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Synthesis of 4,6-dinitrobenzo[*b*]furans from 1,3,5-trinitrobenzene

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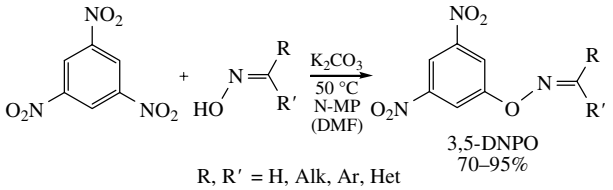
O-3,5-Dinitrophenylketoximes obtained by treatment of ketoximes with 1,3,5-trinitrobenzene undergo acid-catalysed cyclization to give 4,6-dinitrobenzo[*b*]furans substituted at the 2- or 2- and 3-positions.

The aim of this study was to use 1,3,5-trinitrobenzene (TNB) as a versatile synthon prepared from 2,4,6-trinitrotoluene (TNT) for the conversion of TNT into valuable products.[1,2] TNB can be readily obtained from TNT by a two-stage oxidative demethylation process;[3] a technologically attractive method for the oxidation of the TNT methyl group by 80% HNO_3 at elevated temperature and pressure was proposed.[4]

TNB can add nucleophiles at the *ortho* position with respect to the nitro group to give stable anionic σ-H complexes.[5–8] On the other hand, conditions have been found under which O-, S- and N-nucleophiles of certain types replace one or more nitro groups in TNB.[9–14] The resulting substitution products can serve for the synthesis of new polyfunctional aromatic and heterocyclic structures.

Previously,[14] we found that keto- and aldoximes replace a nitro group in TNB in the presence of a base. Thus, a preparative method for the synthesis of hitherto unknown *O*-3,5-dinitrophenyloximes (3,5-DNPO) has been elaborated (Scheme 1).†

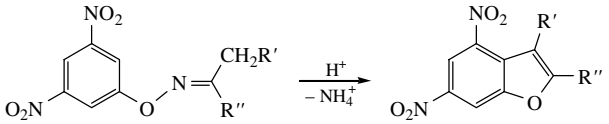


Scheme 1

We found that *O*-3,5-dinitrophenylketoximes **1** containing a methyl group (**1**, R′ = H) or a methylene fragment (**1**, R′ = Alk) at the carbon atom of the C=N bond smoothly undergo cyclisation under mild conditions to give 4,6-dinitrobenzo[*b*]furans **2** substituted at the 2-position (from **1**, R′ = H) or at the 2- and 3-positions (from **1**, R′ = Alk) (Scheme 2).

Cyclisation was observed on heating oximes **1** (above 80 °C) in N-MP or DMF, but the best results were obtained under acidic catalysis: refluxing in a mixture of equal volumes of concentrated hydrochloric acid and ethanol for oximes **1** (R′ = H); heating (80 °C) in a mixture of equal volumes of concentrated H_2SO_4 and MeCOOH for pyridine derivatives (**f**,**g**) to give sulfates **2f**,**g**, 1:1; somewhat more drastic conditions (refluxing

† Scheme 1 in ref. 14 contains an error: in compounds **1b–k** and **2b–k**, R^1 = Me.



a R′ = H, R″ = Me
b R′ = H, R″ = Ph
c R′ = H, R″ = 4-BrC_6H_4
d R′ = H, R″ = 4-FC_6H_4
e R′ = H, R″ = 3,4-methylenedioxy-C_6H_3
f R′ = H, R″ = 4-pyridyl
g R′ = H, R″ = 2-pyridyl
h R′ = H, R″ = 2-$MeOC_6H_4$
i R′ = H, R″ = 2,5-$(MeO)_2C_6H_3$
j R′ = H, R″ = 4-HOC_6H_4
k R′ = H, R″ = 2-furyl
l R′ = H, R″ = 2-thienyl
m R′ + R″ = $(CH_2)_4$
n R′ + R″ = $CH_2CH(Me)(CH_2)_2$
o R′ = Me, R″ = Ph

Scheme 2

in a mixture of concentrated hydrochloric acid and acetic acid, 2:5 v/v) for oximes **1**, R′ = Alk. The reaction was carried out until complete conversion of the original oxime (4–18 h); the yields of 4,6-dinitrobenzo[*b*]furans **2** were 60–95%.‡

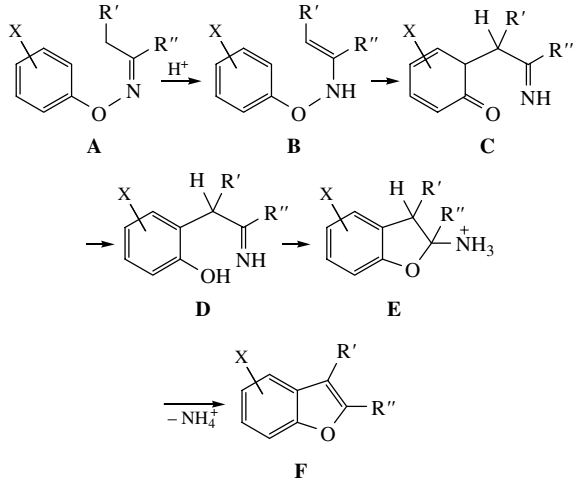
This method is more general for the synthesis of 2-substituted and 2,3-substituted 4,6-dinitrobenzo[*b*]furans. The synthesis of 3-substituted 4,6-dinitrobenzo[*b*]furans has been reported,[15,16] but they were obtained by a different method. Some examples of the synthesis of 2-substituted 4,6-dinitrobenzo[*b*]furans are limited in scope.[17–19]

Note that the acid-catalysed benzofuranisation of O-aryloximes is well known;[20–26] it is analogous to the Fisher conversion of N-arylhydrazones into indoles.[27] However, the benzofuranisation of *O*-3,5-dinitrophenyloximes, which smoothly occurs under mild conditions, is unexpected. In fact, the benzofuranisation of O-aryloximes is assumed to occur according to the mechanism demonstrated in Scheme 3.[24,25]

According to the currently accepted concept,[25] the key step of the process involves an acid-catalysed [3,3]-sigmatropic rearrangement of the enehydroxylamine form of an O-aryloxime (**B**→**C**) followed by the aromatisation of a six-membered ring

(**C→D**), furan ring closure (**D→E**) and aromatisation of the latter by ammonium ion abstraction (**E→F**).

Based on this mechanism and published data, Guzzo *et al.*[25] concluded that electron-donating substituents in the benzene ring should favour the [3,3]-sigmatropic rearrangement, whereas electron-withdrawing substituents should hinder it. Although the benzofuranisation of O-aryloximes with strong electron-withdrawing substituents in the aryl fragment has been reported,[21,23] this required rather drastic conditions in almost all the cases. Note that the electron-withdrawing groups (NO_2, CN, RSO_2, *etc*.) were *meta* with respect to the carbon atom with which the new C–C bond was formed and that the yield of the benzofuranisation product decreased considerably in the presence of two such groups.[21,23]



Scheme 3

In this study, we were the first to perform the benzofuranisation of such O-aryloximes (under mild conditions and in high yields) in which the formation of a new C–C bond occurs at a carbon atom that is *ortho*/*para* with respect to strong electron-withdrawing substituents (two nitro groups). It is likely that such an arrangement of electron-withdrawing substituents hinders the benzofuranisation of O-aryloximes to a smaller extent than in the cases where such substituents are meta with respect to the new C–C bond.

‡ The compounds were characterised by ^{1}H NMR spectra, EI mass spectra and elemental analyses. The ^{1}H NMR spectra were recorded on a Bruker AC-250 spectrometer. The mass spectra were obtained using a Kratos MS-30 instrument. The spectra of all the compounds contain a molecular ion peak (M^+). The course of the reactions was monitored by TLC on Silufol UV-254.

General procedure for the synthesis of 4,6-dinitrobenzo[b]*furans*. 0.01 mol of a corresponding 3,5-dinitrophenyloxime was added to a mixture of ethanol (10 ml) and concentrated hydrochloric acid (36%; 10 ml) [a mixture of 10 ml of AcOH and 4 ml of conc. HCl was used in the case of compounds **m**,**n**,**o**; a mixture of 5 ml of concentrated H_2SO_4 and 5 ml of AcOH was used in the case of compounds **f**,**g** to give the target compounds as sulfates (1:1) in the form of precipitates]. The reaction mixture was refluxed (except for compounds **f**,**g** where heating at 80 °C was used) until the entire parent dinitro compound has been converted (TLC monitoring using $CHCl_3$ as the eluent). The mixture was heated to room temperature; the resulting precipitate was filtered off, crystallised from acetonitrile and dried *in vacuo* (in the case of compounds **2f** and **2g**, the mixture was poured into water, the resulting precipitate of sulfate **2f** or **2g** was filtered off, washed with water on the filter, dried in air and crystallised from acetonitrile).

The resulting compounds are listed below.

2a: rection time, 6 h; yield 93%, mp 143–144 °C). ^{1}H NMR, δ: 8.9 (d, 1H, ^4J 1.9 Hz), 8.78 (d, 1H, ^4J 1.9 Hz), 7.32 (s, 1H), 2.65 (s, 3H).

2b: reaction time, 18 h; yield 95%, mp 178–179 °C. ^{1}H NMR, δ: 8.97 (d, 1H, ^4J 2 Hz), 8.82 (d, 1H, ^4J 2 Hz), 8.15 (m, 3H), 7.57 (m, 3H).

2c: reaction time, 7 h; yield 77%; mp 248–249 °C. ^{1}H NMR, δ: 8.97 (d, 1H, ^4J 2 Hz), 8.85 (d, 1H, ^4J 2 Hz), 8.17 (s, 1H), 8.07 (d, 2H, ^3J 8 Hz), 7.75 (d, 2H, ^3J 8 Hz).

2d: reaction time, 6 h; yield 92%; mp 214–215 °C. ^{1}H NMR, δ: 8.95 (d, 1H, ^4J 2.1 Hz), 8.8 (d, 1H, ^4J 2.1 Hz), 8.17 (t, 2H, ^3J 7.8 Hz), 8.05 (s, 1H), 7.4 (t, 2H, ^3J 7.8 Hz).

2e: reaction time, 4 h; yield 86%; mp 268–269 °C. ^{1}H NMR, δ: 8.82 (d, 1H, ^4J 2 Hz), 8.87 (d, 1H, ^4J 2 Hz), 7.95 (s, 1H), 7.61 (s, 2H), 7.1 (d, 1H), 6.15 (s, 2H).

2f: reaction time, 3 h; yield 88% (sulfate); mp 162–163 °C. ^{1}H NMR, δ: 9.07 (d, 1H, ^4J 2 Hz), 8.85 (d, 1H, ^4J 2 Hz), 8.79 (d, 2H, ^3J 8 Hz), 8.40 (s, 1H), 8.03 (d, 2H, ^3J 8 Hz).

2g: reaction time, 10 h; yield 72% (sulfate); mp 174–175 °C. ^{1}H NMR, δ: 9.02 (d, 1H, ^4J 1.9 Hz), 8.83 (d, 1H, ^4J 1.9 Hz), 8.75 (m, 1H), 8.1 (m, 3H), 7.53 (t, 1H, ^3J 8 Hz).

2h: reaction time, 8 h; yield 80%; mp 227–228 °C. ^{1}H NMR, δ: 8.95 (d, 1H, ^4J 2 Hz), 8.82 (d, 1H, ^4J 2 Hz), 8.05 (d, 1H, J 7 Hz), 7.9 (s, 1H), 7.58 (t, 1H, ^3J 8 Hz), 7.32 (d, 1H, ^3J 8 Hz), 7.21 (t, 1H, ^3J 7.8 Hz), 4.1 (s, 3H).

2i: reaction time, 8 h; yield 84%; mp 252–253 °C. ^{1}H NMR, δ: 9.02 (d, 1H, ^4J 1.9 Hz), 8.83 (d, 1H, ^4J 1.9 Hz), 7.93 (s, 1H), 7.51 (s, 1H), 7.25 (d, 2H, ^3J 8 Hz), 4.07 (s, 3H), 3.85 (s, 3H).

2j: reaction time, 12 h; yield 58%; mp 271–272 °C. ^{1}H NMR, δ: 10.3 (s, 1H), 8.8 (d, 1H, ^4J 2 Hz), 8.84 (d, 1H, ^4J 2 Hz), 7.93 (d, 2H, ^3J 8 Hz), 7.81 (s, 1H), 6.95 (d, 2H, ^3J 8 Hz).

2k: reaction time, 5 h; yield 75%; mp 160–161 °C. ^{1}H NMR, δ: 8.98 (d, 1H, ^4J 1.9 Hz), 8.87 (d, 1H, ^4J 1.9 Hz), 8.09 (s, 1H), 7.77 (s, 1H), 7.48 (d, 1H, J 5 Hz), 6.84 (m, 1H).

2l: reaction time, 6 h; yield 80%; mp 165–166 °C. ^{1}H NMR, δ: 165, 8.8 (d, 1H, ^4J 1.9 Hz), 8.71 (d, 1H, ^4J 1.9 Hz), 7.92 (m, 2H), 7.72 (s, 1H), 7.24 (t, 1H, J 4 Hz).

2m: reaction time, 6 h; yield 85%; mp 102 °C. ^{1}H NMR, δ: 8.85 (d, 1H, ^4J 2 Hz), 8.7 (d, 1H, ^4J 2 Hz), 2.84 (m, 4H), 1.89 (m, 4H).

2n: reaction time, 9 h; yield 71%; mp 88 °C. ^{1}H NMR, δ: 8.75 (d, 1H, ^4J 2 Hz), 8.62 (d, 1H, ^4J 2 Hz), 2.9 (m, 3H), 2.35 (m, 1H), 1.95 (m, 2H), 1.5 (m, 1H), 1.1 (d, 3H).

2o: reaction time, 6 h; yield 73%; mp 151–152 °C. ^{1}H NMR, δ: 8.85 (d, 1H, ^4J 2 Hz), 8.7 (d, 1H, ^4J 2 Hz), 7.85 (m, 2H), 7.62 (m, 3H), 2.42 (s, 3H).

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