Supporting Information

An Approach to New Chiral Bicyclic Imines and Amines *via* Horner–Wadsworth–Emmons reaction

Jakub Iwanejko, Mateusz Sowiński, Elżbieta Wojaczyńska,* and Tomasz K. Olszewski*

Faculty of Chemistry, Wrocław University of Science and Technology,

Wybrzeże Wyspiańskiego 27, 50-370 Wrocław, Poland.

Marcin Górecki

Institute of Organic Chemistry, Polish Academy of Sciences,

Kasprzaka St. 44/52, 01-224 Warsaw, Poland

E-mail: elzbieta.wojaczynska@pwr.edu.pl, tomasz.olszewski@pwr.edu.pl

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General

Melting points were determined on the Schmelzpunkt Bestimmer Apotec melting-point apparatus using the standard open capillary method and are uncorrected. ^{1}H, ^{13}C and ^{31}P NMR spectra were collected on Jeol 400yh, Bruker Avance III 500 and Bruker Avance II 600 instruments. NMR spectra recorded in $CDCl_3$, D_2O and were referenced to the respective residual ^{1}H or ^{13}C signals of the solvents. The reported *J* values are those observed from the splitting patterns in the spectrum and may not reflect the true coupling constant values. NOESY experiments were carried out at 293K. Infrared spectra (4000-400 cm^{-1}) were collected on a Perkin Elmer 2000 FTIR spectrophotometer. High resolution mass spectra were collected using electrospray ionization on Waters LCT Premier XE TOF instrument. Optical rotations were measured using an Optical Activity Ltd. Model AA-5 automatic polarimeter; $[\alpha]^{D}$ values are given in 10^{-1} deg cm^2 g^{-1}. Chromatographic separations were performed on silica gel 60 (70-230 mesh). Thin layer chromatography was carried out using silica gel 60 precoated plates.

Experimental procedures

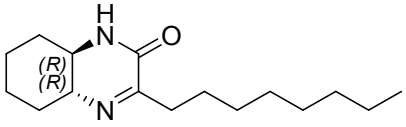
Cyclic imines

Procedures

General procedure for synthesis of cyclic imines **3a** - **s**

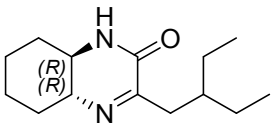
Sodium hydride (60% dispersion in mineral oil, 1.30 mmol, 52.0 mg, 1.30 equiv) was dispersed in anhydrous THF (10 ml) under argon atmosphere. The mixture was cooled to 273 K in an ice bath and then dimethyl-[(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-yl]phosphonate **2** (1.10 mmol, 288 mg, 1.10 equiv) was added. The mixture was stirred for 30 minutes. The aldehyde was added (1.00 mmol, 1.00 equiv) and the reaction continued for 30 minutes in 273 K and then for 60 minutes in a room temperature. Reaction mixture was washed with Et_2O (20 ml) and saturated $NaHCO_3$ solution (20 ml). The organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure. Depending on yield and purity of crude product, the imines were described without additional purification or purified by silica gel column chromatography (eluent: CH_2Cl_2/MeOH 97:3 v/v).

Synthesis



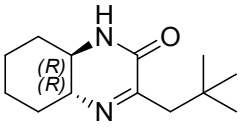
3e 4-octyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Colorless oil; 238 mg; yield = 90%; $[\alpha]_D^{20}$ −109 (c 1.05, CH_2Cl_2); IR (KBr): 724, 1119, 1220, 1318, 1364, 1455, 1628, 1683, 2857, 2927, 3085, 3205 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.24 (br. s, 1H), 2.98-3.11 (m, 2H), 2.59-2.67 (m, 1H), 2.42-2.50 (m, 1H), 2.29-2.31 (m, 1H), 1.75-1.89 (m, 3H), 1.49-1.59 (m, 2H), 1.19-1.41 (m, 14H), 0.85 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.1, 158.7, 62.5, 54.4, 33.9, 31.9, 31.8, 31.2, 29.5, 29.4, 29.3, 27.0, 25.3, 23.8, 22.7, 14.2; HRMS (ESI-TOF) calcd. for $C_{16}H_{28}N_2O$ $[M+H]^+$ *m*/*z*: 265.2280, found: 265.2274.



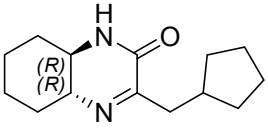
3h 4-(2-ethylbutyl)-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Off-white solid; 196 mg; yield = 83%; mp. 87-90 °C; $[\alpha]_D^{20}$ −98 (c 0.46, CH_2Cl_2); IR (KBr): 811, 1226, 1363, 1456, 1621, 1686, 2856, 2931, 2959, 3068, 3189 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.38 (br. s, 1H), 2.98-3.09 (m, 2H), 2.72 (ddd, *J* = 2.5, 6.4, 16.1 Hz, 1H), 2.24-2.32 (m, 2H), 1.69-1.90 (m, 4H), 1.24-1.41 (m, 8H), 0.85 (t, *J* = 7.6 Hz, 3H), 0.83 (t, *J* = 7.3 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.9, 158.8, 62.6, 54.4, 38.5, 37.8, 31.9, 31.1, 25.7, 25.3, 25.27, 23.8, 10.9, 10.7; HRMS (ESI-TOF) calcd. for $C_{14}H_{24}N_2O$ $[M+H]^+$ *m*/*z*: 237.1967, found: 237.1971.



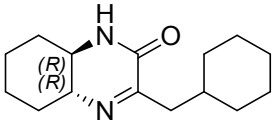
3i 4-neopentyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Colorless solid; 140 mg; yield = 63%; mp. 129-131 °C; $[\alpha]_D^{20}$ −103 (c 1.05, CH_2Cl_2); IR (KBr): 819, 1219, 1316, 1366, 1450, 1611, 1677, 2864, 2941, 3090, 3188 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.30 (br. s, 1H), 3.04-3.07 (m, 3H), 2.33-2.36 (m, 1H), 2.05 (d, *J* = 12.2 Hz, 1H), 1.76-1.91 (m, 3H), 1.30-1.42 (m, 4H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.4, 159.2, 62.9, 54.7, 44.6, 31.9 (2C overlapped), 31.0, 29.8 (3C overlapped), 25.2, 23.8; HRMS (ESI-TOF) calcd. for $C_{13}H_{23}N_2O$ $[M+H]^+$ *m*/*z*: 223.1810, found: 223.1807.



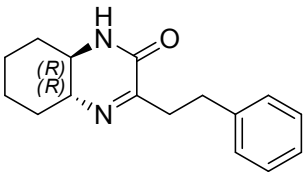
3k 4-(cyclopentylmethyl)-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Off-white solid; 185 mg; yield = 79%; mp. 121-123 °C; $[\alpha]^{20}_D$ - 105 (c 0.66, CH_2Cl_2); IR (KBr): 802, 1052, 1358, 1628, 1686, 2858, 2932, 3068, 3189 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.24 (br. s, 1H), 2.99-3.09 (m, 2H), 2.79 (ddd, *J* = 13.5, 6.7, 2.1 Hz, 1H), 2.29-2.39 (m, 2H), 2.17 (sept, *J* = 7.3 Hz, 1H), 1.14-1.89 (m, 15H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 158.8, 62.5, 54.5, 39.6, 37.8, 32.6, 32.1, 31.9, 31.1, 25.2, 25.1, 25.0, 23.8; HRMS (ESI-TOF) calcd. for $C_{14}H_{22}N_2O$ $[M+H]^+$ *m*/*z*: 235.1810, found: 235.1813.



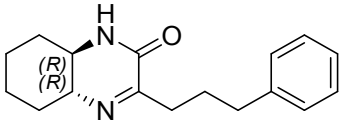
3l 4-cyclohexylmethyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Colorless solid; 169 mg; yield = 68%; mp. 124-125 °C; $[\alpha]_D^{20}$ −104 (c 0.98, CH_2Cl_2); IR (KBr): 810, 1222, 1364, 1444, 1618, 1677, 2851, 2931, 3065, 3095, 3184 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.31 (br. s, 1H), 3.02-3.10 (m, 2H), 2.69 (ddd, *J* = 13.3, 6.3, 1.8 Hz, 1H), 2.28-2.36 (m, 1H), 2.22 (dd, *J* = 13.1, 7.6 Hz, 1H), 1.59-1.89 (m, 8H), 1.09-1.41 (m, 8H), 0.88-1.02 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.6, 158.8, 62.5, 54.5, 41.1, 36.2, 33.5, 33.0, 31.9, 31.1, 26.4, 26.3, 26.2, 25.2, 23.7; HRMS (ESI-TOF) calcd. for $C_{15}H_{24}N_2O$ $[M+H]^+$ *m*/*z*: 249.1967, found: 249.1960.



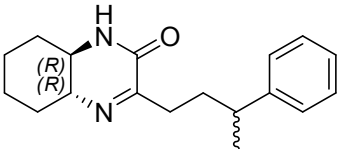
3m 4-phenethyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Pale yellow solid; 179 mg; yield = 70%; mp. 127-128 °C; $[\alpha]_D^{20}$ −110 (c 0.55, CH_2Cl_2); IR (KBr): 499, 711, 756, 1358, 1624, 1678, 2863, 2934, 3064, 3188 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.14-7.28 (m, 5H), 6.52 (br. s, 1H), 2.82-3.03 (m, 6H), 2.29-2.32 (m, 1H), 1.76-1.90 (m, 3H), 1.25-1.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 164.9, 158.6, 141.5, 128.7 (2C overlapped), 128.4 (2C overlapped), 126.0, 62.6, 54.4, 35.4, 32.7, 31.2, 31.1, 25.3, 23.8; HRMS (ESI-TOF) calcd. for $C_{16}H_{21}N_2O$ $[M+H]^+$ *m*/*z*: 257.1654, found: 257.1647.



3n 4-phenylpropyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Off-white solid; 265 mg; yield = 98%; mp. 115-117 °C; $[\alpha]^{20}_D$ - 93 (c 0.40, CH_2Cl_2); IR (KBr): 701, 756, 1360, 1451, 1494, 1627, 1684, 2855, 2926, 3023, 3081, 3171 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13-7.27 (m, 5H), 6.20 (br. s, 1H), 2.97-3.04 (m, 2H), 2.68 (q, *J* = 6.7 Hz, 1H), 2.66 (t, *J* = 7.6 Hz, 2H), 2.57 (q, *J* = 7.6 Hz, 1H), 2.29-2.31 (m, 1H), 1.69-1.94 (m, 5H), 1.24-1.41 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.5, 158.6, 142.2, 128.6 (2C overlapped), 128.4 (2C overlapped), 125.8, 62.5, 54.4, 35.7, 33.5, 31.9, 31.2, 28.5, 25.3, 23.8; HRMS (ESI-TOF) calcd. for $C_{17}H_{22}N_2O$ $[M+H]^+$ *m*/*z*: 271.1810, found: 271.1806.



3o 4-(3-phenylbutyl)-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

Off-white solid; mixture of epimers 1:1; 196 mg; yield = 69%; mp. 93-95 °C; IR (KBr): 696, 760, 1369, 1452, 1493, 1628, 1684, 2858, 2927, 3027, 3062, 3195 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.13-7.28 (m, 5H), 5.96

(br. s, 1H), 2.91-3.00 (m, 2H), 2.74 (sext, *J* = 7.6 Hz, 1H), 2.50 (q, *J* = 6.1 Hz, 1H), 2.27-2.30 (m, 1H), 1.62-1.94 (m, 5H), 1.21-1.41 (m, 5H), 1.27 (dd, *J* = 7.0, 2.3 Hz, 3H), ^{13}C NMR (100 MHz, $CDCl_3$): δ 165.7, 158.5, 147.1, 128.4 (2C overlapped), 127.2 (2C overlapped), 126.0, 62.5, 54.3, 40.0, 34.9, 32.1, 31.9, 31.1, 25.3, 23.8, 22.3; HRMS (ESI-TOF) calcd. for $C_{18}H_{24}N_2O$ [*M*+H]$^+$ *m/z*: 285.1967, found: 285.1963.

Full characteristic of compounds **3b**, **3d** and **3g** can be found in our previous paper (J. Iwanejko, A. Brol, B. Szyja, M. Daszkiewicz, E. Wojaczyńska, T. K. Olszewski, *Tetrahedron*, **2019**, *75*, 1431-1439).

Cyclic amines

Procedures

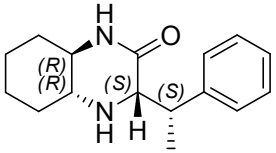
General procedure for synthesis of amines 4a – b

Sodium hydride (60% dispersion in mineral oil, 1.30 mmol, 52.0 mg, 1.30 equiv) was dispersed in anhydrous THF (10 ml) under argon atmosphere. The mixture was cooled to 273 K in an ice bath and then dimethyl-[(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-yl]phosphonate **2** (1.10 mmol, 288 mg, 1.10 equiv) was added. The mixture was stirred for 30 minutes. The ketone (acetophenone or acetone) was added (1.00 mmol, 1.00 equiv) and the reaction continued for 30 minutes in 273 K and then for 60 minutes in a room temperature. Reaction mixture was washed with Et_2O (20 ml) and saturated $NaHCO_3$ solution (20 ml). The organic layer was dried (Na_2SO_4), filtered and evaporated under reduced pressure. The crude product was then dissolved in methanol (10 mL) at room temperature and sodium borohydride (1.30 mmol, 49.2 mg, 1.30 equiv was added). The mixture was stirred for 3 hours. Solvent was evaporated under reduced pressure and the residue was subjected to column chromatography (eluent: CH_2Cl_2/MeOH 95:5 v/v) to obtain pure amines.

General procedure for synthesis of amines 5a – e and 6c

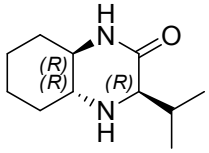
To a solution of an appropriate imine (1.00 mmol, 1.00 equiv) in methanol (10 mL) at room temperature was added sodium borohydride (1.30 mmol, 49.2 mg, 1.30 equiv). The mixture was stirred for 3 hours. Solvent was evaporated under reduced pressure and the residue was subjected to column chromatography (eluent: CH_2Cl_2/MeOH 95:5 v/v) to obtain pure diastereomers of amine.

Synthesis



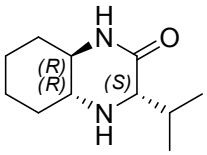
4a (4-((S)-1-phenylethyl))-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless oil; 83 mg; yield = 32%; $[\alpha]_D^{20}$ -16 (c 0.25, CH_2Cl_2); IR (KBr): 706, 772, 1121, 1343, 1357, 1452, 1664, 2855, 2929, 3178, 3447 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.31-7.34 (m, 2H), 7.23-7.28 (m, 2H), 7.18-7.21 (m, 1H), 5.95 (br. s, 1H), 3.78 (dq, *J* = 7.3, 3.4 Hz, 1H), 3.72 (d, *J* = 3.1 Hz, 1H), 2.37-2.41 (m, 2H), 1.60-1.85 (m, 4H), 1.45 (d, *J* = 7.3 Hz, 3H), 0.99-1.34 (m, 5H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 171.7, 141.7, 128.7 (2C overlapped), 128.2 (2C overlapped), 126.7, 64.4, 57.9, 57.7, 40.2, 31.6, 30.9, 24.9, 23.7, 18.1; HRMS (ESI-TOF) calcd. for $C_{16}H_{23}N_2O$ [*M*+H]$^+$ *m/z*: 259.1810, found: 259.1812.



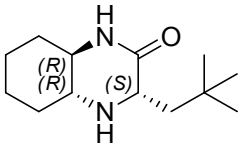
4b isopropyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 123 mg; yield = 63%; mp. 126-127 °C; $[\alpha]_D^{20}$ +27 (c 0.30, CH_2Cl_2); IR (KBr): 1157, 1364, 1464, 1643, 2862, 2935, 3188, 3327, 3449 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 6.89 (br. s, 1H), 3.41 (s, 1H), 2.92-2.98 (m, 1H), 2.42-2.48 (m, 1H), 1.73-1.93 (m, 5H), 1.15-1.46 (m, 4H), 1.30 (s, 3H), 1.25 (s, 3H), 1.02-1.15 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 73.5, 63.5, 59.0, 55.8, 31.2, 30.8, 27.4, 26.6, 25.0, 23.7; HRMS (ESI-TOF) calcd. for $C_{11}H_{21}N_2O$ [*M*+H]$^+$ *m/z*: 197.1654, found: 197.1649.



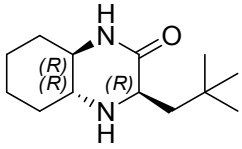
4b' isopropyl-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 49 mg; yield = 25%; mp. 120-122 °C; $[\alpha]_D^{20}$ +33 (c 0.30, CH_2Cl_2); IR (KBr): 827, 1352, 1364, 1465, 1658, 2860, 2931, 3195, 3321, 3418 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.04 (br. s, 1H), 3.32 (d, *J* = 4.6 Hz, 1H), 2.94-3.00 (m, 1H), 2.48-2.54 (m, 1H), 2.39 (dsep, *J* = 7.0, 4.9 Hz, 1H), 1.69-1.88 (m, 5H), 1.08-1.38 (m, 4H), 1.03 (d, *J* = 7.0 Hz, 3H), 0.93 (d, *J* = 7.0 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.6, 77.3, 62.5, 58.9, 55.9, 31.6, 31.0, 24.9, 23.8, 20.3, 18.6; HRMS (ESI-TOF) calcd. for $C_{11}H_{21}N_2O$ $[M+H]^+$ *m*/*z*: 197.1654, found: 197.1649.



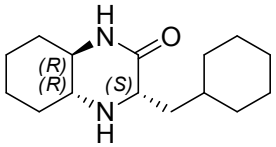
5a 4-neopentyl-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 177 mg; yield = 79%; mp. 182-184 °C; $[\alpha]_D^{20}$ −31 (c 0.16, CH_2Cl_2); IR (KBr): 1144, 1359, 1409, 1476, 1658, 2862, 2938, 3065, 3189, 3282 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.78 (br. s, 1H), 3.50 (dd, *J* = 8.4, 1.8 Hz, 1H), 2.97-3.03 (m, 1H), 2.45-2.51 (m, 1H), 2.23 (dd, *J* = 14.5, 2.5 Hz, 1H), 1.68-1.81 (m, 4H), 1.22-1.41 (m, 6H), 0.97 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.1, 58.7, 58.5, 58.3, 46.0, 31.7, 31.0, 30.6, 30.1 (3C overlapped), 24.8, 23.9; HRMS (ESI-TOF) calcd. for $C_{13}H_{25}N_2O$ $[M+H]^+$ *m*/*z*: 225.1967, found: 225.1964.



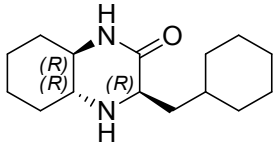
5a' 4-neopentyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 43 mg; yield = 19%; mp. 178-179 °C; $[\alpha]_D^{20}$ +32 (c 0.14, CH_2Cl_2); IR (KBr): 1120, 1362, 1408, 1467, 1659, 2860, 2936, 3058, 3180, 3300 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.70 (br. s, 1H), 3.60 (dd, *J* = 9.2, 4.5 Hz, 1H), 2.93-2.99 (m, 1H), 2.51-2.57 (m, 1H), 1.70-1.81 (m, 5H), 1.60 (dd, *J* = 14.4, 9.2 Hz, 1H), 1.54 (br. s, 1H), 1.12-1.40 (m, 4H), 0.99 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.1, 59.0, 56.4, 53.1, 46.3, 31.8, 31.1, 31.0, 29.9 (3C overlapped), 25.0, 23.9; HRMS (ESI-TOF) calcd. for $C_{13}H_{25}N_2O$ $[M+H]^+$ *m*/*z*: 225.1967, found: 225.1964.



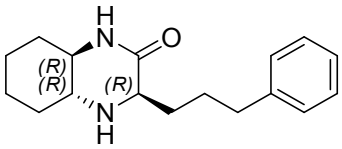
5b 4-(cyclohexylmethyl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 130 mg; yield = 52%; mp. 155-156 °C; $[\alpha]_D^{20}$ +55 (c 0.29, CH_2Cl_2); IR (KBr): 1131, 1146, 1313, 1353, 1412, 1449, 1661, 2852, 2922, 3063, 3187, 3272 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.08 (br. s, 1H), 3.56 (dd, *J* = 9.6, 3.4 Hz, 1H), 2.98-3.03 (m, 1H), 2.45-2.51 (m, 1H), 1.93 (ddd, *J* = 13.8, 10.0, 3.4 Hz, 1H), 1.64-1.86 (m, 10H), 1.11-1.52 (m, 9H), 0.85-1.03 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.0, 58.5, 58.2, 56.9, 39.9, 34.4, 33.8, 31.9, 31.6, 30.8, 26.6, 26.4, 26.2, 24.8, 23.8; HRMS (ESI-TOF) calcd. for $C_{15}H_{27}N_2O$ $[M+H]^+$ *m*/*z*: 251.2123, found: 251.2118.



5b' 4-(cyclohexylmethyl)-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

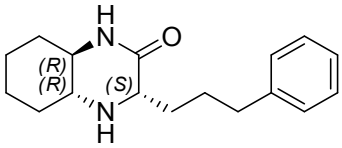
Colorless solid; 83 mg; yield = 33%; mp. 174-175 °C; $[\alpha]_D^{20}$ +46 (c 0.34, CH_2Cl_2); IR (KBr): 1114, 1148, 1359, 1413, 1448, 1659, 2851, 2928, 3058, 3178, 3298 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 6.18 (br. s, 1H), 3.56 (dd, *J* = 7.2, 7.0 Hz, 1H), 2.93-2.99 (m, 1H), 2.48-2.54 (m, 1H), 1.60-1.81 (m, 12H), 1.08-1.30 (m, 8H), 0.84-1.04 (m, 2H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 174.0, 58.9, 55.6, 52.9, 39.9, 34.3, 34.2, 31.9, 31.6, 31.0, 26.6, 26.4, 26.1, 25.0, 23.9; HRMS (ESI-TOF) calcd. for $C_{15}H_{27}N_2O$ $[M+H]^+$ *m*/*z*: 251.2123, found: 251.2118.



5c (3-phenylpropyl)-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

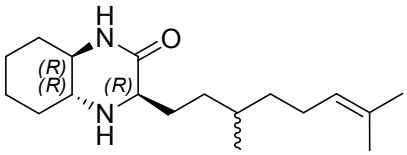
Colorless solid; 114 mg; yield = 42%; mp. 134-135 °C; $[\alpha]_D^{20}$ +36 (c 0.70, CH_2Cl_2); IR (KBr): 696, 752, 1364, 1417, 1452, 1496, 1655, 2857, 2931, 3059, 3174, 3296 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 7.24-7.28 (m, 2H), 7.14-7.19 (m, 3H), 6.29 (br. s, 1H), 3.47 (dd, *J* = 9.2, 4.0 Hz, 1H), 2.93-2.99 (m, 1H), 2.57-2.71 (m, 2H),

2.43-2.49 (m, 1H), 2.30 (br. s, 1H), 1.70-1.95 (m, 8H), 1.11-1.39 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 173.3, 142.3, 128.5 (2C overlapped), 128.4 (2C overlapped), 125.8, 58.9, 58.1, 53.3, 35.8, 32.6, 31.6, 30.9, 28.7, 25.0, 23.8; HRMS (ESI-TOF) calcd. for $C_{17}H_{24}N_2O$ [*M*+H]$^+$ *m*/*z*: 273.1967, found: 273.1971.



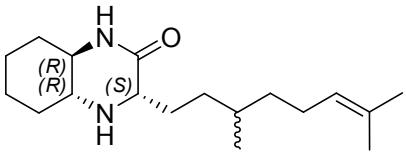
5c' (3-phenylpropyl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 95 mg; yield = 35%; mp. 58-60 °C; $[\alpha]_D^{20}$ −15 (c 0.48, CH_2Cl_2); IR (KBr): 696, 1352, 1409, 1453, 1496, 1659, 2854, 2934, 3026, 3061, 3190, 3269 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.25 (t, *J* = 7.0 Hz, 2H), 7.13-7.17 (m, 3H), 6.25 (br. s, 1H), 3.52-3.55 (m, 1H), 2.93-3.00 (m, 1H), 2.63 (t, *J* = 7.3 Hz, 2H), 2.43-2.49 (m, 1H), 2.00-2.05 (m, 1H), 1.69-1.81 (m, 8H), 1.21-1.36 (m, 4H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 172.3, 142.4, 128.5 (2C overlapped), 128.4 (2C overlapped), 125.8, 59.5, 58.4, 58.2, 36.1, 32.4, 31.5, 30.8, 28.1, 24.8, 23.9; HRMS (ESI-TOF) calcd. for $C_{17}H_{24}N_2O$ [*M*+H]$^+$ *m*/*z*: 273.1967, found: 273.1971.



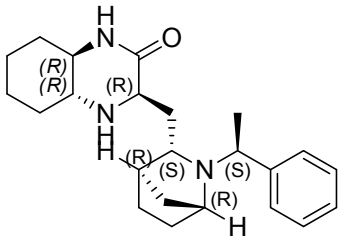
5d (3,7-dimethyloct-6-en-1-yl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 120 mg; yield = 41%; mixture of epimers 1:1; IR (KBr): 812, 844, 1126, 1352, 1363, 1451, 1659, 2858, 2936, 3177, 3299, 3426 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, both isomers present): δ 6.03 (br. s, 2H), 5.05-5.10 (m, 2H), 3.42 (ddd, *J* = 10.0, 3.7, 2.8 Hz, 2H), 2.96-3.02 (m, 2H), 2.49-2.56 (m, 2H), 1.41-2.03 (m, 18H), 1.66 (s, 6H), 1.58 (s, 6H), 1.09-1.54 (m, 18H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.878 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, both isomers present): δ 173.3, 173.27, 131.2 (2C overlapped), 125.0, 124.9, 58.8, 58.77, 58.6 (2C overlapped), 53.3, 53.27, 37.2, 36.9, 34.2, 33.9, 32.6, 32.3, 31.6 (2C overlapped), 30.9 (2C overlapped), 30.5, 30.1, 25.8 (2C overlapped), 25.7, 25.5, 24.9 (2C overlapped), 23.8 (2C overlapped), 19.7, 19.5, 17.7 (2C overlapped); HRMS (ESI-TOF) calcd. for $C_{18}H_{33}N_2O$ [*M*+H]$^+$ *m*/*z*: 293.2593, found: 293.2603.



5d' (3,7-dimethyloct-6-en-1-yl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 58 mg; yield = 20%; mixture of epimers 1:1; IR (KBr): 831, 1121, 1350, 1452, 1664, 2858, 2928, 3258, 3428 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$, both isomers present): δ 6.08 (br. s, 2H), 5.04-5.08 (m, 2H), 3.49 (dd, *J* = 8.3, 3.4 Hz, 2H), 2.99-3.03 (m, 2H), 2.46-2.52 (m, 2H), 1.52-2.02 (m, 18H), 1.65 (s, 6H), 1.57 (s, 6H), 1.09-1.48 (m, 18H), 0.88 (d, *J* = 6.4 Hz, 3H), 0.87 (d, *J* = 6.4 Hz, 3H); ^{13}C NMR (100 MHz, $CDCl_3$, both isomers present): δ 171.8, 171.7, 131.21, 131.2, 124.93, 124.9, 59.8 (2C overlapped), 58.5 (2C overlapped), 57.8 (2C overlapped), 37.2, 36.9, 33.1, 33.0, 32.72, 32.7, 31.6 (2C overlapped), 30.4 (2C overlapped), 29.9 (2C overlapped), 25.8 (2C overlapped), 25.6 (2C overlapped), 24.7 (2C overlapped), 23.8 (2C overlapped), 19.6, 19.5, 17.8 (2C overlapped); HRMS (ESI-TOF) calcd. for $C_{19}H_{33}N_2O$ [*M*+H]$^+$ *m*/*z*: 293.2593, found: 293.2603.



5e 4-(((1*R*,3*S*,4*R*,)-2-((*S*)-1-phenylethyl)-2-azabicyclo[2.2.1]heptan-3-yl)methyl)(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decan

Colorless oil; 115 mg; yield = 43%; IR (KBr): 702, 763, 1128, 1360, 1451, 1627, 1683, 2860, 2936, 3062, 3205 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.19-7.33 (m, 5H), 5.93 (br. s, 1H), 3.79 (q, *J* = 6.4 Hz, 1H), 2.96-3.11 (m, 2H), 2.82-2.90 (m, 1H), 2.47-2.62 (m, 2H), 2.26-2.33 (m, 1H), 2.09-2.16 (m, 1H), 1.59 (q, *J* = 8.0 Hz, 2H), 1.31 (d, *J* = 6.7 Hz, 3H), 1.21-1.89 (m, 13H), 0.86-0.94 (m, 1H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 166.0, 158.7, 146.0, 128.4 (2C overlapped), 126.9, 126.7 (2C overlapped), 62.5, 57.

0, 56.7, 54.4, 40.8, 38.6, 33.4, 32.9, 32.8, 31.9, 31.1, 30.1, 25.3, 24.8, 23.8; HRMS (ESI-TOF) calcd. for $C_{23}H_{34}N_3O$ [*M*+H]$^+$ *m*/*z*: 368.2702, found: 368.2704.

Derivatives of cyclic imine 3i

Procedures

Procedure for the synthesis of 6b

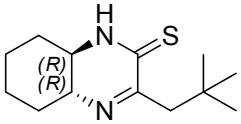
To a solution of imine **3i** (2.00 mmol, 444 mg, 2.00 equiv) in toluene (15 mL), Lawesson`s reagent (1.20 mmol, 485 mg, 0.600 equiv) was added under an argon atmosphere. The reaction mixture was refluxed for 4 hours. Upon completion of the reaction (monitored by TLC), it was quenched with water (20 mL) and extracted with ethyl acetate (3 x 20 mL). The organic layer was dried over Na_2SO_4, filtered, and concentrated under reduced pressure. The crude product was purified by column chromatography (eluent: CH_2Cl_2/MeOH 98 : 2 v/v).

Procedure for the synthesis of dialkyl aminophosphonic acid ester 6d and aminophosphonic acid 6e can be found in the literature (J. Iwanejko, A. Brol, B. M. Szyja, M. Daszkiewicz, E. Wojaczyńska, T. K. Olszewski, *Org. Biomol. Chem.*, **2019**, *17*, 7352-7359.).

Procedure for reduction of 5a to bisamine 6f

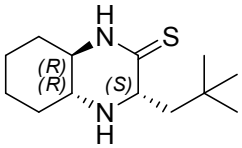
To a solution of **5a** (0.500 mmol, 112 mg, 1.0 equiv) in anhydrous THF (5 mL) under argon atmosphere was added lithium aluminium hydride (0.750 mmol, 28.5 mg, 1.5 quiv). The mixture was heated under reflux for 20 hours and then cooled down to room temperature. The reaction was quenched with addition of water (30 µL), NaOH (15% solution, 30 µL) and water (90 µL). Resulting suspension was filtered through celite and washed with THF. The organic layer was dried (K_2CO_3), filtered and evaporated under reduced pressure and the resulting crude product was purified by column chromatography (eluent: CH_2Cl_2/MeOH 80 : 20 v/v).

Synthesis



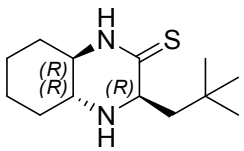
6b 4-(neopentyl)-(1*R*,6*R*)-3-thio-2,5-diazabicyclo[4.4.0]dec-4-ene

Yellow solid; 81 mg; yield = 34%; mp. 104-105 °C; $[\alpha]^{20}_D$ - 147 (c 0.30, CH_2Cl_2); IR (KBr): 1039, 1179, 1314, 1359, 1449, 1520, 1604, 1674, 2862, 2937, 3159 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.48 (br. s, 1H), 3.74 (dd, *J* = 12.4, 1.8 Hz, 1H), 2.97-3.01 (m, 1H), 2.79-2.87 (m, 1H), 2.38-2.40 (m, 1H), 2.15 (d, *J* = 12.5 Hz, 1H), 2.02-2.06 (m, 1H), 1.80-1.87 (m, 2H), 1.29-1.47 (m, 4H), 0.94 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 187.0, 164.3, 62.2, 55.6, 46.7, 32.03, 32.01, 30.0, 29.9 (3C overlapped), 25.0, 24.0;HRMS (ESI-TOF) calcd. for $C_{13}H_{22}N_2S$ [*M*+H]$^+$ *m*/*z*: 239.1582, found: 239.1595.



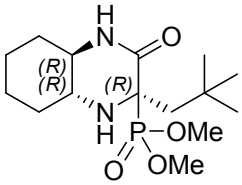
6c 4-neopentyl-(1*R*,4*S*,6*R*)-3-thio-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 122 mg; yield = 51%; mp. 180-182 °C; $[\alpha]_D^{20}$ -89 (c 0.12, 1M HCl); IR (KBr): 1035, 1056, 1288, 1340, 1359, 1541, 2861, 2952, 3153, 3260, 3436 cm^{-1}; ^{1}H NMR (400 MHz, $CDCl_3$): δ 8.38 (br. s, 1H), 3.77 (d, *J* = 8.6 Hz, 1H), 2.91-2.95 (m, 1H), 2.79 (dd, *J* = 14.4, 1.8 Hz, 1H), 2.47-2.53 (m, 1H), 1.77-1.87 (m, 4H), 1.39 (dd, *J* = 14.4, 8.6 Hz, 1H), 1.14-1.41 (m, 5H), 1.00 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 206.9, 63.4, 60.7, 57.5, 50.6, 31.2, 30.9, 30.8, 30.2 (3C overlapped), 24.7, 24.1; HRMS (ESI-TOF) calcd. for $C_{13}H_{25}N_2S$ [*M*+H]$^+$ *m*/*z*: 241.1738, found: 241.1731.



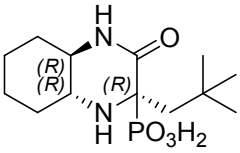
6c' 4-neopentyl-(1*R*,4*R*,6*R*)-3-thio-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 58 mg; yield = 24%; mp. 175-177 °C; $[\alpha]_D^{20}$ +37 (c 0.11, 1M HCl); IR (KBr): 1032, 1061, 1353, 1365, 1543, 2855, 2929, 2950, 3143, 3263, 3436 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 8.17 (br. s, 1H), 3.99 (dd, *J* = 9.3, 1.8 Hz, 1H), 2.89-2.92 (m, 1H), 2.55-2.61 (m, 1H), 2.16 (dd, *J* = 14.2, 1.8 Hz, 1H), 1.79-1.86 (m, 4H), 1.64 (dd, *J* = 14.4, 9.5 Hz, 1H), 1.54 (br. s, 1H), 1.15-1.42 (m, 4H), 1.01 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 207.6, 62.4, 61.1, 51.5, 48.9, 31.4, 31.0, 30.9, 30.0 (3C overlapped), 25.0, 24.2; HRMS (ESI-TOF) calcd. for $C_{13}H_{25}N_2S$ $[M+H]^+$ *m*/*z*: 241.1738, found: 241.1731.



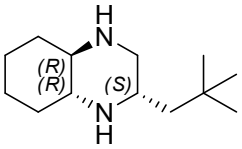
6d dimethyl-[4-neopentyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-yl]-phosphonate

Colorless solid; 308 mg; yield = 87%; mp. 103-105 °C; $[\alpha]^{20}_D$ + 37 (c 0.35, CH_2Cl_2); IR (KBr): 1028, 1059, 1243, 1342, 1463, 1670, 2860, 2952, 3225, 3436 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 5.95 (br. s, 1H), 3.79 (d, *J* = 10.4 Hz, 6H), 3.05-3.07 (m, 2H), 2.36 (dd, *J* = 14.4, 3.1 Hz, 1H), 1.70-1.79 (m, 5H), 1.59 (dd, *J* = 14.4, 12.2 Hz, 1H), 1.15-1.41 (m, 4H), 1.00 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 169.4, 66.9 (d, *J* = 120.7 Hz), 57.5, 55.0, 54.0, 53.9, 53.8, 44.9, 32.2 (d, *J* = 15.0 Hz), 31.2 (3C overlapped), 30.7 (d, *J* = 13.2 Hz), 24.2, 23.9; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 27.2; HRMS (ESI-TOF) calcd. for $C_{15}H_{29}N_2O_4PNa$ $[M+Na]^+$ *m*/*z*: 355.1763, found: 355.1771.



6e [4-neopentyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-yl]-phosphonic acid

Colorless solid; 217 mg; yield = 72%; *dr* = 93:7;; IR (KBr): 557, 1081, 1207, 1261, 1345, 1470, 1601, 1651, 2949, 3051, 3180 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 3.77-3.82 (m, 1H), 3.54-3.57 (m, 1H), 3.20 (s, 2H), 2.56 (dd, *J* = 15.9, 4.6 Hz, 1H), 1.51-2.05 (m, 5H), 1.16-1.30 (m, 2H), 0.92 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 167.9, 67.8 (d, *J* = 120.0 Hz), 57.0, 53.1, 48.9, 43.5, 30.3 (3C overlapped), 30.2, 26.8, 23.6, 22.4; $^{31}P\{^1H\}$ NMR (162 MHz, $CDCl_3$): δ 9.9; HRMS (ESI-TOF) calcd. for $C_{13}H_{26}N_2O_4P$ $[M+H]^+$ *m*/*z*: 303.1474, found: 303.1476.



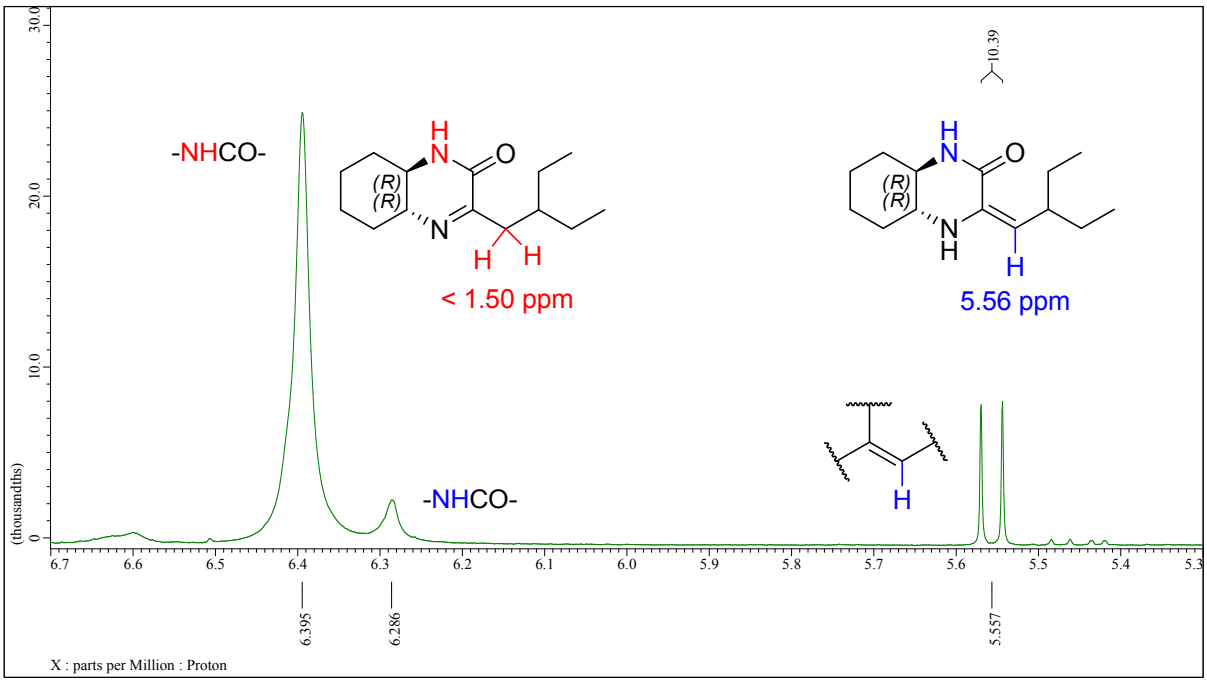
6f 4-neopentyl-(1*R*,4*S*,6*R*)-2,5-diazabicyclo[4.4.0]decane

Colorless solid; 70 mg; yield = 67%; mp. 42-44 °C; $[\alpha]_D^{20}$ +24 (c 0.17, CH_2Cl_2); IR (KBr): 833, 1113, 1325, 1366, 1450, 1466, 1650, 2854, 2927, 3273, 3413 cm^{-1}; ^1H NMR (400 MHz, $CDCl_3$): δ 2.92 (dd, *J* = 11.6, 3.1 Hz, 1H), 2.77-2.82 (m, 1H), 2.49 (dd, *J* = 11.6, 10.4 Hz, 1H), 2.25-2.31 (m, 1H), 2.16-2.21 (m, 1H), 1.58-1.71 (m, 4H), 1.56 (br. s, 2H), 1.14-1.33 (m, 6H), 0.91 (s, 9H); ^{13}C NMR (100 MHz, $CDCl_3$): δ 61.9, 60.5, 54.27, 54.25, 48.8, 32.3, 32.0, 30.5, 30.1 (3C overlapped), 25.1, 24.9; HRMS (ESI-TOF) calcd. for $C_{13}H_{27}N_2$ $[M+H]^+$ *m*/*z*: 211.2174, found: 211.2169.

Spectra

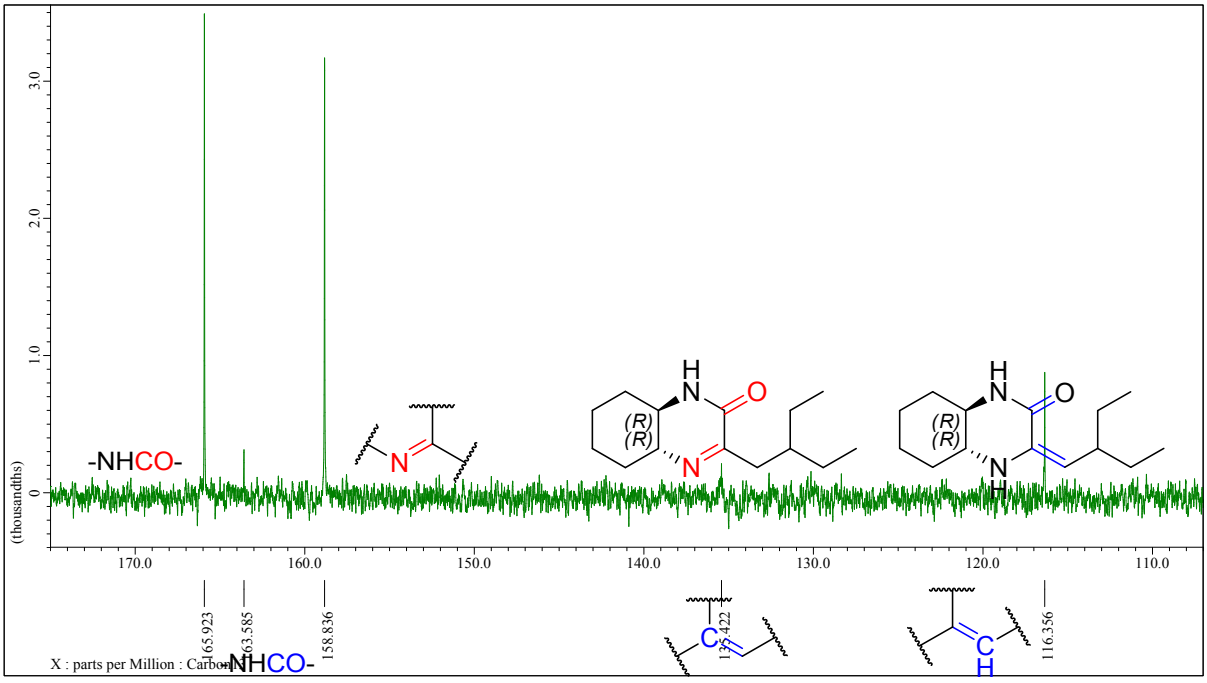
Imine/enamine form differences

A fragment of ^{1}H NMR spectrum of crude reaction mixture of **3h**. Crucial structural features of both



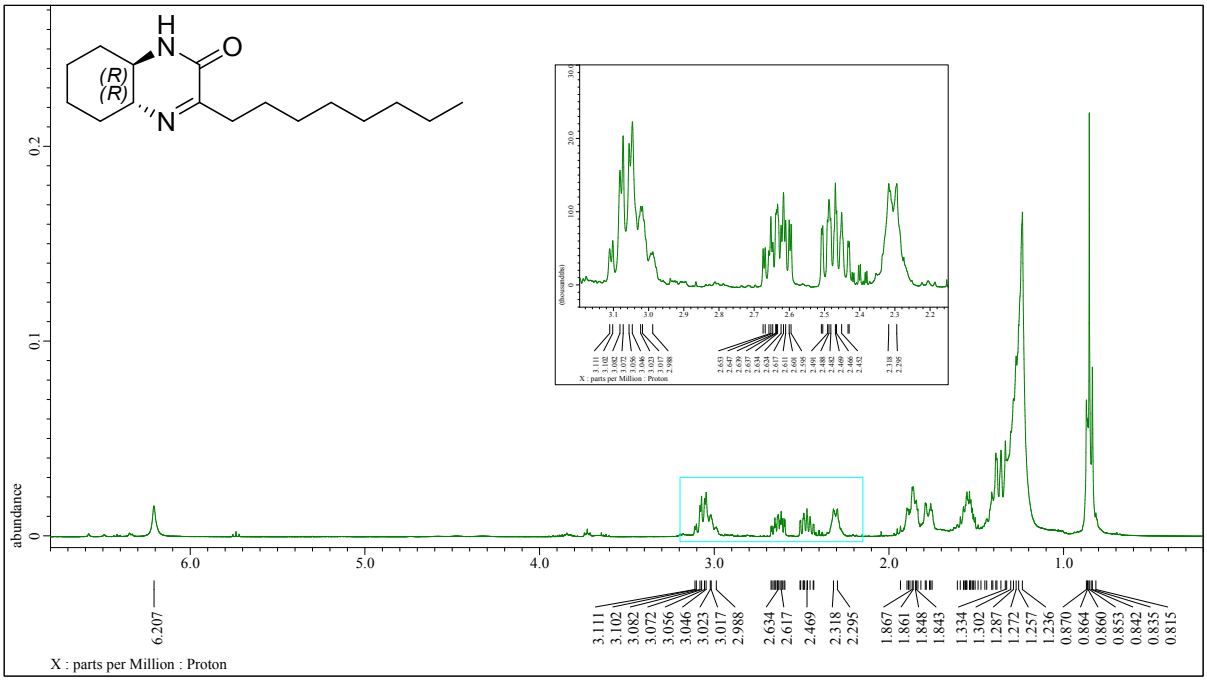
forms and corresponding signals were marked.

A fragment of ^{13}C NMR spectrum of crude reaction mixture of **3h**.



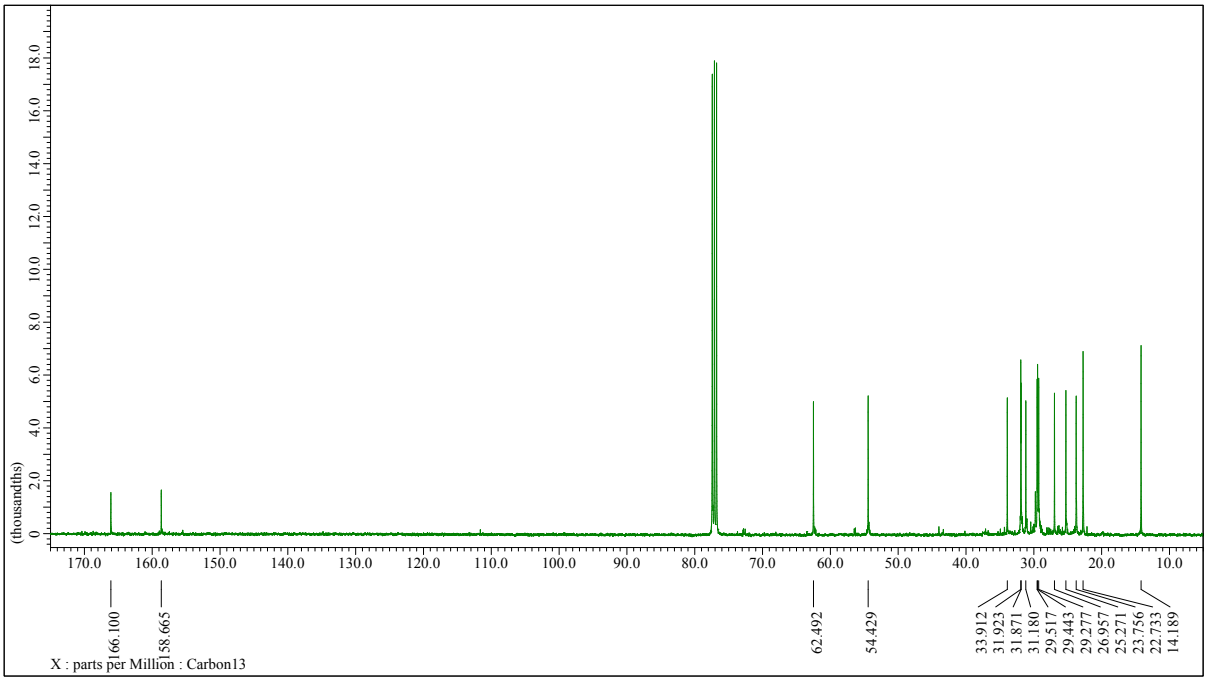
Cyclic imines

3e 4-octyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

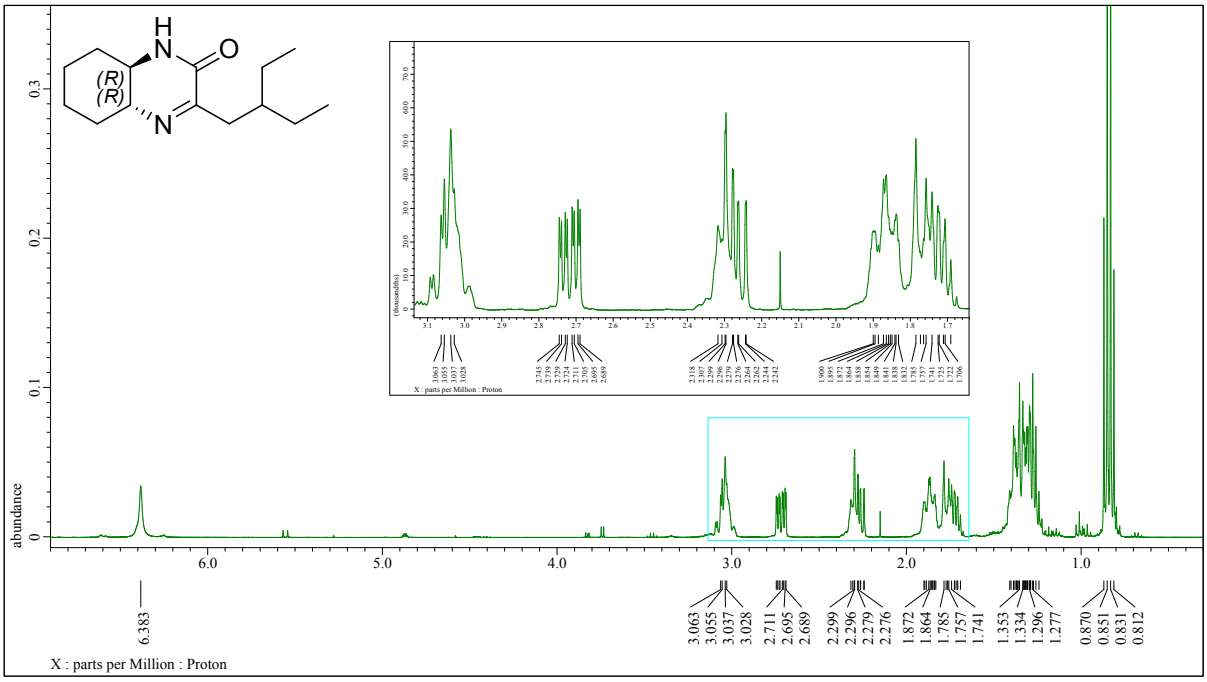


^{1}H NMR spectrum of **3e**

^{13}C NMR spectrum of **3e**

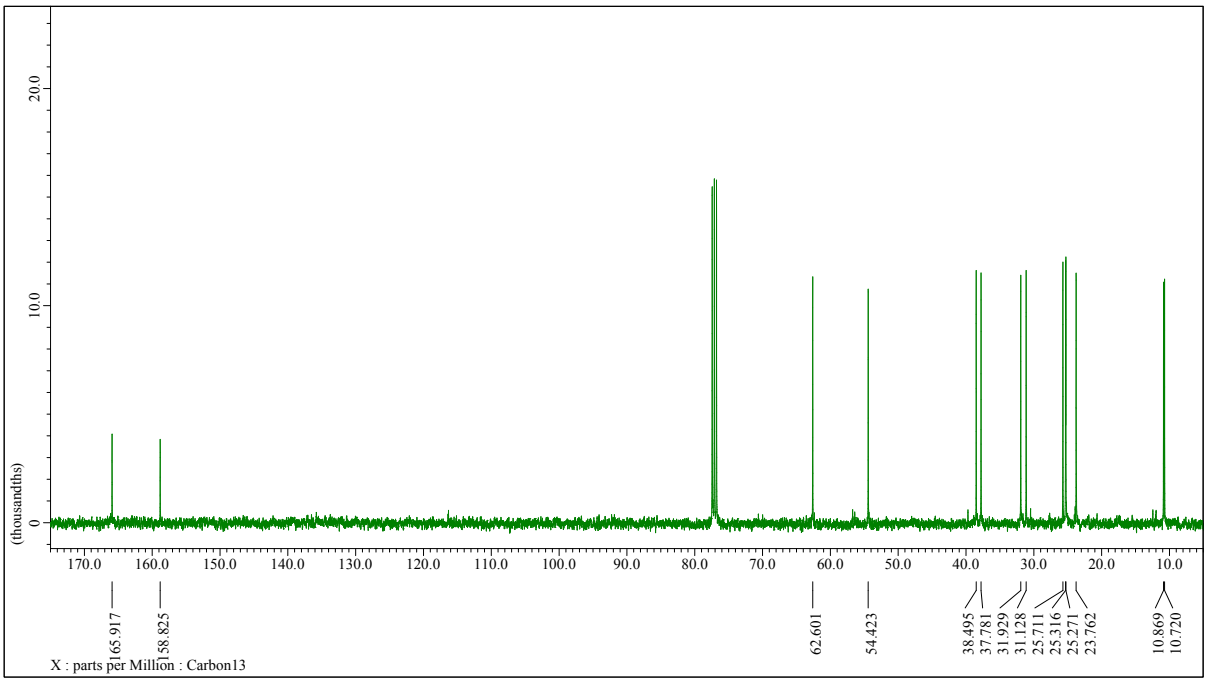


3h 4-(2-ethylbutyl)-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

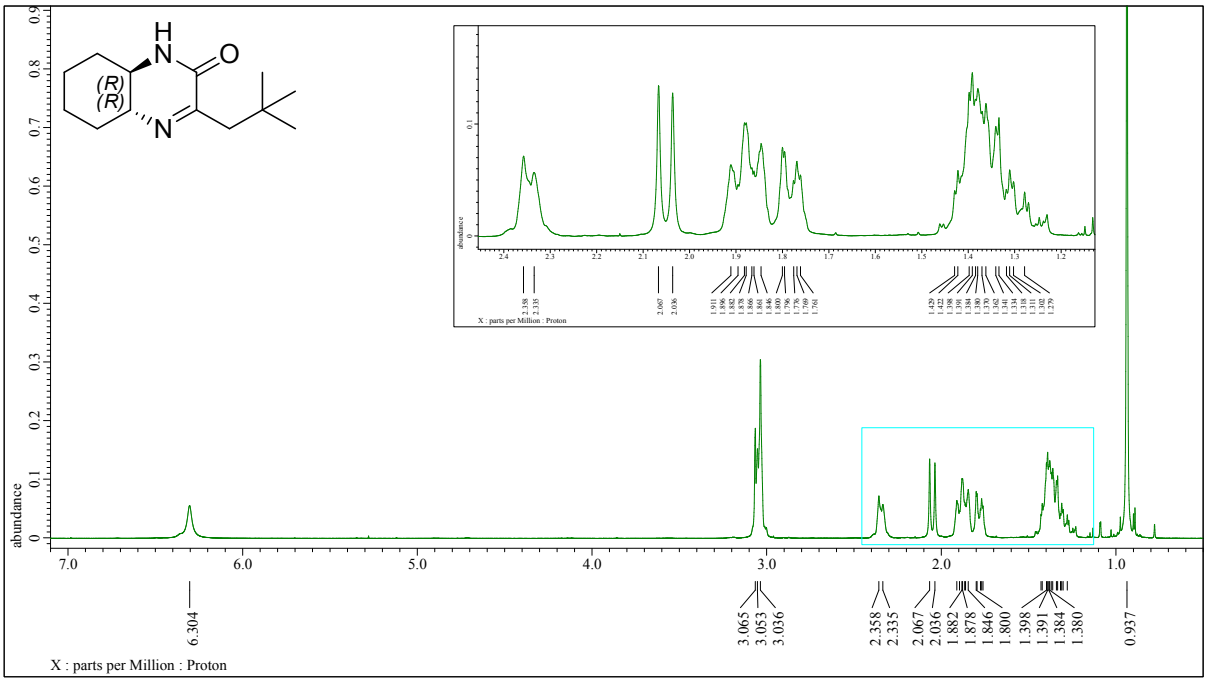


^{1}H NMR spectrum of **3h**

^{13}C NMR spectrum of **3h**

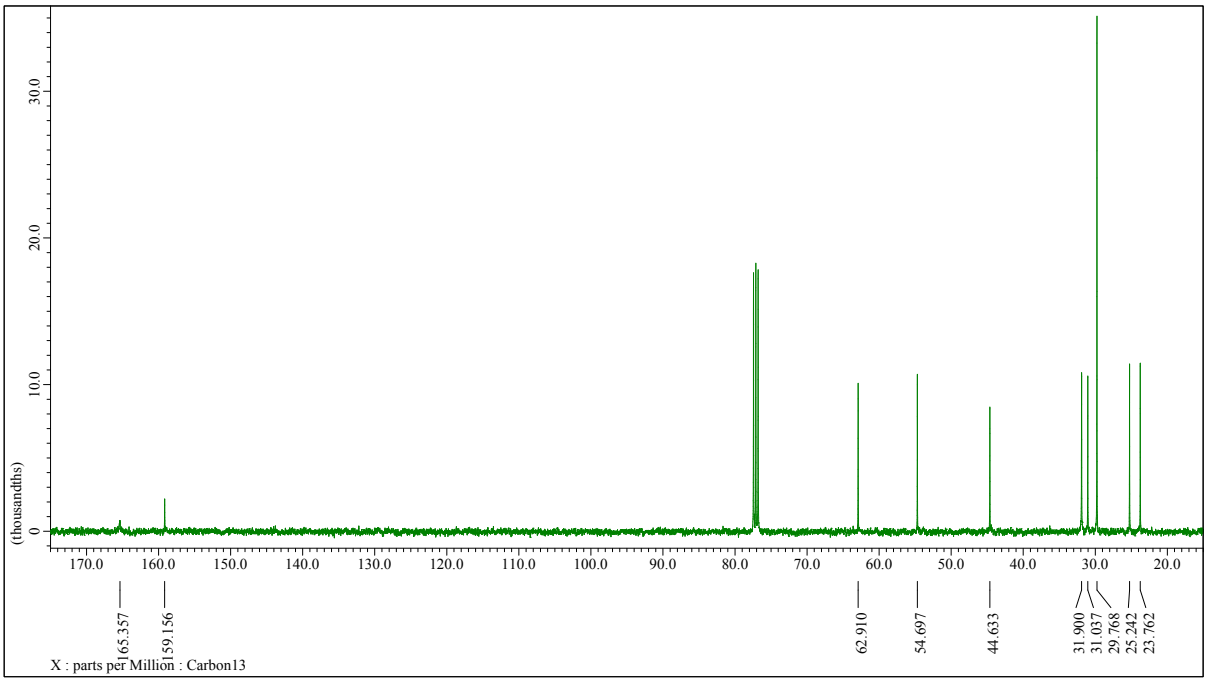


3i 4-neopentyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

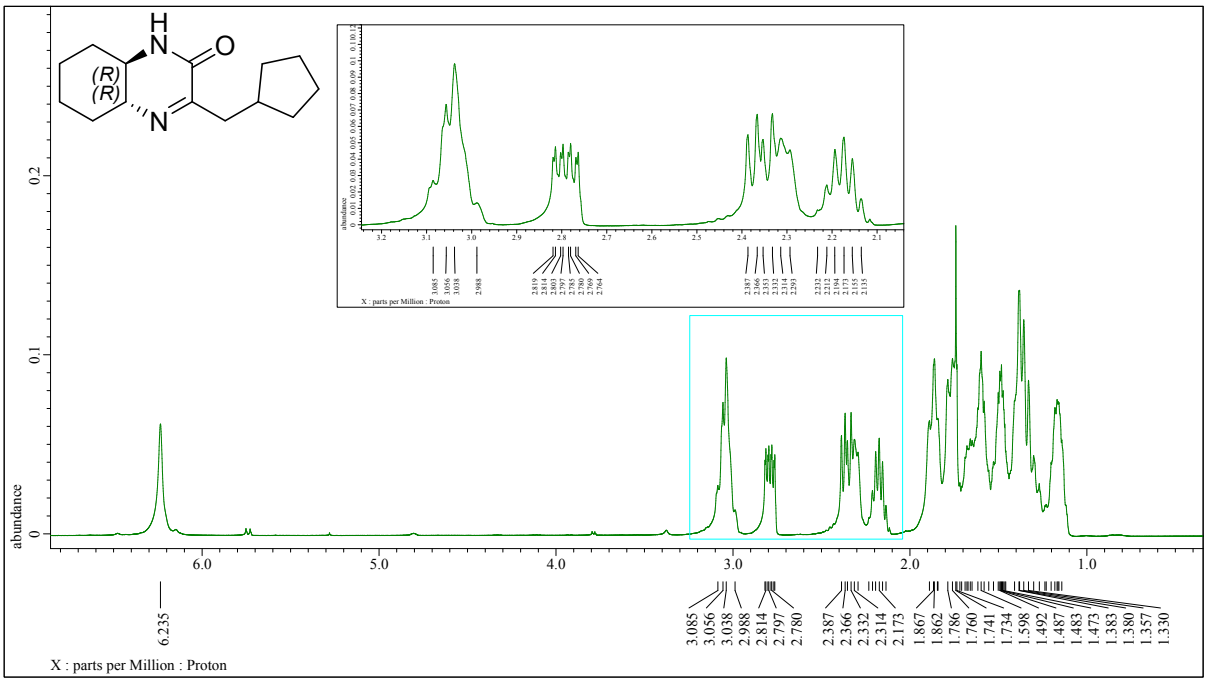


^{1}H NMR spectrum of **3i**

^{13}C NMR spectrum of **3i**

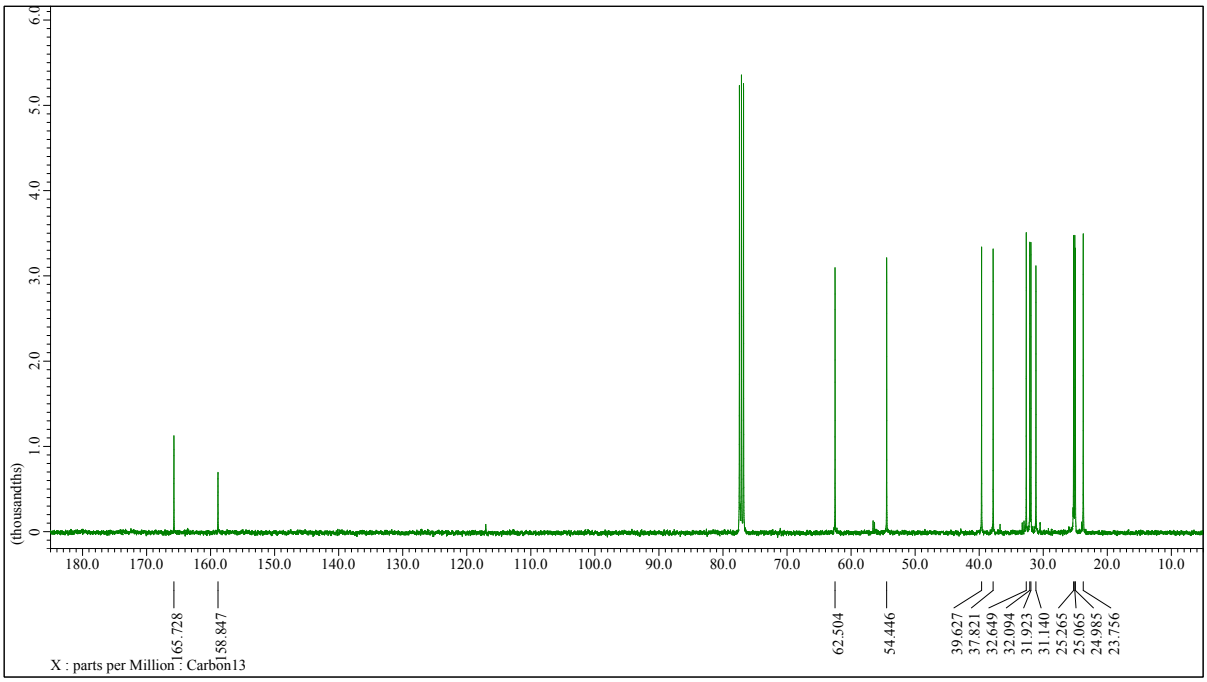


3k 4-(cyclopentylmethyl)-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

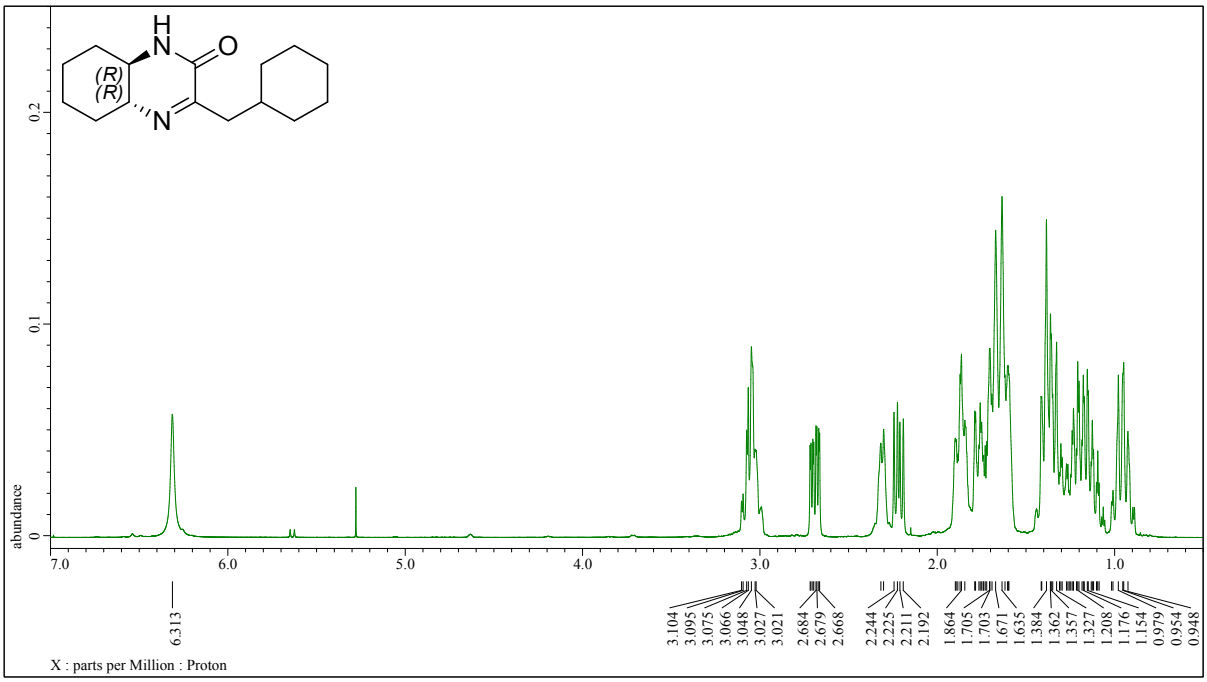


^{1}H NMR spectrum of **3k**

^{13}C NMR spectrum of **3k**

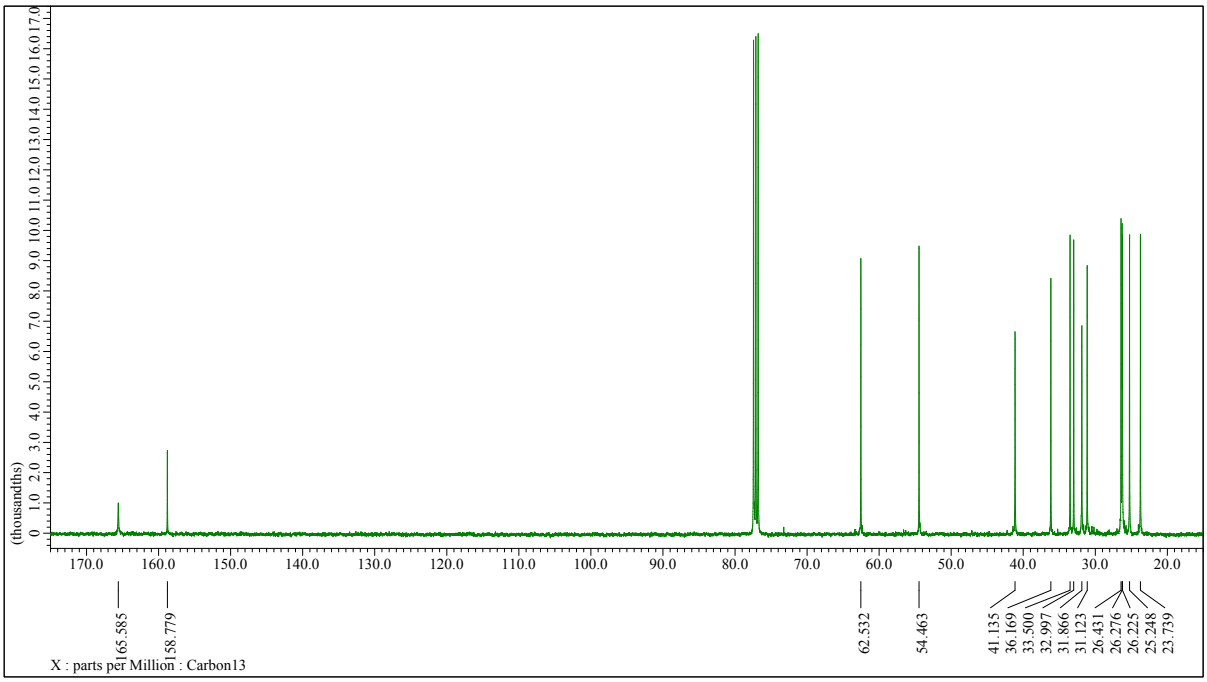


3l 4-cyclohexylmethyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene



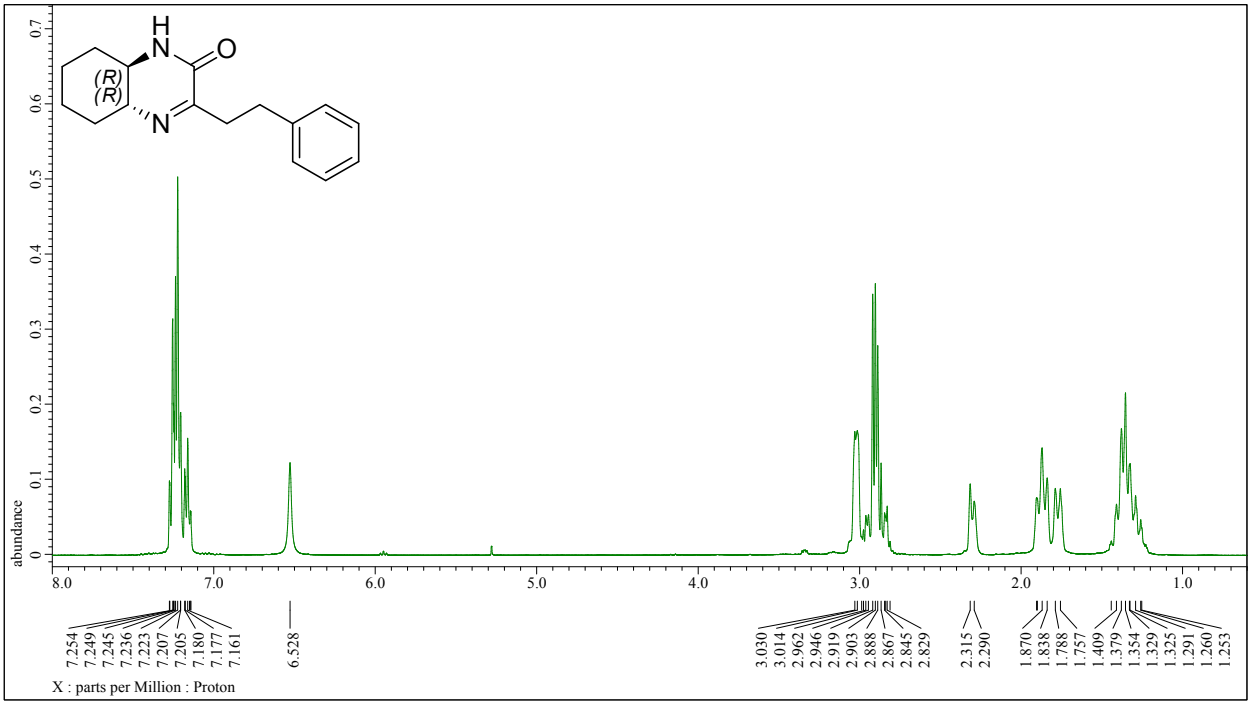
^{1}H NMR spectrum of **3l**

^{13}C NMR spectrum of **3l**

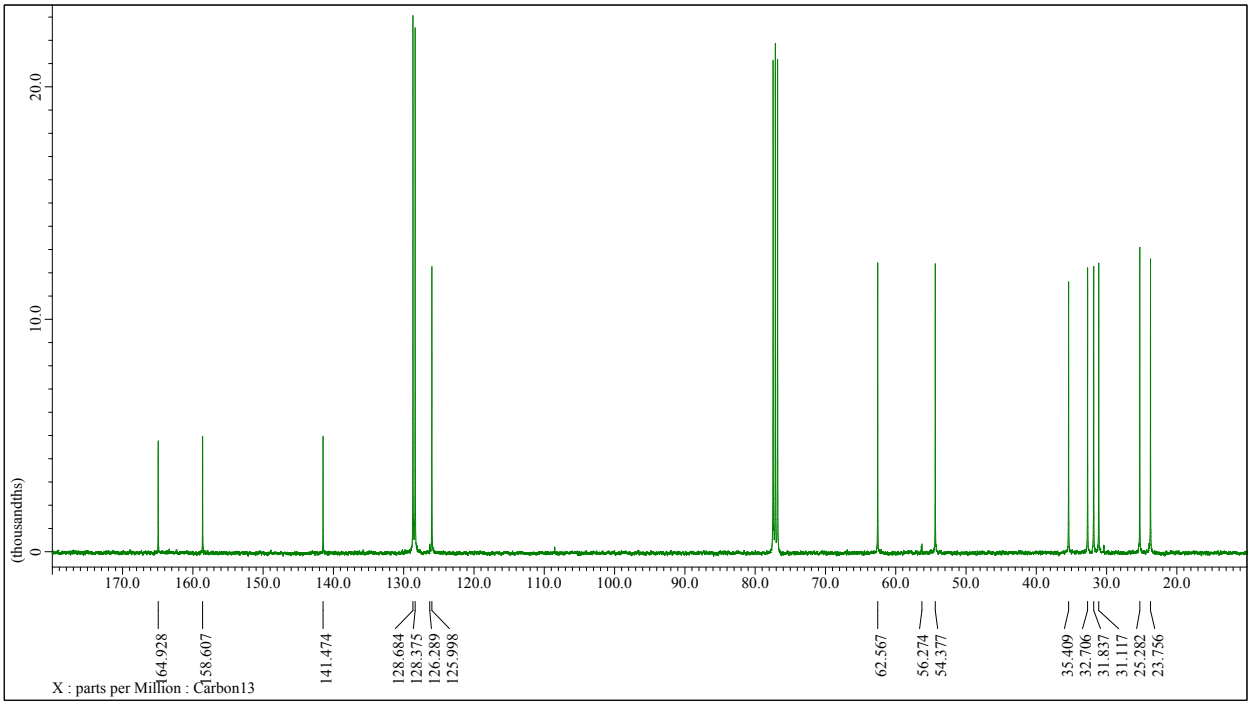


3m 4-phenethyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

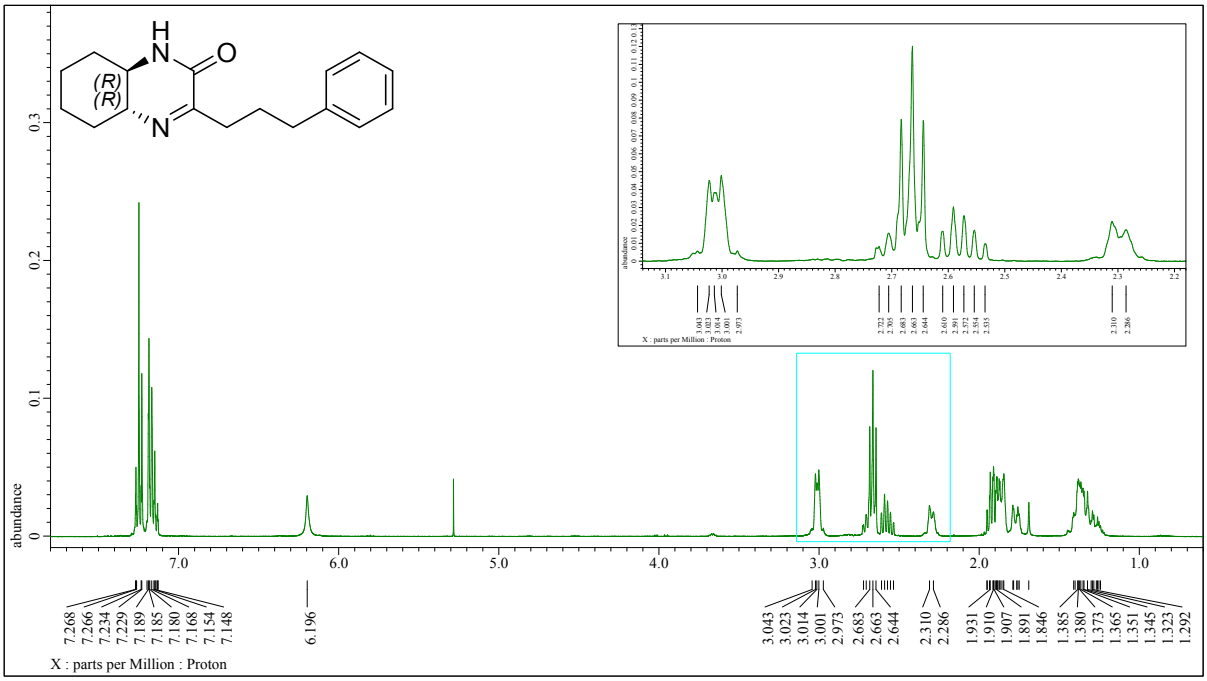
^{1}H NMR spectrum of **3m**



^{13}C NMR spectrum of **3m**

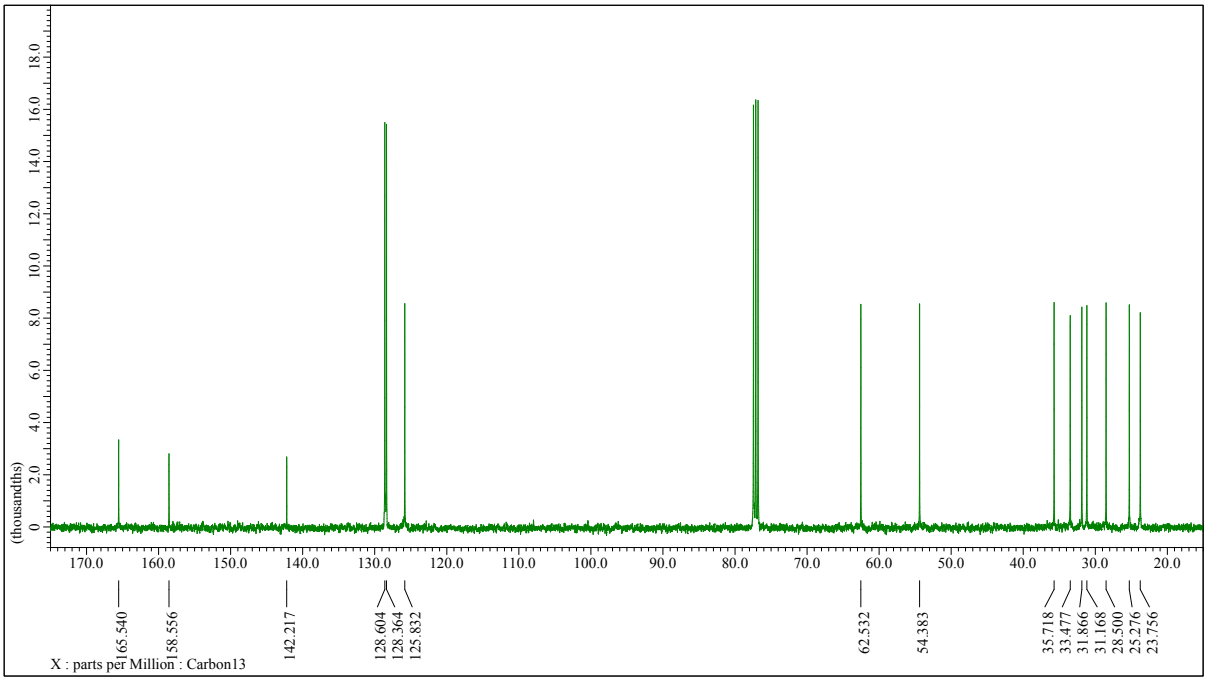


3n 4-phenylpropyl-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene

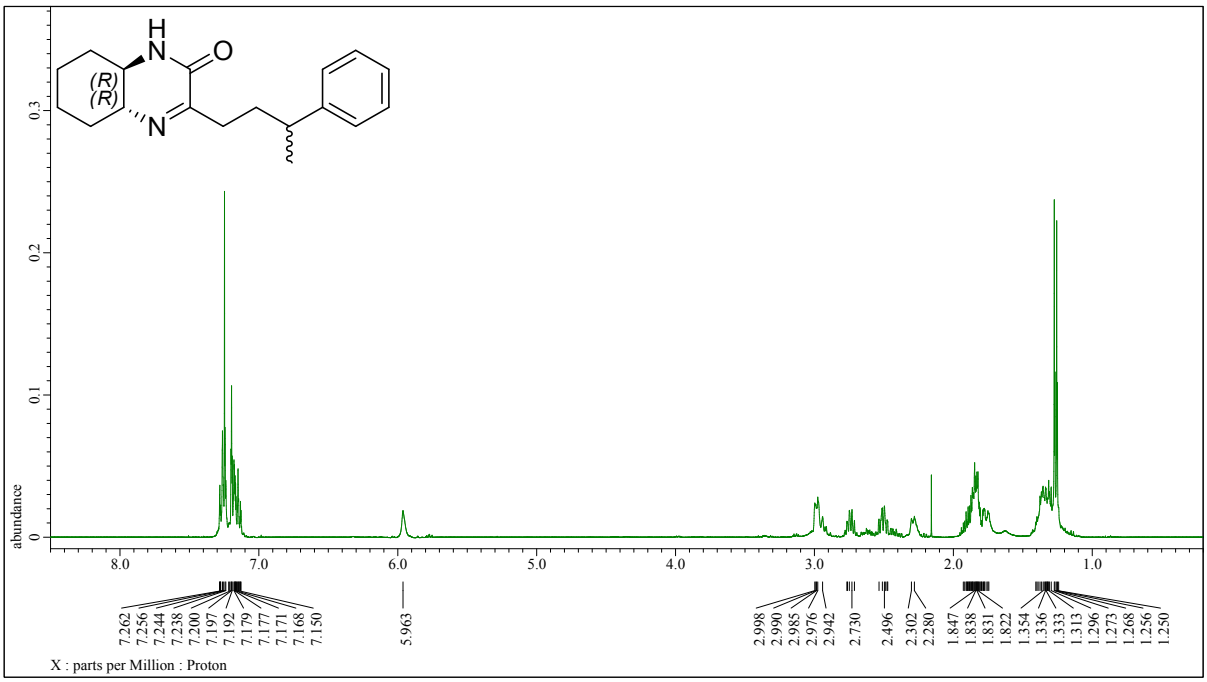


^{1}H NMR spectrum of **3n**

^{13}C NMR spectrum of **3n**

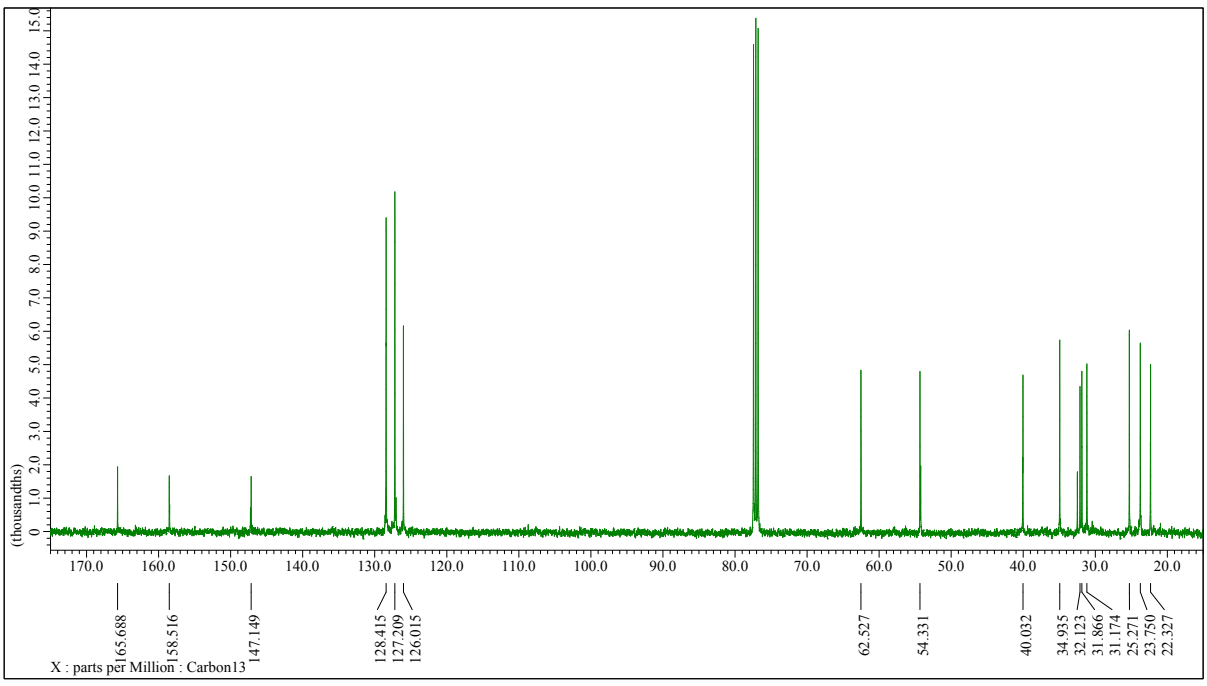


3o 4-(3-phenylbutyl)-(1*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-ene



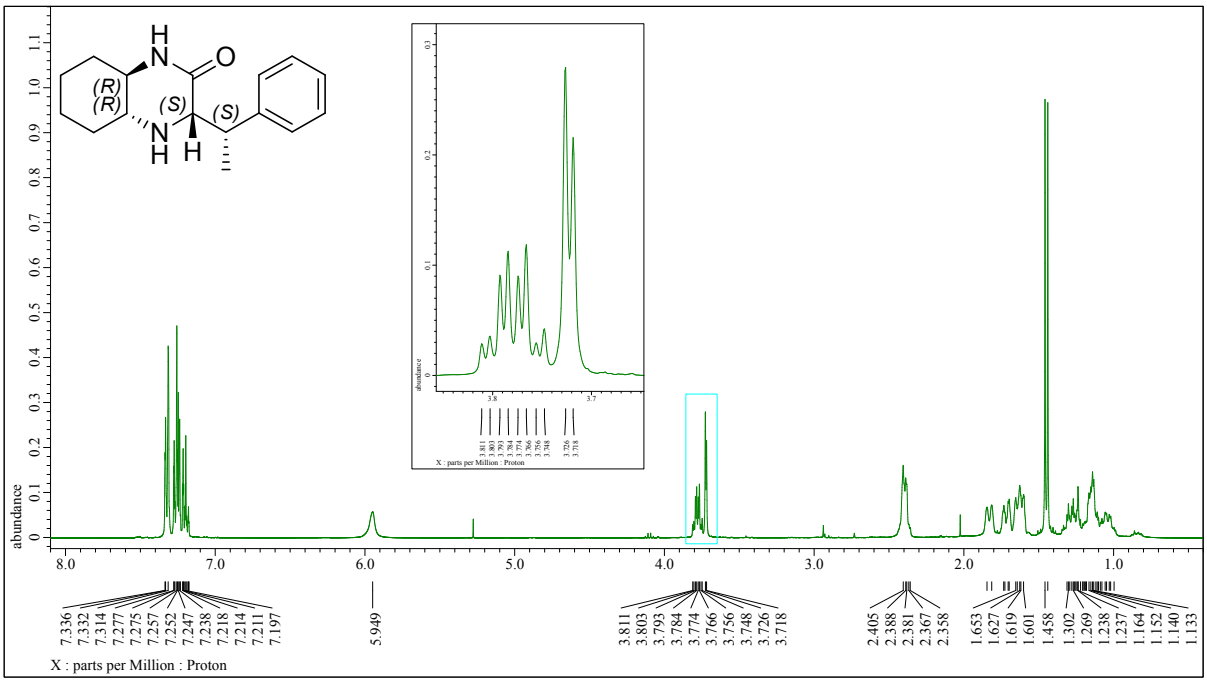
^{1}H NMR spectrum of **3o**

^{13}C NMR spectrum of **3o**



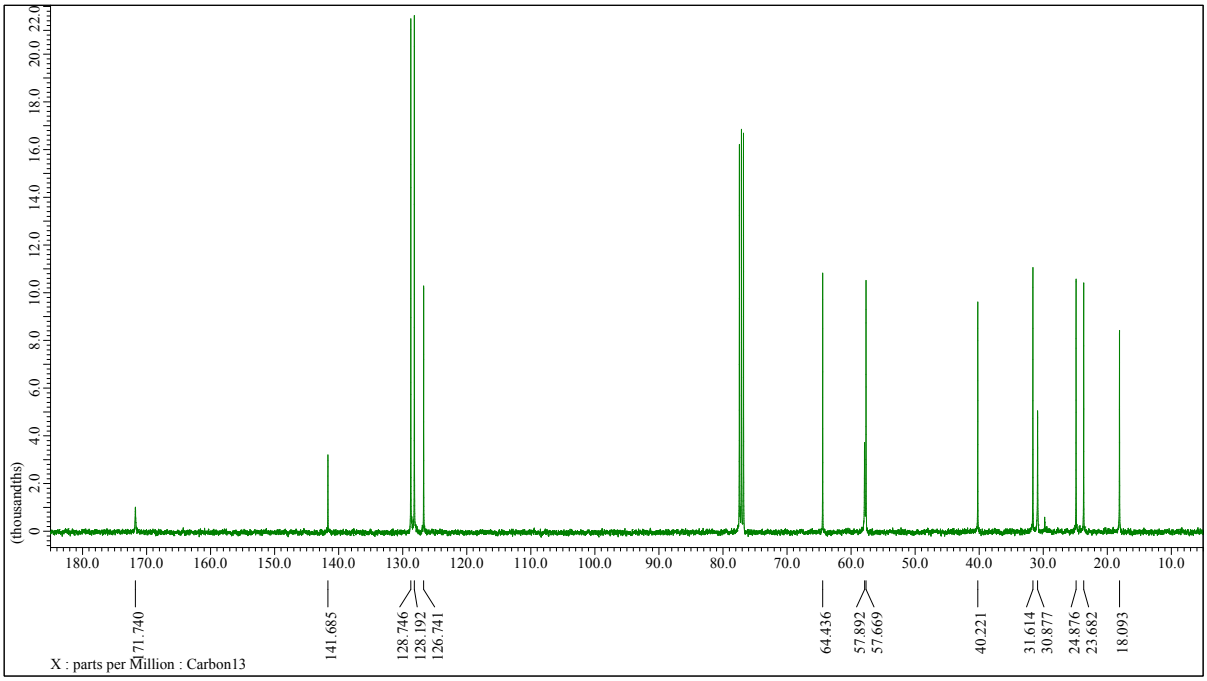
Cyclic amines

4a (4-((*S*)-1-phenylethyl))-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

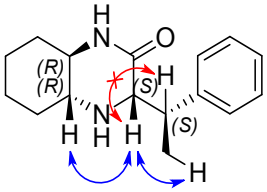


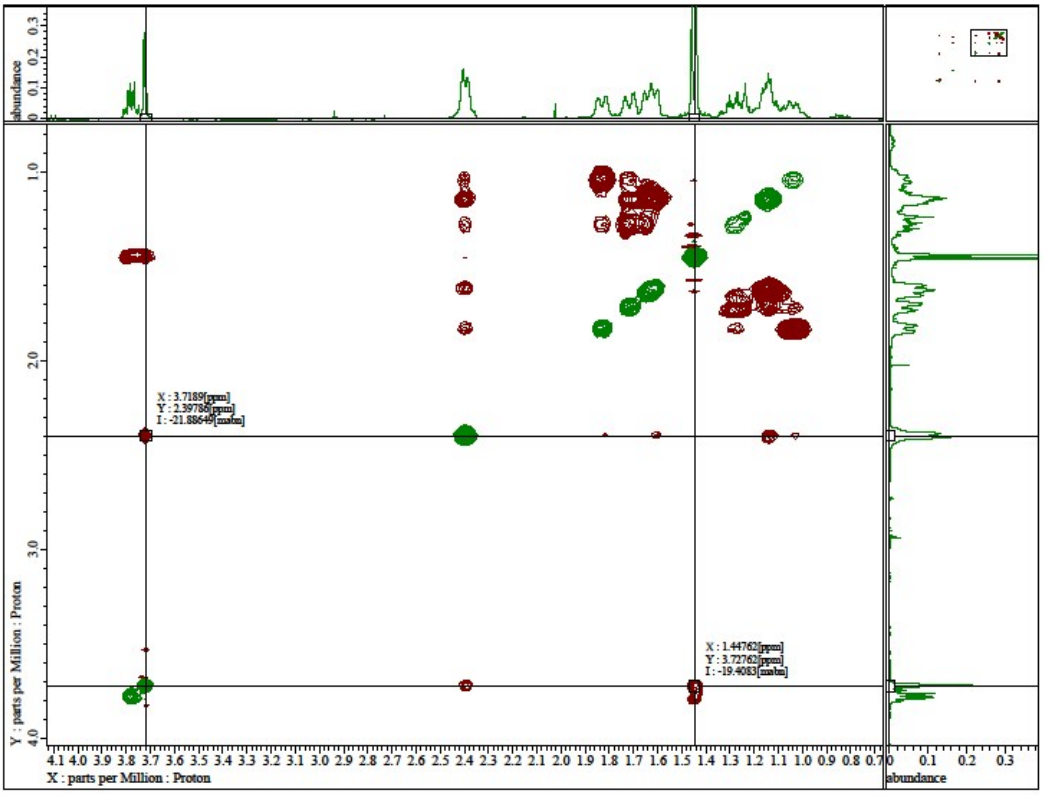
^{1}H NMR spectrum of **4a**

^{13}C NMR spectrum of **4a**

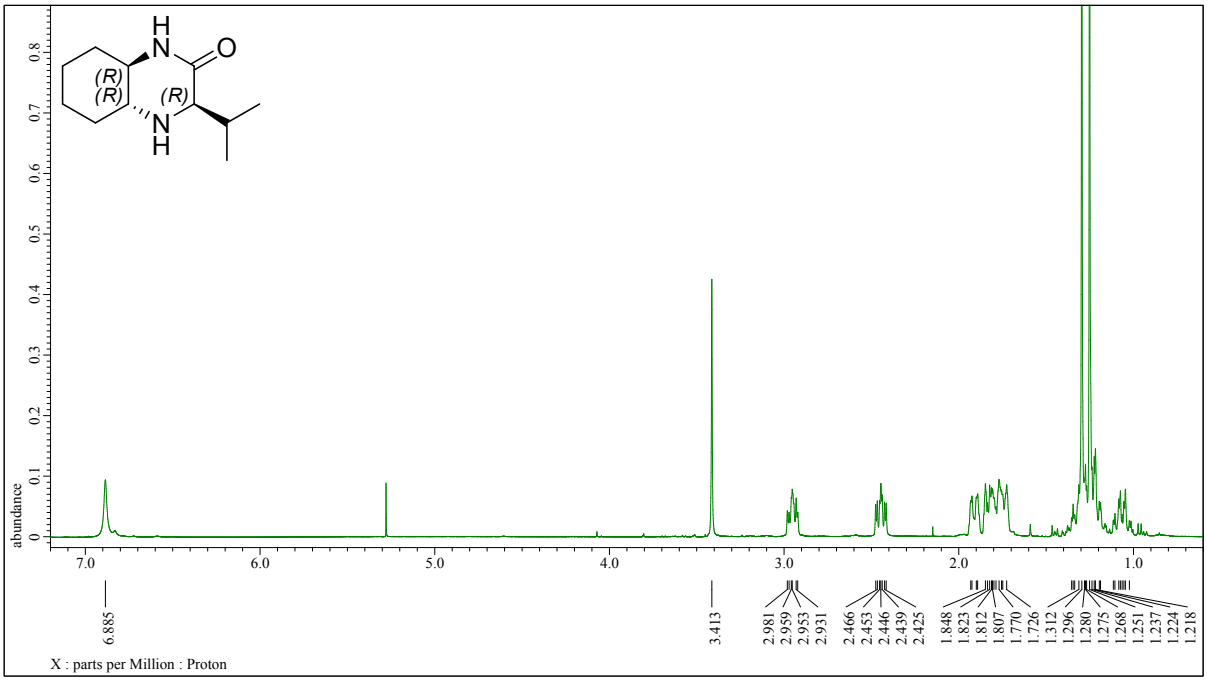


NOESY correlation of **4a**



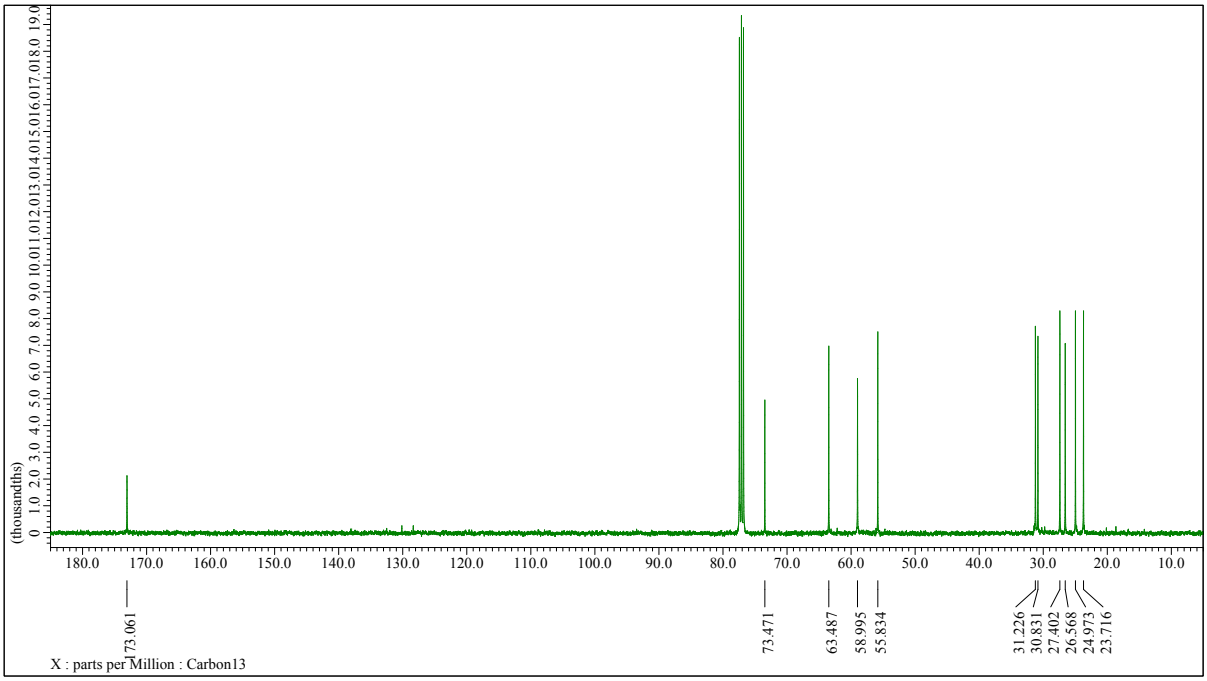


4b isopropyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

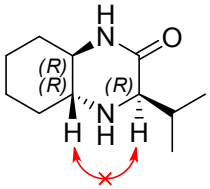


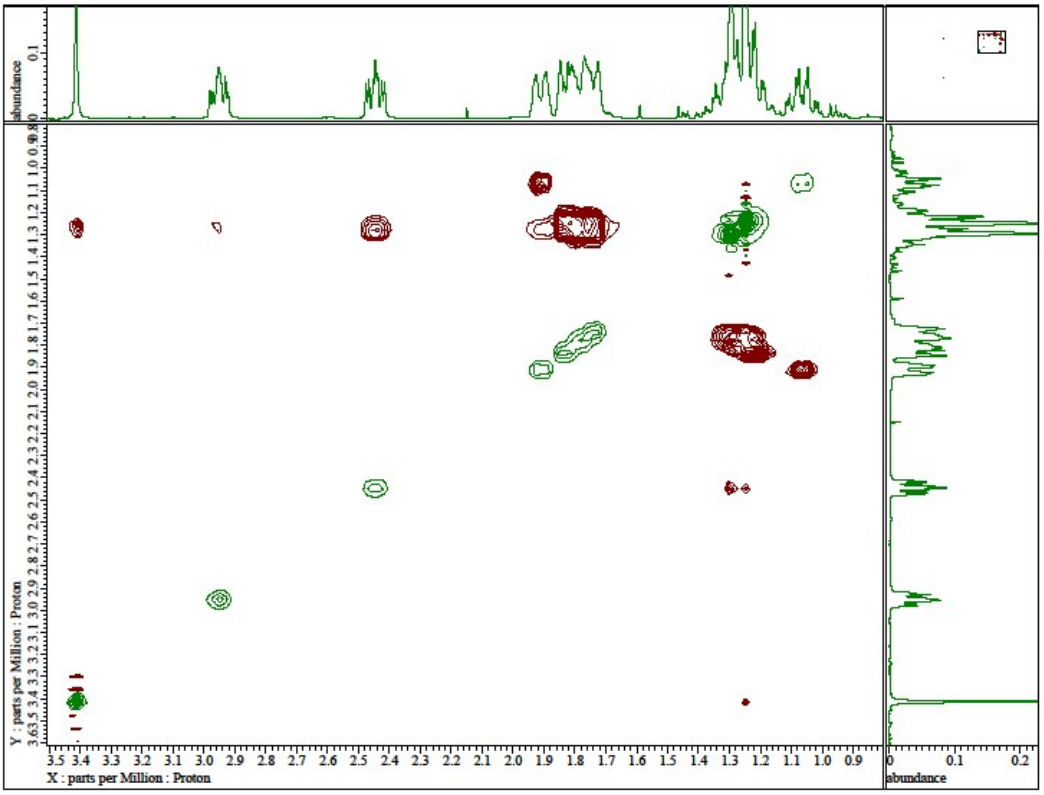
^{1}H NMR spectrum of **4b**

^{13}C NMR spectrum of **4b**

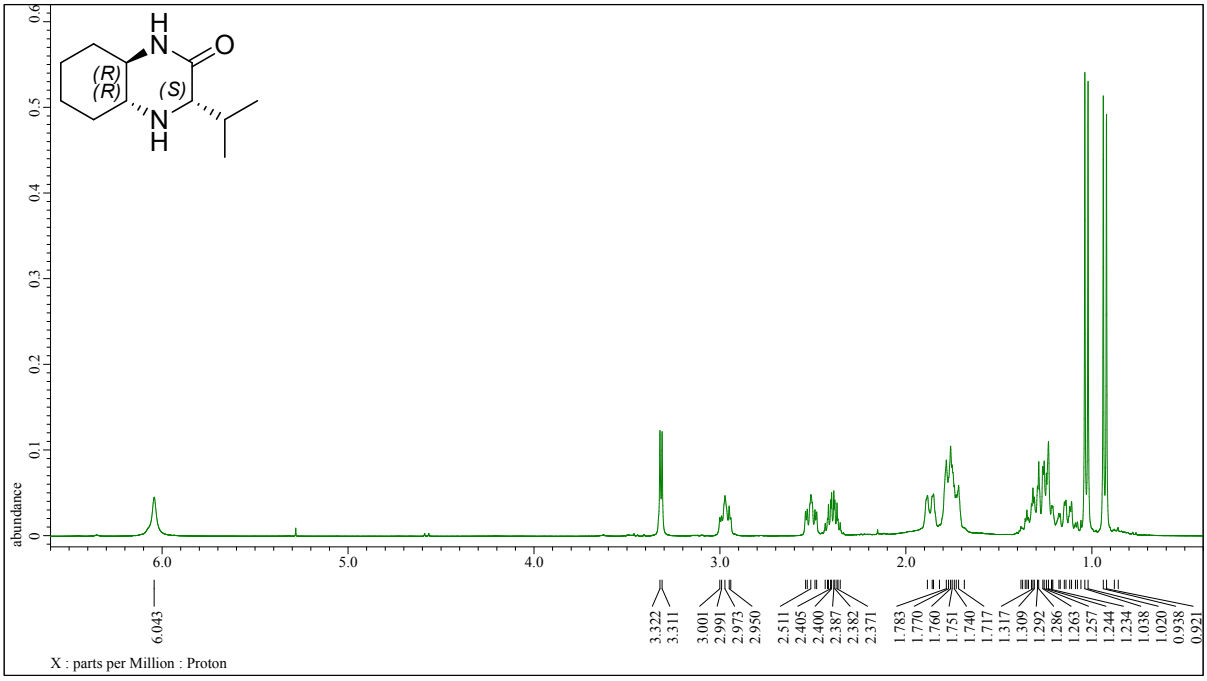


NOESY correlation of **4b**



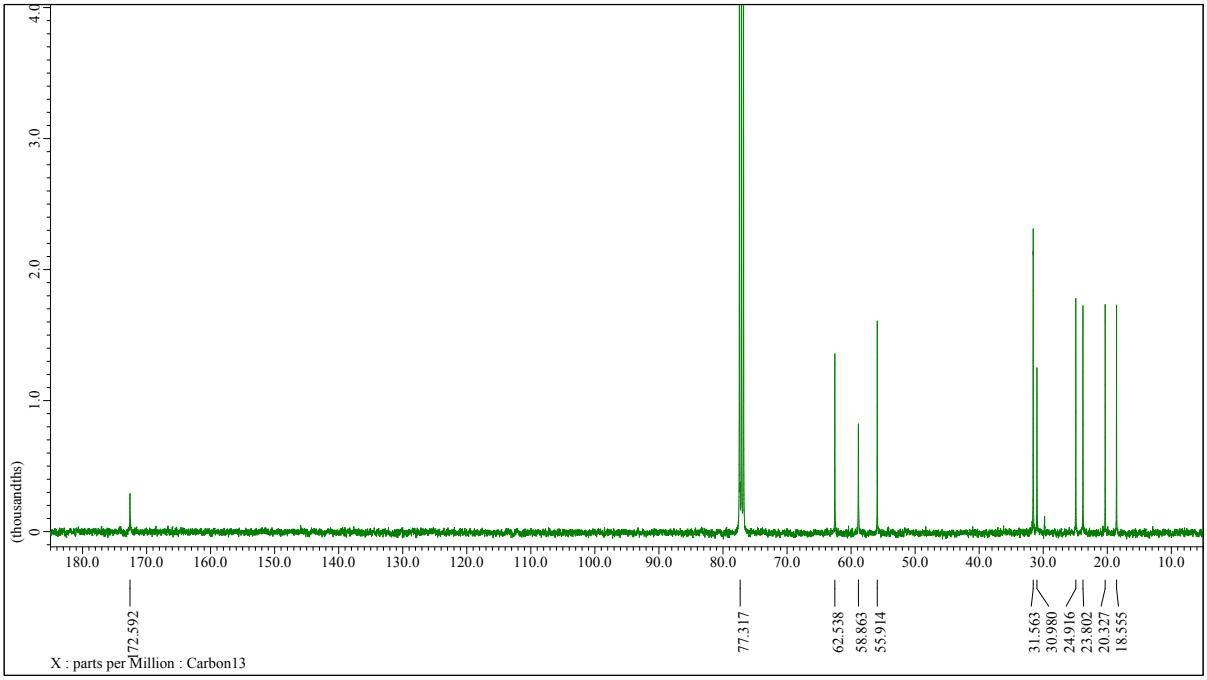


4b’ isopropyl-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

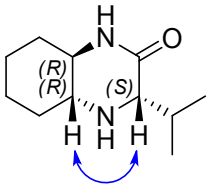


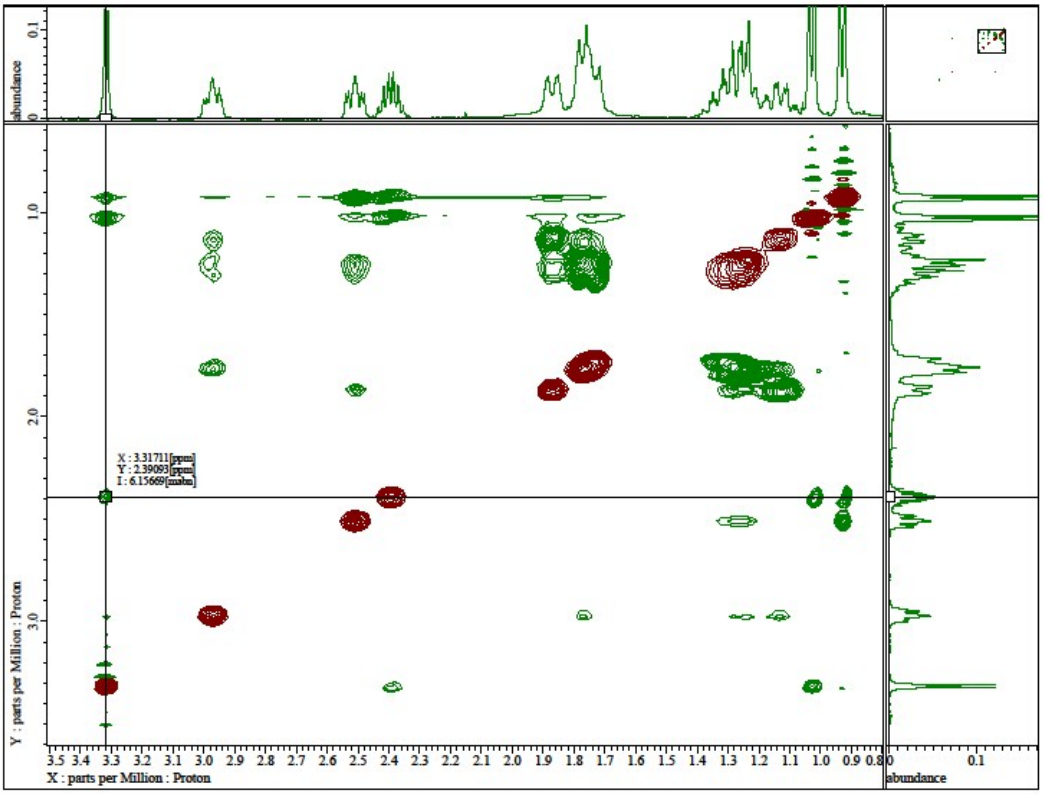
^{1}H NMR spectrum of **4b’**

^{13}C NMR spectrum of **4b’**

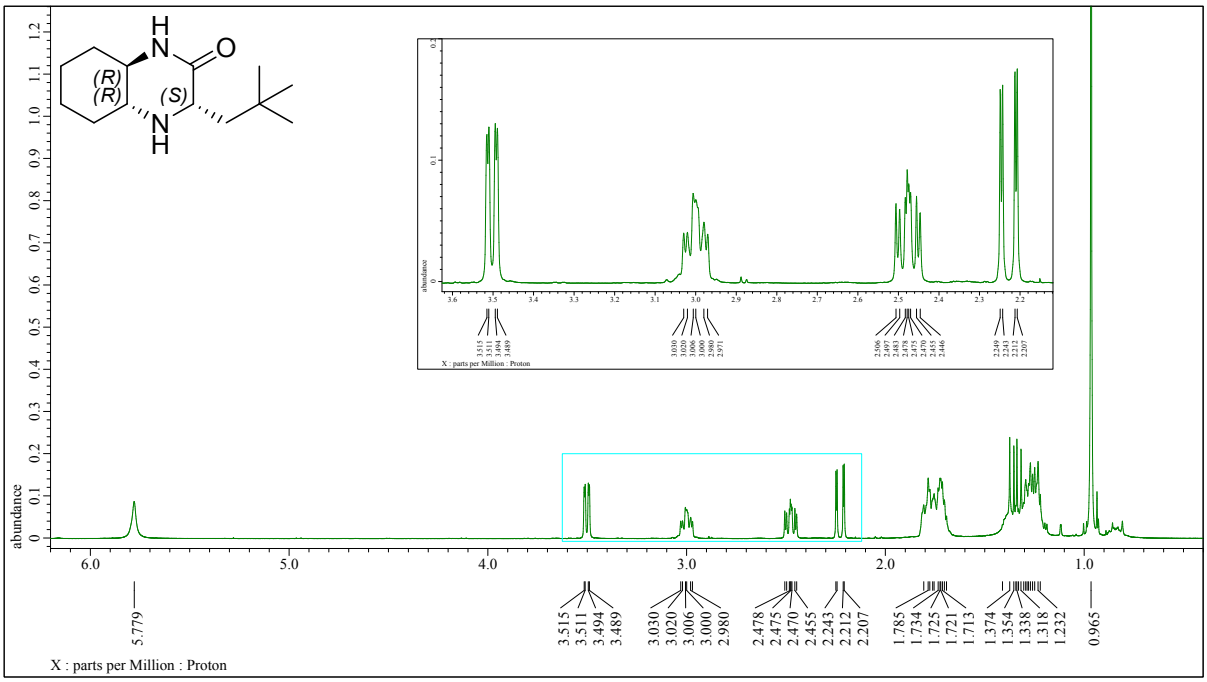


NOESY correlation of **4b'**



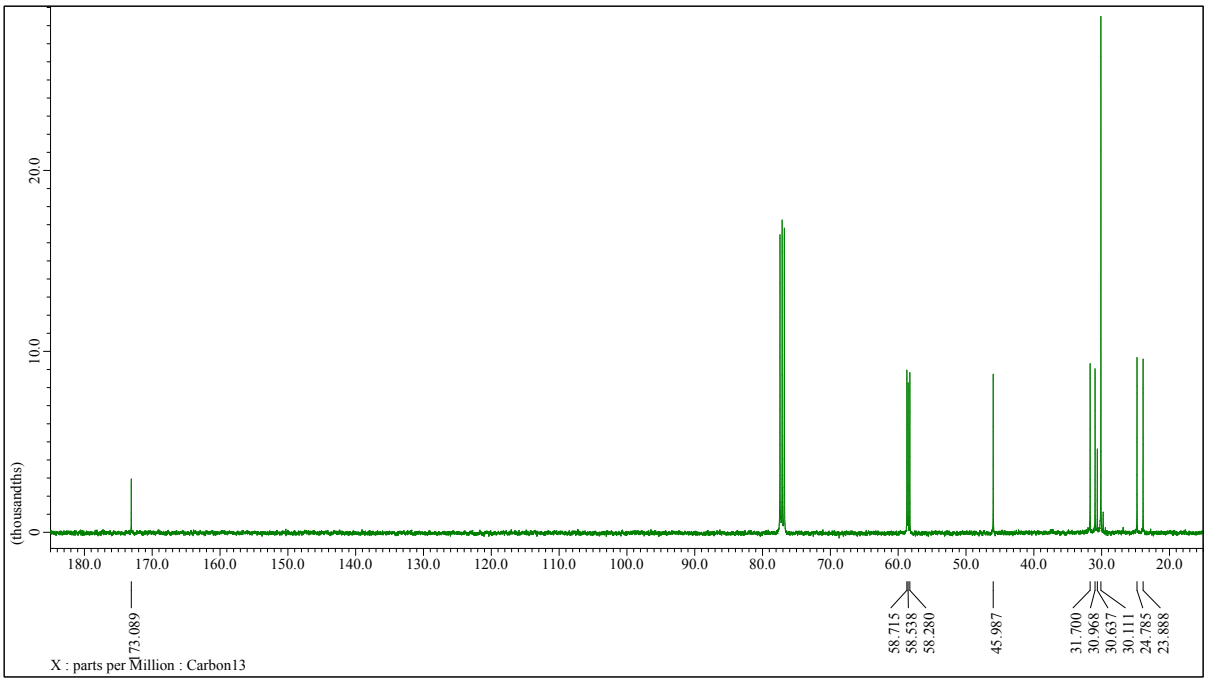


5a 4-neopentyl-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

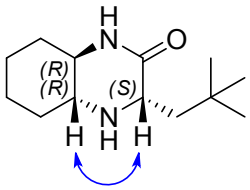


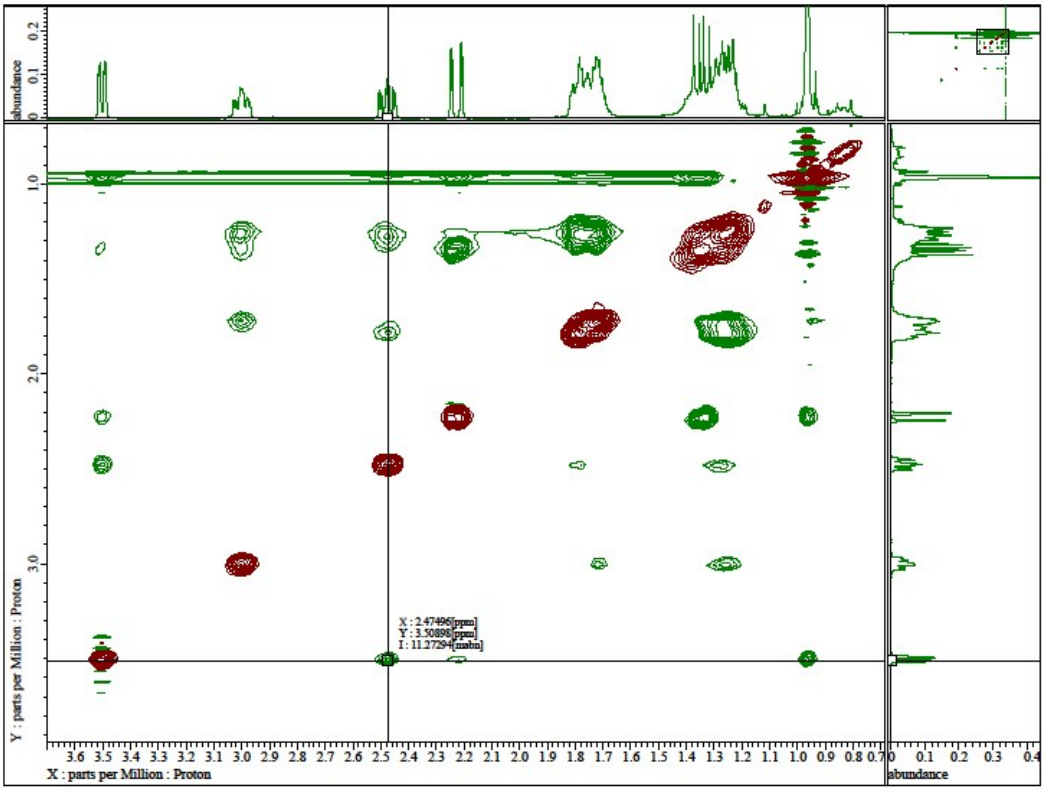
^{1}H NMR spectrum of **5a**

^{13}C NMR spectrum of **5a**

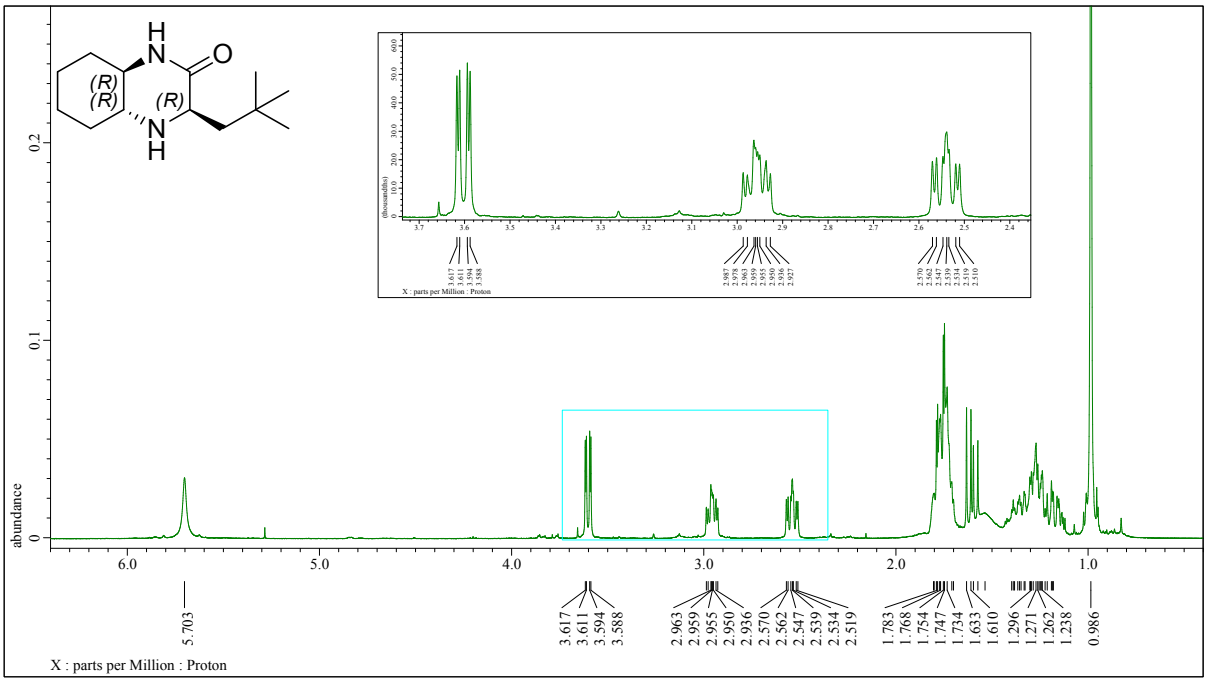


NOESY correlation of **5a**



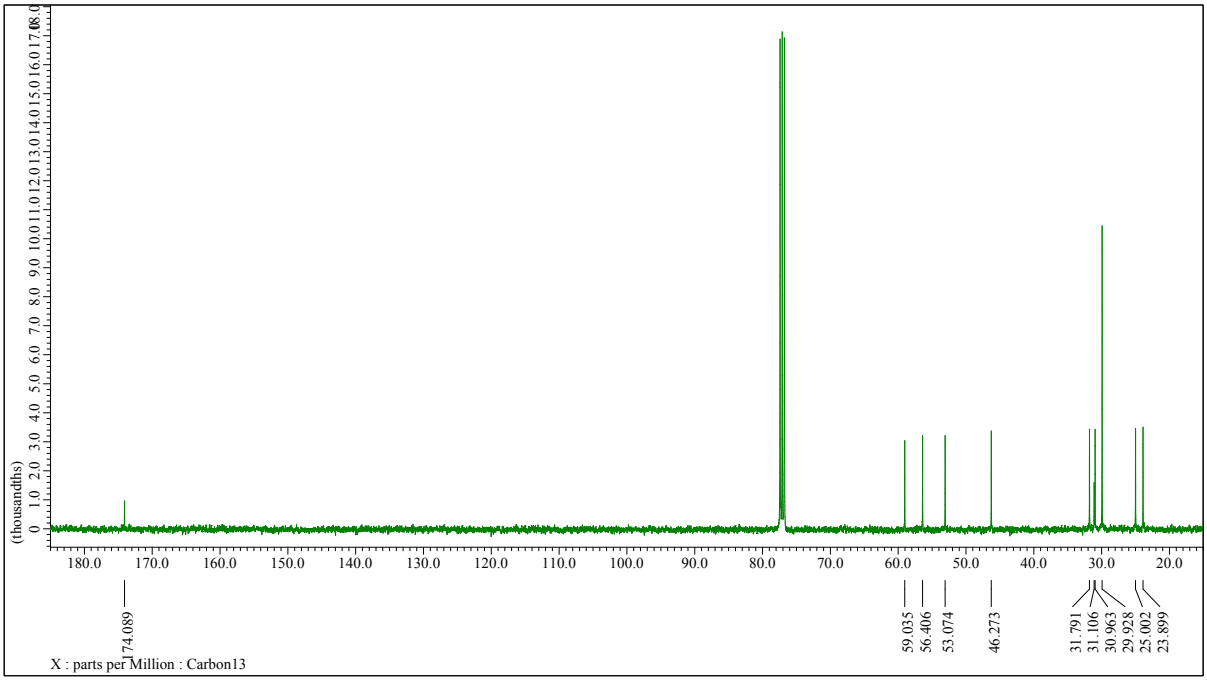


5a’ 4-neopentyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

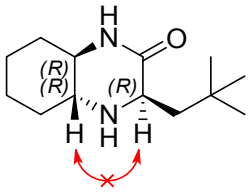


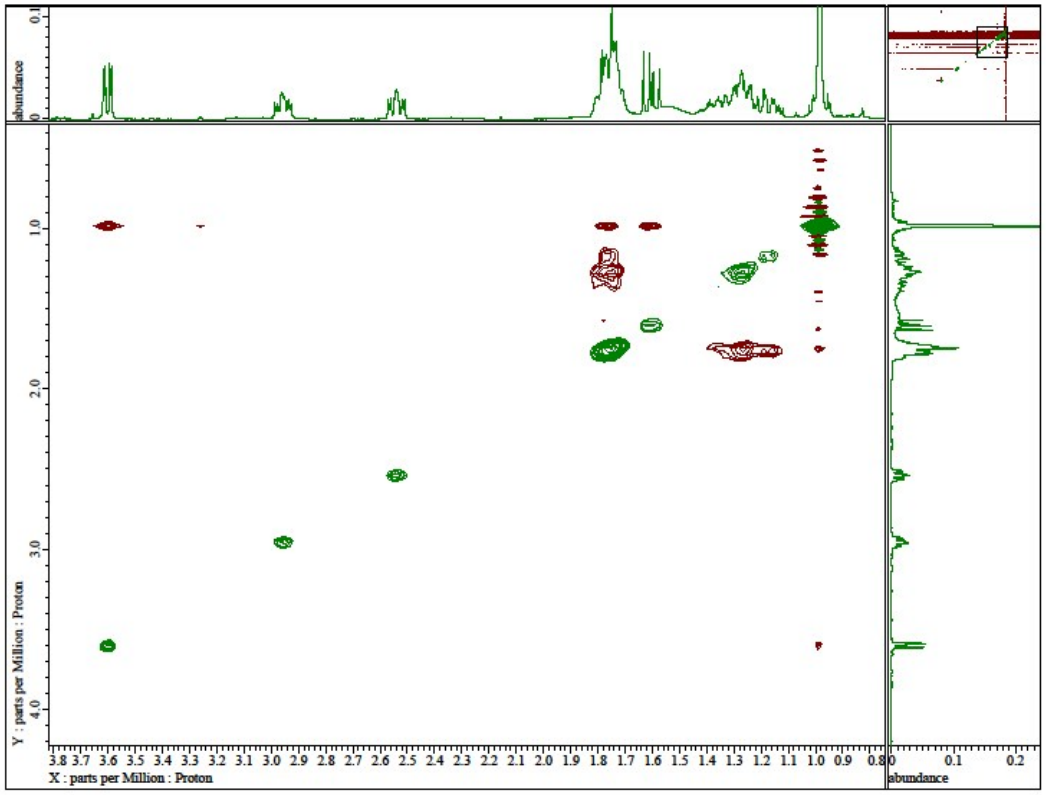
^{1}H NMR spectrum of **5a’**

^{13}C NMR spectrum of **5a’**



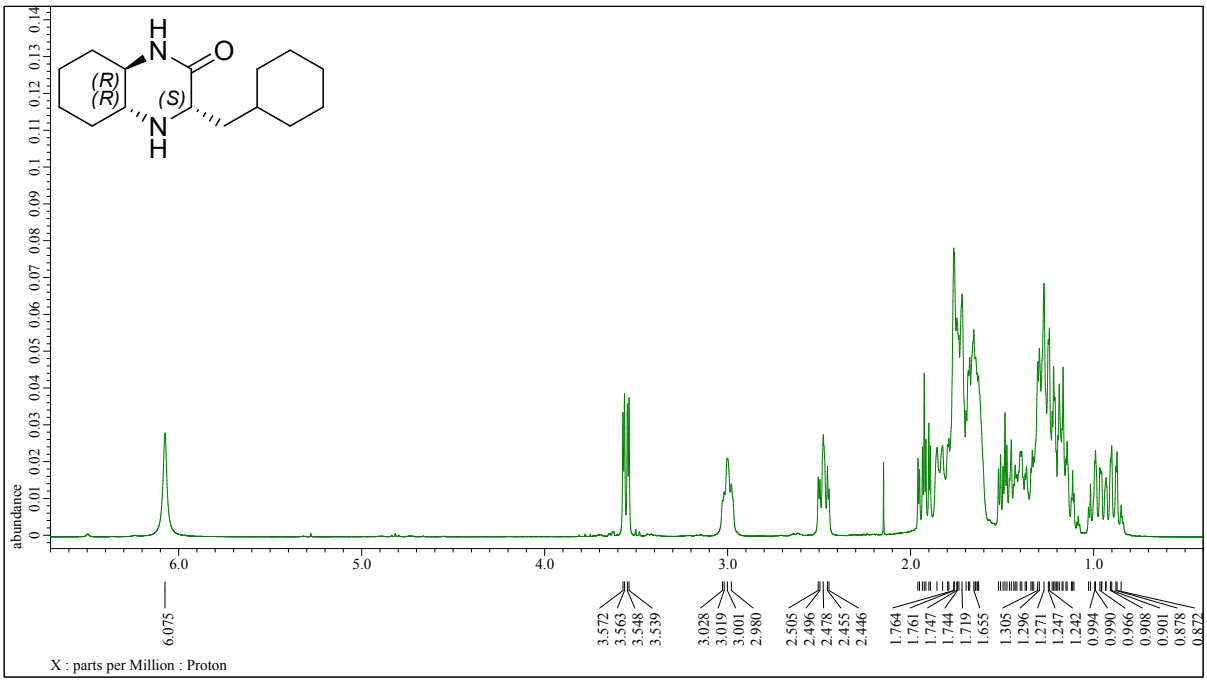
NOESY correlation of **5a'**

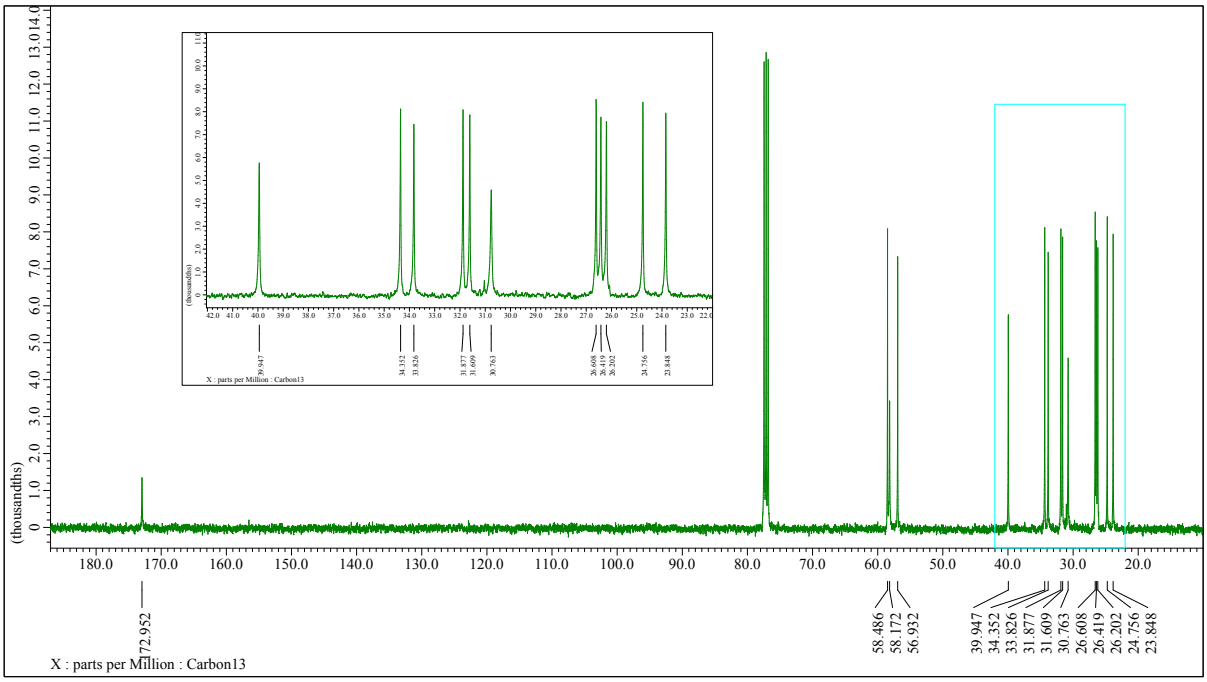




5b 4-(cyclohexylmethyl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

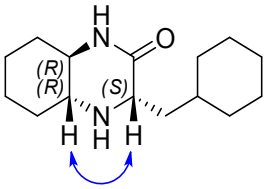
^{1}H NMR spectrum of **5b**

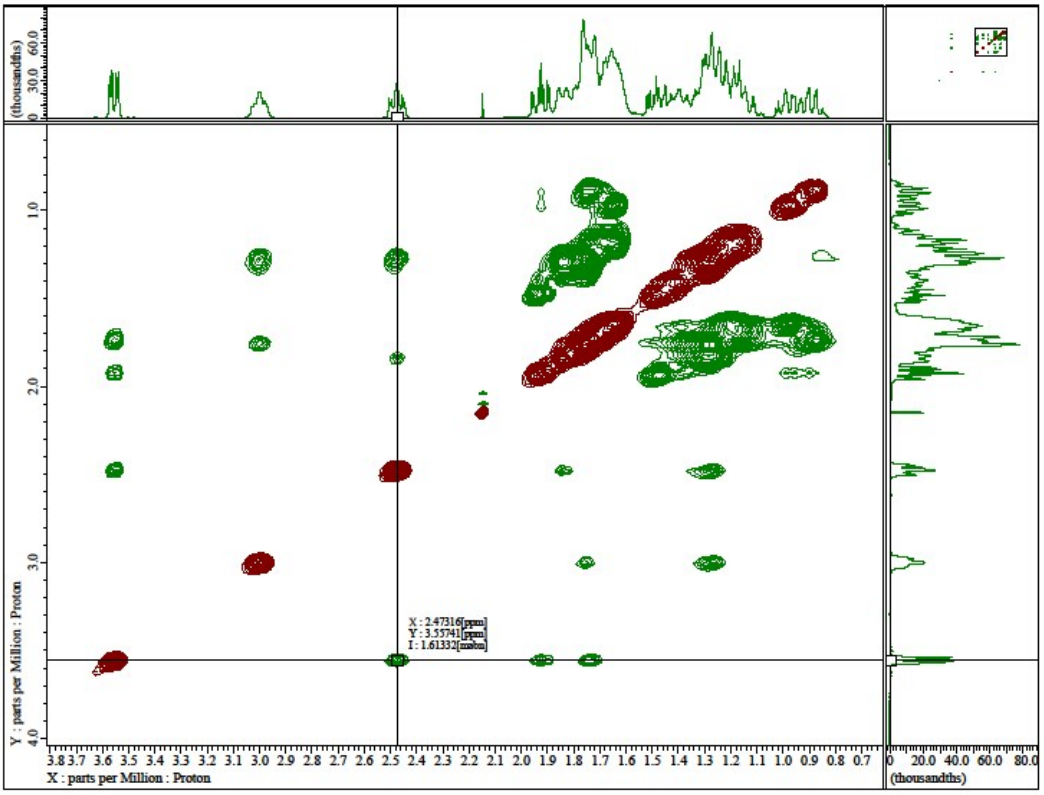




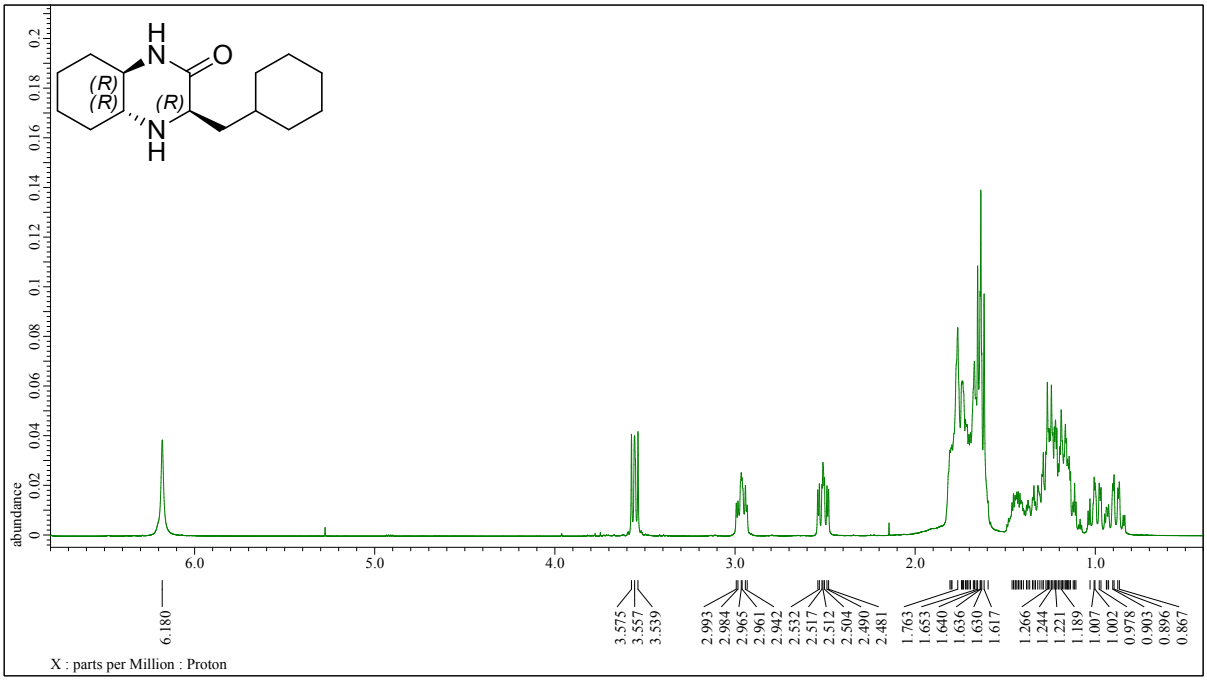
^{13}C NMR spectrum of **5b**

NOESY correlation of **5b**



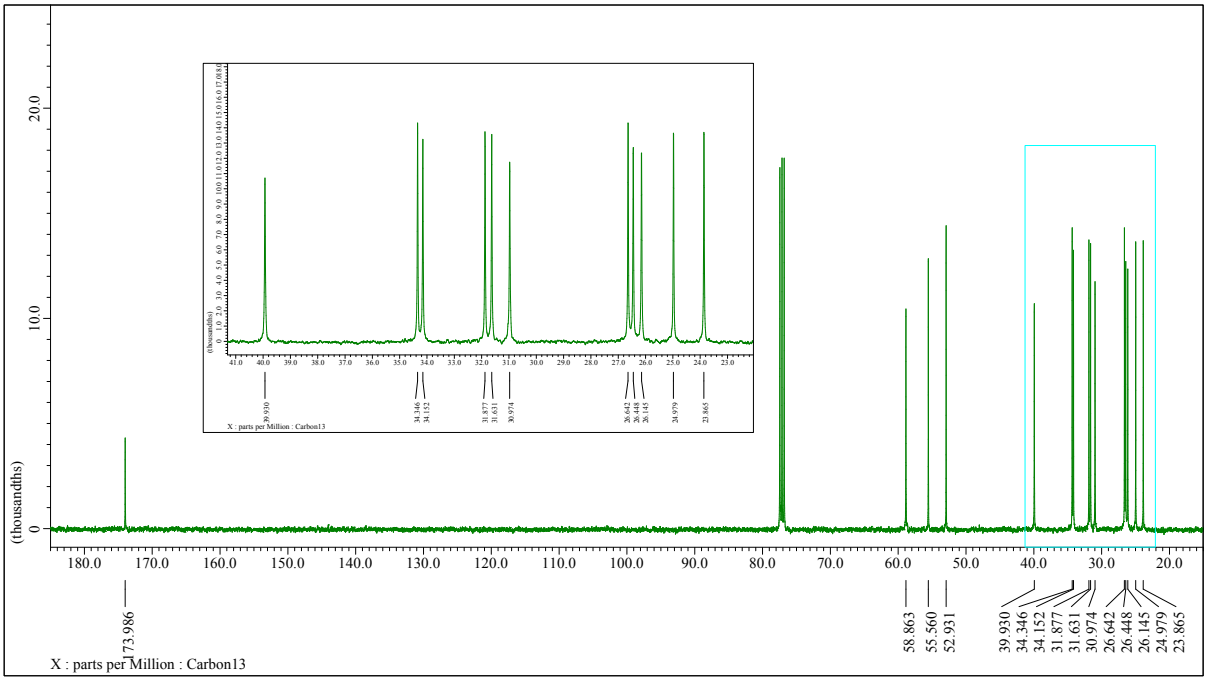


5b’ 4-(cyclohexylmethyl)-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

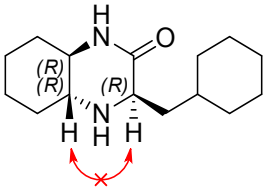


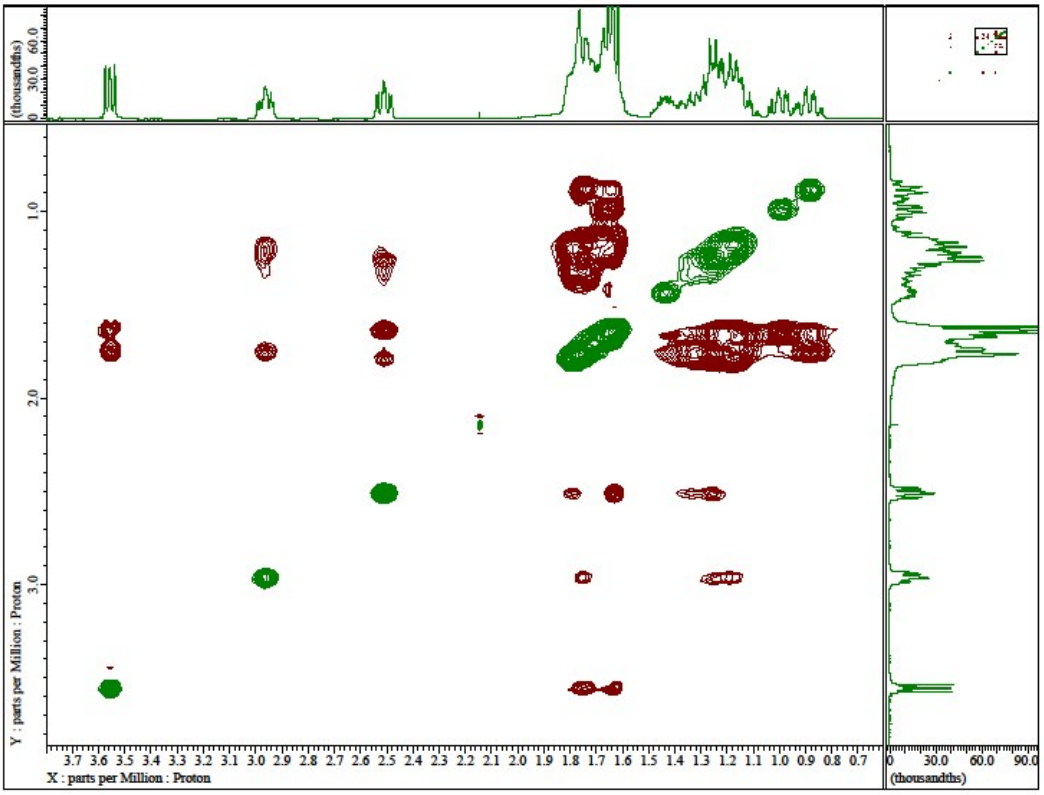
^{1}H NMR spectrum of **5b’**

^{13}C NMR spectrum of **5b’**

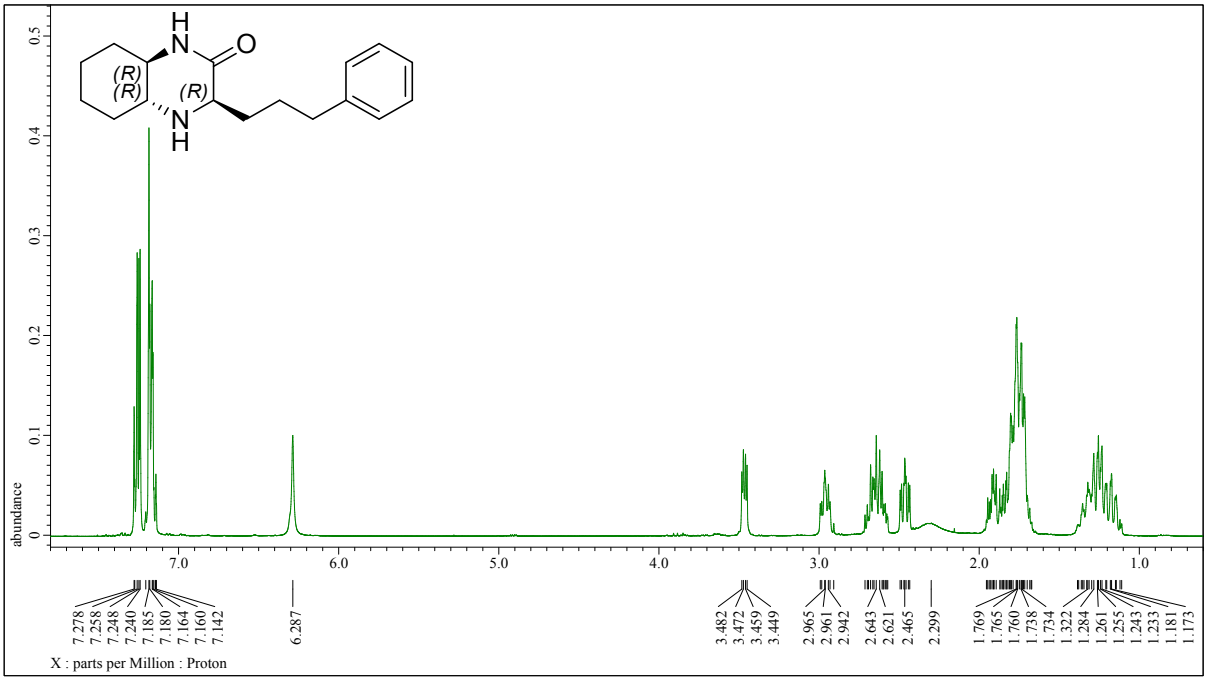


NOESY correlation of **5b'**



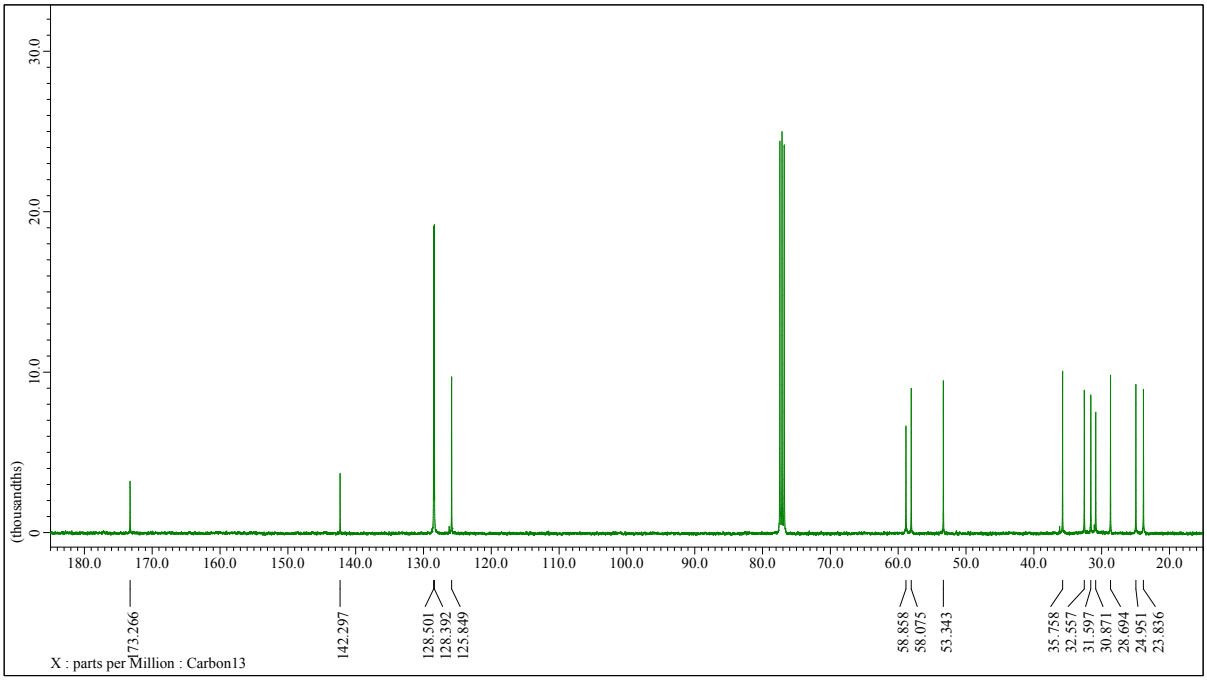


5c (3-phenylpropyl)-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

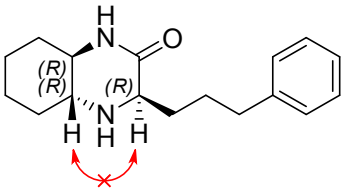


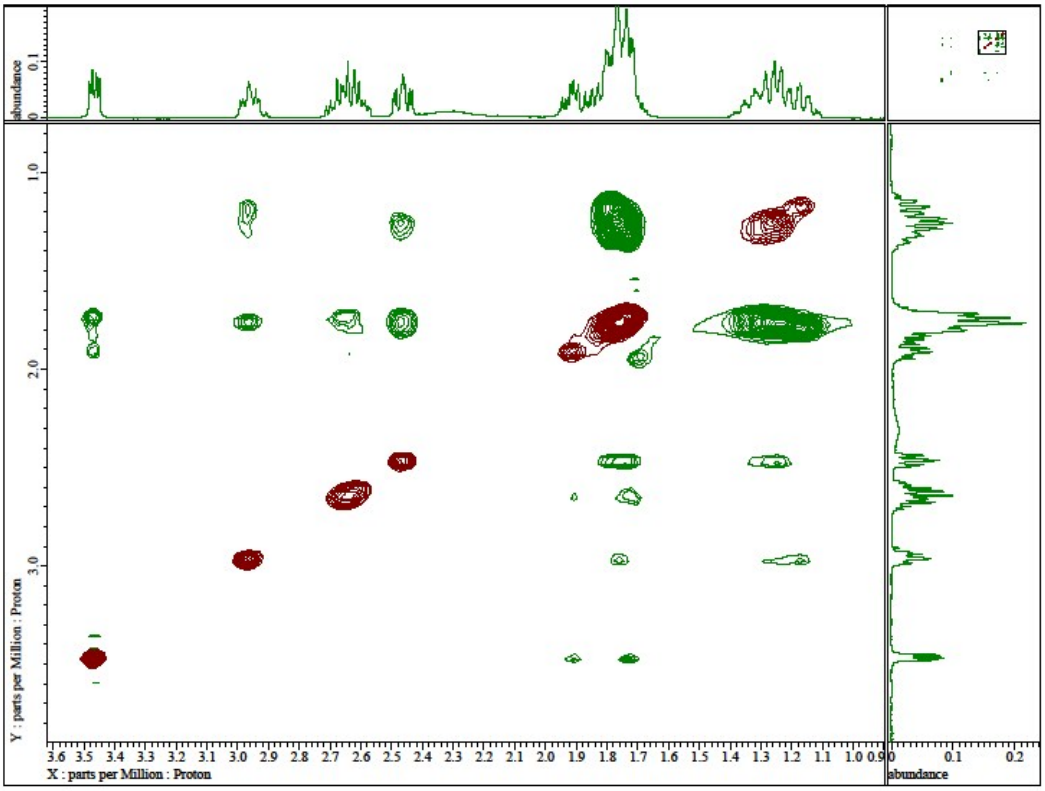
^{1}H NMR spectrum of **5c**

^{13}C NMR spectrum of **5c**

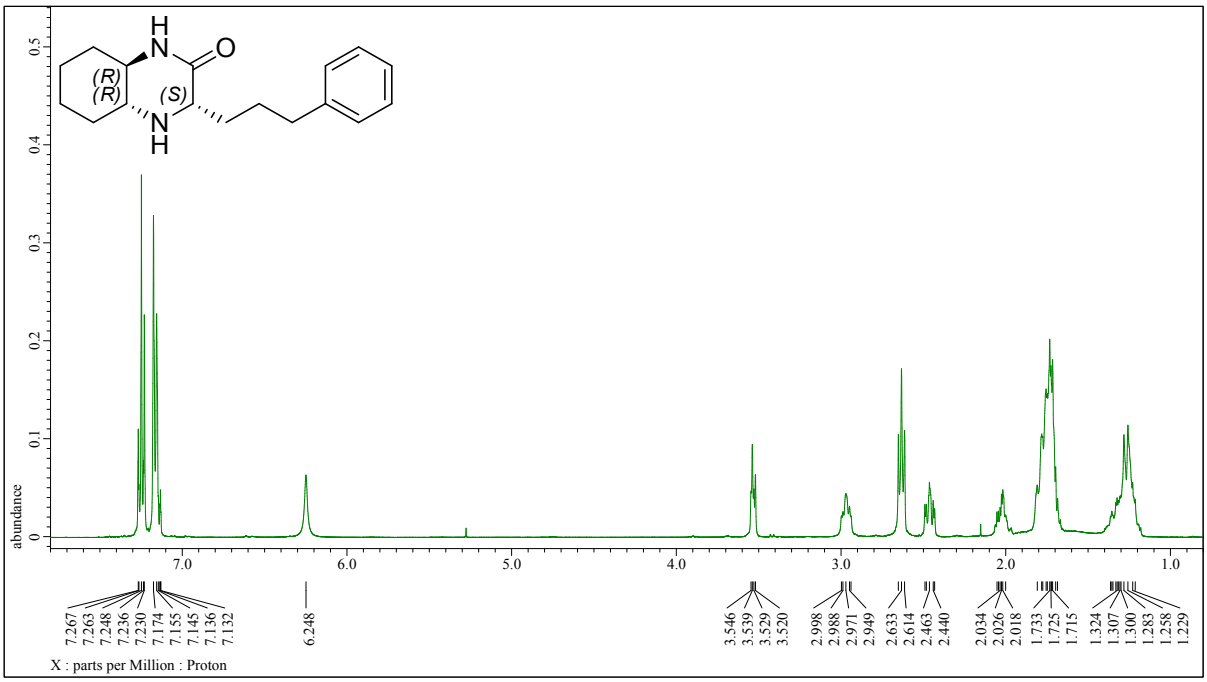


NOESY correlation of **5c**



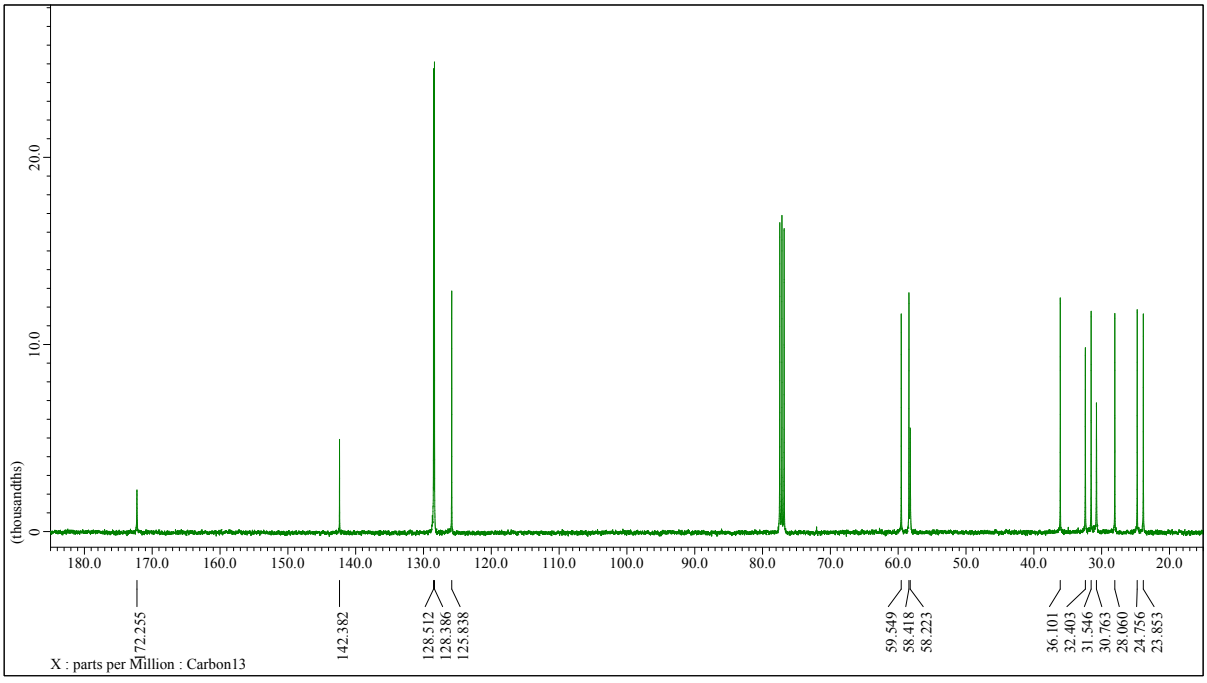


5c’ (3-phenylpropyl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

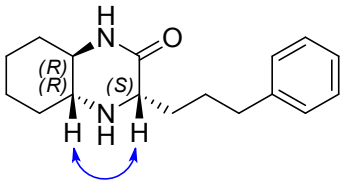


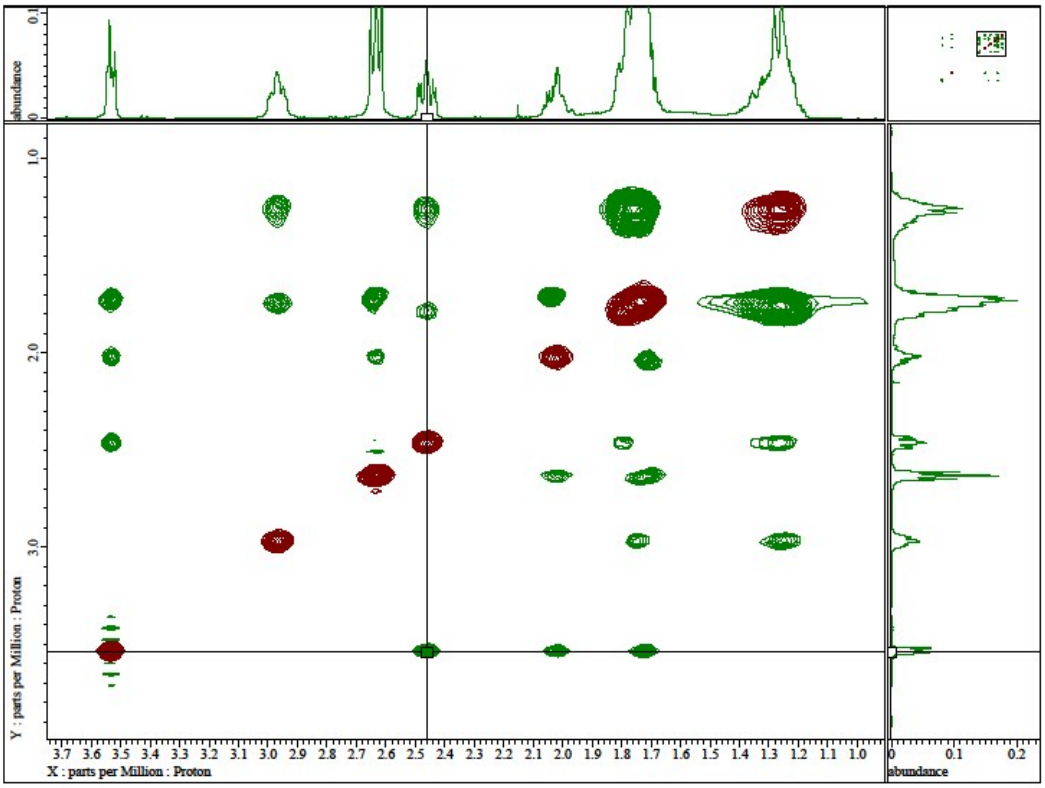
^{1}H NMR spectrum of **5c’**

^{13}C NMR spectrum of **5c’**

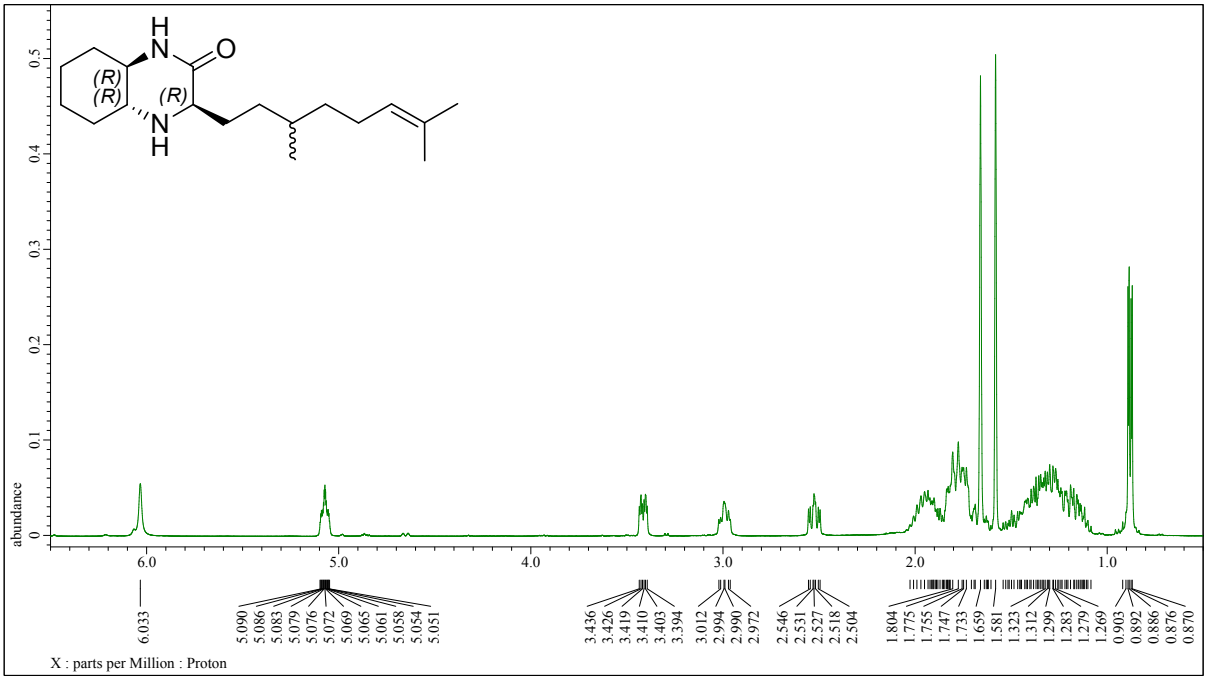


NOESY correlation of **5c'**



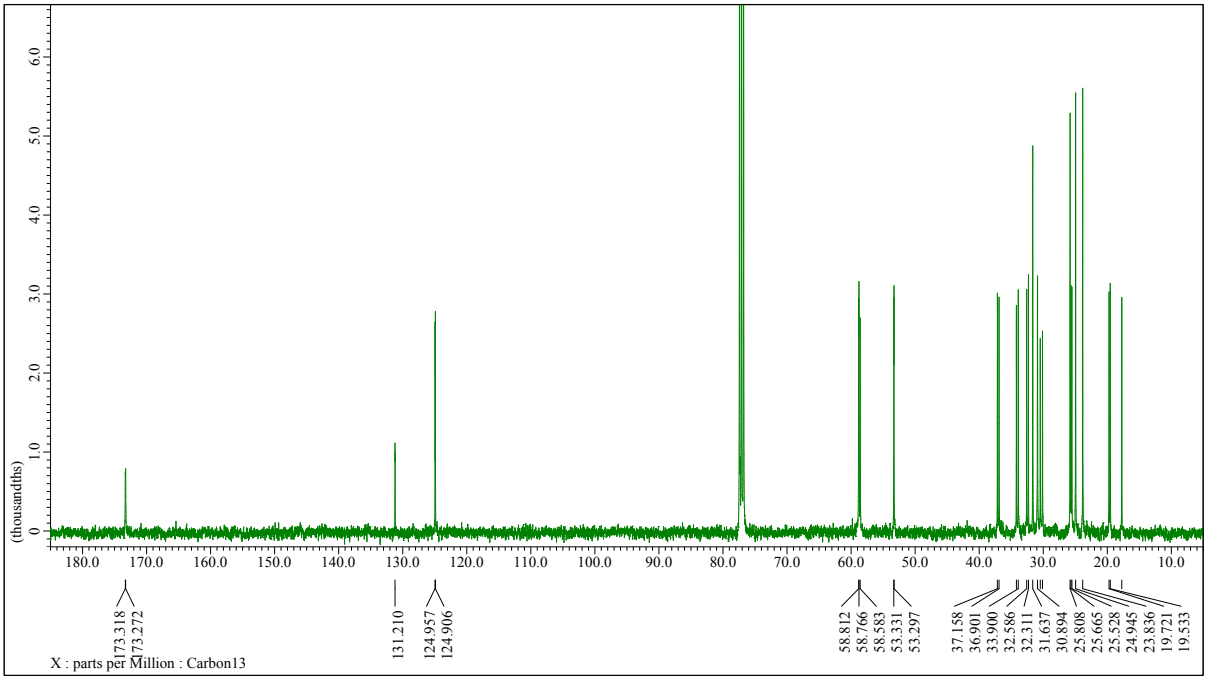


5d (3,7-dimethyloct-6-en-1-yl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

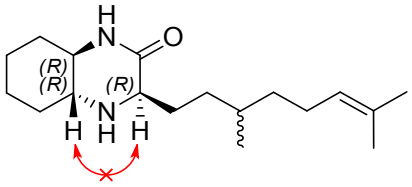


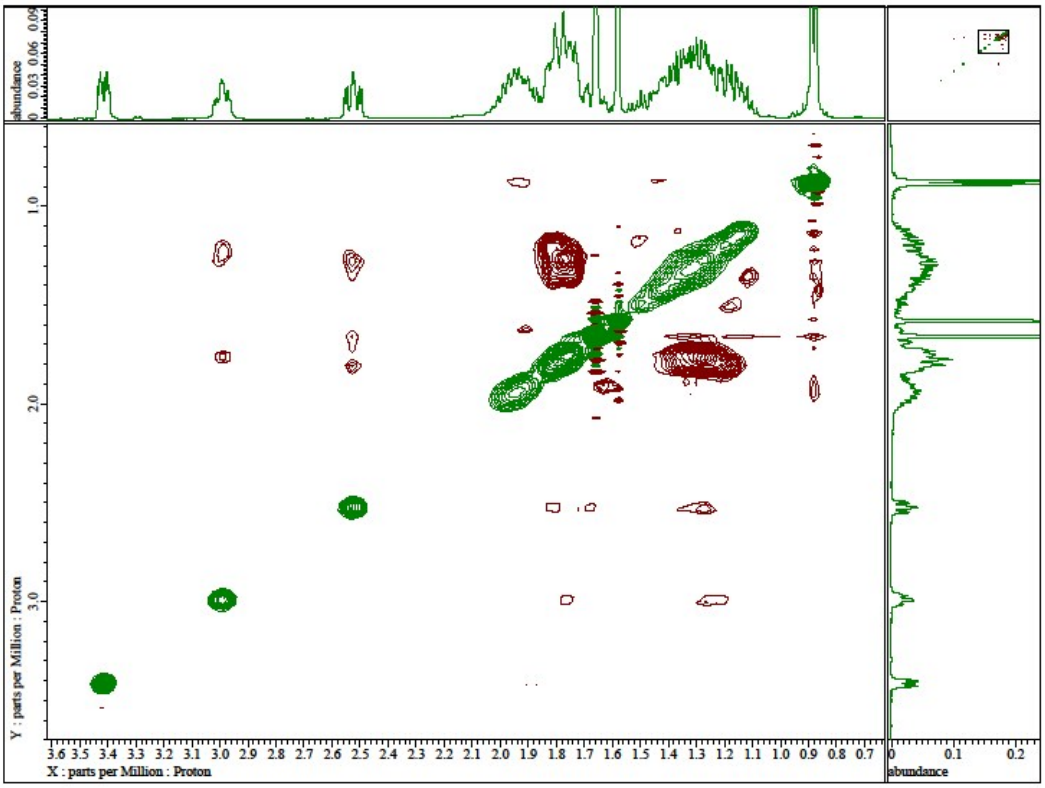
^{1}H NMR spectrum of **5d**

^{13}C NMR spectrum of **5d**



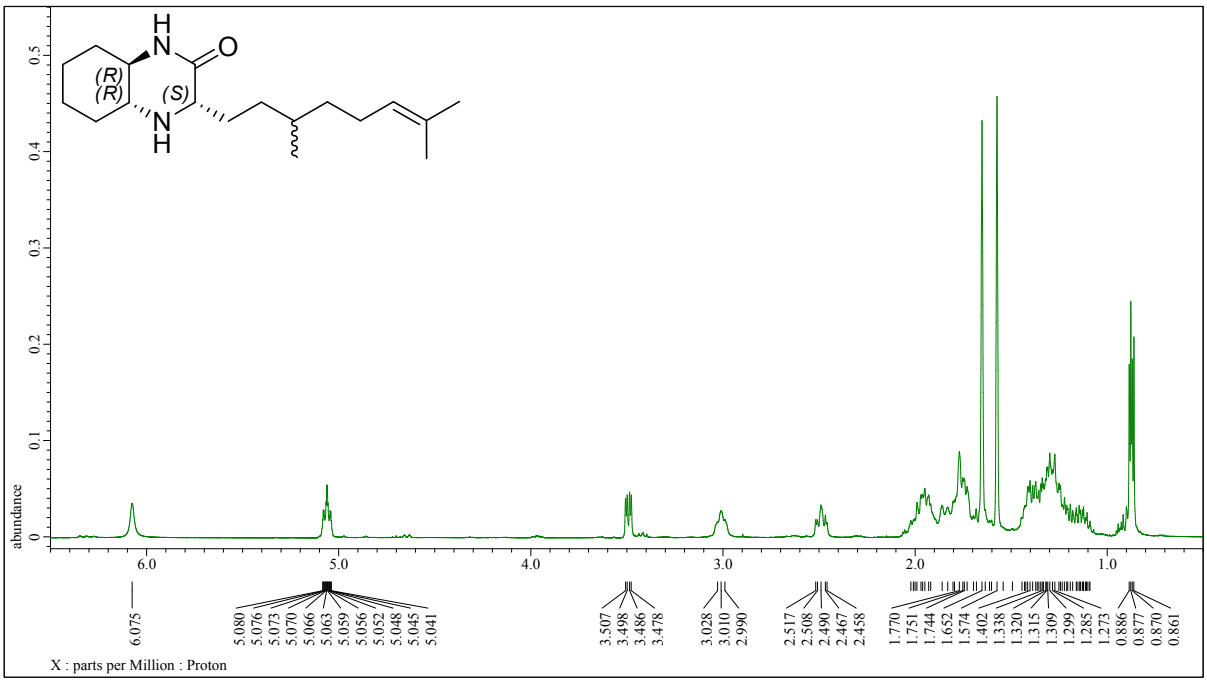
NOESY correlation of **5d**



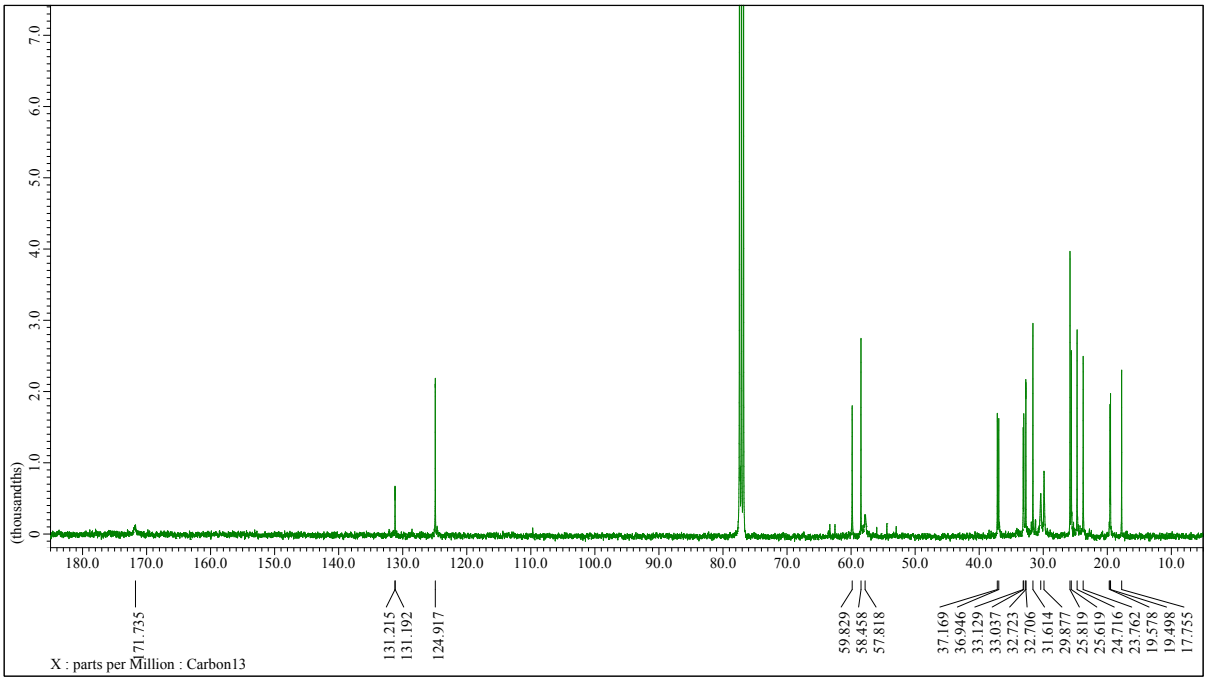


5d’ (3,7-dimethyloct-6-en-1-yl)-(1*R*,4*S*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decane

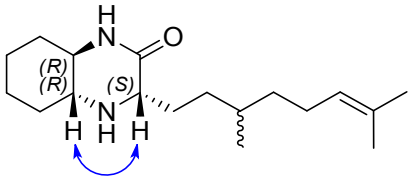
^{1}H NMR spectrum of **5d’**

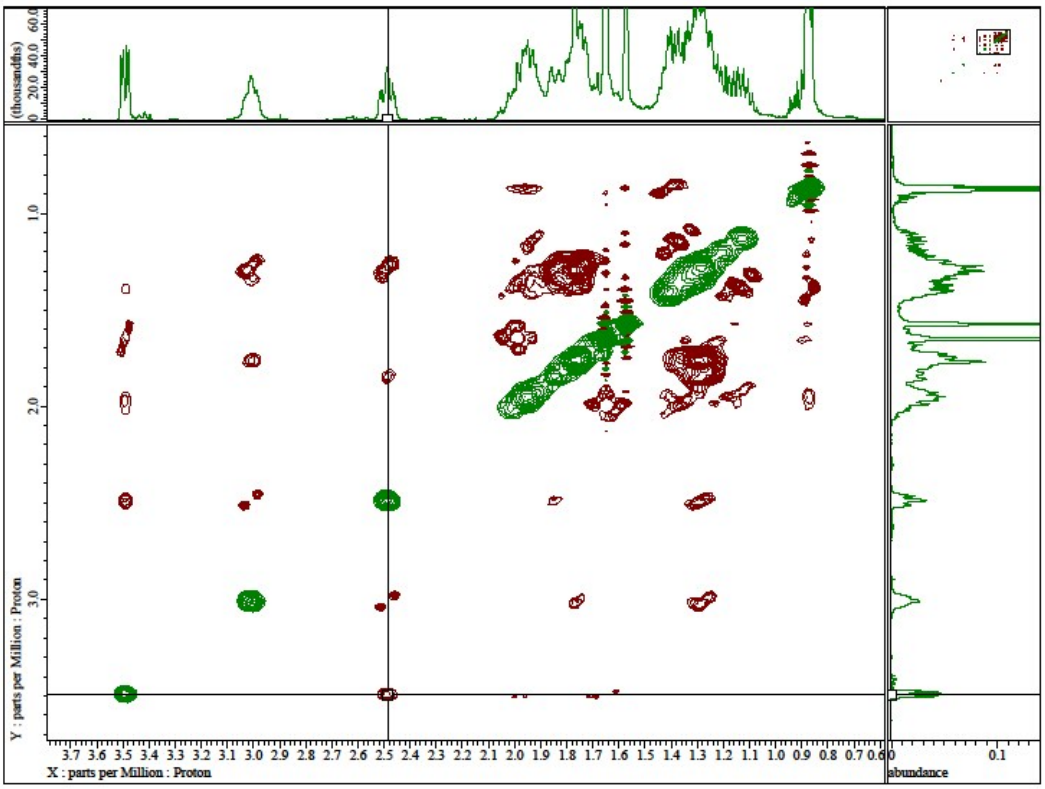


^{13}C NMR spectrum of **5d’**

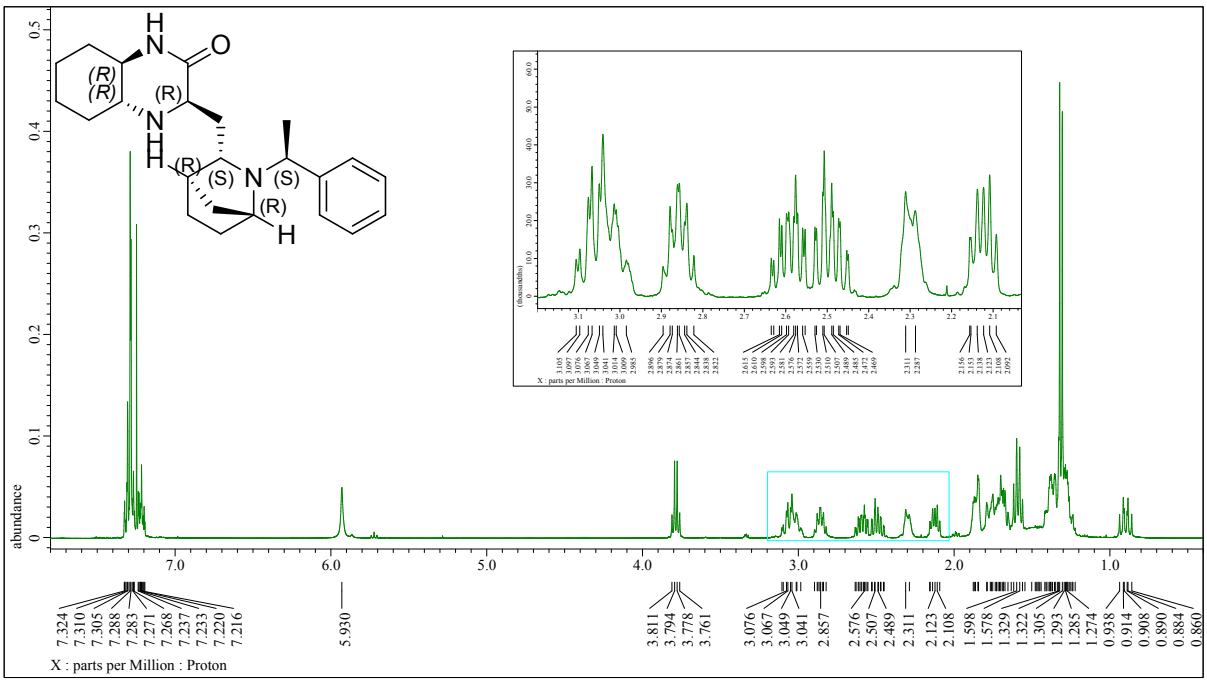


NOESY correlation of **5d'**



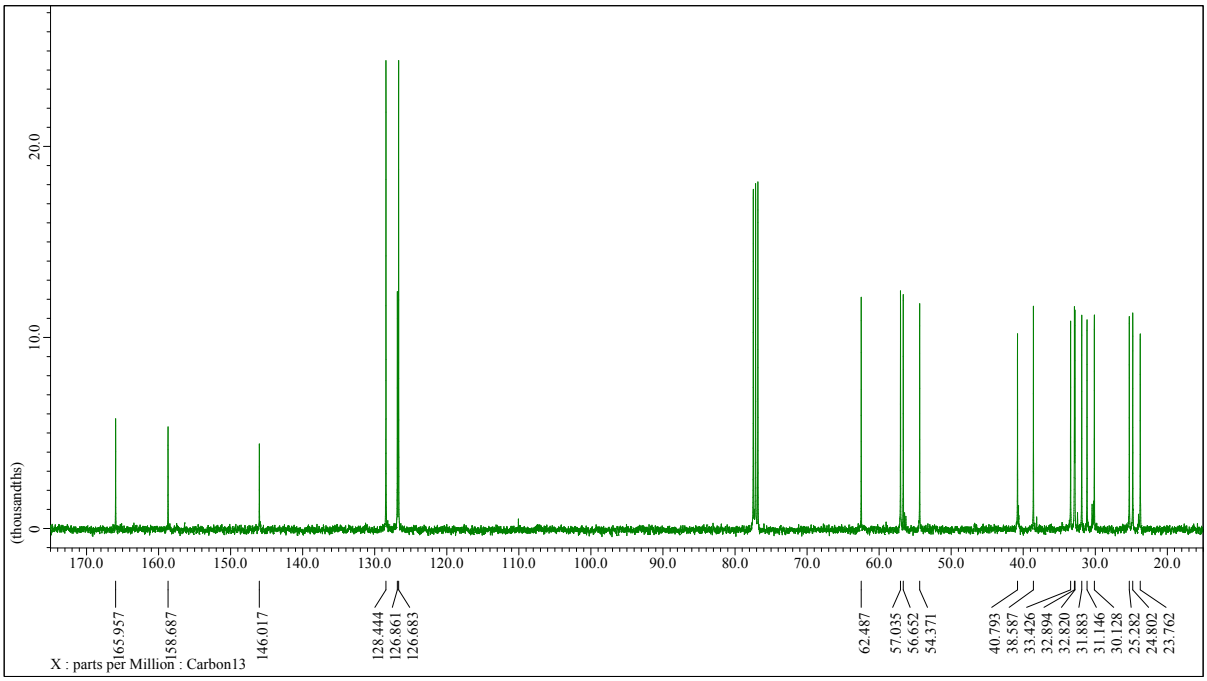


5e 4-(((1*R*,3*S*,4*R*,)-2-((*S*)-1-phenylethyl)-2-azabicyclo[2.2.1]heptan-3-yl)methyl)(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]decan

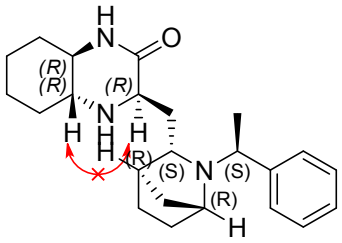


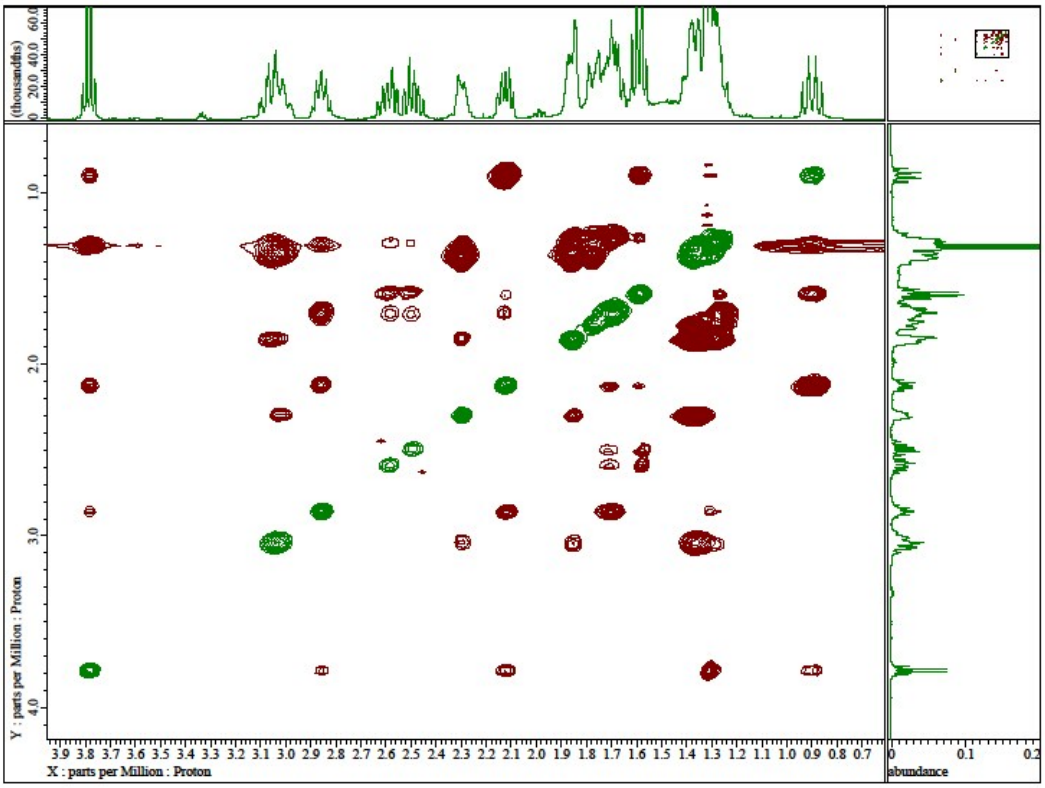
^{1}H NMR spectrum of **5e**

^{13}C NMR spectrum of **5e**



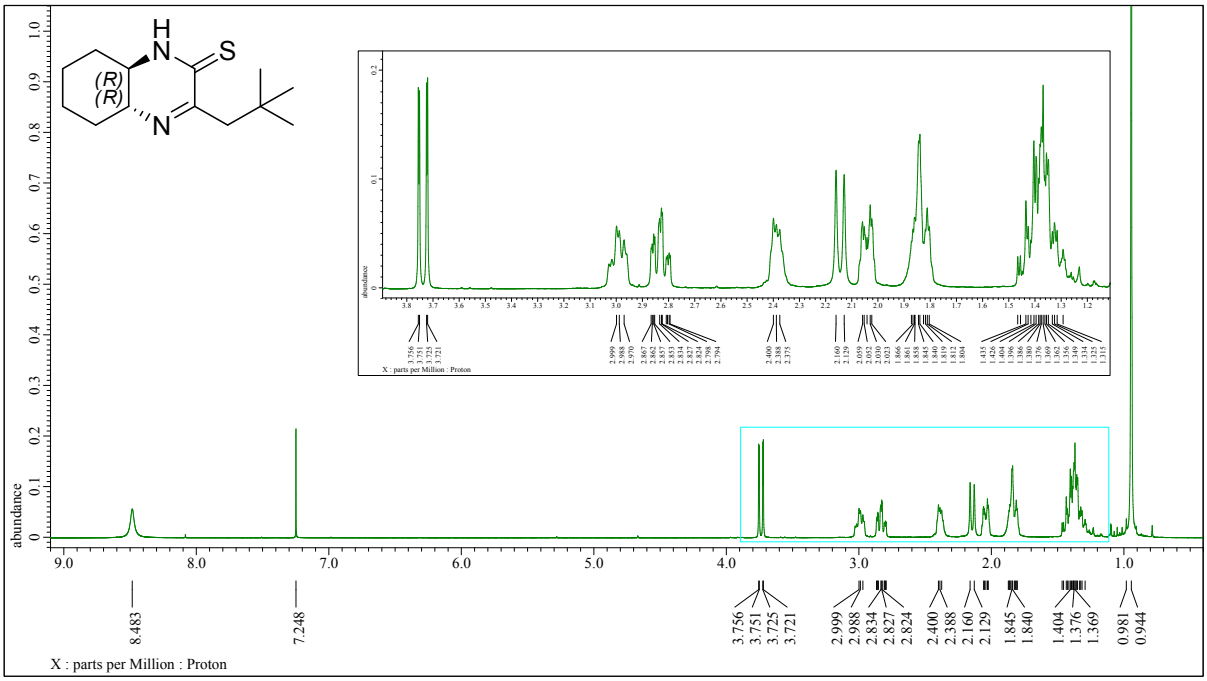
NOESY correlation of **5e**





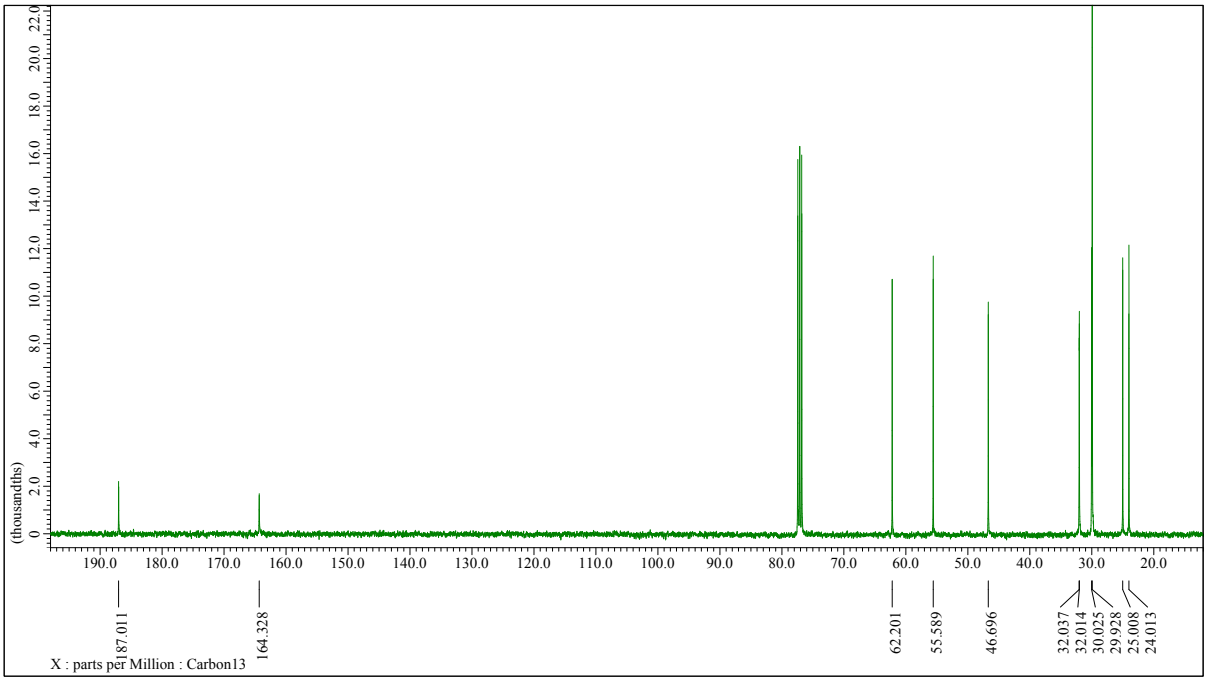
Derivatives of cyclic imine 3i

6b 4-(neopentyl)-(1*R*,6*R*)-3-thio-2,5-diazabicyclo[4.4.0]dec-4-ene

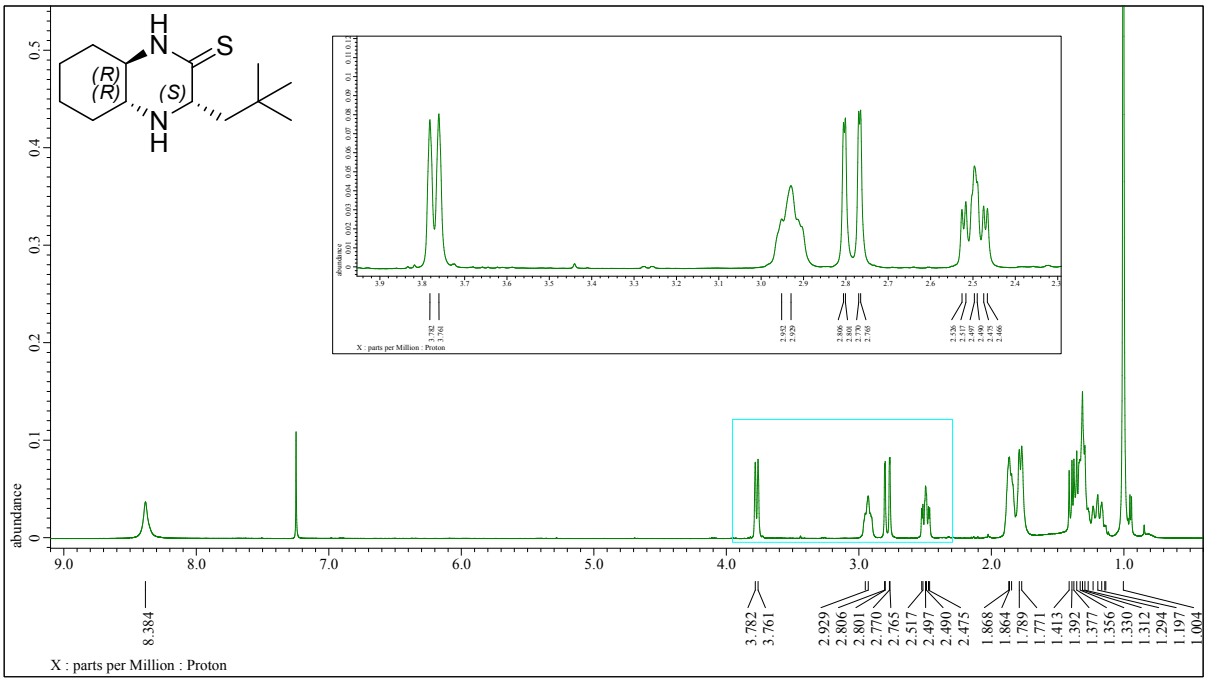


^{1}H NMR spectrum of **6b**

^{13}C NMR spectrum of **6b**

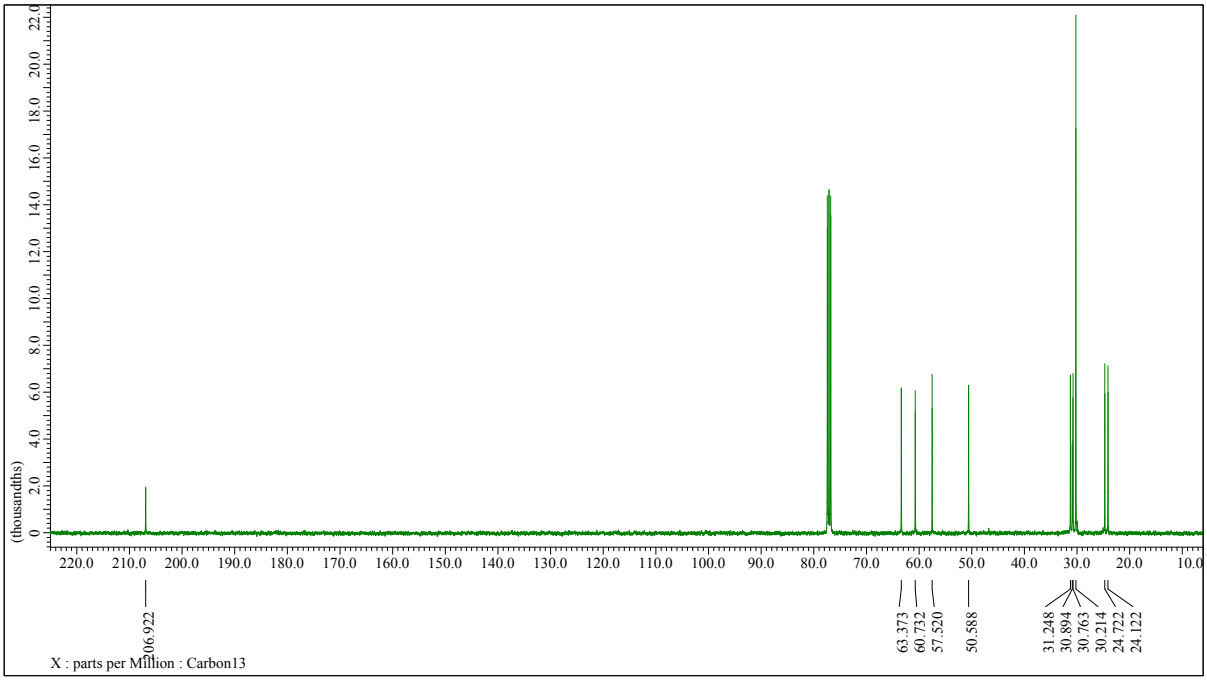


6c 4-neopentyl-(1*R*,4*S*,6*R*)-3-thio-2,5-diazabicyclo[4.4.0]decane

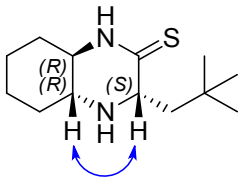


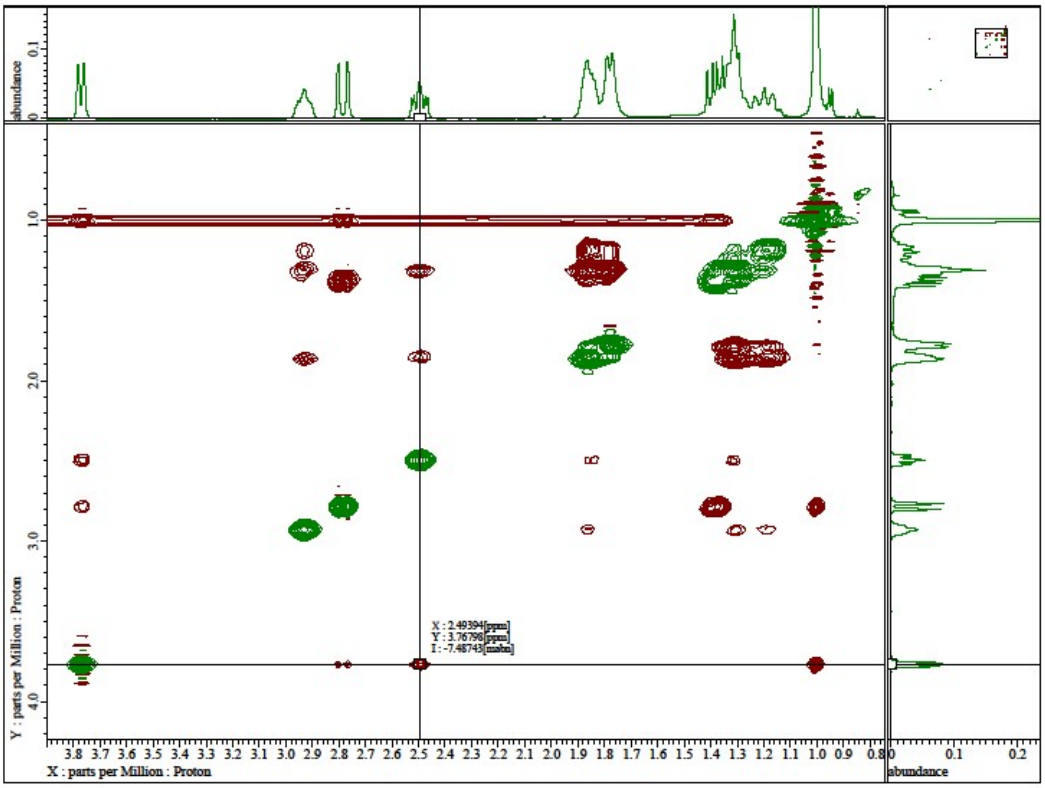
^{1}H NMR spectrum of **6c**

^{13}C NMR spectrum of **6c**

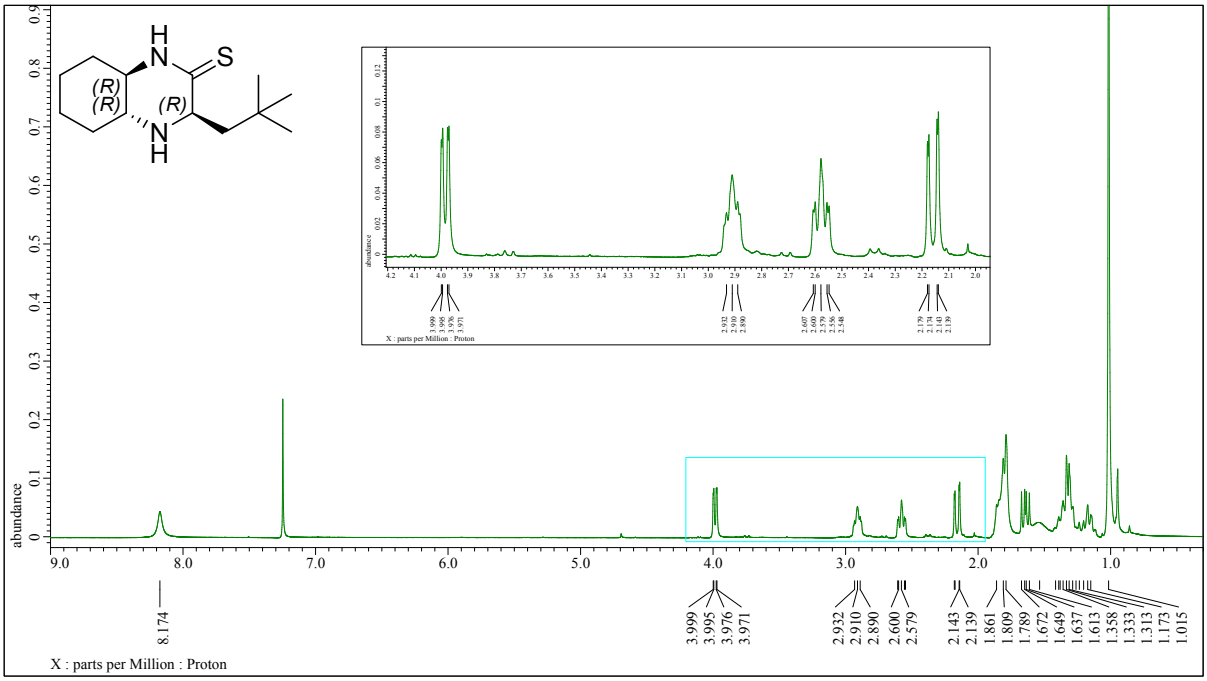


NOESY correlation of **6c**



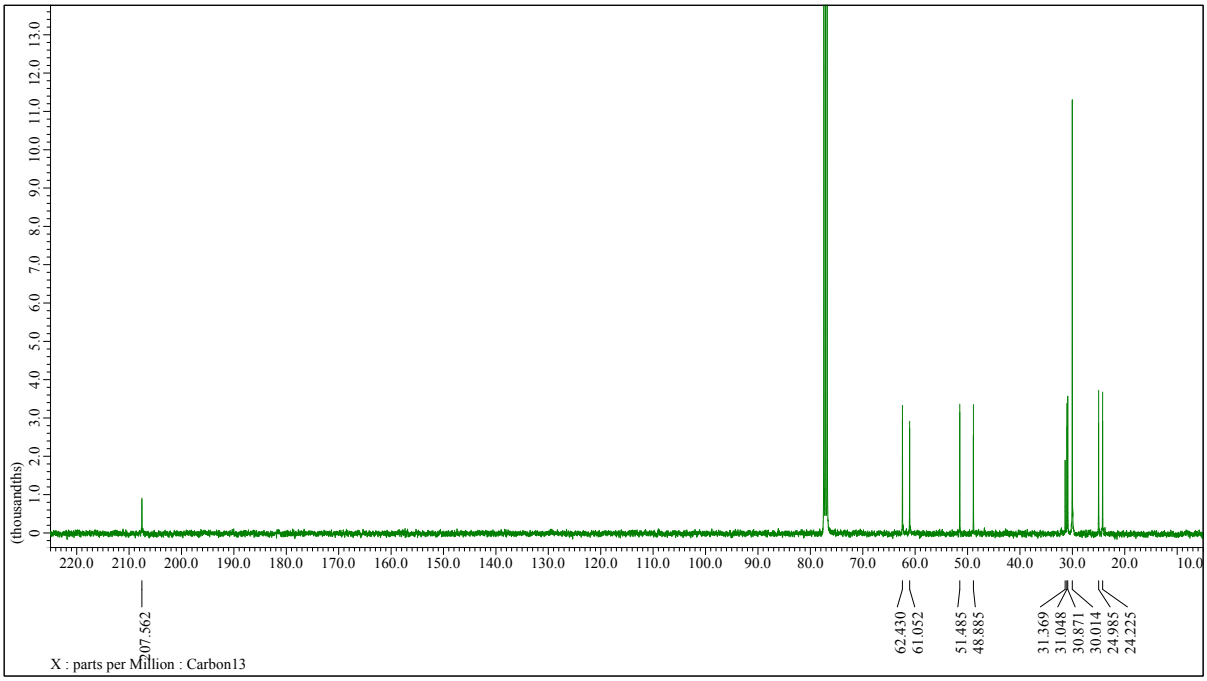


6c’ 4-neopentyl-(1*R*,4*R*,6*R*)-3-thio-2,5-diazabicyclo[4.4.0]decane

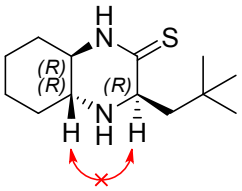


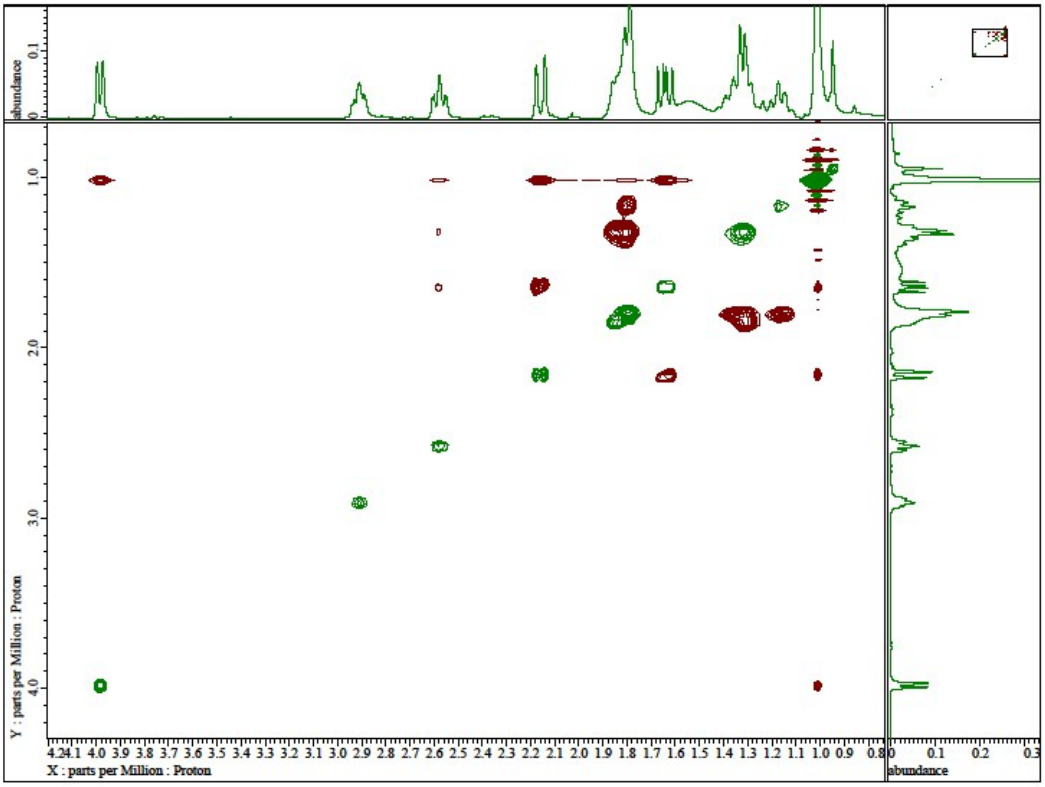
^{1}H NMR spectrum of **6c’**

^{13}C NMR spectrum of **6c’**

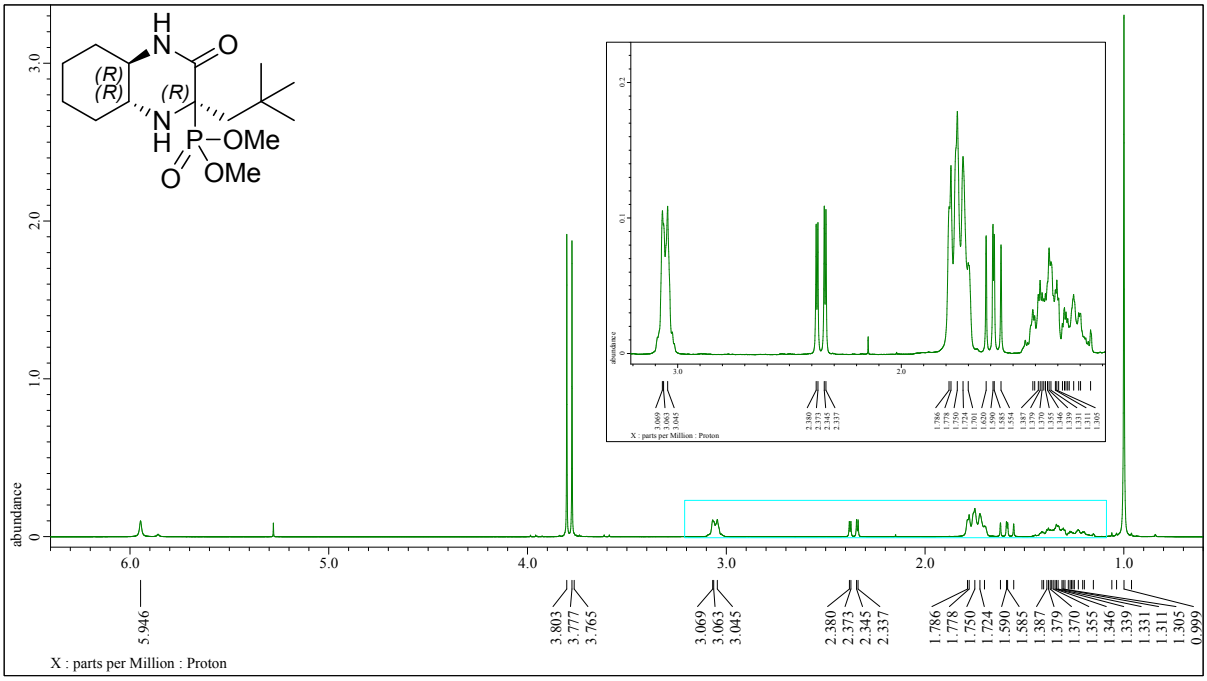


NOESY correlation of **6c'**



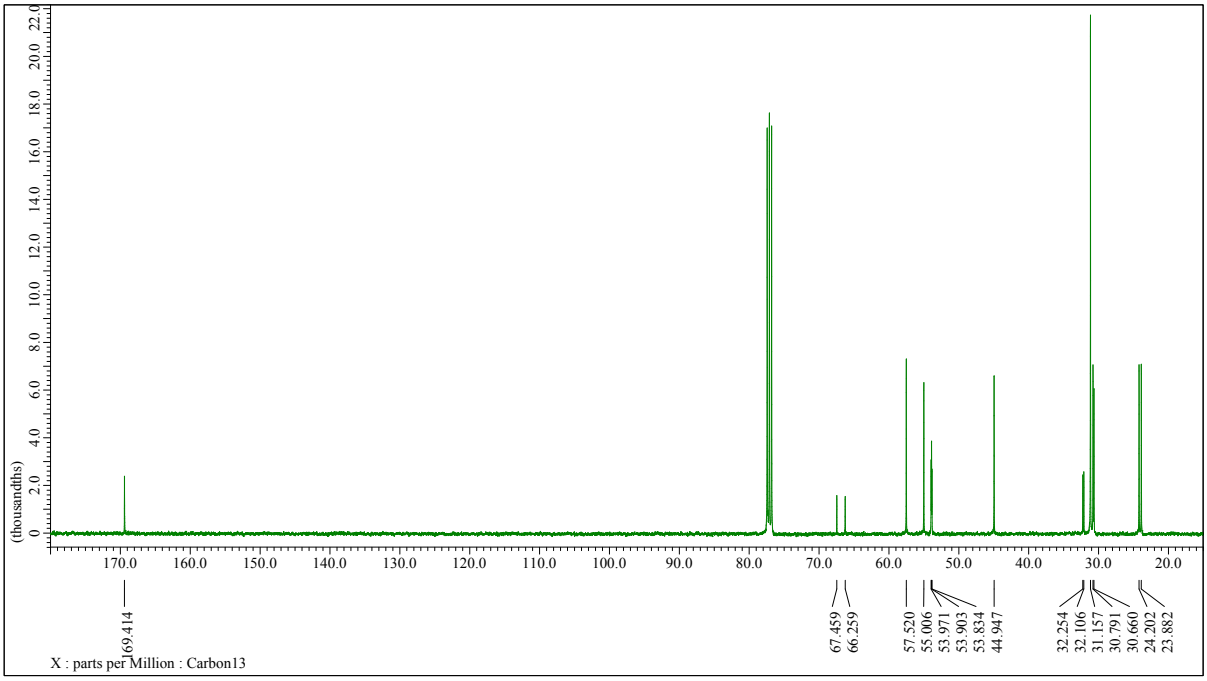


6d dimethyl-[4-neopentyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-yl]-phosphonate

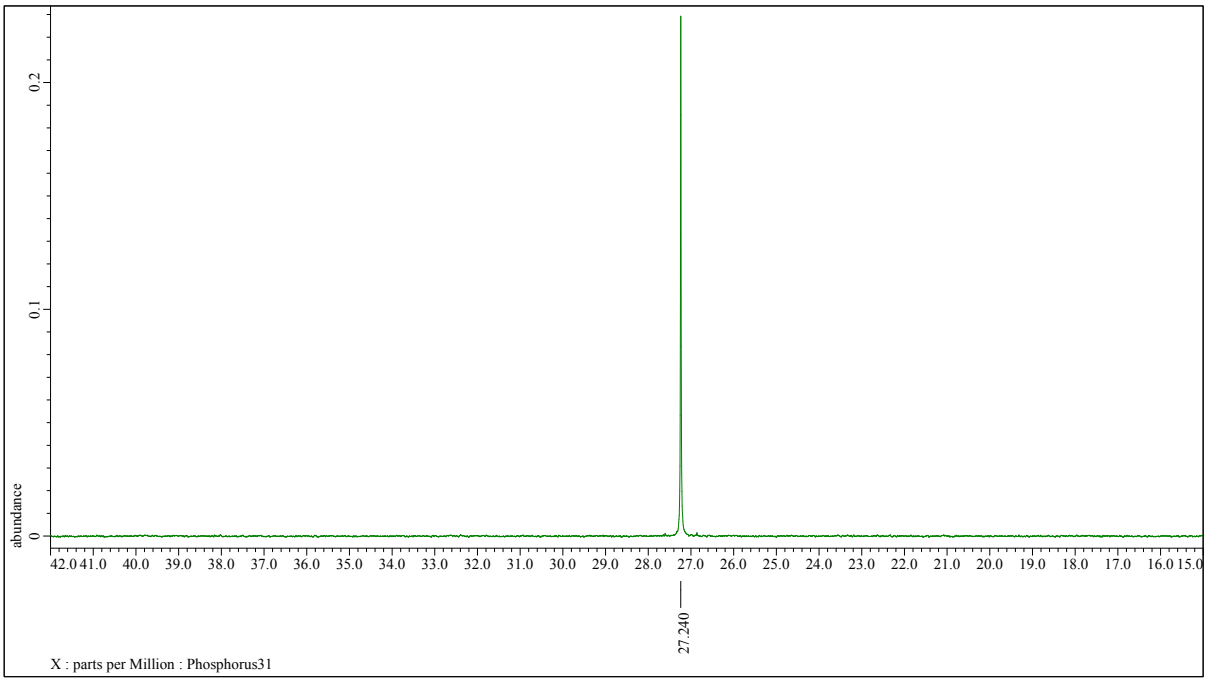


^{1}H NMR spectrum of **6d**

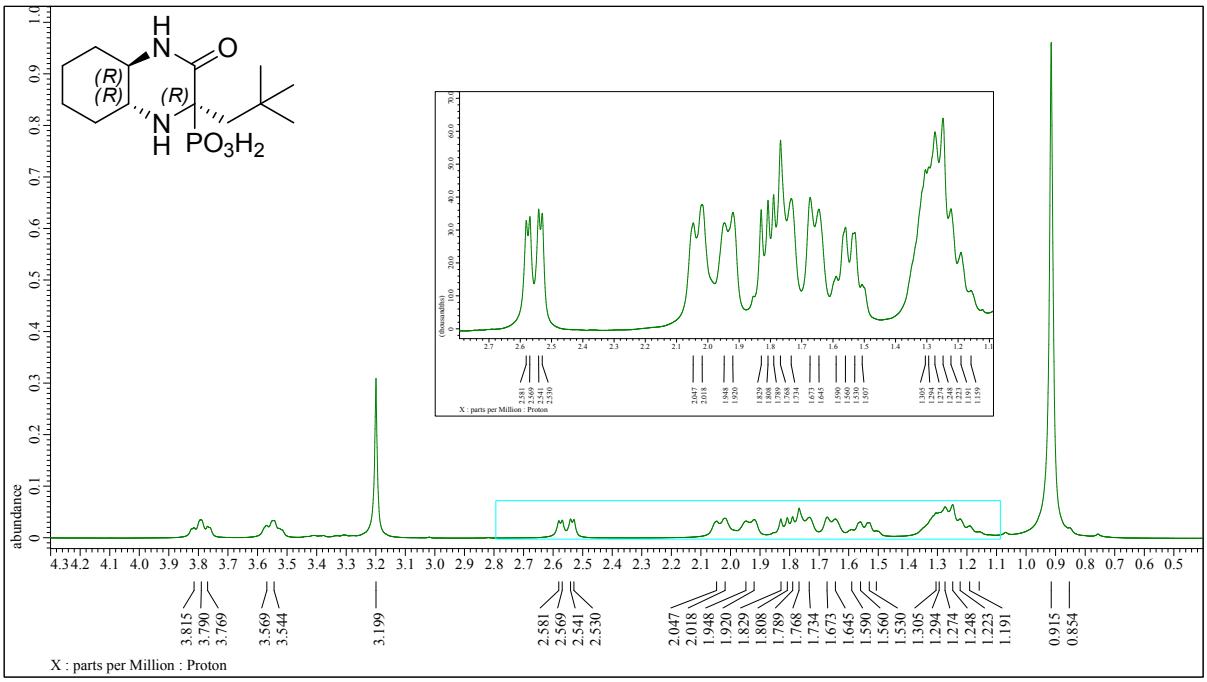
^{13}C NMR spectrum of **6d**



^{31}P NMR spectrum of **6d**

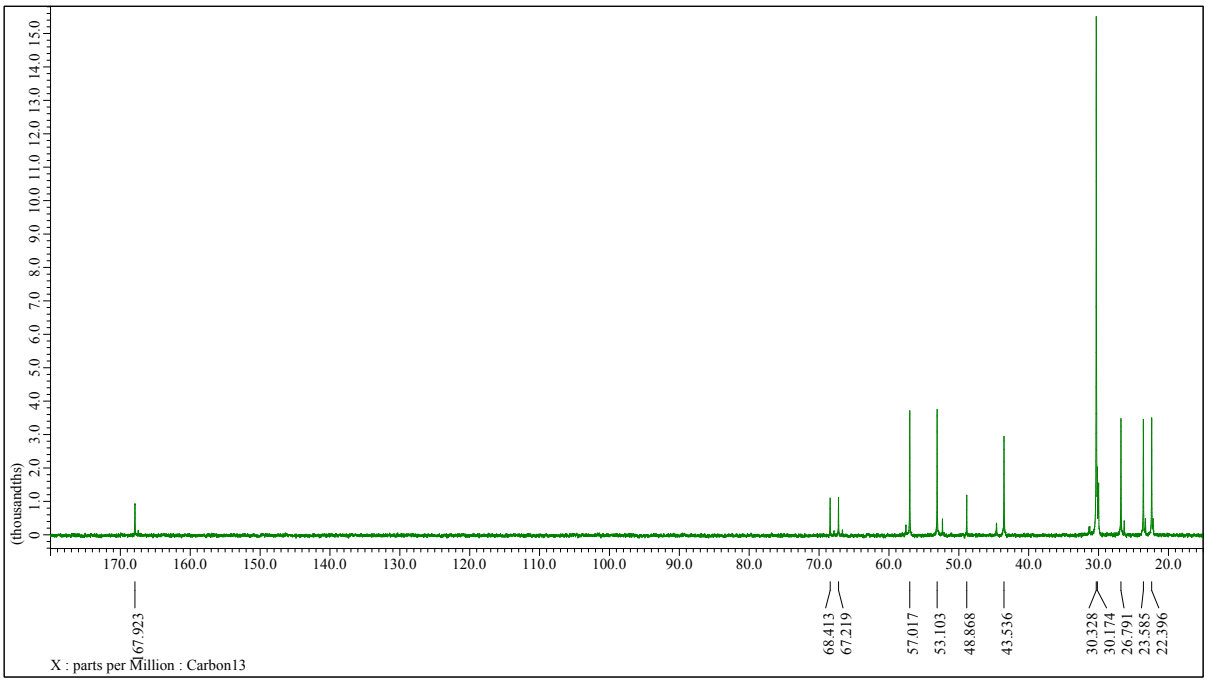


6e [4-neopentyl-(1*R*,4*R*,6*R*)-3-oxo-2,5-diazabicyclo[4.4.0]dec-4-yl]- phosphonic acid

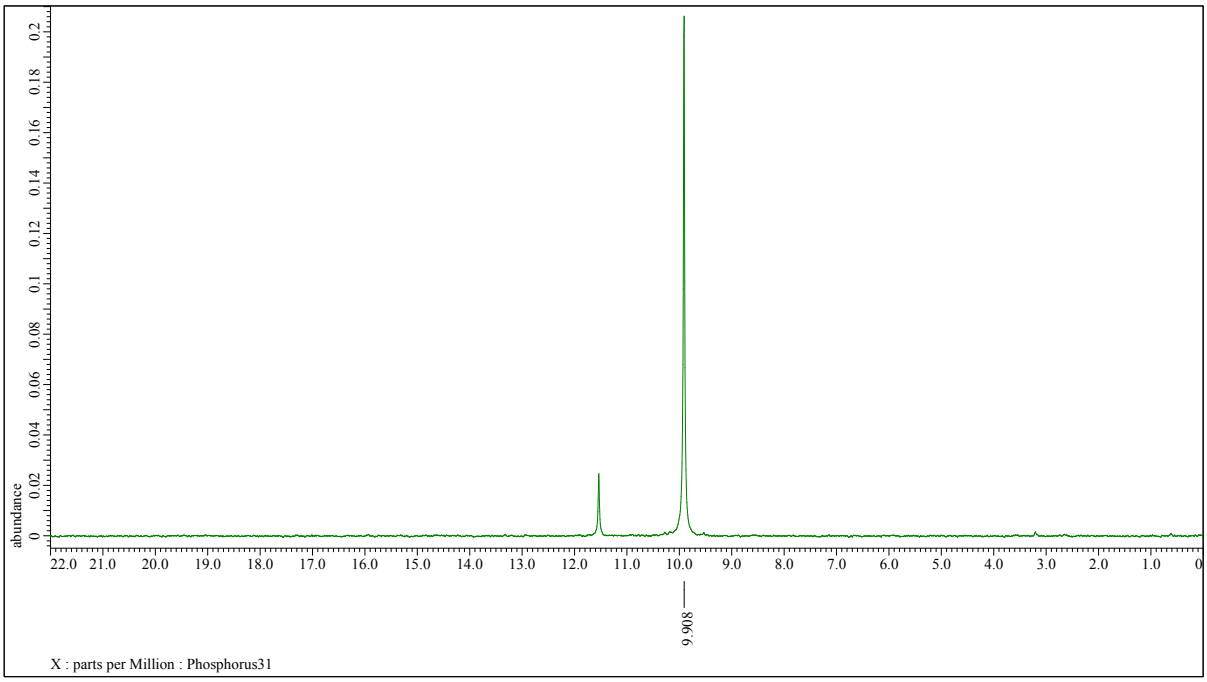


^{1}H NMR spectrum of **6e**

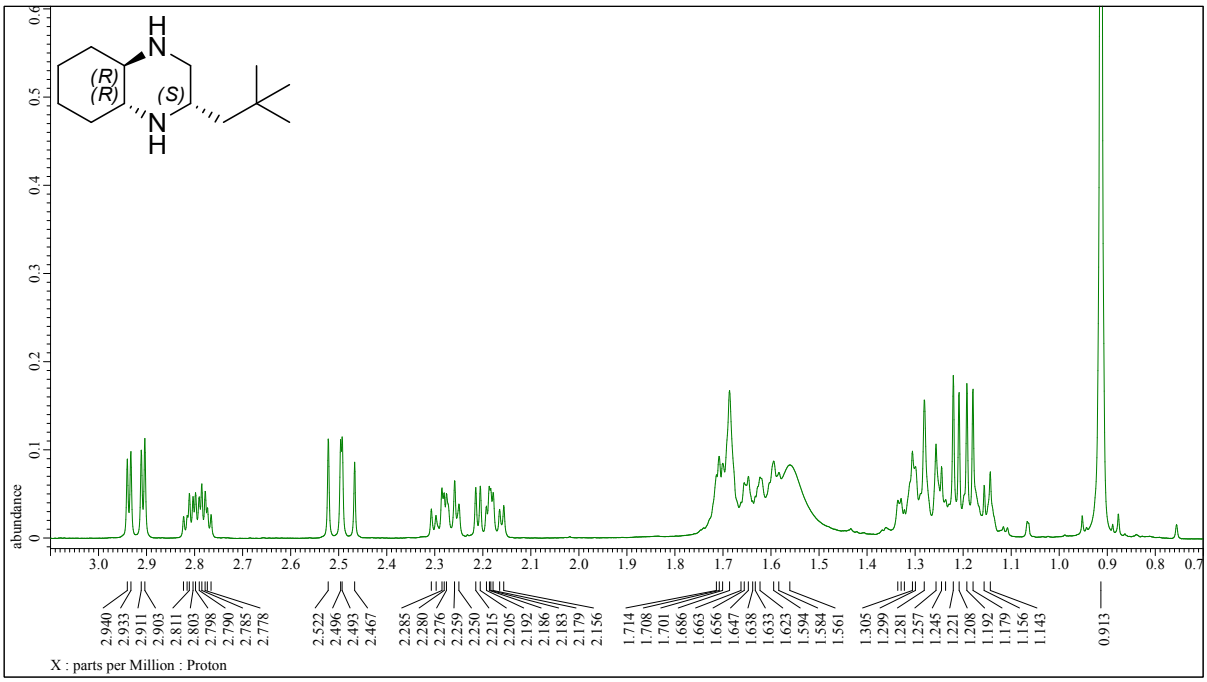
^{13}C NMR spectrum of **6e**



^{31}P NMR spectrum of **6e**

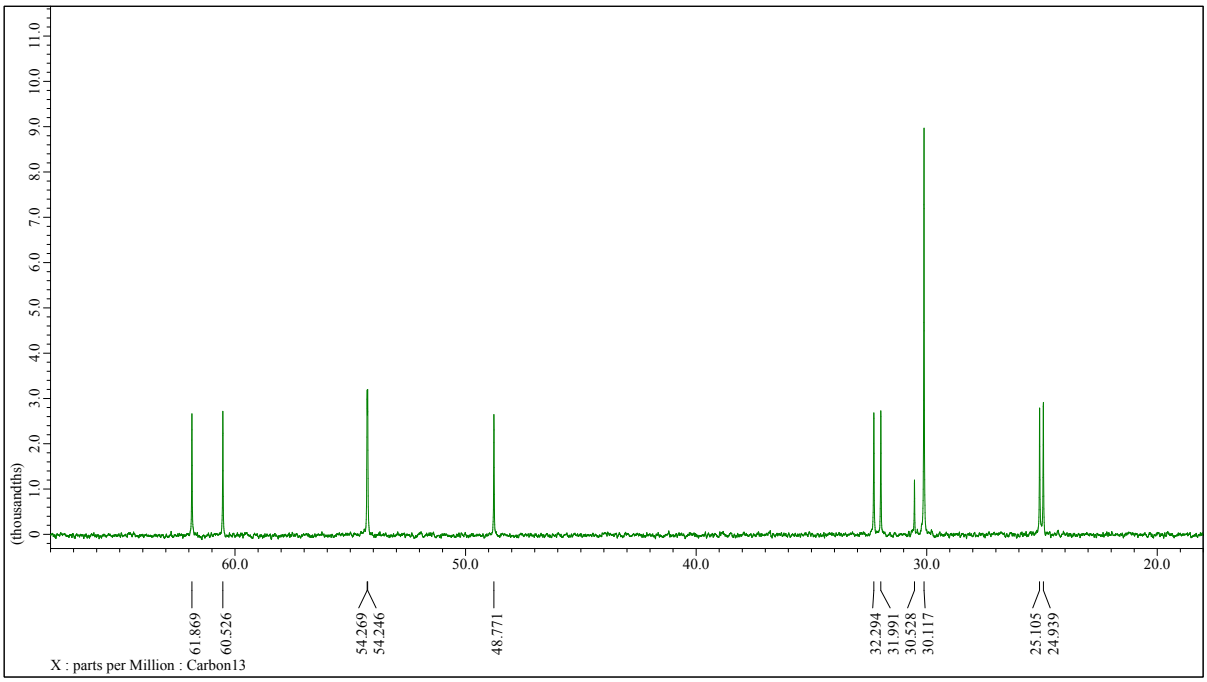


6f 4-neopentyl-(1*R*,4*S*,6*R*)-2,5-diazabicyclo[4.4.0]decane

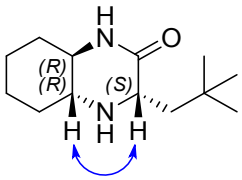


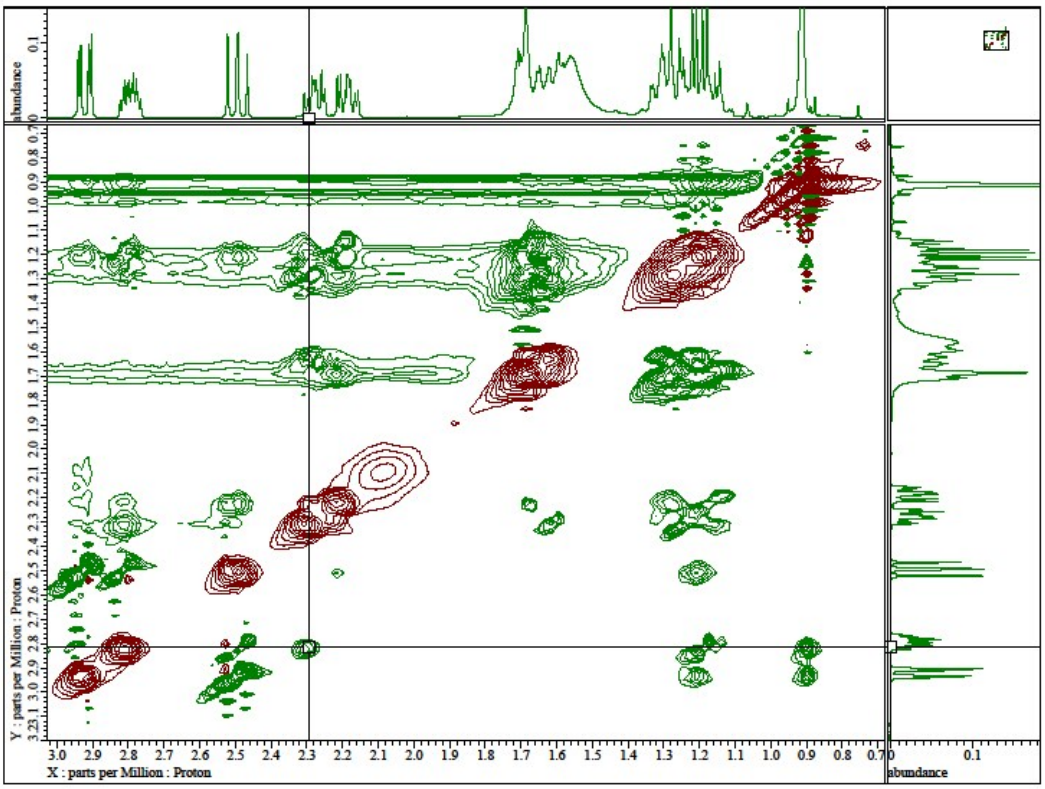
^{1}H NMR spectrum of **6f**

^{13}C NMR spectrum of **6f**



NOESY correlation of **6f**





Chiroptical analysis of (1*R*,4*R*,6*R*)-**6d**

Table S1. Calculated at ωB97X-D/6-311+G(d,p)/PCM/CH_3CN level of theory relative energies (ΔE) and conformer distribution at 25° C for individual conformers of compound (1*R*,4*R*,6*R*)-**6d**.

No.	Pop. [%]	ΔE [kcal mol^{-1}]
Conf. #1	33.11	0
Conf. #2	21.98	0.24
Conf. #3	18.35	0.35
Conf. #4	16.58	0.41
Conf. #5	6.15	1.00
Conf. #6	3.82	1.28

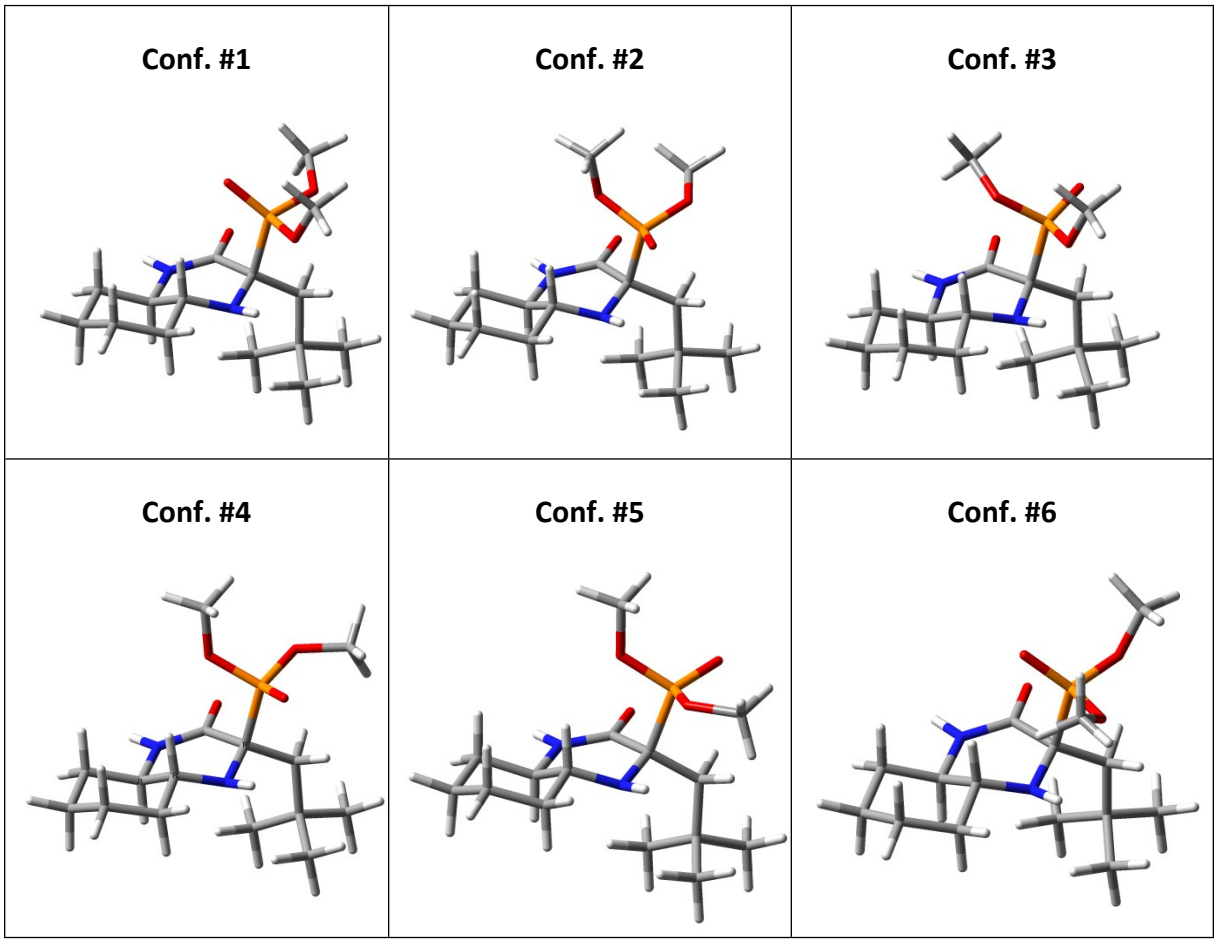


Figure S1. Structure of the conformers found within 1.5 kcal mol^{-1} energy window.

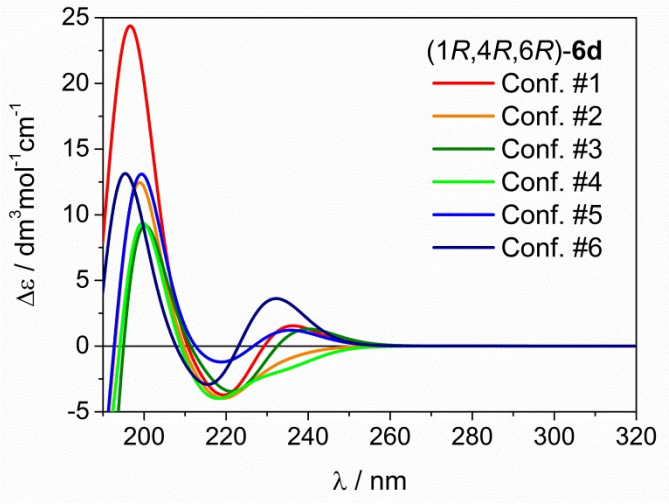


Figure S2. ECD spectra of individual conformers of (1*R*,4*R*,6*R*)-**6d** calculated at CAM-B3LYP/def2-TZVP/PCM(CH_3CN) level of theory (UV shift = +17 nm, σ = 0.3 eV).

***Cartesian coordinates for individual conformers* of (1*R*,4*R*,6*R*)-6d**

Conf. #1
imaginary frequency = 0
ΔE (Hartree) = -1340.91676101

C	-4.67596	-0.02142	0.27784
C	-4.23758	-0.69441	-1.0267
C	-2.90821	-0.12972	-1.53494
C	-1.84244	-0.23943	-0.45316
C	-2.29156	0.50687	0.79265
C	-3.58031	-0.08937	1.34536
N	-0.58295	0.35148	-0.87895
C	0.52498	0.1846	0.04655
C	0.09664	0.38672	1.51227
N	-1.21617	0.47098	1.77576
O	0.94901	0.40938	2.39605
P	1.1456	-1.58981	0.00946
O	0.34068	-2.56895	0.78661
C	1.71569	1.10362	-0.30906
C	1.46708	2.61512	-0.54817
C	2.84365	3.29243	-0.44856
C	0.90321	2.88186	-1.95147
C	0.53572	3.23311	0.4998
O	2.71305	-1.63072	0.34475
C	3.20782	-1.8317	1.6789
O	1.17243	-1.80888	-1.57457
C	1.58166	-3.06441	-2.13813
H	-5.58903	-0.48896	0.65497

H	-4.91714	1.02994	0.07937
H	-4.12795	-1.77232	-0.85748
H	-5.01	-0.5715	-1.79033
H	-2.57946	-0.67002	-2.42821
H	-3.02495	0.92377	-1.81606
H	-1.72998	-1.30314	-0.18513
H	-2.47862	1.55197	0.50903
H	-3.88797	0.45333	2.2445
H	-3.39767	-1.13028	1.63708
H	-0.31493	0.02786	-1.80101
H	-1.4499	0.62357	2.74743
H	2.19609	0.70156	-1.2076
H	2.43896	0.99369	0.50163
H	2.76282	4.36028	-0.67369
H	3.2629	3.18775	0.55703
H	3.5508	2.85114	-1.15862
H	0.84668	3.96022	-2.13322
H	-0.0955	2.45938	-2.06164
H	1.55046	2.44668	-2.7204
H	0.47743	4.31593	0.35213
H	-0.47761	2.83331	0.41377
H	0.89855	3.05043	1.51522
H	4.26988	-2.04539	1.57825
H	2.70129	-2.6767	2.14781
H	3.05257	-0.92857	2.26938
H	1.4545	-2.97294	-3.21426
H	0.95428	-3.8728	-1.75866
H	2.62963	-3.25823	-1.90266

Conf. #2

imaginary frequency = 0

ΔE (Hartree) = -1340.9163748

C	4.52406	-0.69858	0.42504
C	4.2367	-0.29705	-1.02519
C	2.8482	-0.75951	-1.47545
C	1.78553	-0.23543	-0.51954
C	2.07163	-0.72361	0.8906
C	3.42428	-0.21588	1.375
N	0.45699	-0.70788	-0.87883
C	-0.62726	-0.14164	-0.09299
C	-0.28753	-0.08017	1.40754
N	0.9885	-0.29645	1.76664

O	-1.15984	0.19758	2.22424
P	-0.93592	1.61458	-0.68864
O	-0.6926	1.72681	-2.14963
C	-1.95433	-0.90142	-0.3239
C	-1.97481	-2.44839	-0.21607
C	-3.45301	-2.84303	-0.06542
C	-1.42879	-3.11269	-1.48848
C	-1.19831	-2.96519	0.99963
O	0.02401	2.50147	0.24051
C	0.31888	3.8675	-0.09814
O	-2.4288	2.0948	-0.37004
C	-2.92994	2.44213	0.93228
H	5.4897	-0.2974	0.7431
H	4.59823	-1.79088	0.48993
H	4.29804	0.79409	-1.11658
H	5.00014	-0.71268	-1.68796
H	2.80026	-1.85472	-1.49824
H	2.63594	-0.40335	-2.4883
H	1.84584	0.86556	-0.5126
H	2.09478	-1.82218	0.86583
H	3.61487	-0.57193	2.39209
H	3.40476	0.87982	1.40942
H	0.2743	-0.55721	-1.8652
H	1.15914	-0.27908	2.76292
H	-2.33155	-0.63782	-1.31898
H	-2.66969	-0.49556	0.3945
H	-3.5589	-3.93198	-0.048
H	-3.87471	-2.44556	0.86307
H	-4.049	-2.46002	-0.9003
H	-1.56858	-4.19726	-1.43268
H	-0.3659	-2.90703	-1.61483
H	-1.96012	-2.75224	-2.37572
H	-1.32493	-4.04877	1.08611
H	-0.12864	-2.76427	0.90022
H	-1.55534	-2.50836	1.92673
H	0.97441	4.24024	0.68532
H	-0.59638	4.46268	-0.12726
H	0.82514	3.91472	-1.06327
H	-3.87241	2.95802	0.76167
H	-2.23112	3.10412	1.44634
H	-3.08199	1.54306	1.52757

Conf. #3

imaginary frequency = 0
ΔE (Hartree) = -1340.9162046

C	4.25876	-1.46423	-0.00826
C	3.94813	-0.78152	-1.34406
C	2.47152	-0.92544	-1.72367
C	1.58808	-0.40239	-0.59911
C	1.87967	-1.16586	0.68196
C	3.33024	-0.97529	1.10677
N	0.17562	-0.58234	-0.89769
C	-0.74745	-0.01513	0.06792
C	-0.29423	-0.26294	1.52048
N	0.95385	-0.72101	1.71583
O	-1.03767	0.02601	2.45291
P	-0.84397	1.86171	-0.05594
O	-2.06912	2.52045	0.46307
C	-2.19198	-0.52019	-0.15172
C	-2.45416	-2.04298	-0.27977
C	-3.96236	-2.23556	-0.05284
C	-2.11096	-2.56117	-1.68418
C	-1.68811	-2.86275	0.76387
O	-0.58381	2.03028	-1.62478
C	-0.57912	3.33207	-2.23105
O	0.51749	2.46445	0.55205
C	0.62375	2.94151	1.90219
H	5.29994	-1.28669	0.27278
H	4.14165	-2.54889	-0.1206
H	4.19699	0.28402	-1.27096
H	4.57777	-1.1993	-2.13394
H	2.25805	-0.37266	-2.64392
H	2.2274	-1.97784	-1.91166
H	1.84234	0.65526	-0.42604
H	1.70546	-2.23289	0.48509
H	3.52354	-1.5236	2.03389
H	3.50688	0.08738	1.31124
H	-0.04647	-0.24256	-1.82571
H	1.19748	-0.89478	2.68177
H	-2.58545	-0.04157	-1.05629
H	-2.7793	-0.12896	0.6813
H	-4.2406	-3.28442	-0.19423
H	-4.24936	-1.94117	0.96144
H	-4.5455	-1.63446	-0.75824
H	-2.4118	-3.60969	-1.77975

H	-1.04103	-2.48866	-1.87992
H	-2.64357	-1.98933	-2.45156
H	-1.98441	-3.9143	0.69956
H	-0.60986	-2.81313	0.59221
H	-1.89744	-2.51514	1.77936
H	-0.43697	3.17236	-3.29728
H	0.24363	3.92816	-1.8322
H	-1.53044	3.83682	-2.05457
H	1.39921	3.70509	1.90214
H	0.91156	2.11836	2.55811
H	-0.32215	3.37206	2.23298

Conf. #4

imaginary frequency = 0

ΔE (Hartree) = -1340.9161088

C	-4.62622	0.48649	0.10112
C	-4.20633	-0.00497	-1.28772
C	-2.80665	0.48971	-1.66341
C	-1.80282	0.08808	-0.59131
C	-2.22218	0.6641	0.75092
C	-3.58668	0.12767	1.16658
N	-0.47089	0.59768	-0.8824
C	0.57022	0.15116	0.02979
C	0.11438	0.18286	1.50109
N	-1.19734	0.35589	1.73959
O	0.92754	0.01613	2.4034
P	1.02776	-1.61779	-0.38658
O	1.00817	-1.84426	-1.85695
C	1.87587	0.95978	-0.1524
C	1.8196	2.50924	-0.17096
C	3.26095	2.98793	0.06689
C	1.3556	3.04296	-1.53407
C	0.91948	3.078	0.93075
O	-0.00762	-2.47957	0.4699
C	-0.01756	-3.91449	0.38572
O	2.42374	-2.00825	0.29698
C	3.67559	-1.96549	-0.40413
H	-5.59641	0.06321	0.37343
H	-4.75169	1.57573	0.07663
H	-4.21407	-1.10153	-1.30024
H	-4.93065	0.32441	-2.03721

H	-2.49935	0.07187	-2.62717
H	-2.80332	1.58146	-1.76563
H	-1.81605	-1.0108	-0.50392
H	-2.29098	1.7555	0.63964
H	-3.87314	0.54602	2.13646
H	-3.52301	-0.96043	1.28513
H	-0.20033	0.38611	-1.83689
H	-1.44859	0.40669	2.71744
H	2.3474	0.64386	-1.09133
H	2.53999	0.64646	0.65644
H	3.3179	4.07881	0.00335
H	3.61875	2.68567	1.05605
H	3.94189	2.57092	-0.68249
H	1.44159	4.13428	-1.55638
H	0.31773	2.77382	-1.72996
H	1.97684	2.64218	-2.3421
H	0.98505	4.1704	0.93473
H	-0.12676	2.80976	0.76374
H	1.21968	2.71823	1.91866
H	-0.8225	-4.25222	1.03406
H	0.9346	-4.31793	0.73462
H	-0.2095	-4.23249	-0.64047
H	3.52805	-2.16473	-1.46627
H	4.30559	-2.73693	0.03449
H	4.13836	-0.98705	-0.26614

Conf. #5

imaginary frequency = 0

ΔE (Hartree) = -1340.9151732

C	-4.43334	-1.05595	0.19776
C	-4.00239	-0.30027	1.45873
C	-2.52638	-0.54314	1.78618
C	-1.65893	-0.1865	0.5865
C	-2.0732	-1.02019	-0.6143
C	-3.52261	-0.73919	-0.99178
N	-0.2535	-0.46345	0.84196
C	0.6734	-0.07372	-0.20559
C	0.12571	-0.37706	-1.6144
N	-1.16385	-0.74091	-1.71763
O	0.84803	-0.24006	-2.59613
P	1.01439	1.77324	-0.18333

O	2.27377	2.25467	-0.80465
C	2.06573	-0.72282	-0.01077
C	2.17016	-2.24868	0.24054
C	3.63469	-2.6252	-0.03676
C	1.85177	-2.60594	1.69973
C	1.26542	-3.06086	-0.69167
O	0.89403	2.16243	1.37551
C	2.03929	2.40775	2.20551
O	-0.33872	2.37934	-0.77721
C	-0.54203	3.80054	-0.84319
H	-5.46849	-0.81109	-0.05349
H	-4.40191	-2.13447	0.39437
H	-4.16397	0.77398	1.30866
H	-4.62567	-0.59816	2.30592
H	-2.22307	0.0574	2.64958
H	-2.36269	-1.59541	2.04779
H	-1.83243	0.87129	0.33714
H	-1.9806	-2.07974	-0.33671
H	-3.80664	-1.34092	-1.86062
H	-3.62103	0.31494	-1.27667
H	0.039	-0.07717	1.73151
H	-1.46898	-0.96162	-2.65586
H	2.56821	-0.22287	0.82667
H	2.64303	-0.47004	-0.90217
H	3.80629	-3.68337	0.18281
H	3.89579	-2.44848	-1.08477
H	4.3164	-2.03714	0.58651
H	2.04673	-3.66897	1.8755
H	0.8077	-2.40157	1.93654
H	2.4823	-2.03234	2.38763
H	1.45175	-4.12993	-0.55038
H	0.21008	-2.87801	-0.4757
H	1.45447	-2.82129	-1.74187
H	2.85872	2.822	1.61719
H	2.35363	1.47727	2.68228
H	1.72817	3.12211	2.96537
H	-1.52581	3.94758	-1.28244
H	0.21887	4.26317	-1.47367
H	-0.51499	4.23136	0.15941

Conf. #6

imaginary frequency = 0
ΔE (Hartree) = -1340.9147245

C	4.61967	0.06357	-0.25536
C	4.15914	-0.65121	1.01981
C	2.81715	-0.1076	1.51751
C	1.77628	-0.20287	0.41024
C	2.24093	0.60081	-0.79271
C	3.543	0.03253	-1.34466
N	0.49551	0.34351	0.82843
C	-0.59126	0.22198	-0.12833
C	-0.13089	0.50501	-1.57141
N	1.18566	0.61147	-1.79698
O	-0.95128	0.58244	-2.46546
P	-1.16208	-1.56368	-0.16875
O	-0.29773	-2.50709	-0.9256
C	-1.78951	1.11736	0.25828
C	-1.54867	2.61556	0.57601
C	-2.93463	3.28084	0.53743
C	-0.96195	2.82048	1.98066
C	-0.64541	3.29896	-0.45602
O	-2.68809	-1.49839	-0.62998
C	-3.46402	-2.70493	-0.72112
O	-1.26596	-1.92718	1.39721
C	-0.47135	-2.96483	1.99251
H	5.53838	-0.39341	-0.63164
H	4.85903	1.10731	-0.01882
H	4.05762	-1.72383	0.81543
H	4.91581	-0.54909	1.80193
H	2.47706	-0.66534	2.39594
H	2.92056	0.94133	1.81972
H	1.70009	-1.25807	0.09894
H	2.42077	1.6314	-0.45585
H	3.86375	0.61162	-2.21601
H	3.37118	-0.99701	-1.67977
H	0.20905	-0.00523	1.73554
H	1.4406	0.80335	-2.75627
H	-2.27794	0.67141	1.13205
H	-2.50237	1.04245	-0.56432
H	-2.86174	4.3349	0.82204
H	-3.36964	3.22874	-0.46556
H	-3.62503	2.79139	1.23223
H	-0.93421	3.88846	2.22083

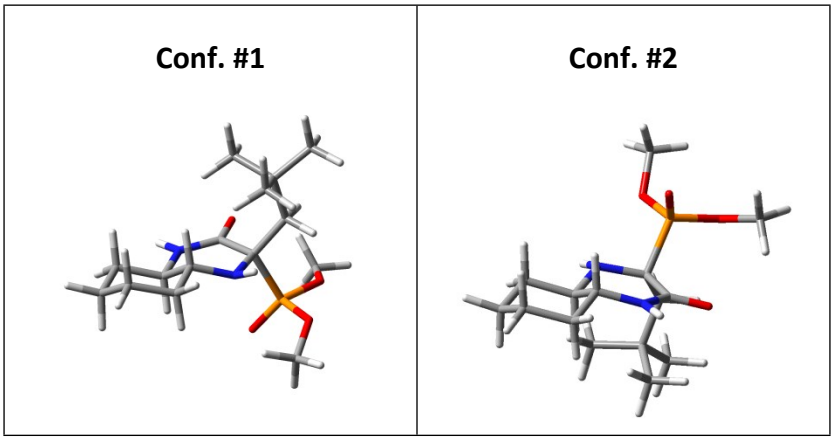
H	0.05029	2.42253	2.04875
H	-1.57958	2.32417	2.73702
H	-0.61021	4.37561	-0.26259
H	0.37899	2.92169	-0.39878
H	-1.01626	3.15056	-1.47385
H	-4.46978	-2.40036	-1.00057
H	-3.48861	-3.21421	0.24473
H	-3.04967	-3.36502	-1.48471
H	-0.71599	-2.96019	3.0525
H	0.59341	-2.76355	1.85836
H	-0.71891	-3.93343	1.55745

Chiroptical analysis of (1*R*,4S,6*R*)-**6d**

Table S2. Calculated at ωB97X-D/6-311+G(d,p)/PCM/CH_3CN level of theory relative energies (*⊿E*) and conformer distribution at 25° C for individual conformers of compound (1*R*,4*S*,6*R*)-**6d**.

No.	**Pop. [%]**	**ΔE [kcal mol^{-1}]**
Conf. #1	43.43	0
Conf. #2	56.57	0.16

Figure S2. Structure of the conformers found within 1.5 kcal mol^{-1} energy window.



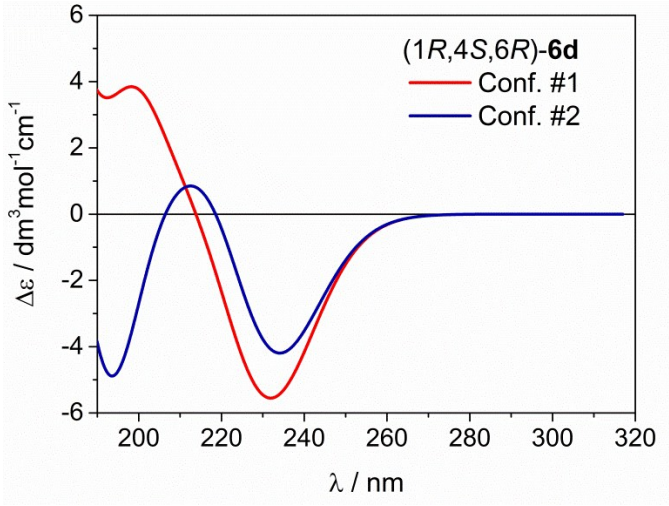


Figure S3. ECD spectra of individual conformers of (1*R*,4*S*,6*R*)-**6d** calculated at CAM-B3LYP/def2-TZVP/PCM(CH_3CN) level of theory (UV shift = +17 nm, ⍰=0.3 eV).

Conf. #1

imaginary frequency = 0

ΔE (Hartree) = -1340.9144443

C	-4.51585	-0.8665	-0.49183
C	-4.32	-0.17037	0.85781
C	-2.9049	-0.38907	1.39685
C	-1.86788	0.05785	0.374
C	-2.05911	-0.68481	-0.93719
C	-3.452	-0.43517	-1.50366
N	-0.52449	-0.20489	0.85442
C	0.59709	0.09927	-0.03638
C	0.22222	0.11303	-1.52771
N	-1.02811	-0.23826	-1.86368
O	1.0707	0.40612	-2.36479
P	1.64448	-1.43536	0.15604
O	1.10368	-2.61113	-0.57322
C	1.44216	1.3347	0.34583
C	0.80068	2.74149	0.44649
C	1.97471	3.71582	0.64457
C	0.0519	3.14094	-0.83015
C	-0.12992	2.88075	1.66122
O	1.78069	-1.59565	1.74129
C	0.99832	-2.55688	2.46837
O	3.17137	-1.07507	-0.15728
C	3.72357	-1.13218	-1.48314
H	-5.51105	-0.65075	-0.88864
H	-4.459	-1.95261	-0.35101
H	-4.50005	0.905	0.7398
H	-5.05346	-0.5362	1.58094

H	-2.75875	0.16518	2.32972
H	-2.74304	-1.44975	1.62176
H	-2.03382	1.12741	0.16142
H	-1.93253	-1.7583	-0.74499
H	-3.57244	-0.98202	-2.44376
H	-3.55845	0.6325	-1.73046
H	-0.36567	0.20185	1.76664
H	-1.2057	-0.30677	-2.8564
H	1.90998	1.11881	1.31362
H	2.25481	1.38751	-0.38194
H	1.60697	4.74068	0.75102
H	2.54532	3.46686	1.54499
H	2.65812	3.68754	-0.2095
H	-0.29722	4.17469	-0.74737
H	-0.8254	2.51435	-1.00945
H	0.70135	3.06724	-1.70609
H	0.36221	2.53568	2.57638
H	-0.39697	3.9322	1.80448
H	-1.06427	2.32945	1.54382
H	1.29559	-2.45799	3.51032
H	1.21497	-3.5662	2.11619
H	-0.06413	-2.33762	2.35643
H	4.8042	-1.10232	-1.36026
H	3.43305	-2.06209	-1.97522
H	3.37878	-0.27915	-2.06674

Conf. #2

imaginary frequency = 0

ΔE (Hartree) = -1340.9141950

C	4.48629	-1.44324	0.19531
C	4.31525	-0.64602	-1.1008
C	2.86478	-0.67667	-1.5874
C	1.92558	-0.18598	-0.49288
C	2.08337	-1.03107	0.75939
C	3.51523	-0.96781	1.27835
N	0.54204	-0.26235	-0.922
C	-0.48822	0.14876	0.02992
C	-0.0629	-0.00838	1.50269
N	1.14047	-0.54289	1.75671
O	-0.83701	0.32454	2.3951
P	-1.78925	-1.1677	-0.1791
O	-1.39541	-2.51278	0.31389
C	-1.14381	1.52892	-0.21842

C	-0.29973	2.82745	-0.2422
C	-1.31917	3.97823	-0.30604
C	0.54834	3.00735	1.0222
C	0.58973	2.92634	-1.49099
O	-2.06813	-1.03261	-1.74628
C	-3.04145	-1.86794	-2.3894
O	-3.18386	-0.65008	0.42141
C	-3.66721	-1.0471	1.71432
H	5.51363	-1.35962	0.55868
H	4.30677	-2.50607	-0.00671
H	4.61655	0.39426	-0.92807
H	4.97564	-1.04175	-1.87669
H	2.74513	-0.05092	-2.47785
H	2.57865	-1.69697	-1.86777
H	2.22487	0.84035	-0.22309
H	1.83535	-2.07003	0.50673
H	3.61109	-1.58464	2.17707
H	3.74553	0.06545	1.56474
H	0.39318	0.18327	-1.81735
H	1.34305	-0.70315	2.73406
H	-1.66896	1.46512	-1.17786
H	-1.91432	1.64023	0.54757
H	-0.80433	4.94222	-0.3578
H	-1.95841	3.88926	-1.19023
H	-1.96234	3.98402	0.57916
H	1.04574	3.98175	0.99987
H	1.32691	2.24619	1.11353
H	-0.07257	2.96067	1.92051
H	0.00676	2.75576	-2.4018
H	1.02528	3.928	-1.55786
H	1.41921	2.21804	-1.47847
H	-2.77162	-2.92003	-2.28058
H	-3.03295	-1.59331	-3.4417
H	-4.0323	-1.68825	-1.96763
H	-3.13762	-0.49297	2.48876
H	-4.72804	-0.80439	1.72909
H	-3.53004	-2.11984	1.8579