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SYNTHESIS OF *cis*-1,5-DIMETHYL-2,4-DINITRO-2,4-DIAZABICYCLO[3.1.0]HEXAN-3-ONE AND *cis*-1,5-DIMETHYL-2,4-DINITRO-2,4-DIAZABICYCLO[3.2.0]HEPTAN-3-ONE

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Abstract: *cis*-1,5-Dimethyl-2,4-dinitro-2,4-diazabicyclo[3.2.0]heptan-3-one and *cis*-1,5-dimethyl-2,4-dinitro-2,4-diazabicyclo[3.1.0]hexan-3-one were both synthesized in three steps each from a common precursor, 1,3-diacetyl-4,5-dimethyl-4-imidazolin-2-one.

Polynitropolycyclic cage compounds and *N*-nitro compounds such as nitramines, nitramides and nitrimines are recognized as classes of compounds that possess the chemical and thermal stability sought in energetic materials.[1] As part of our studies on the synthesis of polynitrated strained materials we recently reported the X-ray crystal structures of two bicyclic *N,N'*-dinitroureas: *cis*-1,5-dimethyl-2,4-dinitro-2,4-diazabicyclo[3.1.0]hexan-3-one (1a) and *cis*-1,5-dimethyl-2,4-dinitro-2,4-diazabicyclo[3.2.0]heptan-3-one (3a).[2] We now wish to report the synthesis of **1a** and **3a** from a common precursor; 1,3-diacetyl-4,5-dimethyl-4-imidazolin-2-one (2a). Imidazolinone **2a** is easily prepared in two steps by refluxing commercially available 3-hydroxy-2-butanone (acetoin), urea, and trifluoroacetic acid[3] and

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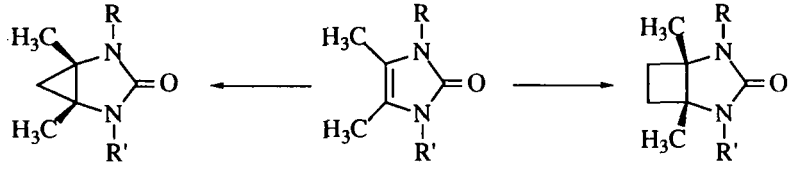


1a R=R'=NO_2
1b R=R'=Ac
1c R=R'=H
1d R=H; R'=NO_2

2a R=R'=Ac
2b R=R'=H
2c R=H; R'=Ac

3a R=R'=NO_2
3b R=R'=Ac
3c R=R'=H
3d R=H; R'=NO_2

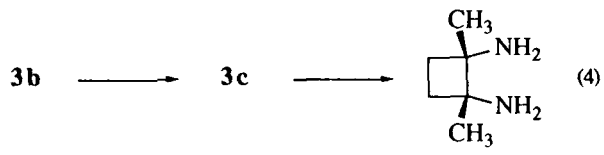
Scheme 1.

subsequently acetylating[4] the reaction product, 4,5-dimethyl-4-imidazolin-2-one (2b).

Simmons-Smith cyclopropanation[5] of **2a** using diiodmethane was employed to prepare 2,4-diacetyl-*cis*-1,5-dimethyl-2,4-diazabicyclo[3.1.0]hexan-3-one (1b). The reaction was carried out in anhydrous ethyl acetate because **2a** was not sufficiently soluble in the more traditional solvents used in cyclopropanations. Acetyl chloride was used to help promote reaction by consuming traces of water or other hydrolytic impurities.[6] Small quantities of hydrogen chloride produced with the addition of acetyl chloride serve to enhance the reaction rate as well by removing oxide from the metal surface.[6] The use of acetyl chloride resulted in only a minimal increase in the overall yield of **1b** as compared to the non-catalyzed reaction. The isolation and purification of the reaction product however was significantly easier for the catalyzed reaction sequence. Although the yield of **1b** is only 21%, a mixture of unreacted **2a** and monoacetylated imidazolinone **2c** was recovered upon chromatography of the reaction mixture. The mixture of **2a** and **2c** was resubjected to the acetylation conditions to provide pure **2a** which was recycled for further reaction.

2,4-Diacetyl-*cis*-1,5-dimethyl-2,4-diazabicyclo[3.2.0]heptan-2-one (3b) was prepared by the [2 + 2] photochemical cycloaddition of **2a** and ethylene.[7]

Deacetylation of **1b** and **3b** was accomplished using a solution of 1N sodium



Scheme 2.

hydroxide in methanol yielding *cis*-1,5-dimethyl-2,4-diazabicyclo[3.1.0]hexan-3-one (1c) and *cis*-1,5-dimethyl-2,4-diazabicyclo[3.2.0]heptan-3-one (3c) in 81% and 87% yields respectively.

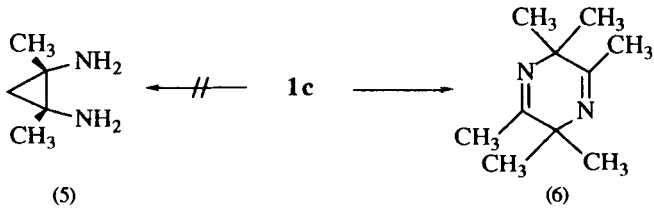
The bicyclo-*N,N'*-dinitroureas **1a** (33%) and **3a** (26%) were prepared from **1c** and **3c** using the method of Suri and Chapman.[8] This method employs ammonium nitrate/trifluoroacetic anhydride nitration conditions with nitromethane as the solvent. Because of solubility problems **3a** was prepared in dichloromethane[9] while **1a** was prepared in ethyl acetate. Extended reaction times of 35-40 hours were required to obtain *N,N'*-dinitroureas **1a** and **3a**. Shorter reaction times resulted in isolation of mononitrated materials **1d** and **3d** which could be resubjected to the nitration conditions to give the dinitroureas **1a** and **3a** respectively.

During the course of this study we found that *cis*-1,2-diamino-1,2-dimethylcyclobutane[7] (4) could be prepared in 88% yield by the barium hydroxide[10] hydrolysis of bicyclic urea **3c**. This reaction coupled with the sodium hydroxide hydrolysis of **3b** described earlier represents a more convenient and improved synthesis of **4** than previously reported.[7]

When the barium hydroxide hydrolysis of urea **1c** was attempted for the preparation of *cis*-1,2-diamino-1,2-dimethylcyclopropane (5) we found that the dilute sulfuric acid work-up of the reaction mixture led instead to a 42% yield of 2,5-dihydro-2,2,3,5,5,6-hexamethylpyrazine (6)[11].

Experimental:

Melting points were obtained on either a Haake-Büchler or Thomas-Hoover melting point apparatus and are uncorrected. Infra-red spectra were recorded on an



(5) (6)

Scheme 3.

Analect FX-6160 spectrometer. ^1H and ^{13}C NMR spectra were acquired at 200.05 MHz and 53.31 MHz respectively. ^1H NMR spectra were obtained in $CDCl_3$ (unless otherwise indicted) using TMS as an internal standard. The center frequency (76.91 ppm) of the $CDCl_3$ triplet was utilized as the internal reference for ^{13}C NMR spectra (unless otherwise noted). Galbraith Laboratories, Inc. of Knoxville, TN or Robertson Microlit Laboratories, Inc. of Madison, NJ were the suppliers of the elemental analyses.

4,5-Dimethyl-4-imidazolin-2-one (2b) was prepared by the method of Butler and Hussian.[3] ^1H NMR (TFA): δ 10.17 (br s, 4H, NH_2^+), 6.3 (s, 6H, CH_3). ^{13}C NMR (TFA): δ 148.6 (C_2), 117.8 (C_4), 6.5 (CH_3).

1,3-Diacetyl-4,5-dimethyl-4-imidazolin-2-one (2a) was prepared by the method of Blitz.[4] ^1H NMR: δ 2.63 (s, 6H, $COCH_3$), 2.23 (C_4CH_3). ^{13}C NMR: δ 170.0 (C_2), 151.6 ($COCH_3$), 117.5 (C_4), 26.4 ($COCH_3$), 11.0 (C_4CH_3).

2,4-Diacetyl-*cis*-1,5-dimethyl-2,4-diazabicyclo[3.1.0]hexan-3-one (1b). Diiodomethane (several drops out of a total of 8.04 g, 30.02 mmol) was added to a mechanically stirred solution of zinc dust (2.94 g, 45 mmol) and cuprous chloride (443.9 mg, 4.48 mmol) in anhydrous EtOAc (25 mL) causing the reaction to reflux. *(Caution: the addition of CH_2I_2 initiates an immediate exothermic reaction!)* This was followed by the dropwise addition of acetyl chloride (70.70 mg, 0.90 mmol) over several minutes. *(The addition of acetyl chloride may also result in a highly exothermic reaction!)* The solution was brought to a gentle reflux and **2a** (2.94 g, 15 mmol) in anhydrous EtOAc (50 mL) was added dropwise over

30 min. The remaining CH_2I_2 in anhydrous EtOAc (25 mL) was added dropwise and the reaction mixture was subsequently refluxed for a total of 15 h while monitoring the ethylene evolution. The reaction mixture was cooled in an ice bath and diluted with saturated NH_4Cl (80 mL; may foam). The resulting solution was carefully filtered through Celite®. *(Caution: pulling air past the activated metal may cause solvent to ignite!)* The reaction flask and solid residue were rinsed with EtOAc (3 x 25 mL) and combined with the filtrate. The filtrate was partitioned and the aqueous layer was washed with EtOAc (2 x 50 mL). The combined organic extracts were washed with 10% NaOH (2 x 50 mL) followed by saturated NaCl (100 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to give a yellow solid (1.97 g). The crude product was purified by flash column chromatography (SiO_2, gradient elution, 10%, 20%, 50% and 100% (v/v) EtOAc/pet ether) monitored by TLC (SiO_2, 20% (v/v) EtOAc/pet ether). Bicyclohexanone **1b** obtained as a white crystalline solid (670 mg, 21%, R_f=0.67). A mixture (716.1 mg) consisting of unreacted starting material **2a** (R_f=0.91) and monoacetylated starting material **2c** (R_f=0.60) was also obtained from the crude product upon chromatography. This mixture of imidazolinones **2a** and **2c** results from the decomposition of the starting material upon chromatography. 2,4-Diacetyl-*cis*-1,5-dimethyl-2,4-diazabicyclo[3.1.0]hexan-3-one (1b). mp 102-103°C. IR (cm^{-1}, KBr): ν 1751 (C=O), 1703 (C=O). ^1H NMR: δ 2.50 (s, 6H, $COCH_3$), 1.58 (s, 6H, C_1CH_3), 0.91 (ABq, 2H, $H_{6,6'}$, $^2J_{6,6'}$=1.23Hz). ^{13}C NMR: δ 171.1 (C_3), 153.0 ($COCH_3$), 38.4 (C_1), 25.0 ($COCH_3$), 24.1 (C_6), 14.4 (C_1CH_3). Anal. Calcd. for $C_{10}H_{14}N_2O_3$: C, 57.16; H, 6.66; N, 13.33. Found: C, 57.12; H, 6.84; N, 13.08. 1-Acetyl-4,5-dimethyl-4-imidazolin-2-one (2c). mp 184-186°C. IR (cm^{-1}, KBr): ν 3047 (N-H), 1710 (C=O). ^1H NMR: δ 8.60-8.20 (br s, 1H, NH), 2.63 (s, 3H, $COCH_3$), 2.22 (q, 3H, C_1CH_3), $^5J_{C1CH3,C5CH3}$=1.11Hz), 1.98 (q, 3H, C_5CH_3, $^5J_{C5CH3,C1CH3}$=1.11Hz). ^{13}C NMR: δ 170.7 (C_2), 153.6 ($COCH_3$), 115.8, 114.7 (C_4 and C_5), 26.0 ($COCH_3$), 11.6 (C_4CH_3), 8.8 (C_5CH_3). Anal. Calcd. for $C_7H_{12}N_2O_2$: C, 54.53; H, 6.55; N, 18.16. Found: C, 54.64; H, 6.66; N, 18.05.

2,4-Diacetyl-*cis*-1,5-dimethyl-2,4-diazabicyclo[3.2.0]heptan-3-one (3b) was prepared by the method of Schultz *et al.*.[7] ^{13}C NMR: δ 171.1 (C_3), 153.8 ($COCH_3$), 61.9 (C_1), 29.9 (C_6), 25.7 ($COCH_3$), 18.1 (C_1CH_3).

***cis*-1,5-Dimethyl-2,4-diazabicyclo[3.1.0]hexan-3-one (1c).** A solution of **1b** (1.23 g, 5.86 mmol) in 1N NaOH (15 mL)/MeOH (20 mL) was stirred at rt for 20 h. The solvent was concentrated *in vacuo* and the aqueous residue was extracted with EtOAc (3 x 75 mL). The combined organic extracts were dried ($MgSO_4$) and the solvent was removed *in vacuo* to give a white solid (601.8 mg, 81%). The crude product was recrystalized (EtOH/ether) to give **1c** (0.50 g, 67%) as a white crystalline solid. mp 240-241°C. IR (cm^{-1}, thin film): ν 3220 (N-H), 1700 (C=O). ^1H NMR: δ 5.1-3.6 (br s, 2H, NH), 1.38 (s, 6H, CH_3), 0.52 (ABq, 2H, $^2J_{6,6'}$=6.25Hz). ^{13}C NMR: δ 181.0 (C_3), 38.8 (C_1), 20.7 (C_6), 15.8 (CH_3). Anal. Calcd. for $C_6H_{10}N_2O$: C, 57.12; H, 8.00; N, 22.19. Found; C, 56.70; H, 8.11; N, 22.08.

***cis*-1,5-Dimethyl-2,4-diazabicyclo[3.2.0]heptan-3-one (3c)** was prepared by the method of Schultz *et al.*.[7] ^{13}C NMR: δ 161.8 (C_3), 61.5 (C_1), 33.1 (C_6), 20.3 (CH_3).

***cis*-1,5-Dimethyl-2,4-dinitro-2,4-diazabicyclo[3.1.0]hexan-3-one (1a).** Preground oven dried NH_4NO_3 (448.0 mg, 6.10 mmol) and **1c** (153.8 mg, 1.22 mmol) were stirred vigorously in TFAA (25 mL) at 0°C for 15 min. Ethyl acetate (10 mL) was added and the reaction mixture was stirred at rt for 45 h. The solvent was removed *in vacuo* and the residue was resuspended in ice/H_2O (25 mL)/EtOAc (3 x 75 mL) and partitioned. The combined organic extracts were washed with saturated $NaHCO_3$ (50 mL, pH=8) and dried ($MgSO_4$). The EtOAc was removed *in vacuo* to give a yellow oil (536.2 mg) which crystallized on standing. ^1H NMR indicated that the crude product consisted mainly of the mono-nitrated material. The crude product was therefore resubmitted to the reaction conditions for an additional 72 h. The resulting material was recrystallized (EtOAc) to give **3a** (69.0 mg, 26%) as a white crystalline solid. *cis*-1,5-dimethyl-2-nitro-2,4-diazabicyclo[3.1.0]hexan-3-one (1d). IR (cm^{-1}, thin film): ν 1764 (C=O), 1558 (NO_2), 1255 (NO_2). ^1H NMR: δ 6.44-6.43 (br s, 1H, NH), 1.61 (s, 3H, C_1CH_3), 1.48 (s, 3H, C_5CH_3), 0.97 (ABq, 2H, $^2J_{6,6'}$=7.28Hz). ^{13}C NMR: δ 150.4 (C_3), 40.6 (C_1), 36.5 (C_5), 24.0 (C_6), 15.3 (C_1CH_3), 14.4 (C_5CH_3). *cis*-1,5-dimethyl-2,4-dinitro-2,4-diazabicyclo[3.1.0]hexan-3-one (1a). mp 240°C (decomp). IR (cm^{-1}, thin film): ν 1795 (C=O), 1593 (NO_2), 1319 (NO_2). ^1H NMR: δ 1.71 (s, 6H, CH_3), 1.36 (ABq, 2H, $H_{6,6'}$, $^2J_{6,6'}$=8.39Hz). ^{13}C NMR

(acetone-d_6): δ 143.3 (C_3), 41.9 (C_1), 23.4 (C_6), 14.1 (CH_3). Anal. Calcd. for $C_6H_8N_4O_5$: C, 33.32; H, 3.74; N, 25.92. Found: C, 33.41; H, 3.62; N, 25.78.

***cis*-1,5-Dimethyl-2,4-dinitro-2,4-diazabicyclo[3.2.0]heptan-3-one (3a).** A solution of **3c** (100.0 mg, 0.71 mmol) in CH_2Cl_2 (10 mL) was added dropwise to an ice cold mixture of preground oven dried NH_4NO_3 (284.7 mg, 3.56 mmol) and TFAA (600 μL, 895 mg, 4.26 mmol) in CH_2Cl_2 (10 mL) and the resulting solution was subsequently stirred at rt for 36-37 h. The solvent was removed *in vacuo* to give a white solid. The solid residue was redissolved in EtOAc (30 mL)/H_2O (25 mL) and partitioned. The organic extract was washed with 10% $NaHCO_3$ (20 mL), H_2O (20 mL) and saturated NaCl (20 mL) and dried ($MgSO_4$). The solvent was removed *in vacuo* to give **3a** as a white crystalline solid (54.8 mg, 33%). mp 200-202°C. IR (cm^{-1}, thin film): ν 1799 (C=O), 1579 (NO_2). ^1H NMR: δ 2.68-2.28 (m, 4H, $H_{6,6'}$), 1.67 (s, 6H, CH_3). ^{13}C NMR: δ 142.6 (C_3), 64.6 (C_1), 29.1 (C_6), 17.5 (CH_3). Anal. Calcd. for $C_7H_{10}N_4O_5$: C, 36.52; H, 4.39; N 24.33. Found: C, 36.57; H, 4.42; N, 23.97.

***cis*-1,2-Diamino-1,2-dimethylcyclobutane (4).** Bicycloheptanone **3c** (401.3 mg, 1.79 mmol), $Ba(OH)_2 \cdot 8H_2O$ (10.02 g, 31.76 mmol) and H_2O (6 mL) were sealed in a polymerization tube and heated at 135-140°C for 4 h. The reaction mixture was cooled to rt and transferred to an Erlenmeyer flask with water (50 mL). A stream of CO_2 was bubbled through the solution until a pH of 7-8 was obtained. The insoluble salts were removed by filtration through Celite®. The filtrate was subsequently acidified using 1% H_2SO_4 (v/v, pH=1). The insoluble barium salts were again removed by filtration through Celite®. The filtrate was concentrated *in vacuo* to give an oily solid. The residue was resuspended in a minimal amount of warm water and triturated with methanol to give the disulfate salt of **4** as a white amorphous powder (590.3 mg, 88%). *cis*-1,2-diamino-1,2-dimethylcyclobutane (4) dihydrosulfate[7] mp >280°C. IR (cm^{-1}, thin film): ν 3009-2824 (NH_3^+), 2758 (C-H), 2104 (NH_3^+). ^1H NMR (D_2O): δ 2.35-2.03 (m, 4H, $H_{3,3'}$), 1.43 (s, 6H, CH_3). ^{13}C NMR (D_2O): δ 58.6 (C_1), 26.5 (C_3), 19.1 (CH_3). *cis*-1,2-diamino-1,2-dimethylcyclobutane (4). Sample was prepared for NMR by $CDCl_3$ extraction of a solution of the diamine salt in 1N NaOH or 5% $NaHCO_3$. ^1H NMR: δ 1.72 (ABq, 4H, $H_{3,3'}$, $^2J_{2,2'}$=5.70Hz), 1.49 (br s, 4H, NH_2), 1.14 (s, 6H, CH_3). ^{13}C NMR: δ 57.0 (C_1), 31.9 (C_3), 24.4 (CH_3).

Barium hydroxide hydrolysis of *cis*-1,5-dimethyl-2,4-diaza bicyclo[3.1.0]hexan-3-one (1c). Bicyclicurea **1c**, $Ba(OH)_2.8H_2O$ and water (5 mL) were sealed in a polymerization tube and heated at 135-140°C for 60 h. The reaction mixture was transferred to a 250-mL Erylnmeyer flask with water (50 mL). A stream of CO_2 was bubbled through the solution until a pH of 7-8 was obtained. The crude reaction mixture was filtered through Celite® to remove the insoluble barium salts. The aqueous solution was acidified with 1% H_2SO_4 (v/v, pH=1) and subsequently refiltered through Celite®. Removal of the water *in vacuo* gave a yellow oil (384.2 mg). This oil was triturated with ether/MeOH to provide 2,5-dihydro-2,2,3,5,5,6-hexamethylpyrazine (6)[11] as a white powder (78.9 mg, 42%). ^1H NMR (D_2O): δ 2.36 (s, 6H), 1.60 (12H). ^{13}C NMR (D_2O): δ 180.3 (C_3), 58.4 (C_2), 30.4 (CH_3), 25.9 (CH_3).

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