One- and Two-Electron Oxidation of Hydrazines by Dimethyldioxirane

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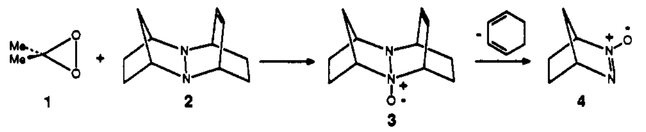
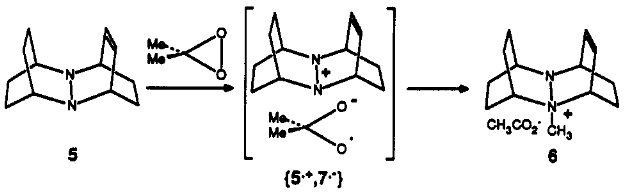
Summary: Dimethyldioxirane (1) reacts with sesquibicyclic hydrazine 2 to give the expected (thermally labile) hydrazine *N*-oxide product and with the homologous hydrazine 5, principally by methyl group transfer, to produce the N-methylated hydrazinium cation acetate 6.

Scheme I



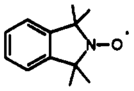
Scheme II



Dimethyldioxirane (1) is a powerful and preparatively useful aprotic oxygenating reagent.[1] In this work, we studied its reaction with some sesquibicyclic hydrazines[2] and discovered a surprising dichotomy between the expected formation of hydrazine *N*-oxides and production of N-methylated hydrazinium cations. Treatment of hydrazine 2[2] with an acetone solution of 1 at −78 °C produced an 85% yield of azo oxide 4,[3] and 15% unreacted 2 was recovered (see Scheme I). It is not surprising that the far more nucleophilic nitrogens of 2 are oxygenated more rapidly than the double bond. Low-temperature ^{1}H-NMR studies in acetone-d_6 showed that hydrazine oxide 3 (δ 6.65 and 6.58 [vinyl multiplets, 1 H each], 4.38, 4.18, 3.99, 3.57 [bridgehead broad s, 1 H each]) is initially produced. Hydrazine oxides have not been previously observed. Although solubility problems prevented quantitative work, the formation of 3 appears to be rapid even at −40 °C. Retro-Diels–Alder cleavage of 3 to 4 and 1,3-cyclohexadiene occurs with a rate constant of 8.6×10^{-4} s^{-1} ($t_{1/2}$ 13 min) at 5 °C, corresponding to ΔG^* of 20.2 kcal/mol.[4]

Despite the small structural difference, the homologous unsaturated hydrazine 5 reacts with 1 to give principally *N*-methylhydrazinium acetate 6 (see Scheme II), which was obtained in 66% yield along with 22% recovered 5, corresponding to an 84% conversion to 6.

Methyl group transfer in a thermal reaction of methyl(trifluoromethyl)dioxirane was recently reported by Adam and co-workers.[5] Addition of nitroxide 8 at 0 °C resulted in immediate formation of the bright red color of the single-electron oxidation product, oxoammonium salt 8^+, and a 9.3% yield of the methyl radical, nitroxide coupling product 9, was isolated upon workup. They also detected 9 (in a far lower, unspecified yield) by HPLC when dimethyldioxirane (1) was employed, but did not see the red color of 8^+.[5] In agreement with their proposed mechanism, we suggest that the methyl-transfer reaction reported here can best be rationalized as proceeding by single-electron transfer (see Scheme II), which would initially produce the ion pair, hydrazine radical cation ($5^{\bullet+}$), $7^{\bullet-}$, the O–O cleaved radical anion derived from 1.[6]



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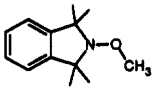

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Protonated 5 is 0.68 p*K* units less acidic than protonated 2 in water,[4b] making it seem unlikely to us that quaternization of a nitrogen of 5 is thermodynamically more difficult than is one of 2. Although steric approach to a nitrogen of 2 is probably slightly easier than to one of 5, we think it unlikely that oxygen transfer rates from 1 to 2 and 5 would differ greatly. We suggest that the only plausible rationalization for the unexpected switch from obtaining the N-oxygenation product from 2 to the methyl-transfer product from 5 would be much faster methyl transfer, which we suggest is initiated by single-electron transfer (see Scheme II). Removal of an electron from 5 (formal oxidation potential E^{f} −0.25 V vs sce[4]) is 6.0 kcal/mol easier than from 2 (E^{f} +0.01) in acetonitrile. Furthermore, the cyclic voltammogram of 1 (studied as the ~0.1 M solution in acetone obtained upon its preparation[1]) shows an irreversible reduction wave which peaks at −0.14 V vs sce (0.5 V/s scan rate) which is not present in blanks containing only acetone. It seems likely that this wave corresponds to reduction of 1. According to Marcus theory, the activation barrier for electron transfer, ΔG^*, is related to the driving force for the electron transfer, ΔG°, and the barrier for vertical electron transfer, λ, by the relationship $\Delta G^* = (\lambda + \Delta G^\circ)^2/4\lambda$.[7] If the only factor causing a

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[1] For reviews, see: (a) Murray, R. W. *Chem. Rev.* 1989, *89*, 1187. (b) Adam, W.; Curci, R.; Edwards, J. O. *Acc. Chem. Res.* 1989, *22*, 205. (c) For preparation and analysis of 1, see: Adam, W.; Chan, Y.; Cremer, D.; Gauss, D.; Scheutzow, D.; Schindler, M. *J. Org. Chem.* 1987, *52*, 2800 and ref 8.

[2] Nelsen, S. F.; Blackstock, S. C.; Frigo, T. B. *J. Am. Chem. Soc.* 1984, *106*, 3366.

[3] Snyder, J. P.; Bandurco, V. T.; Darack, F.; Olsen, H. *J. Am. Chem. Soc.* 1974, *96*, 5158.

[4] (a) Retro-Diels–Alder cleavage of 2 is exothermic (no 2 is detected at equilibrium), and its $t_{1/2}$ at 50 °C in $CDCl_3$ is about 5.5 h.[4b] The cleavage is endothermic for 2-H$^+$ (no protonated azo compound is detected after addition of 1,3-cyclohexadiene).[2] (b) Nelsen, S. F.; Blackstock, S. C.; Frigo, T. B. *Tetrahedron* 1986, *42*, 1769.

[5] Adam, W.; Bottle, S. E.; Mello, R. *J. Chem. Soc., Chem. Commun.* 1991, 771.

[6] (a) AM1 calculations[6b] give the most stable structure for the radical anion derived from 1 with the O,O bond cleaved (∠OCO 105.4°, C,O distances 1.319 and 1.406 Å). (b) AM1: Dewar, M. J. S.; Zoebisch, E. G.; Healy, E. F.; Stewart, J. J. P. *J. Am. Chem. Soc.* 1985, *107*, 3902. Structures were optimized using the substantially improved program VAMP 4.40 (on a Stardent 3000 computer), made available to us by its author, T. Clark, Universität Erlangen-Nürnberg.

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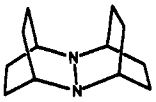
difference in electron-transfer rates were the driving force, which we believe is reasonable for compounds as similar structurally as **2** and **5**, Marcus theory predicts **5** to react over 2500 times as fast as **2** at −78 °C, assuming the ET were 3.5 kcal/mol endothermic to **2** and 2.5 kcal/mol exothermic to **5**. In keeping with the suggestion that electron transfer triggers the methyl-transfer reaction, the even more easily oxidized saturated hydrazine **10** (E^{f} −0.53 V) produces its N-methylated hydrazinium acetate, **11**, even more efficiently than **5** methylates to **6**; a 96% yield of **11** was isolated.



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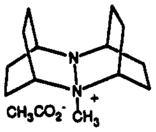

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We are unaware of another type of reaction that efficiently transfers a methyl group by breaking a carbon, methyl bond. It is interesting to consider how important C–Me bond breaking and Me–N bond forming might be at the transition state for methyl transfer. As a test, **10** was reacted with ethylmethyldioxirane,[8] which resulted in a 5:1 ratio of *N*-ethyl-*N*-methyl, acetate/propionate. This corresponds to about a 0.6 kcal/mol lower energy for ethyl-transfer transition state than that involving methyl transfer at −78 °C, as might be expected if which group transfered were principally determined by strength of the C–C bond being cleaved. This is consistent with the methyl transfer being formulated as a β-scission of $7^{\bullet -}$ to acetate anion and a methyl radical,[9] followed by coupling of the methyl radical and the hydrazine radical cation. However, free methyl radicals would be expected to react rapidly with the acetone solvent. The efficient production of **11** observed implies to us that the $\{10^{\bullet +},7^{\bullet -}\}$ pairs are likely to be reacting before they diffuse apart. The activation barrier for cleavage of $7^{\bullet -}$ is calculated to be under 4 kcal/mol,[9] which if true, should allow the cleavage to compete with ion-pair separation.

Our results make it appear that for easily oxidized hydrazines single-electron transfer is more rapid than the usual oxygen-transfer oxidation chemistry shown by **1**, which is a two-electron transfer process, and that rapid β scission of $7^{\bullet -}$ results in formation of methyl- instead of oxygen-transfer product.

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(7) See, for example, eq 47 of: Sutin, N. *Progr. Inorg. Chem.* **1983**, *30*, 441. Also see eq 55 of: Eberson, L. *Adv. Phys. Org. Chem.* **1982**, *18*, 79.

(8) Murray, R. W.; Jeyaraman, R. *J. Org. Chem.* **1985**, *50*, 2847.

(9) (a) AM1 gets $\Delta H^{\ddagger}$ for $Me_2C(O^-)O^\bullet \rightarrow MeCO_2^- + Me^\bullet$ at 3.7 kcal/mol, 23% of the barrier it obtains for methyl extrusion from *tert*-butoxy radical (experimental E_a ca. 13 ± 2 kcal/mol). (b) It has been suggested[1b] that $7^{\bullet -}$ would rapidly rearrange to the radical anion of methyl acetate. We have been unable to find a low-energy transition state for a direct methyl shift reaction which maintains overlap between the methyl group and both the central carbon and an oxygen and believe that this rearrangement would proceed by cleavage and radical coupling. (c) AM1 gets $\Delta H^{\ddagger}$ for ethyl extrusion from $EtMeC(O^-)O^\bullet$ at 2.5 kcal/mol, 1.2 kcal/mol below that for methyl extrusion.