Hydrogen Abstraction From Unactivated Hydrocarbons Using a Photochemically Excited Isoindoline Nitroxide

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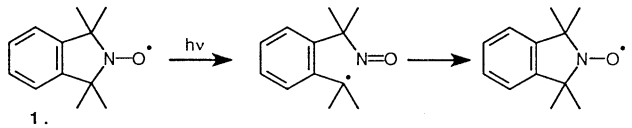
The photochemically excited nitroxide, 1,1,3,3-tetramethylisoindolin-2-yloxyl (**1**$^{\bullet}$), abstracts primary, secondary or tertiary hydrogens from unactivated hydrocarbons including cyclohexane, isobutane and *n*-butane. The resultant carbon-centred radicals are rapidly and efficiently trapped by ground state nitroxide. Hydrogen abstraction from methane may also occur, but is masked by secondary photochemical reactions.

Nitroxides are stable free radical species which, in the ground state, do not normally dimerise, add to alkenes or abstract hydrogens. Photochemically excited nitroxides, however, abstract hydrogens and the resulting radicals are trapped with further ground state nitroxide. This has been demonstrated with TEMPO nitroxides, but only with activated bonds.[1] The TEMPO class of nitroxides suffer from photodegradation by α-cleavage leading to loss of NO and alkene formation. Isoindoline systems on the other hand are more stable and offer several advantages over the less rigid nitroxides.[2] In this letter we report the first use of a photochemically excited isoindoline-based nitroxide 1,1,3,3-tetramethylisoindolin-2-yloxyl (**1**$^{\bullet}$) to abstract *unactivated* tertiary, secondary and even primary hydrogens from a range of alkanes (Scheme 1). The resultant radicals are rapidly and efficiently trapped by ground state nitroxide and can be isolated via standard separation techniques.[3]

Isoindoline systems are more robust towards α-cleavage type photodegradation, as the more rigid system would favour recombination of the resultant carbon-centred radicals and the adjacent nitroso group, therby re-forming the nitroxide and diffusing the excitation energy (Scheme 2).

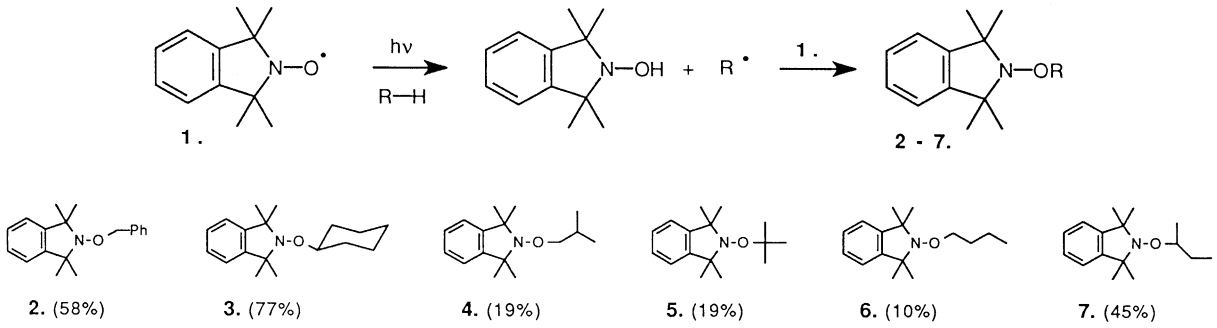


1.

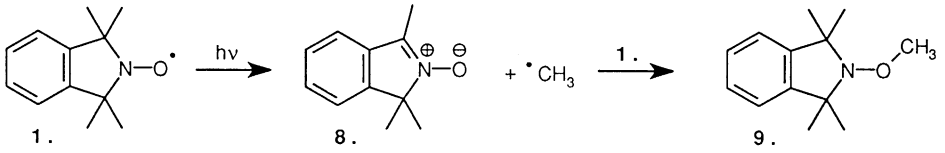
Scheme 2.

Blank experiments involving photolysis of solutions of the nitroxide in benzene as an inert solvent however, demonstrates some β-fragmentation of **1** to generate the nitrone (**8**) and methyl radicals[4] (Scheme 3). This is a novel, as yet unreported, photoprocess for nitroxides, but there is supporting evidence from mass spectroscopy[5] where such fragmentation is the dominant pathway. With methane as the substrate, methyl radical adducts (**9**) were detected, but at levels too close to that arising from nitroxide fragmentation for any conclusions to be drawn. Using broad band photolysis, with prolonged exposure time the trapped alkoxyamine adducts undergo secondary photo-processes leading to degradation. Selection of the appropriate wavelength light should allow greater synthetic yields as well as decrease methyl scission and our studies are continuing in this area.

In a typical procedure[6] involving isobutane, 1,1,3,3-tetramethylisoindolin-2-yloxyl (**1**) (150 mg, 0.79 mmol) was dissolved in liquefied isobutane (30 mL) and the solution irradiated for 2 h in a quartz reaction vessel using a 400LQ medium pressure mercury lamp, without optical filtering, while immersed in acetone-dry ice. Rotary evaporation and HPLC separation gave **4** , 9.7 mg (18.5% based on a 27% conversion of **1**). ^{1}H NMR: δ 1.0 (d, 6H, J_{7Hz}, $H_{3'}$, $H_{4'}$), 1.25 (s, 6H, 2 ring



Scheme 1.



Scheme 3.

CH_3), 1.43 (s, 6H, 2 ring CH_3), 1.95 (m, 1H, $J_{6.7Hz}$, $H_{2'}$), 3.75 (d, 2H, J_{7Hz}, $H_{1'}$), 7.08 (m, 2H, J_{3Hz}, H_5, H_6), 7.17 (m, 2H, J_{3Hz}, H_4, H_7) and **5**, 9.7 mg (18.5% based on a 27% conversion of **1**). ^{1}H NMR: δ 1.30 (s, 9H, $H_{2'}$, $H_{3'}$, $H_{4'}$), 1.32 (s, 6H, 2 ring CH_3), 1.49 (s, 6H, 2 ring CH_3), 7.08 (m, 2H, H_5, H_6), 7.17 (m, 2H, H_4, H_7). ^{13}C NMR: δ 25.5 (ring CH_3), 29 ($C_{2'}$, $C_{3'}$, $C_{4'}$), 30.5 (ring CH_3), 68 (C_1, C_3), 84.2 ($C_{1'}$), 121(C_6, C_5), 127 (C_4, C_7), 145 (C_{3a}, C_{7a}). GC/MS of the mixture gave two peaks (retention 16.9 min and 17.2 minutes, 0.25 mm DB-1 column), each with major ions at m/z = 247 and 191. ($C_{16}H_{25}NO$ requires m/z = 247).

Similarly, 1,1,3,3-tetramethylisoindolin-2-yloxyl (**1**) (254 mg, 1.3 mmol) was irradiated for 1hr in distilled toluene (350 mL). The UV lamp was immersed in the solution during the irradiation. Nitrogen was bubbled continuously through the solvent. After irradiation a dark brown oil was produced upon rotary evaporation of the solvent. The oil was taken up in methanol (5 mL) and reversed phase HPLC separation of the mixture gave the benzyl adduct **2** 150 mg (58% based on a 69% conversion of **1**). ^{1}H NMR: δ 1.45 (s, 12H, ring CH_3), 5.0 (s, 2H, $H_{1'}$), 7.15-7.30 (m, 4H, H_{3a},H_{7a}), 7.3-7.5 (m, 5H, $H_{2'}$-$H_{7'}$); ^{13}C NMR: δ 67 (C_1, C_3), 79.5 ($C_{1'}$), 121.5 (C_6, C_5), 127.1 (C_4, C_7), 127.6 ($C_{5'}$), 128.2 ($C_{6'}$, $C_{4'}$), 128.4 ($C_{3'}$, $C_{7'}$), 138 ($C_{2'}$), 145 (C_{3a}, C_{7a}) which agrees well with literature.[8]

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References and Notes

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2 A.L.J. Beckwith, V.W. Bowry, and K.U. Ingold, *J. Am. Chem. Soc.*, **114**, 4983(1992). b) V.W. Bowry, and K.U. Ingold, *J. Am. Chem. Soc.*, **114**, 4992(1992). c) S.R. Harrison, R.S. Pilkington, and L.H. Sutcliffe, *J. Chem. Soc., Faraday Trans. 1*, **80**, 669(1984).

3 The hydroxylamine by-products are rapidly reoxidised by adventitious oxygen to reform **1** during the experiment and work up.

4 GC/MS of the reaction mixture gave a peak with m/z = 175 attributable to **8** and **9** was isolated from the reaction mixture and fully characterised.

5 J.P. Bartley, W.K. Busfield, I.D. Jenkins, and S. Thang, *Organic Mass Spectrom.*, **23**, 739(1988).

6 All yields reported are for isolated products at high conversion and are based on actual nitroxide consumed. Greater yields (HPLC determined) could be obtained at lower conversions. All products were susceptible to some degree of secondary photodegradation (especially **5**) and isolated ratios reflect this. All compounds were identified by NMR and mass spectrometry and satisfactory elemental analyses were obtained for all new compounds.

7 The comixtures of **4/5** and **6/7** could not be completely separated by preparative HPLC. Yields were calculated from analytical HPLC and supported by NMR integration of the isolated mixtures.

8 R.D. Grant, P.G. Griffiths, G. Moad, E. Rizzardo, and D.H. Solomon, *Aust. J. Chem.*, **44**, 1407(1991).