Supplementary Material (ESI) for Chemical Communications

Supporting Information

Bicyclization Involving Pseudo-Intramolecular Imination with Diamines

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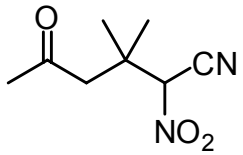
General

The melting points were determined on a Yanaco micro-melting-points apparatus, and were uncorrected. All the reagents and solvents were commercially available and used as received. The ^{1}H spectra were measured on a Bruker DPX-400 or Varian INOVA-400 spectrometer at 400 MHz, with TMS as an internal standard, and the ^{13}C NMR spectra were measured on a Bruker DPX-400 or Varian INOVA-400 spectrometer at 100 MHz. Assignments of ^{13}C NMR spectra were performed by DEPT experiments. The IR spectra were recorded on a Horiba FT-200 IR spectrometer and a JASCO FT/IR-4200 Spectrophotometer. The mass spectra were recorded on a JEOL JMS-AX505HA spectrometer or JEOL-JMS-700 MStation. The elemental microanalyses were performed using a Yanaco MT-3 CHN corder. The X-Ray analysis was carried out with a Rigaku AFC7R diffractometer, using graphite monochromated Mo-Kα radiation.

Preparation of α-nitro-δ-keto nitriles

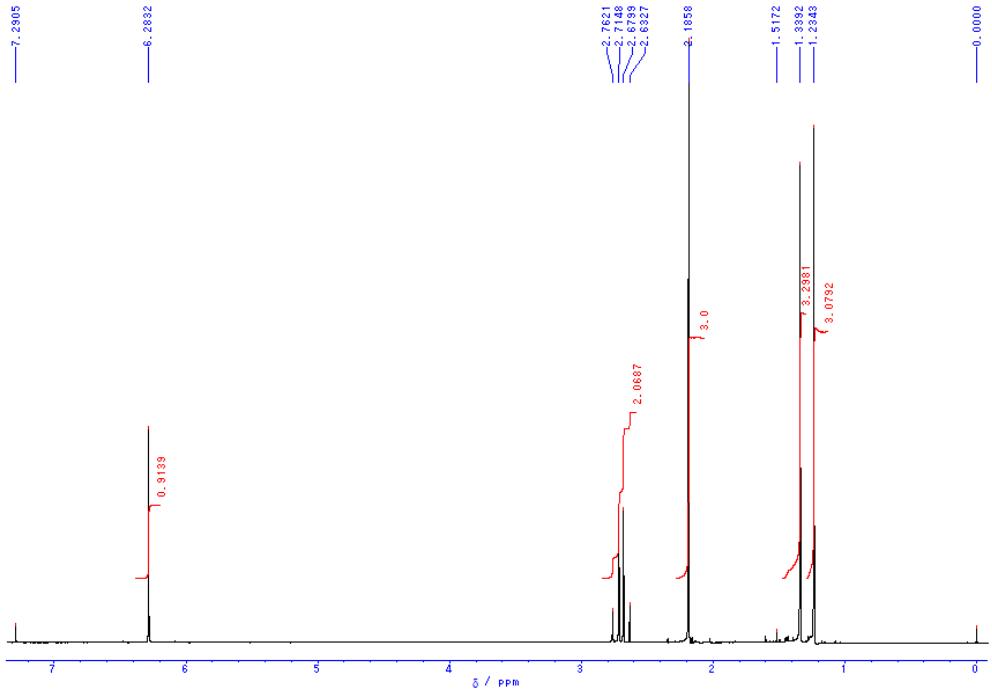
3,3-Dimethyl-2-nitro-5-oxohexanenitrile (1)[1]



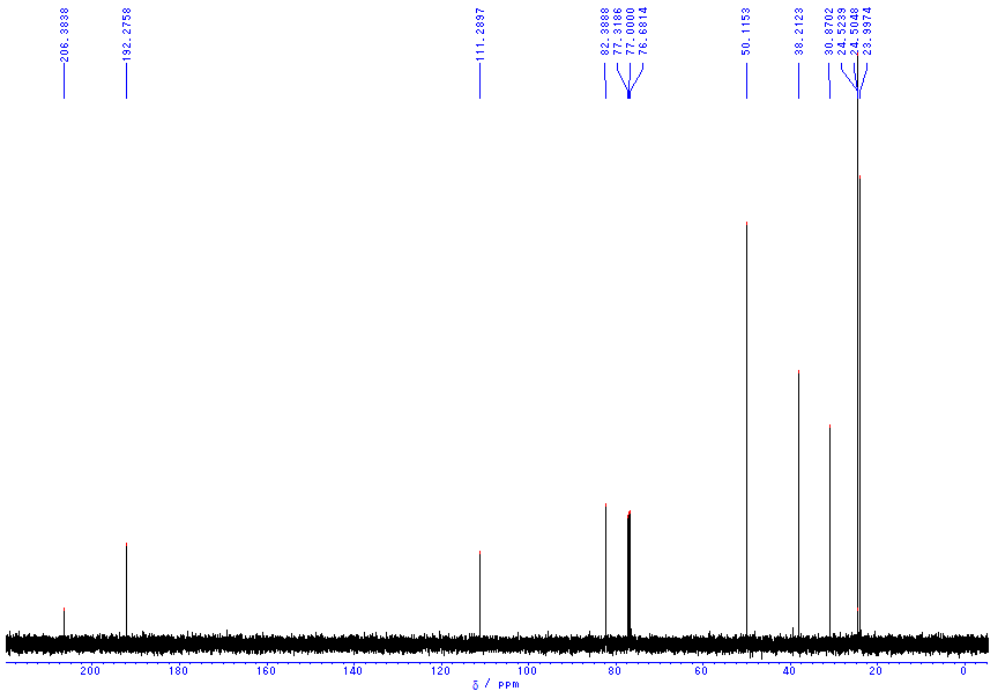
To a suspension of pyridinium 4-nitro-5-oxo-2*H*-isoxazol-2-ide (209 mg, 1.0 mmol) in benzene (3 mL), pyrrolidine (167 µL, 2.0 mmol) was added, and the mixture was stirred at rt for 0.5 h. To the resultant solution, acetone (40 µL, 0.5 mmol) was added. After 2 h of stirring, hexane (10 mL) was added, and the mixture was allowed to stand overnight. Upper solution was decanted off, and the residual white solid was dissolved into acetone (3 mL). After stirring at rt for 1 day, the solvent was evaporated. The residue was dissolved in $CHCl_3$ (20 mL), and washed with 1 M hydrochloric acid (5 mL × 1, 5 mmol).

The organic layer was dried over magnesium sulfate, and was concentrated to afford keto nitrile **1** (167 mg, 0.92 mmol, 92%) as a single product. Yellow solid. Mp 45-46 °C. IR (neat) 1714, 1568, 1365 cm^{-1}; ^{1}H NMR ($CDCl_3$) δ 1.23 (s, 3H), 1.34 (s, 3H), 2.18 (s, 3H), 2.65 (d, J = 18.9 Hz, 1H), 2.73 (d, J = 18.9 Hz, 1H), 6.29 (s, 1H); ^{1}H NMR (DMSO-d_6) δ 1.13 (s, 3H), 1.20 (s, 3H), 2.11 (s, 3H), 2.77 (s, 2H), 6.27 (s, 1H); ^{13}C NMR ($CDCl_3$) δ 24.4 (CH_3), 25.0 (CH_3), 31.3 (CH_3), 38.6 (C), 50.5 (CH_2), 82.8 (CH), 111.8 (C), 206.9 (C); ^{13}C NMR (DMSO-d_6) δ 23.9 (CH_3), 24.3 (CH_3), 31.6 (CH), 38.5 (C), 49.6 (CH_2), 84.7 (CH), 113.0 (C), 207.4 (C). Anal. Calcd for $C_8H_{12}N_2O_3$: C, 52.17; H, 6.57; N, 15.21. Found: C, 52.09; H, 6.58; N, 15.43.

^{1}H NMR of **1** ($CDCl_3$)

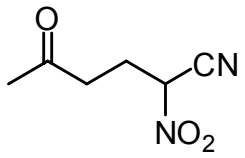


^{13}C NMR of **1** ($CDCl_3$)



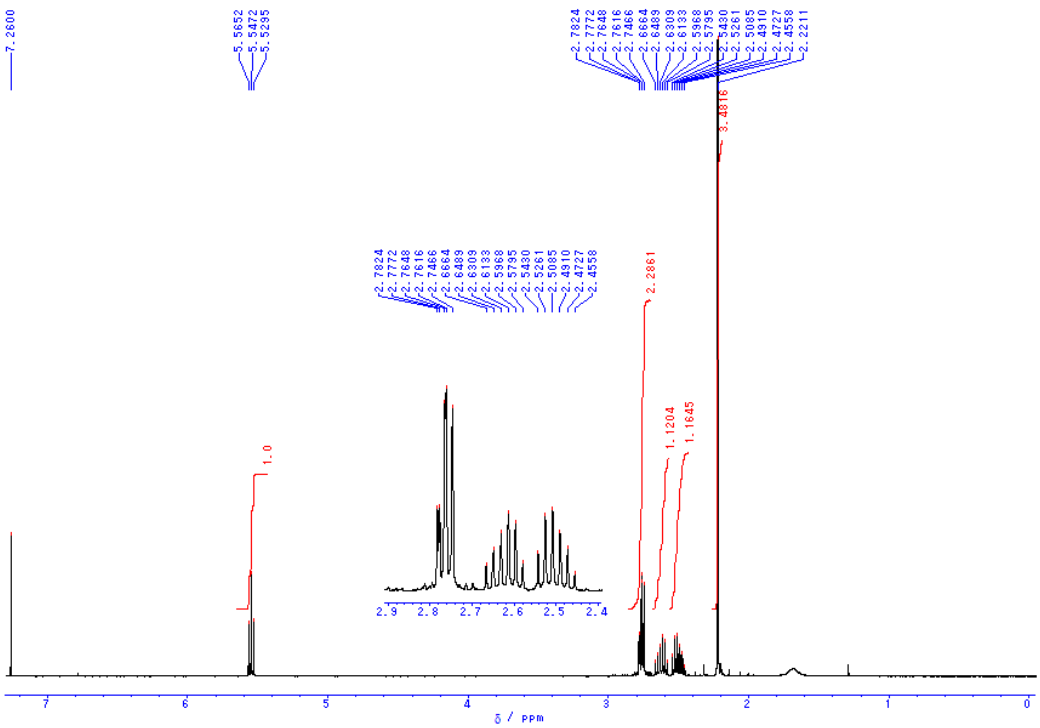
[1] N. Nishiwaki, T. Nogami, M. Ariga, *Heterocycles* **2008**, *75*, 675-681.

2-Nitro-5-oxohexanenitrile (8)

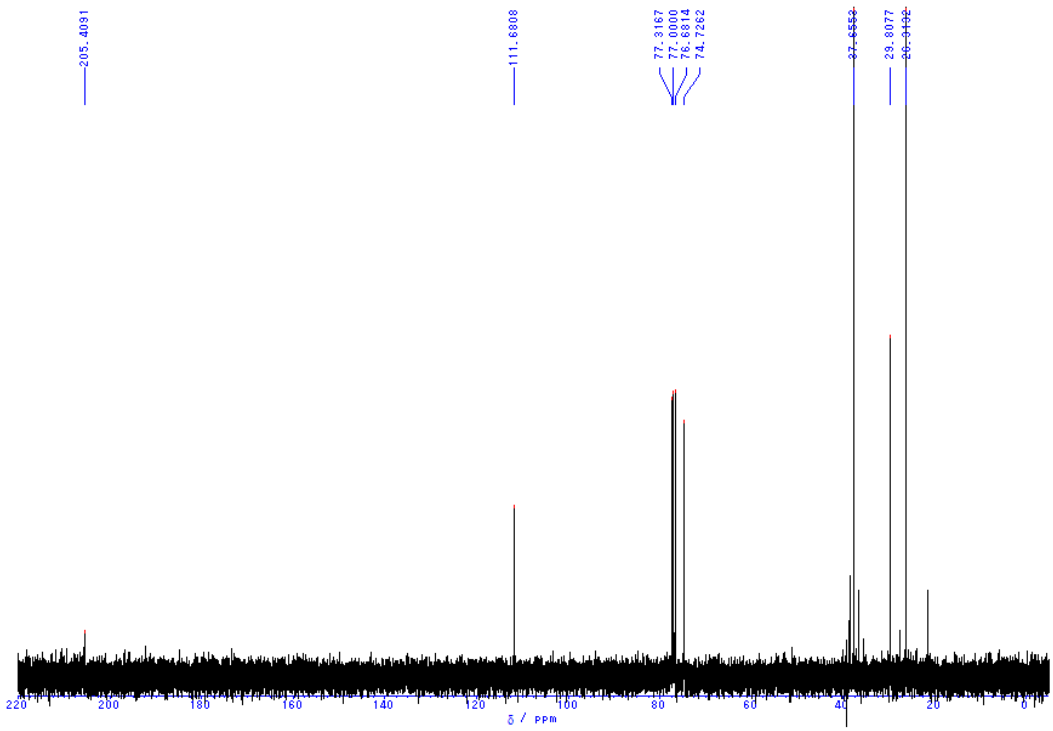


To a suspension of pyridinium 4-nitro-5-oxo-2*H*-isoxazol-2-ide (1.05 g, 5.0 mmol) in benzene (40 mL), were added pyrrolidine (835 μL, 10.0 mmol) and butenone (407 μL, 5.0 mmol), and the mixture was stirred at 30 °C for 2 h. The reaction mixture was washed with 1 M hydrochloric acid (30 mL × 1, 30 mmol). The organic layer was dried over magnesium sulfate, and was concentrated to afford 2-nitro-5-oxohexanenitrile (**9**) (0.69 g, 4.4 mmol, 88%) as a single product. Yellow oil. IR (neat) 2228, 1715, 1574, 1362 cm^{-1}; ^1H NMR ($CDCl_3$) δ 2.22 (s, 3H), 2.50 (dddd, *J* = 14.6, 7.2, 7.0, 6.2 Hz, 1H), 2.62 (dddd, *J* = 14.6, 7.2, 7.0, 6.2 Hz, 1H), 2.76 (dd, *J* = 6.2, 6.2 Hz, 1H), 2.77 (dd, *J* = 7.0, 7.0 Hz, 1H), 5.55 (dd, *J* = 7.2, 7.2 Hz, 1H); ^{13}C NMR ($CDCl_3$) δ 26.6 (CH_2), 30.0 (CH_3), 37.9 (CH_2), 75.0 (CH), 111.9 (C), 205.6 (C). Satisfactory analytical data were not given because of the instability of keto nitrile **8**.

^1H NMR of **8** ($CDCl_3$)



^{13}C NMR of **8** ($CDCl_3$)

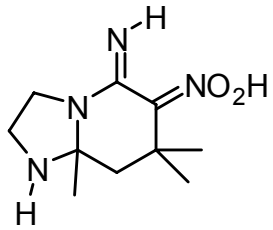


Typical procedure for synthesis of diazabicyclo compounds

To a solution of keto nitrile **1** (184 mg, 1.0 mmol), in acetonitrile (15 mL), 1,2-diaminoethane **4a** (67 μL, 1.0 mmol) was added. After addition of amine, imine **5a** was immediately precipitated as a pale yellow solid. The resultant mixture was heated under reflux for 2 h, and was concentrated under reduced pressure. The brown residual oil was treated with column chromatography on silica gel to afford diazabicyclononane **7a** (172 mg, 0.76 mmol, 76%, eluted with AcOEt/methanol (70/30)) as a colorless solid. Single crystal for X-ray analysis was obtained by recrystallization from a mixed solvent of methanol and acetonitrile (1/2).

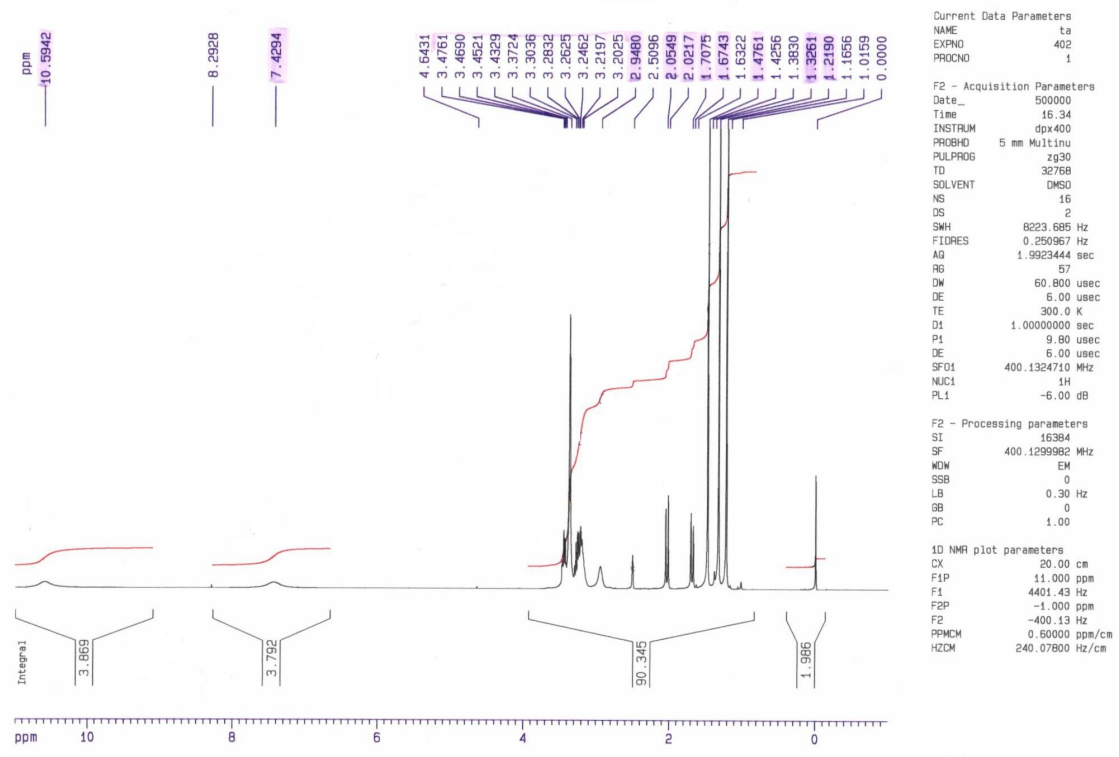
When other diamines and keto nitrile were employed, diazabicyclo compounds were synthesized in a similar way.

1,7-Diaza-2-imino-3-*aci*-nitro-4,4,6-trimethylbicyclo[4.3.0]nonane (7a)

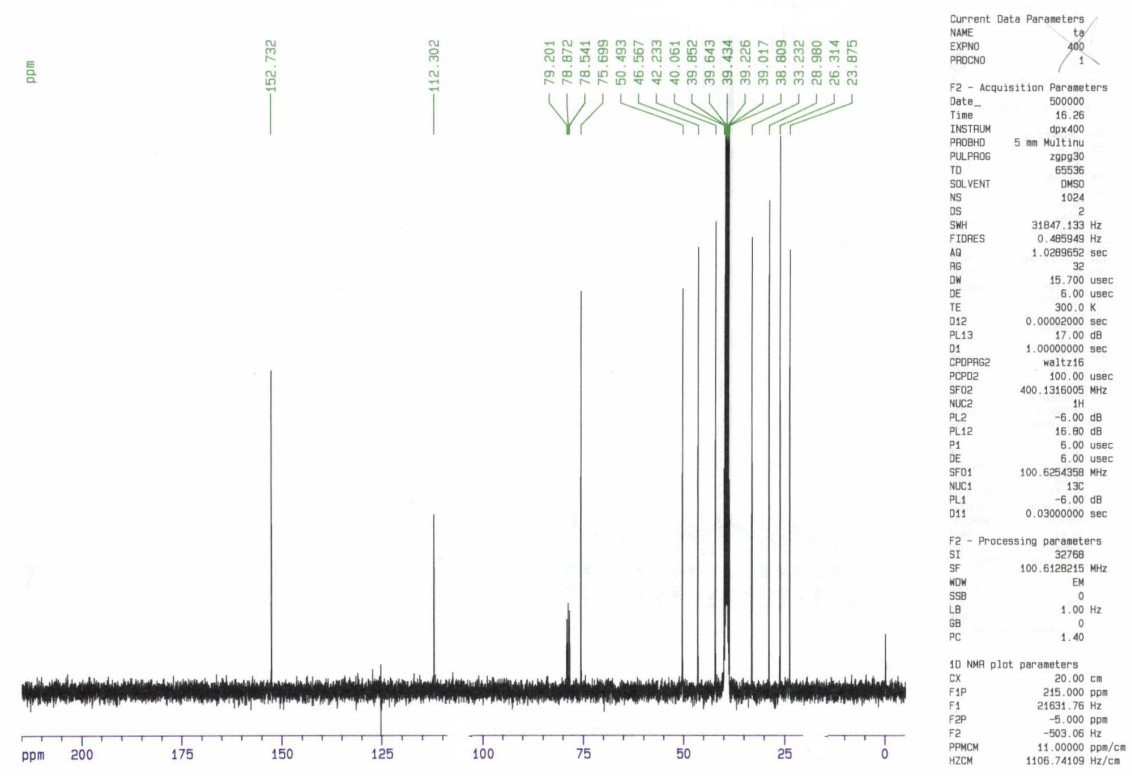


Recrystallized from from a mixed solvent of acetonitrile and methanol (1/2). Colorless prisms. Mp 241-243 °C (dec.). IR (KBr) 3271, 3093, 1641, 1566, 1392, 1371, 1348 cm^{-1}; ^1H NMR (DMSO-*d*$_6$) δ 1.22 (s, 3H), 1.32 (s, 3H), 1.47 (s, 3H), 1.69 (d, *J* = 13.3 Hz, 1H), 2.04 (d, *J* = 13.3 Hz, 1H), 2.9-3.0 (br, 1H), 3.2-3.3 (m, 3H), 3.4-3.5 (m, 1H), 7.3-7.6 (br, 1H), 10.4-10.7 (br, 1H); ^{13}C NMR (DMSO-*d*$_6$) δ 23.9 (CH_3), 26.3 (CH_3), 29.0 (CH_3), 33.2 (C), 42.2 (CH_2), 46.6 (CH_2), 50.5 (CH_2), 75.7 (C), 112.3 (C), 152.7 (C); MS (FAB) 227 (M^++1, 100). Anal. Calcd for $C_{10}H_{18}N_4O_2$: C, 53.08; H, 8.02; N, 24.76%. Found: C, 53.18; H, 8.33; N, 24.69%.

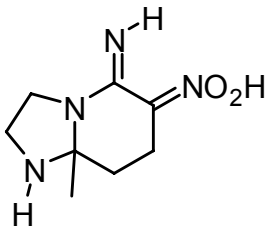
^1H NMR of **7a** (DMSO-*d*$_6$)



^{13}C NMR of **7a** (DMSO-d_6)

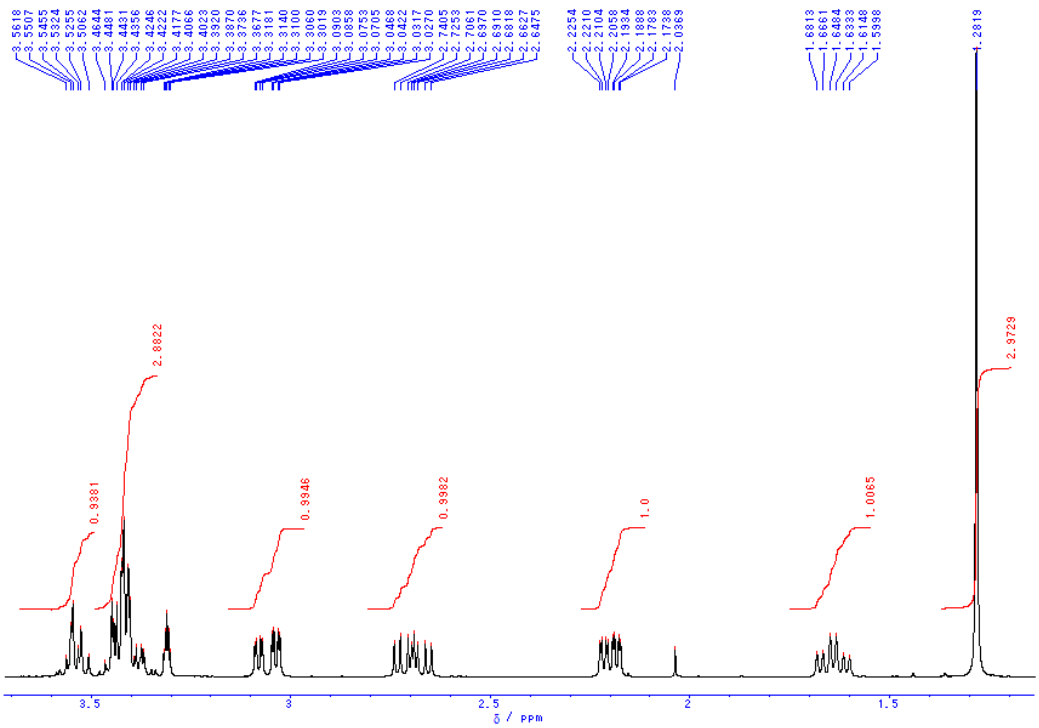


1,7-Diaza-2-imino-6-methyl-3-*aci*-nitrobicyclo[4.3.0]nonane (9)

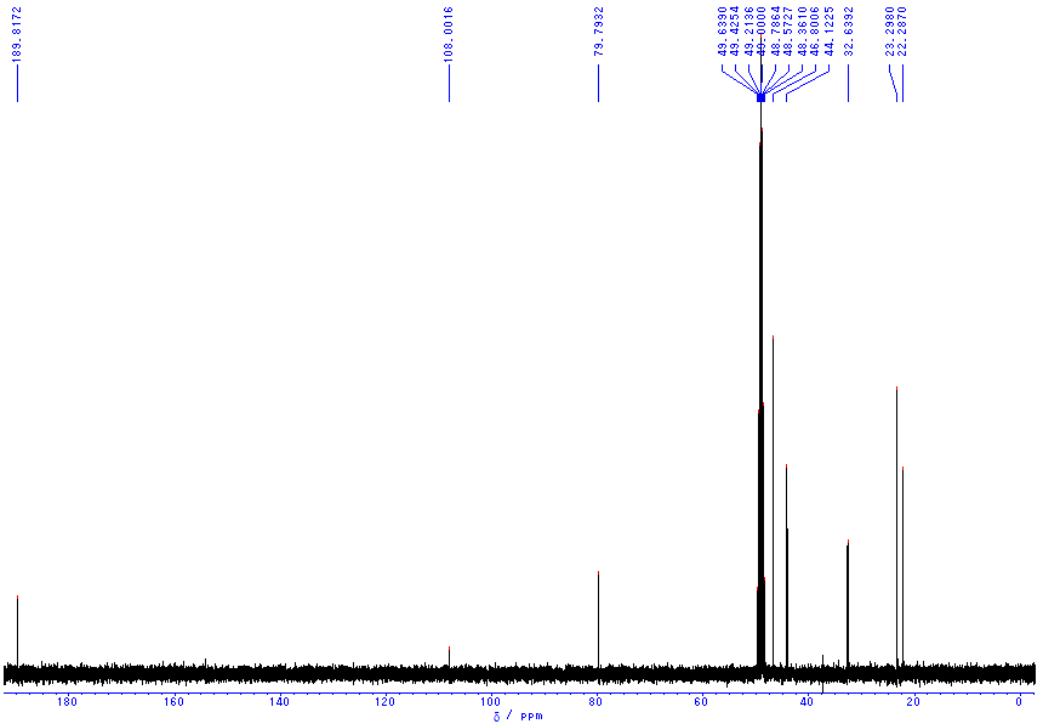


Recrystallized from acetonitrile. Colorless plates. Mp 234-235 °C (dec.). IR (KBr) 3271, 3101, 1624, 1570, 1406 cm^{-1}; ^1H NMR (CD_3OD) δ 1.27 (s, 3H), 1.63 (ddd, J = 13.7, 12.8, 6.1 Hz, 1H), 2.19 (ddd, J = 12.8, 6.0, 1.8 Hz, 1H), 2.68 (ddd, J = 17.4, 13.7, 6.0 Hz, 1H), 3.05 (ddd, J = 17.4, 6.1, 1.9 Hz, 1H), 3.35-3.45 (m, 3H), 3.48-3.59 (m, 1H); ^{13}C NMR (CD_3OD) δ 22.3 (CH_3), 23.3 (CH_2), 32.6 (CH_2), 44.1 (CH_2), 46.8 (CH_2), 79.8 (C), 108.0 (C), 189.8 (C); MS (EI) 198 (40), 181 (29), 166 (54), 152 (82), 85 (100). HRMS Calcd for $C_8H_{14}N_4O_2$: 198.1117. Found: 198.1113.

^1H NMR of **9** (CD_3OD)

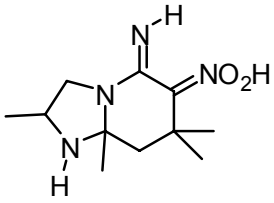


^{13}C NMR of **9** (CD_3OD)

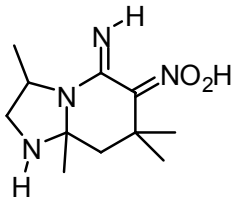


1,5-Diaza-2-imino-3-*aci*-nitro-4,4,6,8-tetramethylbicyclo[4.3.0]nonane (7b)

1,5-Diaza-2-imino-3-*aci*-nitro-4,4,6,9-tetramethylbicyclo[4.3.0]nonane (7b')



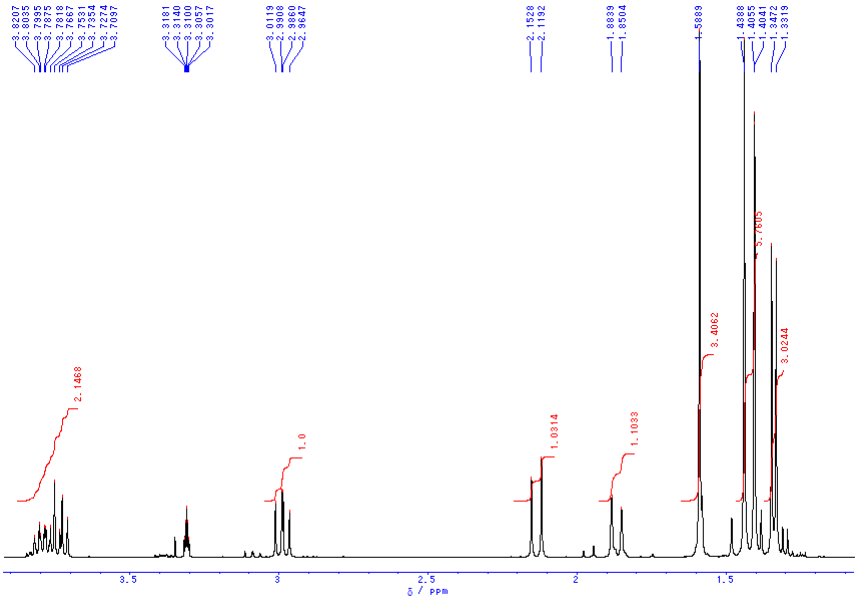
7b



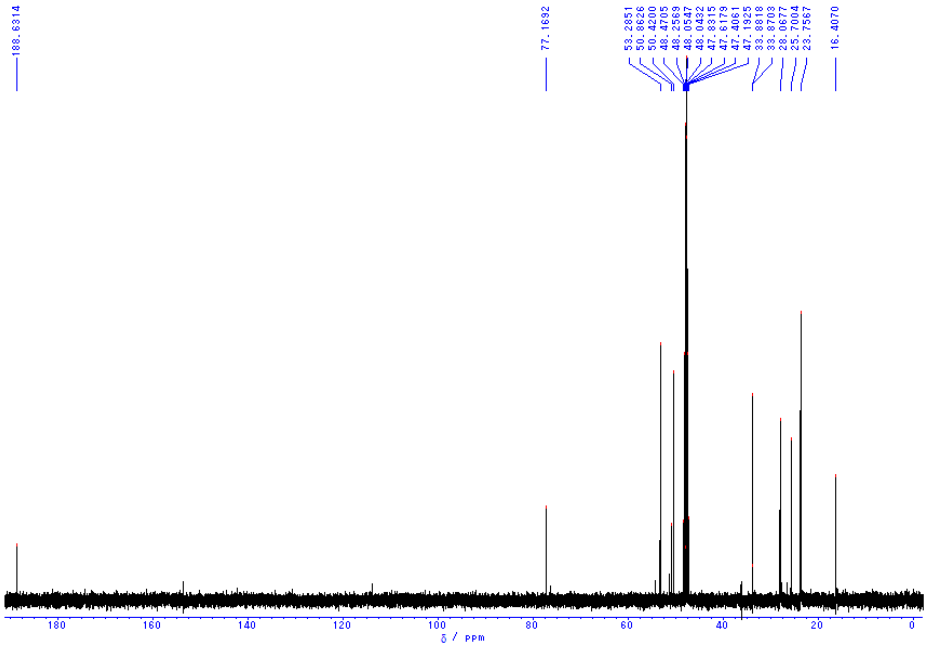
7b'

A mixture of **7b** and **7b'** (1/1) was eluted with a mixed solvent of dichloromethane and methanol (9/1). Recrystallization from a mixed solvent of acetonitrile and methanol (1/2) afforded **7b**. Colorless prisms. Mp 237-238 °C (dec.). IR (KBr) 3258, 2978, 2398, 1618, 1557, 1389, 1356, 1315,1196, 1069 cm^{-1}; ^1H NMR (CD_3OD) δ 1.30 (d, J = 6.5 Hz, 3H), 1.38 (s, 3H), 1.48 (s, 3H), 1.58 (s, 3H), 1.86 (d, J = 13.5 Hz, 1H), 1.96 (d, J = 13.5 Hz, 1H), 3.10 (dd, J = 10.8, 9.4 Hz, 1H), 3.3-3.4 (m, 1H), 3.83 (dd, J = 10.8, 6.0 Hz, 1H); ^{13}C NMR (CD_3OD) δ 16.4 (CH_3), 23.7 (CH_3), 25.7 (CH_3), 28.1 (CH_3), 33.9 (C), 50.4 (CH), 50.9 (CH_2), 53.3 (CH_2), 77.2 (C), 154.8 (C), 188.6 (C); MS (EI) 240 (21), 225 (100), 208 (40), 179 (47), 164 (95), 99 (86). HRMS Calcd for $C_{11}H_{20}N_4O_2$: 240.1586. Found: 240.1582. A correlation between a methyl group at the 5-position and a methyne proton at the 7-position was observed in the ^1H-^1H NOESY 2D spectrum.

^1H NMR of **7b** (CD_3OD)

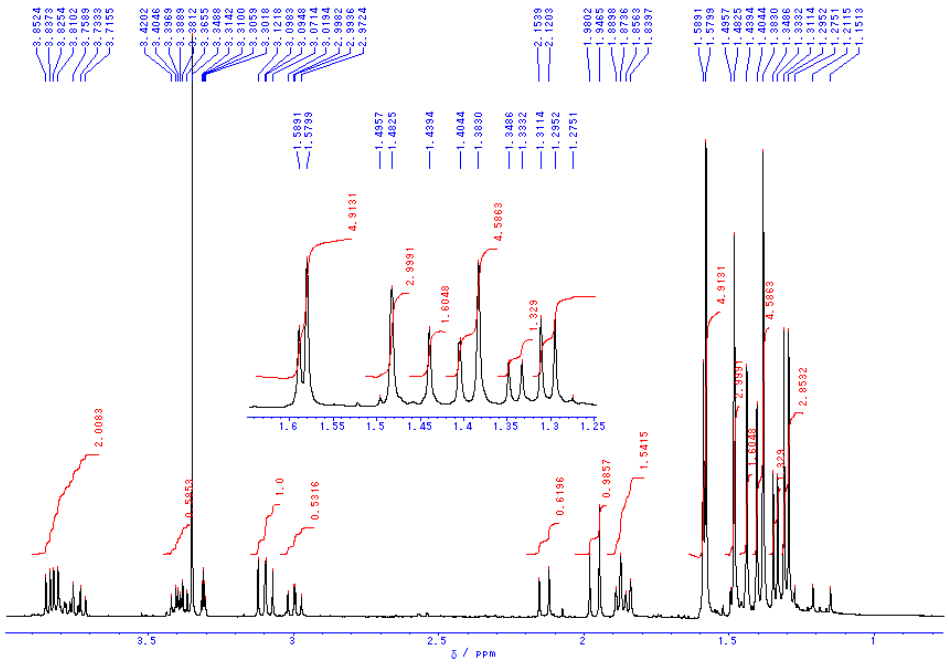


^{13}C NMR of **7b** (CD_3OD)

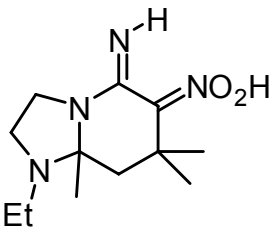


7b' (measured using a mixture with **7b**) ^{1}H NMR (CD_3OD) δ 1.34 (d, J = 6.1 Hz, 3H), 1.41 (s, 3H), 1.44 (s, 3H), 1.59 (s, 3H), 1.85 (d, J = 13.4 Hz, 1H), 2.12 (d, J = 13.4 Hz, 1H), 2.99 (dd, J = 10.4, 8.5 Hz, 1H), 3.73 (dd, J = 10.4, 7.1 Hz, 1H), 3.7-3.8 (m, 1H).

^{1}H NMR of a mixture of **7b** and **7b'** (CD_3OD)

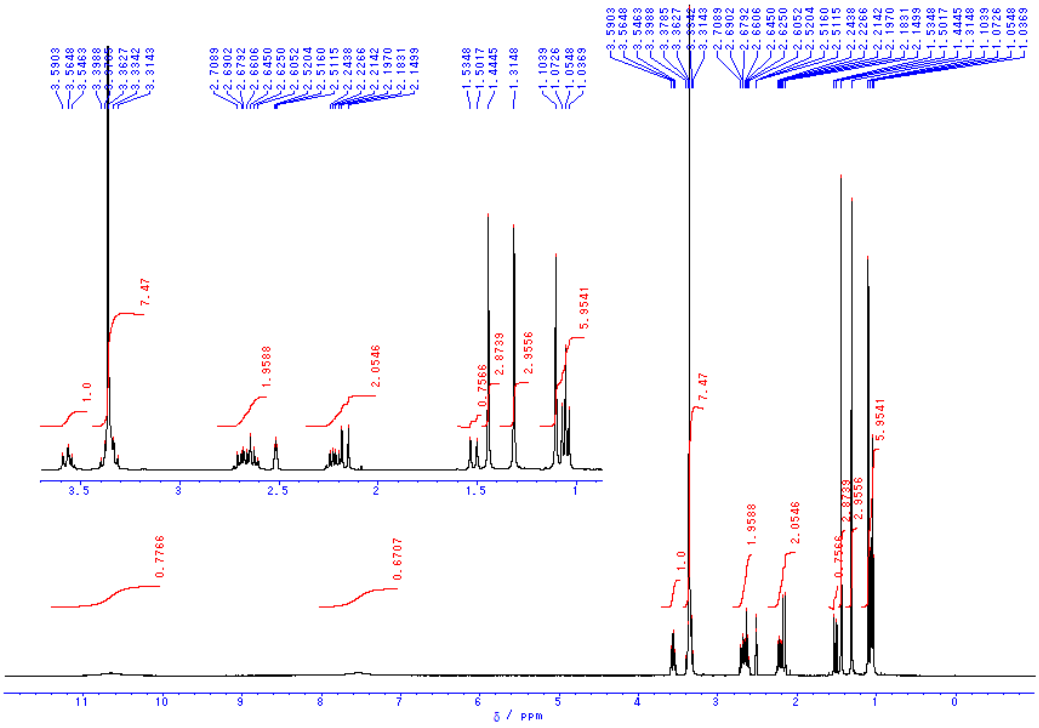


1,7-Diaza-1-ethyl-2-imino-4,4,6-trimethyl-3-*aci*-nitrobicyclo[4.3.0]nonane (7c)

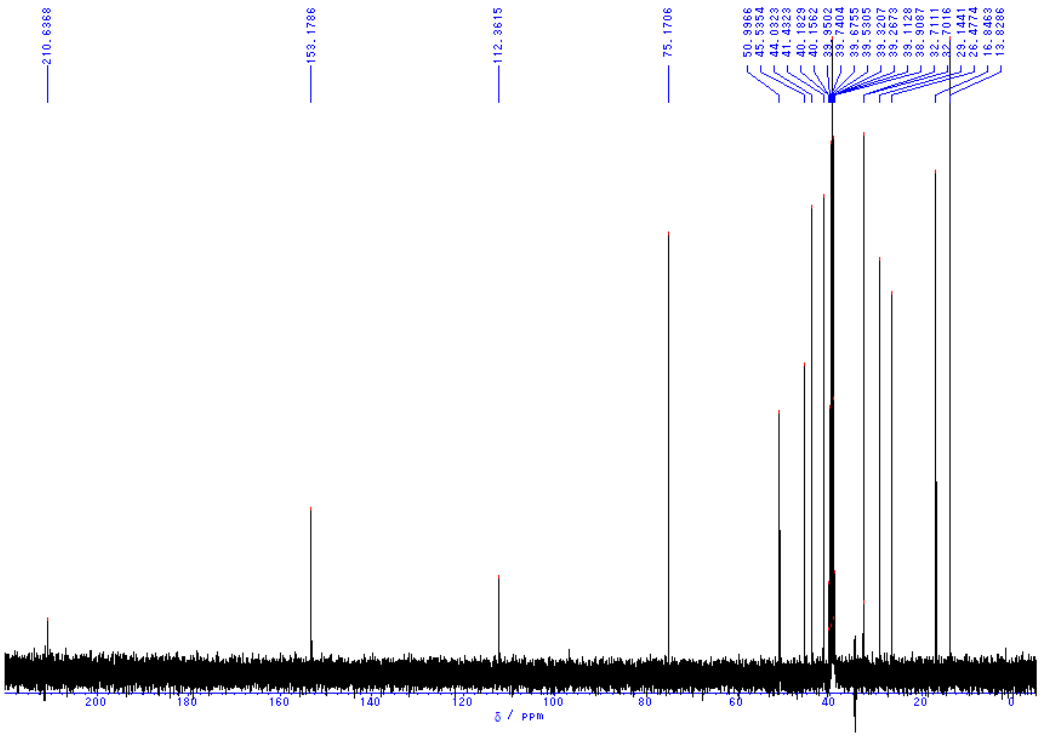


Recrystallized from a mixed solvent of acetonitrile and methanol (1/1). Colorless prisms. Mp 201-204 °C (dec.). IR (KBr) 3250, 1605, 1564, 1389, 1338, cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.05 (t, J= 7.1 Hz, 3H), 1.09 (s, 3H), 1.31 (s, 3H), 1.44 (s, 3H), 1.51 (d, J= 13.2 Hz, 1H), 2.15 (d, J= 13.2 Hz, 1H), 2.20-2.25 (m, 1H), 2.6-2.7 (m, 2H), 3.3-3.45 (m, 2H), 3.5-3.6 (m, 1H), 7.3-7.7 (br, 1H), 10.4-10.8 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 13.7 (CH_3), 16.8 (CH_3), 26.4 (CH_3), 29.0 (CH_3), 32.6 (C), 41.4 (CH_2), 44.0 (CH_2), 45.5 (CH_2), 50.9 (CH_2), 75.1 (C), 112.3 (C), 153.1 (C); MS (EI) 254 (20), 239 (100), 222 (36), 193 (36), 178 (91), 113 (63). HRMS Calcd for $C_{12}H_{22}N_4O_2$: 254.1743. Found: 254.1744.

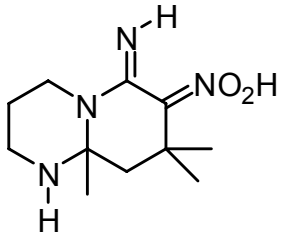
^1H NMR of **7c** (DMSO-d_6)



^{13}C NMR of **7c** (DMSO-d_6)

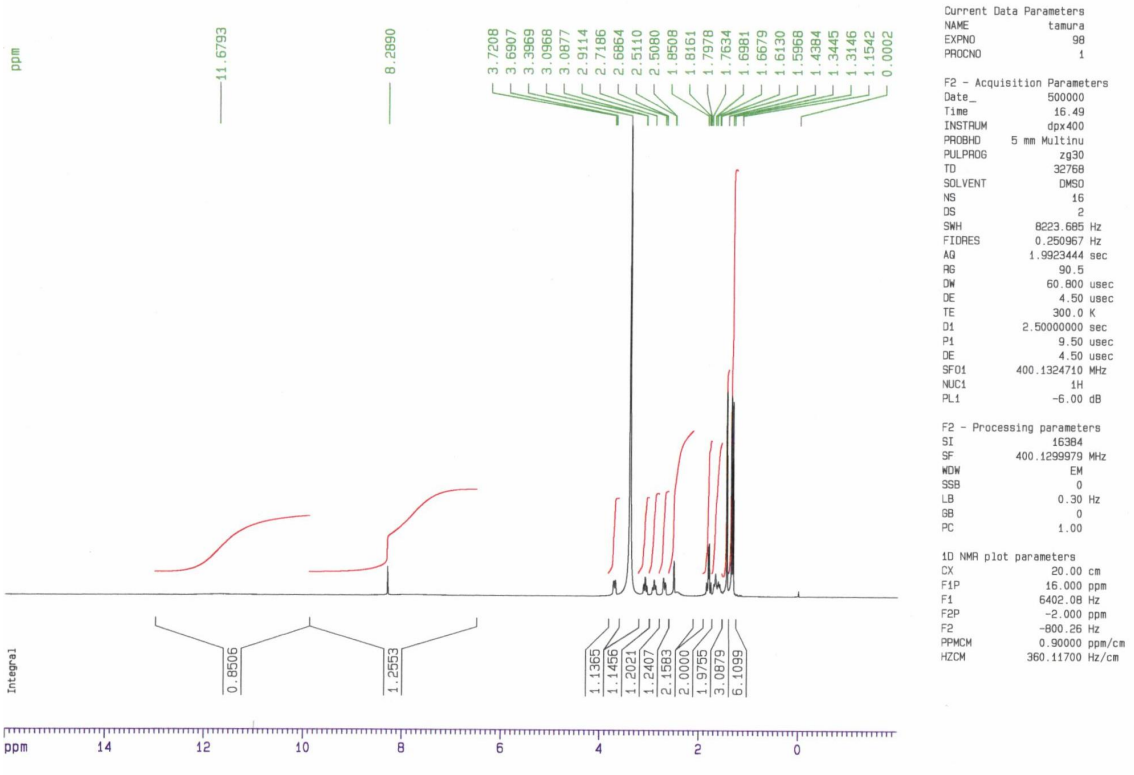


1,7-Diaza-2-imino-3-*aci*-nitro-4,4,6-trimethylbicyclo[4.4.0]decane (7d)

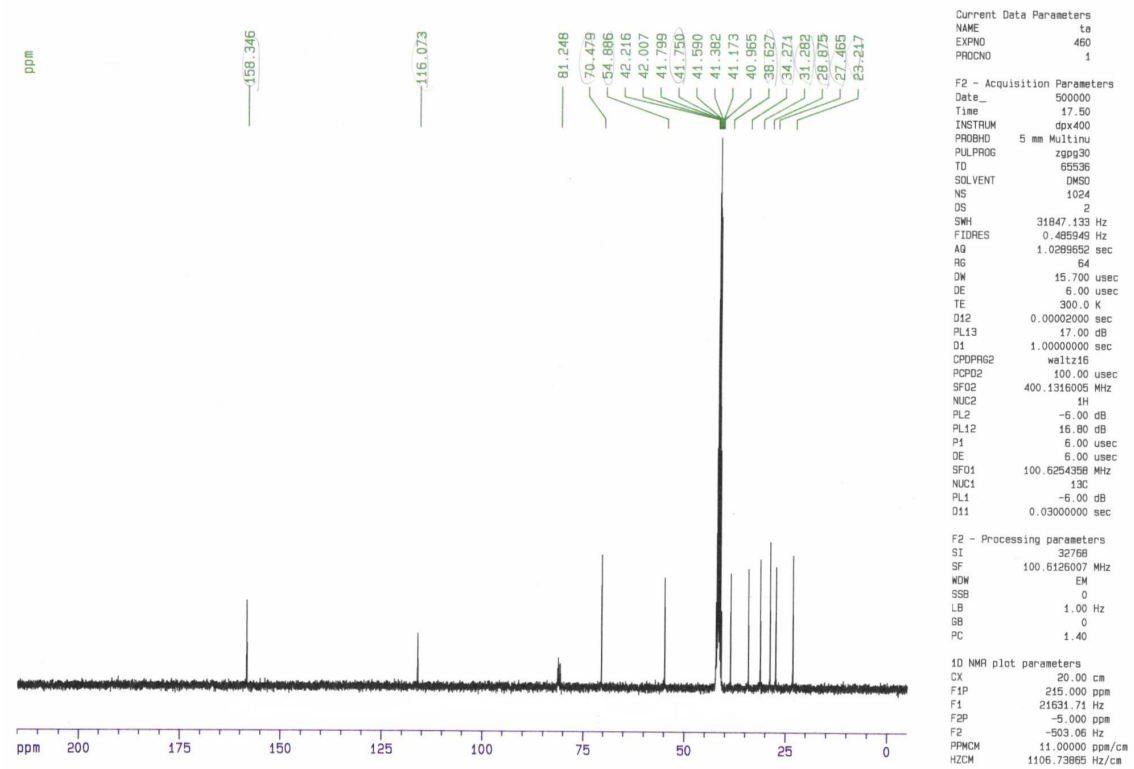


Eluted with chloroform. Pale yellow plates. Mp 204-205 °C (dec.). IR (KBr) 3259, 1606, 1537, 1338 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.31 (s, 3H), 1.34 (s, 3H), 1.44 (s, 3H), 1.55-1.70 (m, 2H), 1.78 (d, J = 13.8 Hz, 1H), 1.83 (d, J = 13.8 Hz, 1H), 2.44 (br, 1H), 2.70 (br d, J = 12.8 Hz, 1H), 2.91 (br dd, J = 11.8, 11.8 Hz, 1H), 3.09 (ddd, J = 12.8, 12.0, 3.6 Hz, 1H), 3.71 (br d, J = 12.0 Hz, 1H), 7.9-8.3 (s, 1H), 11.4-11.9 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 23.2 (CH_3), 27.5 (CH_2), 28.9 (CH_3), 31.3 (CH_3), 34.3 (C), 38.6 (CH_2), 41.8 (CH_2), 54.9 (CH_2), 70.5 (C), 116.1 (C), 158.3 (C); MS (EI) 240 (3), 225 (88), 194 (63), 179 (93), 164 (100). HRMS Calcd for $C_{11}H_{20}N_4O_2$: 240.1586. Found: 240.1585.

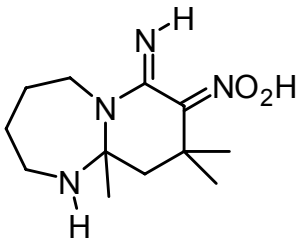
^1H NMR of **7d** (DMSO-d_6)



^{13}C NMR of **7d** (DMSO-d_6)

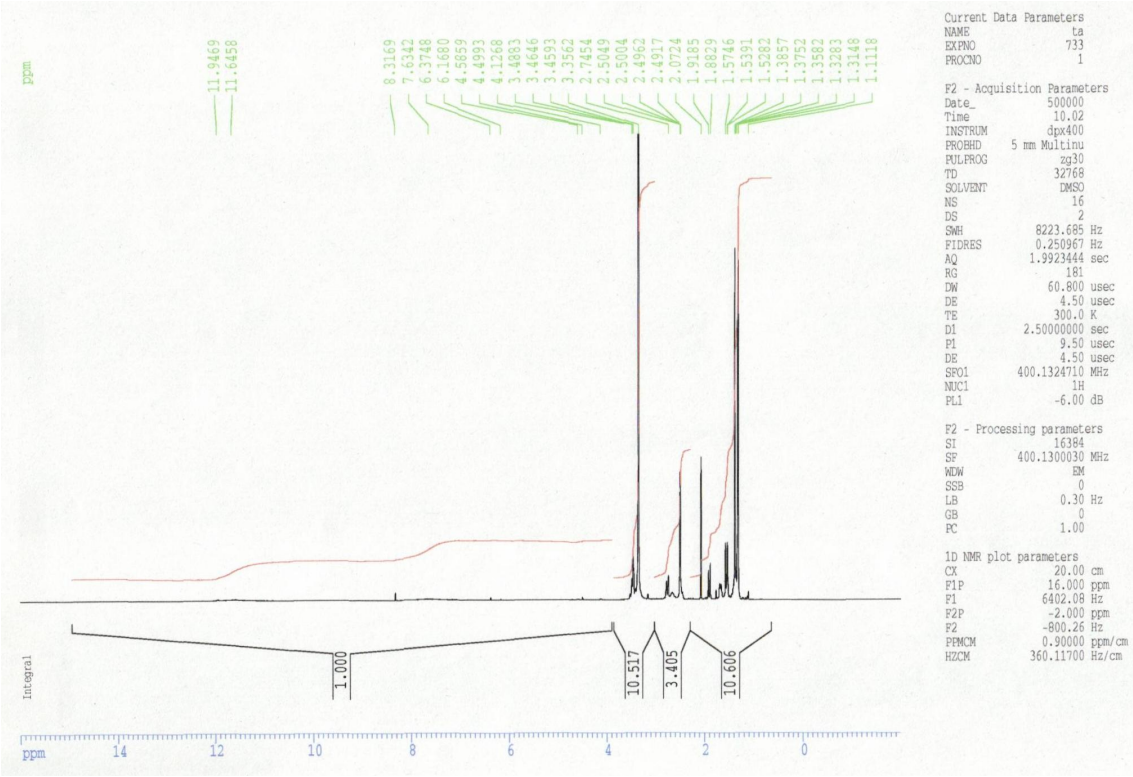


1,7-Diaza-2-imino-3-*aci*-nitro-4,4,6-trimethylbicyclo[5.4.0]undecane (7e)

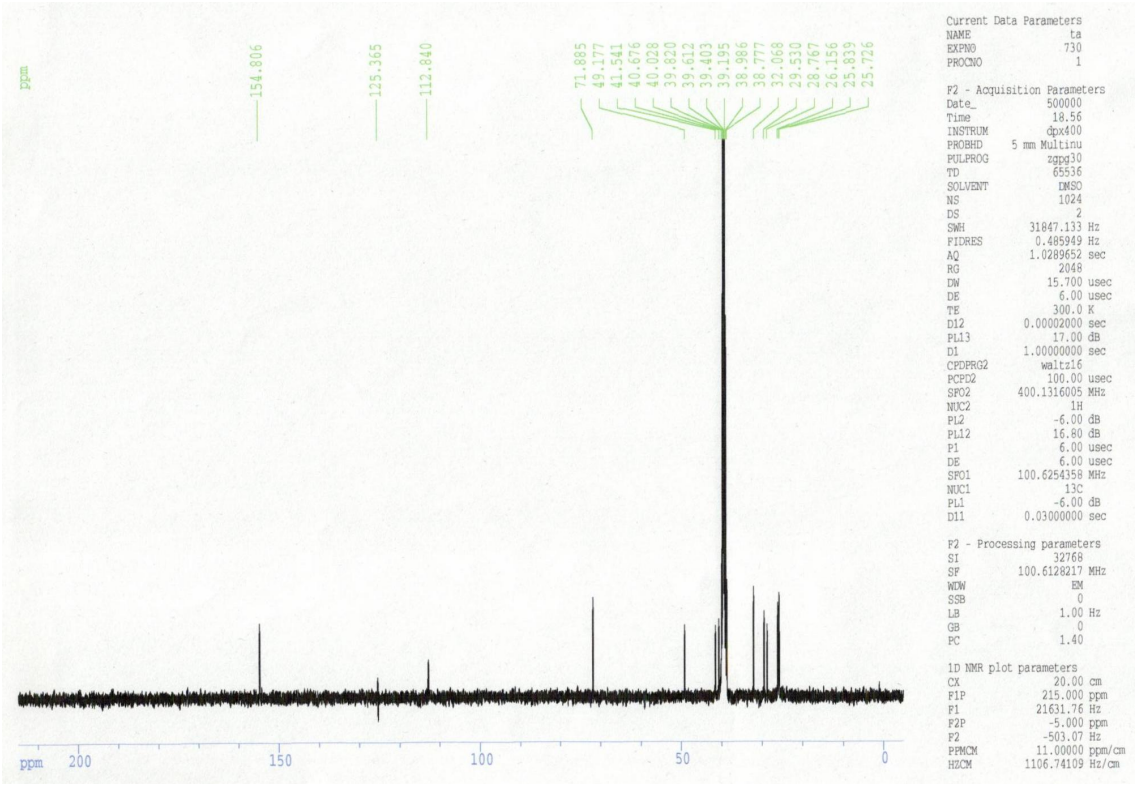


Recrystallized from methanol. Orange granules. Mp 173-178 °C (dec.). IR (KBr) 3275, 2930, 1611, 1560, 1544, 1335 cm^{-1}; ^1H NMR (DMSO-d_6) δ 1.31 (s, 3H), 1.33 (s, 3H), 1.35-1.40 (m, 2H), 1.39 (s, 3H), 1.50-1.55 (m, 1H), 1.56 (d, J = 14.3 Hz, 1H), 1.66-1.69 (m, 1H), 1.90 (d, J = 14.3 Hz, 1H), 2.49-2.53 (m, 1H), 2.6-2.7 (br, 1H), 2.75-2.80 (m, 1H), 3.45-3.50 (m, 2H), 7.4-7.8 (s, 1H), 11.4-11.9 (br, 1H); ^{13}C NMR (DMSO-d_6) δ 25.7 (CH_2), 25.8 (CH_3), 26.2 (CH_3), 28.8 (CH_2), 29.5 (CH_3), 40.7 (CH_2), 41.5 (CH_2), 49.2 (CH_2), 71.9 (C), 112.8 (C), 154.8 (C); MS (EI) 254 (7), 239 (30), 208 (81), 178 (36), 110 (57), 70 (100). HRMS Calcd for $C_{12}H_{22}N_4O_2$: 254.1743. Found: 254.1743.

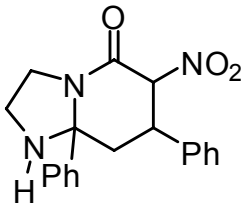
^1H NMR of **7e** (DMSO-d_6)



^{13}C NMR of **7e** (DMSO-d_6)

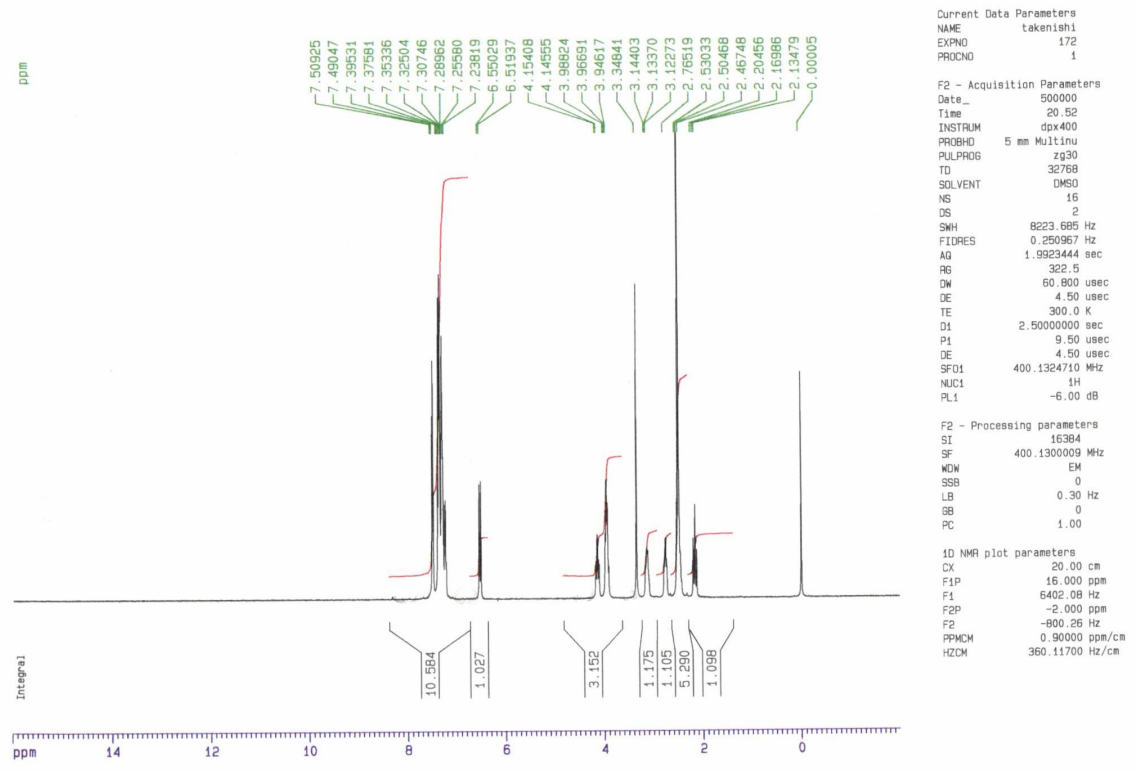


1,7-Diaza -4,6-diphenyl-3-nitro-2-oxobicyclo[4.3.0]nonane (13)

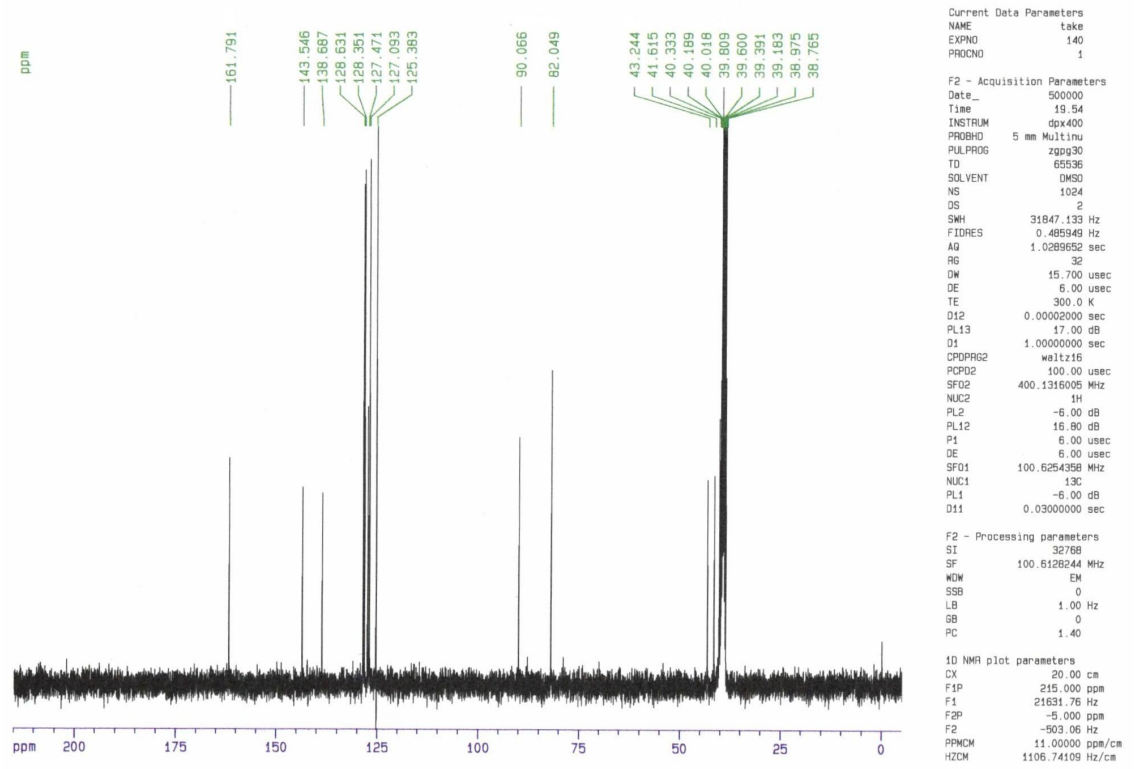


Colorless prisms. Mp 227-230 °C (dec.). IR (KBr) 1652, 1558, 1369 cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.17 (dd, J= 14.0, 3.8 Hz, 1H), 2.50-2.54 (m, 1H), 2.53 (dd, J= 14.0, 3.8 Hz, 1H), 2.74-2.79 (m, 1H), 3.12-3.14 (m, 1H), 3.37 (s, 1H), 3.92-3.99 (m, 1H), 4.15 (ddd, J= 12.4, 3.8, 3.8 Hz, 1H), 6.54 (d, J= 12.4 Hz, 1H), 7.2-7.5 (m, 10H); ^{13}C NMR (DMSO-d_6) δ 40.2 (CH_2), 40.3 (CH), 41.6 (CH_2), 43.2 (CH_2), 82.0 (C), 90.1 (CH), 125.4 (CH), 125.4 (CH), 127.1 (CH), 127.4 (CH), 128.3 (CH), 128.6 (CH), 138.7 (C), 143.5 (C), 161.8 (C); MS (FAB) 338 (M^++1, 100). Anal. Calcd for $C_{19}H_{19}N_3O_3$: C, 67.64; H, 5.68; N, 12.46%. Found: C, 67.63; H, 5.83; N, 12.34%.

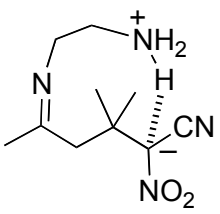
^1H NMR of **13** (DMSO-d_6)



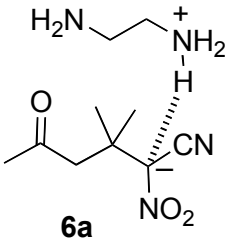
^{13}C NMR of **13** (DMSO-d_6)



7-Ammonio-5-aza-1-cyano-2,2,4-trimethyl-4-heptenenitronate (5a)



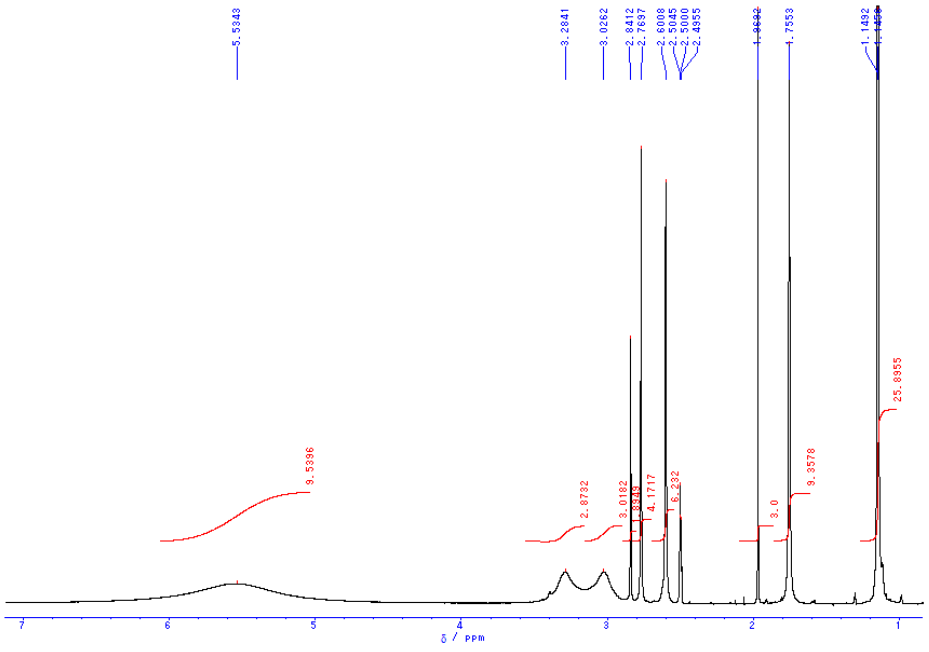
5a

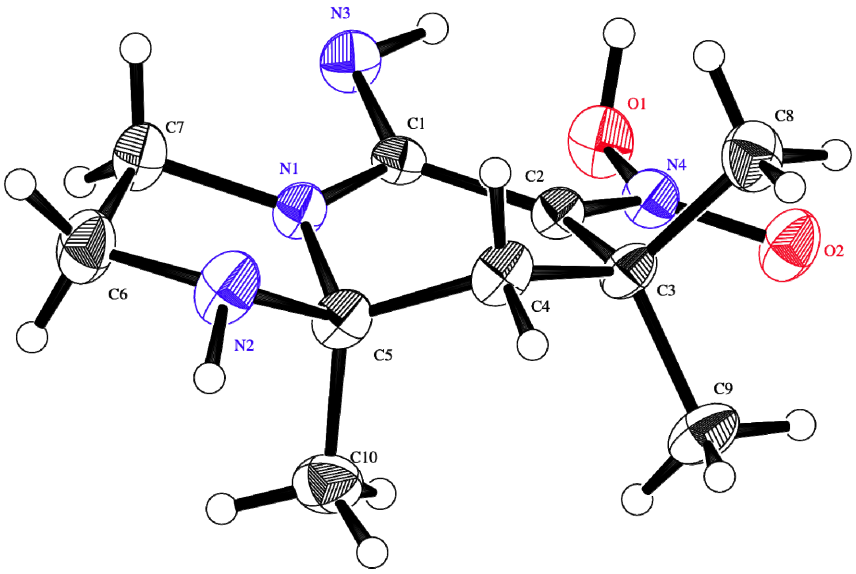


6a

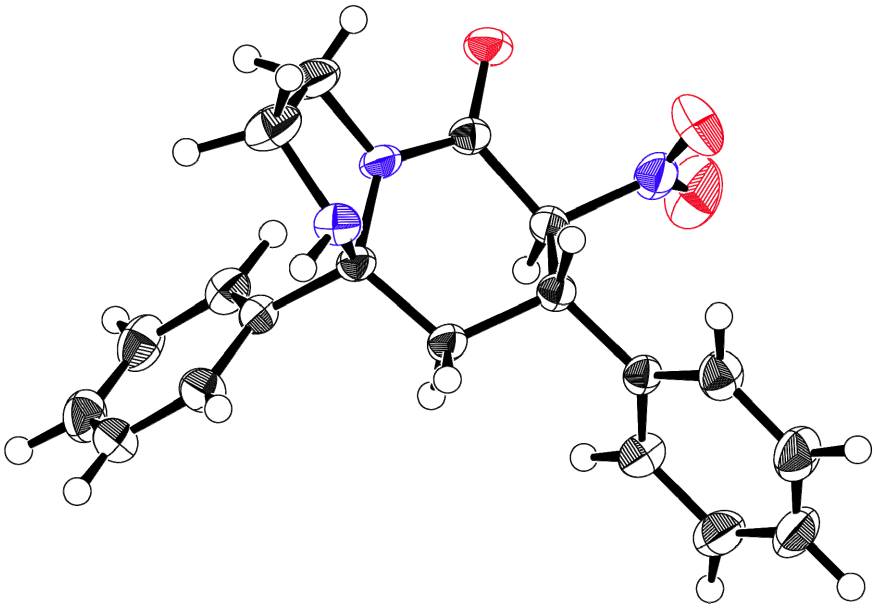
To a solution of keto nitrile **1** (184 mg, 1.0 mmol), in acetonitrile (15 mL), 1,2-diaminoethane **4a** (67 μL, 1.0 mmol) was added. After addition of amine, a pale yellow solid was immediately precipitated, and was collected by filtration to give imine **5a** (226 mg, 1.0 mmol, quant.). Further purification was performed by recrystallization from methanol. Pale yellow prisms. Mp 129-130 °C (dec.). IR (KBr) 2189, 1655, 1464, 1234, 1061 cm^{-1}; MS (EI) 226 (28), 211 (95), 194 (94), 150 (97), 85 (100), 69 (99). HRMS Calcd for $C_{10}H_{18}N_4O_2$: 226.1430. Found: 226.1427. Anal. Calcd for $C_{10}H_{18}N_4O_2$: C, 53.08; H, 8.02; N, 24.76%. Found: C, 52.70; H, 8.18; N, 25.07%.

The ^1H NMR spectrum of the precipitate measured in DMSO-d_6 solution (well soluble) instead of CD_3CN (insoluble) showed signals derived from both imine **5a** and ammonium salt **6a**, which would be ascribed to an equilibrium shift from **5a** to **6a** in DMSO. ^1H NMR (DMSO-d_6) imine **5a** δ 1.14 (s, 6H), 1.73 (s, 3H), 2.59 (s, 2H), 2.9-3.1 (br, 1H), 3.1-3.3 (br, 2H); ammonium salt **6a** δ 1.14 (s, 6H), 1.97 (s, 3H), 2.69 (s, 4H), 2.84 (s, 2H), 5.2-5.8 (br, 5H).





An ORTEP drawing of **7a** with 50% probability thermal ellipsoids. Selected bond length [Å] and angles[°]: N1-C1 1.320(3), N1-C5 1.482(3), N1-C7 1.468(3), C1-C2 1.457(3), C1-N3 1.331(3), N3-O1 2.567(3), C2-N4 1.351(3); C1-N1-C5 123.3(2), C1-N1-C7 125.0(2), C5-N1-C7 111.5(2), N1-C1-N3 119.2(2), N3-C1-C2 122.7(2), N1-C1-C2 118.2(2).



An ORTEP drawing of **13** with 50% probability thermal ellipsoids.