1-Manxyl: A Persistent Tertiary Alkyl Radical that Disproportionates via ϵ-Hydrogen Abstraction

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Herein we present EPR, ENDOR, spin trapping, product studies, and ab initio results for the bicyclo[3.3.3]undec-1-yl, or 1-manxyl, radical **1**. This sterically open radical shows remarkable persistence and unexpectedly small β-hydrogen hyperfine couplings. Surprisingly, unlike their small-ring cousins,[1] simple bridgehead radicals of medium-ring bicycloalkanes have not been reported.

The special structure/strain relationship in medium-ring bicyclic frameworks has allowed the construction of such unusual chemical entities as one- and three-electron bonds,[2] symmetrical C−H−C hydride-bridged carbenium[3] and N−H−N hydrogen-bonded ammonium cations,[4] interbridgehead donor−acceptor complexes,[5] hyperstable olefins,[6] near-planar aliphatic amines,[7] stabilized bridgehead carbocations,[8] and rapidly autoxidizable alkanes.[9] Our interest in through-space perturbation of unpaired electron centers[10] has drawn us to the rich potential of interbridgehead chemistry, for which **1** is a key reference species.

With its 27.2 kcal/mol strain energy (SE)[11] (Table 1) and high bridgehead reactivity,[12] manxane (**2**)[13] readily undergoes hydrogen abstraction by *tert*-butoxyl radicals to yield radical **1**.[14] Figure 1 shows the EPR spectrum obtained from photolysis of a cyclopropane solution of manxane[15] and di-*tert*-butyl peroxide; identical spectra arise in toluene, methylcyclopentane solutions, and neat di-*tert*-butyl peroxide. We assign this spectrum to 1-manxyl radical **1** on the following grounds: (1) the radical is tertiary, showing neither an α C−H hyperfine coupling constant nor a corresponding splitting in the 2,4,6-tri-*tert*-butylnitrosobenzene spin-trapping product;[16] (2) simulation of the spectrum (Figure 1) requires five different sets of three equivalent protons; (3) the radical decays via an extraordinarily slow bimolecular process, and trapping by addition of n-Bu$_3$SnH immediately after photolysis turns off production of its disproportionation products, of which one is [3.3.3]propellane; (4) the known autoxidation of **2** is specific for the bridgehead site.[9,12]

Table 1. Calculated Heats of Formation, Strain Energies and Bond Dissociation Energies[a]

compound	total energy[b]	ΔH_f[c]	SE[d]	BDE[e]
manxane (**2**)	−428.17907	−20.4 (−21.2)[f]	28.0 (27.2)	
1-manxyl (**1**)	−427.56808	14.6	19.9	87.9
2-manxyl (**3**)	−427.55704	21.5	24.6	94.8
3-manxyl (**4**)	−427.55538	22.5	25.6	95.8
1,1-bimanxyl (**7**)	−855.16181	−11.1	80.8	
[3.3.3]propellane (**8**)	−427.04326	−28.7	14.9	
1-manxene (**9**)	−426.97830	13.0	35.0	

[a] In kcal/mol; structures were fully optimized at the HF/6-31G* level, using Spartan 4.0 (Wavefunction Inc., Irvine, CA). [b] Total energies are given in hartrees, 1 hartree = 627.5 kcal/mol. [c] Calculated (experimental) from the Wiberg group equivalents (Wiberg, K. B. *J. Org. Chem.* **1985**, *50*, 5285) for **2**, **7**, **8**, and **9**. The BDE estimates were used to calculate values for the product radicals **1**, **3**, and **4**. [d] Strain energy; from calculated (experimental) ΔH_f and the Benson group equivalents (Benson, S. W. *Thermochemical Kinetics*; John Wiley: New York, 1976) for **2**, **7**, **8**, and **9** and from isodesmic reactions *vs.* isobutane/*tert*-butyl radical for **1** and propane/isopropyl radical for **3** and **4**. [e] Based on BDE (t-Bu−H) = 96.0 kcal/mol (Gutman, D. *Acc. Chem. Res.* **1990**, *23*, 375) and BDE (i-Pr−H) = 98.2 kcal/mol (Russell, J. J.; Seetula, J. A.; Gutman, D. *J. Am. Chem. Soc.* **1988**, *110*, 3092). [f] See ref 11.

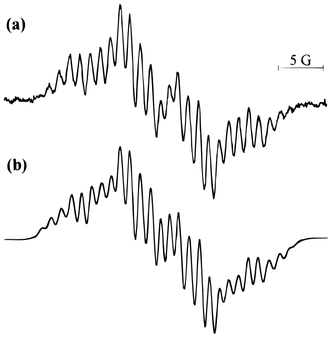

Figure 1. (a) EPR spectrum (9.1 GHz) of 1-manxyl radicals obtained on hydrogen abstraction from manxane by *tert*-butoxyl radicals in cyclopropane at −55 °C (g = 2.0024). (b) Computer simulation.

With 18 secondary and only 2 tertiary C−H bonds in **2**, significant secondary hydrogen abstraction might be expected on statistical grounds, but no evidence for the secondary 2- and 3-manxyl radicals **3** and **4** is seen in the EPR spectra under any conditions. Besides being the unique tertiary sites in manxane, the bridgeheads also afford the greatest strain relief upon

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(12) Manxane (**2**) is autoxidized by air to form a mixture of bridgehead peroxides and hydroperoxides, and 1-manxyl chloride undergoes solvolysis *ca.* 10^4 times faster than *tert*-butyl chloride, consistent with a MM estimate of 6.8 kcal/mol strain relief for bridgehead conversion to a trigonal center. Parker, W.; Tranter, R. L.; Parker, W.; Watt, C. I. F.; Chang, L. W. K.; Schleyer, P. v. R. *J. Am. Chem. Soc.* **1974**, *96*, 7121.

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(15) Manxane (**2**) was prepared by a modified synthesis following Leonard et al.:[13b,c] mp 191 °C (lit. 192 °C); ^{1}H NMR (300 MHz, CDCl$_3$) δ 2.38 (m, 2H), 1.45−1.55 (m, 18H), in accord with previous literature;[13] ^{13}C NMR (300 MHz, CDCl$_3$) δ 30.74 (2 × CH, $J_{^{13}\mathrm{CH}}$ = 120 Hz), 28.96 (6 × CH$_2$, $J_{^{13}\mathrm{CH}}$ = 124.2 Hz), 20.1 (3 × CH$_2$, $J_{^{13}\mathrm{CH}}$ = 125 Hz); MS (EI) m/z (relative intensity) 152 (M$^+$, 31), 124 (27), 109 (47), 96 (100), 81 (91), 67 (85), 55 (60).

(16) Spin trapping of **1** with 2,4,6-tri-*tert*-butylnitrosobenzene (TBN) gives a persistent N-alkoxyanilino radical with g = 2.003, a_N = 9.0 G (1N), a_H = 1.8 G (2H). The 1.8 G *meta*-H hyperfine and the absence of β-hydrogen splittings indicate exclusive addition at the oxygen atom of TBN by an unreactive tertiary radical such as **1**, consistent with the observed multiminute trapping time. Terabe, S.; Konaka, R. *J. Chem. Soc., Perkin Trans. 2* **1973**, 369.

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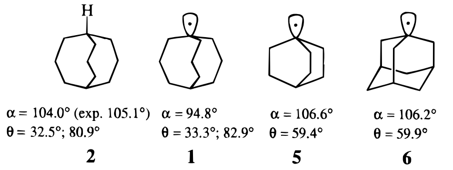

Figure 2. HF/6-31G* geometry-optimized structures of manxane (**2**), 1-manxyl (**1**), 1-bicyclo[2.2.2]octyl (**5**), and 1-adamantyl (**6**) radicals. Legend (C_3 refers to the axis of symmetry): $\alpha = C_3C^{\bullet}C_\beta$ angle; $\theta = C_3C^{\bullet}C_\beta H_\beta$ torsion angle.

hydrogen abstraction, resulting in a BDE (bond dissociation energy) difference of 6.9 kcal/mol (Table 1). Even a fraction of this difference between H-abstraction transition states[17] would easily outweigh the 9:1 statistical factor.

The experimental EPR spectrum of **1**, essentially independent of temperature, can be simulated[18] with the following hyperfine constants: $a_H = 5.3$ G (3H), $a_H = 2.4$ G (3H), $a_H = 0.99$ G (3H), $a_H = 0.88$ G (3H) (see Figure 1); ^{1}H ENDOR[19] studies revealed two more couplings at 0.19 and 0.08 G.[20] INDO calculations[21] performed on PM3 and UHF/6-31G* geometries of **1** reproduce the magnitude of the smaller couplings well but predict a β-hydrogen hyperfine of ~20 G, well above the largest a_H observed (5.3 G). Tentative a_H assignments, based on INDO results, are 5.3 G and 0.88 G for β-H, 2.4 G and 0.99 G for γ-H, 0.08 G for δ-H, and 0.19 G for the ϵ-H.

According to the usual McConnell relation,[22] the 5.3 G β-H splitting for **1** is unexpectedly low. The radical cations of [3.3.3]-propellane[23] and 1,5-diazabicyclo[3.3.3]undecane[24] show β-H couplings of 17 and 22 G, respectively, interpreted as reflecting nearly planar radicals with θ angles (Figure 2) of approximately 30°.[25] The more comparable $a_{H\beta}$ values of 6.64 and 6.58 G for the localized radicals 1-bicyclo[2.2.2]octyl (**5**) and 1-adamantyl (**6**) are attributed to pyramidal geometries at the bridgehead radical sites.[26] For **1**, however, the UHF/6-31G* structure shows only modest pyramidalization and β-hydrogens that are more nearly eclipsed than those in **5** and **6**, leaving the low $a_{H\beta}$ value puzzling.

The decay of **1** in methylcyclopentane, monitored by EPR, is second order with a rate constant of 0.5 $M^{-1}s^{-1}$ at 23 °C and a half-life of 6 h for a 4×10^{-4} M initial radical concentration.[27] Such exceptional persistence is unique considering the lack of steric protection around the radical center.[28] In principle, **1** might dimerize to 1,1-bimanxyl (**7**), but no **7** is detected, and the calculated F-strain (Table 1) in this compound is large, *ca.* 25 kcal/mol. A novel ϵ-disproportionation[29] gives **2** and [3.3.3]-propellane (**8**), whose presence in the product mixture has been confirmed by independent synthesis and GC-MS.[30] A second 150 amu product, seen by GC-MS, is tentatively assigned to 1-manxene (**9**), the Bredt alkene from conventional β-hydrogen disproportionation of **1**. That both these products are derived from **1** is confirmed by their absence in samples where **1** has been quenched after photolysis by the addition of *n*-Bu_3SnH. Ab initio results (Table 1) indicate that ϵ-disproportionation is thermochemically preferred; further studies to confirm the assignment of **9** are underway.

To date, persistent alkyl radicals have depended on steric protection by bulky groups around the radical center. The 1-manxyl radical **1** is the first example of a persistent simple alkyl radical whose exceptionally long lifetime arises not from steric protection but from the high strain of all its decomposition products. The remarkable persistence and puzzlingly low hyperfine splittings for the β-hydrogens in **1** suggest that even such simple entities as bridgehead alkyl radicals have not yet given up all their secrets. In ongoing research, we are exploring related bicyclic systems in which the effects of positioning heteroatoms at the bridgehead opposite to the radical center are probed.

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Supporting Information Available: Details of manxane synthesis; experimental procedures for EPR, ENDOR, spin trapping, and kinetic studies of **1**; INDO calculations on **1**; UHF/6-31G* geometry of **1** (10 pages). See any current masthead page for ordering and Internet access instructions.

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