

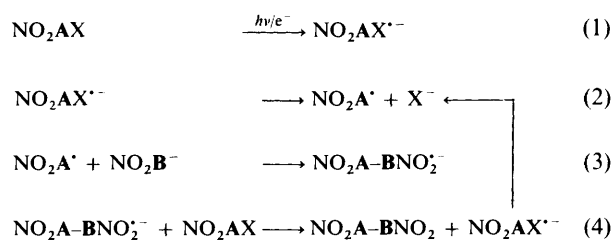
$S_{RN}1$ Synthesis of *vic*-dinitro compounds containing a nitrodioxane subunit

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vic-Dinitro compounds containing a nitrodioxane subunit can be obtained by $S_{RN}1$ reactions between either open chain *gem*-chloronitro derivatives as substrates and an anion from nitrodioxane as the nucleophile or 'reversed' reagents namely *gem*-chloronitrodioxane (substrate) and anions from nitro derivatives. The former access is more efficient and is rationalized on the basis that the structure of the radical anion generated by mono electron transfer to the respective substrates allows an appropriate choice of reagents for optimizing the yield of the title compounds to be made.

Photostimulated $S_{RN}1$ reactions proceeding by the well established four-step chain radical mechanism¹⁻³ depicted in Scheme 1 are efficient for coupling *gem*-halogenonitro compounds NO_2AX as substrates with anions from nitroalkanes NO_2BH as nucleophiles to give *vic*-dinitro derivatives NO_2A-BNO_2 in high yield.

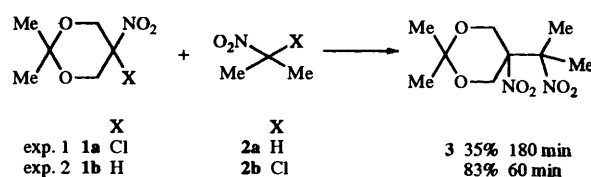


Scheme 1

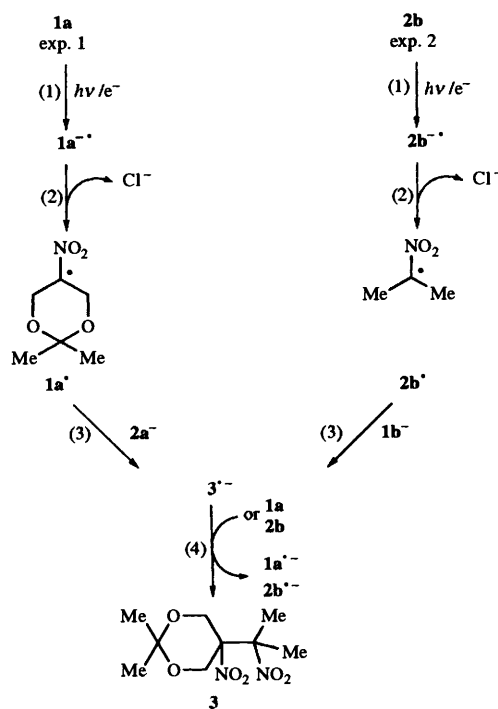
We required a *vic*-dinitro derivative containing a nitrodioxane subunit and we thus carried out a reaction between the *gem*-chloronitro compound **1a** (NO_2ACl) and the anion derived from **2a** (NO_2BH) (Scheme 2, exp. 1) in order to obtain **3**. The yield happened to be poor and the reaction time long compared with related $S_{RN}1$ reactions.³ We then thought that a better yield of this *vic*-dinitro compound **3** could be obtained from a reaction between 'reversed' reagents namely **2b** (NO_2BCl) as the substrate and the anion derived from **1b** (NO_2AH) as the nucleophile. In contrast to exp. 1, and to our surprise, this second experiment was much more satisfactory with regard to yield and reaction time.

Discussion

When considering the structure of the intermediates involved in the four-step chain $S_{RN}1$ mechanism of each reaction (Scheme 3), one can see that the second radical anion $3^{\bullet-}$ which is a precursor of the final product **3** is common to both of them. In exp. 1, it is formed *via* the first radical anion $1a^{\bullet-}$ [eqn. (1)]. Dissociation of $1a^{\bullet-}$ into Cl^- and the radical $1a^{\bullet}$ [eqn. (2)] followed by attack of $1a^{\bullet}$ upon $2a^-$ leads to $3^{\bullet-}$ [eqn. (3)]. In exp. 2, this latter intermediate results from attack of $1b^-$ upon the radical $2b^{\bullet}$, which is itself produced from $2b^{\bullet-}$. In the last



Scheme 2

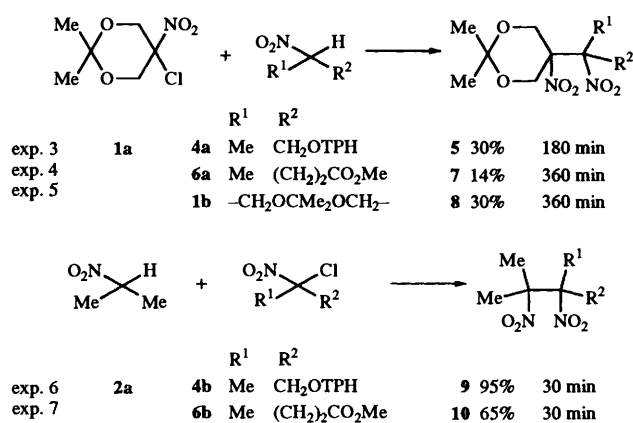


Scheme 3

step of the mechanism [eqn. (4)], which sustains the chain process, the radical anion $3^{\bullet-}$ transfers its extra electron to substrate **1a** (exp. 1) or **2b** (exp. 2) affording the corresponding radical anion $1a^{\bullet-}$ or $2b^{\bullet-}$ along with the final product **3**.

The difference of reactivity between exp. 1 and exp. 2 can tentatively be rationalized by transferring to $S_{RN}1$ reactions in solution at room temperature the conclusions of ESR low temperature matrix studies on radical anions which indicate that: (i) a *gem*-halogenonitrodioxane radical anion⁴ such as $1a^{\bullet-}$ [exp. 1, eqn. (1)] is relatively more stable than the open chain

† Deceased on July 31, 1991.



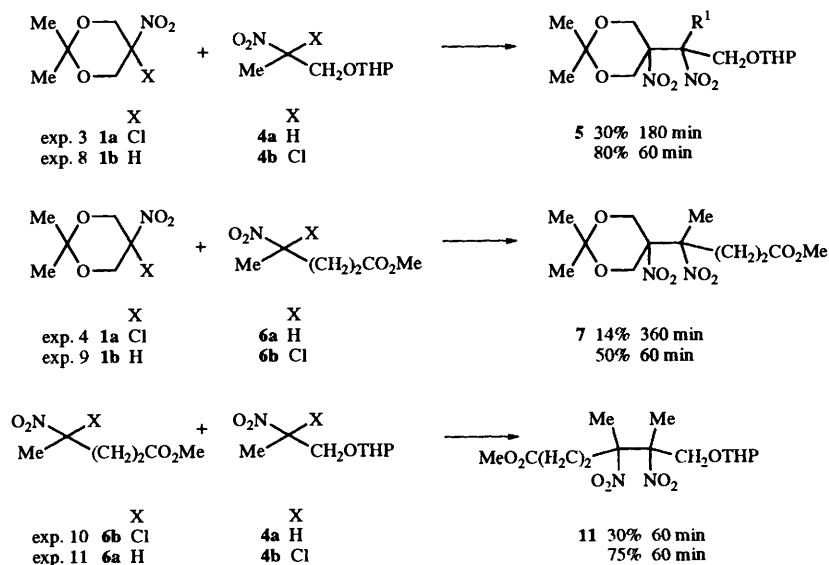
Scheme 4

species **2b**⁻ [exp. 2, eqn. (1)] due to an electronic effect (-I) exerted by the two dioxane oxygen atoms and conformational ring restraints resulting in some stabilization of the C-X σ* bond (where the extra electron is accommodated) before **1a**⁻ reaches planarity concurrent with X⁻ extrusion to give the radical **1a**[•]. (ii) Radical anion breakdown leading to **1a**[•] [exp. 1, eqn. (2)] or to **2b**[•] [exp. 2, eqn. (2)] is precisely rate-determining in the four-step chain process of the S_{RN}1 mechanism.⁵

The reactivity of the radicals thus generated may conceivably be different ‡ so that **2b**[•], because of its longer lifetime is possibly more efficient (to some extent) than **1a**[•] in the electrophilic attack upon their respective nucleophilic partners [eqn. (3)] leading to **3**⁻, the common intermediate to exp. 1 and exp. 2.

More experiments were felt necessary to support the above rationalization. Indeed the lower reactivity of **1a**⁻ was also revealed by reactions of **1a** with functionalized nucleophiles (Scheme 4). The reaction with the anion from **4a** led to **5** (exp. 3) in a yield and reaction time similar to exp. 1. Reaction with the anion from **6a** was sluggish and afforded **7** in very low yield (exp. 4), while that with the anion of **1b** (exp. 5) required 360 min to provide **8** in a yield similar to exp. 1. On the other hand,

‡ We acknowledge one of the referees who pointed out that the planar radical NO₂B[•] is more likely to be stabilized by the nitro group than NO₂A[•] which may be slightly distorted from planarity by interactions between the lone electron pairs of the dioxane oxygen atoms and the half-filled orbital on carbon.



Scheme 5

the reactions between the open chain functionalized substrates **4b**, **6b** and the anion from **2a** were very efficient, leading to **9** (exp. 6) or **10** (exp. 7).

The results of other pairs of S_{RN}1 reactions analogous to the initial one can be predicted by considering the structure of the substrate and of the ensuing radical anion and radical. Thus, the reaction involving the open chain radical anion **4b**⁻ and radical **4b**[•] to give **5** (Scheme 5, exp. 8) was more efficient than that involving the nitrodioxane radical anion **1a**⁻ (exp. 3). Similarly **6b**⁻ (exp. 9) was more reactive than **1a**⁻ and radical **1a**[•] (exp. 4) to give **7**. The last pair of experiments is different from the above ones since it involves open chain reactants. In exp. 11, the very reactive radical anion **4b**⁻ and radical **4b**[•] reacted with **6a**⁻ as nucleophile to give **11**, while the open chain radical anion **6b**⁻ and radical **6b**[•] seemed to be somehow stabilized (possibly by interaction with the ester group) in the reaction with the nucleophile **4a**⁻ (exp. 10).

Although further investigations are necessary to establish on more definite grounds the relevance of the mechanistic equivalence between low temperature ESR studies and S_{RN}1 reactions in solution, our work provides guidance about the choice of reactants for efficient synthesis of *vic*-dinitro compounds containing a nitro dioxane subunit.

Experimental

The IR spectra ($\nu_{\max}/\text{cm}^{-1}$) were recorded on a Nicolet (205, FT) spectrometer in CHCl₃ or CDCl₃ (NMR sample) solution. The mass spectra were recorded on an AEI MS50 (MS-EI) spectrometer. The proton spectra were recorded on a Bruker apparatus 4.7 T (200 MHz), *J* values are reported in Hz and chemical shifts are reported in δ units, (ppm) downfield from tetramethylsilane.

General procedure for S_{RN}1 reactions

Sodium hydride (60% suspension in oil; 0.1 g, 2.1 mmol) was placed in an argon filled two necked flask (25 cm³) and washed with pentane (3 × 5 cm³). The pentane was removed under an argon stream and then anhydrous and degassed dimethylformamide (DMF) (10 cm³) and nitroalkane (1 mmol) in DMF (1 cm³) were successively added using a cannula. After stirring for 10 min, the *gem*-chloronitroalkane (1 mmol) in DMF (1 cm³) was introduced and the reaction system was illuminated by two 25 W neon lamps. The reaction progress was monitored by thin layer chromatography of aliquots.

The reaction was quenched by pouring it into iced 5% aqueous hydrochloric acid (50 cm³) and extracting the resulting mixture with diethyl ether (3 × 50 cm³). The organic phase was washed with brine (2 × 20 cm³) and water (20 cm³), dried over Na₂SO₄ and then evaporated to give a residual oil. Purification was achieved by silica gel column chromatography (elution: methylene chloride-pentane). Yields and reaction times are indicated in Schemes 2, 4 and 5.

2,2-Dimethyl-5-(1-methyl-1-nitro-ethyl)-5-nitro-1,3-dioxane

3. Colourless oil (Found: C, 43.7; H, 6.3. C₉H₁₆N₂O₆ requires C, 43.54; H, 6.45%); $\nu_{\max}/\text{cm}^{-1}$ 1550 and 1200; δ_{H} 1.35 (3 H, s, CH_{3ax}), 1.40 (3 H, s, CH_{3eq}), 1.74 (6 H, s, CH₃), 4.25 (2 H, d, *J* 13.2, dioxane-Hax), and 4.62 (2 H, d, *J* 13.2, dioxane-Heq); m/z 233 (M - CH₃), 203, 149 and 97.

2,2-Dimethyl-5-[1-methyl-1-nitro-2-(tetrahydropyran-2-yl-oxy)ethyl]-5-nitro-1,3-dioxane **5.** Colourless oil; $\nu_{\max}/\text{cm}^{-1}$ 1560 and 1200; δ_{H} 1.36 (3 H, s, CH_{3ax}), 1.45 (3 H, s, CH_{3eq}), 1.56 (6 H, br, CH_{2THP}), 1.74 (3 H, s, CH₃), 3.65 (2 H, m, OCH_{2THP}), 4.10 (2 H, dd, *J* 19, CH_{2OTHP}), 4.40 (2 H, d, *J* 6, dioxane-Hax), 4.45 (1 H, m, OCHO) and 4.70 (2 H, d, *J* 6, dioxane-Heq).

Methyl 4-(2,2-dimethyl-5-nitro-1,3-dioxan-5-yl)-4-nitropentanoate **7.** Colourless oil (Found: C, 45.2; H, 6.65. C₁₂H₂₀N₂O₈ requires C, 45.00; H, 6.25%); $\nu_{\max}/\text{cm}^{-1}$ 1770, 1550, 1440, 1375 and 1200; δ_{H} 1.28 (3 H, s, CH_{3ax}), 1.35 (3 H, s, CH_{3eq}), 1.55 (3 H, s, CH₃), 2.05 (4 H, m, CH₂), 3.62 (3 H, s, CH_{3O}) and 4.30 (4 H, m, dioxane-Hax and -Heq); m/z 321 (MH⁺), 274, 263, 239, 216, 171 and 57.

2,2,2',2'-Tetramethyl-5,5'-dinitro-5,5'-bi(1,3-dioxane) **8.** Colourless oil (Found: C, 45.0; H, 6.2. C₁₂H₂₀N₂O₈ requires C, 45.0; H, 6.25%); $\nu_{\max}/\text{cm}^{-1}$ 1540 and 1200; δ_{H} 1.30 (6 H, s, CH_{3ax}), 1.46 (6 H, s, CH_{3eq}), 1.74 (6 H, s, CH₃) and 4.45 (8 H, s, dioxane-Hax and -Heq); m/z 320 (M⁺), 274, 262, 216, 170 and 132.

2-(2,3-Dimethyl-2,3-dinitrobutoxy)tetrahydropyran **9.** Colourless oil (Found: C, 47.8; H, 7.2. C₁₁H₂₀N₂O₆ requires C,

47.82; H, 7.24%); $\nu_{\max}/\text{cm}^{-1}$ 1545, 1120 and 1060; δ_{H} 1.70 (15 H, br, CH₃ and CH_{2THP}), 3.60 (2 H, m, OCH_{2THP}), 3.85-4.45 (2 H, m, CH_{2OTHP}) and 4.65 (1 H, m, OCHO); m/z 230 (M - NO₂), 192, 130, 101 and 85.

Methyl 4,5-dimethyl-4,5-dinitrohexanoate **10.** Colourless oil (Found: C, 43.5; H, 6.29. C₉H₁₆N₂O₆ requires C, 43.54; H, 6.45%); $\nu_{\max}/\text{cm}^{-1}$ 1720, 1540 and 1200; δ_{H} 1.57 (3 H, s, CH₃), 1.70 (3 H, s, CH₃), 1.75 (3 H, s, CH₃), 2.40 (4 H, m, CH₂) and 3.50 (3 H, s, CH_{3O}); m/z 248 (M⁺), 217, 201, 155, 141 and 115.

Methyl 4,5-Dimethyl-4,5-dinitro-6-(tetrahydropyran-2-yl-oxy)hexanoate **11.** Colourless oil (Found: C, 48.3; H, 6.9. C₁₄H₂₄N₂O₈ requires C, 48.27; H, 6.89%); $\nu_{\max}/\text{cm}^{-1}$ 1740 and 1545; δ_{H} 1.65 (9 H, br, CH₃ and CH_{2THP}), 1.78 (3 H, s, CH₃), 2.30 (4 H, m, CH₂), 3.68 (5 H, m × s, OCH_{2THP} and CH_{3O}), 3.85-4.45 (2 H, m, CH_{2OTHP}) and 4.65 (1 H, m, OCHO); m/z 349 (M + 1), 318, 247, 201, 196, 155 and 85.

References

- 1 N. Kornblum, R. E. Michel and R. C. Kerber, *J. Am. Chem. Soc.*, 1966, **88**, 5660, 5662.
- 2 G. A. Russell and W. C. Danen, *J. Am. Chem. Soc.*, 1966, **88**, 5663.
- 3 Reviews: N. Kornblum, *Angew. Chem., Int. Ed. Engl.*, 1975, **14**, 734; N. Kornblum, in *The Chemistry of Functional Groups*, Suppl. F, *The Chemistry of Amino, Nitroso and Nitro Compounds and their Derivatives*, ed. S. Patai, Wiley, 1983, 361; W. R. Bowman, *Chem. Soc. Rev.*, 1988, **17**, 283; W. R. Bowman, *Photoinduced Electron Transfer*, ed. M. A. Fox and M. Chanon, Elsevier, 1988.
- 4 M. C. R. Symons, R. Beugelmans, W. R. Bowman and A. Lechevallier, *Tetrahedron Lett.*, 1989, **30**, 5949.
- 5 W. R. Bowman and M. C. R. Symons, *J. Chem. Soc., Perkin Trans. 2*, 1983, 25.

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