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Preparation of benzoannulated seven- and eight-membered heterocycles from 2,4,6-trinitrobenzoyl chloride

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Dinitro-substituted 1,2,3-triazolo[1,5-*a*]dibenzo[*b*,*f*][1,4]diazepin-7-one and 10,11-dihydro-11-(4-chlorophenyl)dibenz[*b*,*g*]-[1,5]oxazocin-12-one were prepared in two steps from 2,4,6-trinitrobenzoyl chloride.

Intramolecular nucleophilic displacement of a nitro group in aromatic nitro compounds is a well-known method for preparation of five- and six-membered benzoannulated heterocycles.[1,2] However, this approach was rarely used for preparation of larger heterocycles (seven- and eight-membered),[1,3–5] whereas certain classes of benzoannulated seven-membered heterocycles (in particular, 1,4-benzodiazepines and dibenzo[*b*,*f*]azepines) are widely used in medicine as CNS-affecting drugs (Figure 1).

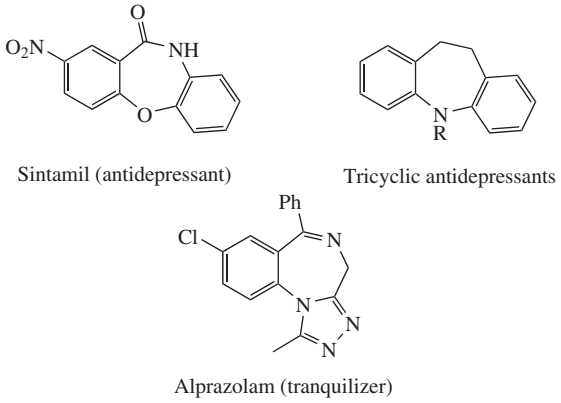
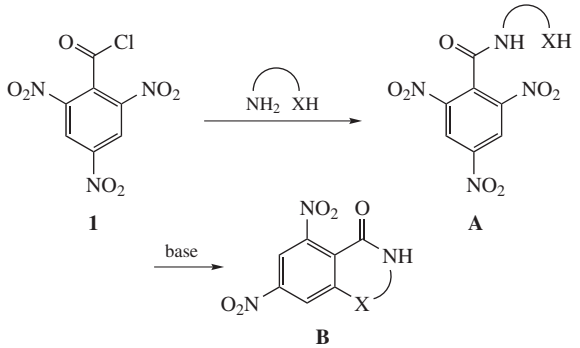


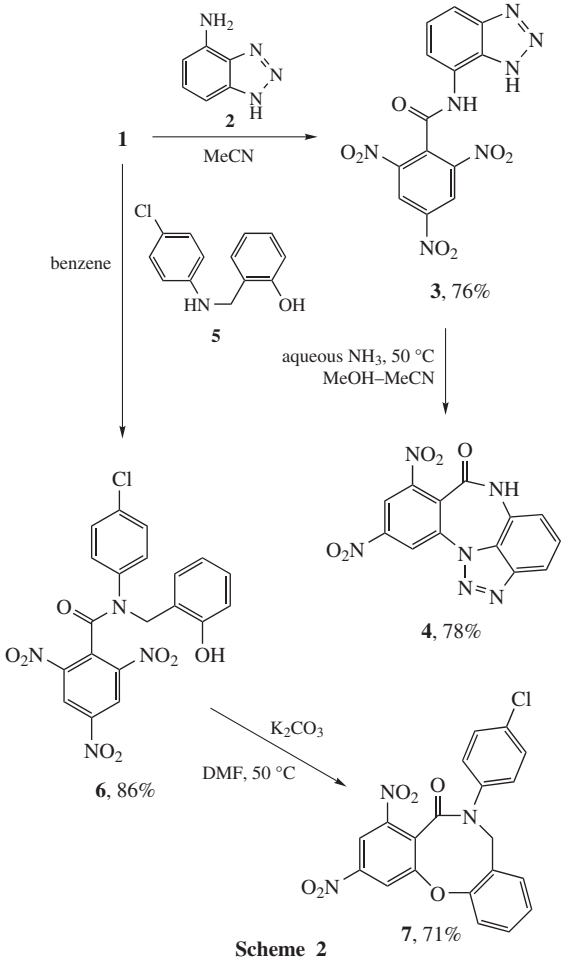
Figure 1 CNS-affecting drugs.

In this work aimed at the utilization of aromatic polynitro compounds, we found that cyclization of *ortho*-nitrobenzoic acid 2-hydroxyanilides afforded dibenz[*b*,*f*][1,4]oxazepin-11(10*H*)-ones.[6,7] We demonstrated that intramolecular nucleophilic displacement of a nitro group in 2,4,6-trinitrobenzoic acid amides **A** is a general method of preparing benzoannulated seven- and eight-membered N-containing heterocycles **B** (Scheme 1).



Scheme 1

† Deceased.



Scheme 2

Cyclization of amide **3** to diazepine **4** (Scheme 2) occurs under mild conditions‡ (MeOH–MeCN, aqueous NH_3, 50 °C, *cf.* ref. 6). At the same time, the conversion of amide **6** to oxazocine **7** under these conditions failed, so in this case the DMF/K_2CO_3 system[7] was used instead (interestingly, the preparation of **4** from **3** in the latter system is accompanied by tar product formation).

Dinitro heterocycles **4** and **7** thus prepared could serve as starting compounds in a synthesis of various derivatives *via* the selective displacement of a nitro group with different nucleophiles.[6]

References

1 S. Radl, *Adv. Heterocycl. Chem*., 2002, **83**, 189.
2 E. Buncel, J. Dust and F. Terrier, *Chem. Rev*., 1995, **95**, 2261.
3 I. G. Abramov, A. V. Smirnov, S. A. Ivanovskii, M. B. Abramova, V. V. Plakhinskii and M. S. Belyasheva, *Mendeleev Commun*., 2001, 80.
4 I. G. Abramov, A. V. Smirnov, L. S. Kalandadze, V. N. Sakharov and V. V. Plakhtinskii, *Heterocycles*, 2003, **60**, 1611.
5 A. V. Smirnov, L. S. Kalandadze, V. N. Sakharov and M. V. Dorogov, *Mendeleev Commun*., 2006, 262.
6 A. V. Samet, V. N. Marshalkin, K. A. Kislyi, N. B. Chernysheva, Yu. A. Strelenko and V. V. Semenov, *J. Org. Chem*., 2005, **70**, 9371.
7 A. V. Samet, K. A. Kislyi, V. N. Marshalkin and V. V. Semenov, *Izv. Akad. Nauk, Ser. Khim*., 2006, 529 (*Russ. Chem. Bull., Int. Ed*., 2006, **55**, 549).
8 M. E. Derieg and L. H. Sternbach, *J. Heterocycl. Chem*., 1966, **3**, 237.

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‡ ^{1}H NMR spectra were recorded in [$^2H_6$]DMSO on a Bruker DRX500 spectrometer (500.13 MHz), mass spectra were measured on a Finnigan MAT LCQ instrument (ESI). Amine **5** was prepared according to a published procedure.[8]

2,4,6-Trinitrobenzoic acid 1,2,3-benzotriazole-4(7)amide **3**. A solution of 4(7)-aminobenzotriazole **2** (0.54 g, 4 mmol) in MeCN (5 ml) was added to a solution of 2,4,6-trinitrobenzoyl chloride **1** (0.55 g, 2 mmol) in MeCN (3 ml) and left overnight. The resulting precipitate was filtered off, the filtrate evaporated to dryness, and the residue triturated with AcOH (2 ml), filtered, thoroughly washed with water and dried. Yield 0.58 g (76%); mp 184–186 °C. ^{1}H NMR, δ: 7.55 (br. s, 2H), 8.2 (br. s, 1H), 9.2 (br. s, 2H), 12.0 (br. s, 1H), 15.9 (br. s, 1H). Found (%): C, 42.21; H, 2.08; N, 25.90. Calc. for $C_{13}H_7N_7O_7$ (%): C, 41.83; H, 1.89; N, 26.27.

*8,10-Dinitro-1,2,3-triazolo[1,5-*a*]dibenzo[*b,f*][1,4]diazepin-7-one* **4**. To a solution of amide **3** (0.50 g, 1.34 mmol) in a mixture of MeOH (2 ml) and MeCN (2 ml), 25% aqueous NH_3 (0.5 ml) was added, and the mixture was heated at 50 °C for 48 h. The resulting glossy reddish brown crystals were filtered off, washed with MeOH (1 ml) and dried. Yield 0.34 g (78%); mp > 300 °C (decomp.). ^{1}H NMR, δ: 7.08 (d, 1H, *J* 7.7 Hz), 7.40 (t, 1H, *J* 8.0 Hz), 7.72 (d, 1H, *J* 8.3 Hz), 8.54 (s, 1H), 9.04 (s, 1H), 11.29 (s, 1H). ^{13}C NMR, δ: 113.5, 114.7, 115.8, 116.6, 121.5, 124.2, 125.3, 127.2, 138.0, 147.6, 149.4, 154.1, 159.5. MS (ESI, MeOH), *m*/*z* (%): 325 $[M - H]^-$ (100), 297 $[M - H - N_2]^-$ (75), 251 $[M - H - N_2 - NO_2]^-$ (10). Found (%): C, 48.04; H, 1.97; N, 25.44. Calc. for $C_{13}H_6N_6O_5$ (%): C, 47.86; H, 1.85; N, 25.76.

2,4,6-Trinitrobenzoic acid N*-(2-hydroxybenzyl)-4-chloroanilide* **6**. A solution of amine **5** (1.17 g, 5 mmol) in benzene (5 ml) was added to a solution of 2,4,6-trinitrobenzoyl chloride **1** (0.69 g, 2.5 mmol) in benzene (10 ml) and left overnight. The resulting precipitate was filtered off and crystallized from MeOH. Yield 1.02 g (86%); mp 176–178 °C. ^{1}H NMR [10:3 mixture of (*Z*)- and (*E*)-isomers with respect to an amide N–C(O) bond]. Major isomer, δ: 5.10 (s, 2H), 6.75 (m, 2H), 7.12 (d, 2H, *J* 8.4 Hz), 7.21 (d, 2H, *J* 8.4 Hz), 7.32 (d, 1H, *J* 8.0 Hz), 8.94 (s, 2H), 9.38 (br. s, 1H). Minor isomer, δ: 4.70 (s, 2H), 6.57 (t, 1H, *J* 7.8 Hz), 6.63 (d, 1H, *J* 8.0 Hz), 6.97 (t, 1H, *J* 7.9 Hz), 7.38 (d, 2H, *J* 8.4 Hz), 7.52 (d, 2H, *J* 8.4 Hz), 9.24 (s, 2H) (some signals overlap). Found (%): C, 51.10; H, 2.61; N, 12.09; Cl, 7.26. Calc. for $C_{20}H_{13}ClN_4O_8$ (%): C, 50.81; H, 2.77; N, 11.85; Cl 7.50.

*10,11-Dihydro-1,3-dinitro-11-(4-chlorophenyl)dibenz[*b,g*][1,5]oxazocin-12-one* **7**. A suspension of amide **6** (0.80 g, 1.7 mmol) and dried K_2CO_3 (0.28 g, 2.03 mmol) in DMF (3 ml) was stirred for 3 h at 50 °C. The mixture was cooled, poured into 30 ml of water, acidified to pH 7, the resulting precipitate was filtered off, washed with hot water (5 ml) and dried. Yield 0.51 g (71%); mp 223–225 °C. ^{1}H NMR, δ: 4.76 (d, 1H, *J* 10.9 Hz), 5.25 (d, 1H, *J* 10.9 Hz), 7.23 (m, 2H), 7.29 (d, 2H, *J* 8.4 Hz), 7.48 (m, 3H), 7.64 (d, 1H, *J* 8.1 Hz), 8.64 (s, 1H), 8.79 (s, 1H). ^{13}C NMR, δ: 52.4, 118.0, 122.3, 124.1, 126.0, 127.0, 127.4, 129.3, 130.4, 130.7, 131.6, 132.6, 139.2, 145.9, 149.6, 151.8, 154.7, 163.0. MS (ESI-MS, MeOH), *m*/*z* (%): 873 $[2M + Na]^+$ (100), 448 $[M + Na]^+$ (20), 426 $[M + H]^+$ (35). Found (%): C, 56.22; H, 3.13; N, 10.19; Cl, 8.15. Calc. for $C_{20}H_{12}ClN_3O_6$ (%): C, 56.42; H, 2.84; N, 9.87; Cl, 8.33.