A Convenient Nitroxide Radical Synthesis

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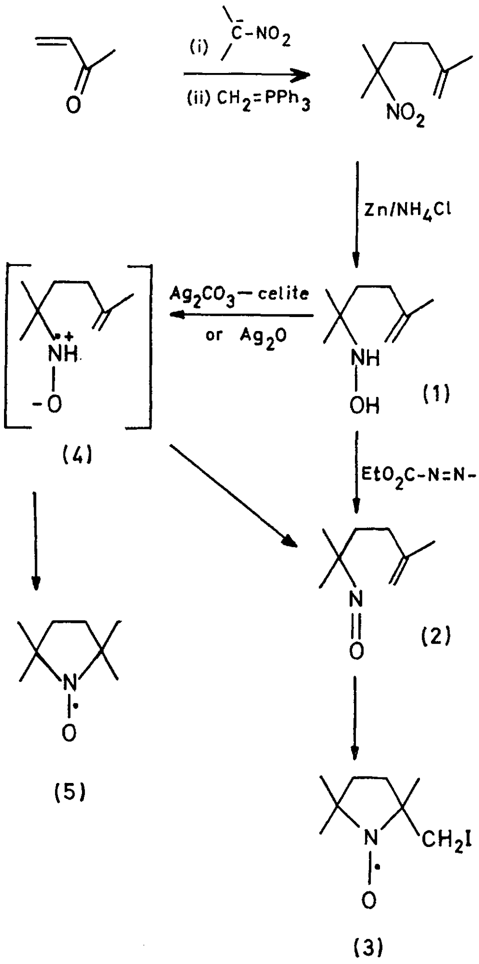
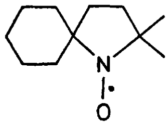
Summary A number of suitably substituted $\delta\epsilon$-unsaturated nitroso-compounds have been prepared and cyclised to pyrrolidino-nitroxide radicals.



Scheme

Some time ago we described the ready formation of a stable nitroxide radical by treatment of an appropriately substituted nitroso-olefin with iodine.[1] We have now examined this general type of reaction using the simpler substrate (**2**) which is readily prepared as outlined in the Scheme. Treatment of (**2**) with iodine in chloroform gives the pure iodo-nitroxide (**3**) as a yellow-orange liquid [$M^+ + 1$ 269,[‡] M^+ 268; e.s.r. ($CHCl_3$) triplet $a_N = 13·6$ Oe, $g = 2·0064$] in 6% yield after column chromatography. The low yield can be ascribed to two major factors: (i) the oxidation (Ag_2CO_3–celite[2] or Ag_2O) of the hydroxyamino-olefin (**1**) does not generate the desired nitroso-olefin (**2**) exclusively. By column chromatography we have been able to isolate the parent nitroxide (**5**)[§] in 20% yield. The exact mechanism of formation of this compound is uncertain but we suggest that the precursor is the monoalkyl nitroxide (**4**)[3] which can undergo cyclisation in a manner analogous to certain olefinic aminium radical cations.[4] This is partially substantiated by the fact that no trace of (**5**) is observed when the oxidation of (**1**) is accomplished with diethyl azodicarboxylate,[5] a reaction which converts a hydroxylamine into a nitroso-compound by a presumed concerted process. (ii) It has been shown that the nitroso-olefin (**2**) is itself rather unstable and readily undergoes intramolecular 'ene' cyclisation.[6]



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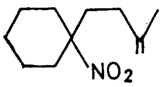

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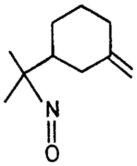

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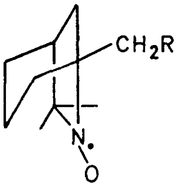

(9)

Similarly, the spiro-nitroxide (**6**) m.p. 29–31·5°, [e.s.r. (Et_2O) triplet $a_N = 13·9$ Oe, $g = 2·0070$)] is prepared in 30% yield from the nitro-olefin (**7**). We have also demonstrated that the stable nitroso-olefin (**8**) (dimer m.p. 77–79°), readily affords the bicyclo-[3,2,1] iodo-nitroxide (**9**, R = I (m.p. 96°, [$M^+ + 1$ 295,[‡] M^+ 294; e.s.r. ($CHCl_3$) triplet $a_N = 14·4$ Oe, $g = 2·0072$] in 40% yield which can be converted into the very volatile liquid nitroxide (**9**, R = H) [$M^+ + 1$ 169,[‡] M^+ 168; e.s.r. ($CHCl_3$) triplet $a_N = 15·6$ Oe, $g = 2·0071$] by Raney nickel reduction followed by re-oxidation of the resultant amine.

This process represents a bifurcated approach to the synthesis of pyrrolidino nitroxide radicals. Preliminary results indicate that the scope of this reaction may also be extended to the piperidino-class. Furthermore, we antici-

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[‡] A strong $M^+ + 1$ peak is a mass spectral characteristic of nitroxide radicals, E. F. J. Duynstee, M. E. A. H. Mevis, H. K. Ostendorf, and R. J. de Kock, *Rec. Trav. Chim.*, 1968, **87**, 945; A. Morrison and A. P. Davies, *Org. Mass Spec.*, 1970, **3**, 353.

[§] This compound is identical to an authentic sample.

pate that the use of other radical initiators or nucleophilic displacement of I$^-$ will augment the versatility of the overall sequence.

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[1] D. M. Hawley, J. S. Roberts, G. Ferguson, and A. L. Porte, *Chem. Comm.*, 1967, 942. For a recent review of nitroxide radical syntheses see, E. G. Rozantsev and V. D. Sholle, *Synthesis*, 1971, 190.

[2] J. A. Maassen and Th. J. de Boer, *Rec. Trav. Chim.*, 1971, **90**, 373.

[3] For references to these species see Th. A. J. W. Wajer, A. Mackor, and Th. J. de Boer, *Tetrahedron*, 1969, **25**, 175.

[4] G. Esposito, R. Furstoss, and B. Waegell, *Tetrahedron Letters*, 1971, 895, 899; J.-M. Surzur, L. Stella, and R. Nouguier, *Tetrahedron Letters*, 1971, 903; Y. L. Chow, R. A. Perry, and B. C. Menon, *Tetrahedron Letters*, 1971, 1549.

[5] E. C. Taylor and F. Yoneda, *Chem. Comm.*, 1967, 199.

[6] W. B. Motherwell and J. S. Roberts, Following Communication.