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# OXIDATIVE ADDITION OF HYDROXIDE ANIONS TO NITROALKENES VIA THE RADICAL ANIONS OF α-NITRO-OXIRANES

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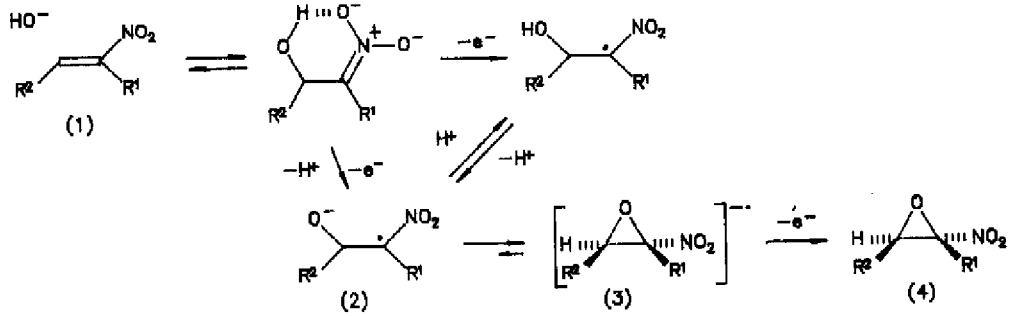
*Key Words: nitro-oxiranes; radical anions; ESR; oxidative addition; α-nitroalkyl radicals*

**Abstract:** Stereoselective oxidative addition of hydroxide anions to nitroalkenes was carried out using potassium ferricyanide to yield α-nitro-oxiranes by a novel non-chain mechanism involving cyclisation of alkoxide anions onto α-nitroalkyl radicals.

As part of our ongoing research into the radical reactions of nitroalkenes[1,2,3] we studied the feasibility of oxidative addition of hydroxide onto nitroalkenes. The addition of hydroxide and other nucleophiles onto the β-position of nitroalkenes is known,[4] and we considered that oxidation of the resulting β-hydroxynitronate might allow cyclisation *via* an α-nitro-oxiranyl radical anion (**3**) (Scheme 1).



**Scheme 1. Oxidative Addition of Hydroxide to Nitroalkenes.**

$K_3Fe(CN)_6$ has been used for the oxidative addition of anions to nitronate anions (Scheme 2).[2,3]

$$R^1R^2C{=}NO_2^- + Fe^{III} \longrightarrow R^1R^2\dot{C}\text{-}NO_2 + Fe^{II}$$
$$R^1R^2\dot{C}\text{-}NO_2 + A^- \longrightarrow [R^1R^2C(A)NO_2]^{\bullet-}$$
$$[R^1R^2C(A)NO_2]^{\bullet-} + Fe^{III} \longrightarrow R^1R^2C(A)NO_2 + Fe^{II}$$

**Scheme 2. Mechanism of Oxidative Addition.** *e.g.* A = $NO_2$, CN, $N_3$, SCN, RS, $RSO_2$, $R_2C{=}NO_2$

**Table 1. Oxidative Addition of Hydroxide to Nitroalkenes.**

| Nitroalkene (1) $R^1$ | $R^2$ | Conditions | % Yield[a] (4) α-nitro-oxirane | % Recovery[a] nitroalkene |
|---|---|---|---|---|
| H | Ph | *b; c*, 24 h | 0, 0 | 12[d], 30[d] |
| Me | Me | *b*; *c*, 24 h, 44 h, 91 h | 0; 10, 13, <5 | -; 29, 25, <5 |
| Me | Et | *b; c*, 24 h, 41 h | 10; 12, 17 | 0; 65, 75 |
| Me | $Pr^i$ | *b*, $O_2$; *b*, $N_2$; *b*, 43 h | 44; 36; 0 | 0; 0; 76 |
| Me | Ph | *b; c*, 24 h | 22, 24; 0 | 0, 0; - |
| Me | *p*-$ClC_6H_4$ | *b; c*, 40 h | 27; 0 | 0; 100 |
| Et | $Pr^i$ | *b* | 55 | 0 |
| -$CH_2CH_2CH_2CH_2$- | | *b; c*, 24 h | 0; 0 | <5; 100 |

[a] % Yields were calculated by $^1H$ NMR spectroscopy using an internal standard. [b] The nitroalkene was added to KOH (5 equiv.) in DMSO/$H_2O$ and stirred for 30 min. Saturated aq. $K_3Fe(CN)_6$ (2 equiv.) and $Et_2O$ were added, and the two phase system stirred for 15 min. [c] A two phase system of $CH_2Cl_2$ and $H_2O$, benzyltrimethylammonium hydroxide (0.05 equiv.), KOH (5 equiv.), $K_3Fe(CN)_6$ (2 equiv.), and the nitroalkene were stirred for the time stated. [d] % Yield of PhCHO.

A range of nitroalkenes[2] and treated with an excess of hydroxide in the presence of two equivalents of $K_3Fe(CN)_6$ under different reaction conditions to give the corresponding α-nitro-oxiranes (Table 1). The α-nitro-oxiranes were purified by Kugelruhr distillation and fully characterised. Most of the nitro-oxiranes were prepared by peroxidation[5] of the nitroalkenes (1) with $H_2O_2/OH^-$ (Scheme 3) [*E*-2-nitrobut-2-ene (43%), *E*-2-nitropent-2-ene (65%), *E*-(4-chlorophenyl)-2-nitroprop-2-ene (51%), and *E*-1-nitrocyclohex-1-ene (28%)] for comparison purposes.

The low yields for the DMSO/$OH^-$ method are due to retro-Henry reactions of the intermediate β-hydroxynitronates. The resulting aldehydes and nitroalkanes were volatile and not recovered except for benzaldehyde in the case of *E*-2-nitro-3-phenylprop-2-ene, but no other products were observed. These harsh conditions were suitable for the conjugated and sterically hindered nitroalkenes but gave complete decomposition of (1), $R^1$ = Me , $R^2$ = Me, Et. Longer reaction times gave decomposition of the nitro-oxiranes, and shorter reaction times gave more unreacted starting nitroalkene. The addition of hydroxide and subsequent cyclisation was only successful in DMSO. No products were obtained when using MeOH or dioxane. The phase transfer catalysis method only worked for the reactive nitroalkenes [(1), $R^1$ = Me, $R^2$ = Me, Et].

The α-alkyl group of the nitroalkene appears to be essential and bulky groups in the β-position hinder decomposition of the nitro-oxirane. Attempts to prepare the nitro-oxiranes by oxidation of the β-hydroxynitro compounds or their dianions failed because of retro-Henry or water elimination reactions. The failure of the oxidative addition of hydroxide to *E*-1-nitrohex-1-ene is unexplained.

Oxidative addition of hydroxide to *m*-dinitrobenzene (CH=$CNO_2$ moiety) using the DMSO/$HO^-$ method gave 1-hydroxy-2,4-dinitrobenzene (3%) after 48 h. Reaction *via* rearrangement of a arene α-nitro-oxirane intermediate is possible but loss of a proton from the *o*-hydroxy α-nitro radical intermediate to yield the radical anion of the product is more likely.

**Mechanism**

No significant change in yield was observed in nitrogen (rigorously oxygen free) or oxygen atmospheres or in the absence of light or with light catalysis at 250 or 350 nm, indicating that singlet oxygen addition or photo-induction are unlikely.

We propose that the mechanism in Scheme 1 is most likely. Cyclisation of the intermediate radical anion (**2**) is favoured by reaction between the strongly nucleophilic alkoxide anion (especially in DMSO) and the strongly electrophilic $\alpha$-nitroalkyl radical[3] and overrides the strain of a three-membered ring transition state. The initial product of cyclisation, the unstable radical anion with the unpaired electron in a C-O $\sigma^*$ molecular orbital, will rapidly relax to the more stable radical anion with the unpaired electron in the $\pi^*$ molecular orbital of the nitro group,[3,6] thereby making ring opening less favourable.

**ESR Spectroscopy of the Radical Anion of *E*-1-methyl-1-nitro-2-isopropyloxirane**

Temperature resolved ESR spectroscopy was used to provide evidence for the cyclised radical anion intermediate (**3**) and for the nature of the equilibrium between the non-cyclised $\beta$-alkoxy-$\alpha$-nitroalkyl radical anion (**2**) and the cyclised radical anion (**3**). We have previously shown that electron-capture by nitro compounds and the structure of unstable radical anion intermediates, can be successfully studied using temperature resolved e.s.r. spectroscopy.[6]

In these studies, electrons are generated using ionising radiation, and electron-capture resulting in stable adducts can be achieved using solid solutions at low temperature (77 K) to ensure that primary products are stabilised by immobility. Methyltetrahydrofuran (MeTHF) is an ideal solvent for observing electron-capture by solutes and it gives a glassy solution at 77 K, so that phase separation is avoided. The electron-loss centres are stabilised as solvent radicals, and electrons are able to migrate to solute molecules with little competition from the solvent. The technique is fully described in the literature.[7]

A good ESR spectrum [Figure 1, $A_{//}$ = 30 G, $A_{\perp}$ = 15 G, $A_{iso}$ = *ca.* 20 G, $2B$ = *ca.* 10 G] was obtained in a solid matrix of MeTHF at 77 K with features characteristic (an asymmetric triplet) of an alkylnitro radical anion ($R\dot{N}O_2^-$)[3,6,7] with no change on annealing apart from a decay at the m.p. No features of the ring-opened radical anion (**2**) were observed in the ESR spectrum. The $\alpha$-nitroalkyl radical feature is easily detected[3,6,7] by ESR spectroscopy and is absent, which indicates that ring closure is particularly favoured and that the equilibrium shown in Scheme 1 lies completely over to the right.

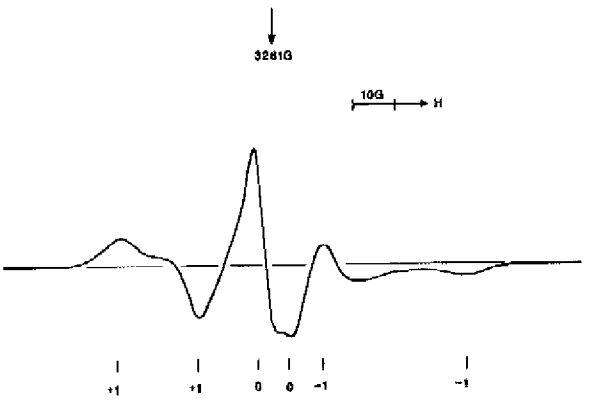


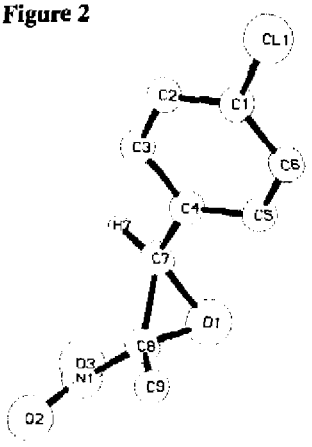

**Figure 1**

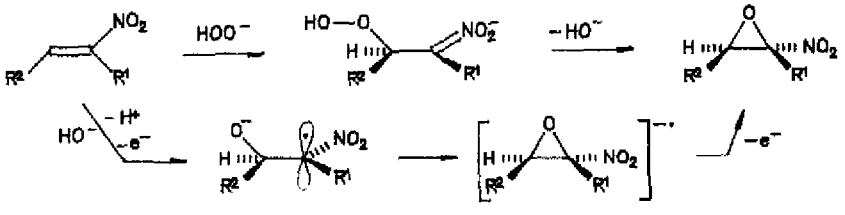
First derivative X-band e.s.r. spectrum for a dilute solution in MeTHF of the radical anions of *E*-1-methyl-1-nitro-2-isopropyl-oxirane after exposure to $^{60}Co$ ϒ-rays at 77 K, showing features assigned to the radical anions.

**Stereochemistry**

There is no data in the literature concerning the stereochemistry of α-nitro-oxiranes. The nitro-oxiranes derived from the oxidative addition and the $H_2O_2/HO^-$ methods are the same and $^1H$ NMR spectroscopy indicated the same stereochemistry for all the oxiranes. The stereochemistry of a sample nitro-oxirane was determined using X-ray crystallography on the crystalline *E*-2-(4-chlorophenyl)-1-methyl-1-nitro-oxirane (Figure 2).[8] The stereochemistry indicates that the alkyl/aryl groups line up *cis* in the intermediates in both methods as shown in Scheme 3.

**Figure 2**




**Scheme 3. Stereochemistry of α-nitroepoxide formation.**

Investigation of analogous reactions with *S*- and *N*-centred anions are underway. A similar cyclisation to a cyclopropane ring *via* a *C*-centred anion has been reported.[9] We wish to thank the SERC for an earmarked studentship (SWJ) and Stephen Hitchcock for an experiment.

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