Facile Preparation of 7,11-Di(4-nitrobenzenesulfonyl)-diaza-1,4-dioxa-7,11-spiro[4,7]dodecan-9-one

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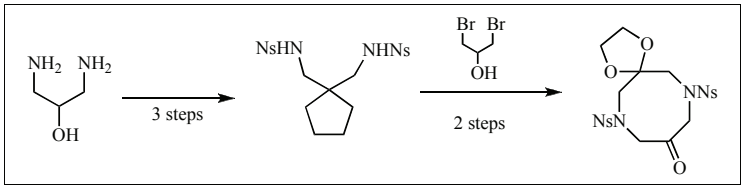

Compound **1** as a key intermediate for the synthesis of 3,3,7,7-tetrakis-(difluoroamino)octahydro-1,5-dinitro-1,5-diazocine (HNFX) and 3,3-bis(difluoroamino)octahydro-1,5,7,7-tetranitro-1,5-diazocine (TNFX) is described. Cycloalkylation of **3** with 1,3-dibromopropan-2-ol (**4**) afforded 1,5-protected-1,5-diazocine **2**, followed by chromic acid oxidation to ketone **1** in good yield.

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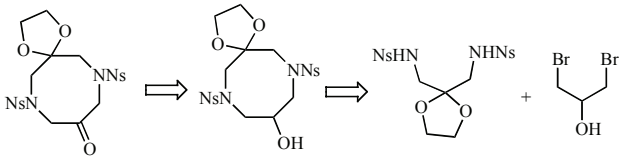
Gem-Bis(difluoroamino)-substituted heterocyclic nitramines have independently been proposed by Zheng *et al.* [1] and Chapman, *et al.* [2] as potentially superior explosives or solid propellant oxidizers. For instance, 3,3,7,7-tetrakis-(difluoroamino)octahydro-1,5-dinitro-1,5-diazocine (HNFX) [3] and 3,3-bis(difluoroamino)octahydro-1,5,7,7-tetranitro-1,5-diazocine (TNFX) [4] have received much attention. Recently, some new synthetic methods have been reported for this intermediate [4-6]. The key intermediates for the synthesis of HNFX and TNFX are 1,5-bis(4-nitrobenzenesulfonyl or acyl)-1,5-diazocin-3,7(2*H*,6*H*)-dione [5,6] and 1,5-bis(4-nitrobenzenesulfonyl)-[1,3]dioxolan-2-yl-1,5-diazacin-3(2*H*)-one [4]. Despite the importance of 3-halo-2-(halomethyl)-1-propenes as a key material for the construction of 1,5-diazacycloocatan-3,7(2*H*,6*H*)-one ring, their use is impeded by high cost and, relatively inefficient preparative procedures [7-9]. The method for the construction of 1,5-diazocine also suffers from one or more limitations including the multistage process, the use of ozone, and the low yield.

This paper reports on a convenient synthesis of 7,11-di(4-nitrobenzenesulfonyl)-1,4-dioxa-7,11-diaza-spiro[4,7]dodecan-9-one (**1**) as a key intermediate for HNFX and TNFX.

The retrosynthesis of compound **1** is shown in Scheme 1, where 1,3-dibromopropan-2-ol (**4**) is a useful moiety for the construction of the 1,5-diazocine ring from compound **3**. Therefore, we selected commercially available compound **4** as a key source of a three carbon synthon.

In our strategy for the synthesis of compound **1** outlined in Scheme 2, the commercially available starting material,

Scheme 1



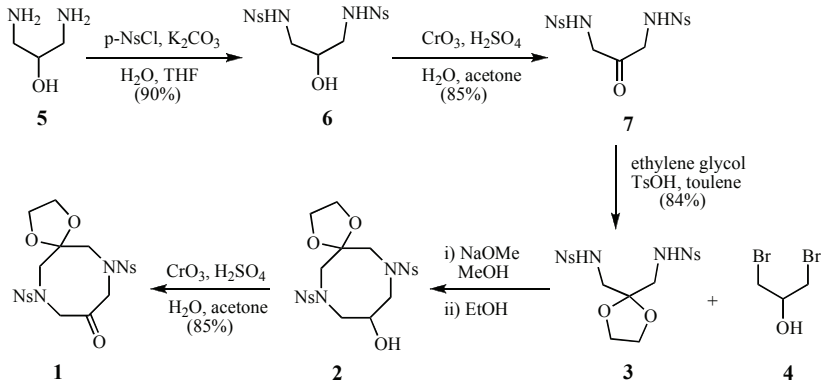
1 **2** **3** **4**

1,3-diaminopropan-2-ol (**5**) was *N*-protected by *p*-nitrobenzenesulfonyl groups, followed by chromic acid oxidation to ketone **7**, and the latter carbonyl function was protected through reaction with ethylene glycol to form its 1,3-dioxolane derivative **3** in 84% yield. Cycloalkylation of **3** with 1,3-dibromopropan-2-ol (**4**) instead of 3-halo-2-(halomethyl)-1-propene afforded 1,5-protected-1,5-diazocine **2** in 81% yield. Oxidation of **2** with chromic acid gave the corresponding ketone **1** in 85% yield.

The structures of synthetic compounds were established by the IR, NMR and elemental analyses. The proton magnetic resonance spectrum of **2** showed proton signals of six CH_2, one CH and one OH involving the proton signals of two phenyl rings. The infrared spectrum of **1** showed the absorption peak of carbonyl group at 1750 cm^{-1} instead of the absorption peak of hydroxyl group. The proton magnetic resonance spectrum of **1** also showed the proton signals of six CH_2 involving the proton signals of two phenyl rings.

In conclusion, our preparation procedures demonstrated that 7,11-di(4-nitrobenzenesulfonyl)-1,4-dioxa-7,11-diaza-spiro[4,7]dodecan-9-one (**1**) was successfully synthesized

Scheme 2



from compound **5** and 1,1-dibromopropen-2-ol (**4**) as a C3- synthon.

EXPEREMENRAL

Melting points were determined with a capillary apparatus and uncorrected. ^{1}H and ^{13}C NMR spectra were recorded on a Varian Inova 500 spectrometer with chemical shifts values reported in δ units (ppm) relative to an internal standard (TMS). IR spectra were obtained on a Hitachi 270-50 IR spectrophotometer. Elemental analyses were performed with a Perkin Elmer 240C. Open-bed chromatography was carried out on silica gel (70 ~ 230 mesh, Merck) using gravity flow. The column was packed as slurries with the elution solvent.

1,3-Di(4-nitrobenzenesulfonamido)propanol (**6**).

Compound **5** (1 g, 11.7 mmol) and potassium carbonate (4.3 g, 31 mmol) were dissolved in water (20 mL). The tetrahydrofuran solution of 4-nitrobenzenesulfonyl chloride (5.8 g, 26.4 mmol, of sulfonyl chloride dissolved in 15 mL of THF) was slowly added to this solution. The reaction mixture was stirred for 12 hours. After evaporating tetrahydrofuran under reduced pressure, the residue was filtered. This residue was washed with excess water, and then methylene chloride (100 mL). The resulting residue was applied to the top of an open-bed silica gel column (3 x 7 cm). The column was eluted with ethyl acetate/*n*-hexane (1:1, v/v). Fractions containing the product were combined, evaporated under reduced pressure and dried in air to give compound **6** in 90% yield as white crystals (ethyl acetate/*n*-hexane = 1:1, v/v), mp 205-207 °C; IR (KBr) 3550, 3300, 2900, 1620, 1530, 1350, 1160 cm^{-1}; ^{1}H NMR (acetone-d_6): δ 2.96 (m, 2H), 3.11 (m, 2H), 3.78 (m, 1H, D_2O exchangeable), 4.40 (d, 1H, *J* = 5.5 Hz, D_2O exchangeable), 6.89 (m, 2H), 8.11 (d, 4H, *J* = 9.15 Hz), 8.42 ppm (d, 4H, *J* = 9.15 Hz); ^{13}C NMR (acetone-d_6): δ 47.4, 69.8, 125.2, 129.2, 147.5, 151.0 ppm.

Anal. Calcd for $C_{15}H_{16}N_4O_9S_2$: C, 39.13; H, 3.50; N, 12.17; S, 13.93. Found: C, 39.21; H, 3.55; N, 12.22; S, 13.98

1,3-Di(4-nitrobenzenesulfonamido)propan-2-one (**7**).

To the solution of **6** (5 g, 11.17 mmol in acetone 150 mL), chromium (VI)oxide solution (2.9 g of CrO_3 and 3 mL of H_2SO_4 in 8 mL of water) was added slowly stirring at 20 °C. The mixture was stirred for 12 hours at room temperature. After pouring the mixture into ice water (200 mL) with stirring, the resulting residue was filtered and washed with excess water to give an 85% yield of **7** as white crystals (THF/*n*-hexane = 1:2, v/v), mp. 202-204 °C; IR (KBr) 3300, 2900, 1750, 1620, 1540, 1360, 1160 cm^{-1}; ^{1}H NMR (acetone-d_6): δ 4,13 (s, 4H), 7.12 (s, 2H), 8.11 (d, *J* = 8.7, 4H), 8.40 ppm (d, 4H, *J* = 8.7 Hz); ^{13}C NMR (acetone-d_6): δ 49.1, 124.3, 127.9, 146.1, 149.4, 199.9 ppm.

Anal. Calcd for $C_{15}H_{14}N_4O_9S_2$: C, 39.30; H, 3.08; N, 12.22; S, 13.99. Found: C, 39.38; H, 3.11; N, 12.31; S, 14.02.

2-Ethylenedioxy-1,3-di(4-nitrobenzenesulfonamido)propane (**3**).

A mixture of **7** (6 g, 26 mmol), ethylene glycol (3 g, 48 mmol), *p*-toluene sulfonic acid monohydrate (0.25 g) and toluene (100 mL) was refluxed for 3 days in a two necked flask equipped with a Dean-Stark tube. After cooling to room temperature, the mixture was filtered and washed with methylene chloride to give an 84% yield of **3**, White crystals (THF), mp 224-226 °C; IR (KBr) 3300, 3150, 2900, 1620, 1540, 1370, 1180, 1060 cm^{-1}; ^{1}H NMR (DMSO-d_6): δ 2.96 (d, 4H, *J* = 6.4 Hz), 3.59 (s, 4H), 7.99 (d, 4H, *J* = 9.1 Hz), 8.13 (s, 2H), 8.37 ppm (d, 4H, *J* = 8.84 Hz); ^{13}C NMR (DMSO-d_6): δ 45.9, 65.0, 106.7, 124.2, 127.8, 146.7, 149.3 ppm.

Anal. Calcd for $C_{17}H_{18}N_4O_{10}S_2$: C, 40.64; H, 3.61; N, 11.15; S, 12.76. Found: C, 40.71; H, 3.70; N, 11.21; S, 12.81.

7,11-Di(4-nitrobenzenesulfonyl)-1,4-dioxa-7,11-diaza-spiro[4,7]dodecan-9-ol (**2**).

To a methanolic solution of **3** (3 g, 7.2 mmol in 200 mL of dry methanol), methanolic sodium methoxide (NaOMe, 0.5 g, 21 mmol in 50 mL of dry methanol) was added slowly with stirring. The mixture was refluxed for 1 hour. After evaporating methanol under reduced pressure, the resulting residue was dissolved in ethanol (200 mL). A solution of **4** (2.3 g, 10.8 mmol in 50 mL of ethanol) was added slowly to the above ethanol solution with stirring. The reaction mixture was refluxed for 24 hours. After cooling to room temperature, the mixture was poured into ice water (300 mL). The solution was adjusted to pH 10 using *conc*-HCl. The resulting precipitate was filtered and washed with excess water. The residue was applied to the top of an open-bed silica gel column (3 x 7 cm). The column was eluted with ethyl acetate/methylene chloride (0.5:9.5, v/v). The

fraction containing the product were combined and evaporated under reduced pressure to give an 81% yield of **2**, Pale yellow crystals (THF/*n*-hexane = 1:2, v/v), mp. 249-251 °C; IR (KBr) 3500, 3110, 2900, 1620, 1530, 1360, 1100 cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.11 (m, 2H), 3.25 (d, 2H, *J* = 14.1 Hz), 3.43 (m, 2H), 3.63 (d, 2H, *J* = 14.1 Hz), 3.83 (m, 1H), 3.92 (s, 4H), 5.27 (bs, 1H, deuterium oxide-exchangeable), 8.12 (d, 4H, *J* = 8.4 Hz), 8.41 ppm (d, 4H, *J* = 8.4 Hz); ^{13}C NMR (DMSO-d_6): δ 53.87, 54.94, 64.61, 67.87, 105.65, 124.57, 128.82, 143.71, 149.83ppm.

Anal. Calcd for $C_{20}H_{22}N_4O_{11}S_2$: C, 43.01; H, 3.97; N, 10.03; S, 11.48. Found: C, 43.09; H, 4.04; N, 10.21; S, 11.53.

7,11-Di(4-nitrobenzenesulfonyl)-1,4-dioxa-7,11-diaza-spiro[4,7]-dodecan-9-one (**1**).

To a solution of **2** (1 g, 1.8 mmol in acetone 50 mL), chrominium (VI) oxide solution (0.54 g of CrO_3 and 1 mL of H_2SO_4 in 8 mL of water) was added slowly stirring at 20 °C. The mixture was stirred for 12 hours at room temperature. After pouring the mixture into ice water (100 mL) with stirring, the resulting residue was collected by filtration and washed with excess water to give an 82% yield of **1** as beige crystals (THF/*n*-hexane = 1:1, v/v), mp. 240-242 °C; IR (KBr) 3150, 1750, 1620, 1540, 1360, 1160, 1100, 1000, 860, 800 cm^{-1}; ^1H NMR (DMSO-d_6): δ 3.60 (s, 4H), 3.94 (s, 4H), 3.96 (s, 4H), 8.20 (d, 4H, *J* = 8.6 Hz), 8.41 ppm (d, 4H, *J* = 8.6 Hz); ^{13}C NMR (DMSO-d_6): δ 55.15, 64.85, 66.94, 106.54, 124.77, 128.77, 142.94, 150.10, 202.42 ppm.

Anal. Calcd. for $C_{20}H_{20}N_4O_{11}S_2$: C, 43.16; H, 3.62; N, 10.07; S, 11.52. Found: C, 43.22; H, 3.70; N, 10.13; S, 11.59.

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