

Nitration of 1,3,5-trimethoxybenzene

Anthony J. Bellamy^{a*}, Peter Golding^b, Simon J. Ward^a
and (in part) Nicholas W. Mitchell^a

^aCranfield University, Royal Military College of Science, Shrivenham, Swindon SN6 8LA, UK

^bAWE Aldermaston, Reading RG7 4PR, UK

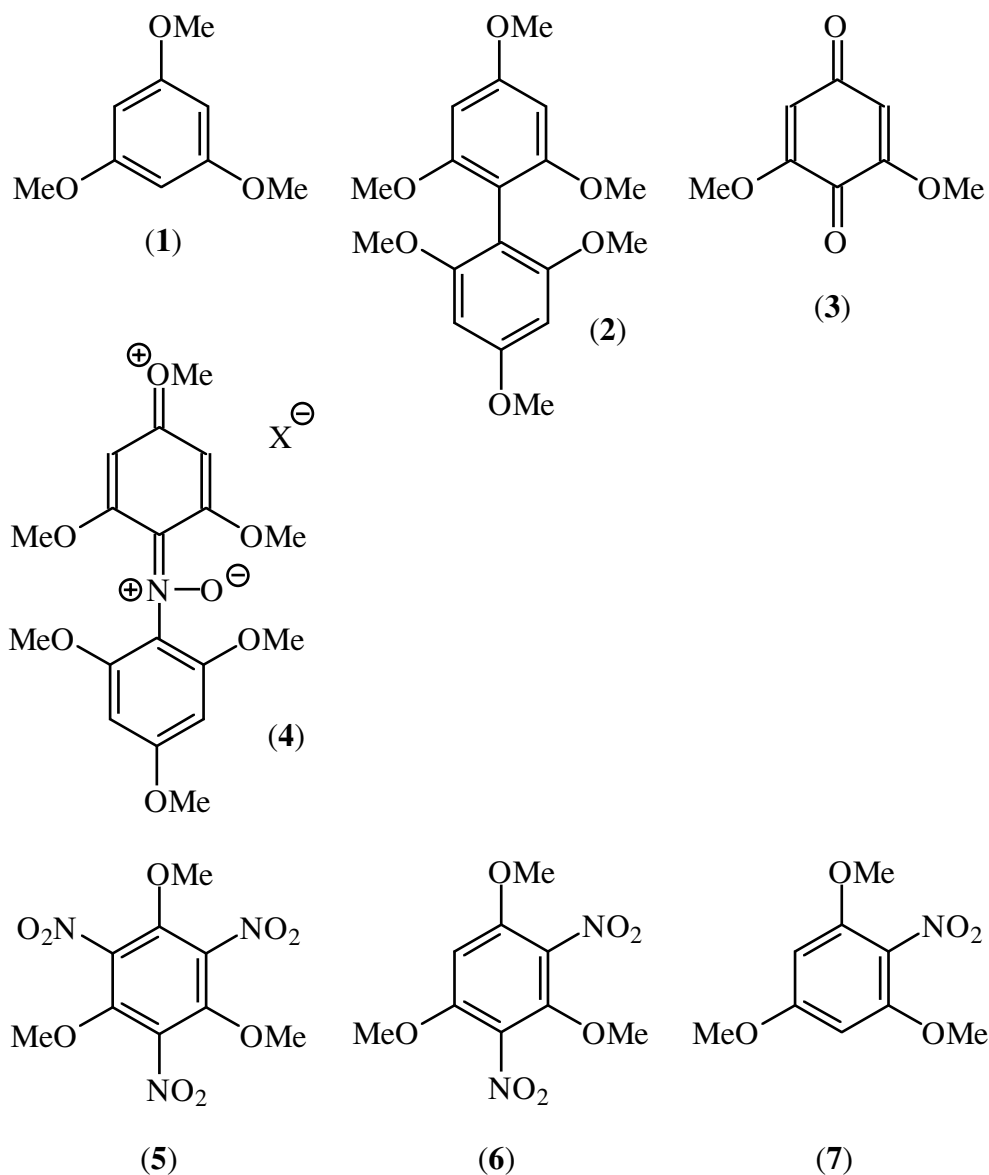
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1,3,5-Trimethoxybenzene has been nitrated with N_2O_5 in organic solvents to give modest yields of the desired 1,3,5-trimethoxy-2,4,6-trinitrobenzene but side reactions involving oxidation and coupling appear to limit the usefulness of this method.

Keywords: 1,3,5-Trimethoxybenzene, nitration, N_2O_5

We have recently described a new, three stage, synthetic route to the explosive compound 1,3,5-triamino-2,4,6-trinitrobenzene (TATB), using 1,3,5-trihydroxybenzene as the starting material.¹ One variant of the reaction sequence involved nitration to 1,3,5-trihydroxy-2,4,6-trinitrobenzene, methylation to 1,3,5-trimethoxy-2,4,6-trinitrobenzene and amination to TATB. Another possible route to TATB from the same starting

material was also considered, namely methylation, nitration, amination. However, whilst the methylation and amination stages of this latter route were found to work satisfactorily, nitration of 1,3,5-trimethoxybenzene (**1**) to give 1,3,5-trimethoxy-2,4,6-trinitrobenzene (**5**) in sufficient yield and purity was disappointing.



* To receive any correspondence. E-mail: A.J.Bellamy@rmcs.cranfield.ac.uk

The nitration of alkoxybenzenes, and 1,3,5-trimethoxybenzene in particular, has been widely studied. Whilst 1,3-dimethoxybenzene can be nitrated to its trinitro derivative in high yield,² reported studies on the nitration of 1,3,5-trimethoxybenzene indicate that it does not give simple nitration products. Nitrations using nitric acid have been reported to give a low yield of the mono-nitro derivative and hexamethoxybiphenyl (**2**),³ 2,6-dimethoxybenzoquinone (**3**),⁴ and quinoidal 2,2',4,4',6,6'-hexamethoxydiphenylamine N-oxide salts (**4**),⁵ usually accompanied by the formation of deep blue reaction mixtures. In an attempt, both to avoid the formation of these unwanted by-products, and to achieve more extensive nitration, we have studied the nitration of 1,3,5-trimethoxybenzene using N₂O₅ in organic solvents.

Nitrations using N₂O₅ dissolved in either dichloromethane or acetonitrile, under a variety of reaction conditions *e.g.* normal and reverse addition, low temperature, in the presence of nitric or sulfuric acid, were performed (see Table 1 for details). In all experiments where sufficient N₂O₅ to convert the substrate into the tri-nitro derivative was used, the yield of products was low (only 22-65% starting material accounted for; see Table 2), and the isolated material was usually a mixture of di- (**6**) and tri-nitrotrimethoxybenzenes, with, in some cases, 3,5-dimethoxydinitrophenols and 2,6-dimethoxybenzoquinone (**3**) (see Table 2). Furthermore, the low recovery of material, the blue coloration of the reaction mixtures (as reported by earlier workers), and the darkly coloured product mixtures, suggest that under these conditions too, extensive coupling and the formation of water-soluble by-products are significant side reactions. Only when a rather limited quantity of N₂O₅ was used (partial nitration, Tables 1 and 2, experiment j) was the yield and accountability high, but even then the mixture of mono- (**7**) and di-nitro derivatives was accompanied by phenolic and benzoquinone derivatives.

The highest conversion into 1,3,5-trimethoxy-2,4,6-trinitrobenzene (**5**) was achieved when sulfuric acid was present (experiment h; 65% yield of crude product, recrystallised to give 45% yield of pure product), but too much sulfuric acid caused the yield to be drastically reduced.

Since nitration using nitric acid appears to cause significant side-reactions (see references cited above), and since aromatic nitration with N₂O₅ would normally liberate HNO₃ as a by-product, nitration using N₂O₅ in acetonitrile in the presence of sodium fluoride was also examined. Sodium fluoride is known to remove HNO₃ from acetonitrile solutions through precipitation of sodium nitrate and complexation of the liberated HF

with fluoride ion.⁶ It was thus anticipated that the presence of NaF would maintain an HNO₃-free environment. Whilst this approach seemed to work to a degree (experiment i; 65% accountability of starting material), the major product was the di-nitro derivative.

Since conditions for the clean nitration of 1,3,5-trimethoxybenzene (**1**) to give 1,3,5-trimethoxy-2,4,6-trinitrobenzene (**5**) could not be found, we subsequently focused on developing the alternative route to TATB, namely initial nitration of 1,3,5-trihydroxybenzene (or its triacetate) followed by alkylation and amination, which is reported elsewhere.¹

Table 1. Nitration of 1,3,5-trimethoxybenzene (TMB) with N₂O₅

Table 2. Product analysis

References 7

Formulae 7

Caution: See the warning concerning the potential explosive nature of some of the compounds concerned: the Experimental Section of the full-text version: J Chem Res(M) 0921.

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