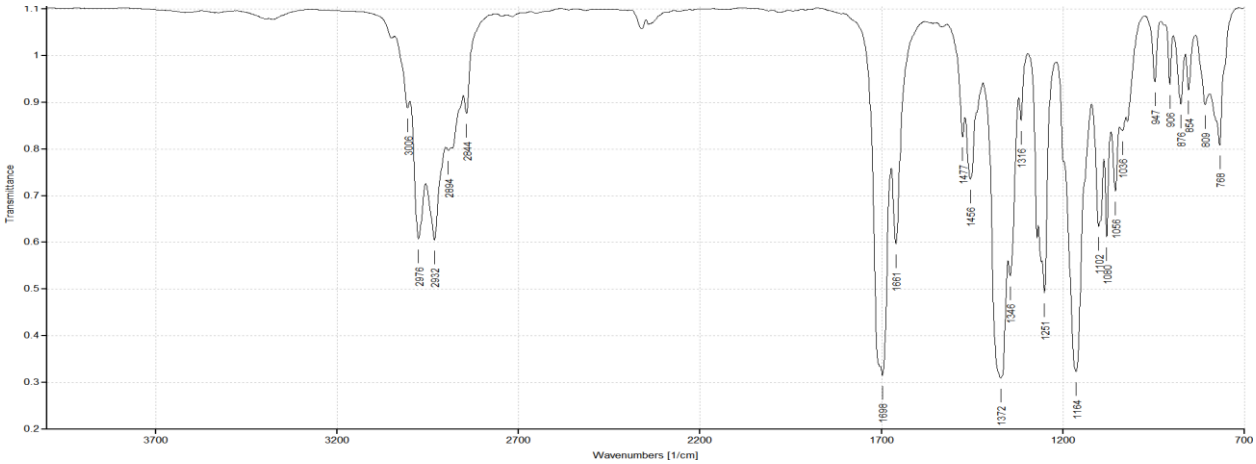
Pale yellow oil. R_f 0.3 [EtOAc/petroleum ether 5%, PMA, UV-active]. IR (neat) ν 2976 (m), 2932 (m), 2894 (m), 1698 (s, C=O), 1661 (m), 1456 (m), 1372 (s), 1346 (m), 1164 (s), 1102 (m), 1080 (m), 1056 (m), 768 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.48 (9 H, s, H8), 1.75 (2 H, m, H2), 2.04 (3 H, s, H9), 2.04 (2 H, m, H3), 3.54 (2 H, m, H1), 4.85 (1 H, br t, J 3.0, H4). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 22.6 (C9), 23.0, 23.1 (C2, C3), 28.3 (C8), 44.5 (C1), 80.2 (C7), 111.1 (C4), 135.5 (C5), 153.6 (C6). MS (positive CI, NH_3): *m/z* 98, 122, 142 ($M'H^+$),[a] 143, 198 (MH^+), 199. MS (EI): *m/z* 117, 121, 124 ($[M-tBuO]^+$),[a] 126, 140, 141, 142, 162, 197 ($M^{+\bullet}$). HRMS (EI): *m/z* 197.1423 ($M^{+\bullet}$ $C_{11}H_{19}NO_2^{+\bullet}$ requires 197.1411).

[a] M' =  ; $[M-tBuO]^+$ =  (tentative assignments)

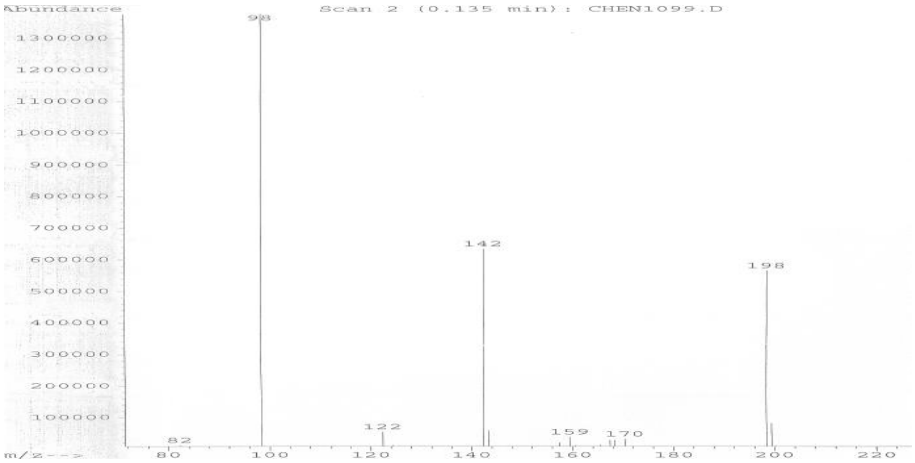
12− S. Kim, J.-Y. Yoon, *Synthesis* **2000**, 1622−1630.



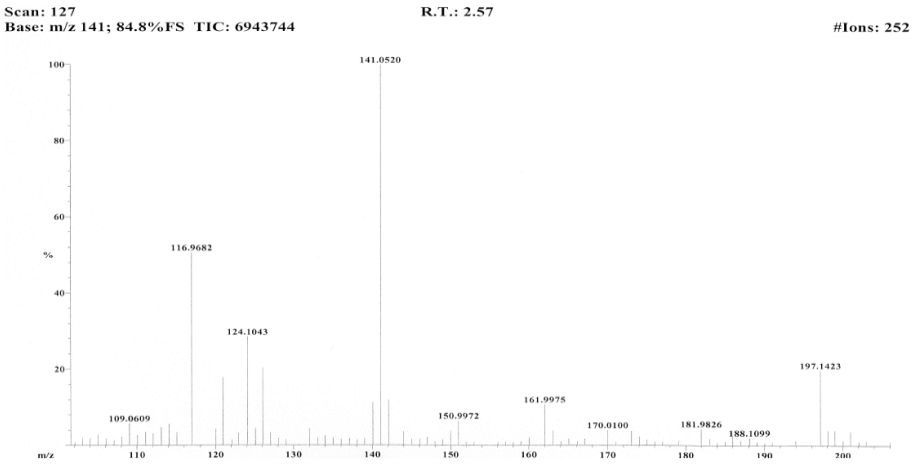
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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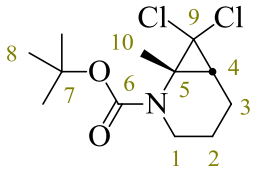
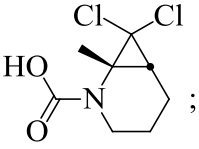
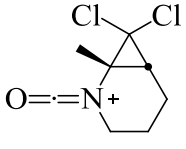
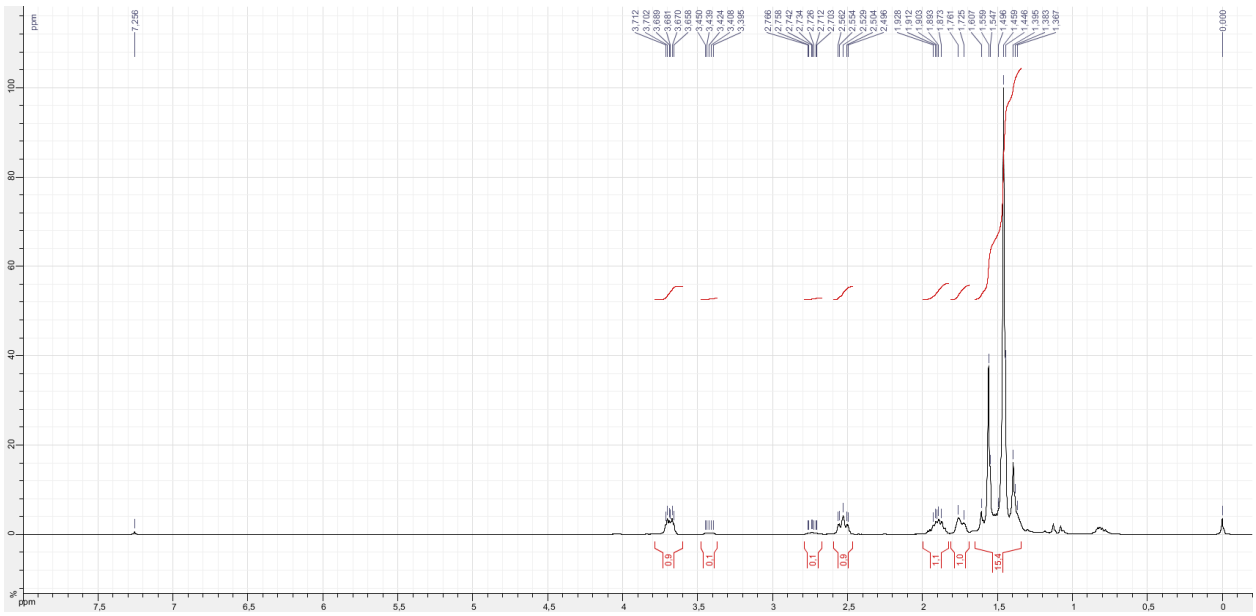
tert-Butyl 7,7-dichloro-1-methyl-2-azabicyclo[4.1.0]heptane-2-carboxylate **2e**

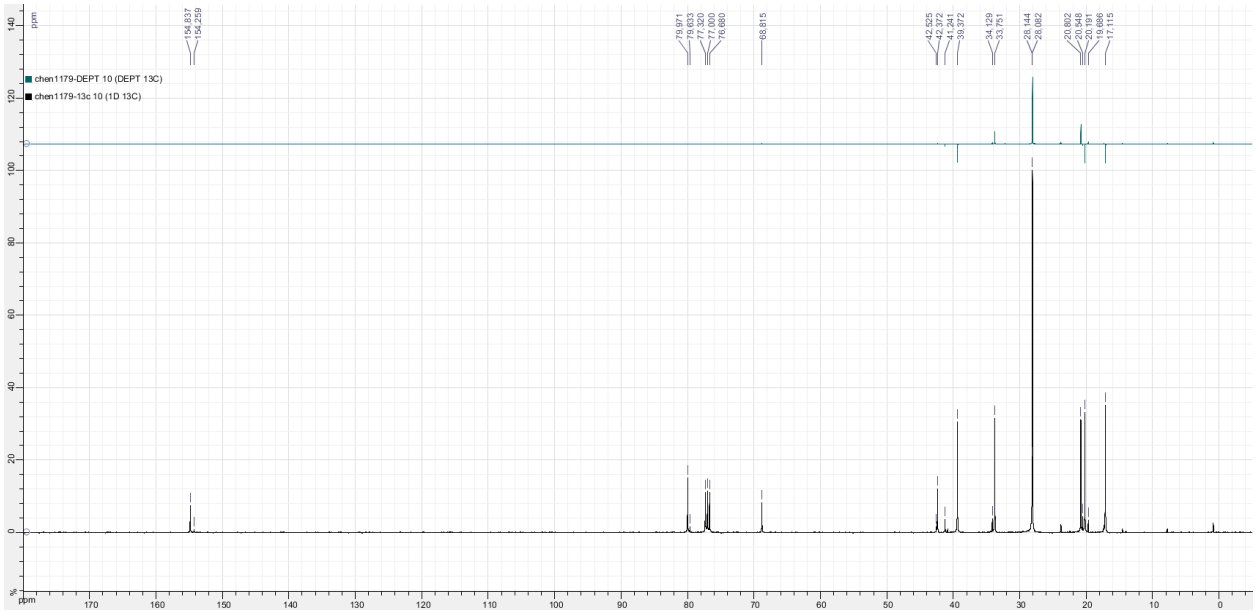


White solid. M.p. 72.0–73.6 °C. R_f 0.2 [EtOAc/petroleum ether 10%, PMA, not UV-active]. IR (neat) *v* 2989 (m), 2976 (m), 2937 (m), 2879 (m), 1695 (s, C=O), 1455 (m), 1385 (m), 1362 (m), 1353 (m), 1343 (m), 1257 (m), 1172 (m), 1157 (m), 1093 (m), 1053 (m), 1034 (m), 894 (m), 844 (m), 771 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz), 90 : 10 mixture of two rotamers. Major rotamer: δ 1.32−1.65 (3 H, m, H2a, H2b, H3a), 1.46 (9 H, s, H8), 1.56 (3 H, s, H10), 1.74 (1 H, br d, *J* 14.5, H4), 1.83−1.98 (1 H, m, H3b), 2.53 (1 H, ddd, *J* 12.5, 11.0, 3.0, H1a), 3.69 (1 H, ddd, *J* 12.5, 5.0, 4.0, H1b). Minor rotamer, characteristic signals: δ 1.45 (9 H, s, H8), 1.55 (3 H, s, H10), 2.73 (1 H, ddd, *J* 12.5, 9.5, 3.5, H1a), 3.42 (1 H, ddd, *J* 12.5, 6.0, 4.0, H1b). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 90 : 10 mixture of two rotamers. Major rotamer: δ 17.1 (C3), 20.2 (C2), 20.8 (C10), 28.1 (C8), 33.8 (C4), 39.4 (C1), 42.4 (C5), 68.8 (C9), 80.0 (C7), 154.8 (C6). Minor rotamer, characteristic signals: δ 19.7 (C10), 20.5 (C2), 28.1 (C8), 34.1 (C4), 41.2 (C1), 42.5 (C5), 79.6 (C7), 154.3 (C6). MS (positive CI, NH_3): *m/z* 224 ($M'H^+$ with two ^{35}Cl),[a] 225, 226 ($M'H^+$ with one ^{35}Cl and one ^{37}Cl),[a] 228 ($M'H^+$ with two ^{37}Cl),[a] 241 ($M'H^+..NH_3$ with two ^{35}Cl),[a] 242, 243 ($M'H^+..NH_3$ with one ^{35}Cl and one ^{37}Cl),[a] 246 ($M'H^+..NH_3$ with two ^{37}Cl),[a] 280 (MH^+ with two ^{35}Cl), 282 (MH^+ with one ^{35}Cl and one ^{37}Cl), 297 ($MH^+..NH_3$ with two ^{35}Cl), 299 ($MH^+..NH_3$ with one ^{35}Cl and one ^{37}Cl). MS (EI): *m/z* 140, 144, 146, 179, 188, 206 ($[M-tBuO]^+$ with two ^{35}Cl),[a] 208 ($[M-tBuO]^+$ with one ^{35}Cl and one ^{37}Cl),[a] 223, 225, 279 ($M^{+\bullet}$ with two ^{35}Cl). HRMS (EI): *m/z* 279.0788 ($M^{+\bullet}$ $C_{12}H_{19}{}^{35}Cl_2NO_2{}^{+\bullet}$ requires 279.0788).

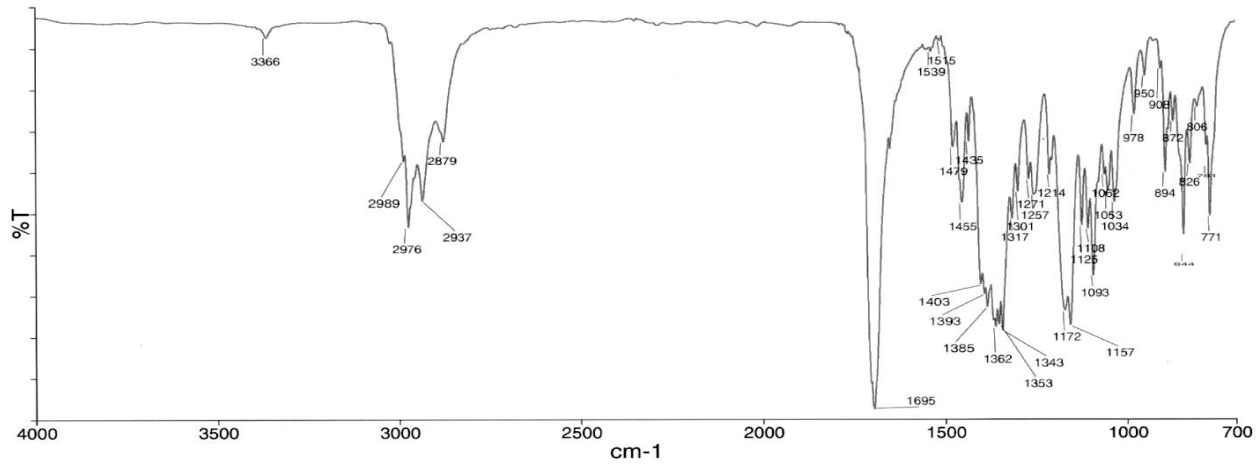
[a] M' =  ; $[M-tBuO]^+$ =  (tentative assignments)



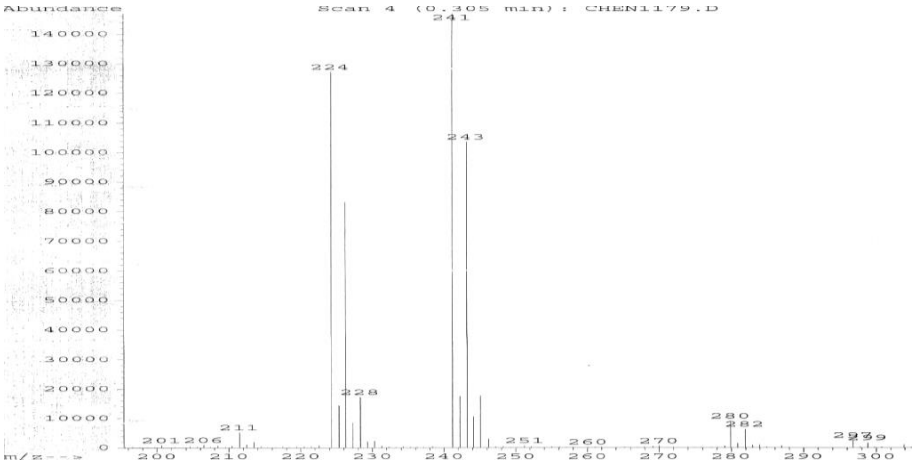
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



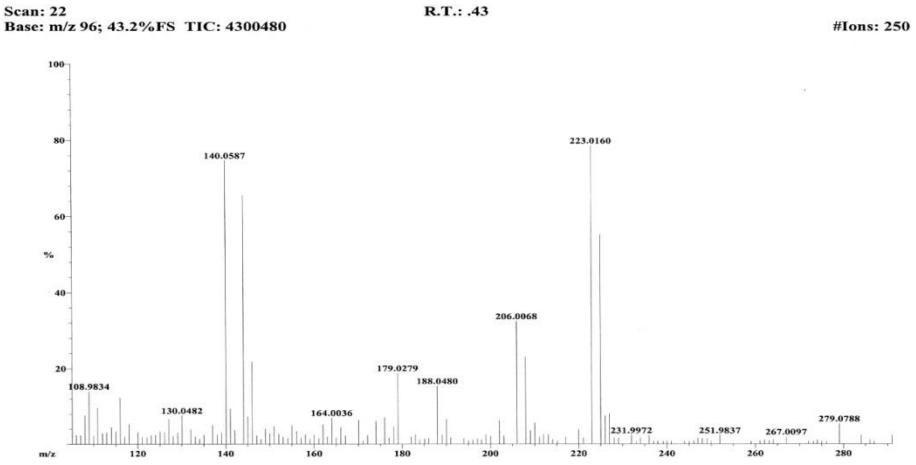
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (CI, NH_3).



MS spectrum (EI).

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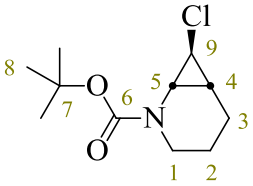
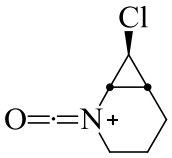
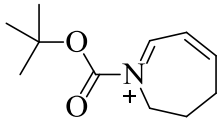
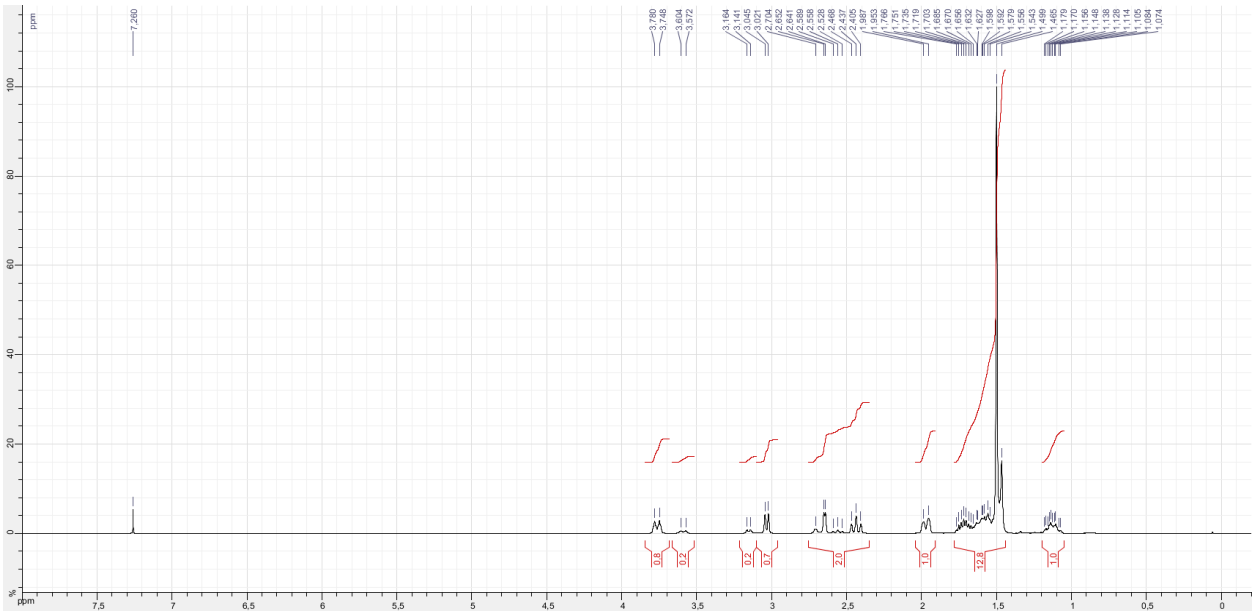
tert-Butyl (1*R**,6*S**,7*R**)-7-chloro-2-azabicyclo[4.1.0]heptane-2-carboxylate *exo*-**8**



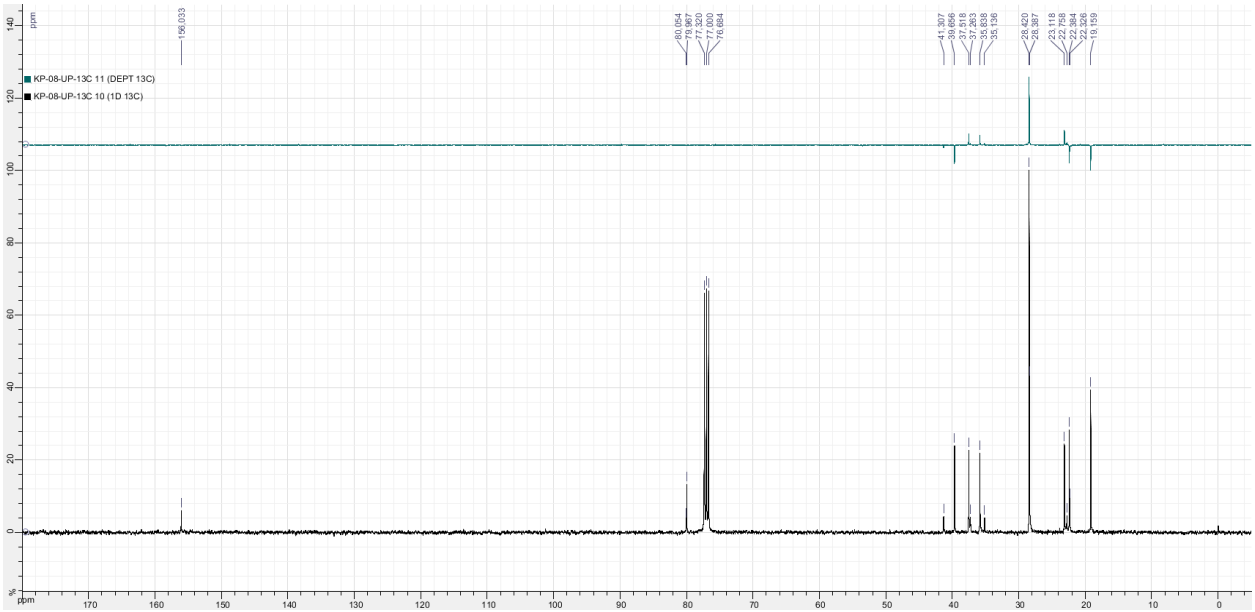
Colourless oil. R_f 0.5 [EtOAc/petroleum ether 10%, anisaldehyde or PMA, not UV-active]; 0.15 [EtOAc/petroleum ether 5% eluted two times]. IR (neat) *v* 2977 (m), 2934 (m), 2868 (w), 1702 (s, C=O), 1447 (w), 1418 (m), 1384 (m), 1366 (m), 1300 (w), 1269 (w), 1246 (w), 1164 (m), 1131 (m), 1035 (w), 1005 (w), 774 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz), 79 : 21 mixture of two rotamers. Major rotamer: δ 1.12 (1 H, tddd, *J* 13.0, 12.0, 4.5, 3.5, H2a), 1.50 (9 H, s, H8), 1.57 (1 H, br ddd, *J* 9.5, 6.0, 4.0, H4), 1.61 (1 H, dddd, *J* 13.0, 6.0, 3.5, 2.0, H2b), 1.72 (1 H, ddt, *J* 13.5, 13.0, 6.0, H3a), 1.97 (1 H, br dd, *J* 13.5, 4.5, H3b), 2.43 (1 H, ddd, *J* 13.0, 12.0, 2.0, H1a), 2.65 (1 H, dd, *J* 4.0, 1.5, H9), 3.03 (1 H, dd, *J* 9.5, 1.5, H5), 3.76 (1 H, dt, *J* 13.0, 3.5, H1b). Minor rotamer: δ 1.45−1.77 (4 H, m, H2, H3a, H4), 1.46 (9 H, s, H8), 1.97 (1 H, br d, *J* 13.5, H3b), 2.56 (1 H, br t, *J* 12.5, H1a), 2.71 (1 H, br d, *J* 3.5, H9), 3.15 (1 H, br d, *J* 9.5, H5), 3.59 (1 H, br d, *J* 12.5, H1b). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 79 : 21 mixture of two rotamers. Major rotamer: δ 19.2 (C3), 22.4 (C2), 23.1 (C4), 28.4 (C8), 35.8 (C9), 37.5 (C5), 39.7 (C1), 80.0 (C7), 156.0 (C6). Minor rotamer: δ 19.2 (C3), 22.3 (C2), 22.8 (C4), 28.4 (C8), 35.1 (C9), 37.3 (C5), 41.3 (C1), 80.1 (C7), 156.0 (C6). MS (EI) *m/z* 98, 110, 130, 140, 158 ([M−*t*BuO]$^+$

with ^{35}Cl),[a] 160 ([M−*t*BuO]$^+$ with ^{37}Cl),[a] 179, 196 ([M−Cl]$^+$).[a] HRMS *m/z* (EI) 158.0370 ([M−*t*BuO]$^+$ $C_7H_9ClNO^+$ requires 158.0368).[a]

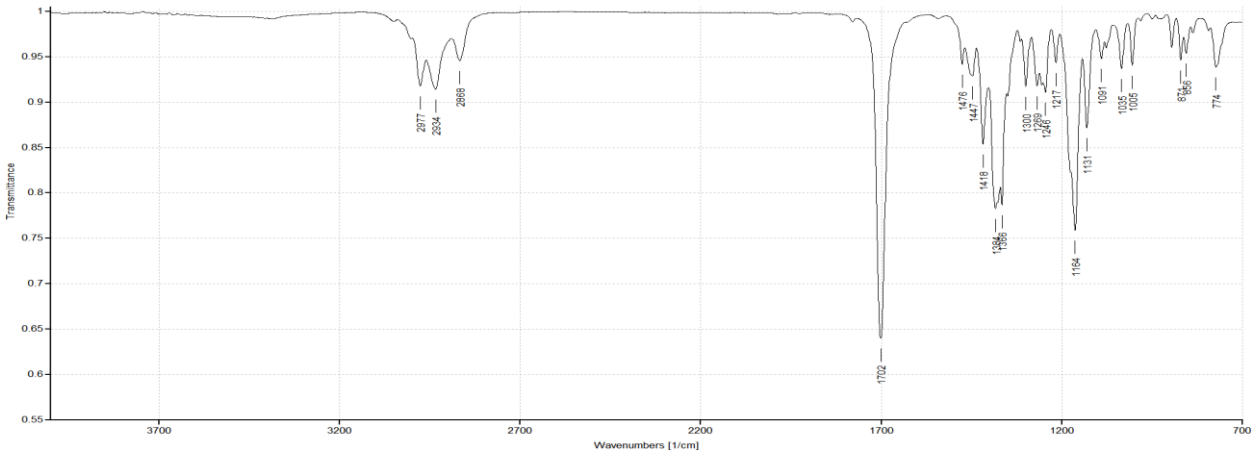
[a] [M–*t*BuO]$^+$ =  ; [M–Cl]$^+$ =  (tentative assignments)



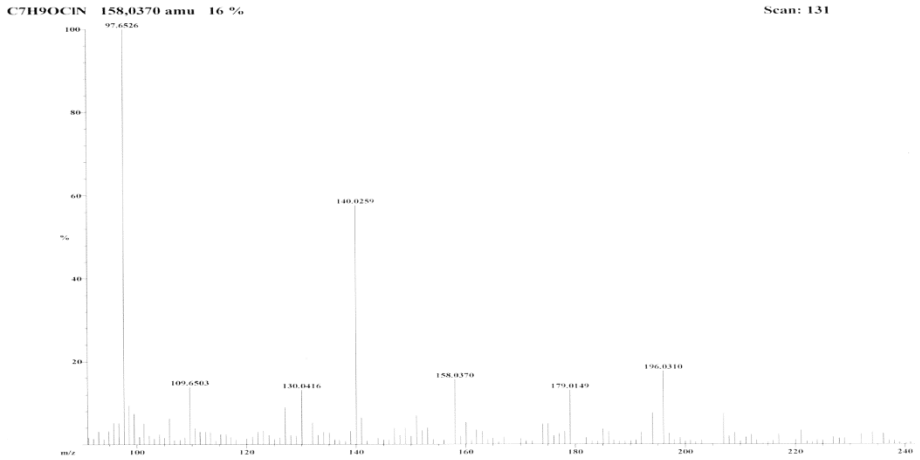
^{1}H NMR spectrum ($CDCl_3$, 300 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (EI).

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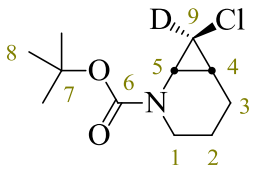
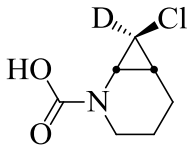
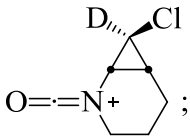
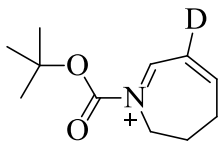
tert-Butyl (1*R**,6*S**,7*R**)-7-chloro-7-deuterio-2-azabicyclo[4.1.0]heptane-2-carboxylate *exo*-**8**-*d*



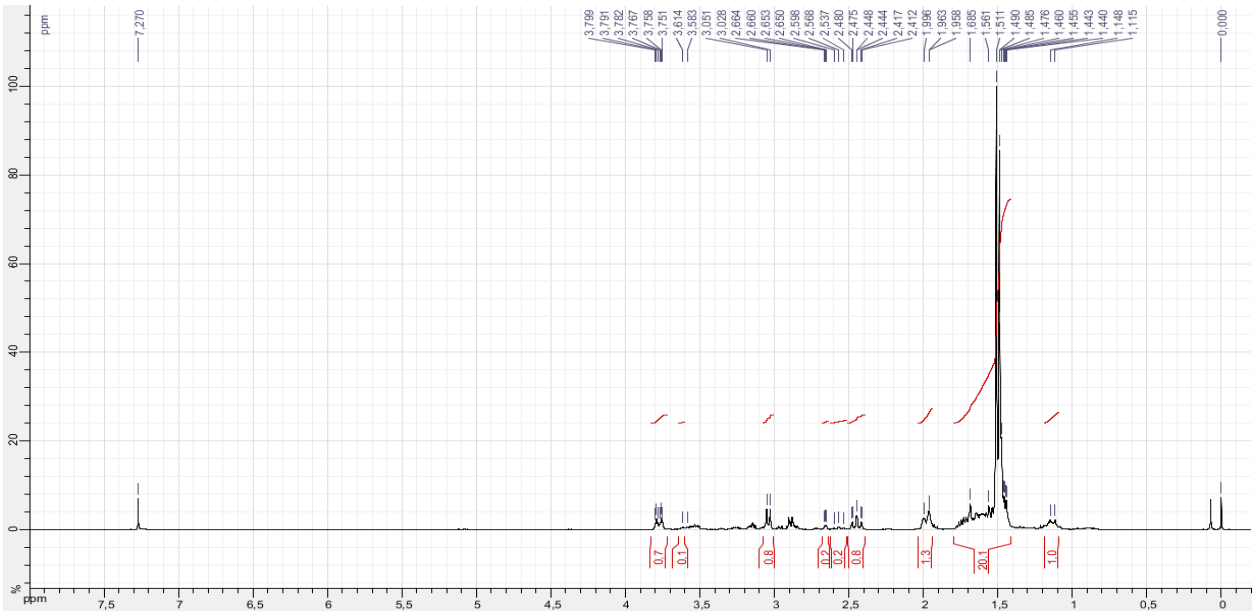
(82%-*d*, determined by ^{1}H NMR spectroscopy)

Colourless oil. R_f 0.15 [EtOAc/petroleum ether 5% eluted two times, PMA, not UV-active]. IR (neat) *v* 2976 (m), 2934 (m), 2868 (w), 1702 (s, C=O), 1477 (w), 1453 (w), 1412 (m), 1379 (m), 1366 (m), 1301 (w), 1269 (w), 1257 (w), 1165 (m), 1132 (m), 1091 (w), 1076 (w), 1037 (w), 998 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz), 76 : 24 mixture of two rotamers. Major rotamer: δ 1.13 (1 H, m, H2a), 1.51 (9 H, s, H8), 1.56 (1 H, m, H4), 1.63 (1 H, m, H2b), 1.73 (1 H, m, H3a), 1.98 (1 H, br d, *J* 13.5, H3b), 2.45 (1 H, ddd, *J* 13.0, 12.0, 2.0, H1a), 3.04 (1 H, d, *J* 9.5, H5), 3.77 (1 H, dt, *J* 13.0, 3.5, H1b). Minor rotamer, characteristic signals: δ 1.49 (9 H, s, H8), 2.57 (1 H, t, *J* 12.5, H1a), 3.60 (1 H, br d, *J* 12.5, H1a). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 76 : 24 mixture of two rotamers. Major rotamer: δ 19.2 (C3), 22.4 (C2), 23.1 (C4), 28.5 (C8), 37.5 (C5), 39.7 (C1), 80.0 (C7), 156.1 (C6). The signal of C9 could not be detected with certainty but a residual peak at 35.8 ppm was observed, corresponding to a small amount of non-deuteriated molecule. Minor rotamer, characteristic signals: δ 19.2 (C3), 22.5 (C2), 28.4 (C8), 40.9 (C1), 79.6 (C7), 156.5 (C6). MS (positive CI, NH_3): *m/z* 98, 176 (M'H$^+$ with ^{35}Cl and no deuterium),[a] 177 (M'H$^+$ with ^{35}Cl),[a] 178 (M'H$^+$ with ^{37}Cl and no deuterium),[a] 179 (M'H$^+$ with ^{37}Cl),[a] 193

($M'H^+..NH_3$ with ^{35}Cl and no deuterium),[a] 194 ($M'H^+..NH_3$ with ^{35}Cl),[a] 195 ($M'H^+..NH_3$ with ^{37}Cl and no deuterium),[a] 196 ($M'H^+..NH_3$ with ^{37}Cl),[a] 232 (MH^+ with ^{35}Cl and no deuterium), 233 (MH^+ with ^{35}Cl), 234 (MH^+ with ^{37}Cl and no deuterium), 235 (MH^+ with ^{37}Cl). MS (EI): *m/z* 111, 125, 139, 141, 147, 159 ($[M-tBuO]^+$ with ^{35}Cl),[a] 197 ($[M-Cl]^+$),[a] 221. HRMS (EI): *m/z* 159.0439 ($[M-tBuO]^+$ $C_7H_8D^{35}ClNO^+$ requires 159.0430).[a]

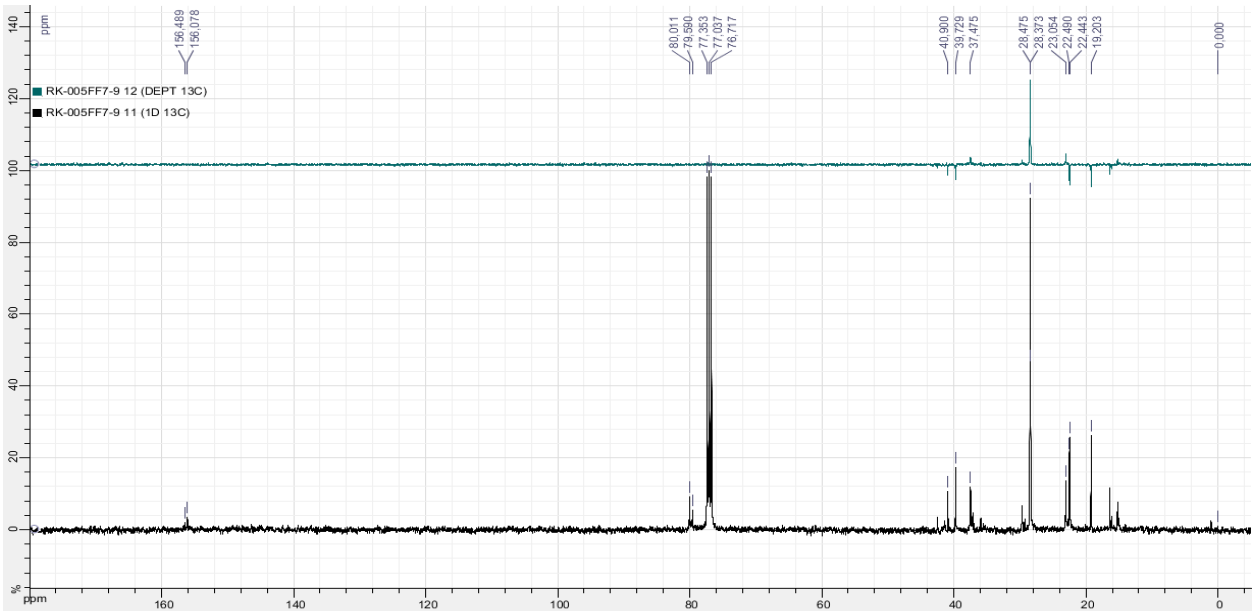
[a] M' =  ; $[M-tBuO]^+$ =  ; $[M-Cl]^+$ = 

(tentative assignments)



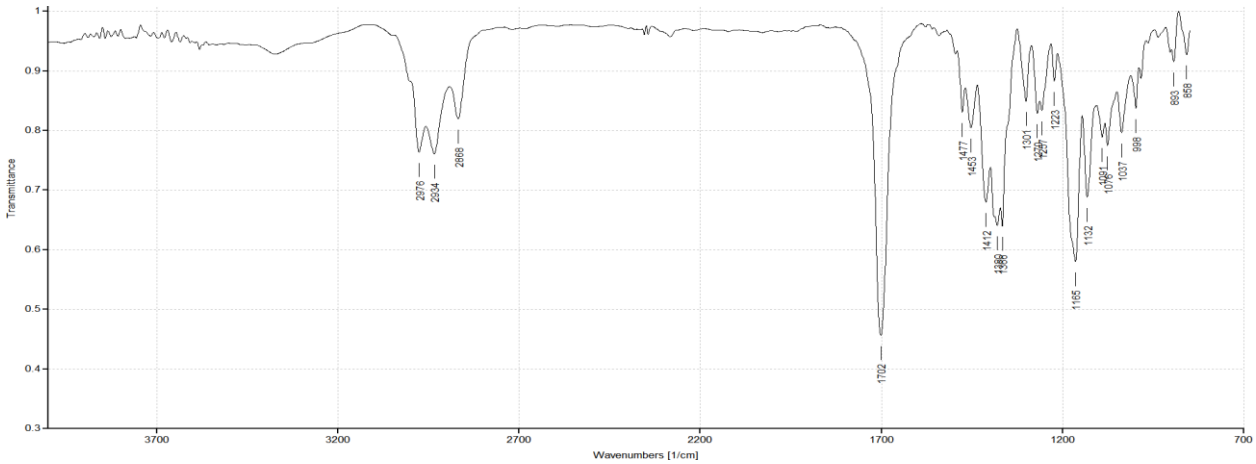
^1H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this sample contained a minor amount of the other diastereoisomer *endo*-**8**-*d*.



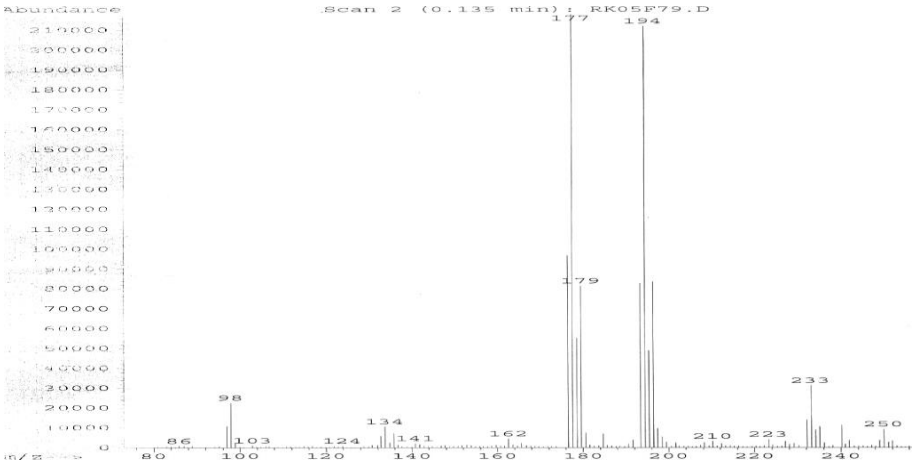
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

Note: this sample contained a minor amount of the other diastereoisomer *endo*-**8**-*d*.



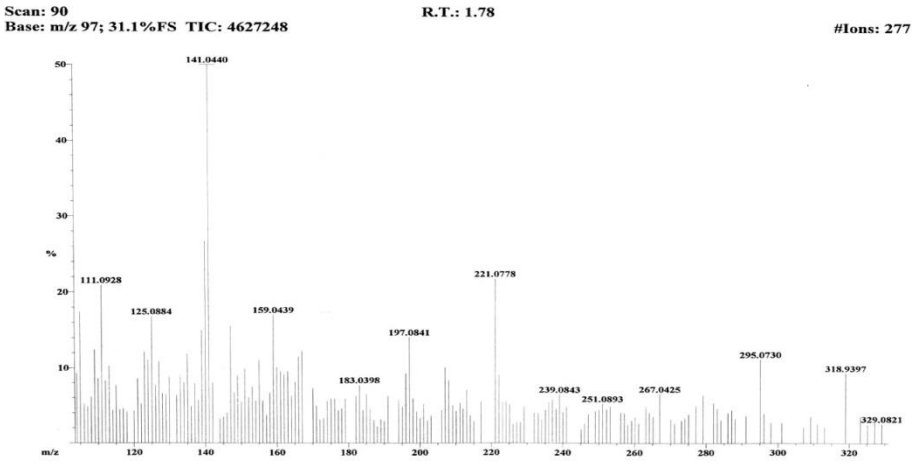
IR spectrum.

Note: this sample contained a minor amount of the other diastereoisomer *endo*-**8**-*d*.



MS spectrum (CI, NH_3).

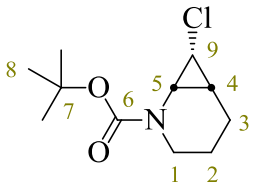
Note: this sample contained a minor amount of the other diastereoisomer *endo*-**8**-*d*.



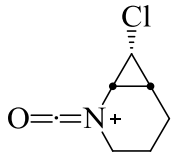
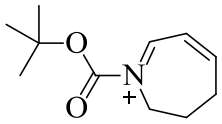
MS spectrum (EI).

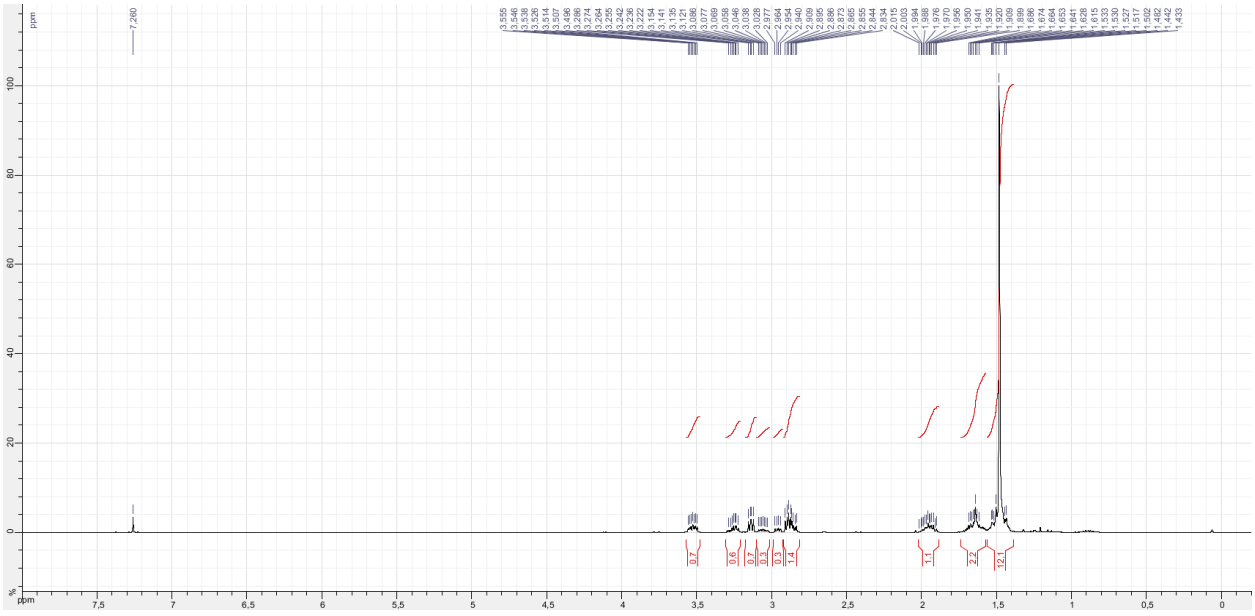
Note: this sample contained a minor amount of the other diastereoisomer *endo*-**8**-*d*.

tert-Butyl (1*R**,6*S**,7*S**)-7-chloro-2-azabicyclo[4.1.0]heptane-2-carboxylate *endo*-**8**

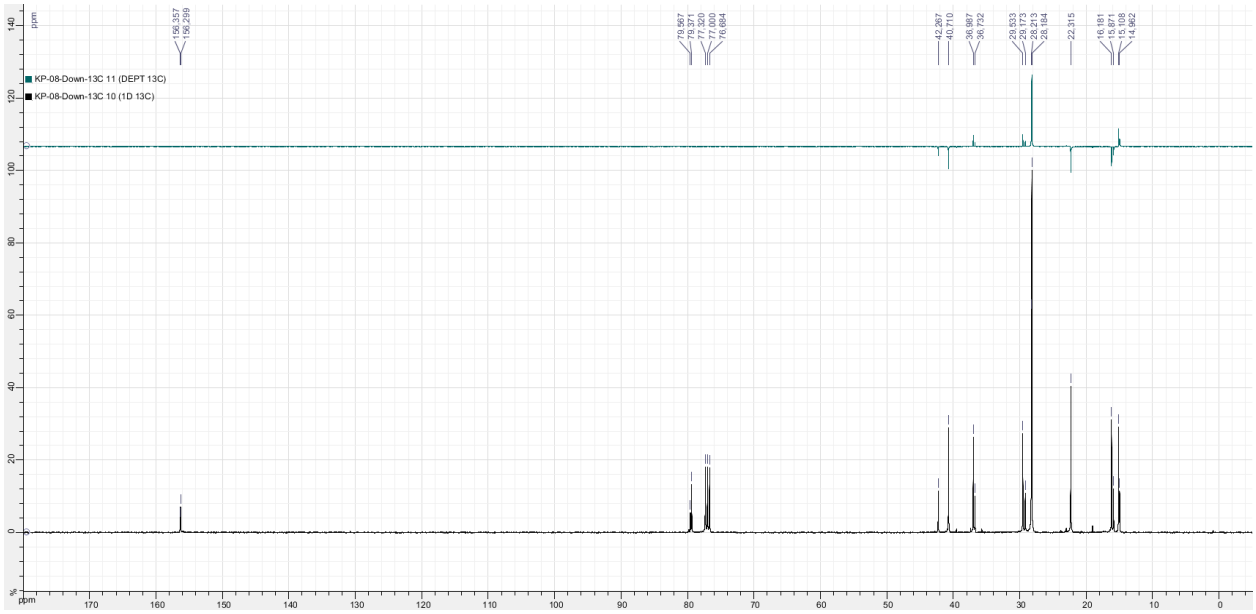


Colourless crystals. M.p. 62−64 °C. R_f 0.45 [EtOAc/petroleum ether 10%, anisaldehyde or PMA, not UV-active]; 0.15 [EtOAc/petroleum ether 5% eluted two times]. IR (neat) ν 2975 (m), 2933 (m), 2869 (w), 1700 (s, C=O), 1478 (w), 1454 (w), 1407 (m), 1391 (m), 1365 (m), 1309 (m), 1272 (w), 1256 (w), 1169 (m), 1137 (m), 1066 (w), 963 (w), 774 (m), 712 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz), 72 : 28 mixture of two rotamers. Major rotamer: δ 1.40−1.73 (4 H, m, H2, H3), 1.48 (9 H, s, H8), 1.94 (1 H, m, H4), 2.86 (1 H, ddd, *J* 12.0, 8.5, 4.0, H1a), 2.89 (1 H, dd, *J* 9.0, 5.5, H5), 3.14 (1 H, dd, *J* 8.0, 5.5, H9), 3.53 (1 H, ddd, *J* 12.0, 7.0, 4.5, H1b). Minor rotamer: δ 1.40−1.73 (4 H, m, H2, H3), 1.48 (9 H, s, H8), 1.98 (1 H, m, H4), 2.96 (1 H, dd, *J* 9.0, 5.5, H5), 3.06 (1 H, ddd, *J* 12.5, 7.0, 4.0, H1a), 3.24 (1 H, dd, *J* 8.0, 5.5, H9), 3.26 (1 H, ddd, *J* 12.5, 8.5, 4.0, H1b). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 72 : 28 mixture of two rotamers. Major rotamer: δ 15.1 (C4), 16.2 (C3), 22.3 (C2), 28.2 (C8), 29.5 (C9), 37.0 (C5), 40.7 (C1), 79.4 (C7), 156.3 (C6). Minor rotamer: δ 15.0 (C4), 15.9 (C3), 22.3 (C2), 28.2 (C8), 29.5 (C9), 36.7 (C5), 42.3 (C1), 79.6 (C7), 156.4 (C6). MS (EI) *m/z* 96, 98, 99, 140, 141, 158 ([M−*t*BuO]$^+$ with ^{35}Cl),[a] 160 ([M−*t*BuO]$^+$ with ^{37}Cl),[a] 175, 196 ([M−Cl]$^+$).[a] HRMS *m/z* (EI) 196.1335 ([M−Cl]$^+$ $C_{11}H_{18}NO_2^+$ requires 196.1333).[a]

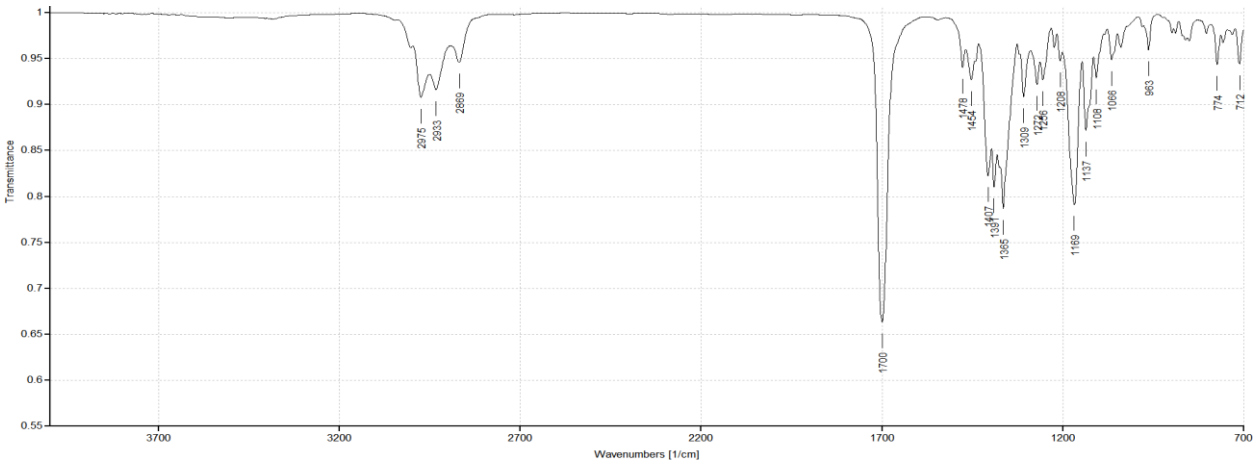
[a] [M−*t*BuO]$^+$ =  ; [M−Cl]$^+$ =  (tentative assignments)



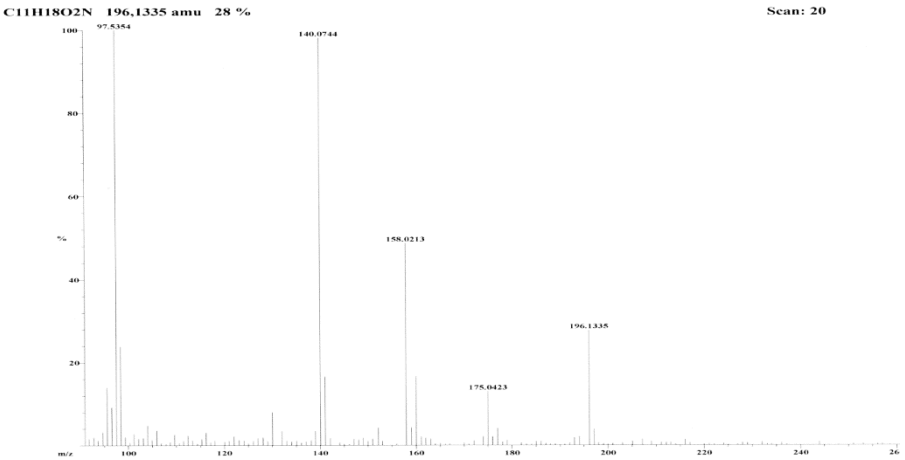
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



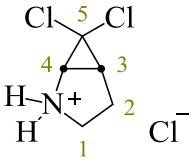
IR spectrum.



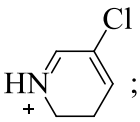
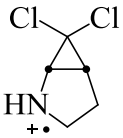
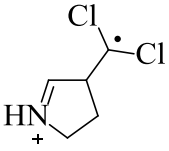
MS spectrum (EI).

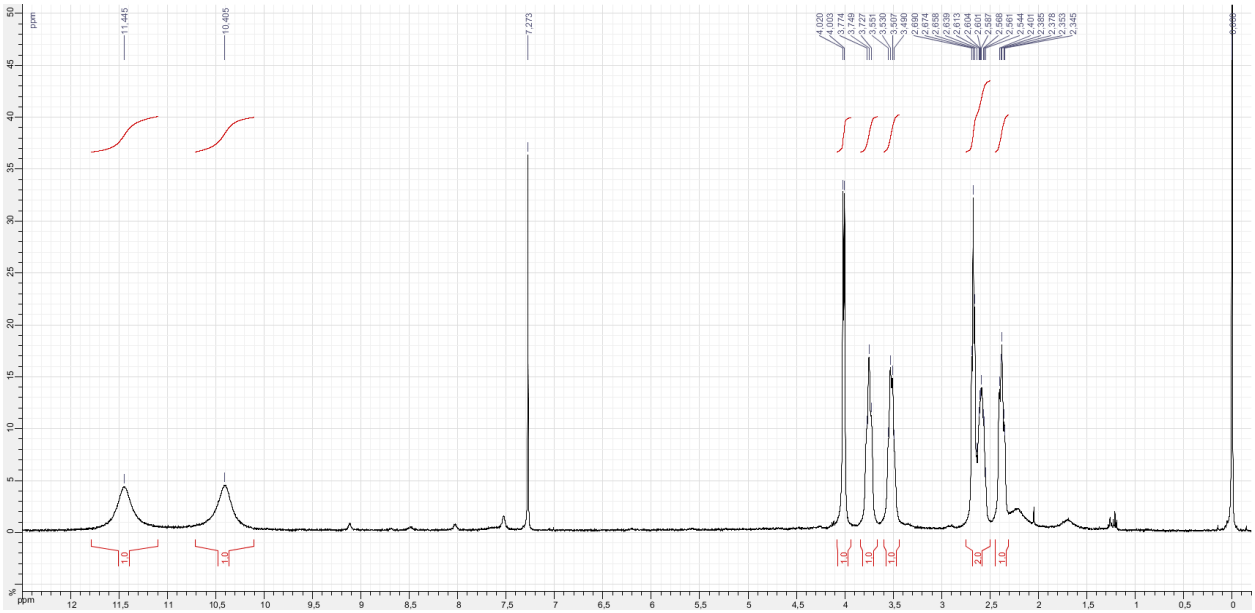
II. Cyclopropylammonium salts

6,6-Dichloro-2-azoniabicyclo[3.1.0]hexane chloride **3a**

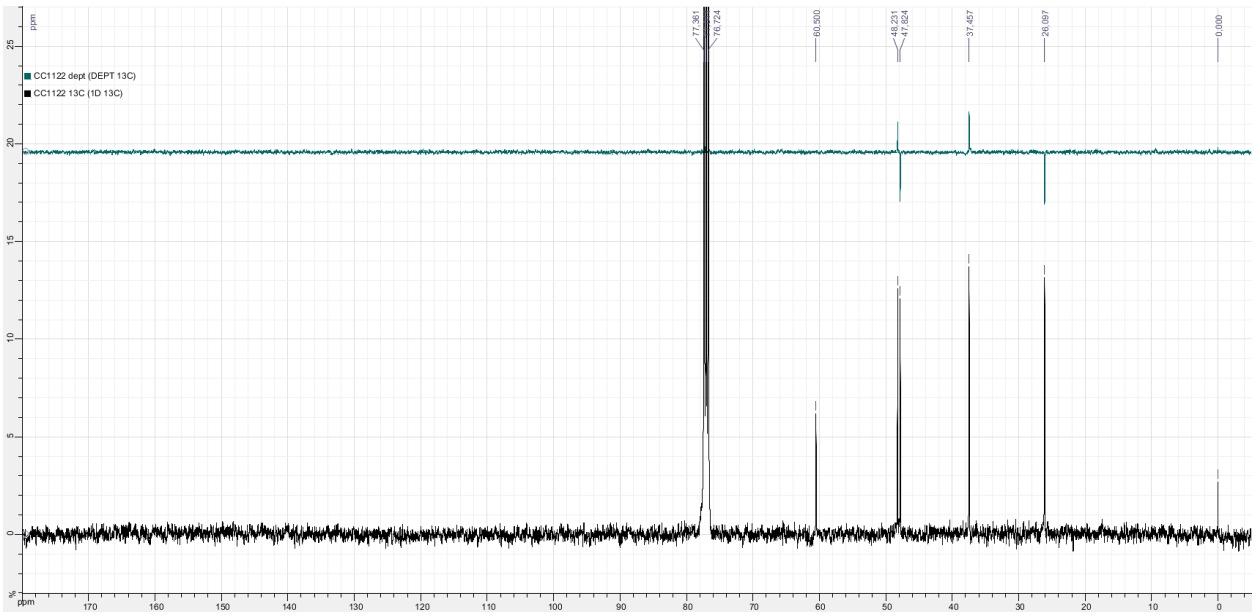


White solid. M.p. 93.5–95.0 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.38 (1 H, br ddd, *J* 14.5, 8.5, 3.5, H2a), 2.59 (1 H, br ddt, *J* 14.5, 9.5, 6.5, H2b), 2.37 (1 H, br t, *J* 6.5, H3), 3.52 (1 H, br ddd, *J* 11.0, 8.5, 6.5, H1a), 3.75 (1 H, br ddd, *J* 11.0, 9.5, 3.5, H1b), 4.01 (1 H, br d, *J* 6.5, H4), 10.40 (1 H, br s, NH), 11.44 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 26.1 (C2), 37.5 (C3), 47.8 (C1), 48.2 (C4), 60.5 (C5). MS (positive CI, NH_3): *m/z* 114, <u>116</u> (M'$^{+}$ with ^{35}Cl),[a] 117, 118 (M'$^{+}$ with ^{37}Cl),[a] 148, 150, 152, 154, 182, 184. MS (EI): *m/z* <u>113</u>, 115, 116 (M'$^{+}$ with ^{35}Cl),[a] 117, 118 (M'$^{+}$ with ^{37}Cl),[a] 130, 151 (M"$^{+\bullet}$ with two ^{35}Cl),[a] 153 (M"$^{+\bullet}$ with one ^{35}Cl and one ^{37}Cl).[a] HRMS (EI): *m/z* 150.9957 (M"$^{+\bullet}$ $C_5H_7{}^{35}Cl_2N^{+\bullet}$ requires 150.9951).[a]

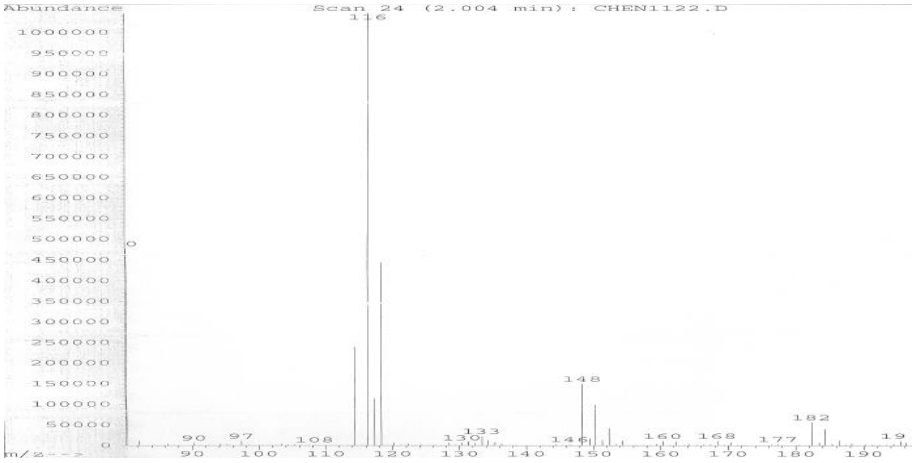
[a] M'$^{+}$ =  ; M"$^{+\bullet}$ =  or  (tentative assignments)



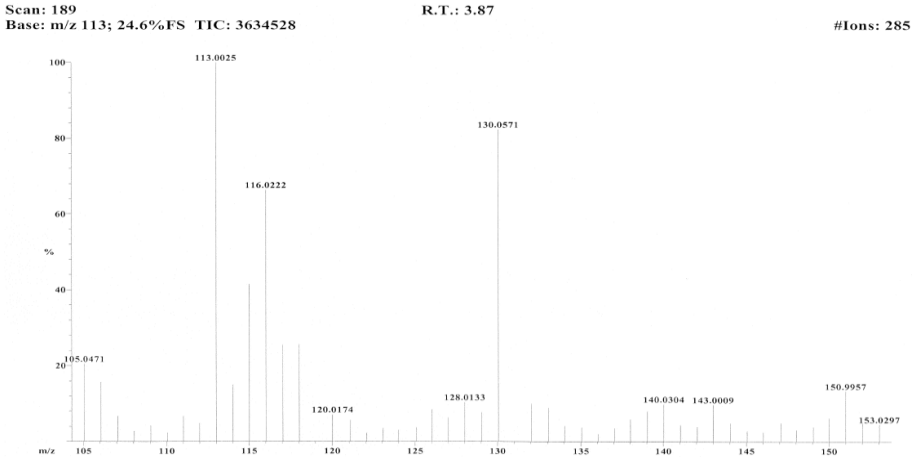
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

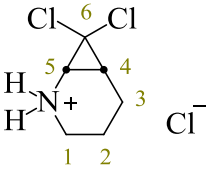


MS spectrum (CI, NH_3).

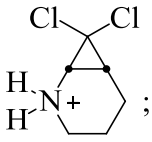
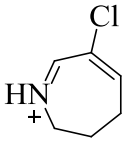
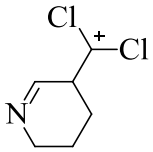


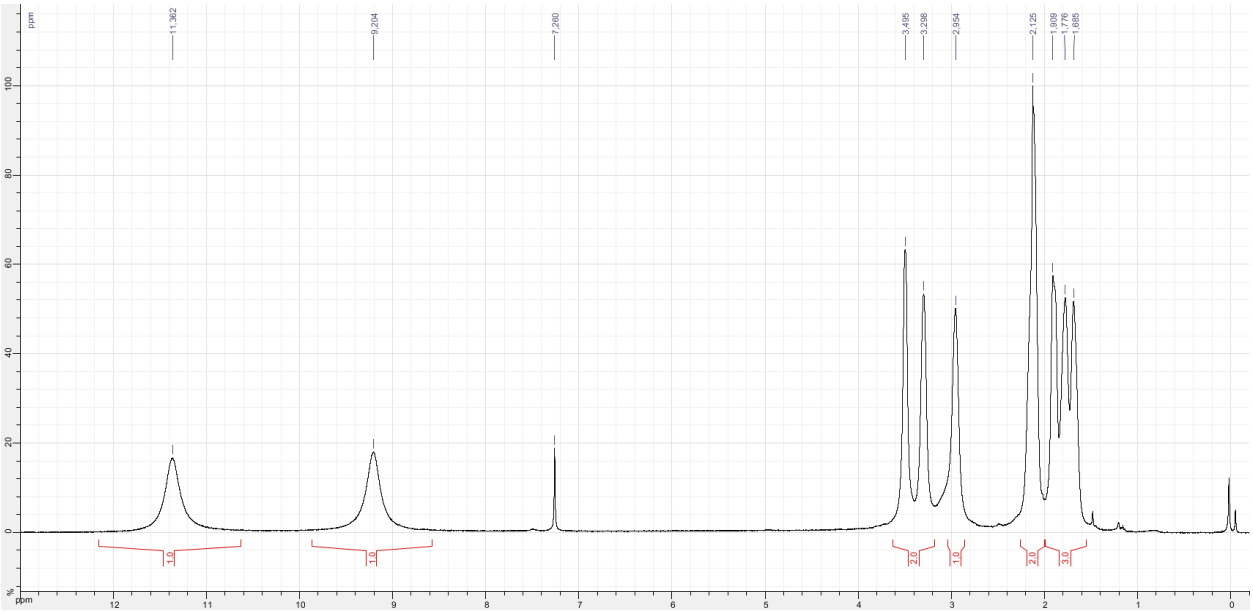
MS spectrum (EI).

7,7-Dichloro-2-azoniabicyclo[4.1.0]heptane chloride **3b**

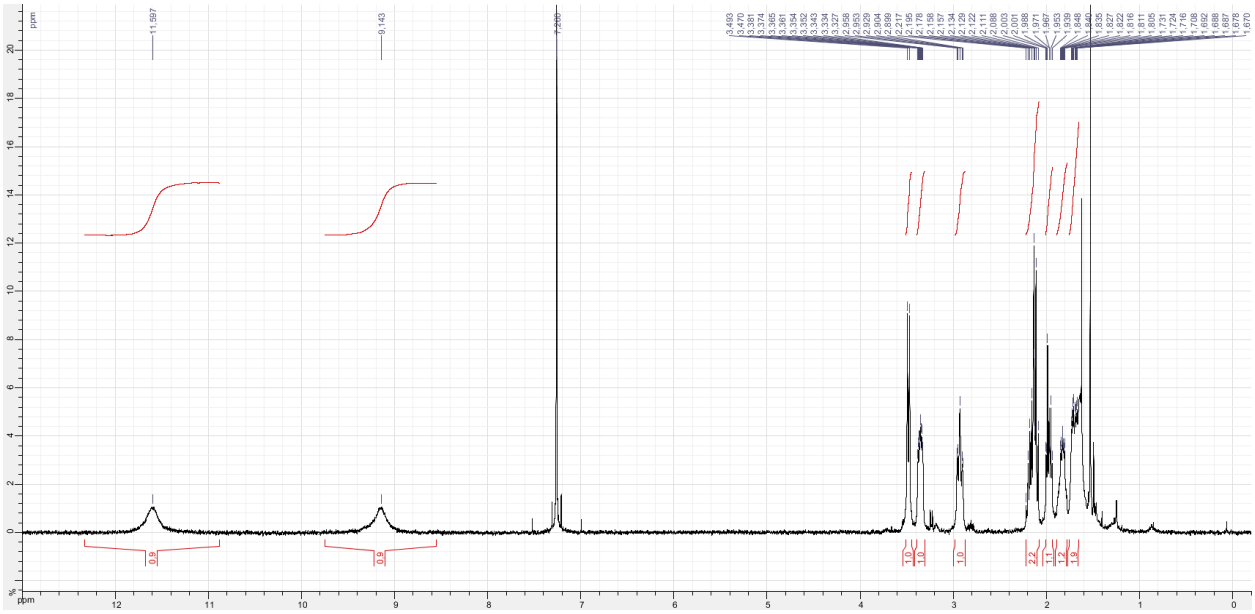


White solid. M.p. 136.5 °C (decomposition). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.69 (1 H, m, H2a), 1.83 (1 H, br s, H2b), 1.97 (1 H, br ddd, *J* 13.5, 6.5, 5.5, H3a), 2.08−2.22 (2 H, m, H3b, H4), 2.93 (1 H, br ddd, *J* 12.5, 9.5, 3.0, H1a), 3.35 (1 H, br ddd, *J* 12.5, 7.0, 3.0, H1b), 3.48 (1 H, br d, *J* 9.5, H5), 9.14 (1 H, br s, NH), 11.60 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 15.0 (C3), 16.5 (C2), 25.2 (C4), 36.6 (C5), 40.5 (C1), 59.3 (C6). MS (positive CI, NH_3): *m/z* 130 (M'$^{+}$ with ^{35}Cl),[a] 132 (M'$^{+}$ with ^{37}Cl),[a] 166 ([M−Cl]$^{+}$ with two ^{35}Cl),[a] 168 ([M−Cl]$^{+}$ with one ^{35}Cl and one ^{37}Cl),[a] 170 ([M−Cl]$^{+}$ with two ^{37}Cl),[a] 183 ([M−Cl]$^{+}$..NH_3 with two ^{35}Cl), 185 ([M−Cl]$^{+}$..NH_3 with one ^{35}Cl and one ^{37}Cl). MS (EI): *m/z* 94, 102, 103, 104, 130 (M'$^{+}$ with ^{35}Cl),[a] 131, 132 (M'$^{+}$ with ^{37}Cl),[a] 164 (M"$^{+}$ with two ^{35}Cl),[a] 166 ([M−Cl]$^{+}$ with two ^{35}Cl), 167.[a] HRMS (EI): *m/z* 164.0039 (M"$^{+}$ $C_6H_8{}^{35}Cl_2N^{+}$ requires 164.0029).[a]

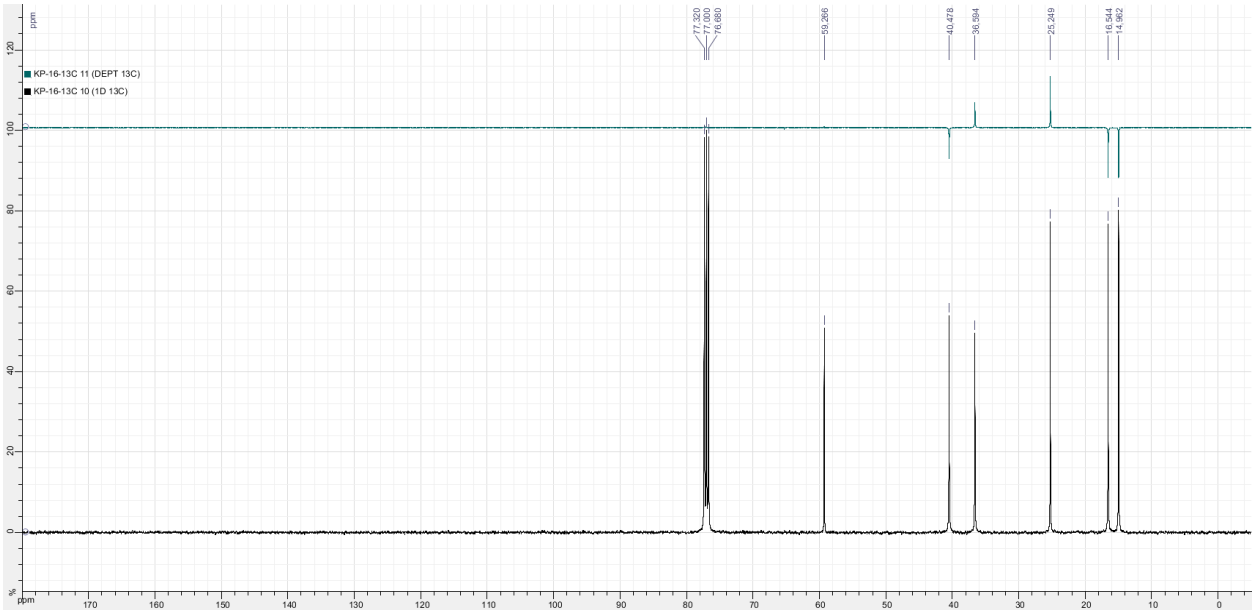
[a] $[M–Cl]^{+}$ =  ; M'$^{+}$ =  ; M"$^{+}$ =  (tentative assignments)



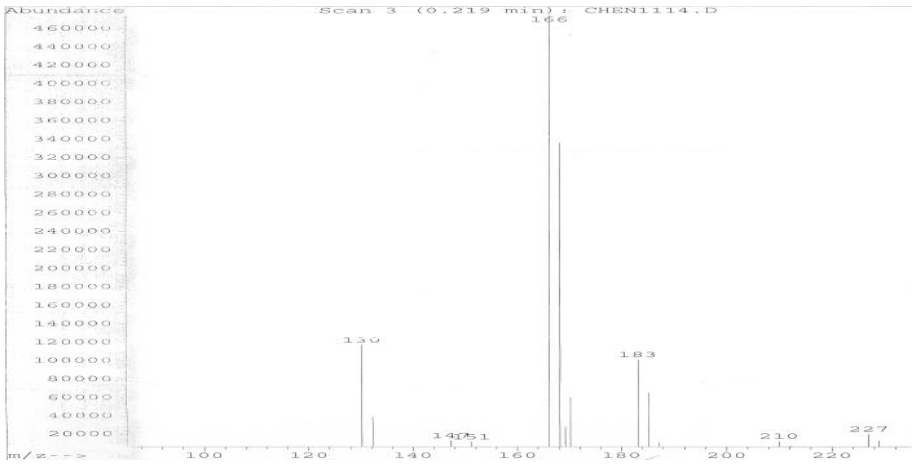
^{1}H NMR spectrum ($CDCl_3$, 400 MHz) at high concentration.



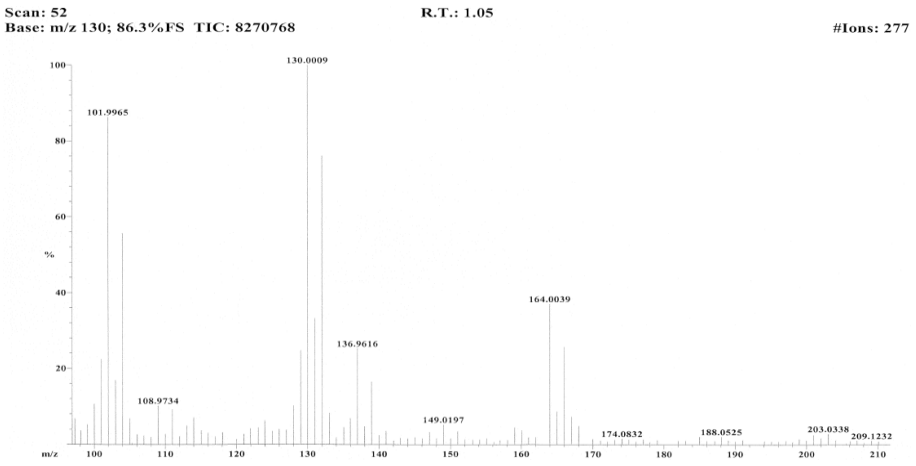
^{1}H NMR spectrum ($CDCl_3$, 400 MHz) at low concentration.



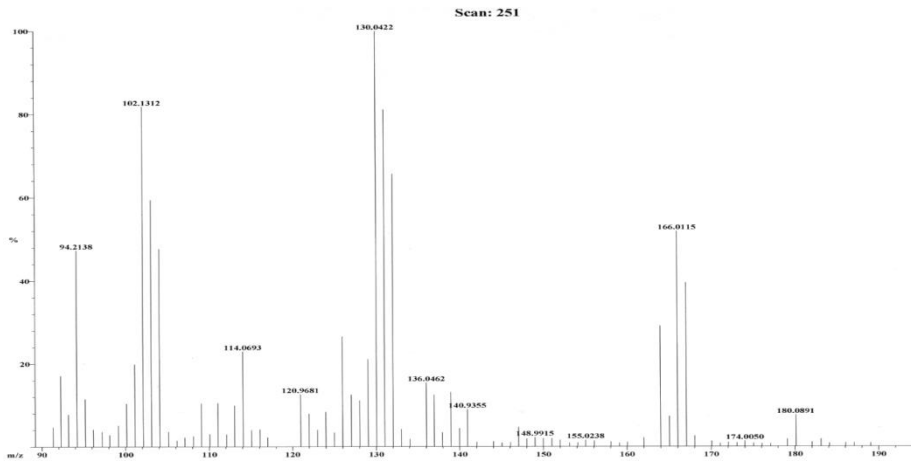
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



MS spectrum (CI, NH_3).

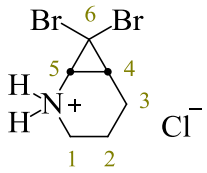


MS spectrum (EI).

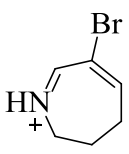


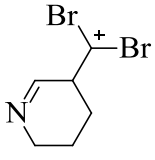
MS spectrum (EI), different run.

7,7-Dibromo-2-azoniabicyclo[4.1.0]heptane chloride **3c**

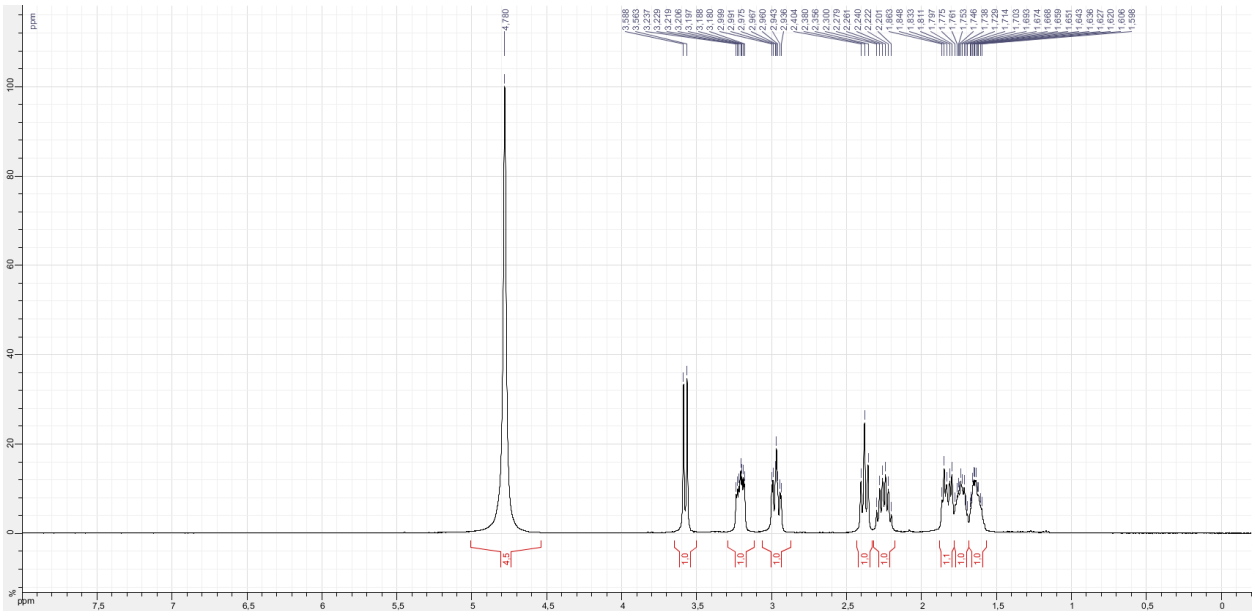


White solid. M.p. 160.9 °C (decomposition). ^{1}H NMR (D_2O, 400 MHz): δ 1.63 (1 H, m, H2a), 1.73 (1 H, m, H2b), 1.83 (1 H, dddd, *J* 15.0, 6.5, 5.5, 1.5, H3a), 2.25 (1 H, dddd, *J* 15.0, 9.5, 7.5, 7.0, H3b), 2.38 (1 H, td, *J* 9.5, 1.5, H4), 2.97 (1 H, ddd, *J* 12.5, 9.5, 3.0, H1a), 3.21 (1 H, ddd, *J* 12.5, 7.0, 3.0, H1b), 3.58 (1 H, d, *J* 9.5, H5), 4.78 (2 H, br s, NH). ^{13}C NMR (D_2O, 100.6 MHz): δ 16.5, 16.5 (C2, C3), 26.0 (C4), 27.1 (C6), 37.9 (C5), 41.1 (C1). MS (positive CI, NH_3): *m/z* 96, 97, 145, 174 (M'$^+$ with ^{79}Br),[a] 176 (M'$^+$ with ^{81}Br),[a] 208, 210, 252 (M"$^+$ with two ^{79}Br),[a] 254 (M"$^{+\bullet}$ with one ^{79}Br and one ^{81}Br),[a] 256 (M"$^+$ with two ^{81}Br). MS (EI): *m/z* 144, 145, 146, 147, 148, 162, 173, 174 (M'$^+$ with ^{79}Br),[a] 175, 176 (M'$^+$ with ^{81}Br),[a] 252 (M"$^+$ with two ^{79}Br),[a] 254 (M"$^{+\bullet}$ with one ^{79}Br and one ^{81}Br),[a] 256 (M"$^+$ with two ^{81}Br).[a] HRMS (EI): *m/z* 251.9031 (M"$^+$ $C_6H_8{}^{79}Br_2N^+$ requires 251.9018).[a]

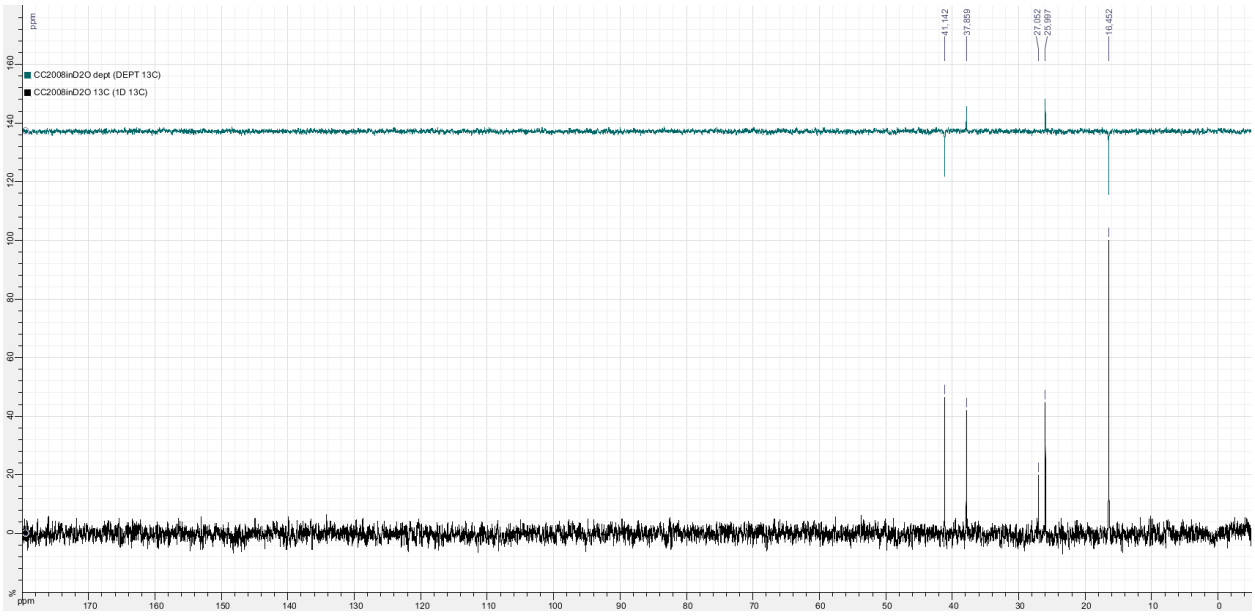
[a] M'$^+$ = 

; M"$^+$ = 

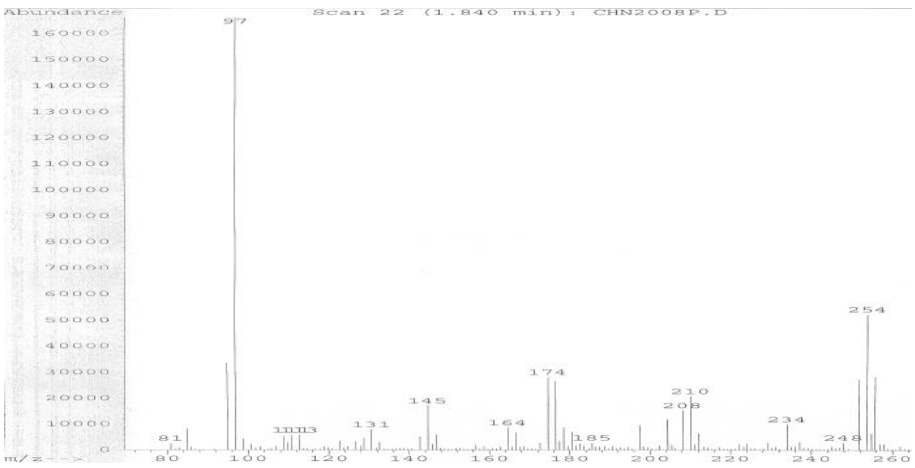
(tentative assignments)



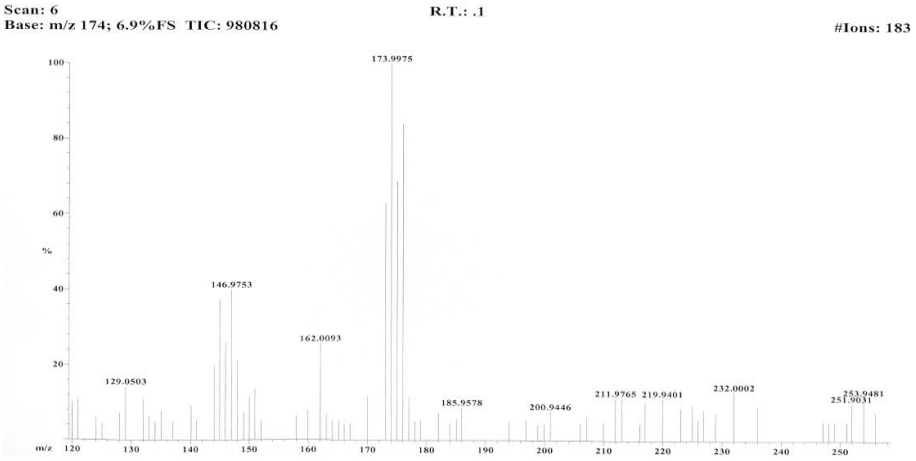
^{1}H NMR spectrum (D_2O, 400 MHz).



^{13}C NMR and DEPT135 spectra (D_2O, 400 MHz).

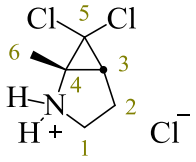


MS spectrum (CI, NH_3).

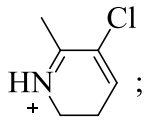
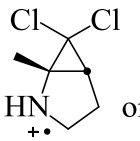
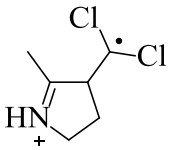


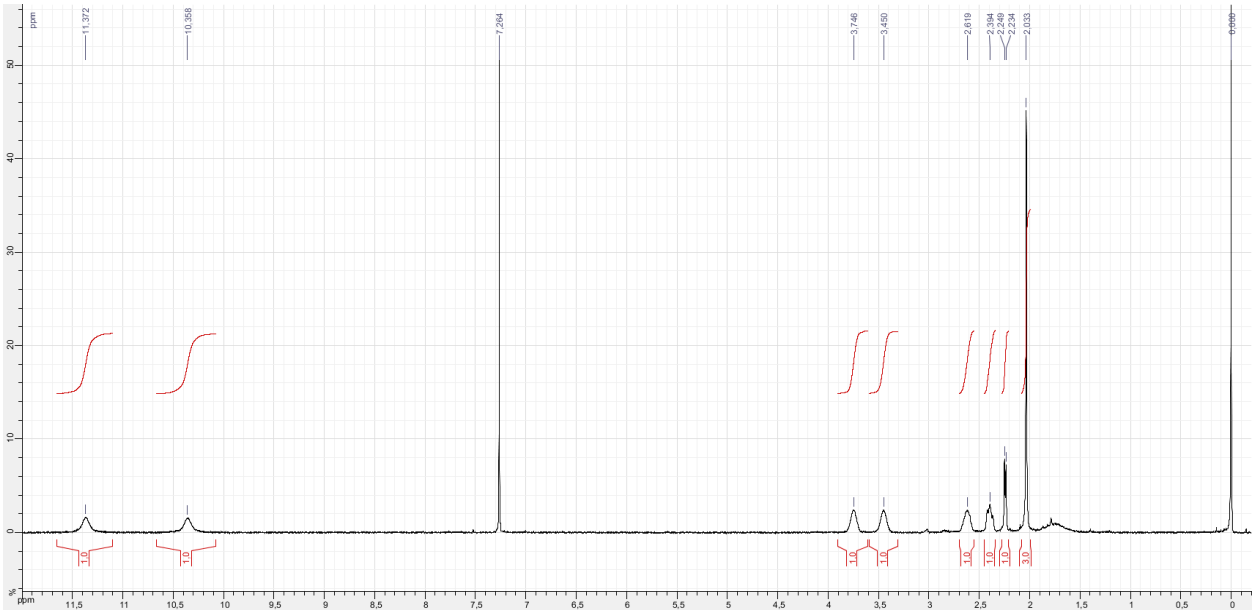
MS spectrum (EI).

6,6-Dichloro-1-methyl-2-azoniabicyclo[3.1.0]hexane chloride **3d**

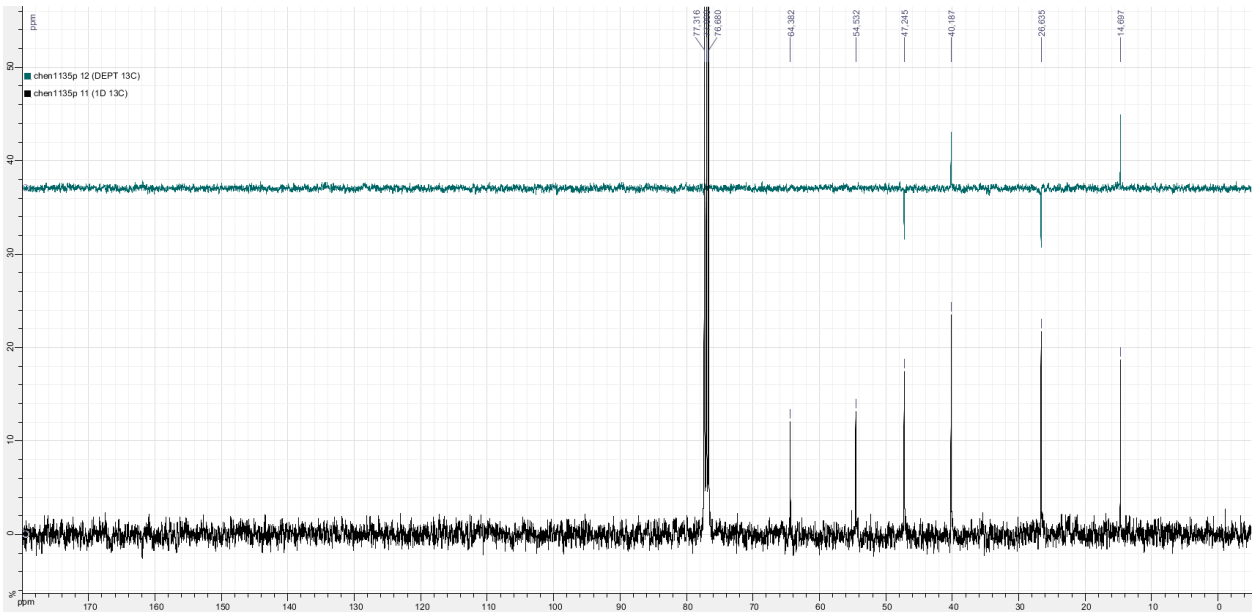


White powder. M.p. 93.1−94.6 °C. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.03 (3 H, s, H6), 2.24 (1 H, br d, *J* 6.0, H3), 2.39 (1 H, m, H2a), 2.62 (1 H, m, H2b), 3.45 (1 H, br s, H1a), 3.75 (1 H, br s, H1b), 10.36 (1 H, br s, NH), 11.37 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 14.7 (C6), 26.6 (C2), 40.2 (C3), 47.2 (C1), 54.5 (C4), 64.4 (C5). MS (EI): *m/z* 127, 128, 129, 130 (M'^{+} with ^{35}Cl),[a] 132 (M'^{+} with ^{37}Cl).[a] HRMS (EI): *m/z* 165.0113 ($M''^{+\bullet}$ $C_6H_9{}^{35}Cl_2N^{+\bullet}$ requires 165.0107).[a]

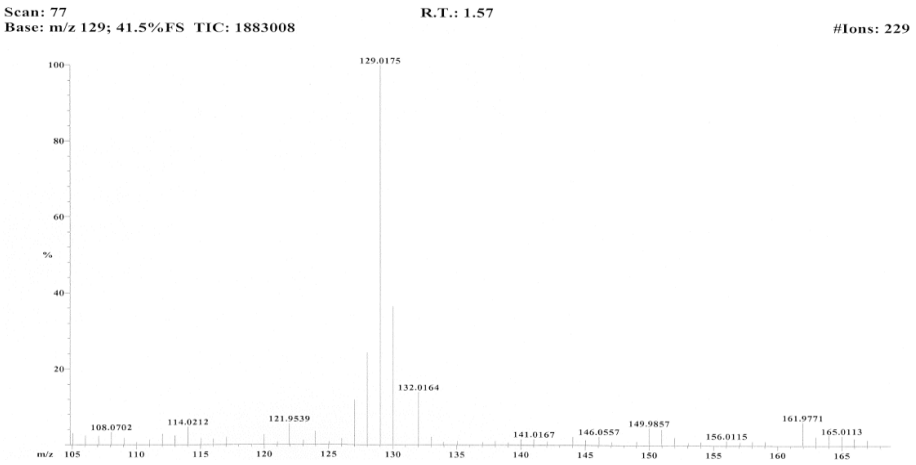
[a] M'^{+} =  ; $M''^{+\bullet}$ =  or  (tentative assignments)



^{1}H NMR spectrum ($CDCl_3$, 400 MHz) at low concentration.

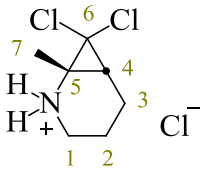


^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

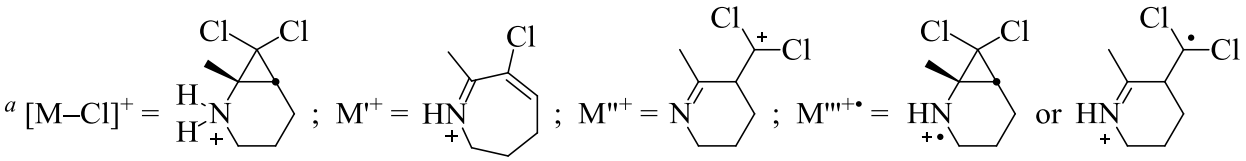


MS spectrum (EI).

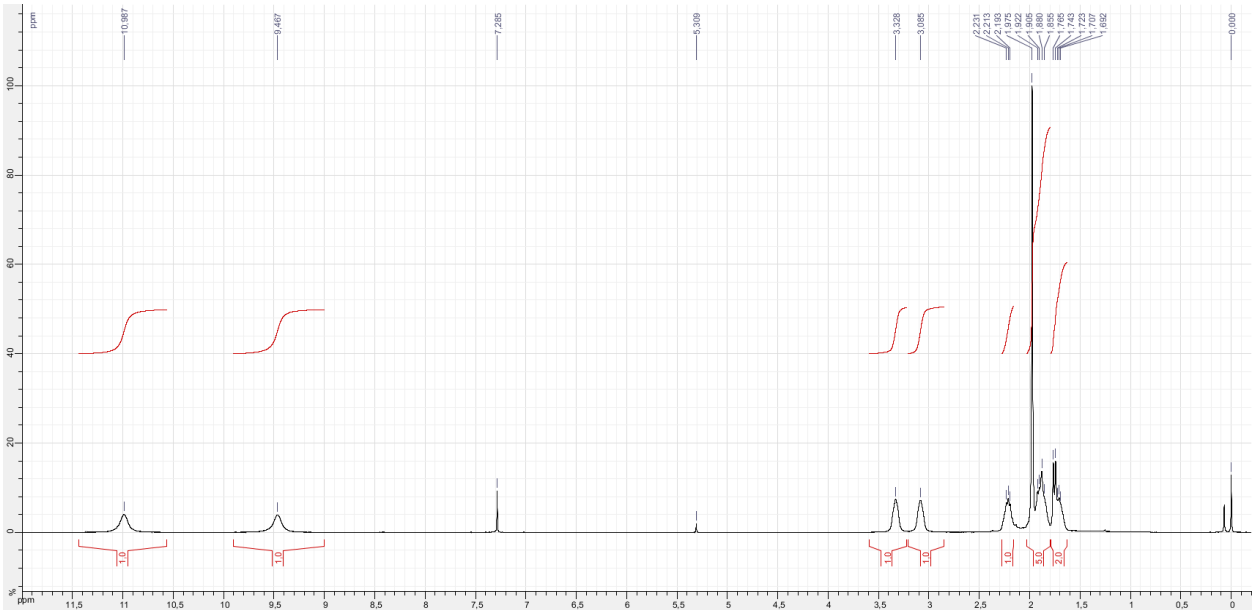
7,7-Dichloro-1-methyl-2-azoniabicyclo[4.1.0]heptane chloride **3e**



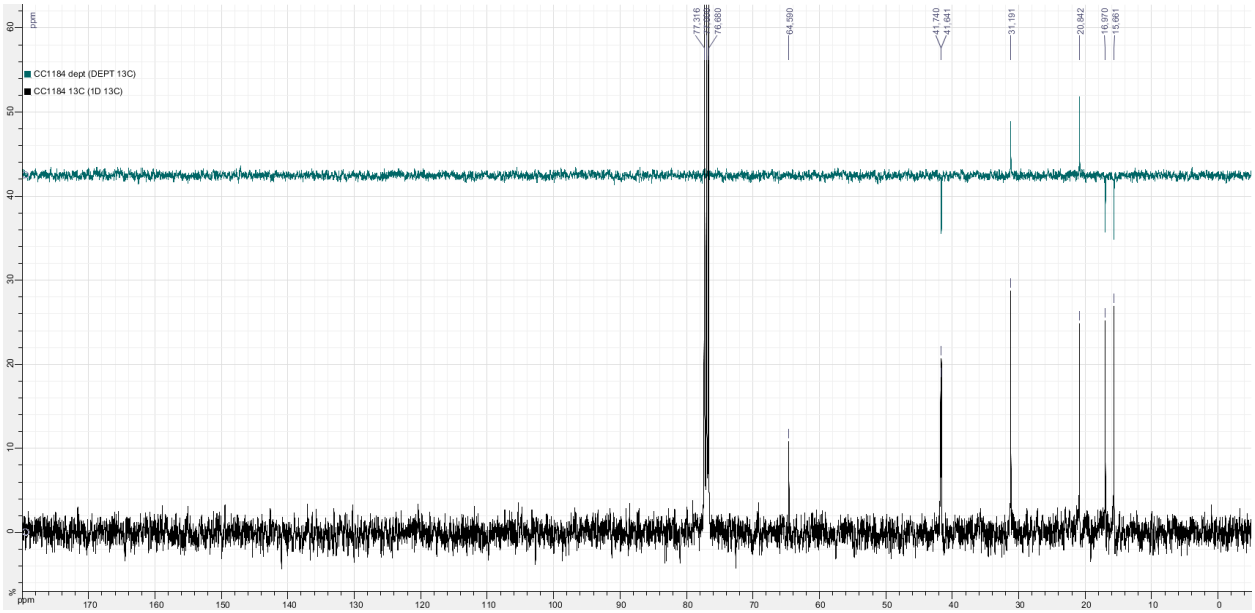
White solid. M.p. 146.5 °C (decomposition). ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.71 (1 H, m, H2a), 1.75 (1 H, br d, *J* 9.0, H4), 1.80−1.95 (2 H, m, H2b, H3a), 1.97 (3 H, s, H7), 2.22 (1 H, m, H3b), 3.08 (1 H, br s, H1a), 3.33 (1 H, br s, H1b), 9.47 (1 H, br s, NH), 10.99 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 15.7, 17.0 (C2, C3), 20.8 (C7), 31.2 (C4), 41.6 (C1), 41.7 (C5), 64.6 (C6). MS (positive CI, NH_3): *m/z* 145, 146, 147, 178, 180 ([M−Cl]$^+$ with two ^{35}Cl),[a] 181, 182 ([M−Cl]$^+$ with one ^{35}Cl and one ^{37}Cl),[a] 184 ([M−Cl]$^+$ with two ^{37}Cl).[a] MS (EI): *m/z* 108, 109, 115, 116, 117, 118, 143, 144 (M'$^+$ with ^{35}Cl),[a] 145, 146 (M'$^+$ with ^{37}Cl),[a] 164, 166, 178 (M''$^+$ with two ^{35}Cl),[a] 179 (M'''$^{+\bullet}$ with two ^{35}Cl),[a] 180 (M'' $^+$ with one ^{35}Cl and one ^{37}Cl),[a] 181 (M'''$^{+\bullet}$ with two ^{37}Cl).[a] HRMS (EI): *m/z* 179.0265 (M'''$^{+\bullet}$ $C_7H_{11}{}^{35}Cl_2N^{+\bullet}$ requires 179.0264).[a]



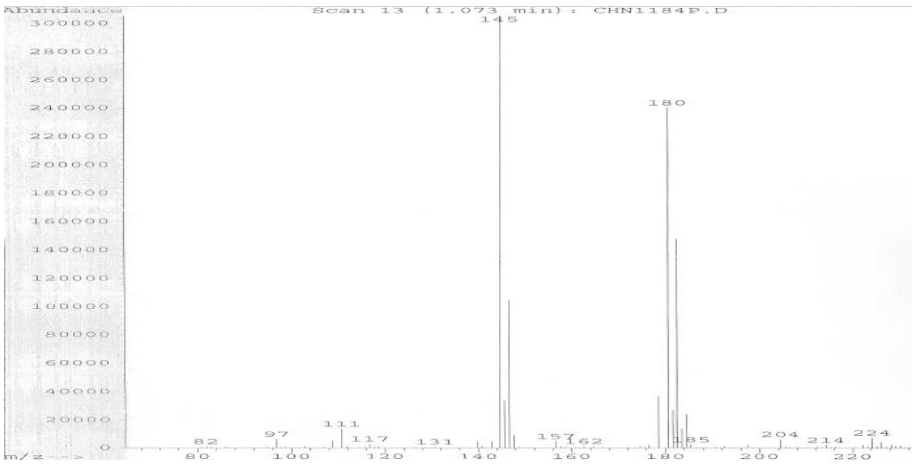
(tentative assignments)



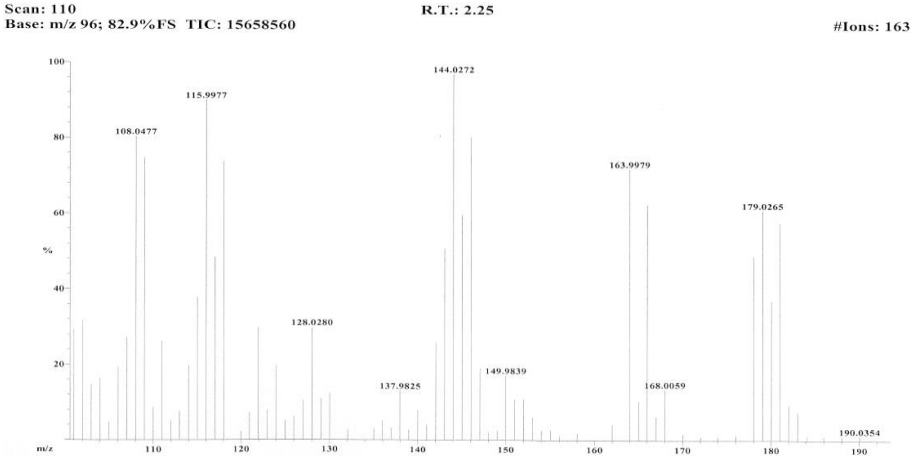
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

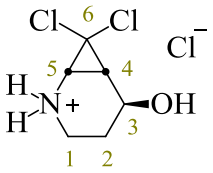


MS spectrum (CI, NH_3).

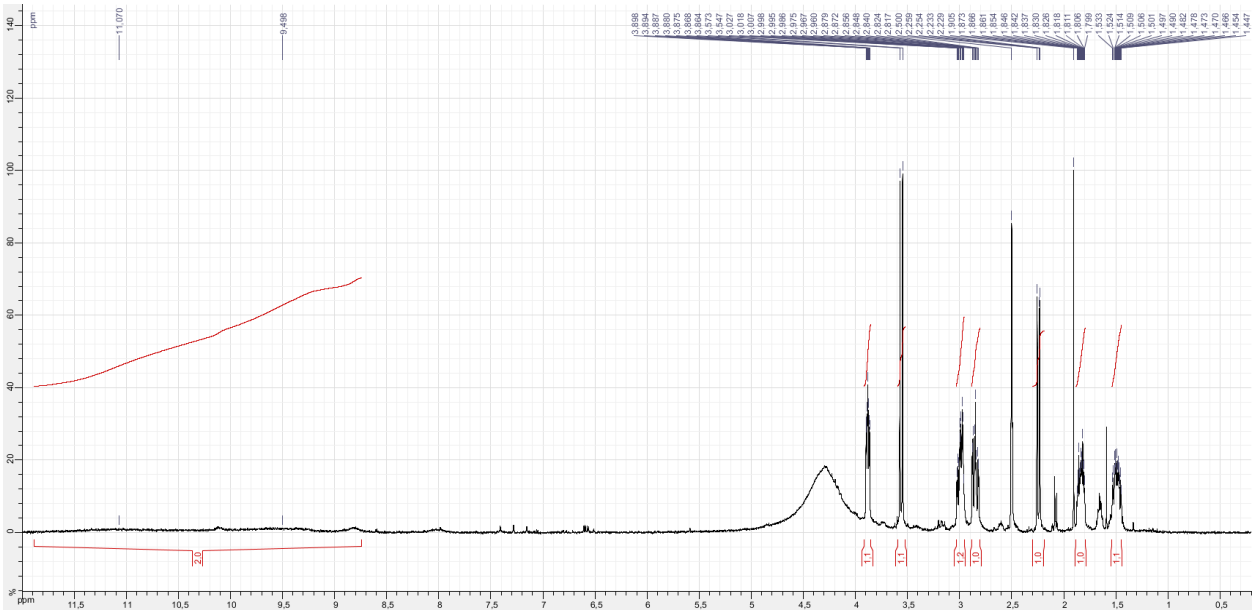


MS spectrum (EI).

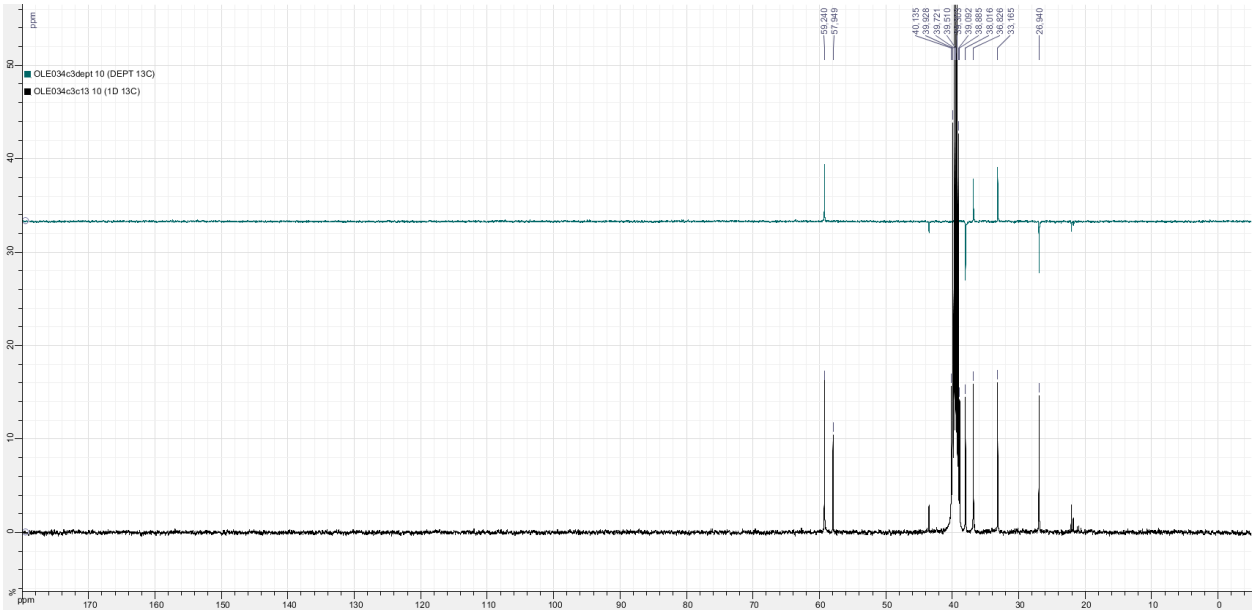
(1*R**,5*R**,6*R**)-7,7-Dichloro-2-azoniabicyclo[4.1.0]heptan-5-ol chloride **3f**



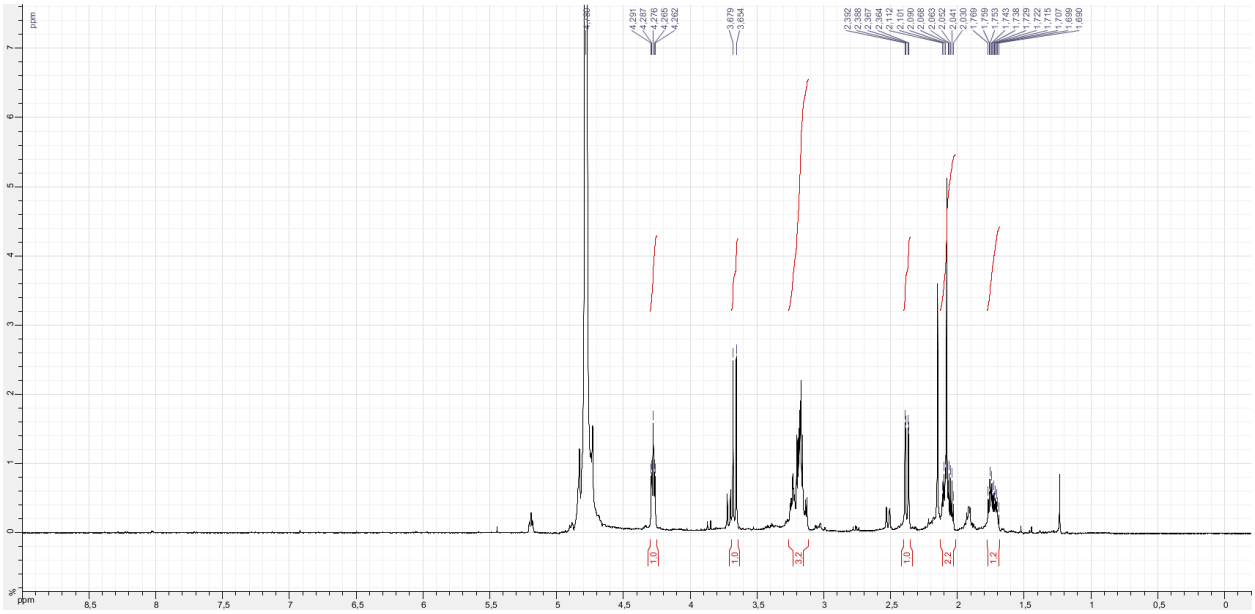
Viscous oil. ^{1}H NMR (DMSO-d_6, 400 MHz): δ 1.49 (1 H, dddd, *J* 14.5, 9.5, 7.5, 3.0, H2a), 1.84 (1 H, dddd, *J* 14.5, 8.0, 4.5, 3.0, H2b), 2.24 (1 H, dd, *J* 10.0, 1.5, H4), 2.85 (1 H, ddd, *J* 13.0, 9.5, 3.0, H1a), 3.00 (1 H, ddd, *J* 13.0, 8.0, 3.0, H1b), 3.56 (1 H, d, *J* 10.0, H5), 3.88 (1 H, ddd, *J* 7.5, 4.5, 1.5, H3), 9.50 (1 H, br s, NH), 11.07 (1 H, br s, NH). ^{13}C NMR (DMSO-d_6, 100.6 MHz): δ 26.9 (C2), 33.2 (C4), 36.8 (C5), 38.0 (C1), 57.9 (C6), 59.2 (C3). ^{1}H NMR (D_2O, 400 MHz): δ 1.73 (1 H, dddd, *J* 12.5, 9.5, 6.0, 3.5, H2a), 2.07 (1 H, m, H2b), 2.38 (1 H, dd, *J* 10.0, 1.5, H5), 3.12-3.26 (2 H, m, H1), 3.67 (1 H, d, *J* 10.0, H5), 4.28 (1 H, ddd, *J* 6.0, 4.5, 1.5, H3). ^{13}C NMR (D_2O, 100.6 MHz): δ 26.2 (C2), 32.4 (C4), 37.5 (C5), 38.5 (C1), 56.3 (C6), 59.1 (C3).



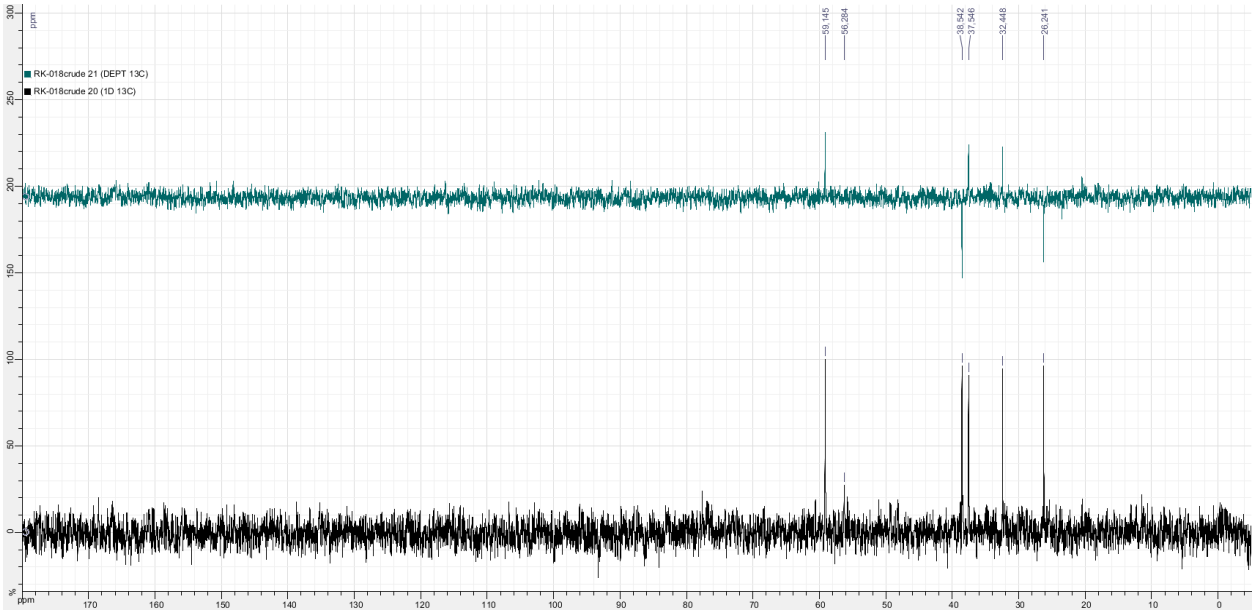
^{1}H NMR spectrum (DMSO-*d*6, 400 MHz).



^{13}C NMR and DEPT135 spectra (DMSO-*d*6, 100.6 MHz).

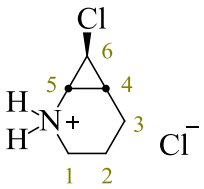


^{1}H NMR spectrum (D_2O, 400 MHz).

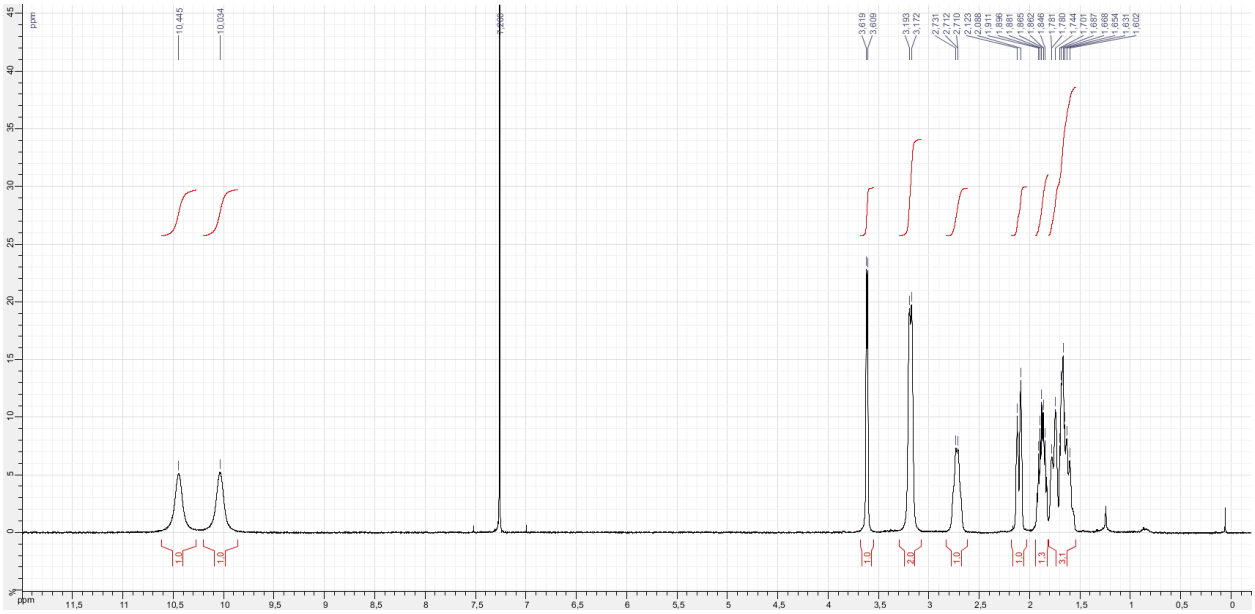


^{13}C NMR and DEPT135 spectra (D_2O, 100.6 MHz).

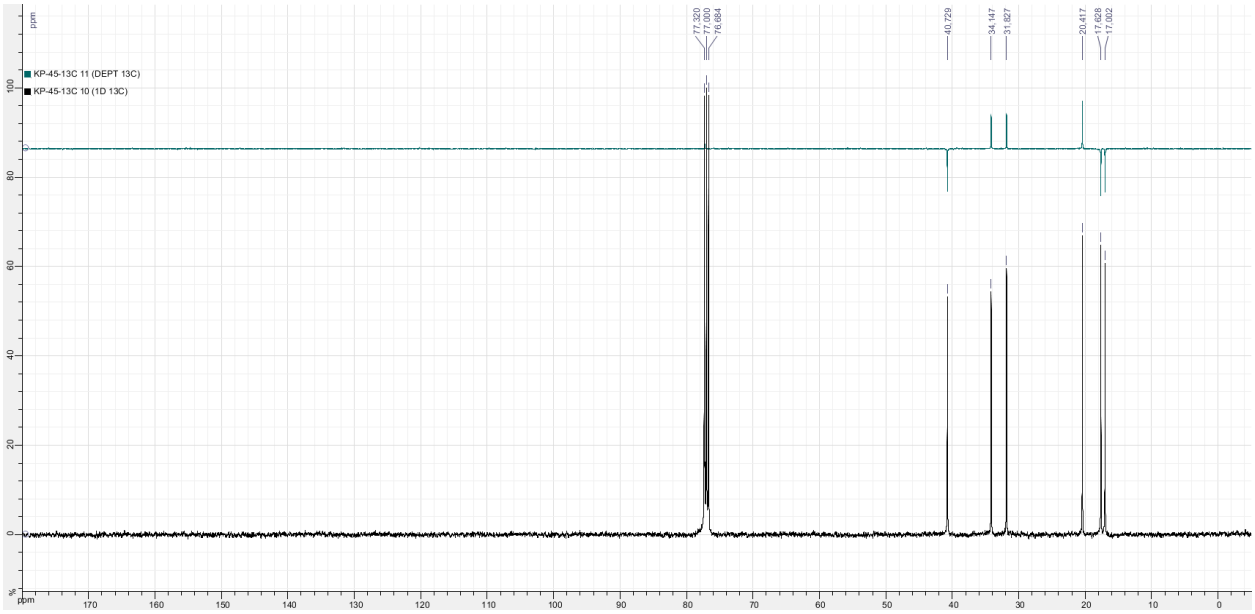
(1*R**,6*S**,7*R**)-7-Chloro-2-azoniabicyclo[4.1.0]heptane chloride *exo*-**9**



Thick colourless oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.54–1.82 (3 H, m, H2, H4), 1.88 (1 H, br ddt, *J* 14.0, 12.0, 6.0, H3a), 2.11 (1 H, br dt, *J* 14.0, 3.5, H3b), 2.72 (1 H, br td, *J* 11.0, 8.5, H1a), 3.18 (2 H, br d, *J* 8.5, H5, H1b), 3.61 (1 H, br d, *J* 4.5, H6), 10.03 (1 H, br s, NH), 10.44 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 17.0 (C2), 17.6 (C3), 20.4 (C4), 31.8 (C6), 34.1 (C5), 40.7 (C1).

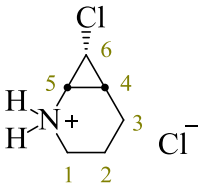


^{1}H NMR spectrum ($CDCl_3$, 400 MHz) at low concentration.

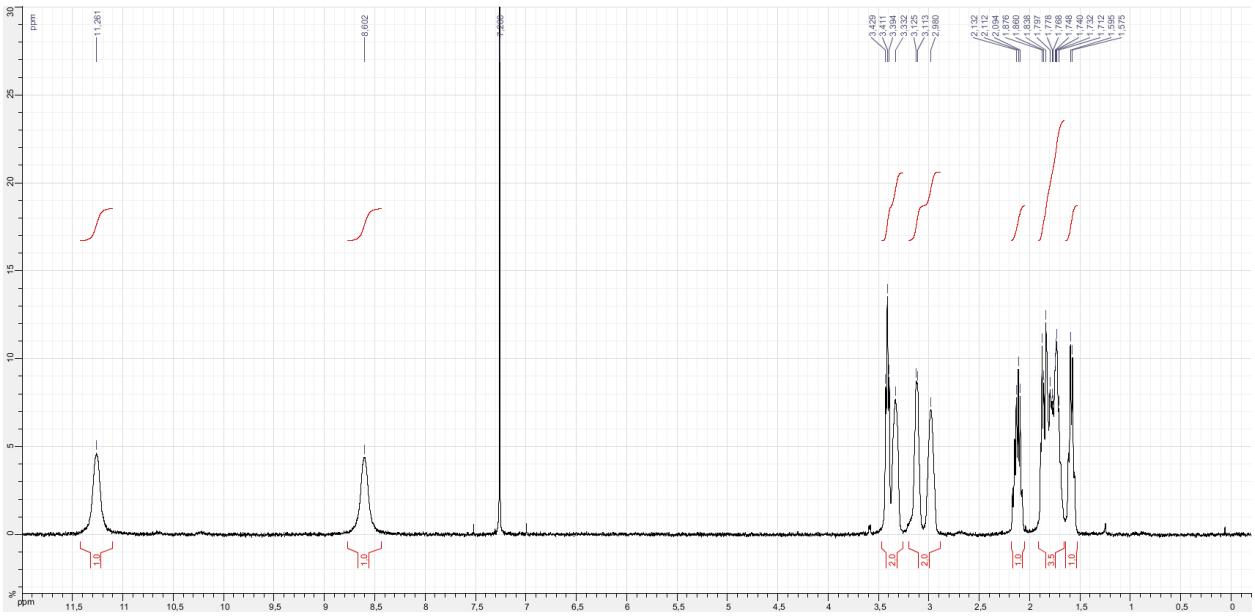


^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

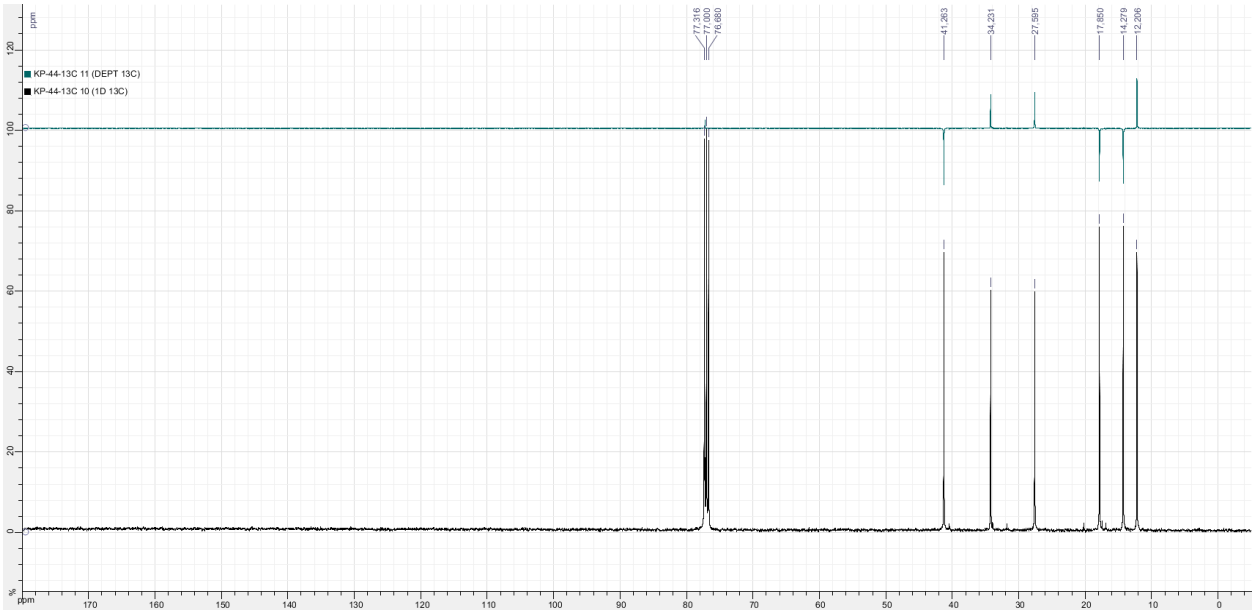
(1*R**,6*S**,7*S**)-7-Chloro-2-azoniabicyclo[4.1.0]heptane chloride *endo*-**9**



Thick pale yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.59 (1 H, br ddd, *J* 9.0, 8.5, 7.0, H4), 1.66−1.91 (3 H, m, H2, H3a), 2.12 (1 H, br ddt, *J* 14.0, 8.5, 7.5, H3b), 2.98 (1 H, br s, H5), 3.12 (1 H, br td, *J* 7.0, 5.0, H1a), 3.33 (1 H, br s, H1b), 3.41 (1 H, br t, *J* 7.0, H6), 8.60 (1 H, br s, NH), 11.26 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 12.2 (C4), 14.3 (C3), 17.8 (C2), 27.6 (C5), 34.2 (C6), 41.3 (C1).



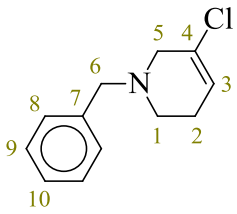
^{1}H NMR spectrum ($CDCl_3$, 400 MHz) at low concentration.



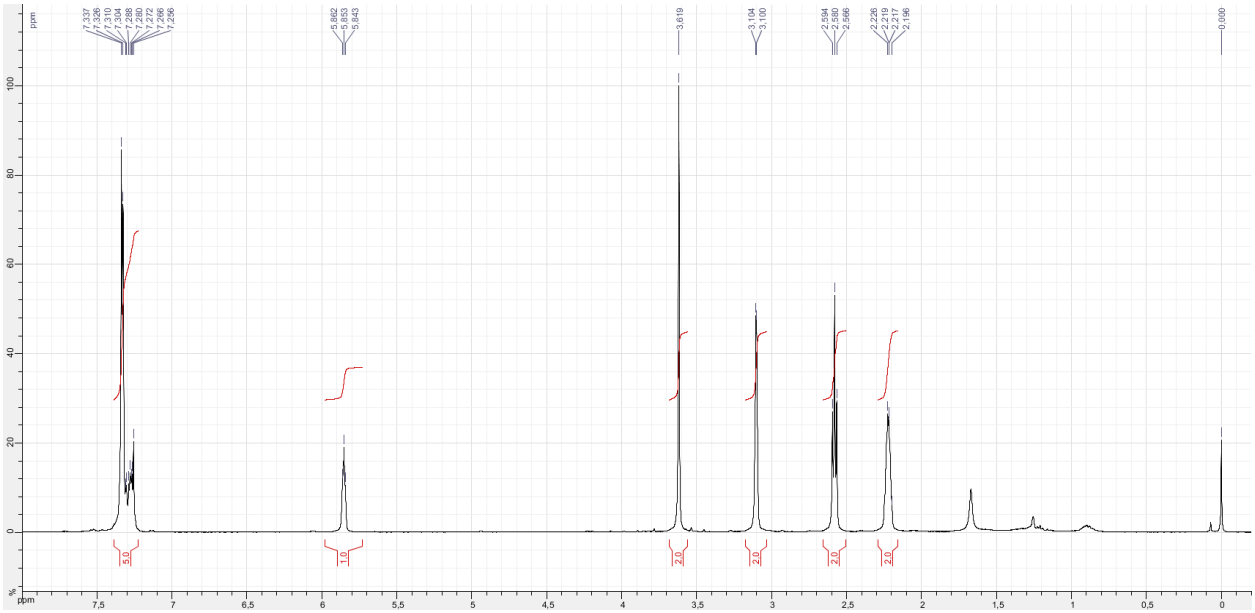
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

III. Transformation compounds from aminocyclopropane derivatives

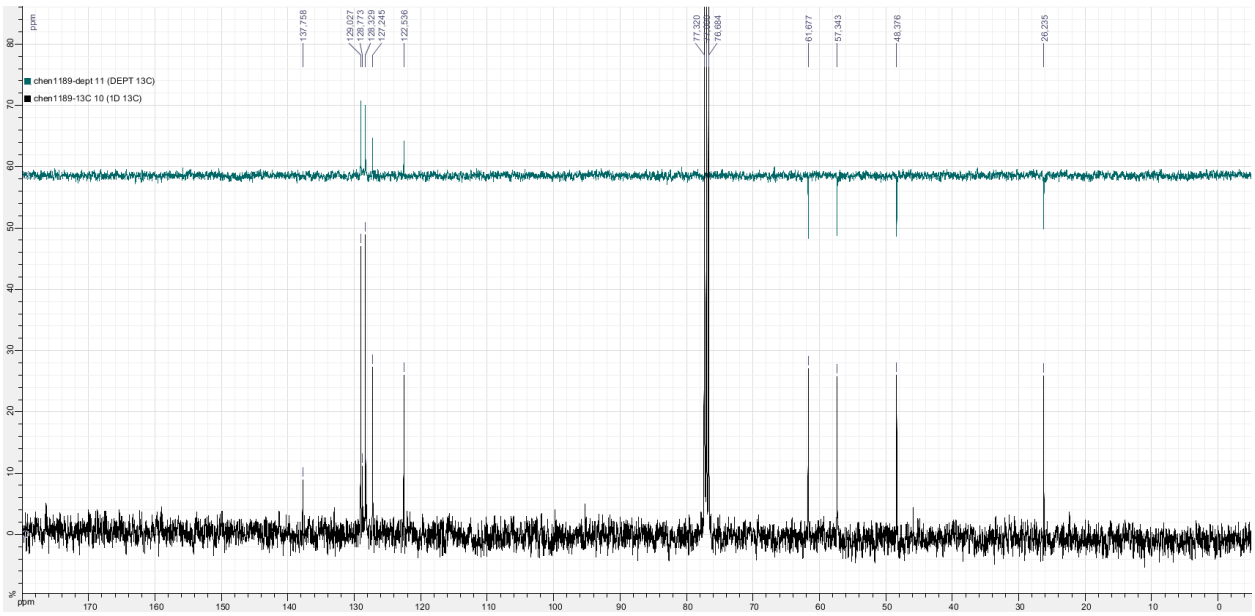
1-Benzyl-5-chloro-3,6-dihydro-2*H*-pyridine **5aa**



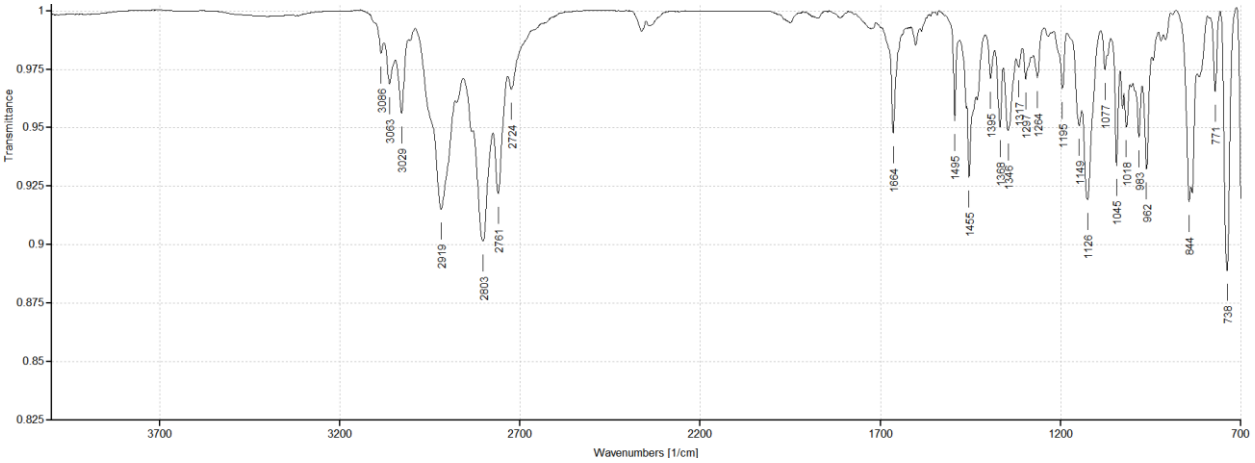
Pale yellow oil. R_f 0.15 [EtOAc/petroleum ether 5%, anisaldehyde (white spot), UV-active]. IR (neat) *v* 3063 (w), 3029 (m), 2919 (s), 2803 (s), 2761 (m), 2724 (w), 1664 (m), 1495 (m), 1455 (m), 1368 (m), 1347 (m), 1149 (m) 1126 (s), 1045 (m), 962 (m), 844 (s), 835 (s), 738 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.22 (2 H, tdt, *J* 5.5, 4.0, 2.5, H2), 2.58 (2 H, t, *J* 5.5, H1), 3.10 (2 H, td, *J* 2.5, 1.5, H5), 3.62 (2 H, s, H6), 5.85 (1 H, tt, *J* 4.0, 1.5, H3), 7.24−7.38 (5 H, m, H8−H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 26.2 (C2), 48.4 (C1), 57.3 (C5), 61.7 (C6), 122.5 (C3), 127.2 (C10), 128.3 (C8 or C9), 128.8 (C4), 129.0 (C8 or C9), 137.8 (C7). MS (positive CI, NH_3): *m/z* 92, 208 (MH^+ with ^{35}Cl), 209, 210 (MH^+ with ^{37}Cl), 211. MS (EI): *m/z* 116, 117, 118, 172, 207 ($M^{+\bullet}$ with ^{35}Cl), 209 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 207.0819 ($M^{+\bullet}$ $C_{12}H_{14}{}^{35}ClN^{+\bullet}$ requires 207.0810).



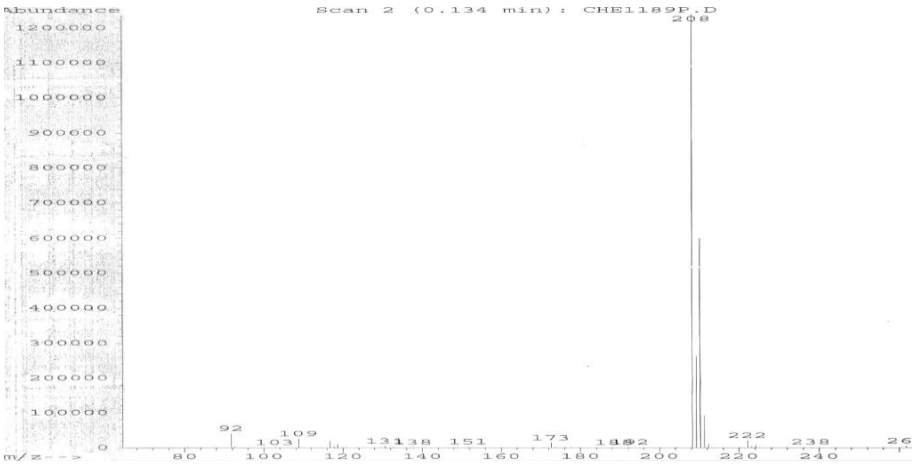
^1H NMR spectrum ($CDCl_3$, 400 MHz).



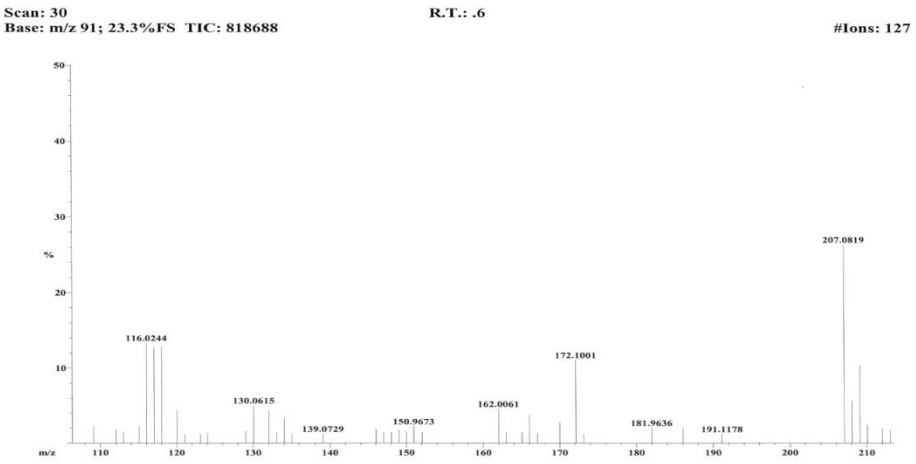
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

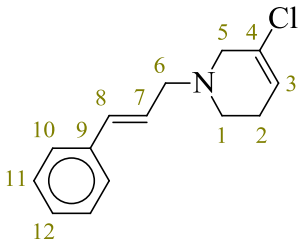


MS spectrum (CI, NH_3).

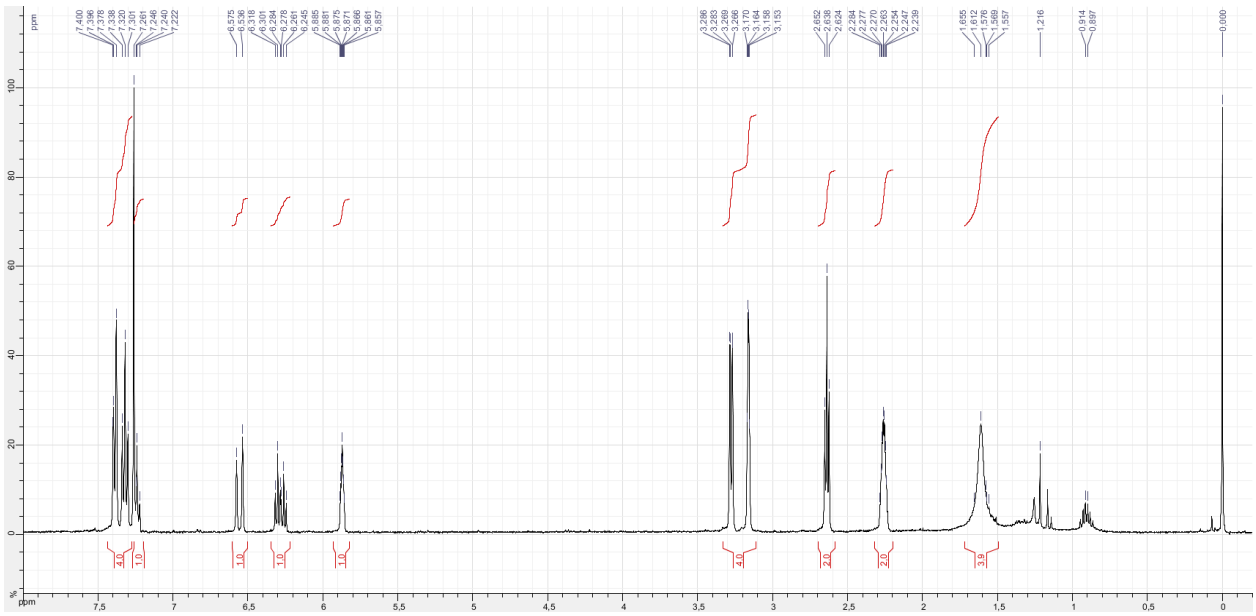


MS spectrum (EI).

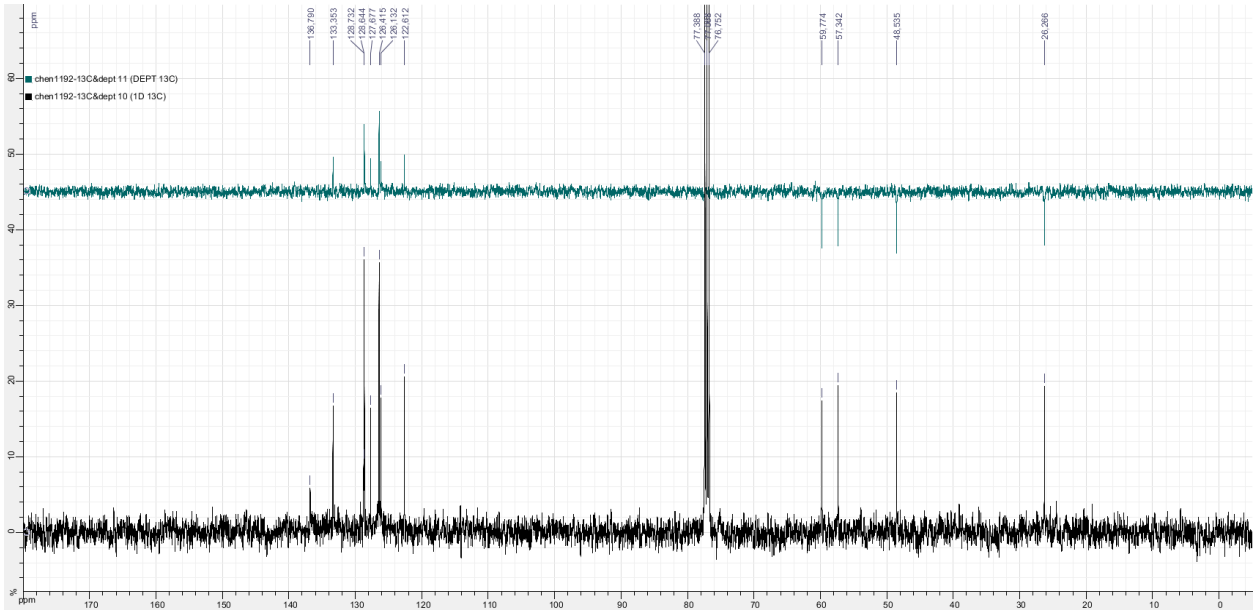
5-Chloro-1-[(*E*)-cinnamyl]-3,6-dihydro-2*H*-pyridine **5ab**



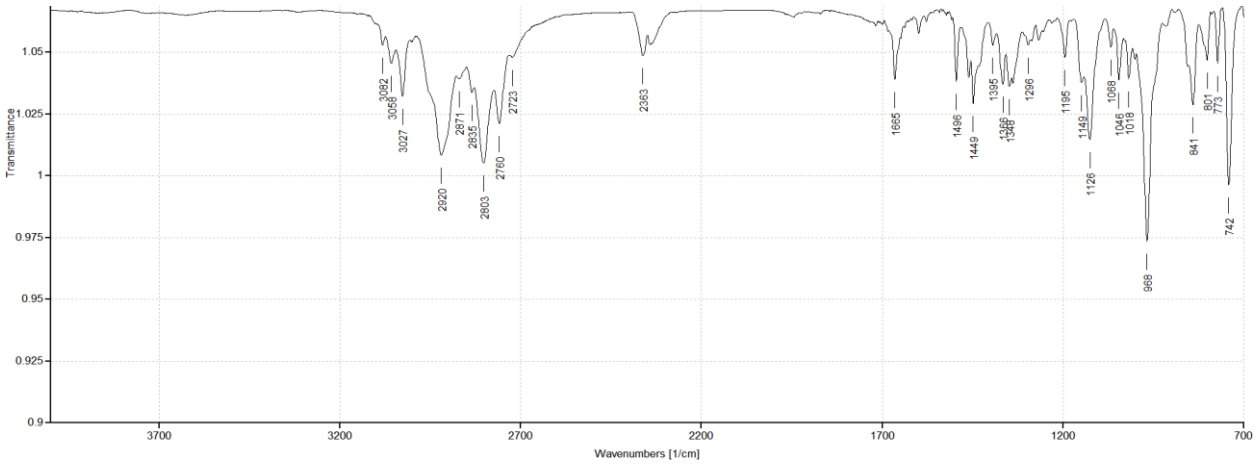
Pale yellow oil. R_f 0.3 [EtOAc/petroleum ether 20%, anisaldehyde (white spot), UV-active]. IR (neat) *v* 3058 (w), 3027 (m), 2920 (m), 2871 (w), 2885 (m), 2803 (m), 2760 (m), 2363 (w), 2342 (w),1665 (w), 1496 (w), 1460 (w), 1449 (m), 1366 (w), 1348 (w), 1339 (w), 1126 (m), 1046 (w), 1018 (w), 968 (s), 841 (m), 742 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.26 (2 H, tdt, *J* 5.5, 4.0, 2.5, H2), 2.64 (2 H, t, *J* 5.5, H1), 3.16 (2 H, q, *J* 2.5, H5), 3.28 (2 H, dd, *J* 7.0, 1.0, H6), 5.87 (1 H, tt, *J* 4.0, 1.5, H3), 6.42 (2 H, AB part of an ABX_2 system, δ_A 6.28, δ_B 6.55, J_{AB} 16.0, J_{AX} 7.0, J_{BX} 1.0, H7, H8), 7.24 (1 H, br t, *J* 7.0, H12), 7.32 (2 H, br dd, *J* 8.0, 7.0, H11), 7.39 (2 H, br d, *J* 8.0, H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 26.3 (C2), 48.5 (C1), 57.3 (C5), 59.8 (C6), 122.6 (C3), 126.1 (C7), 126.4 (C10), 127.7 (C12), 128.6 (C11), 128.7 (C4), 133.4 (C8), 136.8 (C9). MS (positive CI, NH_3): *m/z* 118, 143, <u>234</u> (MH^+ with ^{35}Cl), 235, 236 (MH^+ with ^{37}Cl), 237, 238. MS (EI): *m/z* 115, <u>117</u>, 118, 142, 144, 233 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 233.0970 ($M^{+\bullet}$ $C_{14}H_{16}{}^{35}ClN^{+\bullet}$ requires 233.0966).



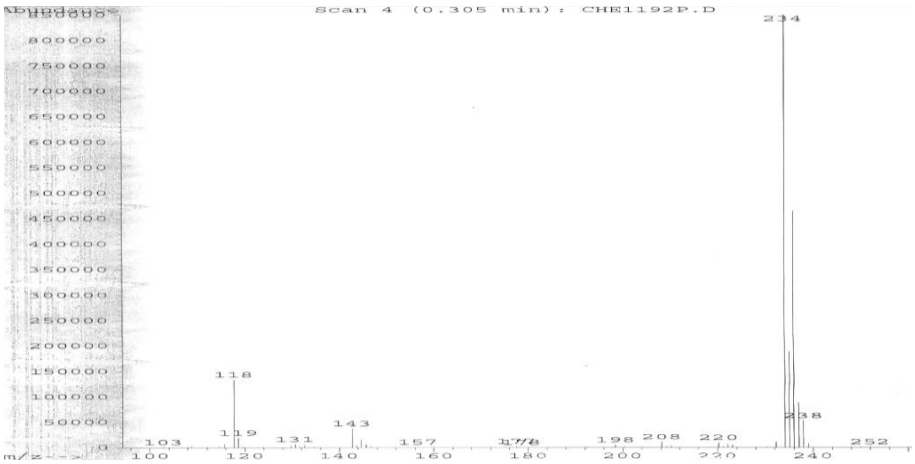
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



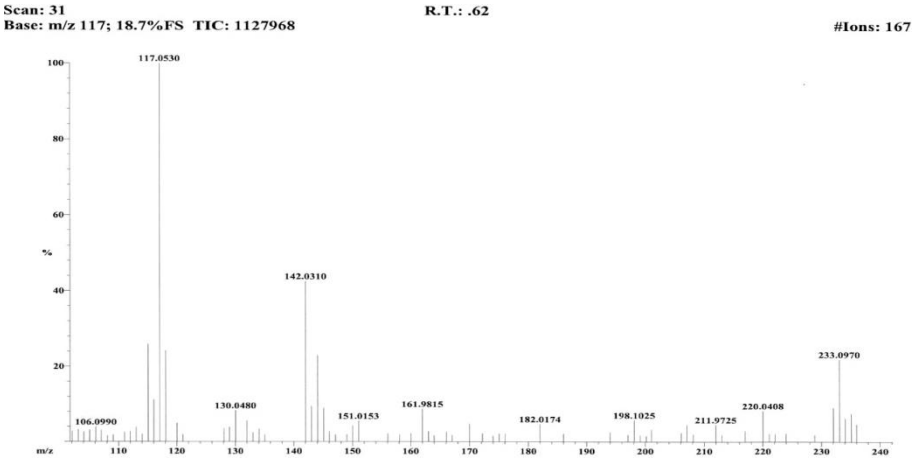
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

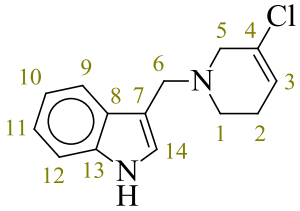


MS spectrum (CI, NH_3).

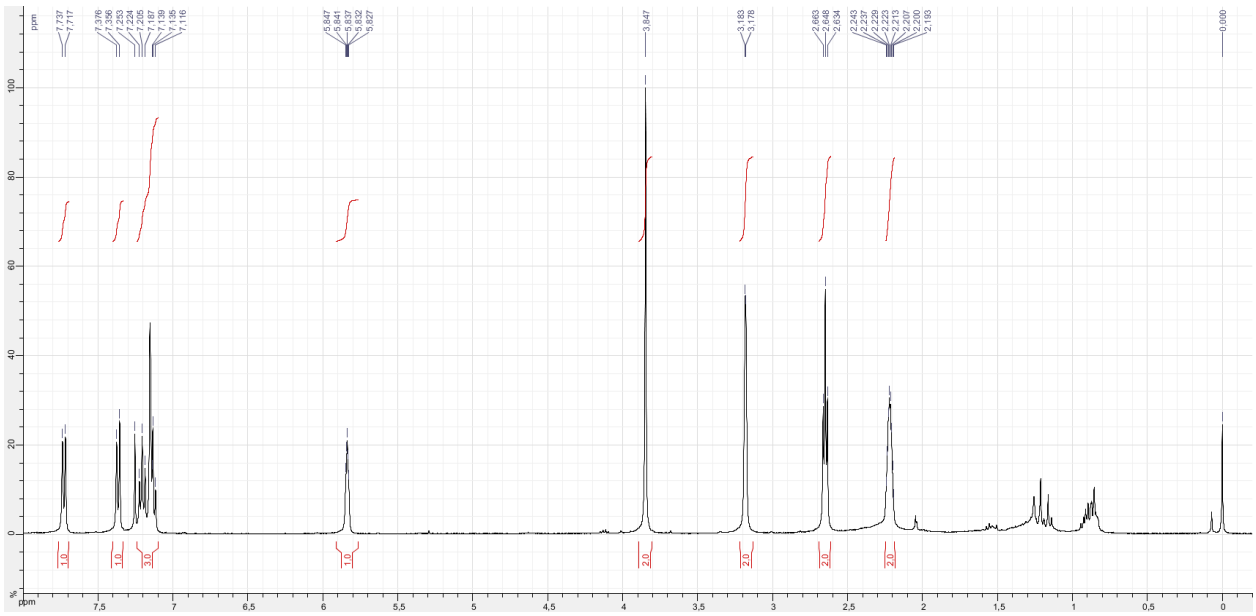


MS spectrum (EI).

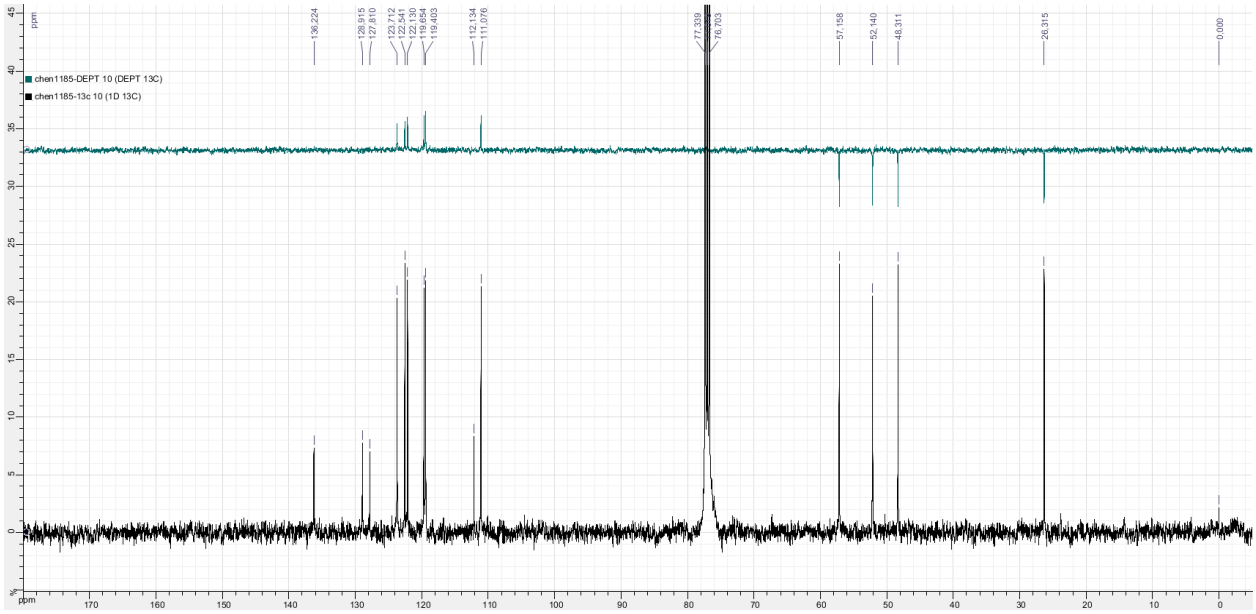
3-((3-Chloro-5,6-dihydropyridin-1(2*H*)-yl)methyl)-1*H*-indole **5ac**



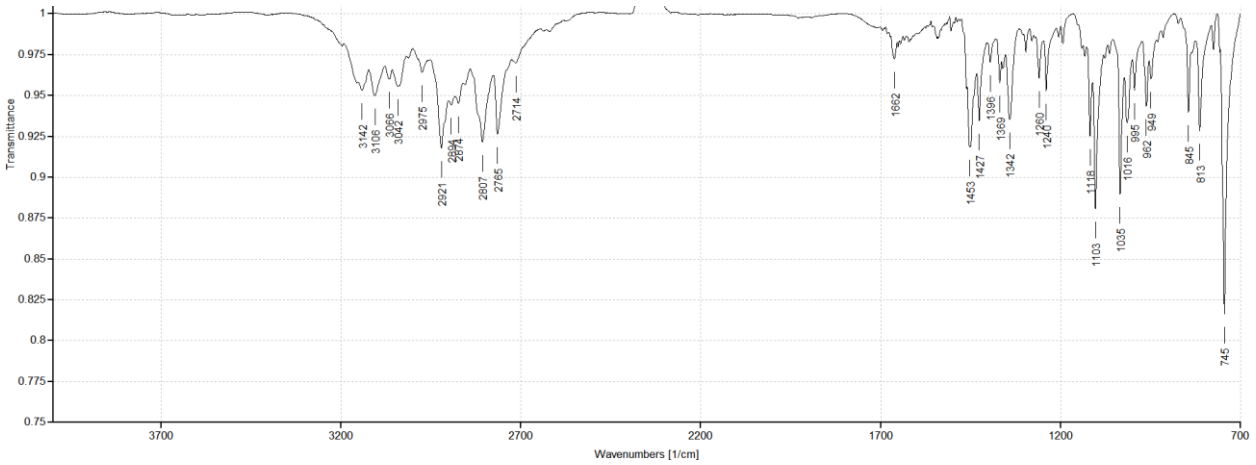
Pale yellow oil. R_f 0.15 [EtOAc/petroleum ether 50%, anisaldehyde (pink-brown spot), UV-active]. IR (neat) *v* 3142 (w), 3106 (w), 3066 (w), 3042 (w), 2921 (m), 2894 (w), 2874 (w), 2807 (m), 2765 (m), 1453 (m), 1427 (m), 1342 (m), 1118 (m), 1103 (m), 1035 (m), 845 (m), 813 (m), 745 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 2.22 (2 H, tdt, *J* 5.5, 4.0, 2.5, H2), 2.65 (2 H, t, *J* 5.5, H1), 3.18 (2 H, td, *J* 2.5, 2.0, H5), 3.85 (2 H, s, H6), 5.84 (1 H, tt, *J* 4.0, 2.0, H3), 7.13 (1 H, t, *J* 7.5, H10), 7.15 (1 H, s, H14), 7.21 (1 H, dd, *J* 8.0, 7.0, H11), 7.37 (1 H, d, *J* 8.0, H12), 7.73 (1 H, d, *J* 8.0, H9), 8.16 (1 H, br s, NH). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 26.3 (C2), 48.3 (C1), 52.1 (C6), 57.2 (C5), 111.1 (C12), 112.1 (C7), 119.4 (C9), 119.7 (C10), 122.1 (C11), 122.5 (C3), 123.7 (C14), 127.8 (C8), 128.9 (C4), 136.2 (C13). MS (positive CI, NH_3): *m/z* 119, 121, 131, 132, 247 (MH^+ with ^{35}Cl), 248, 249 (MH^+ with ^{37}Cl). MS (EI): *m/z* 129, 130, 131, 246 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 246.0926 ($M^{+\bullet}$ $C_{14}H_{15}{}^{35}ClN_2{}^{+\bullet}$ requires 246.0919).



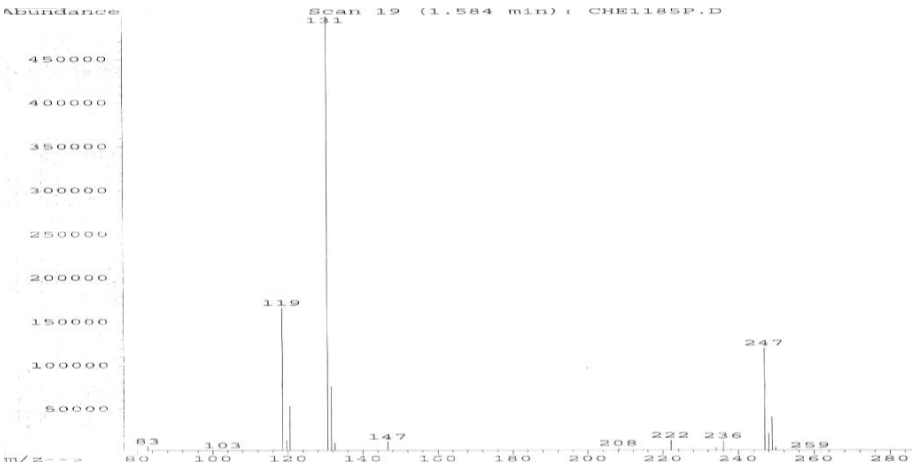
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



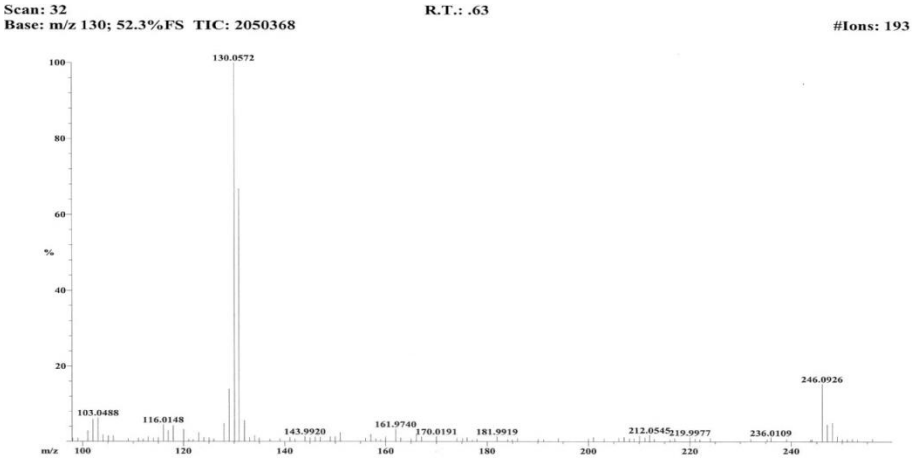
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

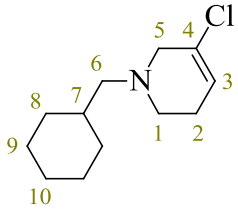


MS spectrum (CI, NH_3).

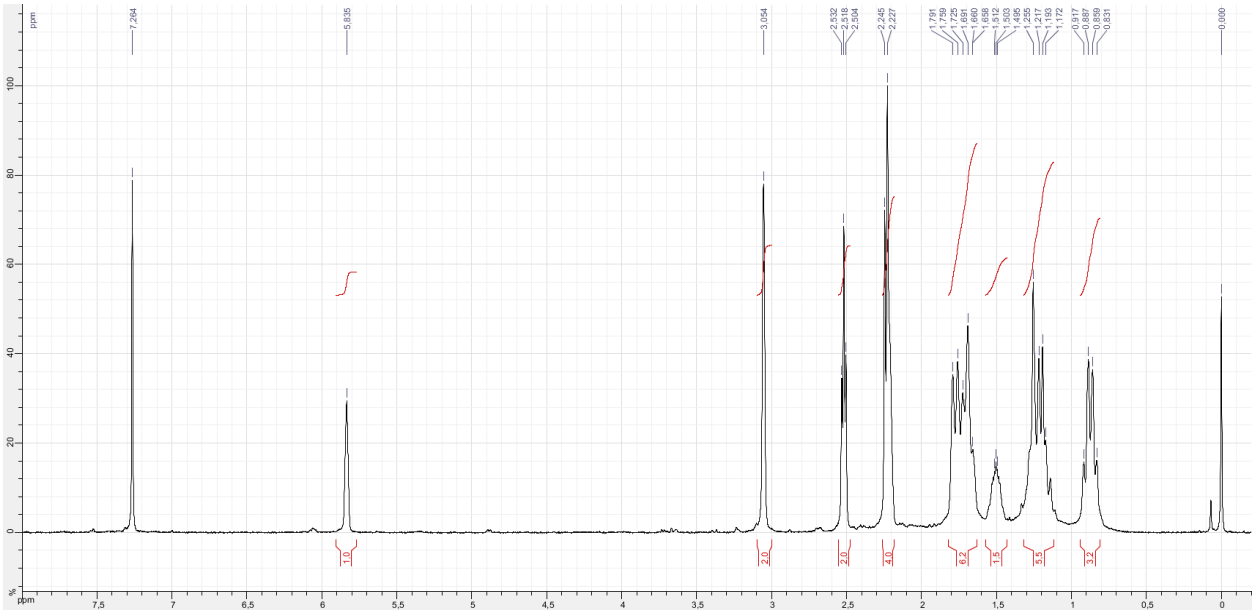


MS spectrum (EI).

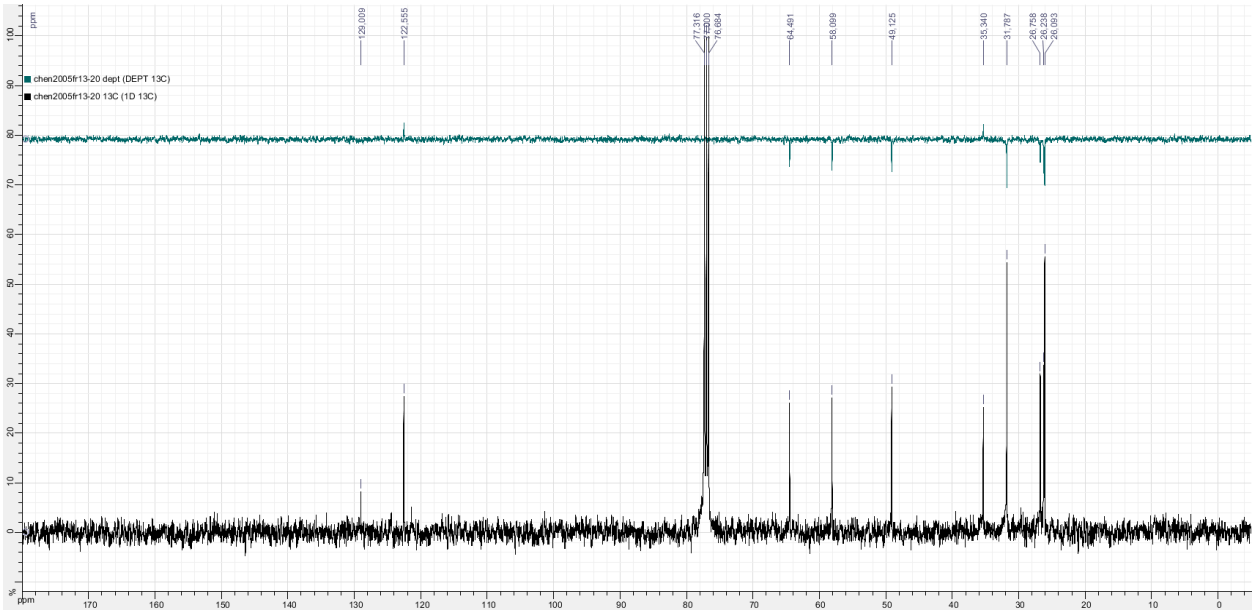
5-Chloro-1-(cyclohexylmethyl)-3,6-dihydro-2*H*-pyridine **5ad**



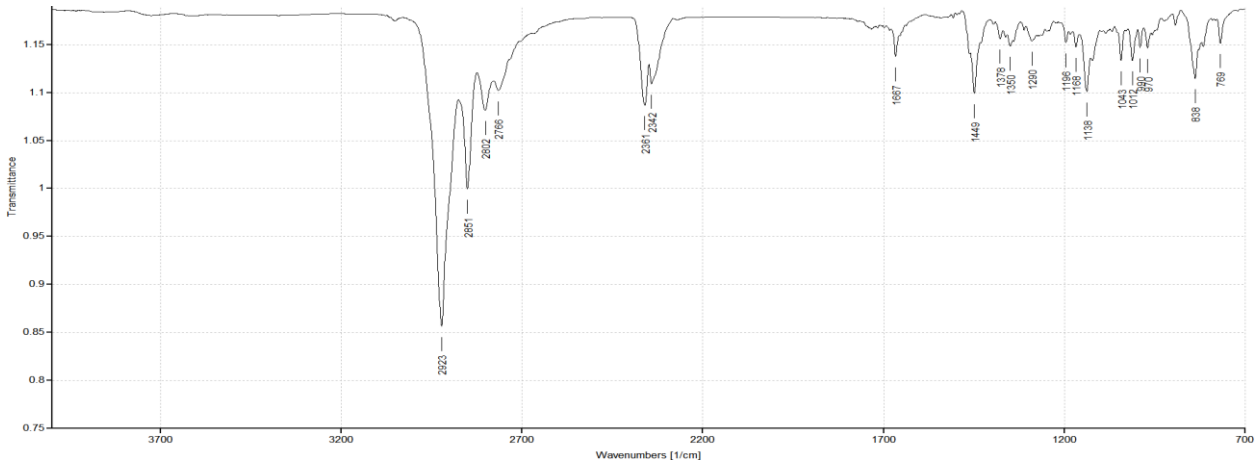
Pale yellow oil. R_f 0.2 [EtOAc/petroleum ether 5%, I_2, anisaldehyde (white spot), not UV-active]. IR (neat) *v* 2923 (s), 2851 (m), 2802 (w), 2766 (w), 2361 (w), 2342 (w), 1667 (w), 1449 (w), 1138 (w), 838 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 0.87 (2 H, dt, *J* 12.0, 11.5, H8a), 1.12−1.31 (1 H, m, H10a), 1.20 (2 H, m, H9a), 1.50 (1 H, ttt, *J* 11.5, 7.0, 3.5, H7), 1.63−1.82 (1 H, m, H10b), 1.69 (2 H, m, H9b), 1.78 (2 H, br d, *J* 12.0, H8b), 2.18−2.26 (2 H, m, H2), 2.24 (2 H, d, *J* 7.0, H6), 2.52 (2 H, t, *J* 5.5, H1), 3.05 (2 H, br s, H5), 5.83 (1 H, br s, H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 26.1 (C9), 26.2 (C2), 26.8 (C10), 31.8 (C8), 35.3 (C7), 49.1 (C1), 58.1 (C5), 64.5 (C6), 122.6 (C3), 129.0 (C4). MS (positive CI, NH_3): *m/z* 131, <u>214</u> (MH^+ with ^{35}Cl), 215, 216 (MH^+ with ^{37}Cl), 217, 228. MS (EI): *m/z* 105, 116, 118, <u>130</u>, 132, 149, 170, 211, 213 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 213.1288 ($M^{+\bullet}$ $C_{12}H_{20}{}^{35}ClN^{+\bullet}$ requires 213.1279).



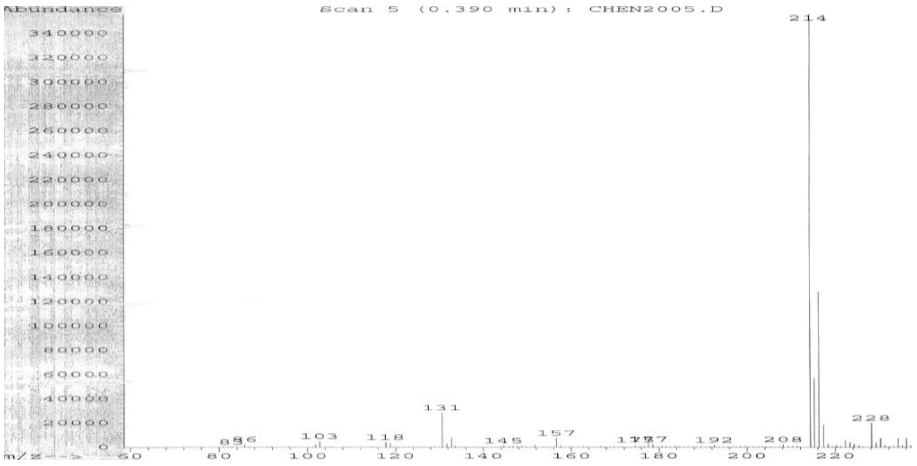
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



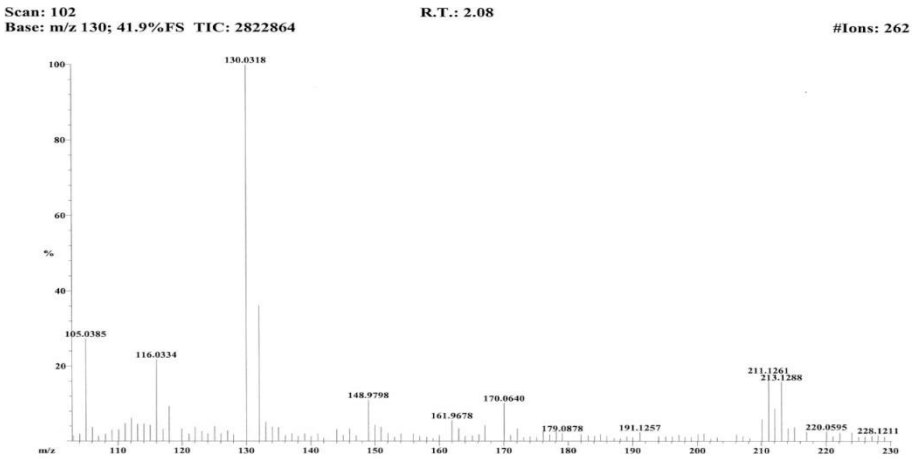
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

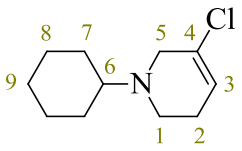


MS spectrum (CI, NH_3).

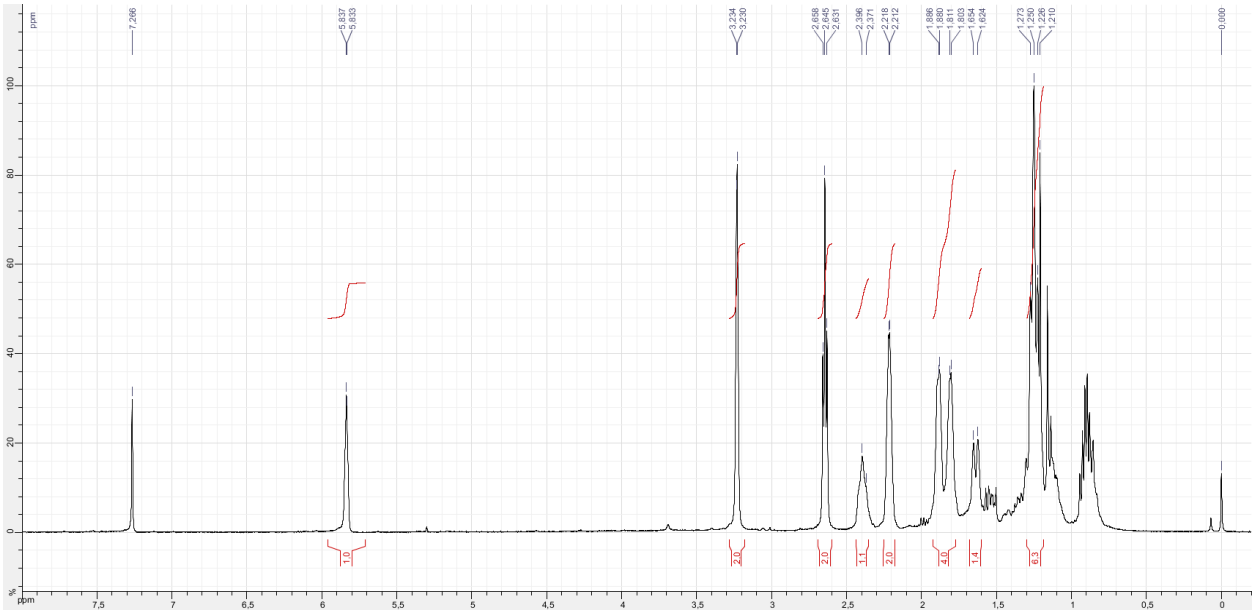


MS spectrum (EI).

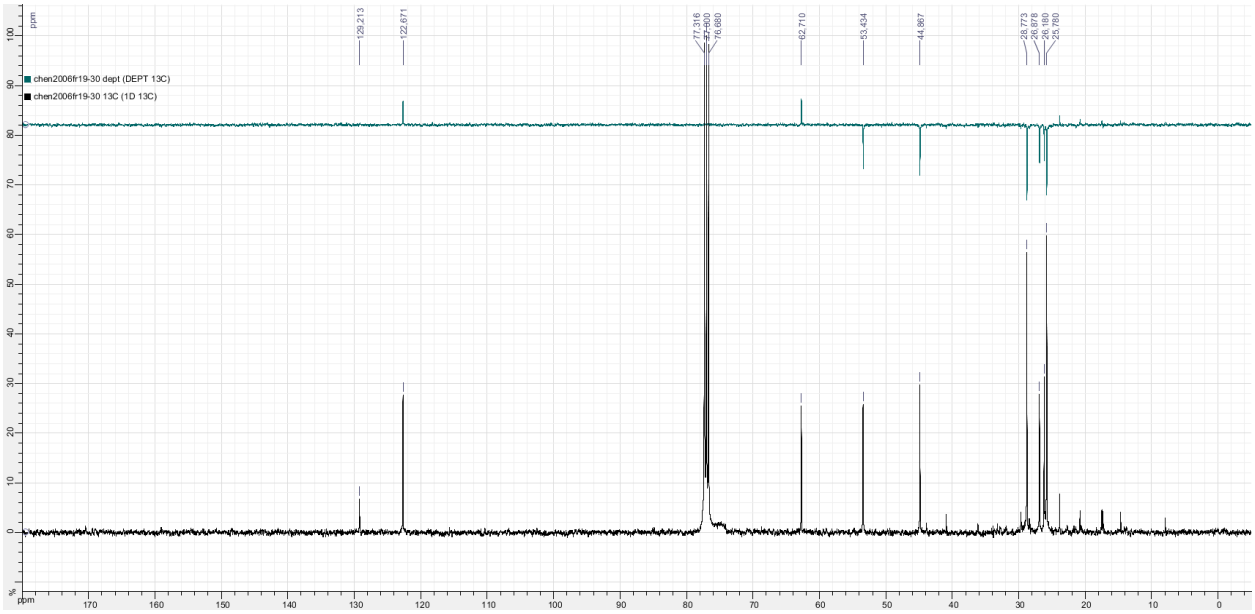
5-Chloro-1-cyclohexyl-3,6-dihydro-2*H*-pyridine **5ae**



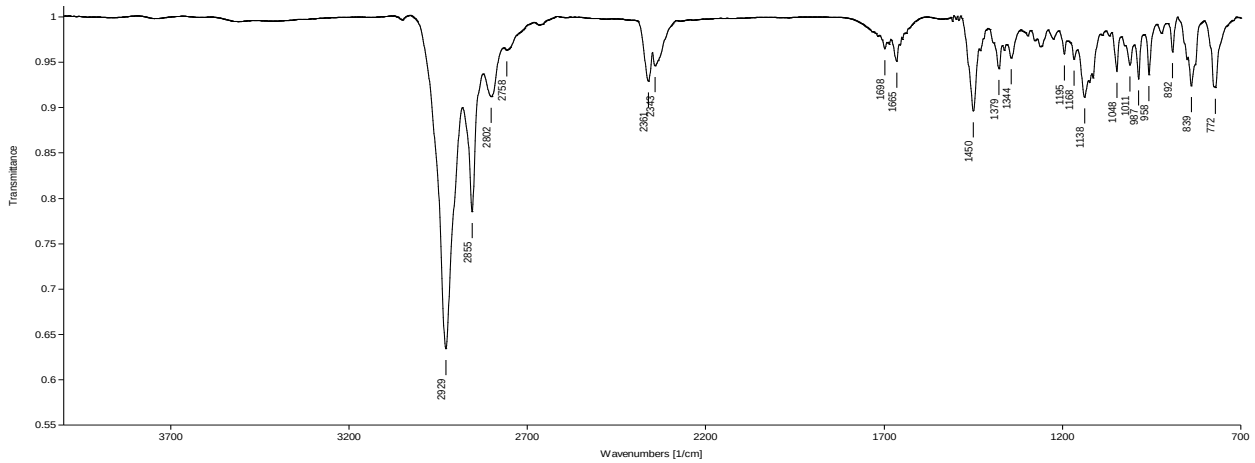
Pale yellow oil. R_f 0.15 [EtOAc/petroleum ether 10%, I_2, anisaldehyde (pink spot), not UV-active]. IR (neat) *v* 2929 (s), 2855 (m), 2802 (w), 2361 (w), 2343 (w), 1665 (w), 1450 (m), 1379 (w), 1138 (w), 987 (w), 958 (w), 839 (w), 772 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.18−1.30 (1 H, m, H9a), 1.24 (2 H, m, H7a), 1.25 (2 H, m, H8a), 1.64 (1 H, br d, *J* 12.0, H9b), 1.81 (2 H, m, H8b), 1.89 (2 H, m, H7b), 2.22 (2 H, tdt, *J* 5.5, 4.0, 2.5, H2), 2.40 (1 H, m, H6), 2.64 (2 H, t, *J* 5.5, H1), 3.23 (2 H, td, *J* 2.5, 2.0, H5), 5.84 (1 H, tt, *J* 4.0, 2.0, H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 25.8 (C8), 26.2 (C9), 26.7 (C2), 28.8 (C7), 44.9 (C1), 53.4 (C5), 62.7 (C6), 122.7 (C3), 129.2 (C4). MS (positive CI, NH_3): *m/z* 157, <u>200</u> (MH^+ with ^{35}Cl), 201, 202 (MH^+ with ^{37}Cl), 204. MS (EI): *m/z* 130, 132, <u>156</u>, 158, 170, 199 ($M^{+\bullet}$ with ^{35}Cl), 201 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 199.1134 ($M^{+\bullet}$ $C_{11}H_{18}{}^{35}ClN^{+\bullet}$ requires 199.1123).



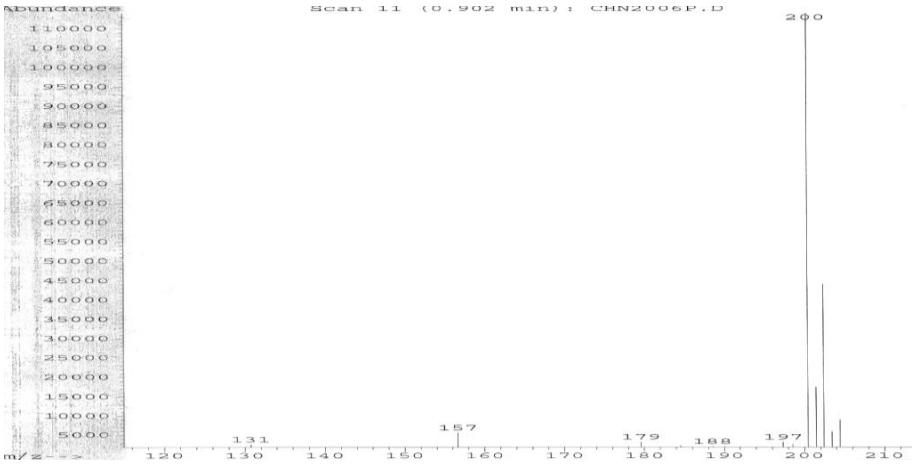
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



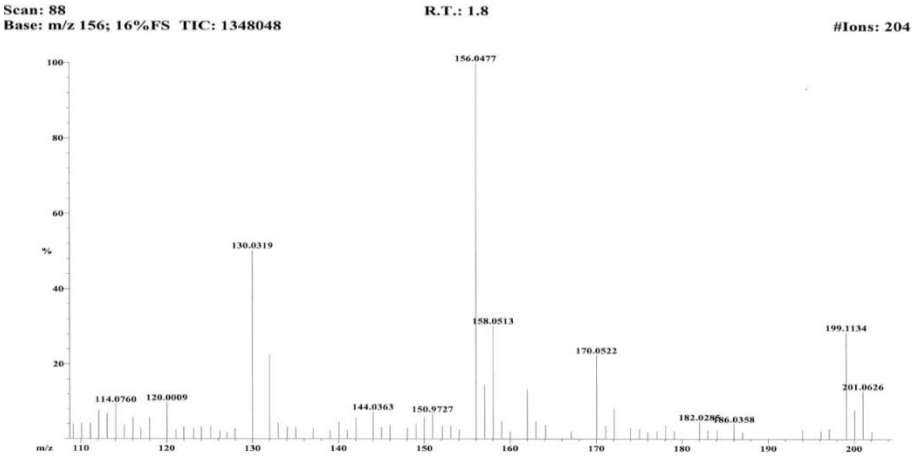
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

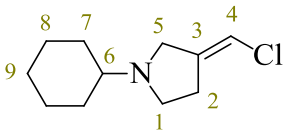


MS spectrum (CI, NH_3).



MS spectrum (EI).

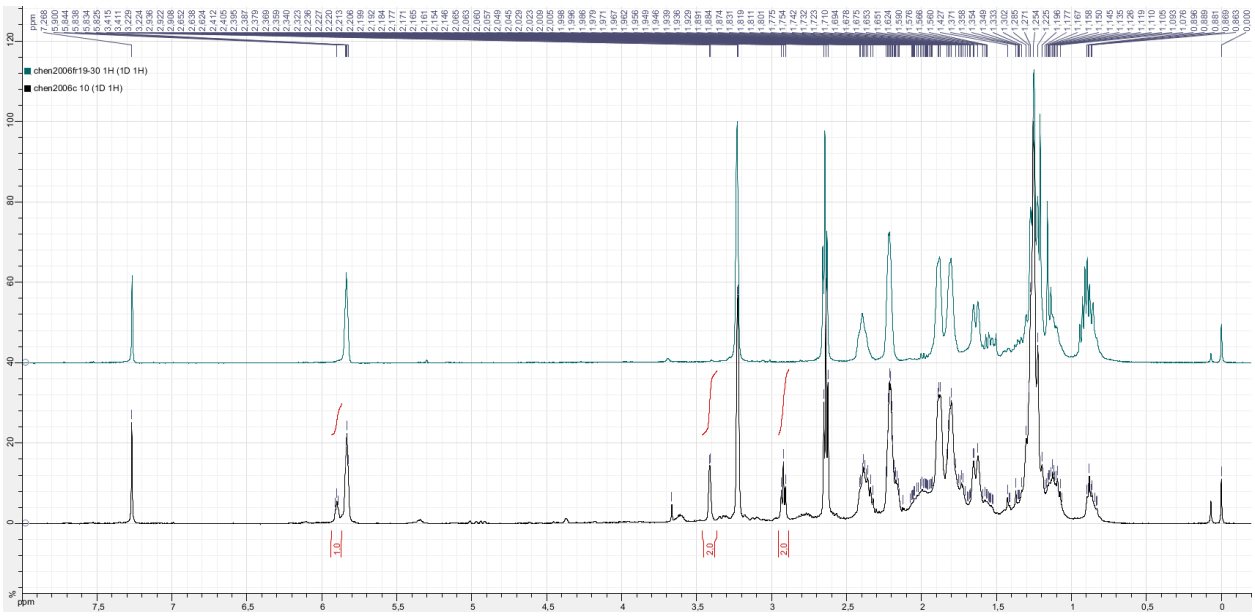
(*E*)-3-(Chloromethylene)-1-cyclohexyl-pyrrolidine **7ae** (tentative structure)[13]



^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: δ 2.92 (2 H, t, *J* 6.0, H1), 3.41 (2 H, td, *J* 2.5, 1.5, H5), 5.90 (1 H, tt, *J* 4.0, 1.5, H5).

Note: this compound was observed in a crude product but was not isolated.

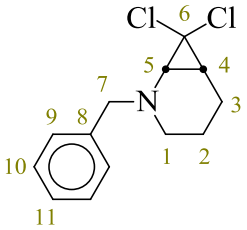
13− This proposed structure is consistent with the by-products observed starting from other compounds in the series. Moreover, the NMR chemical shifts observed for the pyrrolidine protons α to the nitrogen atom are very close to those reported for a derivative where the chlorine atom is replaced with a hydrogen atom: M. Déry, K. Assouvie, N. Heinrich, I. Rajotte, L.-P. D. Lefebvre, M.-A. Legault, C. Spino, *Org. Lett.* **2015**, *17*, 1312–1315 (supporting information).



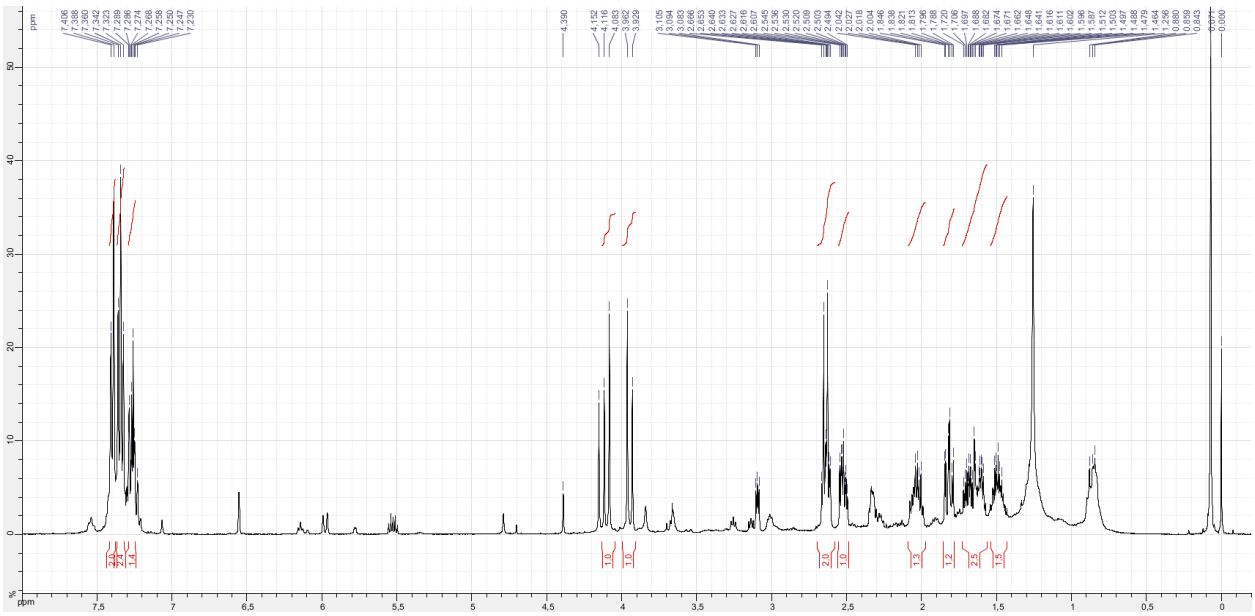
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product containing 5-chloro-1-cyclohexyl-3,6-dihydro-2*H*-pyridine **5ae** as the major component. Signals that are thought to belong to **7ae** have been integrated and a spectrum of pure **5ae** is shown in green.

2-Benzyl-7,7-dichloro-2-azabicyclo[4.1.0]heptane **4ba**

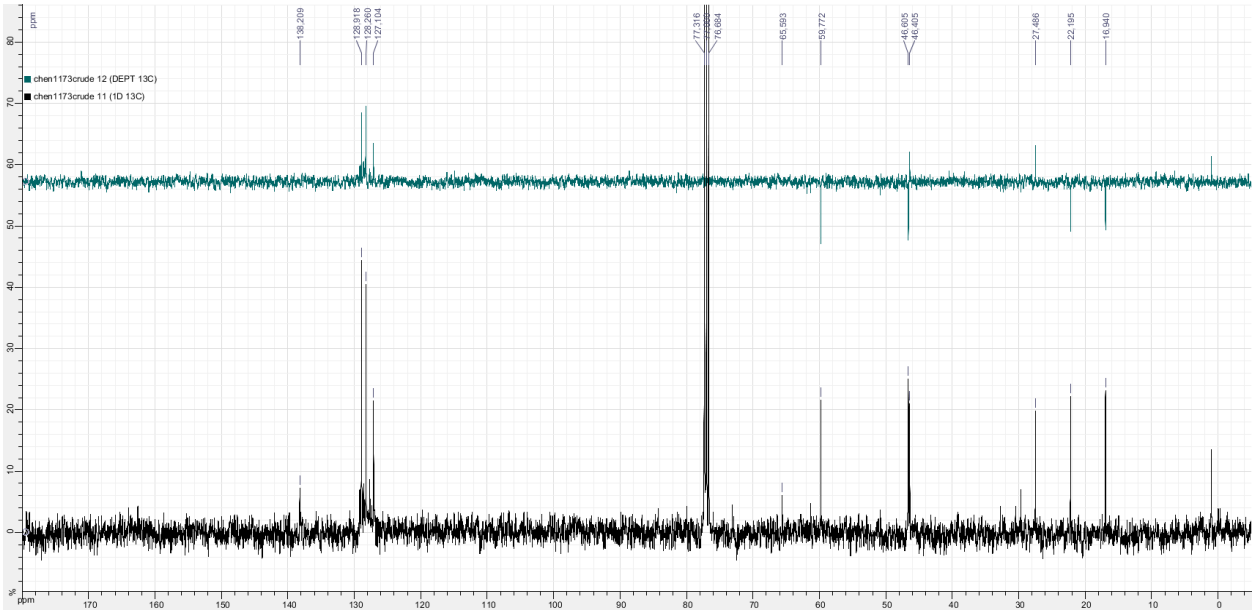


^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.49 (1 H, m, H2a), 1.60 (1 H, m, H2b), 1.68 (1 H, dddd, *J* 14.5, 9.5, 5.5, 3.5, H3a), 1.82 (1 H, ddd, *J* 10.5, 9.5, 3.5, H4), 2.03 (1 H, ddt, *J* 14.5, 9.5, 5.5, H3b), 2.52 (1 H, ddd, *J* 10.5, 6.0, 4.0, H1a), 2.64 (1 H, ddd, *J* 10.5, 9.5, 3.5, H1b), 2.64 (1 H, d, *J* 10.5, H5), 4.02 (2 H, AB system, δ_A 3.95, δ_B 4.10, J_{AB} 13.5, H7), 7.27 (1 H, br t, *J* 7.0, H11), 7.34 (2 H, dd, *J* 7.5, 7.0, H10), 7.40 (2 H, br d, *J* 7.5, H9). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 16.9 (C3), 22.2 (C2), 27.5 (C4), 46.4 (C5), 46.6 (C1), 59.8 (C7), 65.6 (C6), 127.1 (C11), 128.3 (C10), 128.9 (C9), 138.2 (C8).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

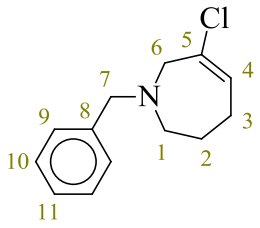
Note: this is the spectrum of a crude product containing 2-benzyl-7,7-dichloro-2-azabicyclo[4.1.0]heptane **4ba** as the major component. Signals that are thought to belong to this compound have been integrated.



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

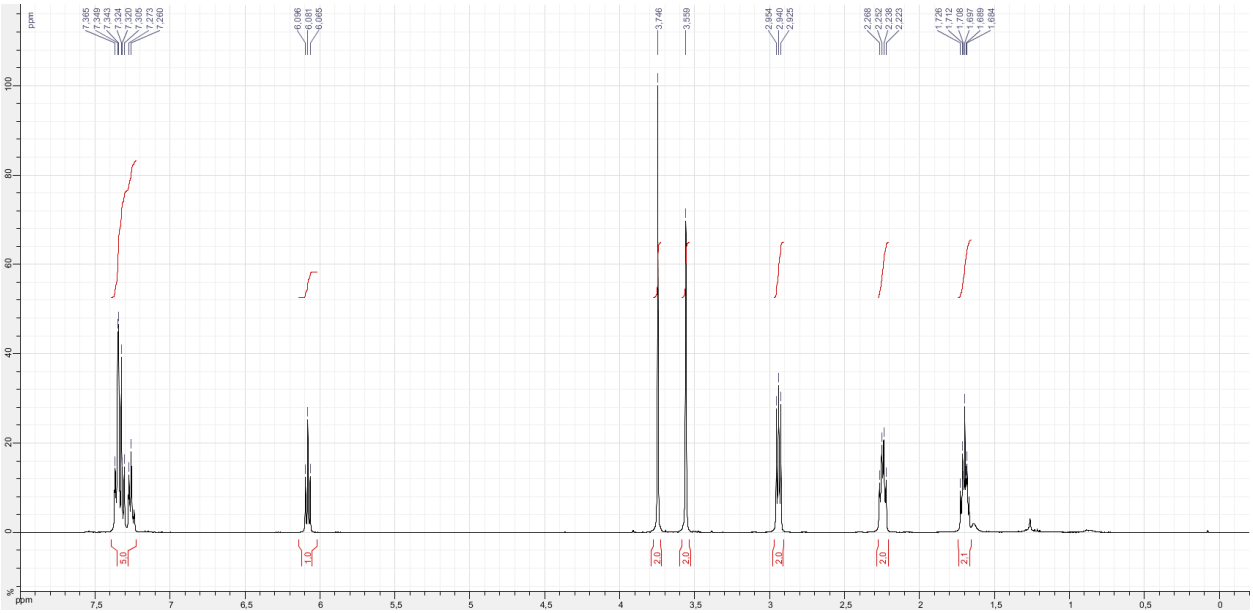
Note: this is the spectrum of a crude product containing **4ba** as the major component.

1-Benzyl-6-chloro-2,3,4,7-tetrahydroazepine **5ba**

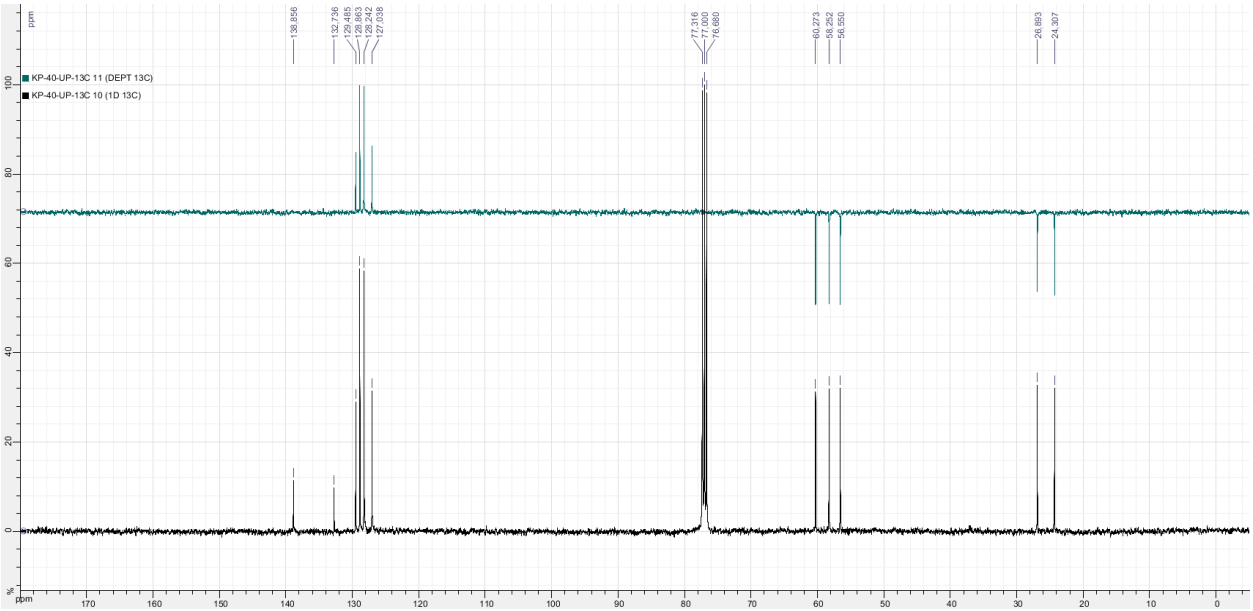


Pale yellow oil. R_f 0.3 [EtOAc/petroleum ether 10%, anisaldehyde (white spot), UV-active]. IR (neat) ν 3063 (w), 3029 (w), 2930 (s), 2839 (m), 2810 (m), 1642 (w), 1494 (m), 1453 (m), 1436 (m), 1361 (w), 1118 (m), 1028 (w), 1015 (w), 969 (w), 951 (w), 822 (w), 757 (m), 733 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.70 (2 H, tt, J 6.0, 5.5, H2), 2.24 (2 H, dtt, J 6.5, 5.5, 1.0, H3),

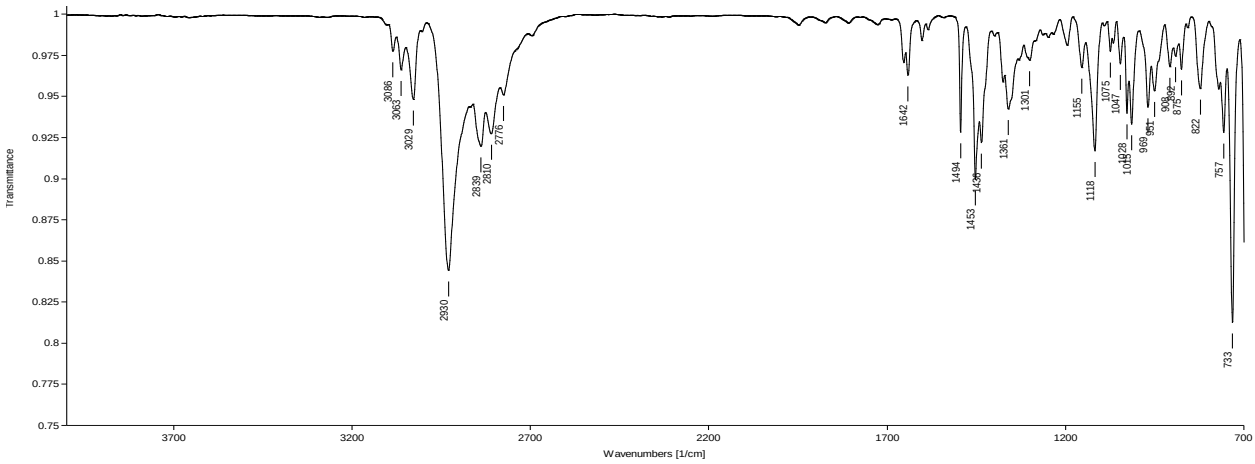
2.94 (2 H, t, *J* 6.0, H1), 3.56 (2 H, t, *J* 1.0, H6), 3.75 (2 H, s, H7), 6.08 (1 H, t, *J* 6.5, H4), 7.26 (1 H, disorted tt, *J* 7.0, 1.5, H11), 7.29−7.38 (4 H, m, H9−H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz): *δ* 24.2 (C2), 26.9 (C3), 56.5 (C1), 58.2, 60.2 (C6, C7), 127.1 (C11), 128.3, 128.9 (C9, C10), 129.6 (C4), 132.6 (C5), 138.7 (C8). MS (positive CI, NH_3): *m/z* 121, 147, 176, 177, 178, 222 (MH^+ with ^{35}Cl), 223, 224 (MH^+ with ^{37}Cl). MS (EI): *m/z* 91 (Bn^+), 92, 120, 121, 130, 186 ($[M-Cl]^+$), 220, 221 ($M^{+\bullet}$ with ^{35}Cl), 222, 223 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 221.0977 ($M^{+\bullet}$ $C_{13}H_{16}{}^{35}ClN^{+\bullet}$ requires 221.0966).



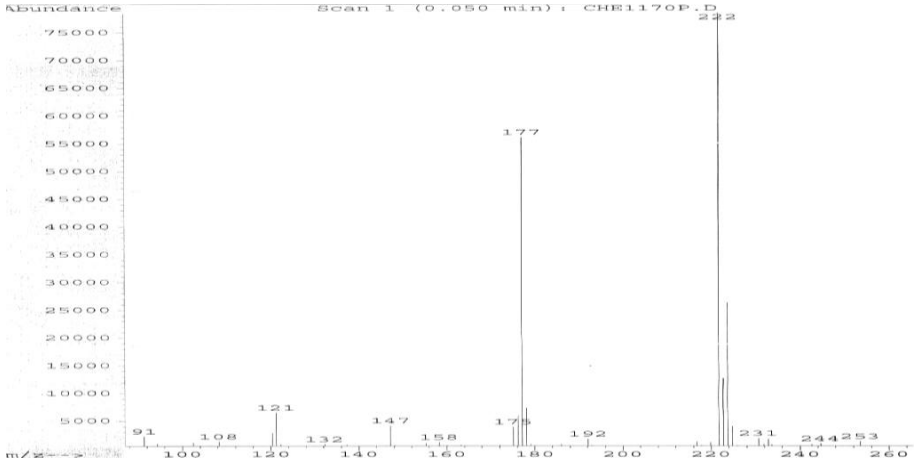
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



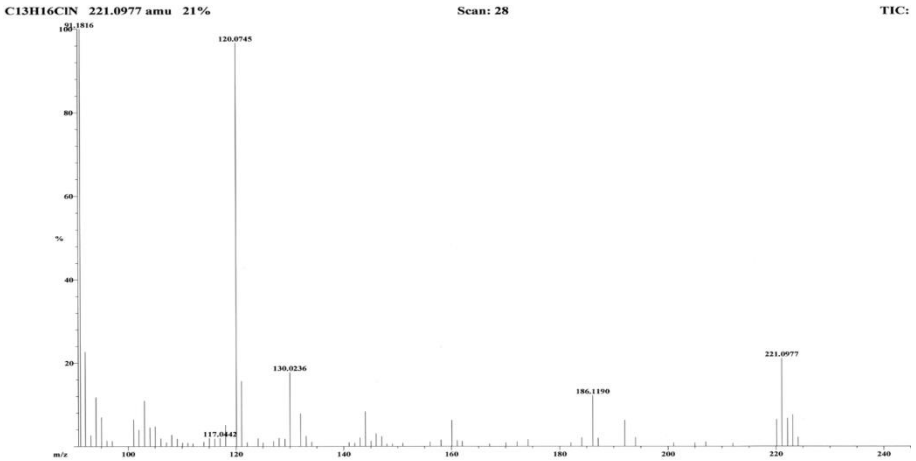
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

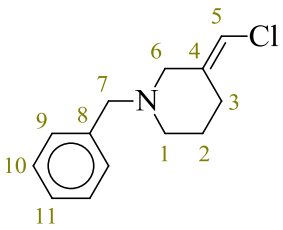


MS spectrum (CI, NH_3).

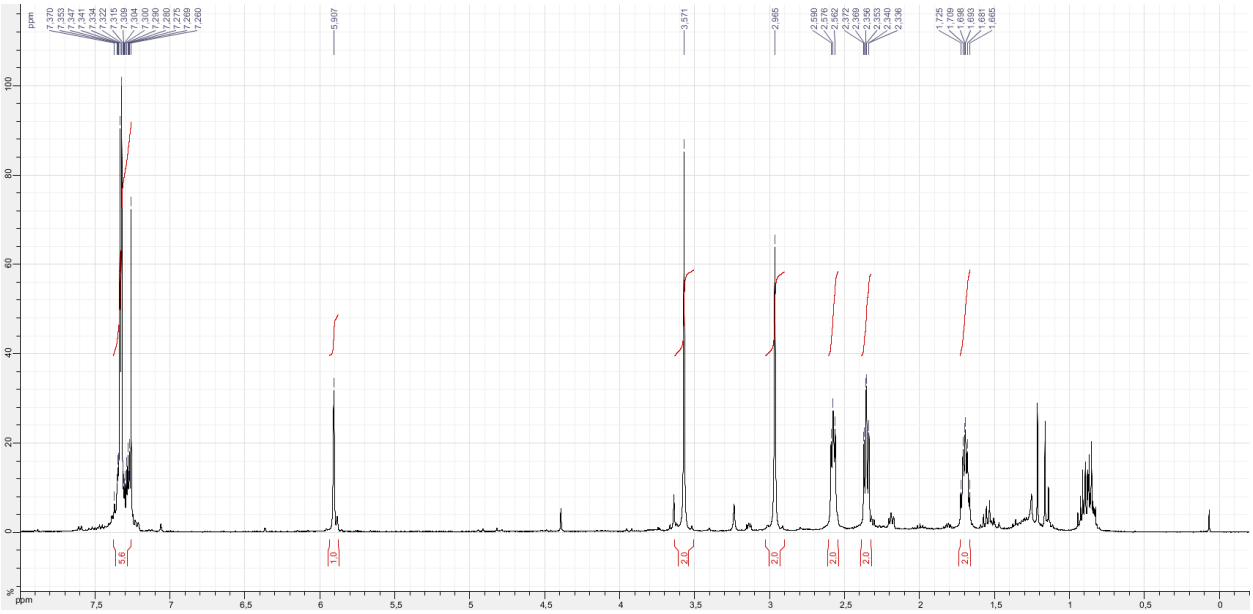


MS spectrum (EI).

(*E*)-1-Benzyl-3-(chloromethylene)piperidine (*E*)-**7ba**[14]

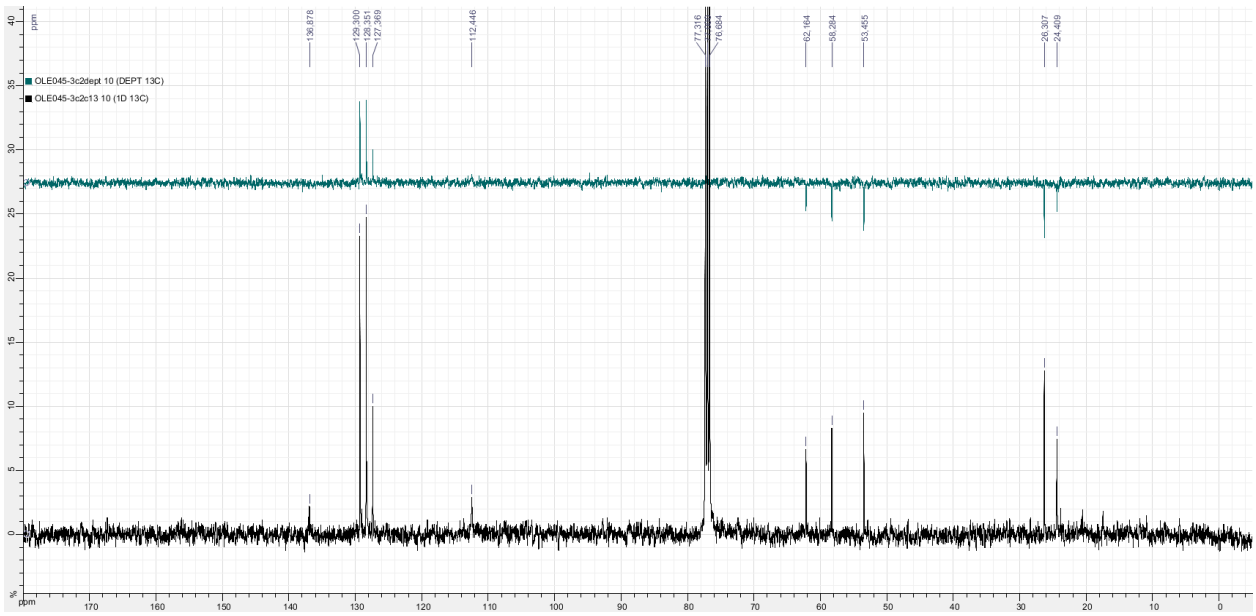


Colourless oil. R_f 0.25 [EtOAc/petroleum ether 10%, $KMnO_4$]. IR (neat): *v* 3555 (w), 2961 (s), 2931 (s), 2874 (m), 2857 (m), 2799 (w), 2752 (w), 1613 (s), 1455 (m), 1366 (m), 1353 (m), 1341 (m), 1312 (m), 1308 (m), 1177 (m), 1138 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.69 (2 H, tt, J 6.5, 5.5, H2), 2.35 (2 H, td, *J* 6.5, 1.0, H3), 2.58 (2 H, t, *J* 5.5, H1), 2.96 (2 H, s, H6), 3.57 (2 H, s, H7), 5.91 (1 H, t, *J* 1.0, H5), 7.26−7.38 (5 H, m, H9−H11). Noesy spectrum: H5 ↔ H6 clearly visible. ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 24.4 (C2), 26.3 (C3), 53.5 (C1), 58.3 (C7), 62.2 (C6), 112.4 (br s, C5), 127.4 (C11), 128.4, 129.3 (C9, C10), 136.9, 136.9 (C4, C8). MS (EI): *m/z* 130, 132, 144, 172, 186 ([M−Cl]$^+$), 187, 201, 220 ([M−H]$^+$ with ^{35}Cl), 221 ($M^{+\bullet}$ with ^{35}Cl), 222 ([M−H]$^+$ with ^{37}Cl), 223 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 221.0975 ($M^{+\bullet}$ $C_{13}H_{16}{}^{35}ClN^{+\bullet}$ requires 221.0966).

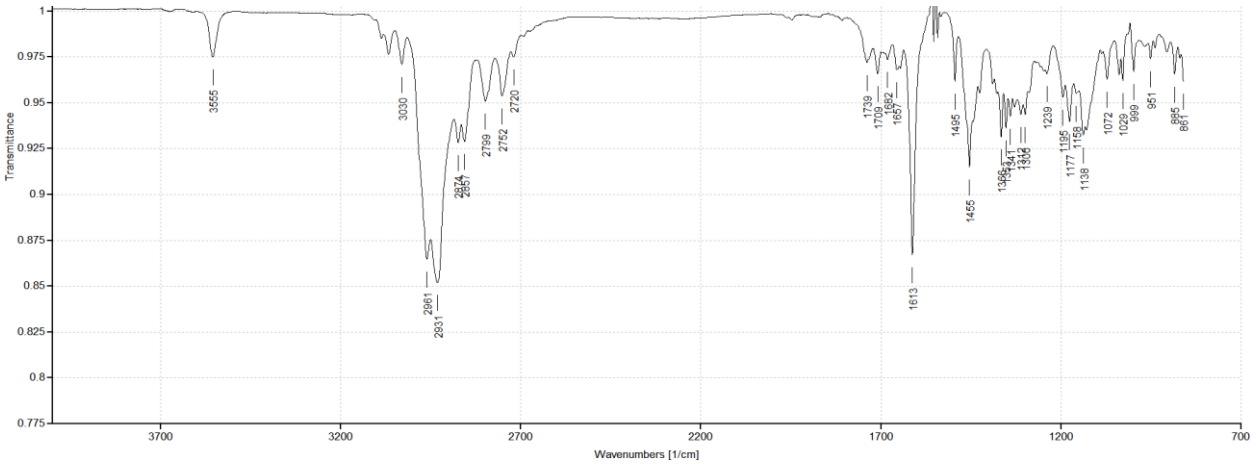


^1H NMR spectrum ($CDCl_3$, 400 MHz).

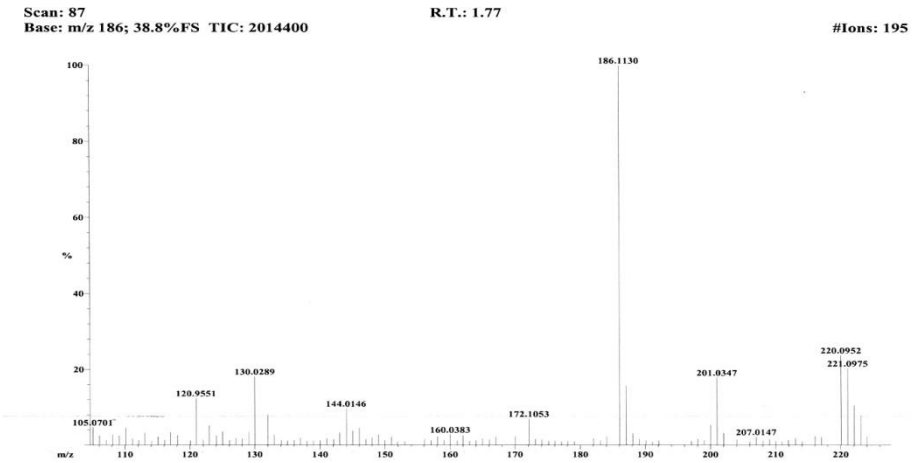
14− Another preparation of this compound is described in the literature; however, no characterisation data is provided: M. Yoshinori, L. E. Overman, *Heterocycles* **1996**, *42*, 549–552.



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

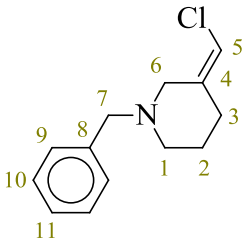


IR spectrum.

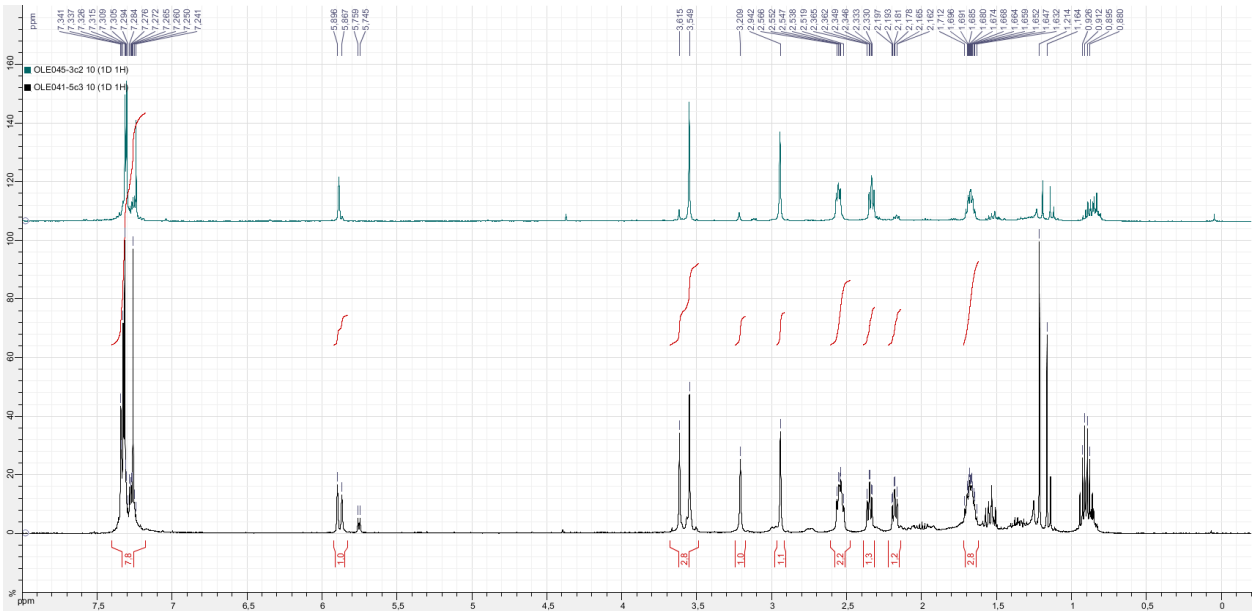


MS spectrum (EI).

(*Z*)-1-Benzyl-3-(chloromethylene)piperidine (*Z*)-**7ba** [15]

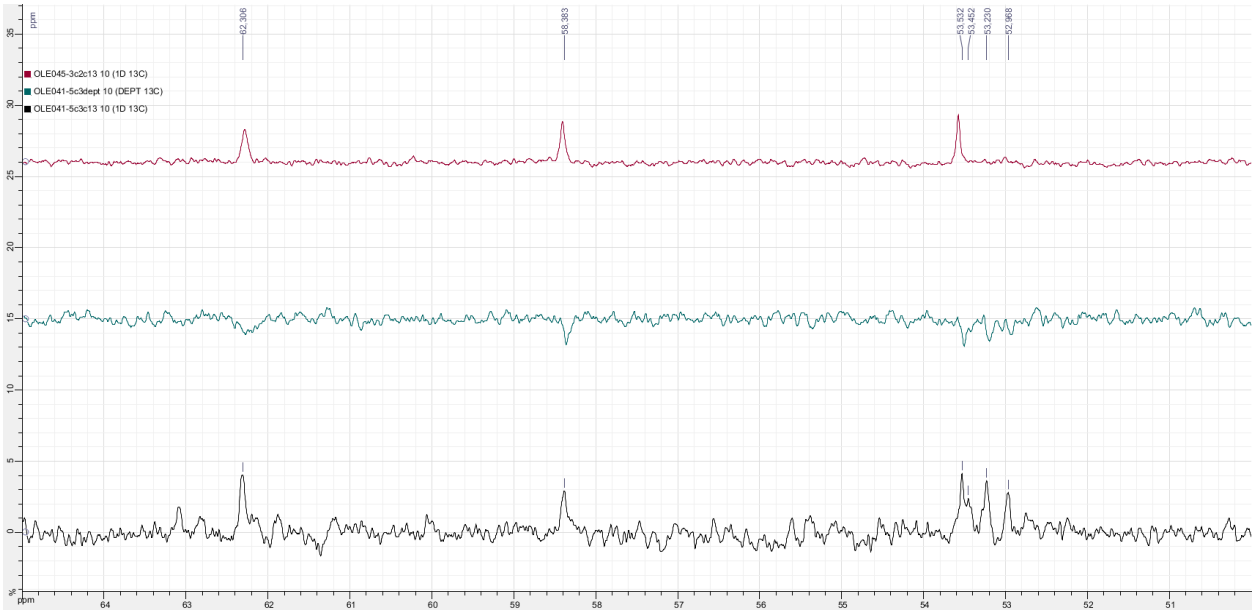


^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.66 (2 H, tt, J 6.5, 5.5, H2), 2.18 (2 H, td, *J* 6.5, 1.0, H3), 2.53 (2 H, t, *J* 5.5, H1), 3.21 (2 H, s, H6), 3.61 (2 H, s, H7), 5.87 (1 H, t, *J* 1.0, H5), 7.26−7.38 (5 H, m, H9−H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz), characteristic signals: δ 31.6 (C3), 53.0, 53.2, 53.5 (C1, C6, C7).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

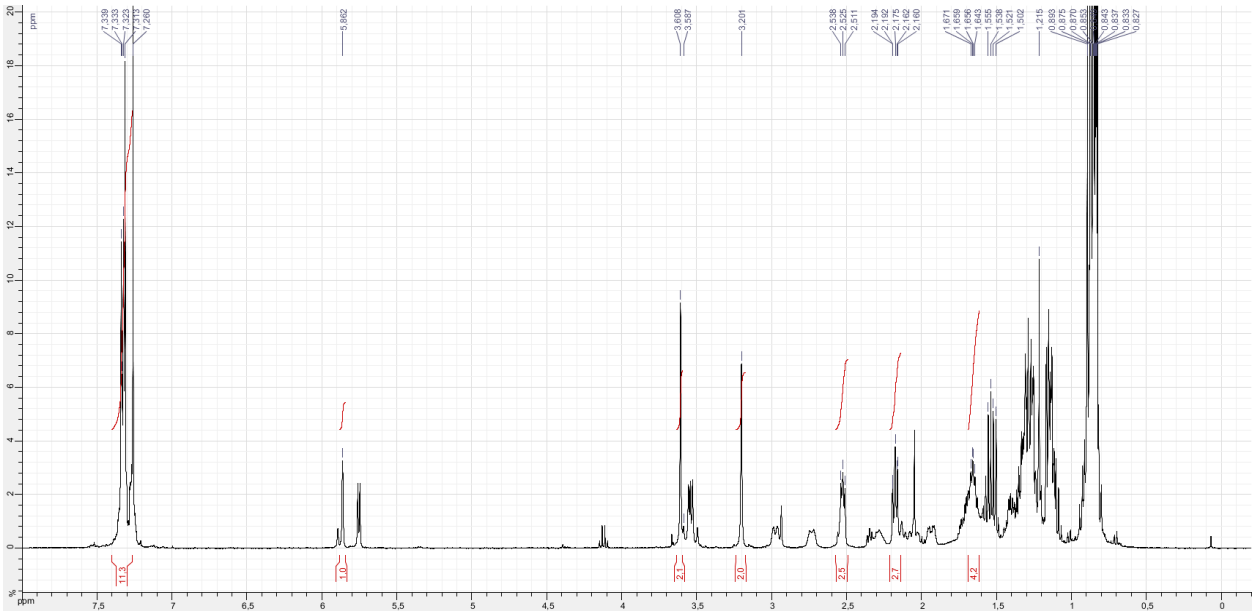
Note: this is the spectrum of a sample containing a 53 : 47 mixture of the (*E*) and (*Z*) isomers. The spectrum of the pure (*E*) isomer is displayed at the top, in green.



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

15− This compound was not obtained in pure form.

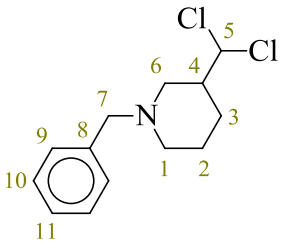
Note: this is a part of the spectrum of a sample containing a 53 : 47 mixture of the (*E*) and (*Z*) isomers. The spectrum of the pure (*E*) isomer is displayed at the top, in red.



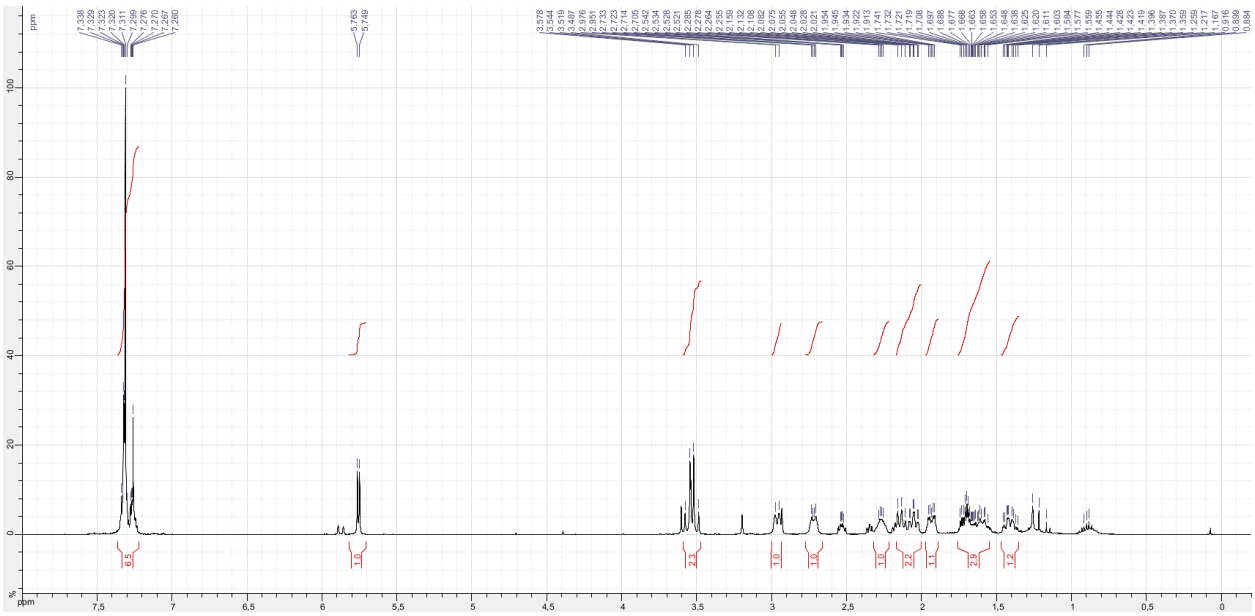
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a sample containing a ≈ 50 : 50 mixture of (*Z*)-1-benzyl-3-(chloromethylene)piperidine (*Z*)-**7ba** and 1-benzyl-3-(dichloromethyl)piperidine **16ba**.

1-Benzyl-3-(dichloromethyl)piperidine **16ba**[15]

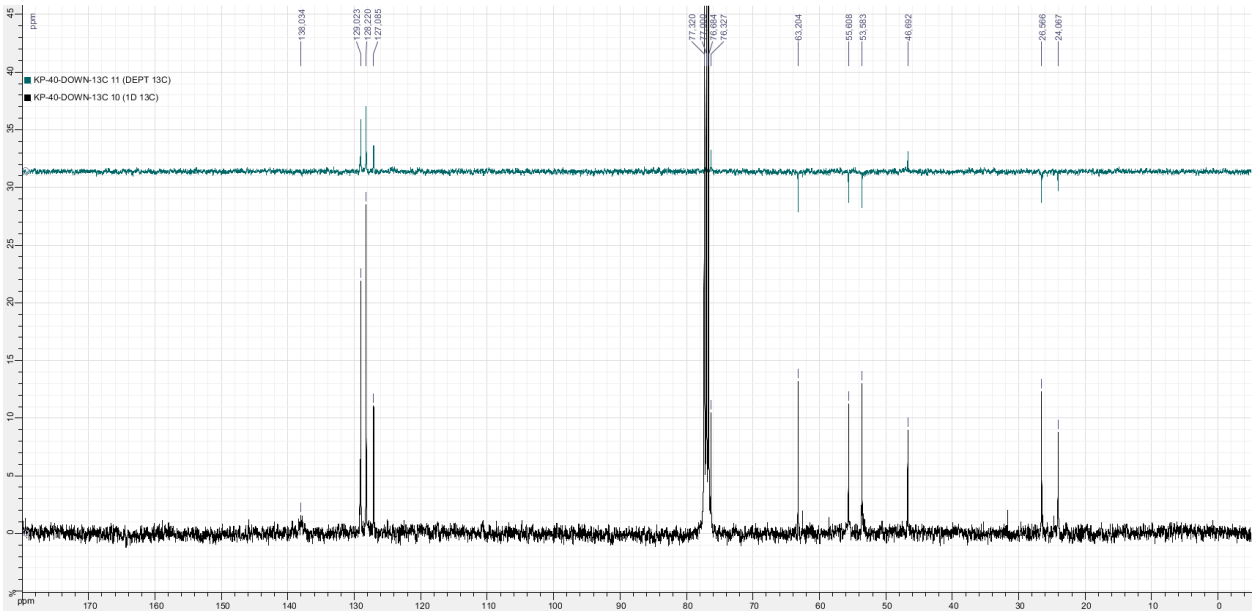


Colourless oil. R_f 0.2 [EtOAc/petroleum ether 10%, $KMnO_4$, not UV-active]. IR (neat) ν 3028 (w), 2939 (m), 2802 (m), 2770 (m), 1608 (w), 1494 (w), 1454 (m), 1352 (w), 1297 (w), 1104 (w), 1072 (w), 1028 (w), 794 (w), 752 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.41 (1 H, dddd, *J* 13.0, 11.0, 10.0, 4.5, H3a), 1.55−1.76 (2 H, m, H2), 1.93 (1 H, dq, *J* 13.0, 3.8, H3b), 2.04 (1 H, ddd, *J* 11.0, 10.5, 3.0, H1a), 2.13 (1 H, dd, *J* 10.5, 9.0, H6a), 2.27 (1 H, m, H4), 2.72 (1 H, br d, *J* 11.0, H1b), 2.96 (1 H, br d, *J* 10.5, H6b), 3.53 (2 H, AB system, δ_A 3.51, δ_B 3.56, J_{AB} 13.5, H7), 5.68 (1 H, d, *J* 5.5, H5), 7.22−7.36 (5 H, m, H9−H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 24.1 (C2), 26.6 (C3), 46.7 (C4), 53.6 (C1), 55.6 (C6), 63.2 (C7), 76.3 (C5), 127.1 (C11), 128.2 (C9), 129.0 (C10), 138.0 (C8). MS (EI) *m/z* 90, 91, 130, 186, 220, 222 ($[M-Cl]^+$ with ^{35}Cl), 223, 224 ($[M-Cl]^+$ with ^{37}Cl), 225, 257 ($M^{+\bullet}$ with two ^{35}Cl), 259 ($M^{+\bullet}$ with one ^{35}Cl and one ^{37}Cl), 260, 261 ($M^{+\bullet}$ with two ^{37}Cl). HRMS *m/z* (EI) 257.0742 ($M^{+\bullet}$ $C_{13}H_{17}{}^{35}Cl_2N^{+\bullet}$ requires 257.0733).



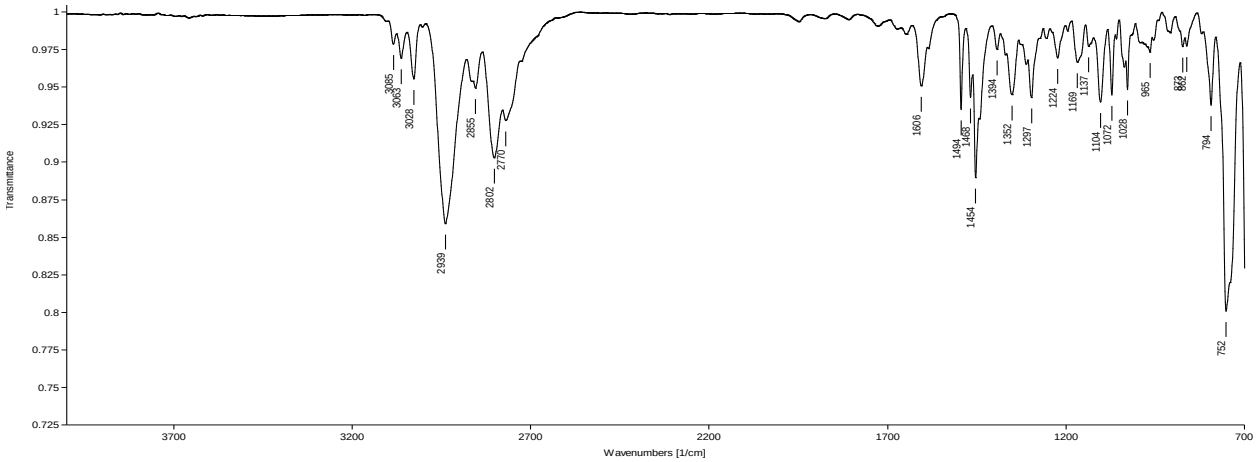
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a sample containing minor amounts of (*E*)- and (Z)-**7ba**.



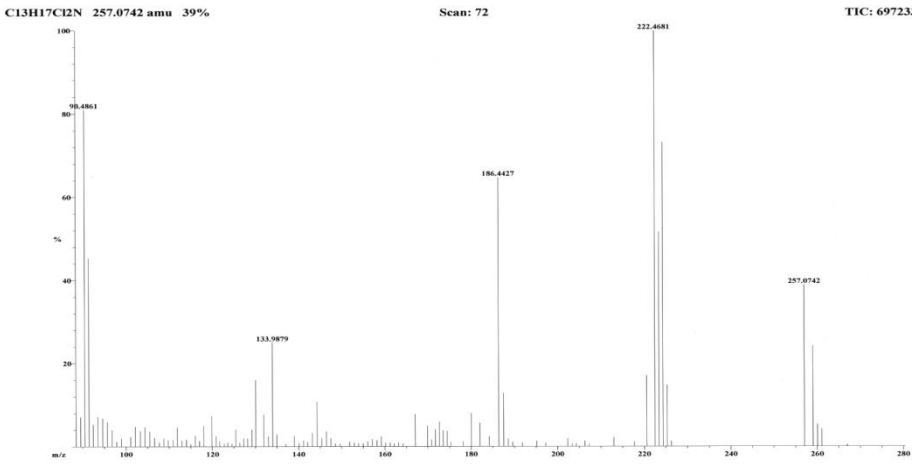
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

Note: these are spectra of a sample containing minor amounts of (*E*)- and (Z)-**7ba**.



IR spectrum.

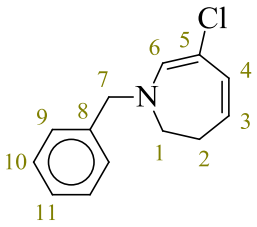
Note: this is the spectrum of a sample containing minor amounts of (*E*)- and (Z)- **7ba**.



MS spectrum (EI).

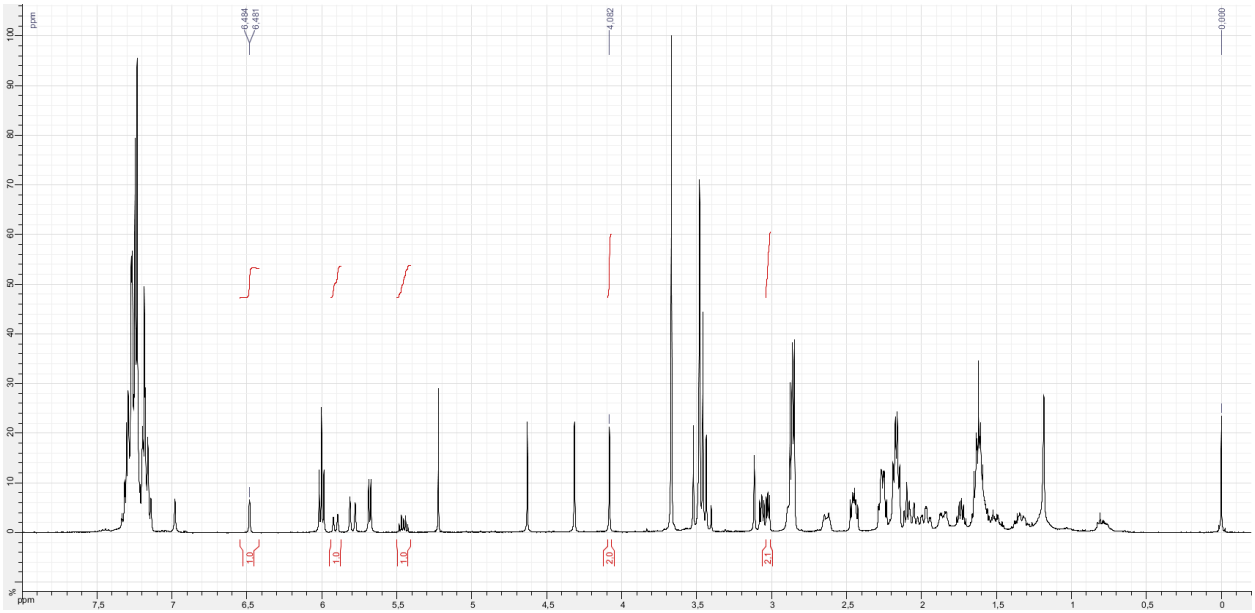
Note: this is the spectrum of a sample containing minor amounts of (*E*)- and (Z)- **7ba**.

1-Benzyl-6-chloro-2,3-dihydroazepine **17ba**
(tentative structure)



^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: δ 3.02 (1 H, distorted t, *J* 4.0, H1), 4.08 (2 H, s, H7), 5.46 (1 H, dt, *J* 11.5, 6.0, H3), 5.91 (1 H, dtd, *J* 11.5, 1.5, 1.0, H4), 6.48 (1 H, d, *J* 1.0, H6).

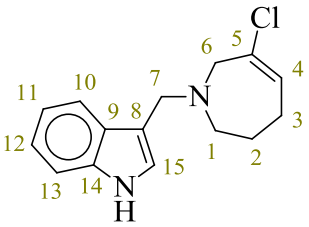
Note: this molecule was observed in crude products containing it as a minor component.
It was not isolated.



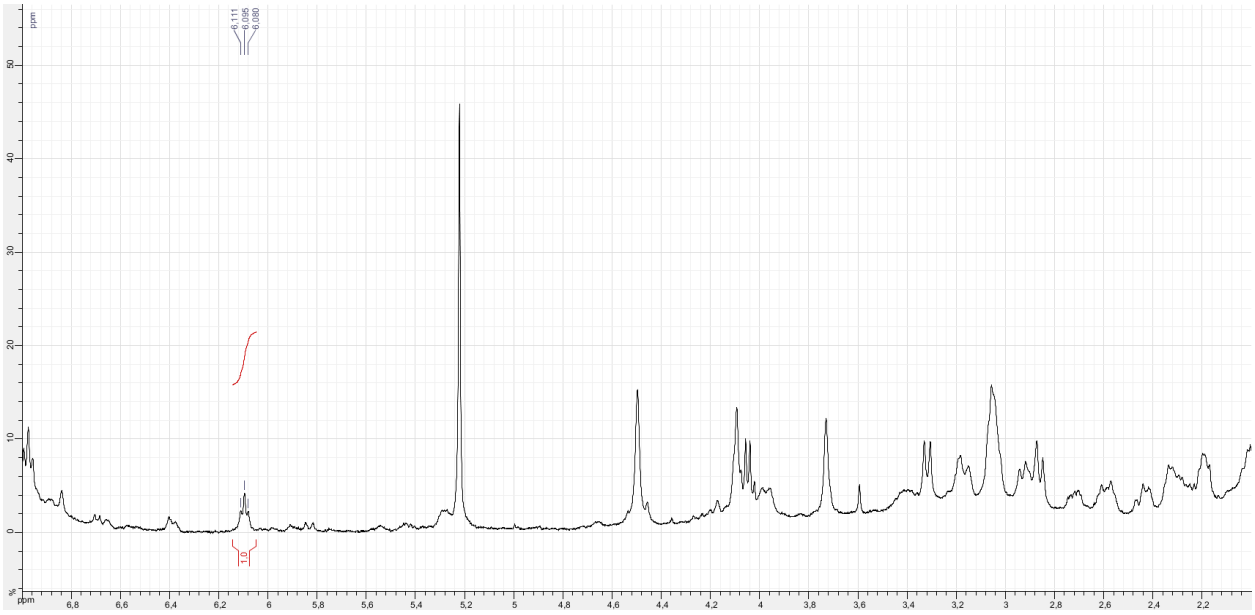
^{1}H NMR spectrum of ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product. Signals that are thought to belong to **17ba** have been integrated.

3-[(6-Chloro-2,3,4,7-tetrahydroazepin-1-yl)methyl]-1*H*-indole **5bc**



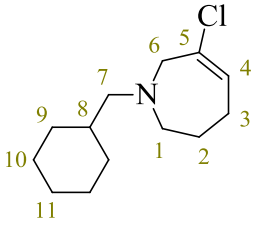
^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signal: δ 6.09 (1 H, t, *J* 6.0, H4).



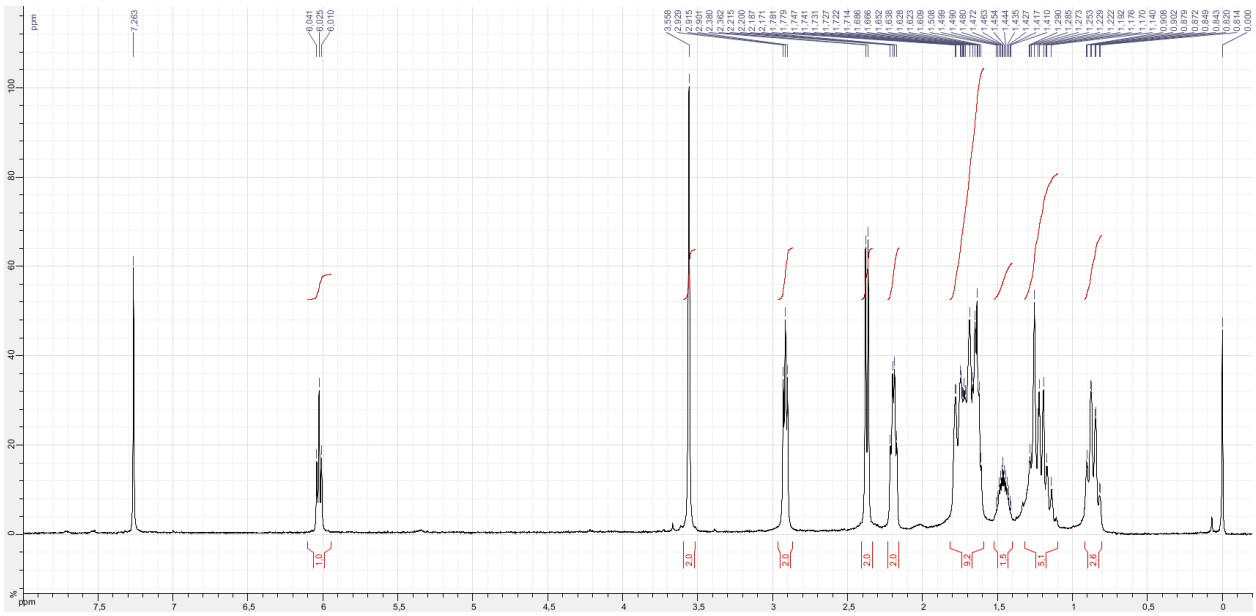
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is part of the spectrum of a crude product, showing an expected characteristic signal of **5bc** (integrated).

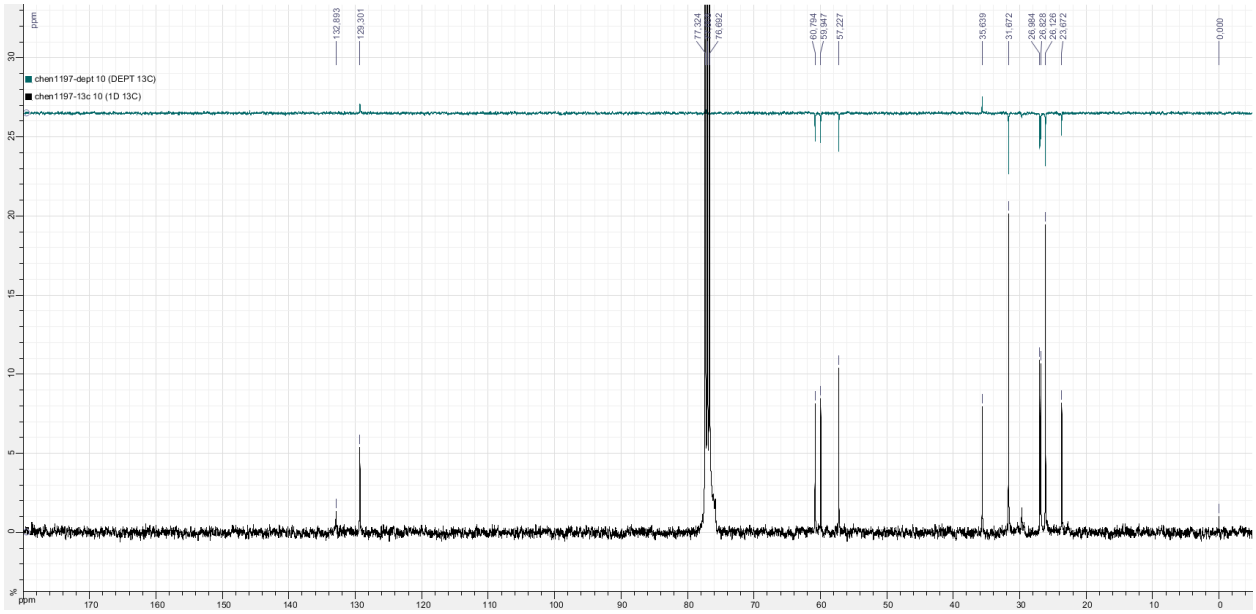
6-Chloro-1-(cyclohexylmethyl)-2,3,4,7-tetrahydroazepine **5bd**



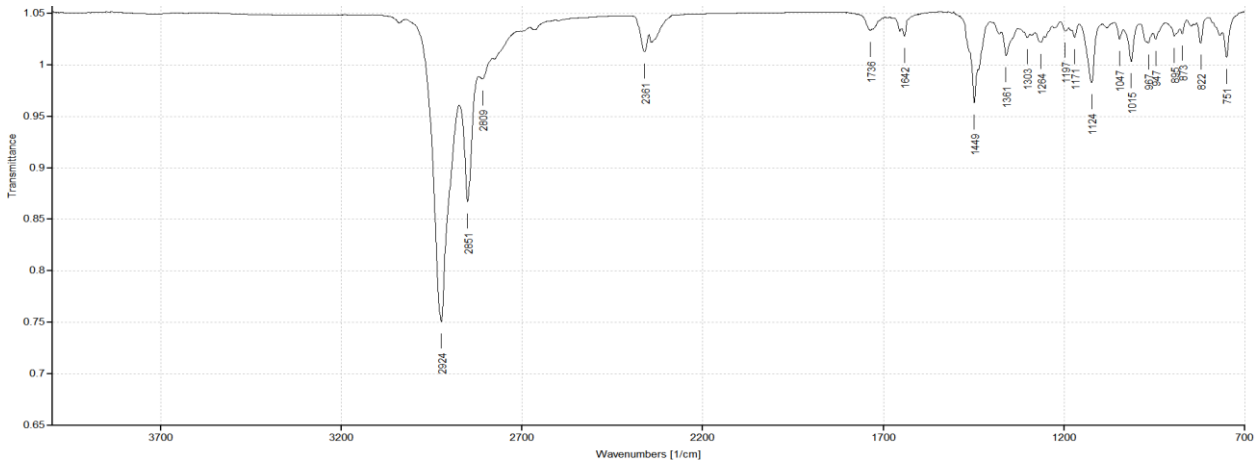
Pale yellow oil. R_f 0.35 [EtOAc/petroleum ether 5%, I_2, UV-active]. IR (neat) ν 2924 (s), 2851 (m), 2809 (w), 2361 (w), 1449 (m), 1360 (w), 1361 (w), 1124 (w), 1015 (w), 751 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.86 (2 H, dtd, *J* 12.0, 11.5, 2.5, H9a), 1.09−1.29 (1 H, m, H11a), 1.21 (2 H, m, H10a), 1.46 (1 H, ttt, *J* 11.5, 7.0, 3.5, H8), 1.60−1.75 (1 H, m, H11b), 1.64 (2 H, quint, *J* 5.5, H2), 1.69 (2 H, m, H10b), 1.77 (2 H, br d, *J* 12.0, H9b), 2.37 (2 H, d, *J* 7.0, H7), 2.19 (2 H, dt, *J* 6.5, 5.5, H3), 2.92 (2 H, t, *J* 5.5, H1), 3.56 (2 H, br s, H6), 6.02 (1 H, t, *J* 6.5, H4). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 23.7 (C2), 26.1 (C10), 26.8 (C11), 27.0 (C3), 31.7 (C9), 35.6 (C8), 57.2 (C1), 59.9 (C7), 60.8 (C6), 129.3 (C4), 132.9 (C5). MS (positive CI, NH_3): *m/z* 109, 145, 146, 147, 192, 226, 227, 228 (MH^+ with ^{35}Cl), 229, 230 (MH^+ with ^{37}Cl), 231. MS (EI): *m/z* 108, 109, 144 ([M−cyclohexyl]$^+$ with ^{35}Cl), 145, 146 ([M−cyclohexyl]$^+$ with ^{37}Cl), 227 ($M^{+\bullet}$ with ^{35}Cl), 229 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 227.1438 ($M^{+\bullet}$ $C_{13}H_{22}{}^{35}ClN^{+\bullet}$ requires 227.1436).



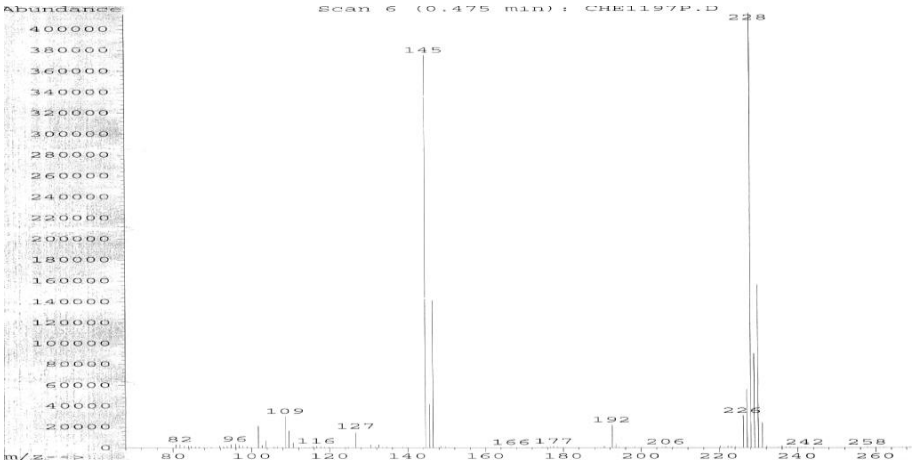
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



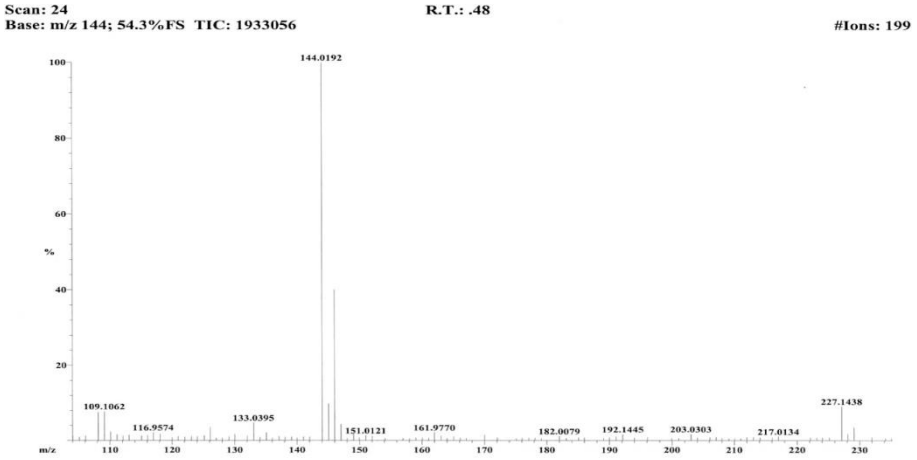
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

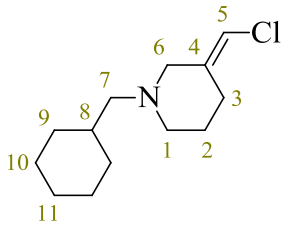


MS spectrum (CI, NH_3).



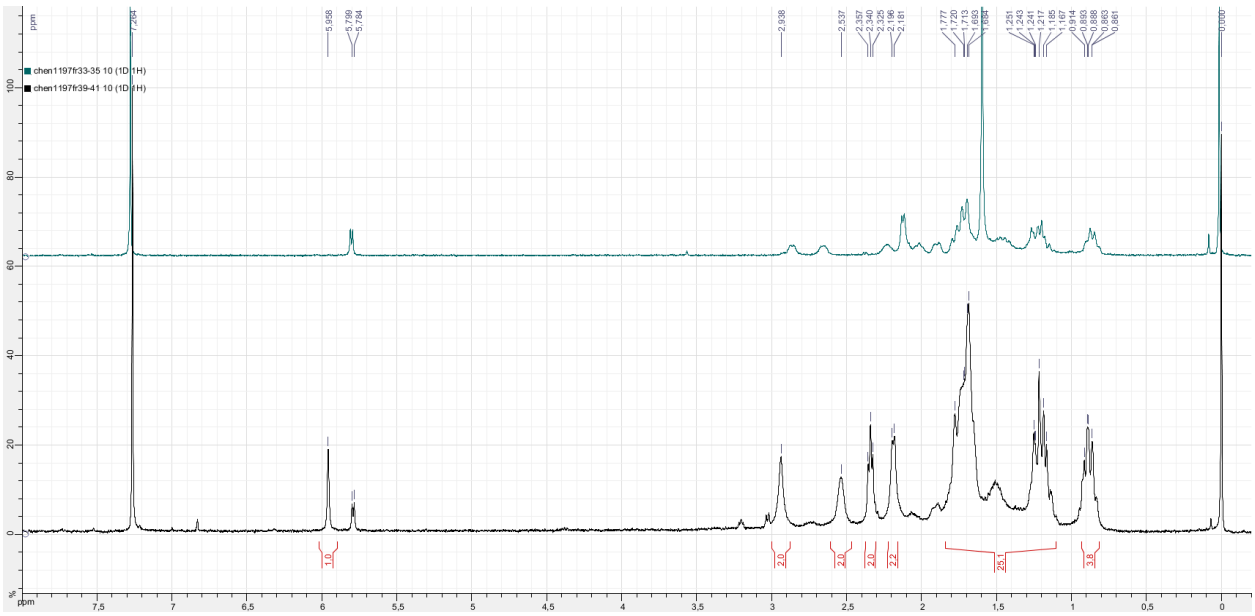
MS spectrum (EI).

(*E*)-3-(Chloromethylene)-1-(cyclohexylmethyl)piperidine (*E*)-**7bd**



R_f 0.15 [EtOAc/petroleum ether 5%, I_2]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.87 (2 H, m, H9a), 1.10−1.84 (13 H, m, H2, H8−H11), 2.14−2.24 (2 H, m, H7), 2.34 (2 H, br t, *J* 6.5, H3), 2.54 (2 H, br s, H1), 2.94 (2 H, s, H6), 5.96 (1 H, br s, H5).

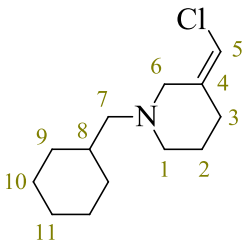
Note: this compound was not isolated in pure form, but as a mixture with a small amount of 1-(cyclohexylmethyl)-3-(dichloromethyl)piperidine **16bd**.



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a sample containing a minor amount of **16bd**.

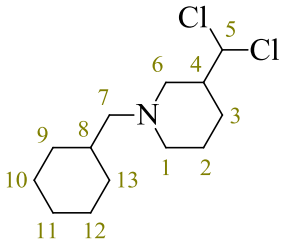
(*Z*)-3-(Chloromethylene)-1-(cyclohexylmethyl)piperidine (*Z*)-**7bd**



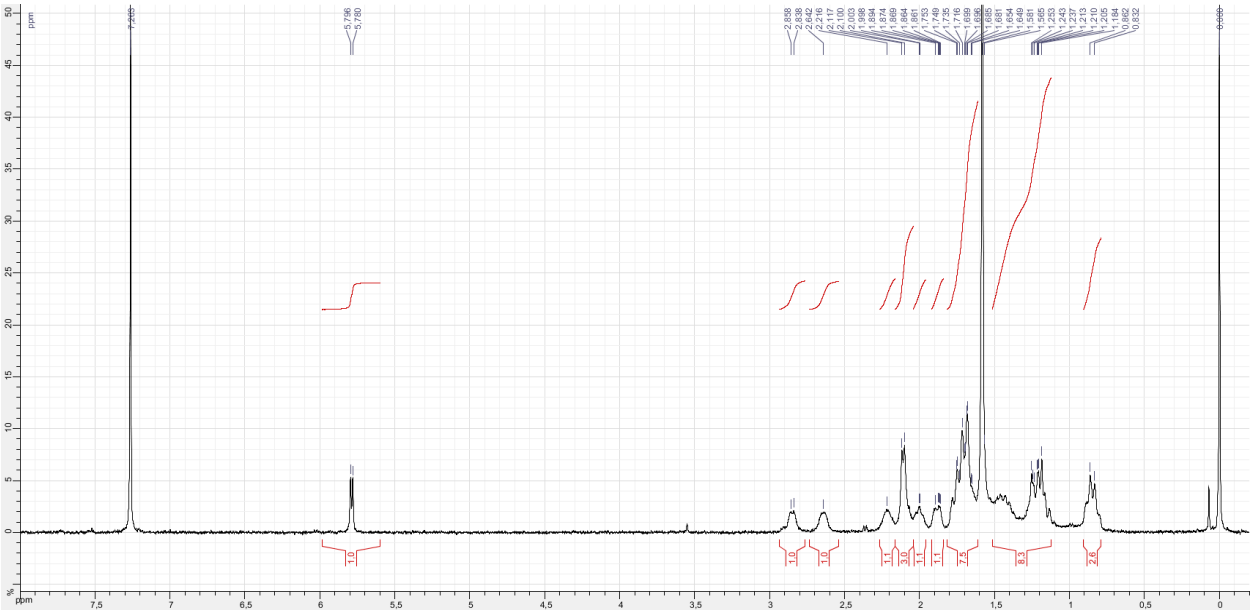
^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signal: δ 5.83 (1 H, br s, H5).

Note: this compound was observed as a minor component in a crude product and was not isolated.

1-(Cyclohexylmethyl)-3-(dichloromethyl)piperidine **16bd**

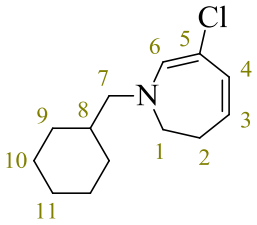


R_f 0.25 [EtOAc/petroleum ether 5%, I_2, not UV-active]. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 0.85 (2 H, m, H9a, H13a), 1.10−1.82 (12 H, m, H2, H3a, H8, H9b, H10−H12, H13b), 1.88 (1 H, br d, *J* 13.0, H3b), 2.00 (1 H, m, H1a), 2.04−2.16 (3 H, m, H6a, H7), 2.22 (1 H, m, H4), 2.64 (1 H, m, H1b), 2.85 (1 H, br d, *J* 8.5, H6b), 5.79 (1 H, d, *J* 6.0, H5).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

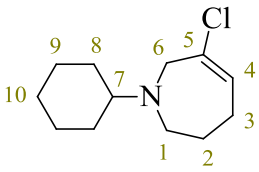
6-Chloro-1-(cyclohexylmethyl)-2,3-dihydroazepine **17bd**



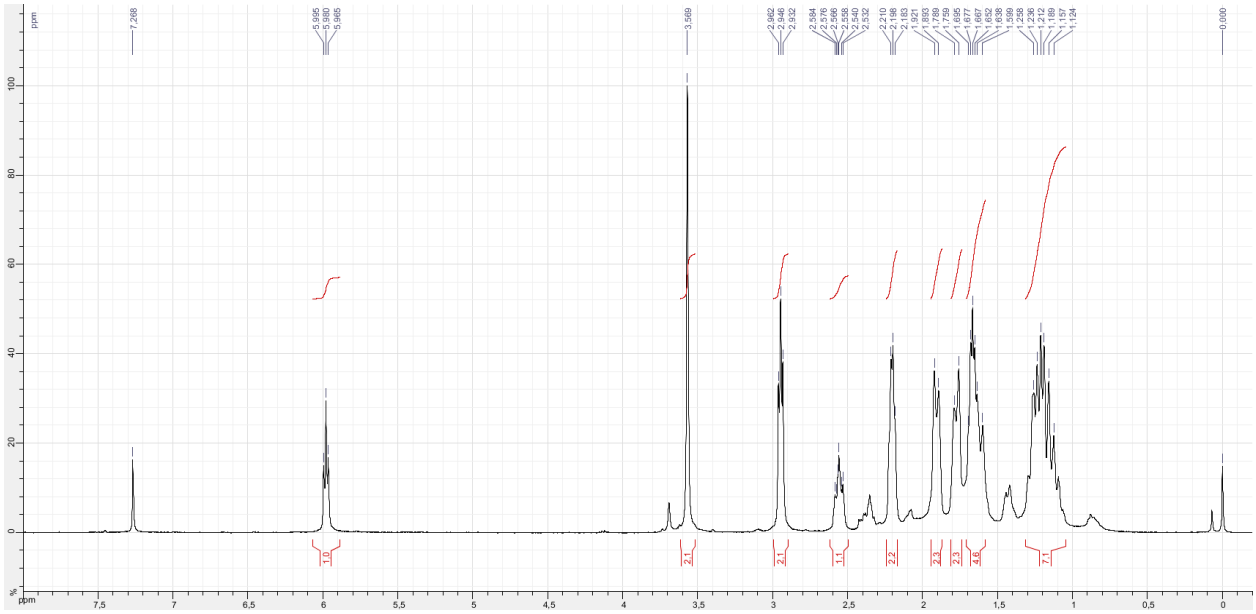
^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: δ 5.46 (1 H, dt, *J* 11.5, 6.0, H3), 5.95 (1 H, br d, *J* 11.5, H4), 6.35 (1 H, br s, H6).

Note: this compound was observed as a minor component in a crude product and was not isolated.

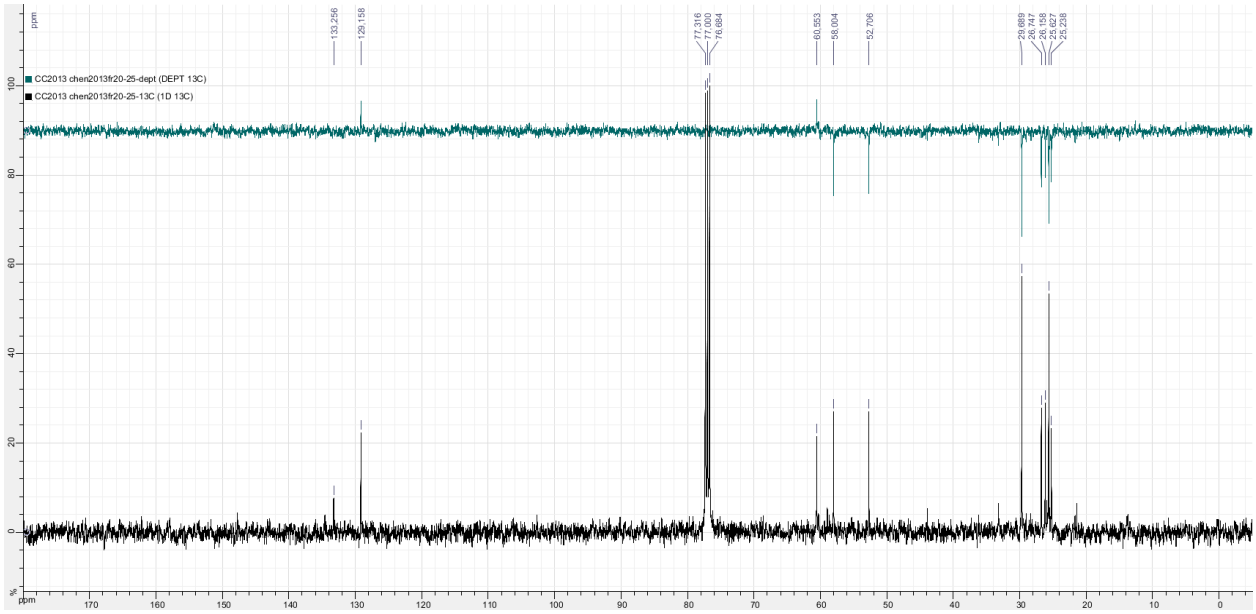
6-Chloro-1-cyclohexyl-2,3,4,7-tetrahydroazepine **5be**



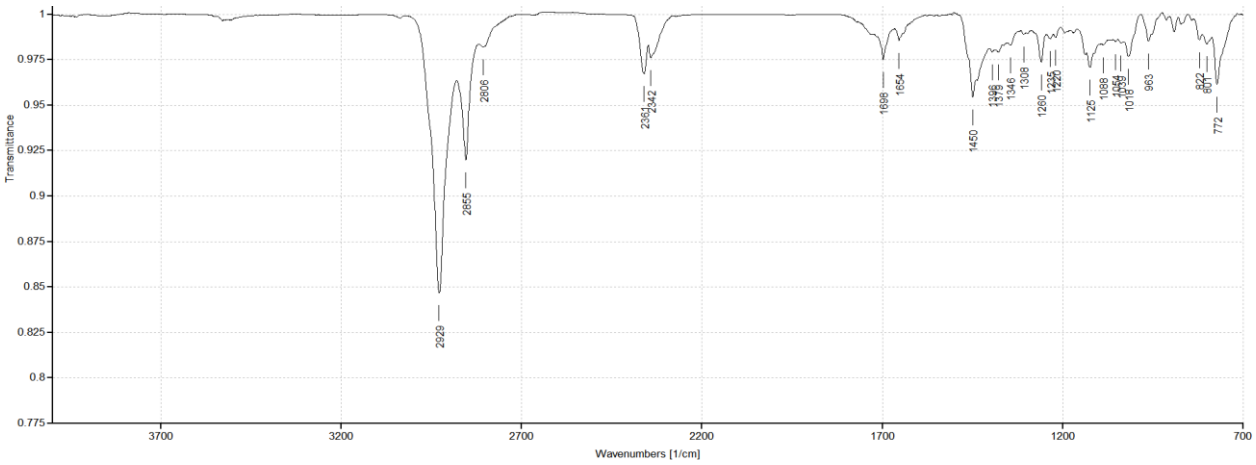
Pale yellow oil. R_f 0.5 [EtOAc/petroleum ether 20%, I_2, not UV-active]. IR (neat) ν 2929 (s), 2855 (m), 2806 (w), 2361 (w), 2342 (w), 1698 (w), 1450 (w), 1260 (w), 1125 (w), 1018 (w), 963 (w), 772 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.04−1.32 (3 H, m, H8a, H9a, H10a), 1.61 (1 H, dm, *J* 12.5, H10b), 1.67 (2 H, tt, *J* 6.0, 5.5, H2), 1.77 (2 H, dm, *J* 12.0, H9b), 1.91 (2 H, br d, *J* 11.5, H8b), 2.20 (2 H, dt, *J* 6.0, 5.5, H3), 2.56 (1 H, tt, *J* 10.5, 30, H7), 2.95 (2 H, t, *J* 6.0, H1), 3.57 (2 H, br s, H6), 5.98 (1 H, br t, *J* 6.0, H4). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 25.2 (C2), 25.6 (C9), 26.2 (C10), 26.7 (C3), 29.7 (C8), 52.7 (C1), 58.0 (C6), 60.6 (C7), 129.2 (C4), 132.3 (C5). MS (positive CI, NH_3): *m/z* 131, 170, 179, 178, 204, 214 (MH^+ with ^{35}Cl), 215, 216 (MH^+ with ^{37}Cl), 217, 236. MS (EI): *m/z* 112, 170, 171, 172, 213 ($M^{+\bullet}$ with ^{35}Cl), 215 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 213.1279 ($M^{+\bullet}$ $C_{12}H_{20}{}^{35}ClN^{+\bullet}$ requires 213.1279).



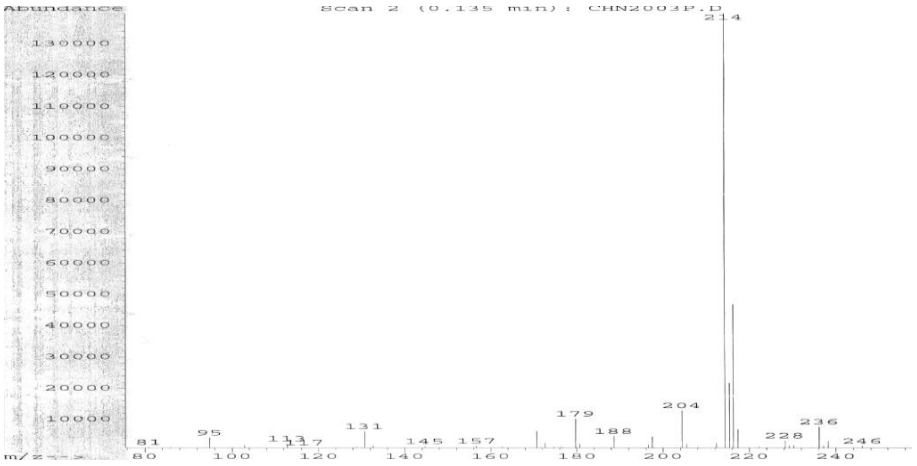
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



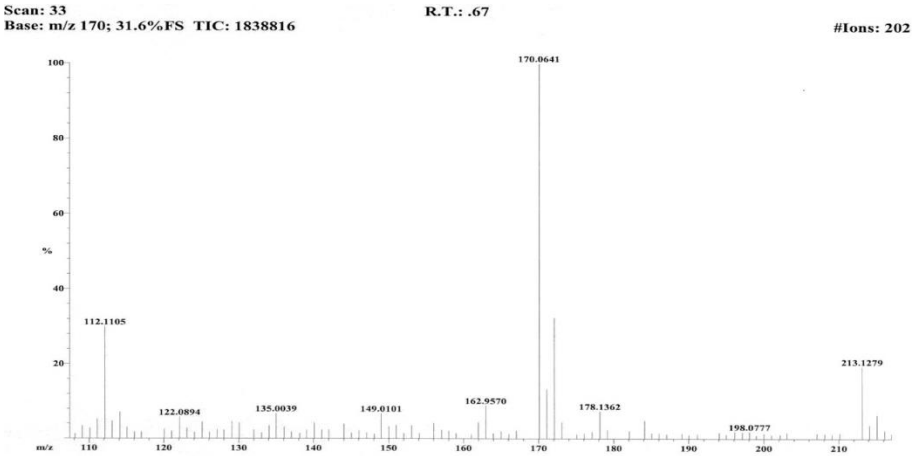
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

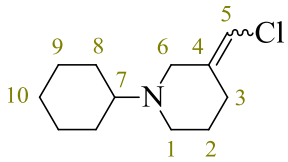


MS spectrum (CI, NH_3).



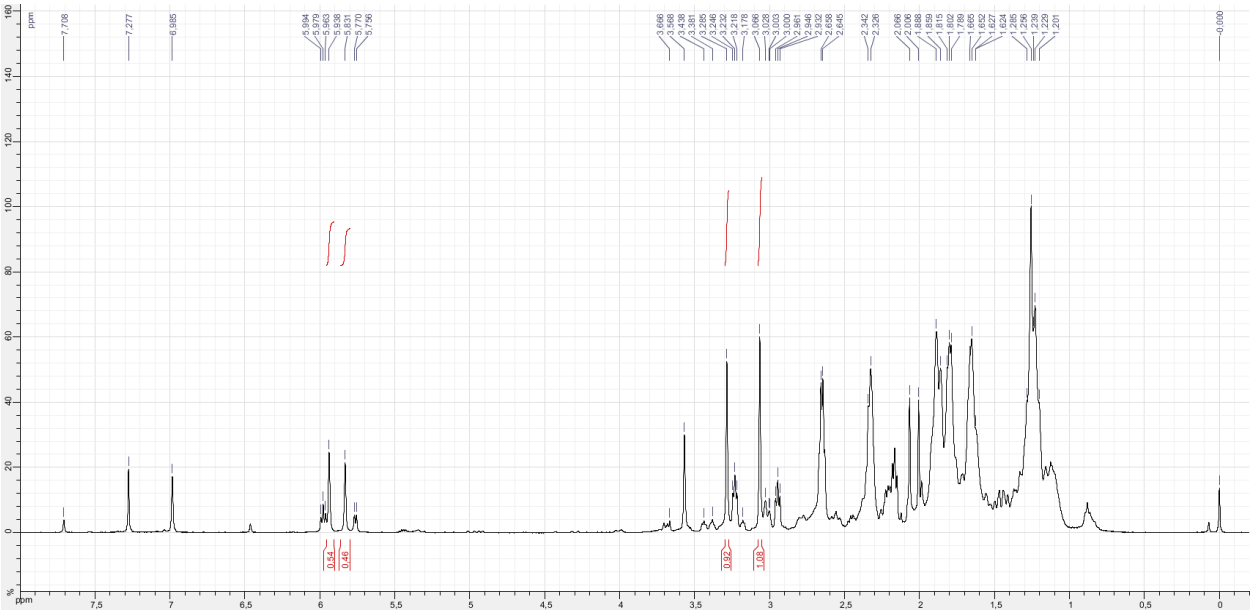
MS spectrum (EI).

3-(Chloromethylene)-1-cyclohexyl-piperidine **7be**



^{1}H NMR ($CDCl_3$, 400 MHz), 54:46 mixture of *E* and *Z* isomers. *E* isomer, characteristic signals: δ 3.07 (2 H, s, H6), 5.94 (1 H, br s, H5). *Z* isomer, characteristic signals: δ 3.28 (2 H, s, H6), 5.83 (1 H, br s, H5).

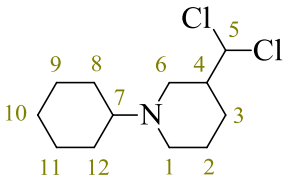
Note: these isomeric compounds were observed in a crude product but were not isolated.
Their proposed structures are consistent with those of by-products isolated in the *N*-benzyl series.



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product, showing the expected characteristic signals of (*E*)- and (*Z*)-3-(chloromethylene)-1-cyclohexyl-piperidine.

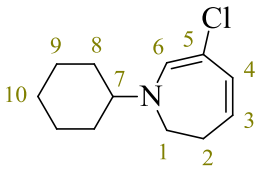
1-Cyclohexyl-3-(dichloromethyl)piperidine **16be**



^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signal: δ 5.76 (1 H, d, *J* 5.5, H5).

Note: this compound was observed as a minor component in a crude product and was not isolated. Its proposed structure is consistent with that of a by-product isolated in the *N*-benzyl series.

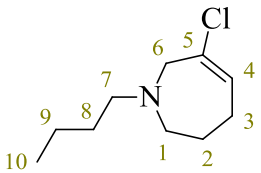
6-Chloro-1-cyclohexyl-2,3-dihydroazepine **17be**



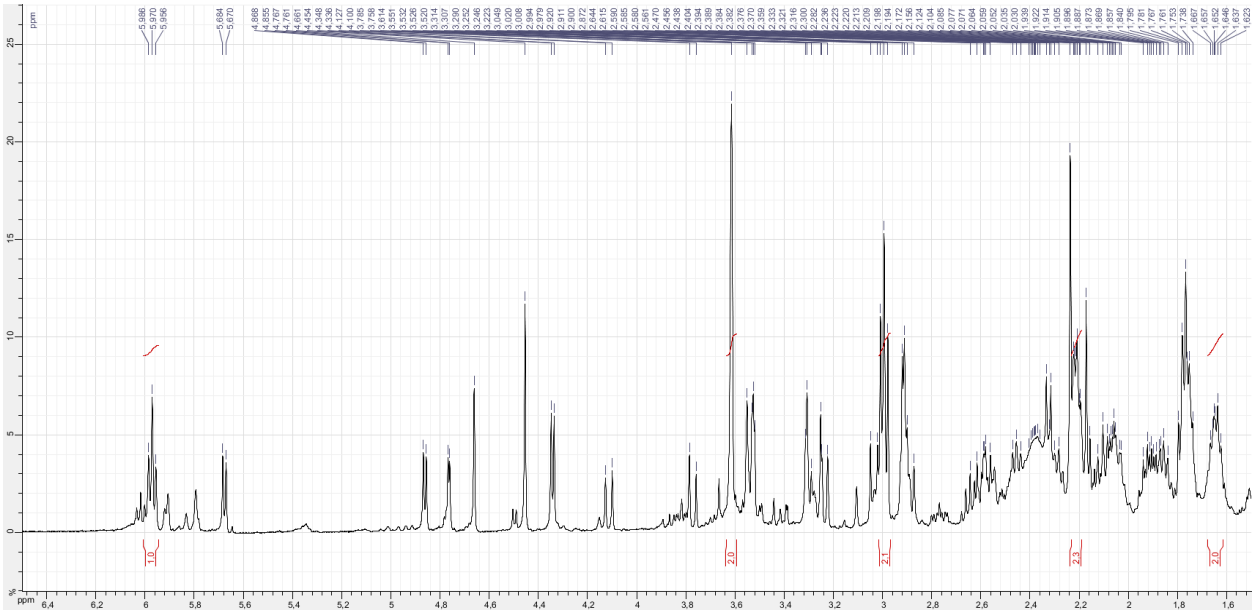
^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: δ 5.44 (1 H, dt, *J* 11.5, 5.5, H3), 6.46 (1 H, br s, H6).

Note: this compound was observed as a minor component in a crude product and was not isolated. Its proposed structure is consistent with that of a by-product isolated in the *N*-benzyl series.

6-Chloro-1-butyl-2,3,4,7-tetrahydroazepine **5bf**



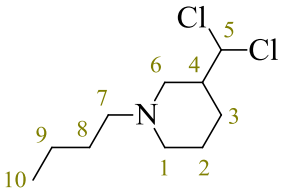
^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: δ 1.64 (2 H, tt, *J* 6.0, 5.5, H2), 2.22 (2 H, dt, *J* 6.0, 5.5, H3), 2.99 (2 H, t, *J* 6.0, H1), 3.61 (2 H, br s, H6), 5.97 (1 H, t, *J* 6.0, H4).



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

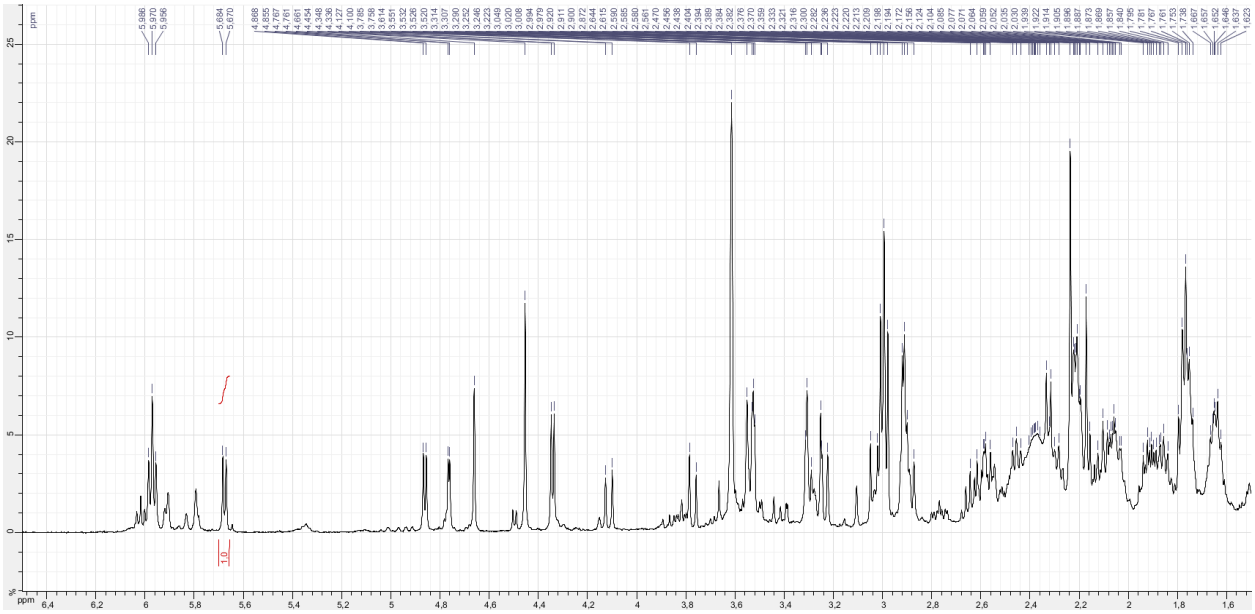
Note: this is the spectrum of a crude product, showing the expected characteristic signals of **5bf** (integrated).

1-Butyl-3-(dichloromethyl)piperidine **16bf**



^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signal: δ 5.68 (1 H, d, *J* 5.5, H5).

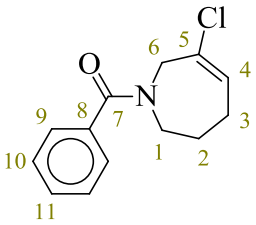
Note: this compound was observed in a crude product but not isolated.
This proposed structure is consistent with that of **16ba**, isolated in the *N*-benzyl series.



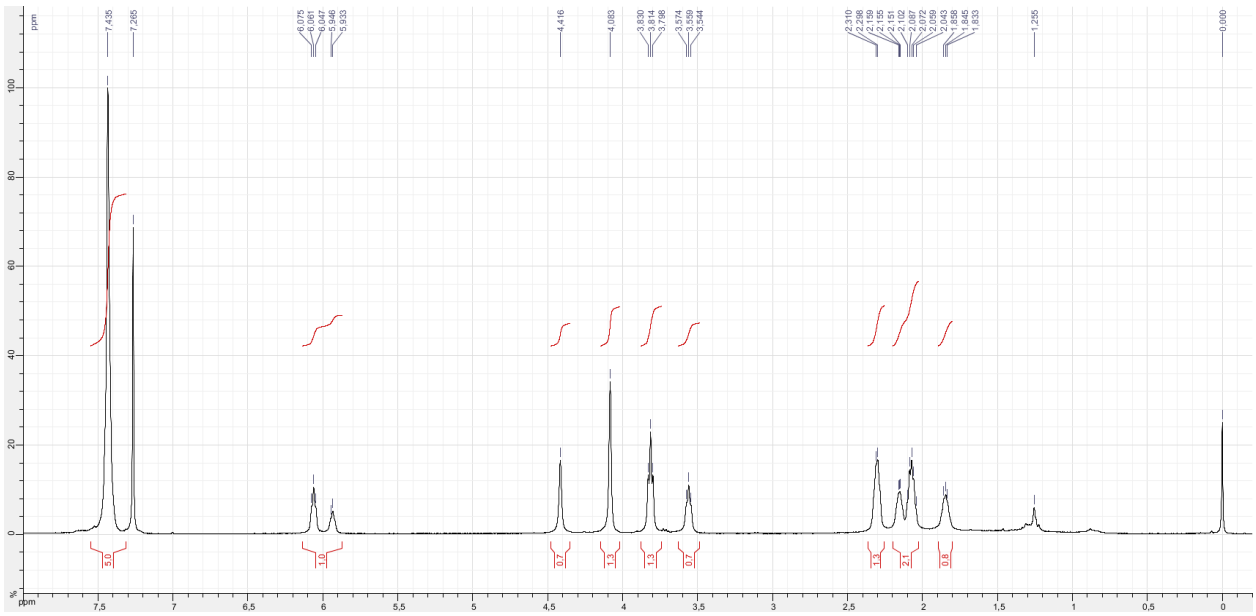
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product, showing the expected characteristic signal of the $CHCl_2$ proton of **16bf** (integrated).

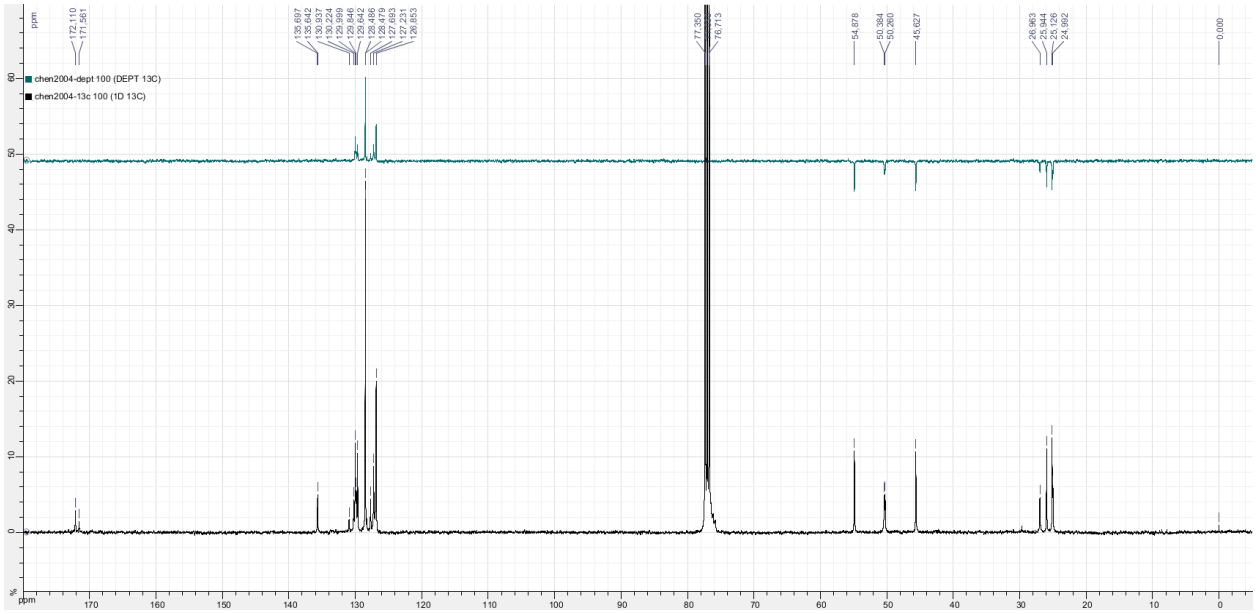
(6-Chloro-2,3,4,7-tetrahydroazepin-1-yl)-phenyl-methanone



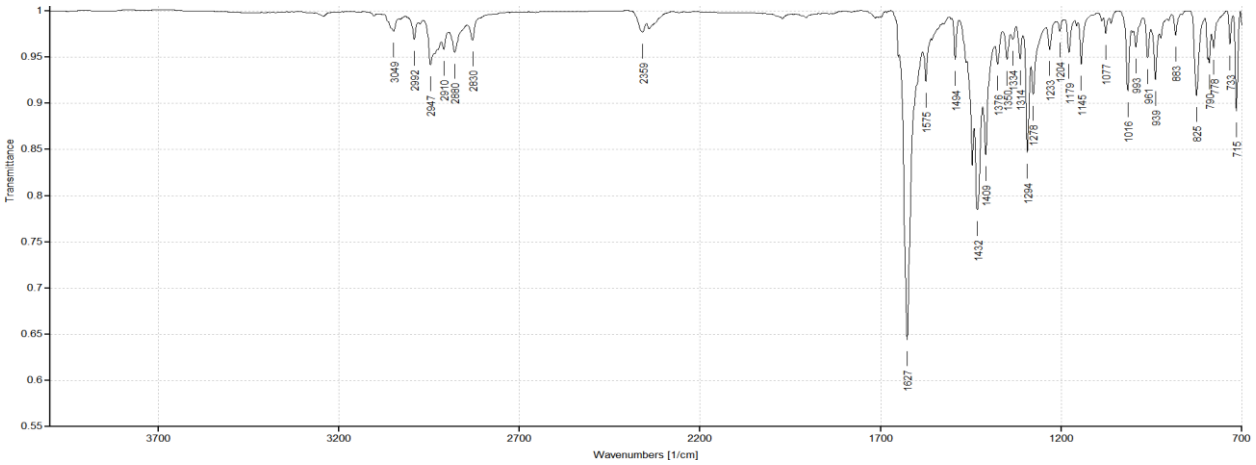
Pale yellow oil. R_f 0.2 [EtOAc/petroleum ether 20%, $KMnO_4$, UV-active]. IR (neat) ν 3049 (w), 2992 (w), 2947 (w), 2910 (w), 2880 (w), 2830 (w), 1627 (s, C=O), 1446 (m), 1432 (m), 1409 (m), 1294 (m), 1016 (w), 939 (w), 825 (w), 715 (w) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz), 63 : 37 mixture of two rotamers. Major rotamer: δ 2.07 (2 H, tt, J 6.5, 5.5, H2), 2.30 (2 H, br td, J 6.5, 5.0, H3), 3.81 (2 H, t, J 6.5, H1), 4.08 (2 H, br s, H6), 6.06 (1 H, t, J 5.0, H4), 7.43 (5 H, br s, H9–H11). Minor rotamer: δ 1.84 (2 H, quint, J 6.0, H2), 2.15 (2 H, br td, J 6.0, 5.0, H3), 3.56 (2 H, t, J 6.0, H1), 4.42 (2 H, br s, H6), 5.93 (1 H, t, J 5.0, H4), 7.43 (5 H, br s, H9–H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 63 : 37 mixture of two rotamers. Major rotamer: δ 25.1 (C3), 25.9 (C2), 45.6 (C1), 54.9 (C6), 126.9, 128.5 (C9, C10), 129.6 (C4), 130.0 (C11), 130.2 (C5), 135.6 (C8), 172.1 (C7). Minor rotamer, characteristic signals: δ 25.0 (C3), 27.0 (C2), 50.3, 50.4 (C1, C6), 127.2, 127.7, 128.5, 129.8 (C4, C9–C11), 130.9 (C5), 135.7 (C8), 171.6 (C7). MS (positive CI, NH_3): *m/z* 106, 204, 236 (MH^+ with ^{35}Cl), 237, 238 (MH^+ with ^{37}Cl), 239. MS (EI): *m/z* 105, 106, 134, 170, 200, 235 ($M^{+\bullet}$ with ^{35}Cl), 236, 237 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 235.0761 ($M^{+\bullet}$ $C_{13}H_{14}{}^{35}ClNO^{+\bullet}$ requires 235.0759).



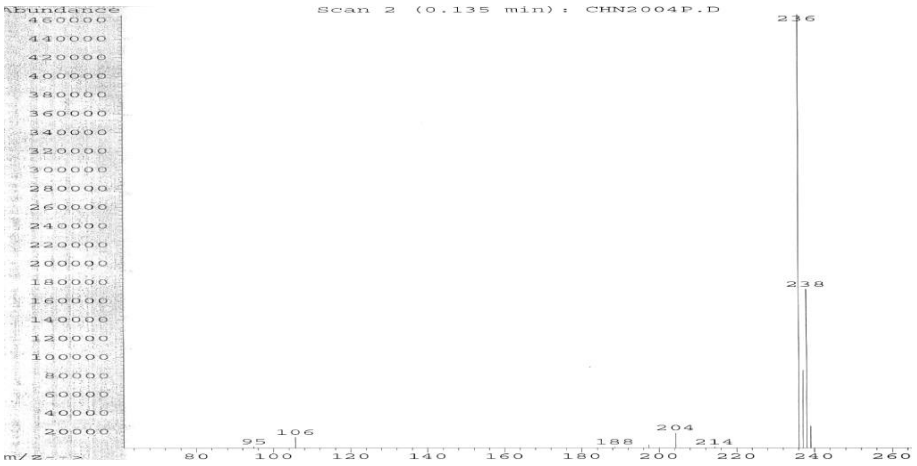
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



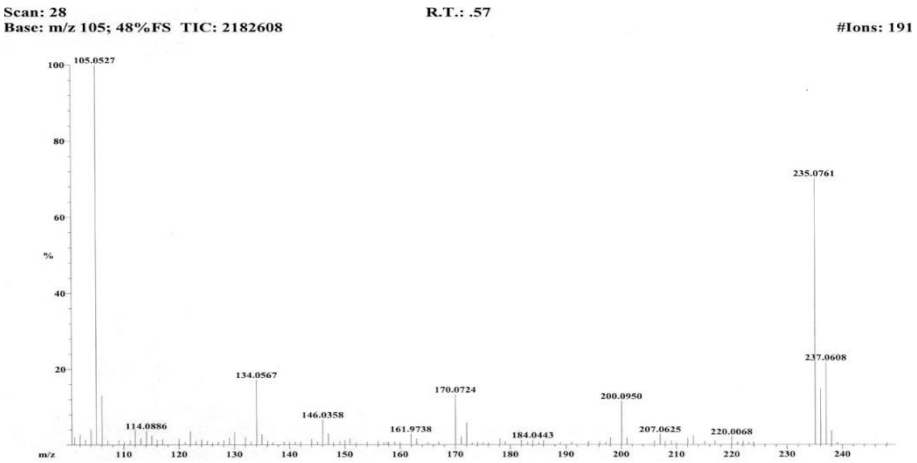
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

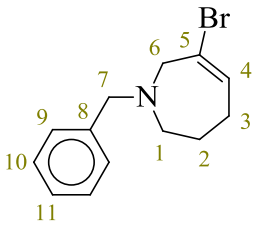


MS spectrum (CI, NH_3).

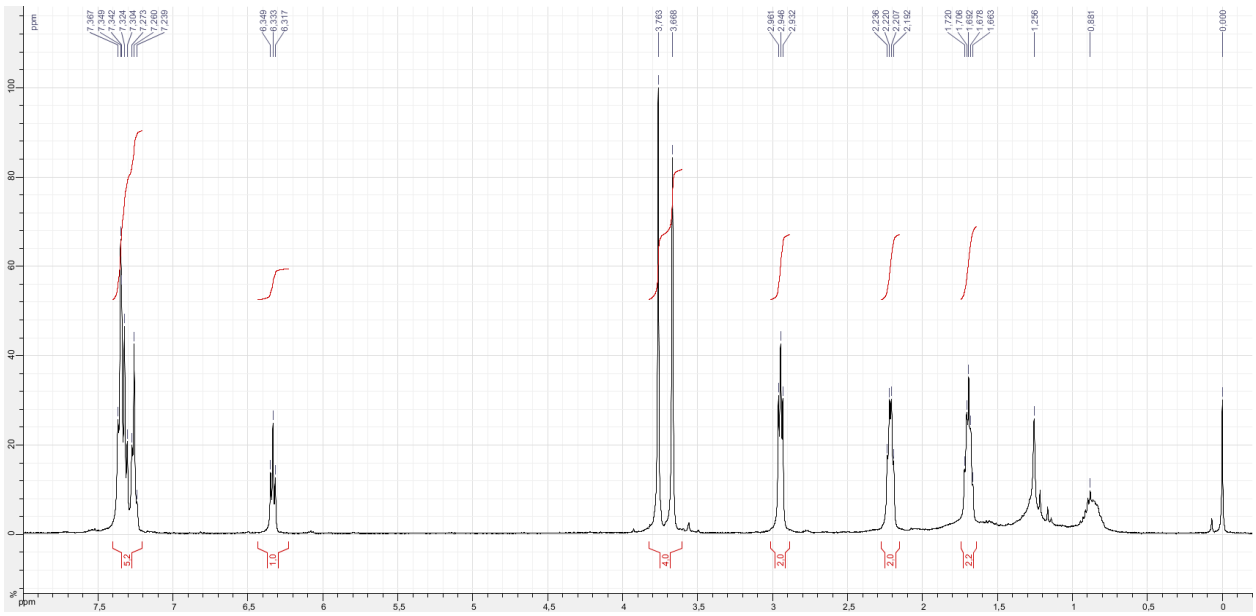


MS spectrum (EI).

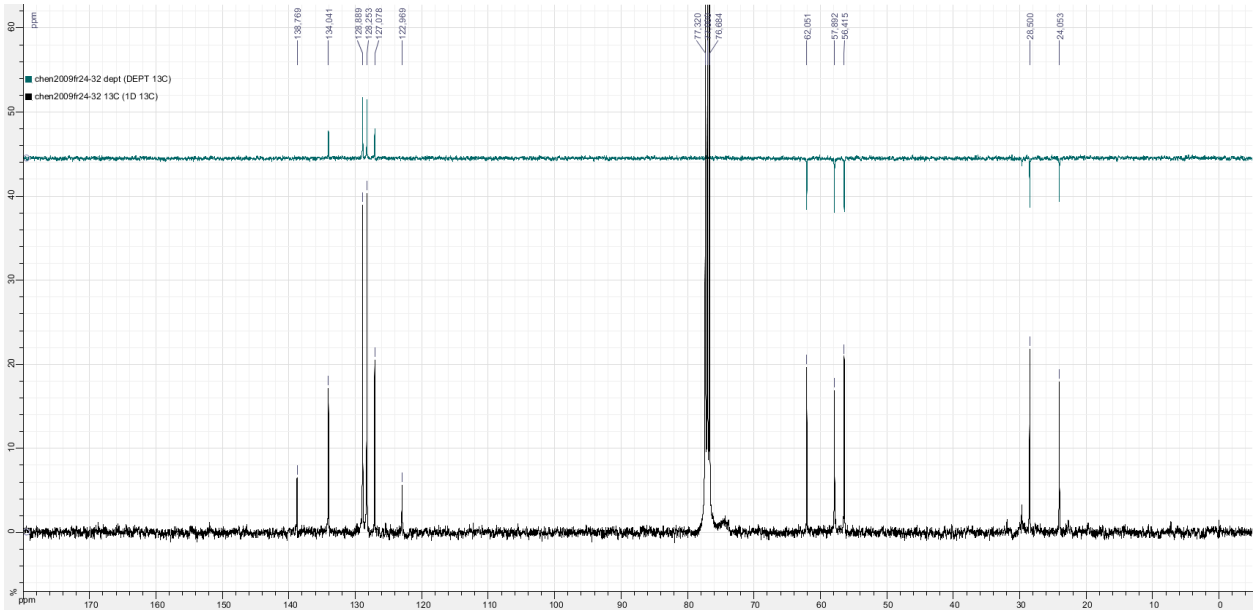
1-Benzyl-6-bromo-2,3,4,7-tetrahydroazepine **5ca**



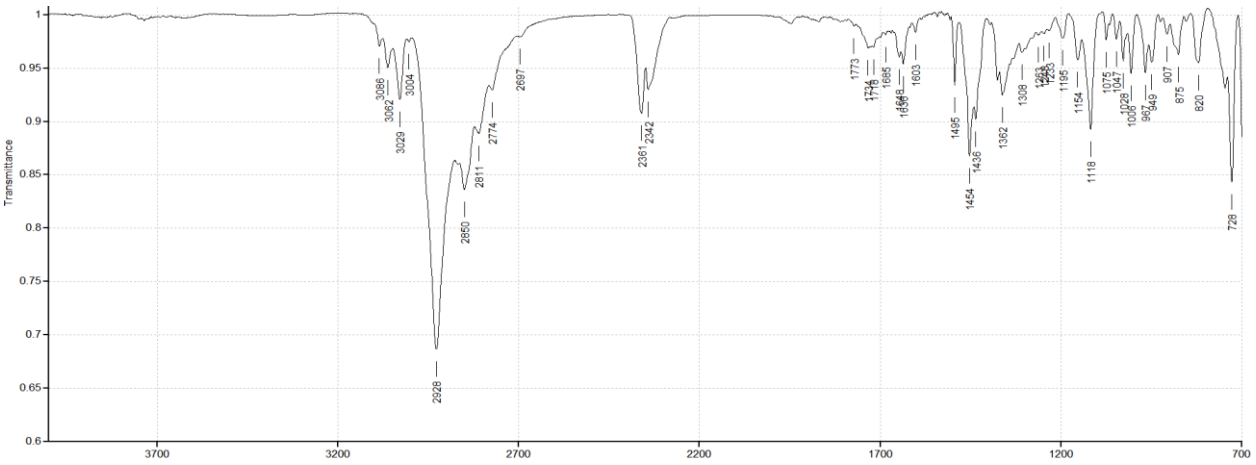
Pale yellow oil. R_f 0.3 [EtOAc/petroleum ether 10%, anisaldehyde (white spot), UV-active]. IR (neat) *v* 3029 (w), 2928 (s), 2850 (m), 2811 (m), 2361 (w), 2342 (w), 1495 (w), 1454 (m), 1436 (w), 1362 (w), 1118 (m), 728 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.69 (2 H, quint, *J* 5.5, H2), 2.21 (2 H, dt, *J* 6.5, 5.5, H3), 2.95 (2 H, t, *J* 5.5, H1), 3.67 (2 H, s, H6), 3.76 (2 H, s, H7), 6.33 (1 H, t, *J* 6.5, H4), 7.22−7.40 (5 H, m, H9−H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 24.1 (C2), 28.5 (C3), 56.4 (C1), 57.9 (C7), 62.1 (C6), 123.0 (C5), 127.1 (C11), 128.3, 128.9 (C9, C10), 134.0 (C4), 138.8 (C8). MS (positive CI, NH_3): *m/z* 222, <u>266</u> (MH^+ with ^{79}Br), 267, 268 (MH^+ with ^{81}Br), 269. MS (EI): *m/z* <u>120</u>, 121, 130, 186 ($[M-Br]^+$), 265 ($M^{+\bullet}$ with ^{79}Br), 267 ($M^{+\bullet}$ with ^{81}Br). HRMS (EI): *m/z* 265.0468 ($M^{+\bullet}$ $C_{13}H_{16}{}^{79}BrN^{+\bullet}$ requires 265.0461).



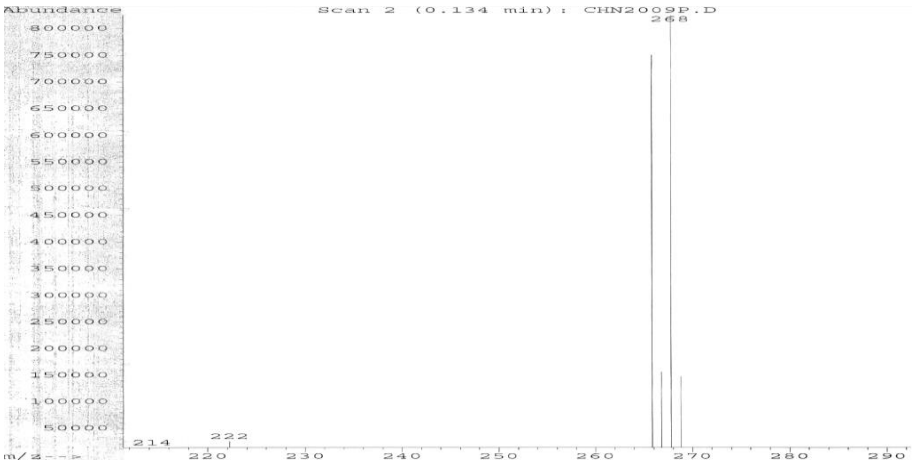
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



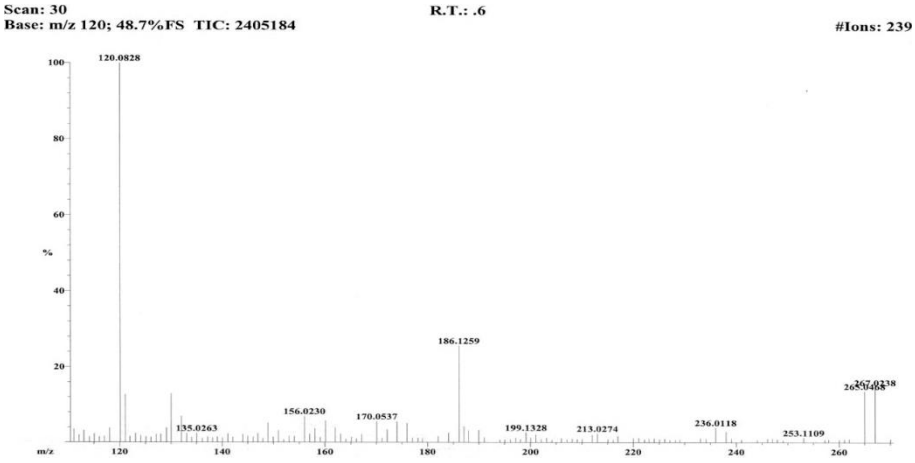
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

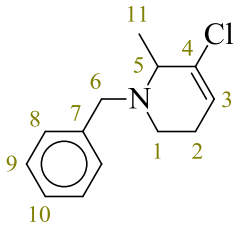


MS spectrum (CI, NH_3).

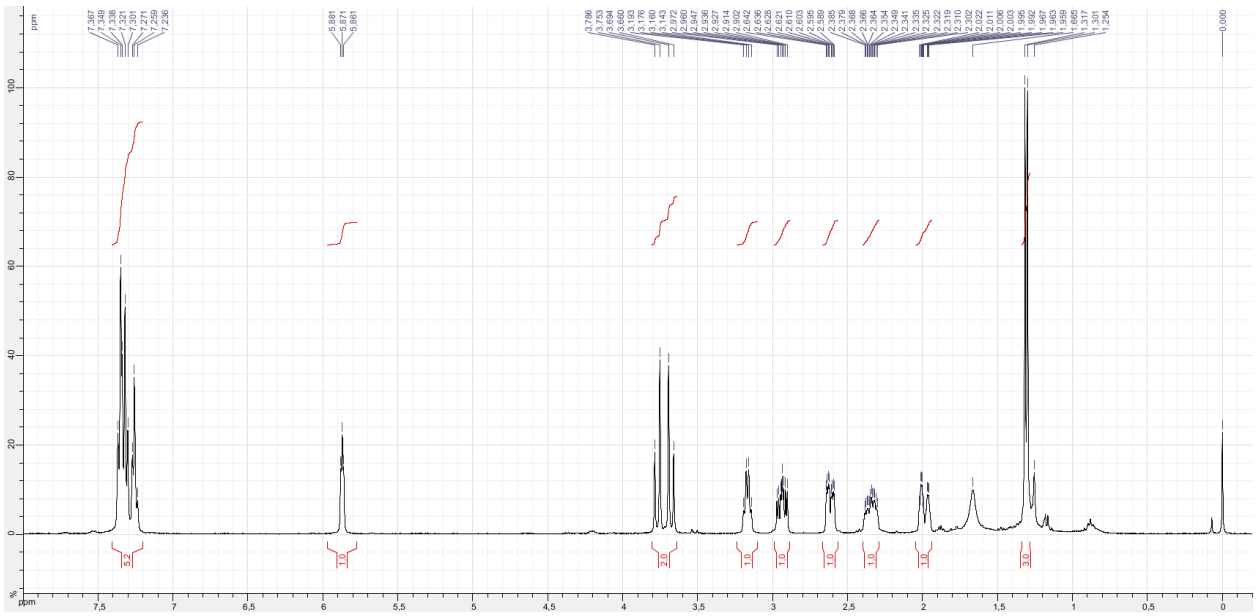


MS spectrum (EI).

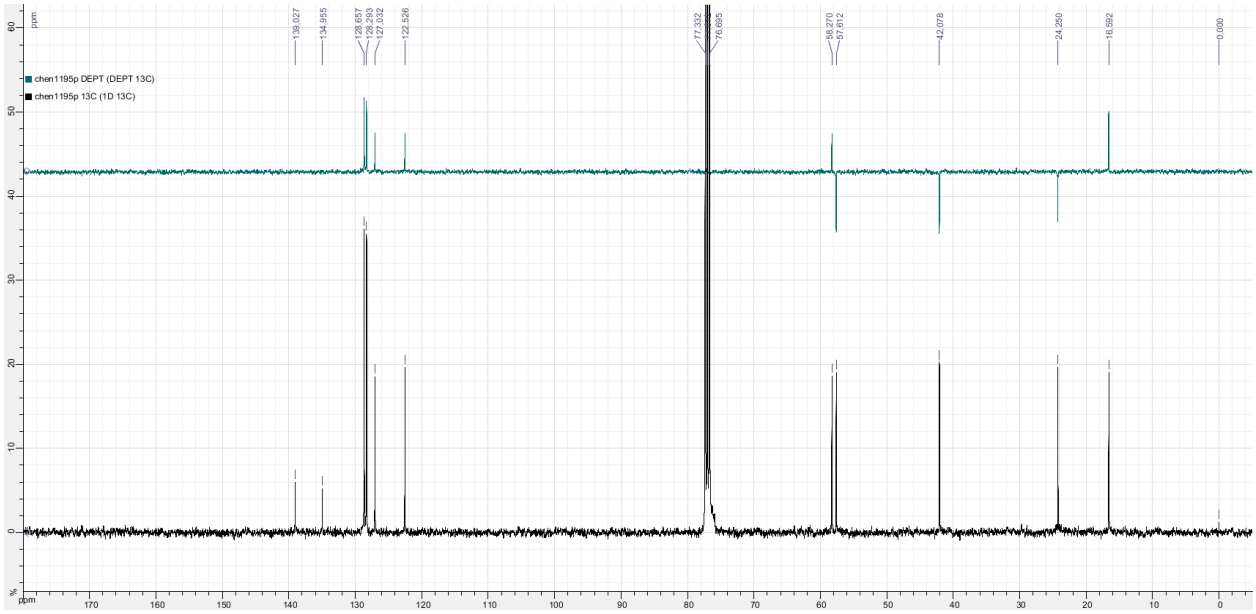
1-Benzyl-5-chloro-6-methyl-3,6-dihydro-2*H*-pyridine **5da**



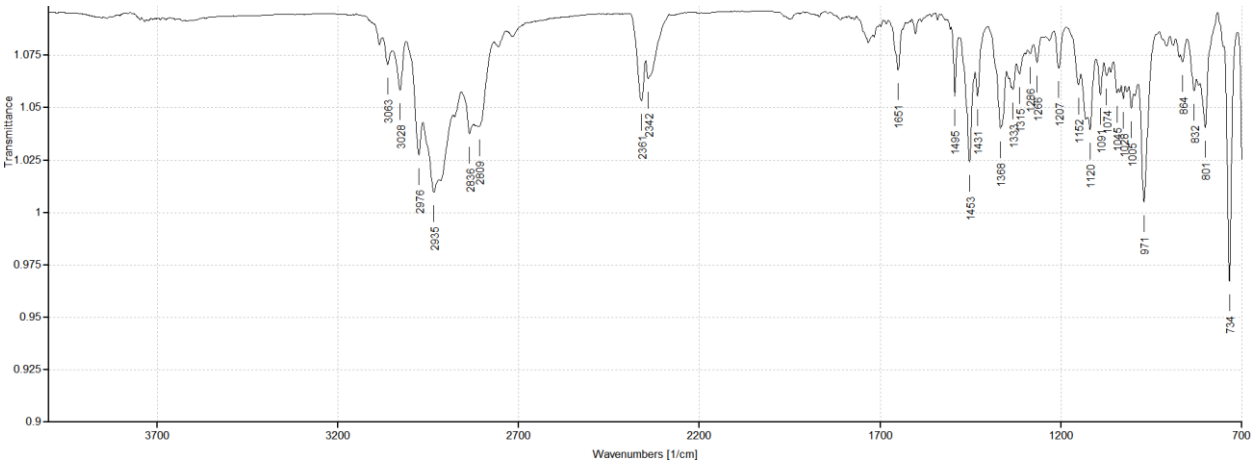
Pale yellow oil. R_f 0.3 [EtOAc/petroleum ether 10%, anisaldehyde (white spot), UV-active]. IR (neat) *v* 3028 (w), 2976 (m), 2935 (m), 2836 (m), 2809 (m), 2361 (w), 2342 (w), 1495 (w), 1453 (m), 1368 (m), 1120 (m), 970 (m), 801 (m), 734 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.31 (3 H, d, *J* 6.5, H11), 1.99 (1 H, dddd, *J* 17.0, 5.5, 5.0, 3.0, H2a), 2.34 (1 H, dddd, *J* 17.0, 10.0, 3.0, 2.5, H2b), 2.62 (1 H, ddd, *J* 13.0, 5.5, 2.5, H1a), 2.94 (1 H, ddd, *J* 13.0, 10.0, 5.0, H1b), 3.17 (1 H, q, *J* 6.5, H5), 3.72 (2 H, AB system, δ_A 3.68, δ_B 3.77, J_{AB} 13.5, H6), 5.87 (1 H, t, *J* 4.0, H3), 7.22−7.39 (5 H, m, H8−H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 16.6 (C11), 24.2 (C2), 42.1 (C1), 57.6 (C6), 58.3 (C5), 122.5 (C3), 127.0 (C10), 128.3, 128.7 (C8, C9), 135.0 (C4), 139.0 (C7). MS (positive CI, NH_3): *m/z* 92, 206, 208, 222 (MH^+ with ^{35}Cl), 223, 224 (MH^+ with ^{37}Cl), 225, 236. MS (EI): *m/z* 120, 206 ($[M–Me]^+$ with ^{35}Cl), 207, 208 ($[M–Me]^+$ with ^{37}Cl), 221 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 221.0971 ($M^{+\bullet}$ $C_{13}H_{16}{}^{35}ClN^{+\bullet}$ requires 221.0966).



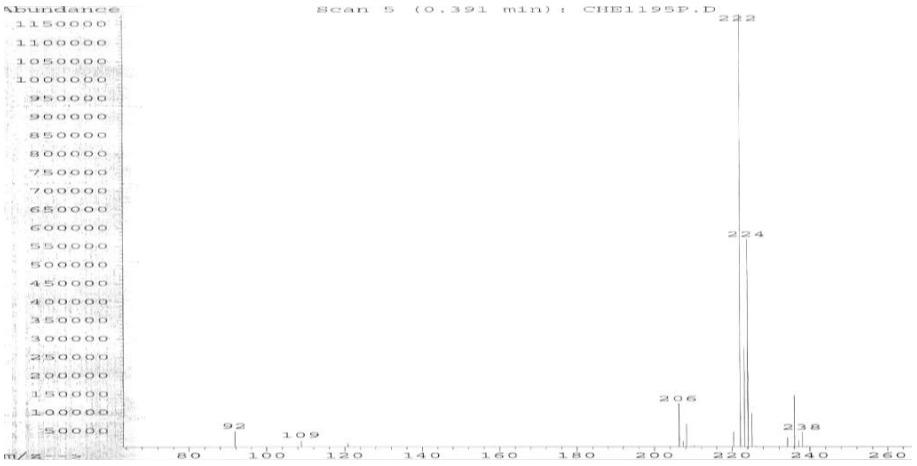
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



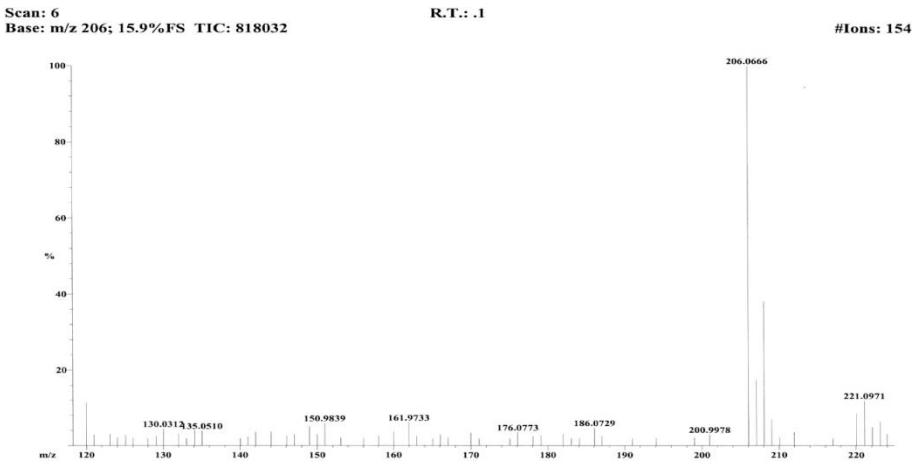
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

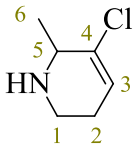


MS spectrum (CI, NH_3).



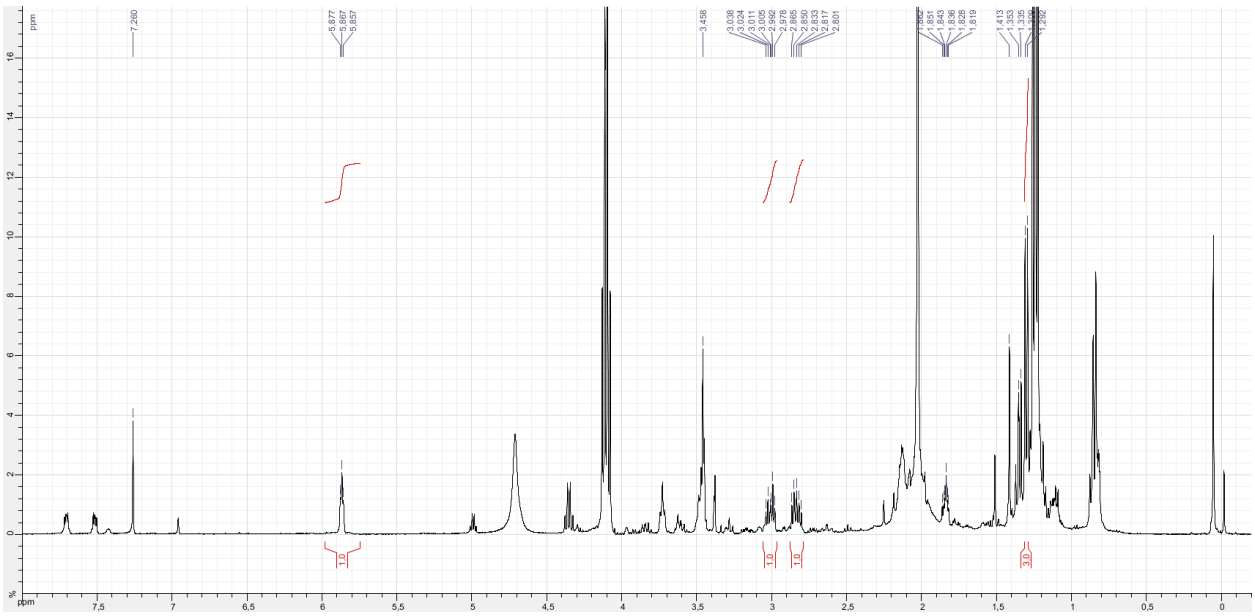
MS spectrum (EI).

5-Chloro-6-methyl-1,2,3,6-tetrahydropyridine



Yellow oil. ^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signals: δ 1.30 (3 H, d, *J* 7.0, H6), 2.83 (1 H, ddd, *J* 13.7, 7.0, 5.0, H1a), 3.01 (1 H, dt, *J* 13.5, 5.0, H1b), 5.87 (1 H, t, *J* 4.0, H3).

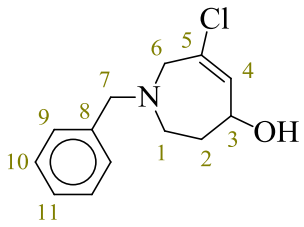
Note: this compound was observed in a crude product but was not isolated.



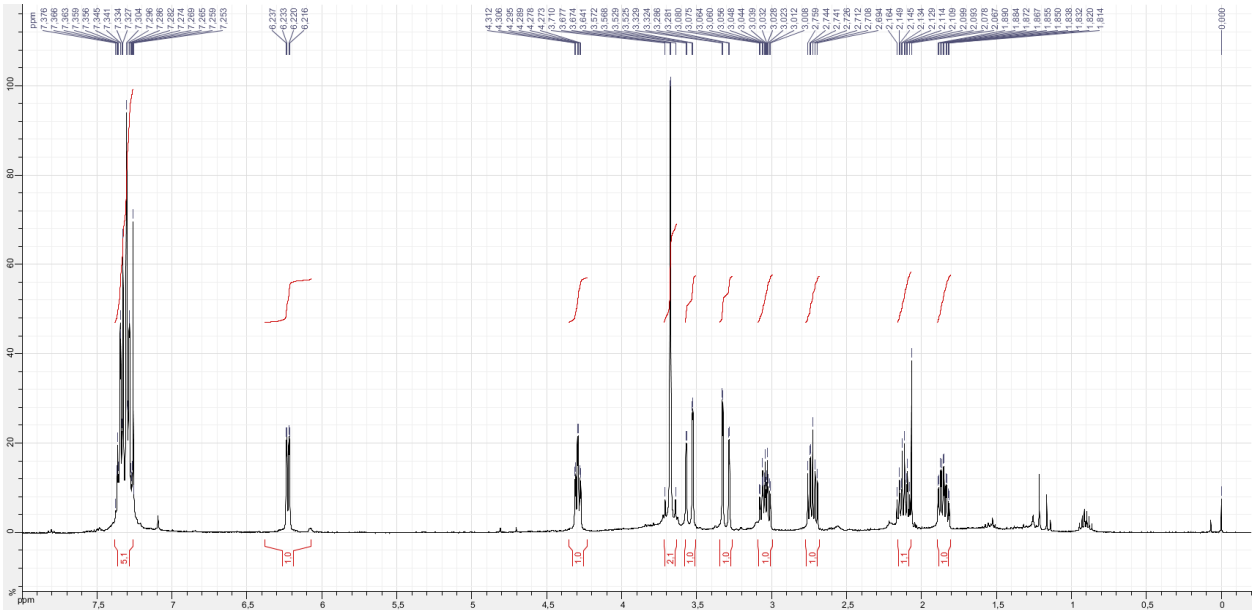
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product containing 5-chloro-6-methyl-1,2,3,6-tetrahydropyridine.

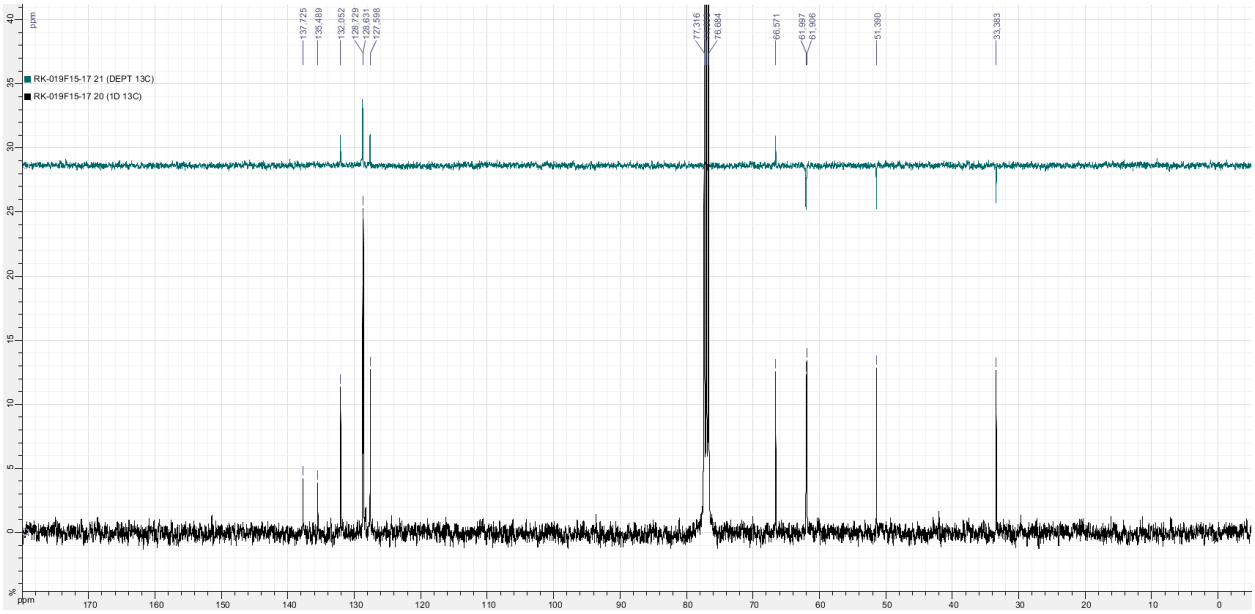
1-Benzyl-6-chloro-2,3,4,7-tetrahydroazepin-4-ol **5fa**



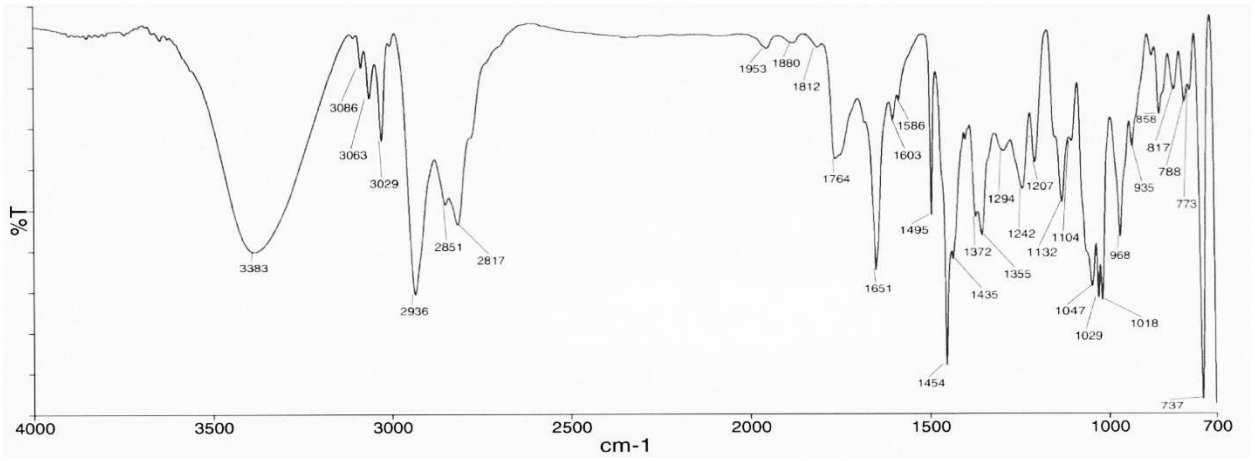
Yellow oil. R_f 0.05 [EtOAc/petroleum ether 20%, PMA, UV-active]. IR (neat) ν 3383 (br, m), OH), 3029 (w), 2936 (m), 2851 (m), 2817 (m), 1764 (m), 1651 (m), 1495 (m), 1454 (s), 1435 (m), 1372 (m), 1355 (m), 1242 (m), 1132 (m), 1047 (m), 1029 (m), 1018 (m), 968 (m), 737 (s) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.85 (1 H, dddd, J 14.0, 7.0, 6.5, 2.5, H2a), 2.12 (1 H, dddd, J 14.0, 8.0, 6.5, 6.0, H2b), 2.73 (1 H, ddd, J 13.0, 7.0, 6.0, H1a), 3.04 (1 H, dddd, J 13.0, 8.0, 6.5, 2.0, H1b), 3.43 (2 H, AB part of an ABX system, δ_A 3.31, δ_B 3.55, J_{AB} 17.0, J_{AX} 2.0, J_{BX} 2.0, H6), 3.68 (2 H, AB system, δ_A 3.67, δ_B 3.68, J_{AB} 13.5, H7), 4.29 (1 H, td, J 6.5, 2.5, H3), 6.23 (1 H, dd, J 6.5, 2.0, H4), 7.25−7.38 (5 H, m, H9, H10, H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 33.4 (C2), 51.4 (C1), 61.9, 62.0 (C6, C7), 66.6 (C3), 127.6 (C11), 128.6, 128.7 (C9, C10), 132.1 (C4), 135.5 (C5), 137.7 (C8). MS (positive CI, NH_3): *m/z* 121, 220, 238 (MH^+ with ^{35}Cl), 239, 240 (MH^+ with ^{37}Cl), 241. MS (EI): *m/z* 120, 121, 200, 201, 202, 237 ($M^{+\bullet}$ with ^{35}Cl), 239 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 237.0909 ($M^{+\bullet}$ $C_{13}H_{16}{}^{35}ClNO^{+\bullet}$ requires 237.0915).



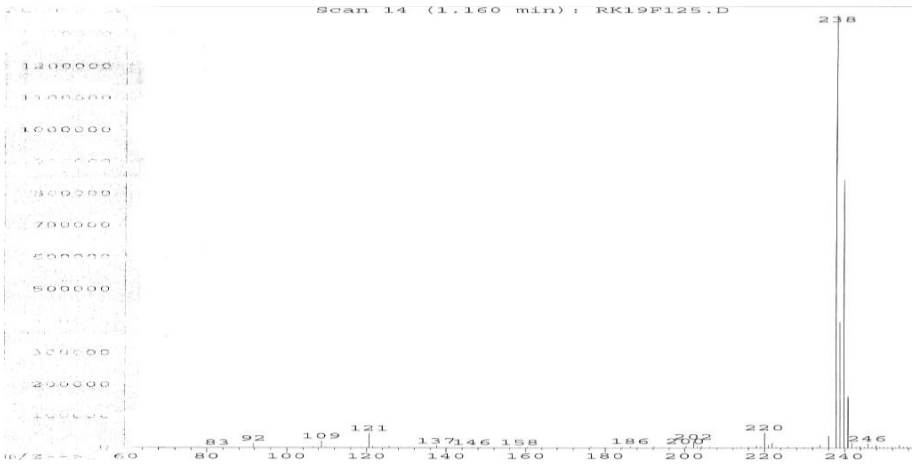
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



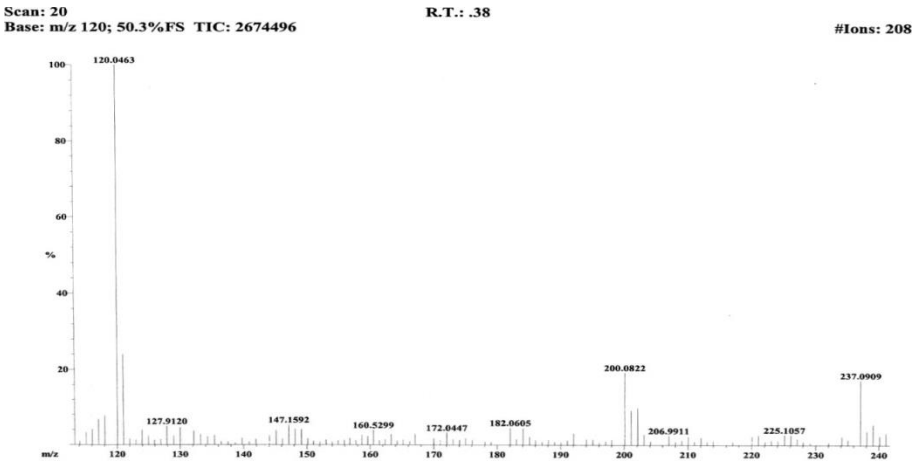
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

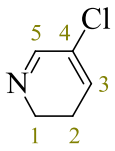


MS spectrum (CI, NH_3).



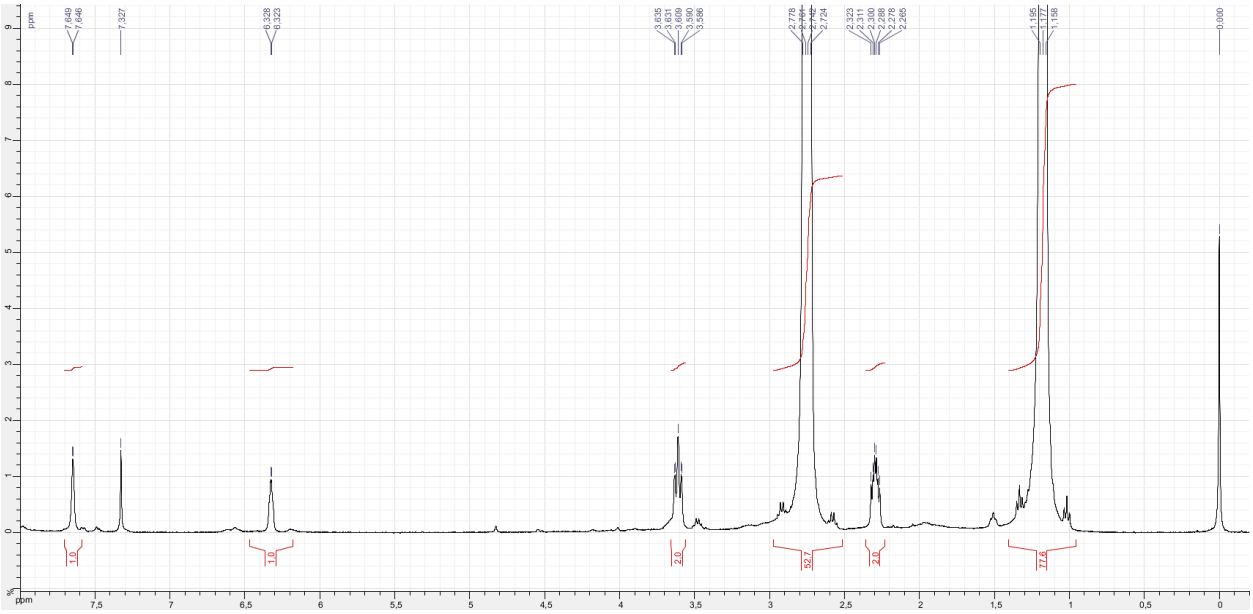
MS spectrum (EI).

5-Chloro-2,3-dihydropyridine **6a**



^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.29 (2 H, td, *J* 9.0, 5.0, H2), 3.61 (2 H, td, *J* 9.0, 2.0, H1), 6.33 (1 H, td, *J* 5.0, 2.0, H3), 7.65 (1 H, q, *J* 2.0, H5).

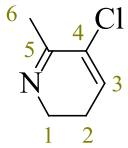
Note: this compound was directly observed by NMR as a solution in $CDCl_3$ but was not isolated.



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

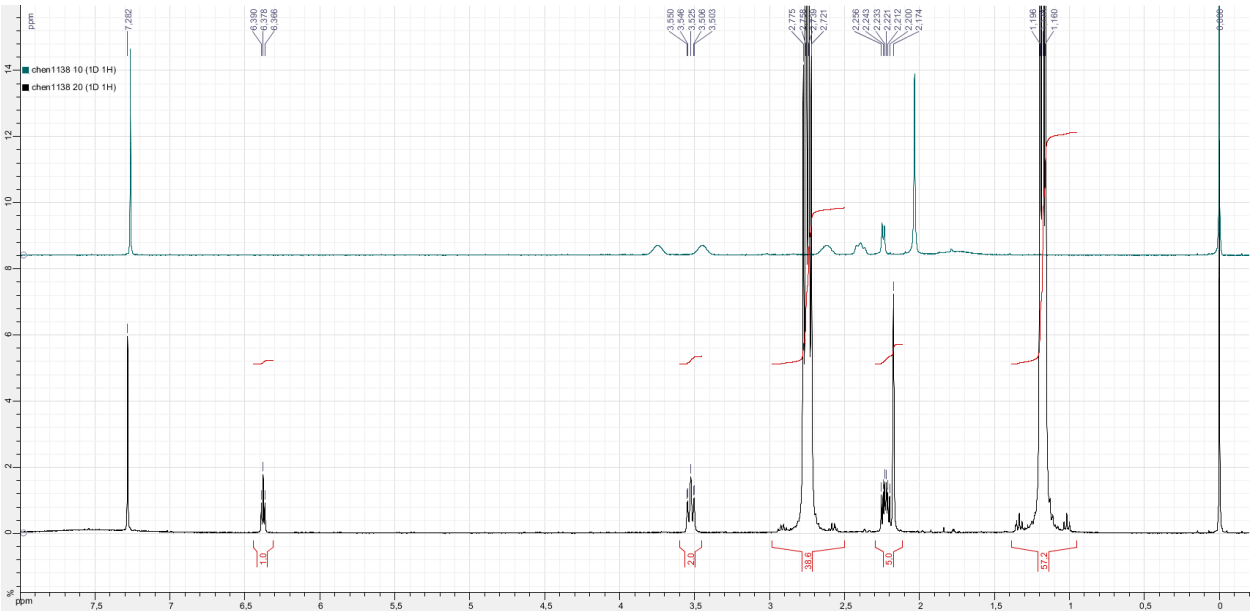
Note: the signals of triethylamine / triethylamine hydrochloride are visible, together with those of **6a**.

5-Chloro-6-methyl-2,3-dihydropyridine **6d**



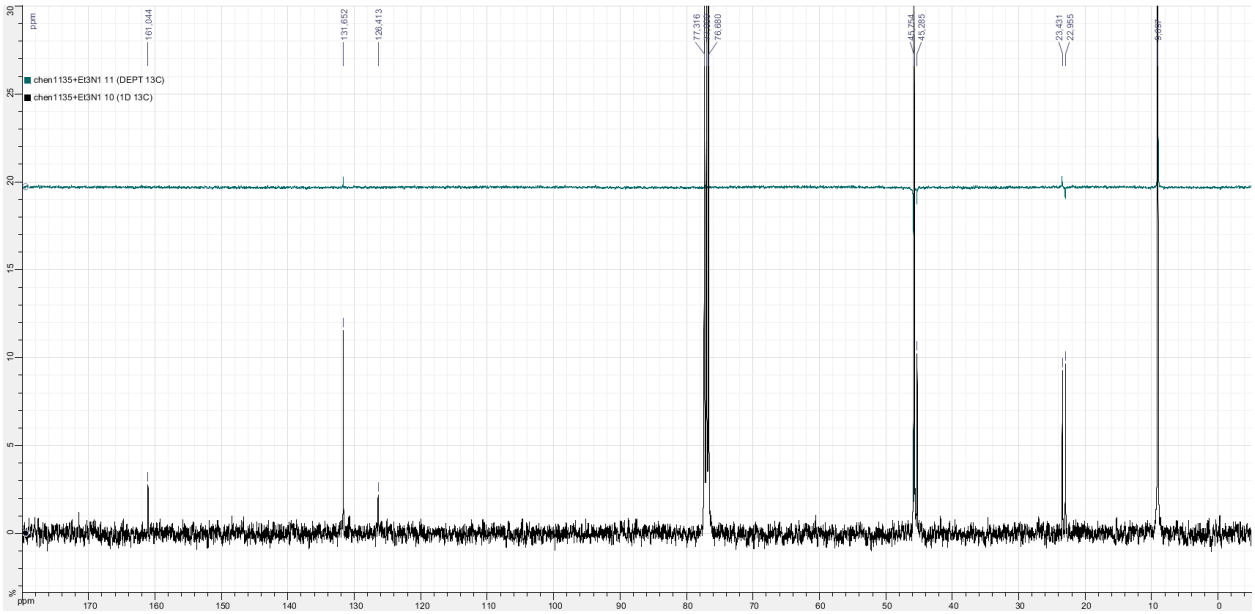
^{1}H NMR ($CDCl_3$, 400 MHz): δ 2.17 (3 H, t, *J* 1.5, H6), 2.23 (2 H, td, *J* 9.0, 5.0, H2), 3.53 (2 H, tq, *J* 9.0, 1.5, H1), 6.38 (1 H, t, *J* 5.0, H3). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 23.0 (C2), 23.4 (C6), 45.3 (C1), 126.4 (C4), 131.7 (C3), 161.0 (C5).

Note: this compound was directly observed by NMR as a solution in $CDCl_3$ but was not isolated.



^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

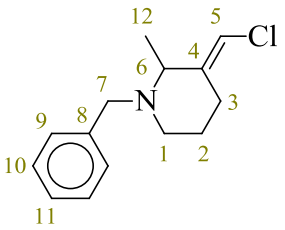
Note: on top, in green, is displayed the spectrum of the starting material **3d**, before addition of several equivalents of triethylamine. The spectrum of the solution after addition of Et_3N is shown at the bottom, in black. The signals of triethylamine / triethylamine hydrochloride are visible, together with those of the product **6d**.



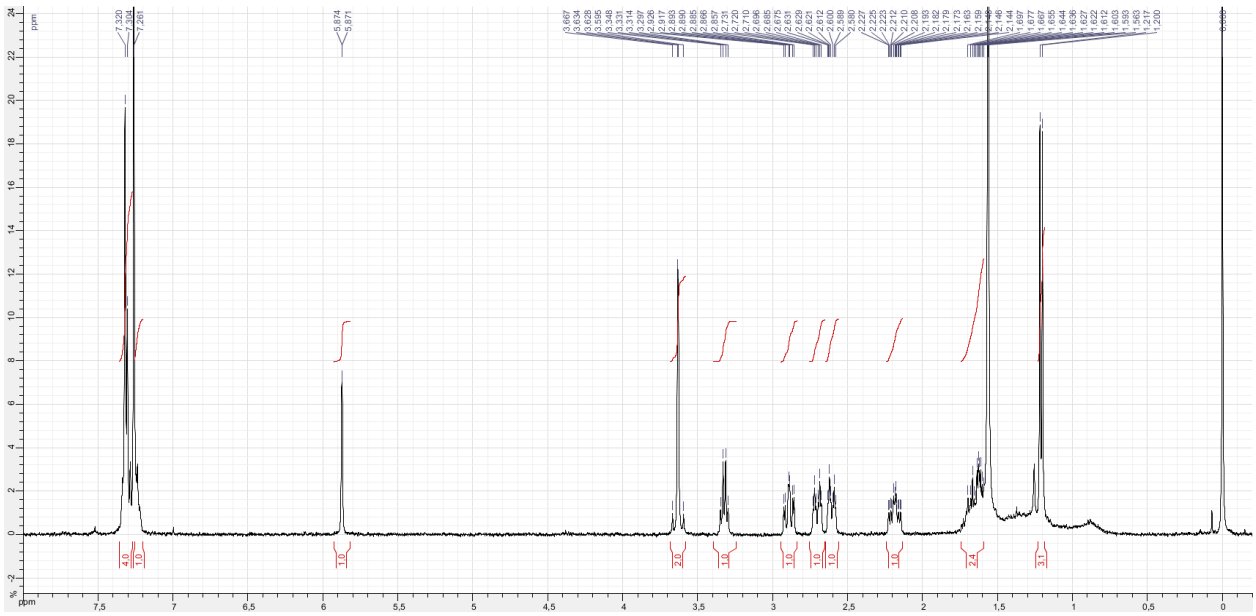
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

Note: the signals of triethylamine / triethylamine hydrochloride are visible, together with those of the product **6d**.

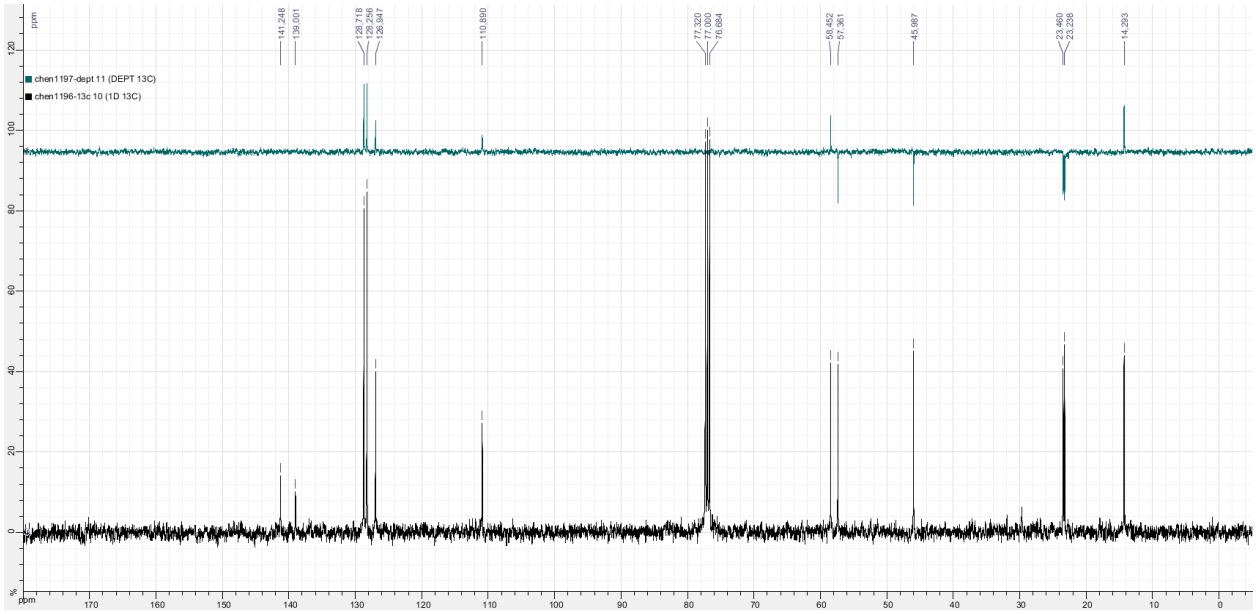
(*E*)-1-Benzyl-3-(chloromethylene)-2-methyl-piperidine **7ea**



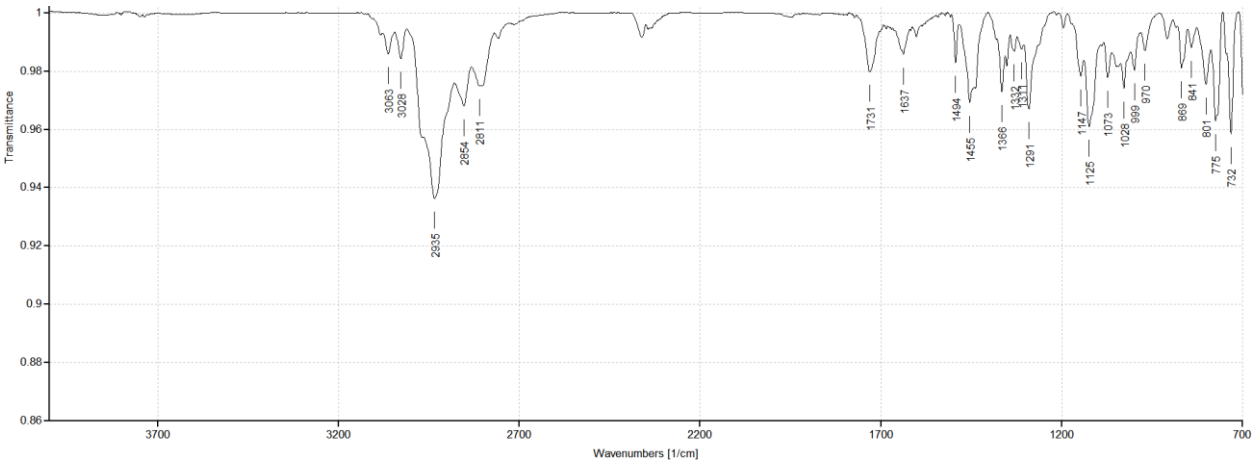
Pale yellow oil. R_f 0.15 [EtOAc/petroleum ether 5%, anisaldehyde (white spot), UV-active]. IR (neat) *v* 3063 (w), 3028 (w), 2935 (s), 2854 (m), 2811 (m), 1731 (w), 1637 (w), 1494 (w), 1455 (m), 1366 (m), 1291 (m), 1125 (m), 1028 (m), 775 (m), 732 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz): δ 1.21 (3 H, d, *J* 7.0, H12), 1.55−1.74 (2 H, m, H2), 2.19 (1 H, dddd, *J* 14.0, 12.0, 5.5, 1.5, H3a), 2.61 (1 H, dt, *J* 13.0, 3.5, H1a), 2.70 (1 H, dt, *J* 14.0, 4.0, H3b), 2.89 (1 H, ddd, *J* 13.0, 11.0, 3.5, H1b), 3.32 (1 H, qdd, *J* 7.0, 1.5, 1.0, H6), 3.63 (2 H, AB system, δ_A 3.62, δ_B 3.64, J_{AB} 14.0, H7), 5.87 (1 H, d, *J* 1.0, H5), 7.24 (1 H, br t, *J* 7.0, H11), 7.31 (2 H, br dd, *J* 7.5, 7.0, H10), 7.34 (2 H, br d, *J* 7.5, H9). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 14.3 (C12), 23.2, 23.5 (C2, C3), 46.0 (C1), 57.4 (C7), 58.5 (C6), 110.9 (C5), 126.9 (C11), 128.3, 128.7 (C9, C10), 139.0 (C8), 141.2 (C4). MS (positive CI, NH_3): *m/z* 208, 220, <u>236</u> (MH^+ with ^{35}Cl), 237, 238 (MH^+ with ^{37}Cl), 239. MS (EI): *m/z* 117, 149, <u>220</u> ($[M–Me]^+$ with ^{35}Cl), 221, 222 ($[M–Me]^+$ with ^{37}Cl), 235 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 235.1131 ($M^{+\bullet}$ $C_{14}H_{18}{}^{35}ClN^{+\bullet}$ requires 235.1123).



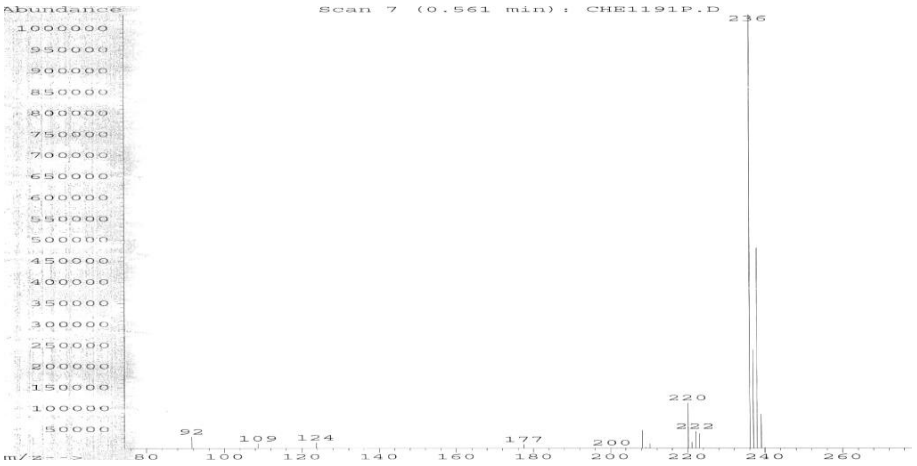
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



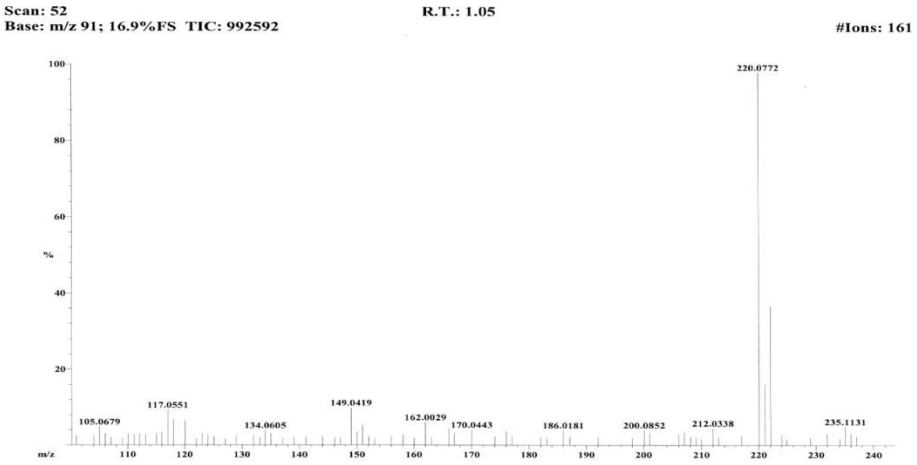
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

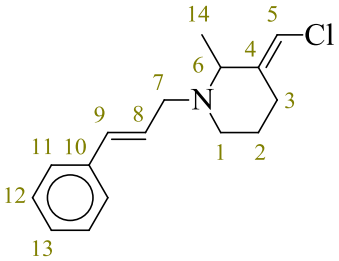


MS spectrum (CI, NH_3).

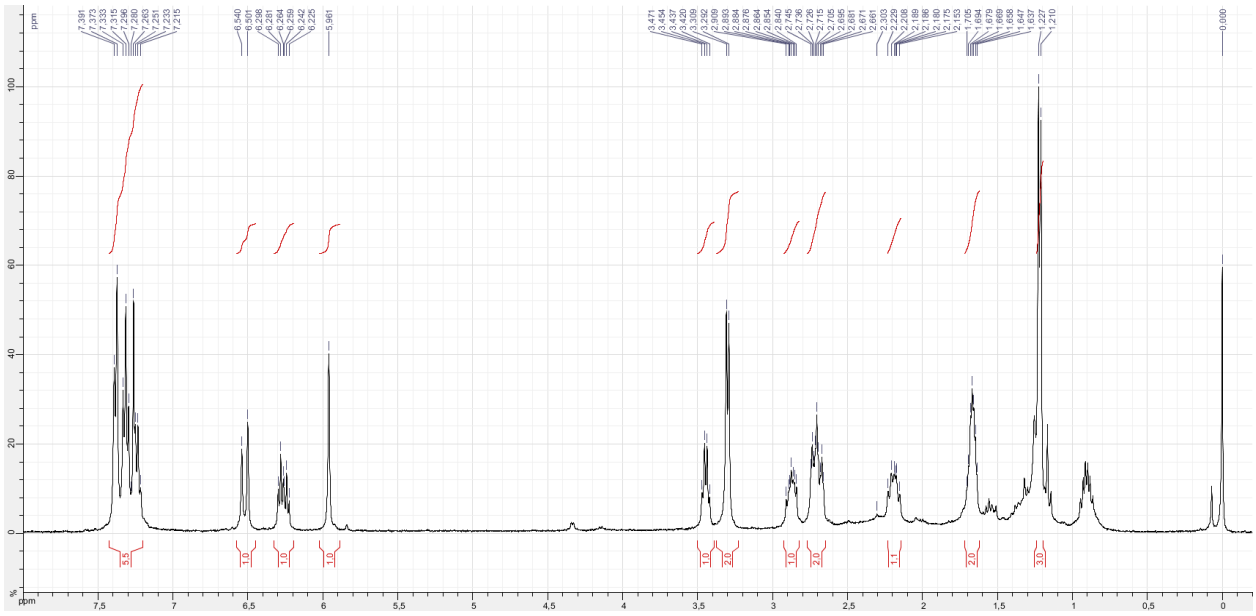


MS spectrum (EI).

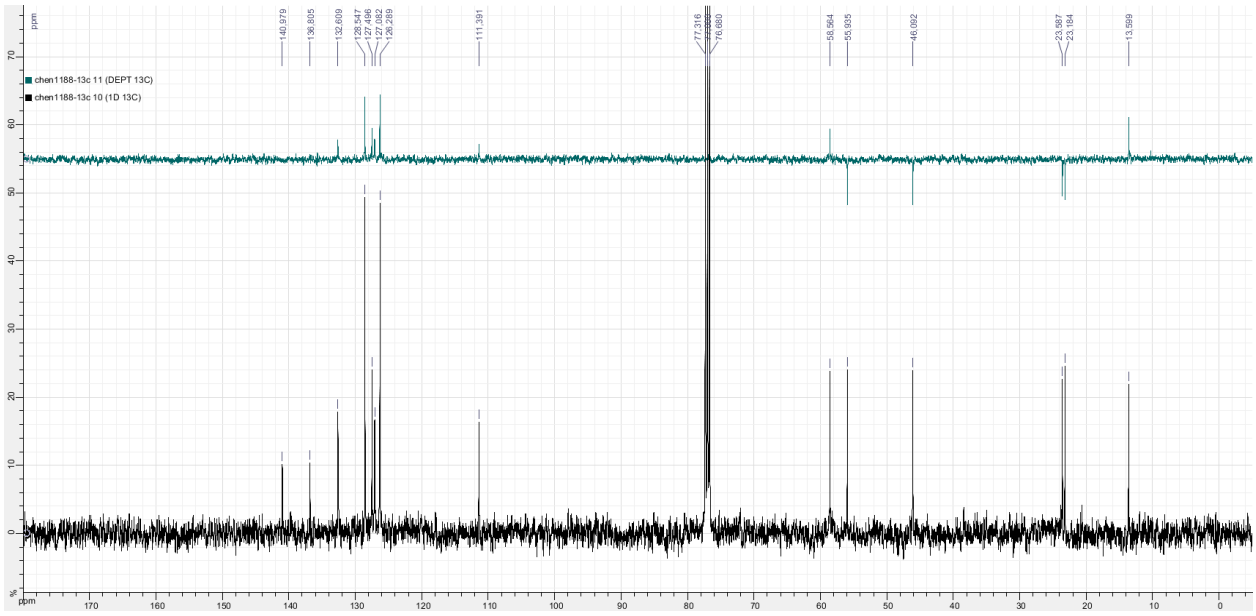
(*E*)-3-(Chloromethylene)-1-[(*E*)-cinnamyl]-2-methyl-piperidine **7eb**



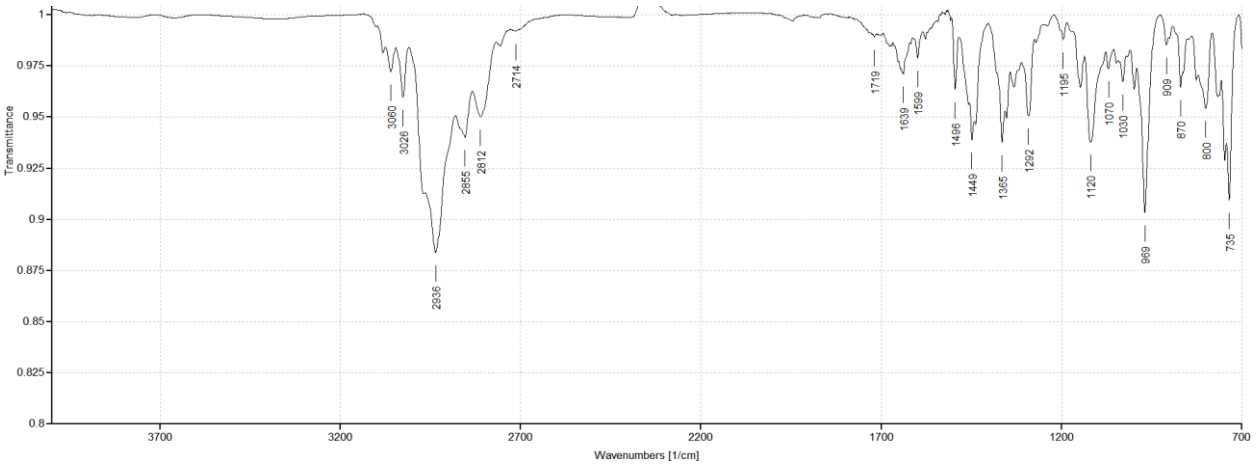
Pale yellow oil. R_f 0.2 [EtOAc/petroleum ether 30%, anisaldehyde (white spot), UV-active]. IR (neat) *v* 3060 (w), 3026 (w), 2936 (s), 2855 (m), 2812 (w), 1639 (w), 1496 (w), 1449 (m), 1365 (m), 1292 (m), 1120 (m), 969 (m), 800 (w), 735 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.22 (3 H, d, *J* 6.5, H14), 1.67 (2 H, m, H2), 2.19 (1 H, m, H3a), 2.65−2.76 (2 H, m, H3b, H1a), 2.87 (1 H, ddd, *J* 13.0, 9.0, 5.5, H1b), 3.30 (2 H, br d, *J* 6.5, H7), 3.45 (1 H, q, *J* 6.5, H6), 5.96 (1 H, s, H5), 6.39 (2 H, AB part of an ABX_2 system, δ_A 6.26, δ_B 6.52, J_{AB} 15.5, J_{AX} 6.5, J_{BX} 0.0, H8, H9), 7.23 (1 H, br t, *J* 7.0, H13), 7.31 (2 H, br dd, *J* 7.5, 7.0, H12), 7.38 (2 H, br d, *J* 7.5, H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 13.6 (C14), 23.2 (C3), 23.6 (C2), 46.1 (C1), 55.9 (C7), 58.6 (C6), 111.4 (C5), 126.3 (C11), 127.1 (C8), 127.5 (C13), 128.6 (C12), 132.6 (C9), 136.8 (C10), 141.0 (C4). MS (positive CI, NH_3): *m/z* 246, 248, 262 (MH^+ with ^{35}Cl), 263, 264 (MH^+ with ^{37}Cl), 265. MS (EI): *m/z* 115, 117, 118, 162, 246 ($[M–Me]^+$ with ^{35}Cl), 248 ($[M–Me]^+$ with ^{37}Cl), 261 ($M^{+\bullet}$ with ^{35}Cl). HRMS (EI): *m/z* 261.1284 ($M^{+\bullet}$ $C_{16}H_{20}{}^{35}ClN^{+\bullet}$ requires 261.1279).



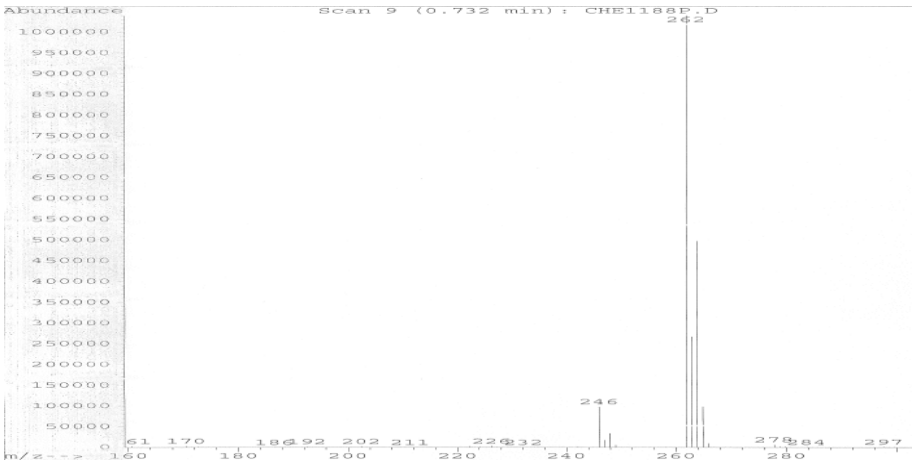
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



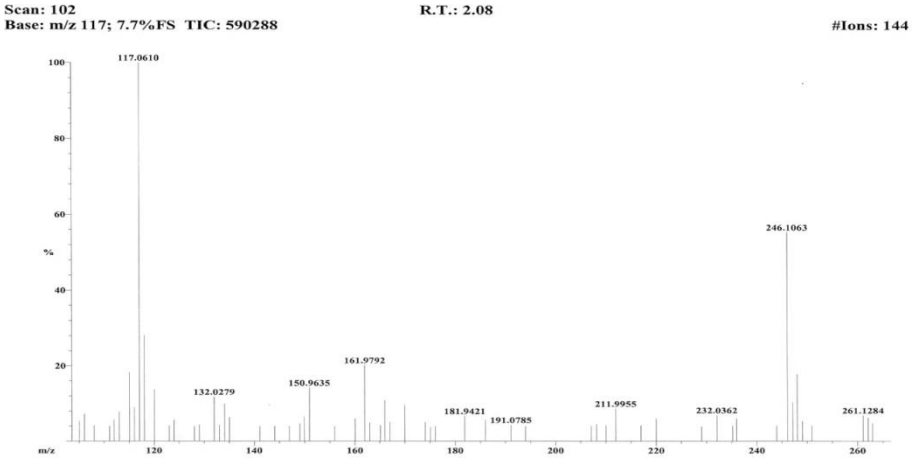
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.

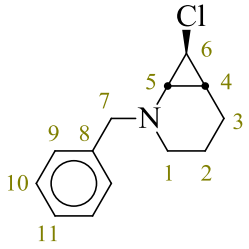


MS spectrum (CI, NH_3).

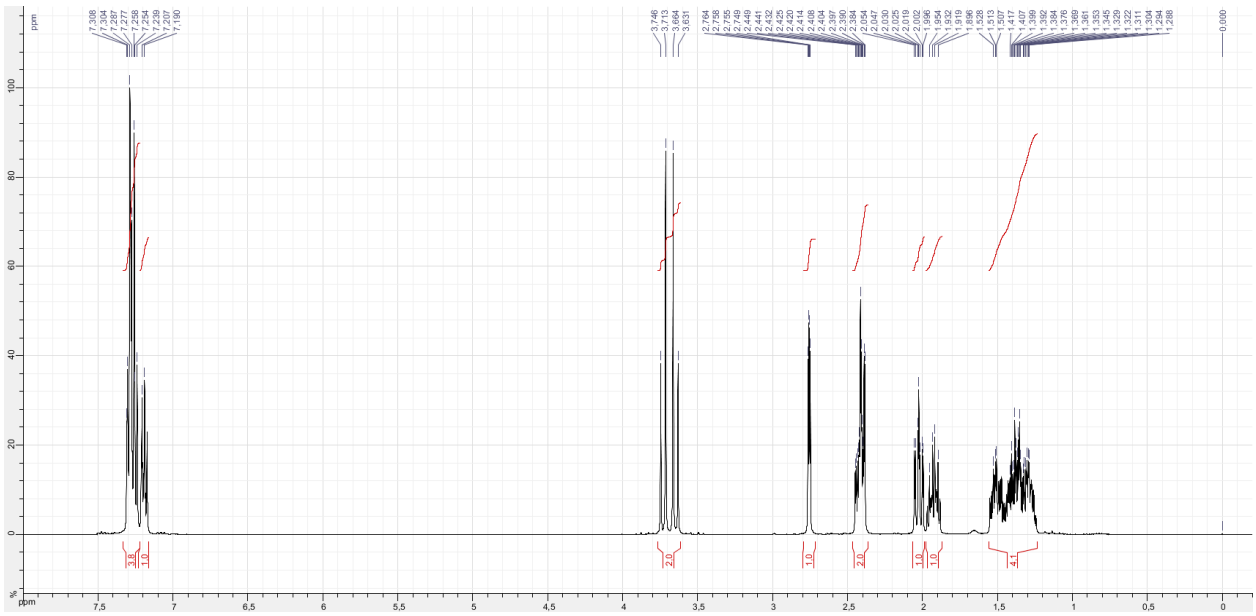


MS spectrum (EI).

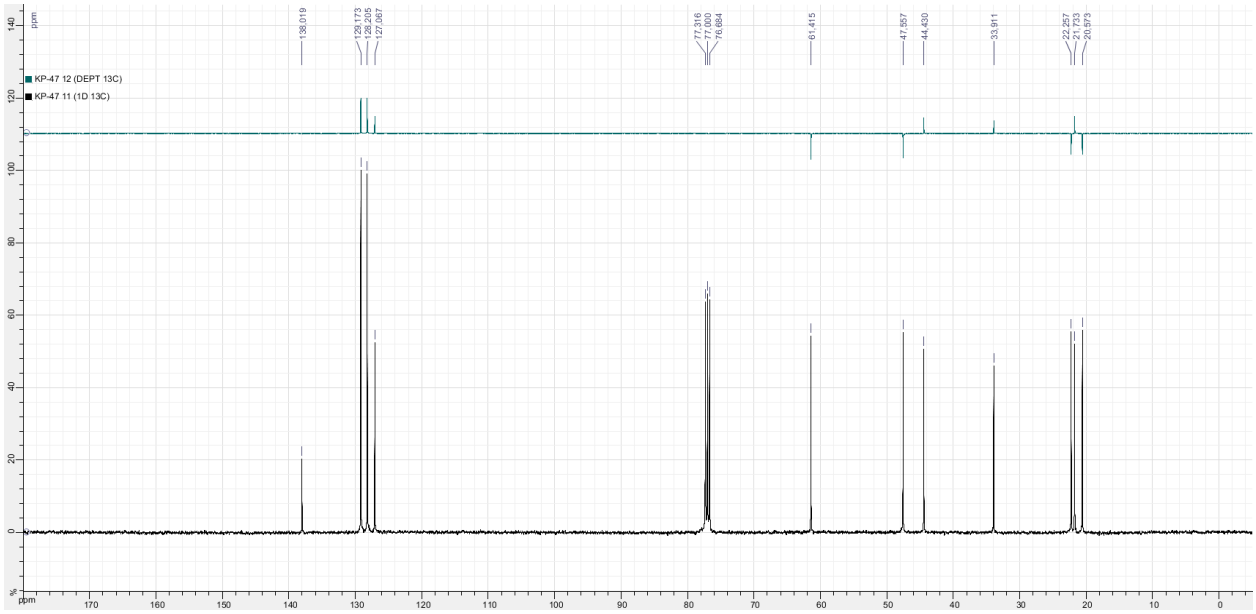
(1*R**,6*S**,7*R**)-2-Benzyl-7-chloro-2-azabicyclo[4.1.0]heptane *exo*-**10**



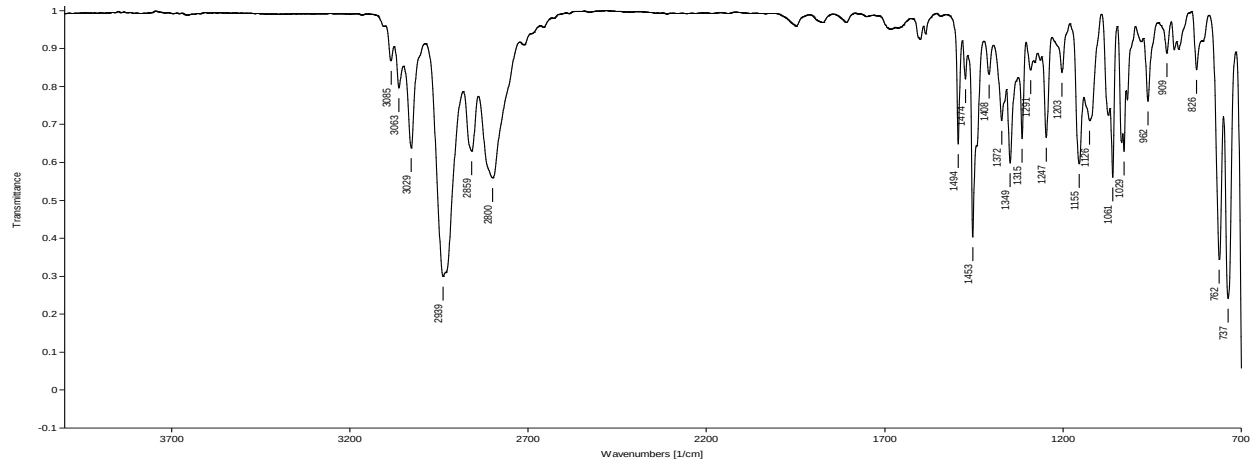
Colourless oil. R_f 0.5 [EtOAc/petroleum ether 10%, $KMnO_4$, UV-active]. IR (neat) ν 3029 (m), 2939 (s), 2859 (m), 2800 (m), 1494 (m), 1453 (s), 1349 (m), 1315 (m), 1247 (m), 1155 (m), 1061 (m), 1029 (m), 762 (s), 737 (s) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 1.28 (1 H, ddtd, J 13.0, 6.5, 5.5, 2.5, H2a), 1.35 (1 H, dddd, J 9.5, 9.0, 3.5, 2.5, H4), 1.42 (1 H, ddddd, J 13.0, 9.5, 9.0, 5.5, 3.0, H2b), 1.51 (1 H, dddd, J 14.0, 9.0, 5.5, 2.5, H3a), 1.93 (1 H, ddt, J 14.0, 9.0, 5.5, H3b), 2.02 (1 H, ddd, J 11.5, 9.5, 2.5, H1a), 2.40 (1 H, dd, J 9.5, 2.5, H5), 2.42 (1 H, ddd, J 11.5, 6.5, 3.0, H1b), 2.76 (1 H, dd, J 3.5, 2.5, H6), 3.69 (2 H, AB system, δ_A 3.65, δ_B 3.73, J_{AB} 13.0, H7), 7.19 (1 H, br t, J 7.0, H11), 7.23−7.32 (4 H, m, H9−H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 20.6 (C3), 21.7 (C4), 22.3 (C2), 33.9 (C6), 44.4 (C5), 47.6 (C1), 61.4 (C7), 127.1 (C11), 128.2 (C10), 129.2 (C9), 138.0 (C8). MS (EI): *m/z* 91 (Bn^+), 92, 94, 95, 102, 186 ($[M-Cl]^+$), 187, 220, 221 ($M^{+\bullet}$ with ^{35}Cl), 222. HRMS (EI): *m/z* 186.1273 ($[M-Cl]^+$ $C_{13}H_{16}N^+$ requires 186.1278), 221.0989 ($M^{+\bullet}$ $C_{13}H_{16}{}^{35}ClN^{+\bullet}$ requires 221.0966).



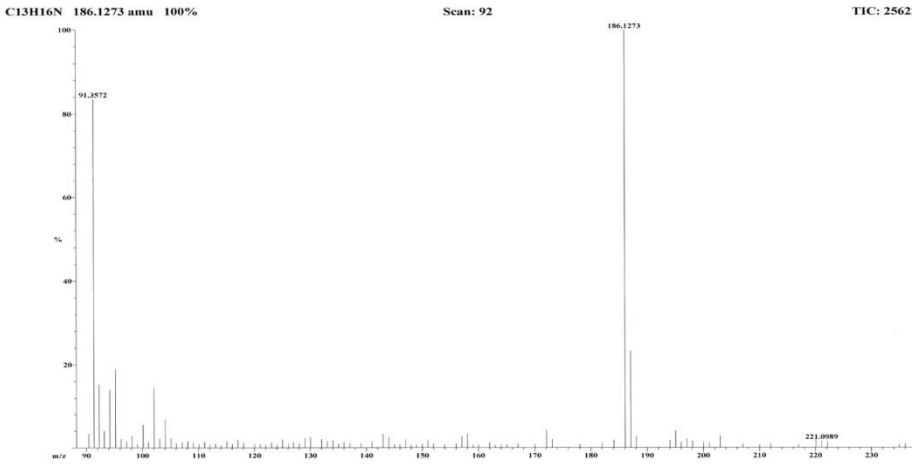
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

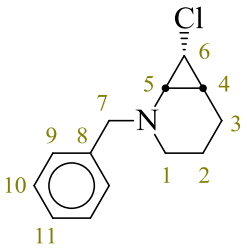


IR spectrum.



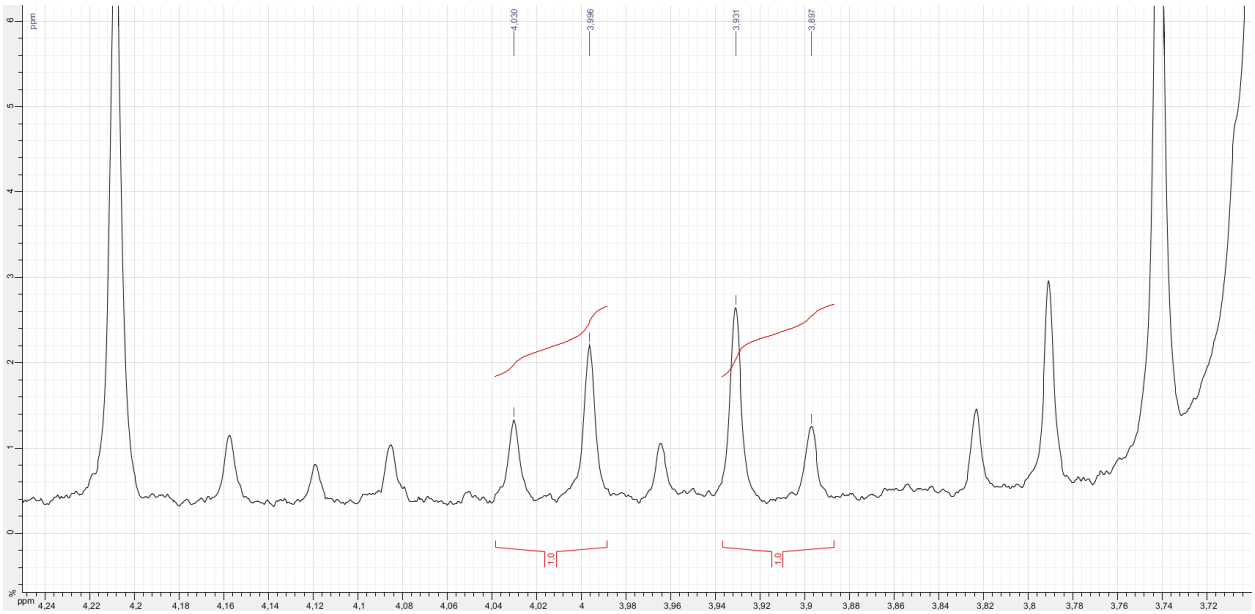
MS spectrum (EI).

(1*R**,6*S**,7*S**)-2-Benzyl-7-chloro-2-azabicyclo[4.1.0]heptane *endo*-**10**



^{1}H NMR ($CDCl_3$, 400 MHz), characteristic signal: 3.96 (2 H, AB system, δ_A 3.92, δ_B 4.01, J_{AB} 13.5, H7).

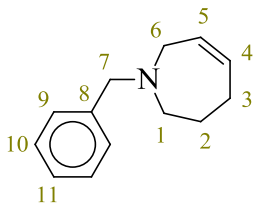
Note: the AB system described above, observed in a $CDCl_3$ solution of a crude product, has been tentatively assigned to this structure but no other experimental confirmation was obtained.



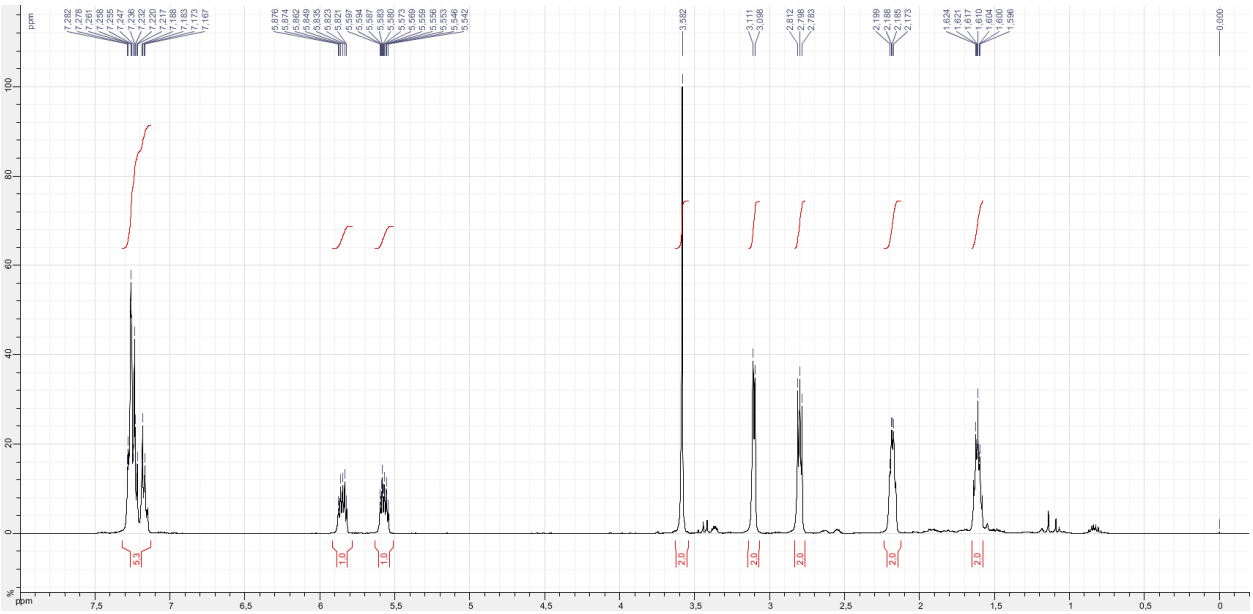
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

Note: this is the spectrum of a crude product. Only the part where the characteristic AB system lies is displayed.

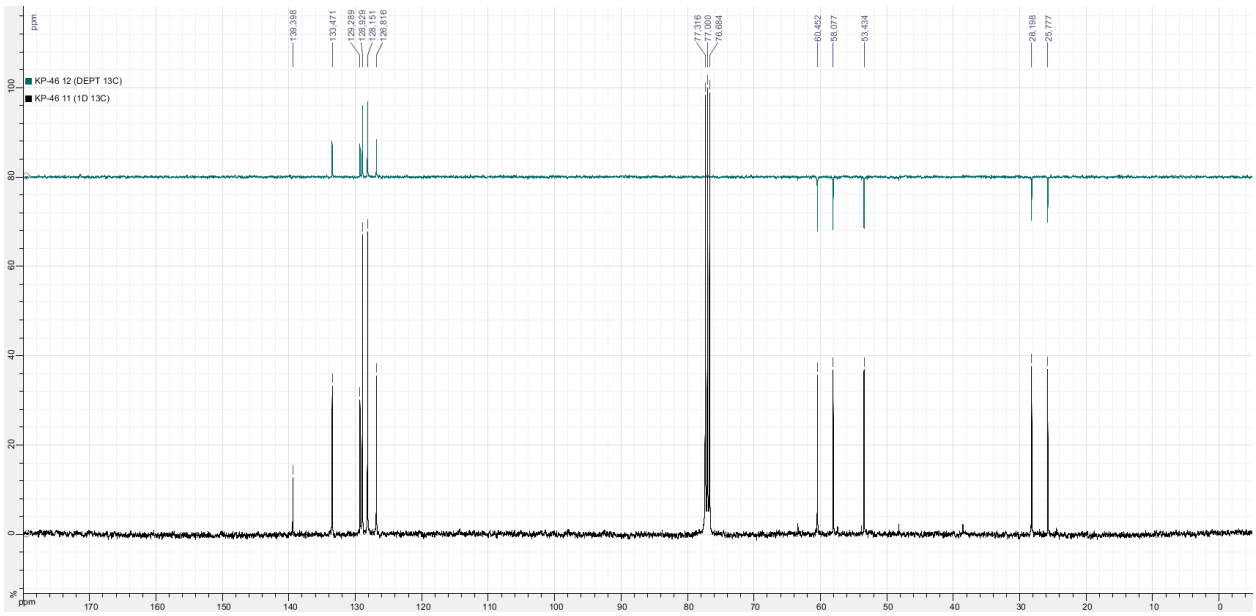
1-Benzyl-2,3,4,7-tetrahydroazepine **11**



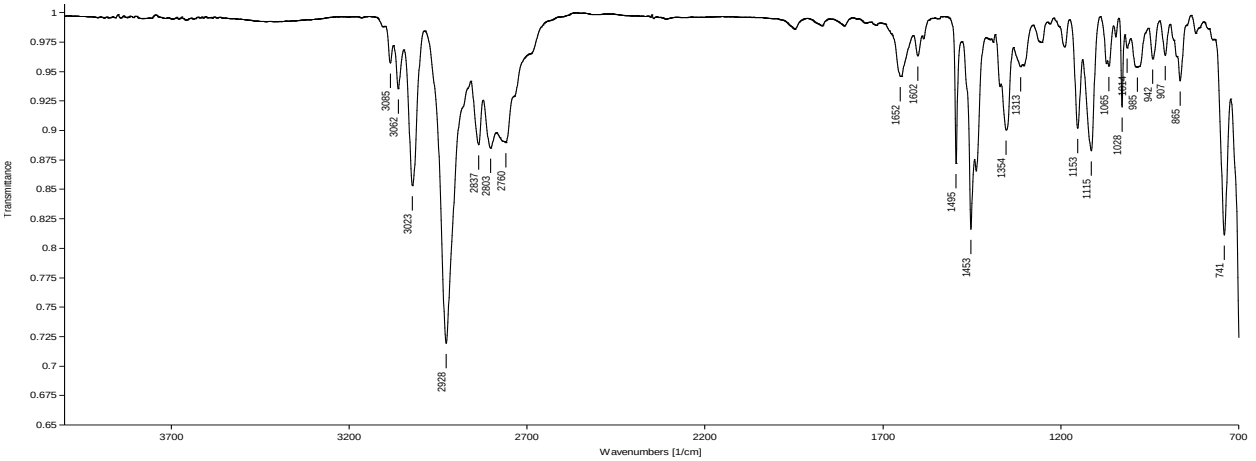
Colourless oil. R_f 0.4 [EtOAc/petroleum ether 20%, $KMnO_4$, not UV-active]. IR (neat) ν 3023 (m), 2928 (s), 2837 (m), 2803 (m), 2760 (m), 1652 (w), 1495 (m), 1453 (m), 1354 (m), 1153 (m), 1115 (m), 1028 (w), 741 (m) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz): δ 1.61 (2 H, distorted quint, J 5.5, H2), 2.18 (2 H, br qd, J 5.5, 1.0, H3), 2.80 (2 H, distorted t, J 5.5, H1), 3.10 (2 H, dd, J 5.5, 1.0, H6), 3.58 (2 H, s, H7), 5.57 (1 H, dtt, J 11.0, 5.5, 1.0, H5), 5.85 (1 H, dtt, J 11.0, 5.5, 1.0, H4), 7.14−7.30 (5 H, m, H9−H11). ^{13}C NMR ($CDCl_3$, 100.6 MHz): δ 25.8 (C2), 28.2 (C3), 53.4 (C6), 58.1 (C1), 60.5 (C7), 126.8 (C11), 128.2, 128.9 (C9, C10), 129.3 (C5), 133.5 (C4), 139.4 (C8). MS (EI): *m/z* 91 (Bn^+), 92, 96, 110, 120, 131, 172, 186, 187 ($M^{+\bullet}$), 188. HRMS (EI): *m/z* 187.1354 ($M^{+\bullet}$ $C_{13}H_{17}N^{+\bullet}$ requires 187.1356).



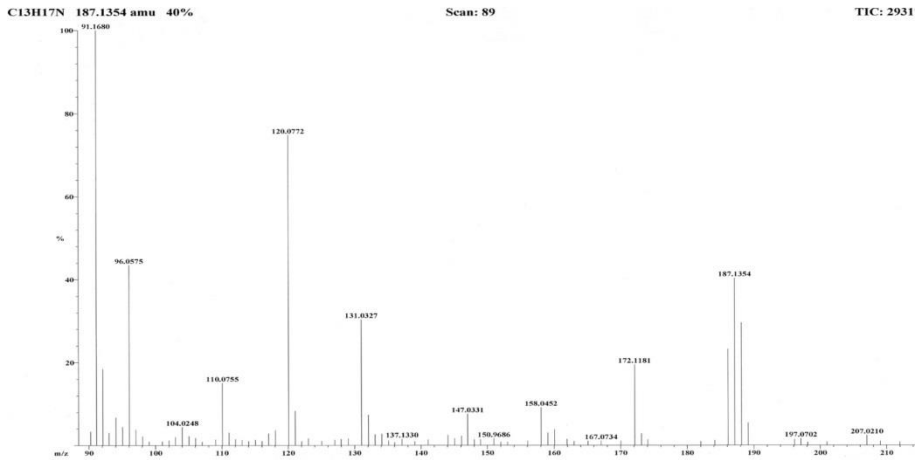
^1H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

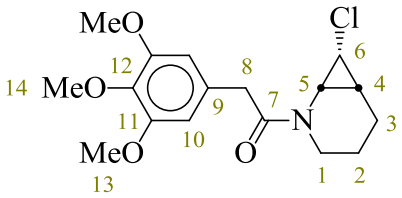


IR spectrum.

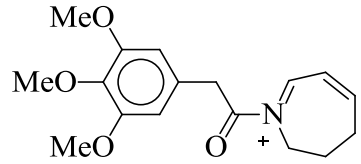


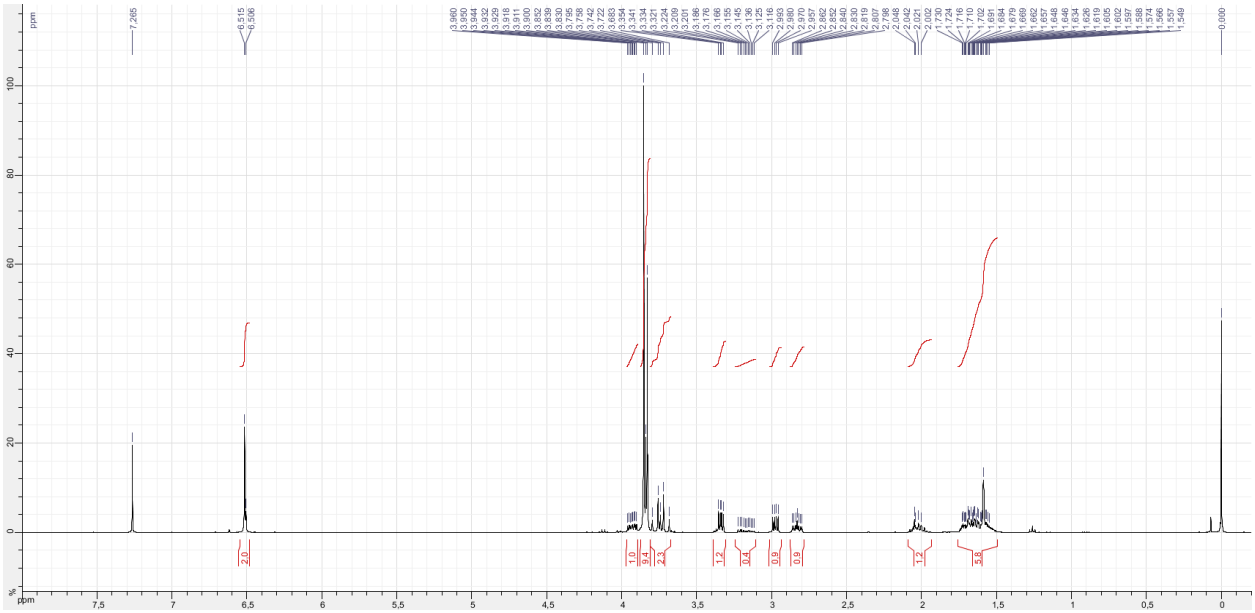
MS spectrum (EI).

1-[(1*R**,6*S**,7*S**)-7-Chloro-2-azabicyclo[4.1.0]heptan-2-yl]-2-(3,4,5-trimethoxyphenyl)ethanone *endo*-**14**

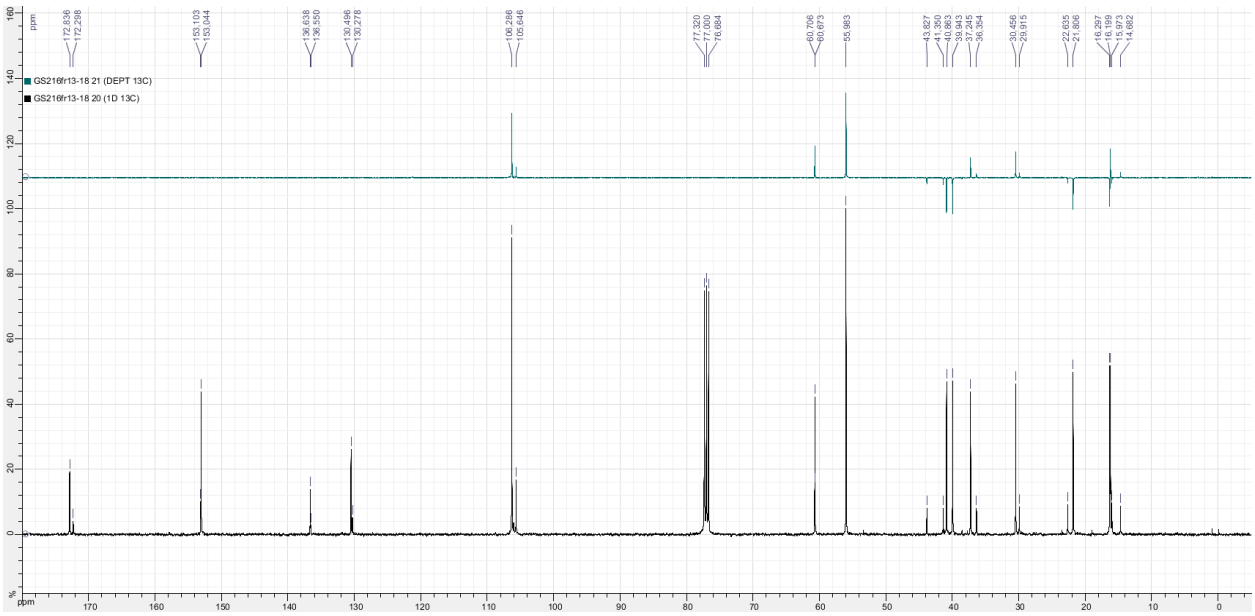


Thick pale yellow oil. R_f 0.1 [EtOAc/petroleum ether 50%, anisaldehyde, UV-active]. IR (neat) *v* 2996 (w), 2939 (m), 2871 (w), 2838 (w), 1651 (s, C=O), 1590 (m), 1508 (m), 1457 (m), 1424 (m), 1334 (m), 1240 (m), 1125 (s), 1008 (m), 789 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz), 84:16 mixture of two rotamers. Major rotamer: δ 1.50−1.75 (4H, m, H2, H3a, H4), 2.02 (1H, m, H3b), 2.83 (1H, ddd, *J* 13.0, 8.5, 3.5, H1a), 2.98 (1H, dd, *J* 9.5, 5.0, H6), 3.34 (1H, dd, *J* 8.0, 5.0, H5), 3.74 (2 H, AB system, δ_A 3.71, δ_B 3.77, J_{AB} 15.0, H8), 3.83 (3H, s, H14), 3.85 (6H, s, H13), 3.93 (1H, ddd, *J* 13.0, 6.5, 4.0, H1b), 6.51 (2H, s, H10). Minor rotamer, characteristic signals: δ 3.15 (1H, ddd, *J* 12.0, 8.0, 4.0, H1a), 3.21 (1H, dd, *J* 9.0, 6.0, H6), 3.35 (1 H, m, H1b), 6.51 (2H, s, H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz), 84:16 mixture of two rotamers. Major rotamer: δ 16.2 (C4), 16.3 (C3), 21.8 (C2), 30.5 (C6), 37.2 (C5), 39.9 (C1), 40.9 (C8), 56.0 (C13), 60.7 (C14), 106.3 (C10), 130.5 (C9), 136.6 (C12), 153.0 (C11), 172.8 (C7). Minor rotamer: δ 14.7 (C4), 16.0 (C3), 22.6 (C2), 29.9 (C6), 36.4 (C5), 41.3 (C8), 43.8 (C1), 56.0 (C13), 60.7 (C14), 105.6 (C10), 130.3 (C9), 136.5 (C12), 153.1 (C11), 172.3 (C7). MS (EI): *m/z* 96, 97, 181, 182, 208, 244, 246, 304 ($[M-Cl]^+$),[a] 339 ($M^{+\bullet}$ with ^{35}Cl), 341 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 339.1228 ($M^{+\bullet}$ $C_{17}H_{22}{}^{35}ClNO_4{}^{+\bullet}$ requires 339.1232).

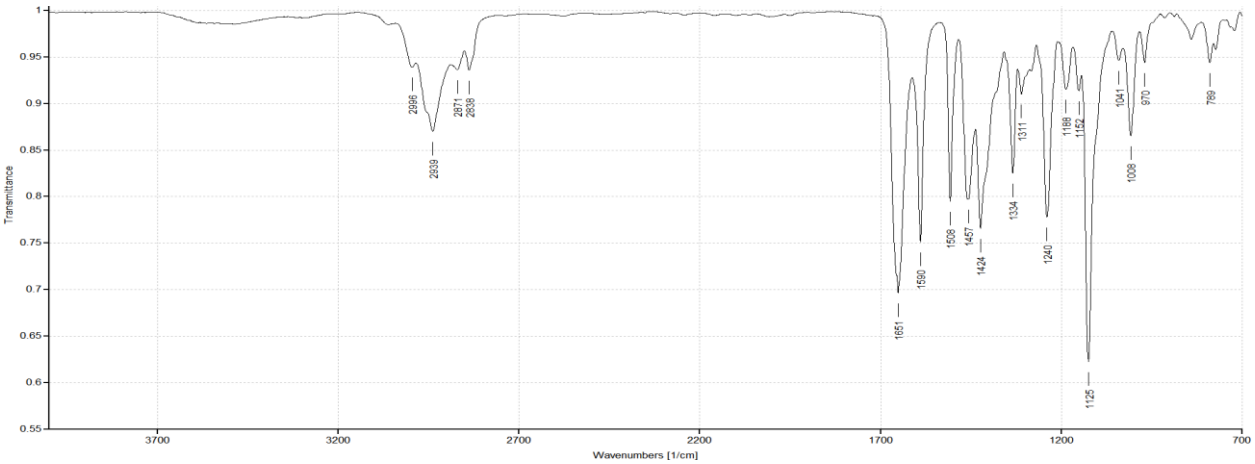
[a] $[M-Cl]^+$ =  (tentative assignment)



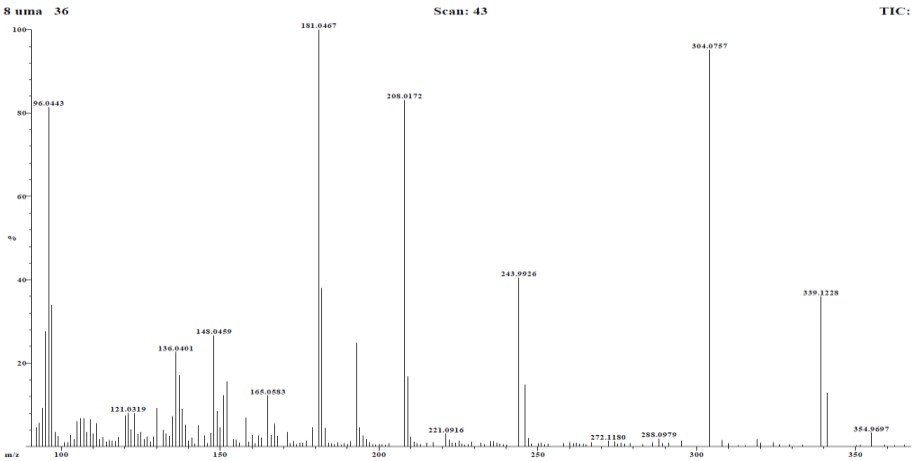
^1H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).

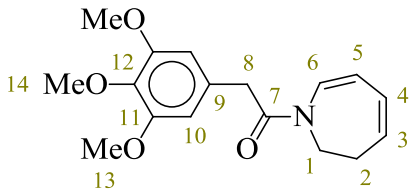


IR spectrum.

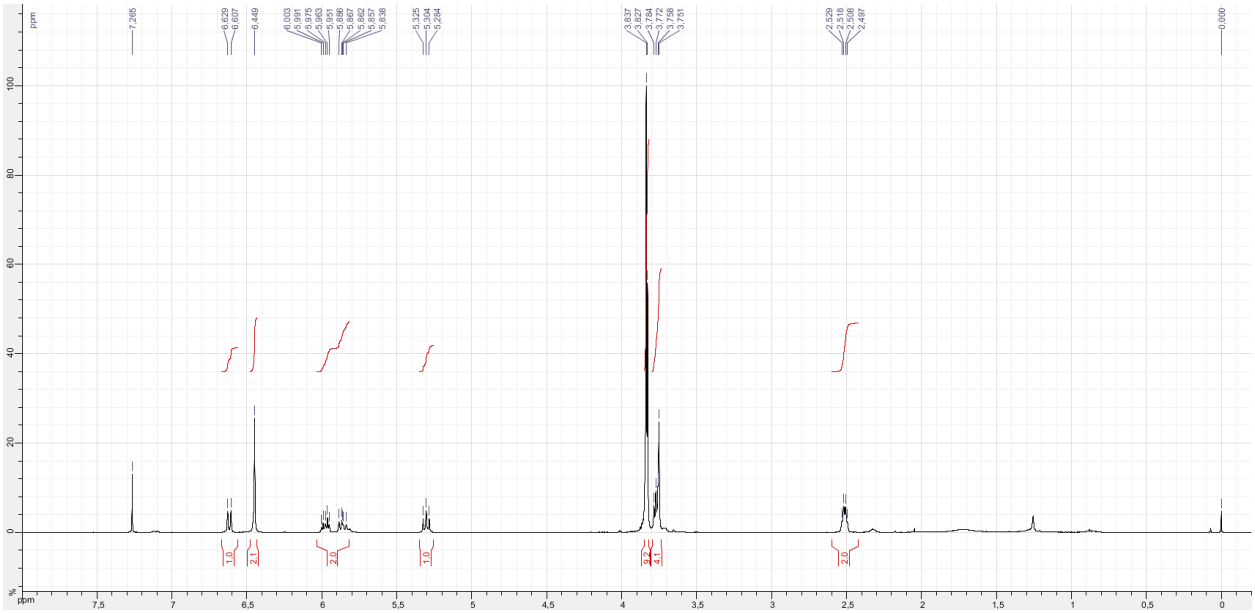


MS spectrum (EI).

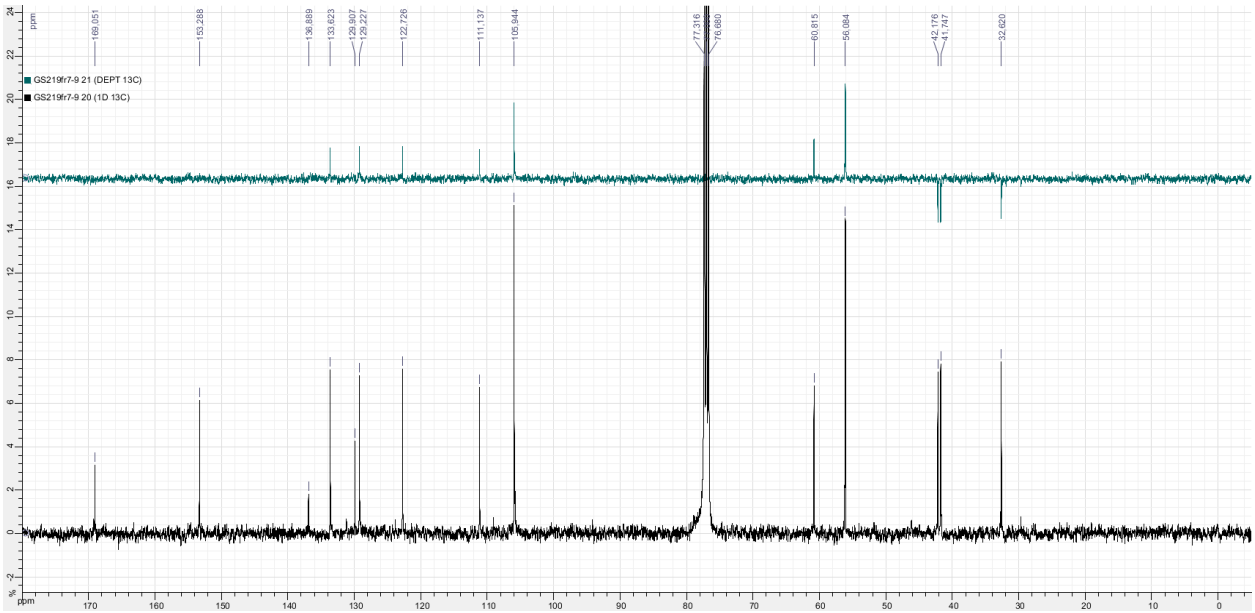
1-(2,3-Dihydroazepin-1-yl)-2-(3,4,5-trimethoxyphenyl)ethanone **15**



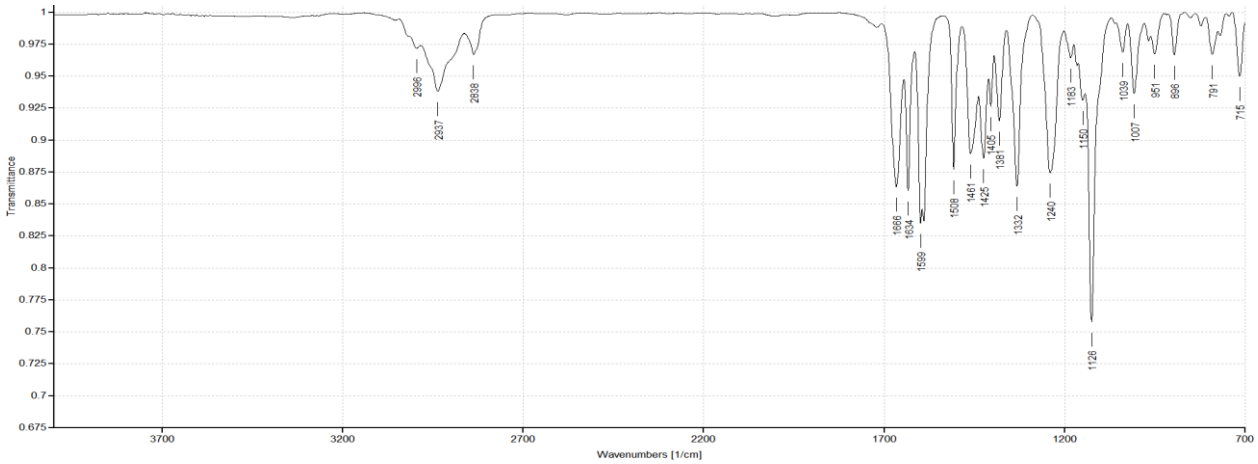
Pale yellow oil. R_f 0.15 [EtOAc/petroleum ether 20%, anisaldehyde, UV-active]. IR (neat) *v* 2996 (w), 2937 (w), 2838 (w), 1666 (m, C=O), 1634 (m), 1599 (m), 1591 (m), 1508 (m), 1461 (m), 1425 (m), 1332 (m), 1240 (m), 1126 (s), 1007 (w), 715 (w) cm^{-1}. ^1H NMR ($CDCl_3$, 400 MHz) δ 2.51 (2H, qd, *J* 5.0, 1.5, H2), 3.75 (2H, s, H8), 3.77 (2H, t, *J* 5.0, H1), 3.83 (3H, s, H14), 3.84 (6H, s, H13), 5.30 (1H, dd, *J* 9.0, 7.5, H5), 5.86 (1H, ddt, *J* 11.5, 7.5, 1.5, H4), 5.98 (1H, dt, *J* 11.5, 5.0, H3), 6.45 (2H, s, H10), 6.62 (1H, d, *J* 9.0, H6). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 32.6 (C2), 41.7 (C8), 42.2 (C1), 56.1 (C13), 60.8 (C14), 105.9 (C10), 111.1 (C5), 122.7 (C4), 129.2 (C6), 129.9 (C9), 133.6 (C3), 136.9 (C12), 153.3 (C11), 169.1 (C7). MS (EI): *m/z* 95, 97, 109, 111, 121, 123, 125, 135, 147, 193, 208, 221, 303 ($M^{+\bullet}$).



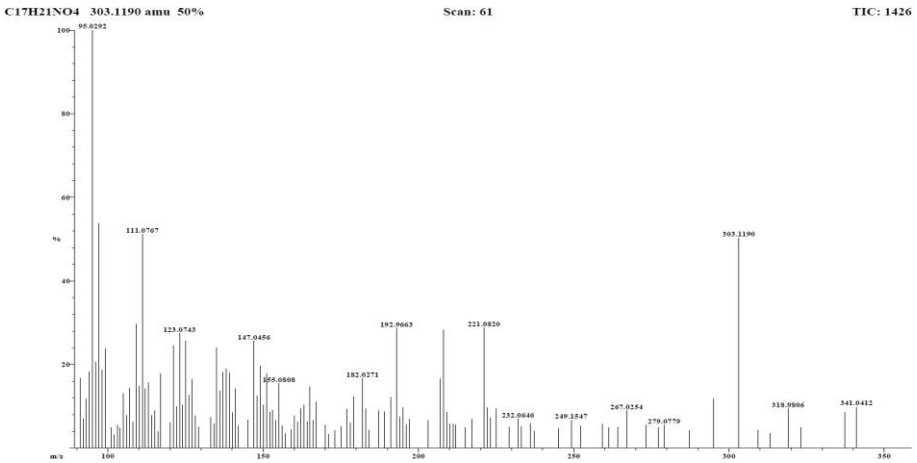
^1H NMR spectrum ($CDCl_3$, 400 MHz).



^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (EI).

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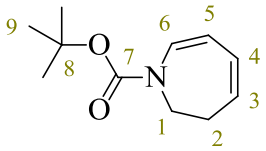
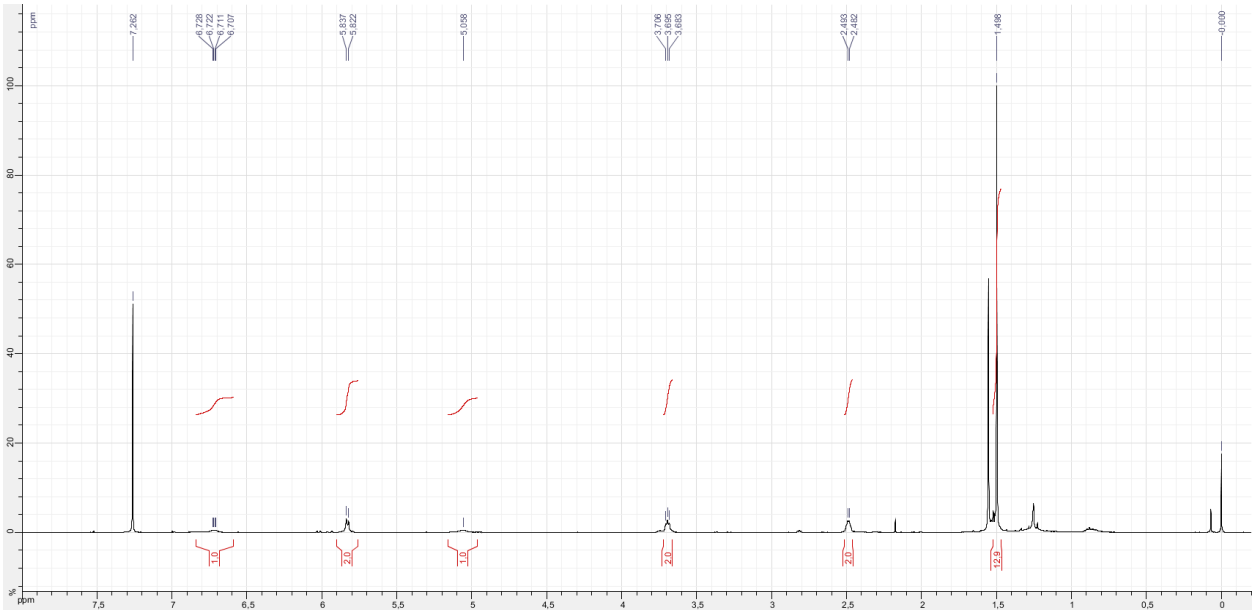
tert-Butyl 2,3-dihydroazepine-1-carboxylate

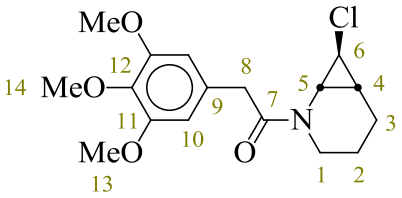


Colourless oil. R_f 0.8 [EtOAc/petroleum ether 5%]. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.50 (9 H, s, H9), 2.49 (2H, br td, *J* 4.5, 3.5, H2), 3.69 (2H, br t, *J* 4.5, H1), 5.06 (1H, br s, H5), 5.78−5.88 (2H,m, H3−H4), 6.72 (1H, br d, *J* 6.5, H6).



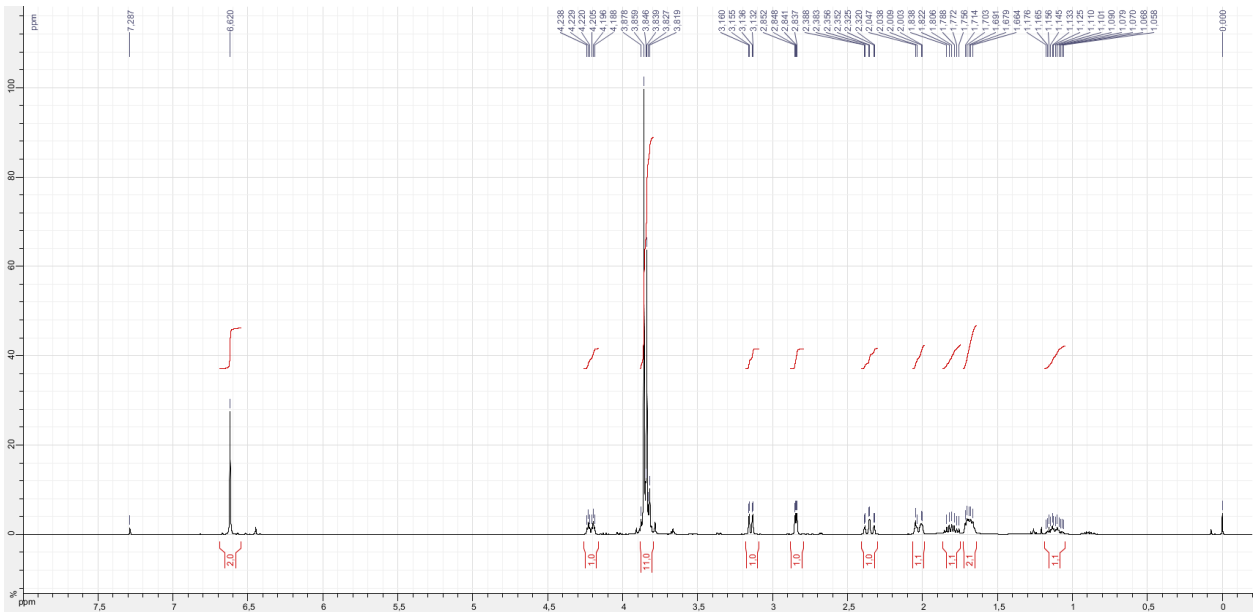
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).

1-[(1*R**,6*S**,7*R**)-7-Chloro-2-azabicyclo[4.1.0]heptan-2-yl]-2-(3,4,5-trimethoxyphenyl)ethanone *exo*-**14**

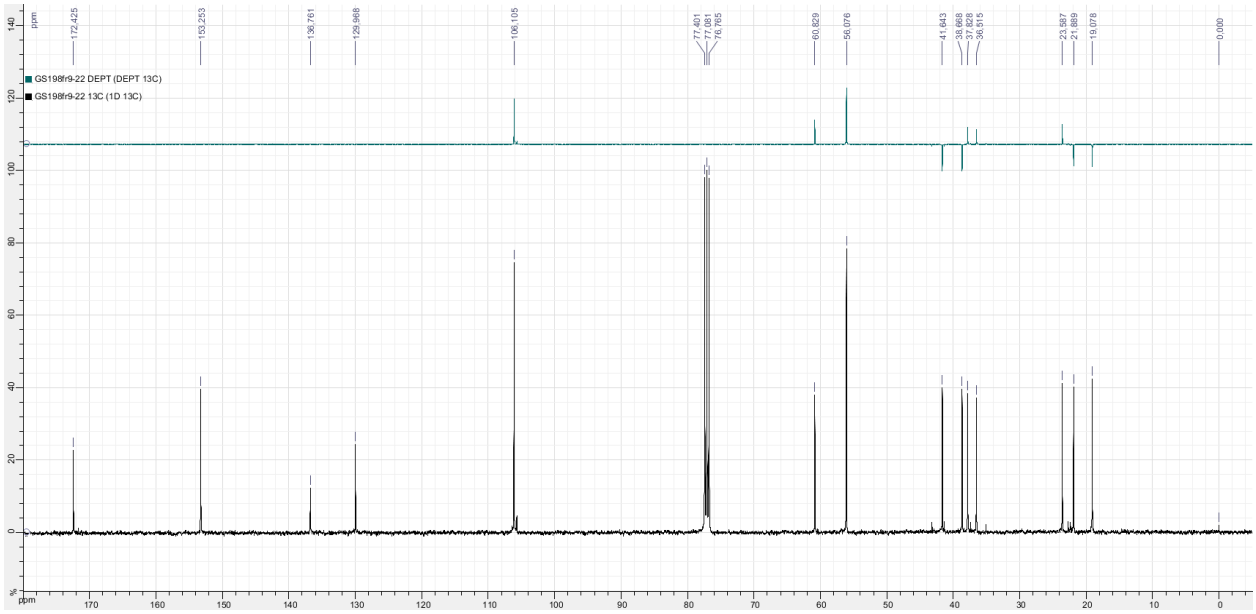


Pale yellow oil. R_f 0.2 [EtOAc/petroleum ether 50%, anisaldehyde, UV-active]. IR (neat) *v* 2996 (w), 2939 (m), 2869 (w), 2838 (w), 1656 (m, C=O), 1590 (m), 1507 (m), 1460 (m), 1424 (m), 1387 (m), 1334 (m), 1241 (m), 1183 (w), 1153 (w), 1126 (s), 1038 (w), 1007 (m) cm^{-1}. ^{1}H NMR ($CDCl_3$, 400 MHz) δ 1.12 (1 H, ddddd, *J* 13.5, 13.0, 12.0, 4.5, 3.5, H2a), 1.64−1.73 (2 H, m, H2b, H4), 1.81 (1 H, dddd, *J* 13.5, 13.0, 7.0, 5.5, H3a), 2.03 (1 H, br dd, *J* 13.5, 4.5, H3b), 2.35 (1 H, ddd, *J* 13.0, 12.0, 2.0, H1a), 2.84 (1 H, dd, *J* 4.5, 1.5, H6), 3.15 (1 H, dd, *J* 9.5, 1.5, H5), 3.81−3.89 (2 H, m, H8), 3.84 (3 H, s, H14), 3.86 (6 H, s, H13), 4.21 (1 H, dt, *J* 13.0, 3.5, H1b), 6.62 (2 H, s, H10). ^{13}C NMR ($CDCl_3$, 100.6 MHz) δ 19.1 (C3), 21.9 (C2), 23.6 (C4), 36.5 (C6), 37.8 (C5), 38.7 (C1), 41.6 (C8), 56.1 (C13), 60.8 (C14), 106.1 (C10), 130.0 (C9), 136.8 (C12), 153.3 (C11), 172.4 (C7). MS (ES-API): *m/z* 102, 274, 340 (MH^+ with ^{35}Cl), 342 (MH^+ with ^{37}Cl), 362 (MNa^+ with ^{35}Cl), 363, 364 (MNa^+ with ^{37}Cl).[16] MS (EI): *m/z* 97, 98, <u>180</u>, 181, 208, 245, 303, 304, 339 ($M^{+\bullet}$ with ^{35}Cl), 341 ($M^{+\bullet}$ with ^{37}Cl). HRMS (EI): *m/z* 339.1252 ($M^{+\bullet}$ $C_{17}H_{22}{}^{35}ClNO_4{}^{+\bullet}$ requires 339.1232).

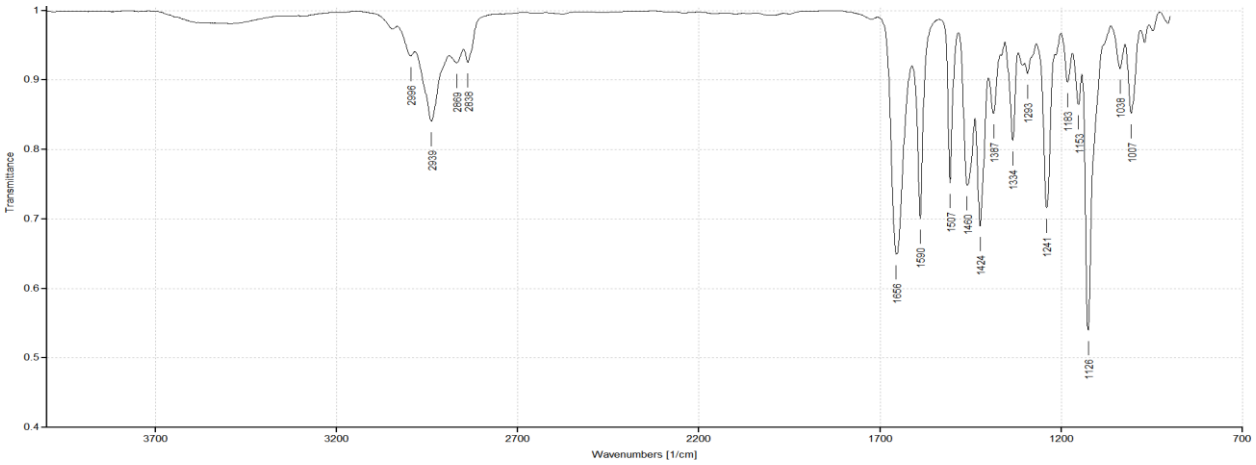
16− Peaks with higher *m/z* values were also observed, which we were not able to assign: 520.9, 690.3, <u>691.4</u>, 691.9, 692.3, 692.8, 693.3, 692.



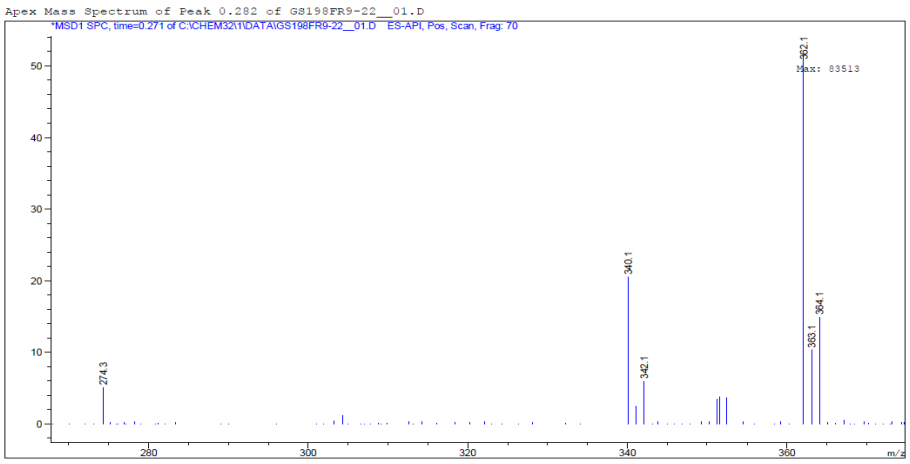
^{1}H NMR spectrum ($CDCl_3$, 400 MHz).



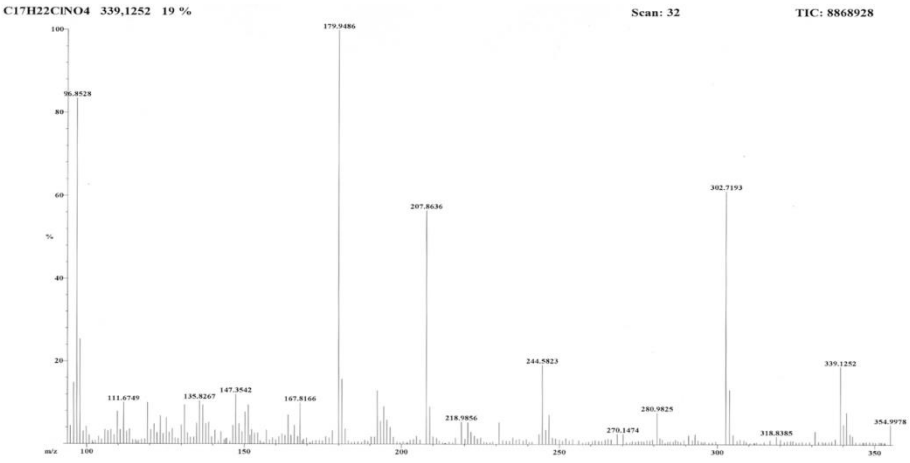
^{13}C NMR and DEPT135 spectra ($CDCl_3$, 100.6 MHz).



IR spectrum.



MS spectrum (ES-API).[16]



MS spectrum (EI).