Synthesis of nitro-substituted benzoannelated seven-membered heterocycles from trinitrotoluene

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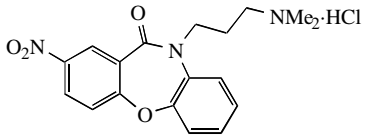
10.1070/MC2001v011n03ABEH001426

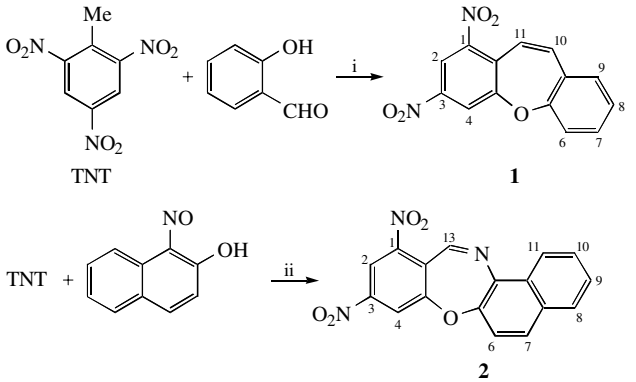
Dibenzo[*b*,*f*]oxepine, dibenzo[*b*,*f*]-1,4-oxazepinone and benzo[*f*]naphtho[2,1-*b*]-1,4-oxazepine were synthesised starting from 2,4,6-trinitrotoluene.

While investigating the utilization of 2,4,6-trinitrotoluene (TNT), it was found to be a promising starting compound for the synthesis of benzoannelated five-membered heterocycles (indoles, indazoles, benzothiophenes and benzo[*d*]isothiazoles).[1–4]

This communication deals with the synthesis of seven-membered N- and O-containing benzoannelated heterocycles with nitro groups at the benzene ring from TNT. These compounds are of special interest because of their pharmaceutical activity.[5,6] Thus, the antidepressant Sintamil possesses a structure of dibenzo[*b*,*f*]-1,4-oxazepinone:[7]



Reactions of TNT with salicylaldehyde and 1-nitroso-2-naphthol afforded dibenzo[*b*,*f*]oxepine **1** and benzo[*f*]naphtho[2,1-*b*]-1,4-oxazepine **2**, respectively (Scheme 1).†



Scheme 1 *Reagents and conditions*: i, morpholine, reflux, 3 h, 75%; ii, Et_3N, MeCN, 5 min, 31%.

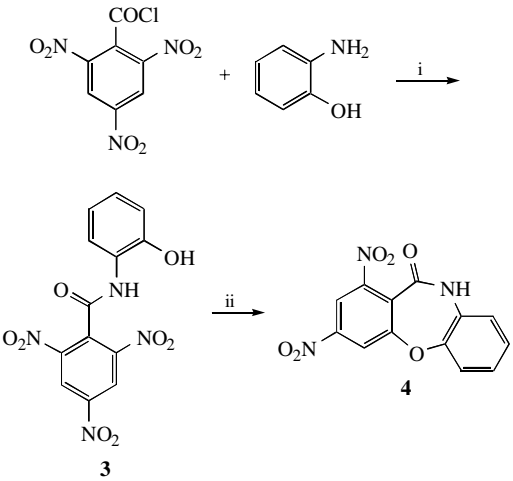
† ^{1}H NMR spectra were recorded in [$^2H_6$]DMSO on a Bruker DRX500 spectrometer (500.13 MHz), mass spectra were measured on a Kratos MS-30 instrument. ^{1}H NMR spectra for the reaction products of TNT with salicylaldehydes, 1-nitroso-2- and 2-nitroso-1-naphthols and the ^{1}H NMR spectra of the products of nucleophilic substitution in oxazepines **2** and **4** are placed on the web-site *http://www.chemical-block.com*.

1,3-Dinitrodibenzo[b,f]*oxepine* **1**: to a mixture of 10 mmol (2.27 g) of TNT and 35 mmol (4.27 g) salicylaldehyde, morpholine (10 mol% on an aldehyde basis) was added, and the mixture was heated for 3 h at 135 °C. Then, the reaction mixture was cooled, dissolved in hot AcOH and filtered. The filtrate was cooled; the precipitate was filtered off and dried. Yield 2.13 g (75%), yellowish brown crystals, mp 148–150 °C. ^{1}H NMR, δ: 7.02 (d, 1H, *J* 12.1 Hz), 7.29 (m, 2H), 7.43 (d, 1H, *J* 8.1 Hz), 7.50 (m, 2H), 8.51 (s, 1H, H-2 or H-4), 8.59 (s, 1H, H-2 or H-4). MS, *m*/*z* (%): 284 (M^+, 15), 255 (59), 225 (53), 179 (100), 163 (61).

1,3-Dinitrobenzo[f]*naphtho[2,1-*b*]-1,4-oxazepine* **2**: to a solution of 0.346 g (2 mmol) of 1-nitroso-2-naphthol and 0.454 g (2 mmol) of TNT in 3 ml of MeCN, 0.20 g (2 mmol) of Et_3N was added with stirring. After 5 min, the precipitate was filtered off, washed with MeOH and acetone and dried. Yield 0.208 g (31%), deeply orange crystals, mp 276–278 °C. ^{1}H NMR, δ: 7.55–7.65 (m, 3H), 7.92 (m, 2H), 8.32 (d, 1H, *J* 8.4 Hz), 8.60 (s, 1H, H-2 or H-4), 8.68 (s, 1H, H-2 or H-4), 9.19 (s, 1H, H-13). MS, *m*/*z* (%): 335 (M^+, 100), 243 (68), 231 (43), 214 (41).

Probably, in both cases the methyl group of TNT reacts first (with the C=O or N=O group of the reagent molecule) followed by cyclization of the intermediate product *via* intramolecular nucleophilic replacement of the *o*-nitro group by the OH group. Substituted salicylaldehydes, as well as 2-nitroso-1-naphthol, react in a similar way.

Dibenzo[*b*,*f*]-1,4-oxazepine **4** was obtained from 2,4,6-trinitrobenzoyl chloride (readily prepared from TNT[2]).‡ In this case, intermediate amide **3** can be isolated, and its cyclization to oxazepinone **4** occurs slowly (Scheme 2).



Scheme 2 *Reagents and conditions*: i, C_6H_6, reflux, 8 h, 81%; ii, aqueous NH_3, EtOH–MeCN, 50 °C, 60 h, 91%.

Dinitro-substituted compounds **1**, **2** and **4** react with O- and S-nucleophiles to yield nucleophilic substitution products in which one or two nitro groups are replaced. These results will be published elsewhere.

References

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‡ *2,4,6-Trinitrobenzoic acid (2-hydroxyphenyl)amide* **3**: prepared in 81% yield according to the general procedure for 2,4,6-trinitrobenzamides.[2] Grey powder, mp 201–203 °C. ^{1}H NMR, δ: 6.80–7.00 (m, 3H), 8.05 (d, 1H, *J* 8.3 Hz), 9.10 (s, 2H), 9.70 (br. s, 1H, OH), 10.35 (br. s, 1H, NH). MS, *m*/*z* (%): 348 (M^+, 5), 153 (69), 126 (81), 108 (99), 80 (83), 79 (100).

1,3-Dinitrodibenzo[b,f]*-1,4-oxazepin-11(10*H*)-one* **4**: to a solution of 0.348 g (1 mmol) of amide **3** in a mixture of EtOH (2 ml) and MeCN (2 ml), 7 drops of 25% aqueous NH_3 were added, and the mixture was heated for 60 h at 50 °C until the starting amide disappeared (TLC monitoring). Then, the precipitate was filtered off, washed with EtOH and dried. Yield 0.275 g (91%), black needles (orange needles after chromatography on silica gel; eluent, benzene–EtOAc), mp 289–290 °C. ^{1}H NMR, δ: 7.15–7.30 (m, 3H), 7.48 (d, 1H, H-9, *J* 8.5 Hz), 8.49 (s, 1H, H-2 or H-4), 8.51 (s, 1H, H-2 or H-4), 11.20 (br. s, 1H, NH). MS, *m*/*z* (%): 301 (M^+, 49), 211 (32), 181 (42), 153 (57), 126 (94), 74 (100).

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Received: 17th January 2001; Com. 01/1752