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IMPROVED SYNTHESIS OF AN ENERGETIC MATERIAL, 1,3,3-TRINITROAZETIDINE EXPLOITING 1-AZABICYCLO[1.1.0]BUTANE

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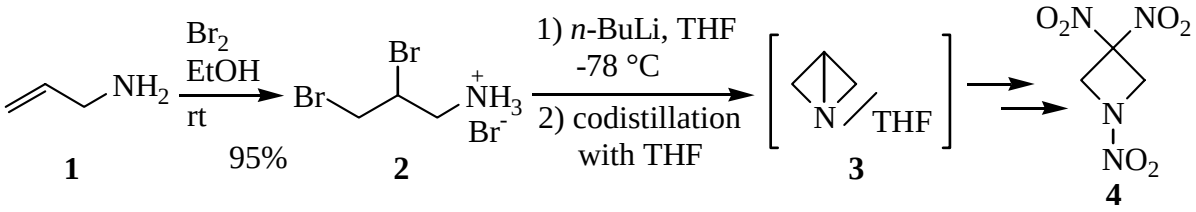
Abstract- Expeditious synthesis of 1-nitroso-3-nitroazetidine (**6**), a useful key intermediate for the synthesis of 1,3,3-trinitroazetidine (**4**), was investigated by using 1-azabicyclo[1.1.0]butane (**3**) and $NaNO_2$ in the presence of some acids. The most efficient method was achieved in 26% yield by treatment of **3** with $NaNO_2$ in the presence of H_2SO_4. Conversion of **6** into **4** was also carried out.

1-Azabicyclo[1.1.0]butanes have been characterized to be highly strained bicyclic structures.[1] Since the first report of the synthesis and reactivity of these compounds, little attention has been paid to the unusual ring system.[2] Specifically, the synthetic utility of 1-azabicyclo[1.1.0]butane (**3**), which must be expected to be useful for the preparation of various 1,3-disubstituted and 3-monosubstituted azetidines, has scarcely reported because of its synthetic difficulty due to the remarkably strained structure.[1-3] In the meantime, the usefulness of the compound (**3**) and its related compound as a key intermediate in the synthesis of a particular compound, 1,3,3-trinitroazetidine (TNAZ, **4**) was reported.[4] TNAZ (**4**) has been noteworthy from the viewpoint of a new important energetic material involving numerous applications to the explosive and propellant technology.[5] Hence, efficient and environmentally benign methods for the large-scale synthesis of TNAZ (**4**) have been required.[6] Although there have been several reports for the synthesis of TNAZ (**4**), its preparation exploiting a highly strained molecule (**3**) seems to be a quite elegant method.[4,7] However, the earlier methods using **3** resulted in the very poor yields of TNAZ (**4**) or of its synthetic intermediate.[4] Recently, we have developed a new efficient procedure for the synthesis of

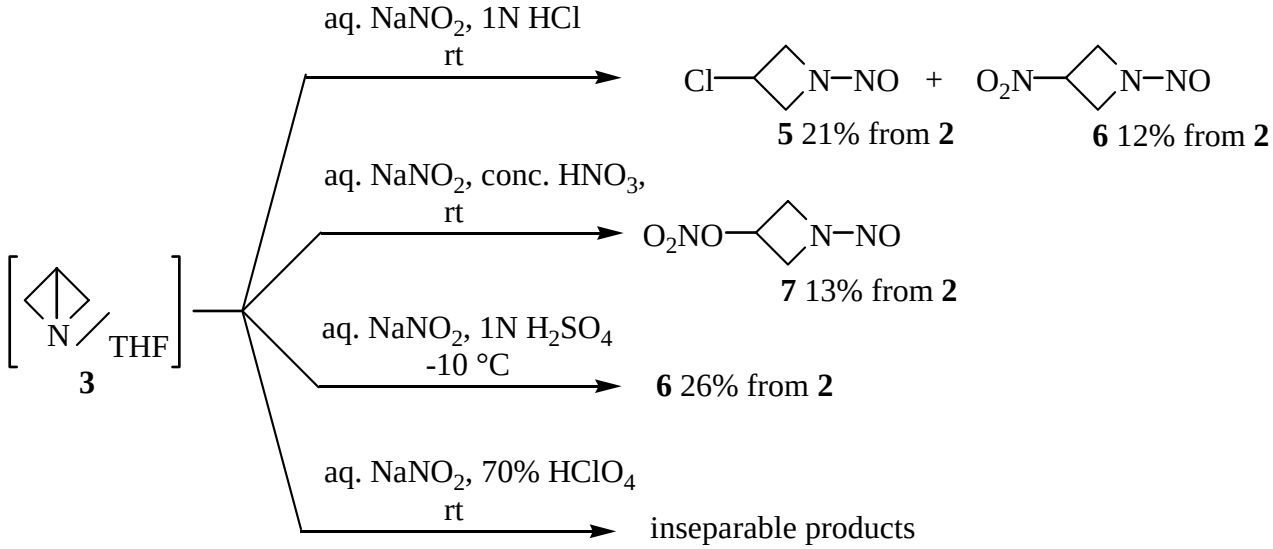
3 starting from an inexpensive compound, allylamine (**1**) *via* its bromination followed by treatment of the resultant dibromide **2** with *n*-BuLi, as shown in Scheme 1.[8] We describe here an expeditious synthesis of TNAZ (**4**) by exploiting 1-azabicyclo[1.1.0]butane (**3**).

Scheme 1



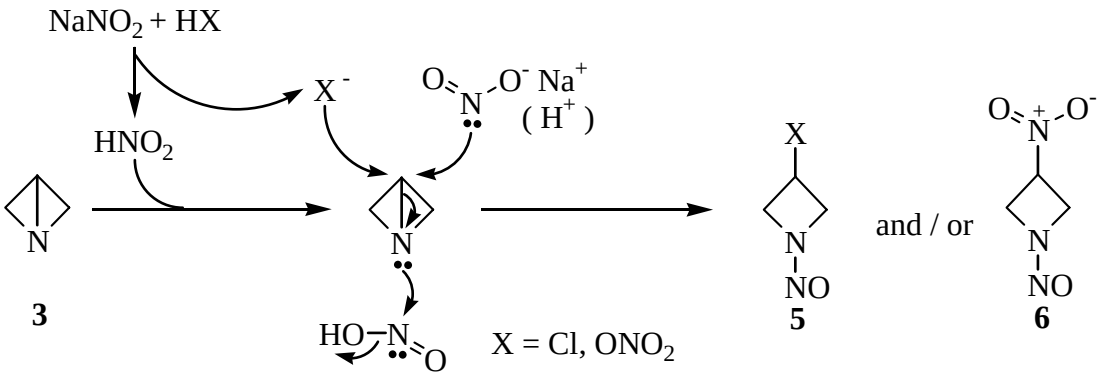
First of all, preparation of a key intermediate (**6**) was investigated by treatment of **3** with $NaNO_2$ in the presence of some mineral acids. All experimental results are summarized in Scheme 2. A THF solution

Scheme 2



of **3**, obtained from the reaction of **2** with *n*-BuLi in THF at -78°C for 1 h followed by codistillation along with THF, was treated with an aqueous solution of $NaNO_2$ in the presence of 1N HCl at room temperature for 3 h to give 3-chloro-1-nitrosoazetidine (**5**) and 3-nitro-1-nitrosoazetidine (**6**) in 21% and 12% yields from **2**, respectively.[9] Similar treatment of the THF solution of **3** with aqueous $NaNO_2$ - conc. HNO_3 afforded only 3-nitrooxy-1-nitrosoazetidine (**7**) in 13% yield from **2**. It was presumed that the reactions described above might be promoted by concomitant N1-nitrosation with nucleophilic addition of X^-(X = Cl, ONO_2) or nitrite anion (NO_2^-) involving cleavage of the strained C3-N bond in the molecule (**3**), as shown in Scheme 3.

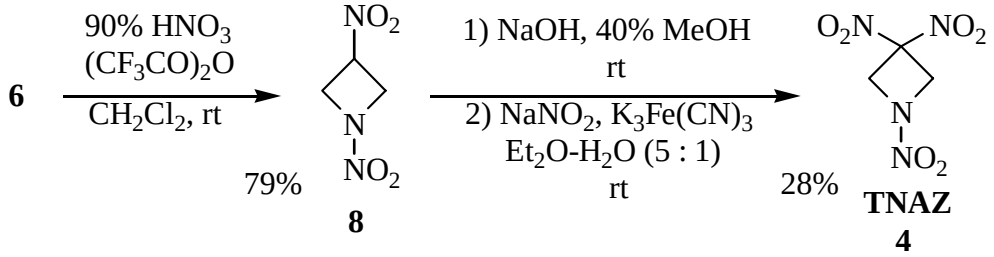
Scheme 3



Based on this assumption, the use of the acid composed of a weak nucleophilic counter anion was predicted to afford the desired compound (**6**) selectively. Thus, **3** was treated with aqueous $NaNO_2$ - 1N H_2SO_4, and **6** was obtained in 26% yield from **2**.[9] However, the reaction of **3** with aqueous $NaNO_2$ - 70% $HClO_4$ gave inseparable many products.

Finally, conversion of **6** into TNAZ (**4**) was performed according to the known reaction route[4a] represented in Scheme 4. Oxidation of the NO group of **6** with 90% HNO_3 - $(CF_3CO)_2O$ gave 1,3-dinitroazetidine (**8**) (79% yield), whose sodium nitronate was subjected to the oxidative nitration with $NaNO_2$ - $K_3Fe(CN)_3$ to obtain TNAZ (**4**) in 28% yield. We have achieved an improved synthetic method for the TNAZ exploiting 1-azabicyclo[1.1.0]butane (**3**), which must be fairly better than the earlier procedure.

Scheme 4



EXPERIMENTAL

All melting points were measured using a Yanagimoto apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 1720 infrared Fourier transform spectrophotometer. ^1H NMR (200 MHz, 400 MHz) and ^{13}C NMR (100 MHz) spectra were taken on a JEOL JNM-FX 200 or JEOL JNM-GSX 400 spectrometer with tetramethylsilane as an internal standard, and chemical shifts are recorded in δ values. HR-MS (FAB and EI) was measured on a JEOL JMS SX-102A mass spectrometer using a direct inlet system. Combustion analyses were performed by a Yanagimoto CHN Corder.

1-Amino-2,3-dibromopropane hydrobromide (2)

To an EtOH (100 mL) solution of Br_2 (40 mL, 785 mmol) was added dropwise allylamine (**1)** (28 mL, 374 mmol) at 0 °C, and the mixture was stirred at rt for 18 h. The resulting precipitate was filtered off, washed with ether, and recrystallized from MeOH. Compound (**2)** (106 g, 95%) was obtained as colorless prisms. mp 176-180 °C. ^{1}H NMR (200 MHz, CD_3OD) δ 3.38 (1H, dd, *J* = 9.5 and 13.9 Hz), 3.70 (1H, dd, *J* = 3.2 and 13.9 Hz), 3.94 (1H, dd, *J* = 8.3 and 11.0 Hz), 4.01 (1H, dd, *J* = 4.6 and 11.0 Hz), 4.5-4.7 (1H, m); IR (KBr) 1978, 1591, 1430, 1393, 1225, 1170, 1094, 1054 cm^{-1}; HRMS (FAB): Calcd for $C_3H_7NBr_2$: 215.9023, Found *m*/*z*: 215.9041 ($(M+1)^+$); Anal. Calcd for $C_3H_8NBr_3$: C, 12.10; H, 2.71; N, 4.70. Found: C, 12.20; H, 2.67; N, 4.57.

THF solution of 1-azabicyclo[1.1.0]butane (3)[8]

A hexane solution of *n*-BuLi (50.4 mmol) was added dropwise to a suspension of **2** (5.00 g, 16.8 mmol) in anhydrous THF (50 mL) at -78 °C under argon, and the mixture was stirred at -78 °C for 1 h. Then the reaction was quenched with 50% KOH and distilled at 80 °C. The resulting THF solution was dried over K_2CO_3 and filtered. The filtrate was adjusted to the 100 mL volume with THF. This THF solution was used in next reaction. ^{1}H NMR (400 MHz, THF-d_8) δ 0.85 (2H, m), 2.07 (2H, m), 2.29 (1H, m); ^{13}C NMR (100 MHz, THF-d_8) δ 17.2, 51.1.

3-Chloro-1-nitrosoazetidine (5) and 3-nitro-1-nitrosoazetidine (6)

To a water (3 mL) solution of $NaNO_2$ (2.0 g, 29.0 mmol) was added a THF solution of **3** (20 mL), and the mixture was stirred at rt for 20 min. Then, 1N HCl (77 mL, 77 mmol) was added dropwise, and the mixture was stirred at rt for 3 h. The reaction mixture was extracted with AcOEt, and the extract was washed with saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel by elution with $CHCl_3$ - acetone (95 : 5). The first chromatography fraction afforded **5** (93 mg, 21% yield based on **2**) as a yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.1-4.3 (1H, m), 4.6-4.8 (1H, m), 4.8-5.0 (2H, m), 5.3-5.5 (1H, m) [lit.,[3b] ^{1}H NMR ($CDCl_3$) δ 4.07-4.20 (1H, m), 4.50-4.73 (1H, m), 4.78-4.88 (2H, m), 5.23-5.34 (1H, m)].

Further elution of the column with $CHCl_3$ - acetone (95 : 5) afforded **6** (54 mg, 12% yield based on **2**) as a pale yellow crystalline solid. mp 77-79 °C (lit.,[3a] mp 77-78 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.59 (2H, d, *J* = 3.9 Hz), 5.3-5.5 (3H, m).

3-Nitrooxy-1-nitrosoazetidine (7)

To a water (3 mL) solution of $NaNO_2$ (2.0 g, 29.0 mmol) was added a THF solution of **3** (20 mL), and the resulting mixture was stirred at rt for 20 min. Then, concentrated aqueous HNO_3 (2.65 mL, 29 mmol) was added dropwise, and the mixture was stirred at rt for 3.5 h. The reaction mixture was extracted with

AcOEt, and the extract was washed with saturated aqueous $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by column chromatography on silica gel with $CHCl_3$ - acetone (95 : 5). Compound (**7**) (148 mg, 13% yield based on **2**) was obtained as a pale yellow oil. ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.18 (1H, ddd, *J* = 2.2, 3.7 and 13.9 Hz), 4.56 (1H, ddd, *J* = 2.2, 6.6 and 13.9 Hz), 4.92 (1H, ddd, *J* = 2.2, 3.7 and 12.2 Hz), 5.30 (1H, ddd, *J* = 2.2, 6.6 and 12.2 Hz), 5.5-5.7 (1H, m); IR (neat) 1402, 1376, 1354, 1309, 1121, 1069 cm^{-1}; HRMS (EI): Calcd for $C_3H_5N_3O_4$: 147.0280, Found *m/e*: 147.0285 (M^+).

3-Nitro-1-nitrosoazetidine (6)

To a water (3 mL) solution of $NaNO_2$ (2.0 g, 29.0 mmol) was added a THF solution of **3** (20 mL), and the resulting mixture was stirred at rt for 20 min. Then, 1N H_2SO_4 (18.4 mL, 9.2 mmol) was added dropwise at –10 °C, and the mixture was stirred for 30 min. The reaction mixture was extracted with AcOEt, and the extract was washed with saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and filtered, and the filtrate was concentrated *in vacuo*. The residue was chromatographed on a silica gel column with $CHCl_3$ - acetone (95 : 5). Compound (**6**) (113 mg, 26% yield based on **2**) was obtained as a pale yellow crystalline solid.

1,3-Dinitroazetidine (8)

To a mixture of trifluoroacetic anhydride (9.3 mL, 66 mmol) and 90% HNO_3 (9.1 mL, 227 mmol) was added **6** (448 mg, 3.32 mmol) in one portion with stirring at 0 °C. The mixture was stirred at rt for 22 h. The reaction mixture then was poured over crushed ice, and the resulting aqueous suspension was extracted with CH_2Cl_2. The extract was washed with saturated $NaHCO_3$ and brine. The organic layer was dried over $MgSO_4$ and filtered, and the filtrate was concentrated *in vacuo*. The residue was purified by silica gel column chromatography with hexane - AcOEt (75 : 25). Compound (**8)** (429 mg, 79%) was obtained as a white crystalline solid. mp 60-62 °C (lit.,[3a] mp 62-63 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 4.7-5.0 (4H, m), 5.1-5.3 (1H, m).

1,3,3-Trinitroazetidine (4)

To a solution of NaOH (32 mg, 0.80 mmol) in 40% aqueous MeOH (9.0 mL) was added **8** (100 mg, 0.613 mmol) with stirring, and the solution was stirred at rt for 30 min. This solution was added rapidly with stirring to a mixture of $K_3Fe(CN)_6$ (1.04 g, 3.16 mmol), $NaNO_2$ (440 mg, 6.48 mmol), water (10 mL), and Et_2O (50 mL). After stirring at rt for 30 min, the organic layer was separated, and the aqueous layer was extracted with CH_2Cl_2. The combined organic extract was washed with water and brine, and dried over $MgSO_4$. After filtration, the filtrate was concentrated *in vacuo* to give an oily residue, which was purified by preparative TLC with CH_2Cl_2. Pure compound (**4**) (35 mg, 28%) was obtained as colorless needles. mp 95-97 °C (lit.,[3a] mp 98-99 °C). ^{1}H NMR (200 MHz, $CDCl_3$) δ 5.21 (4H, s) [lit.,[3a]

^{1}H NMR ($CDCl_3$) δ 5.20 (4H, s)].

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9. Earlier similar method for the preparation of **6** using **3** resulted in the 1% and 5.5% yield. [4a,b]