Evidence for *Reversible* Ring-opening of the α-Cyclopropylbenzyl Radical

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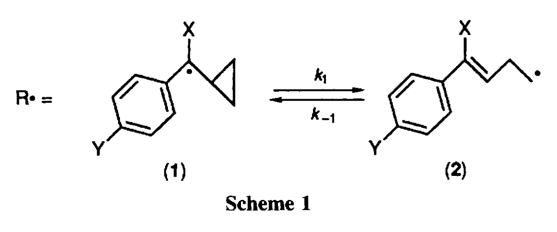
Kinetic absorption spectroscopy, EPR, and tributylstannane product data indicate that the α-cyclopropylbenzyl radical (**1a**) undergoes reversible ring-opening to the 4-phenylbut-3-enyl radical (**2a**) and that equilibrium favours the ring-closed form, (**1a**).

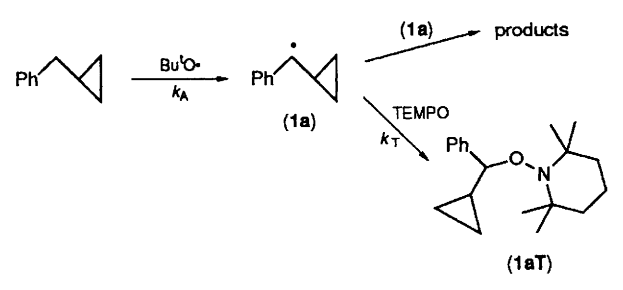
It has recently been reported[1] that α-arylcyclopropylcarbinyl radicals (**1**), formed by pulse radiolysis of appropriate benzoate esters, rearrange to the corresponding 4-arylbut-3-enyl radicals (**2**) and that the reverse ring-closing reaction 'must occur at least about an order of magnitude slower than the ring-opening process,' *i.e.* Scheme 1 with $k_1 \geqslant 10k_{-1}$. In particular, the UV absorption attributed to α-cyclopropylbenzyl radical (**1a**) (X = Y = H) was reported to decay with a first-order rate constant of 2.7×10^5 s^{-1} at 22 °C, implying that $k_1 = 2.7 \times 10^5$ s^{-1} and $k_{-1} \leqslant 3 \times 10^4$ s^{-1}.

In contrast, a nitroxide radical trapping study[2] has suggested that ring-opening of (**1a**) is not only reversible but that equilibrium may favour the ring-closed form. Thermochemical calculations[3] also indicate that ring-opening (**1a**) → (**2a**) is thermodynamically disfavoured with $\Delta\Delta G°(300\ \text{K})$ +14 kJ mol^{-1} (which implies $k_{-1} >> k_1$). In conformity with this thermodynamic information, we report herein direct evidence that the ring-opening of (**1a**) is not detectable even under conditions where radical–radical reactions are the predominant mode of radical decay. We also report evidence that ring-closure of (**2a**) is over two orders of magnitude faster than the upper limit estimated from the pulse radiolysis data (*vide supra*).[1]

Laser flash photolysis (LFP)[4] (308 nm) of a solution containing α-cyclopropyltoluene (0.5 M) and di-t-butyl peroxide (0.4 M) in benzene (see Scheme 2) afforded a UV absorption spectrum with a sharp maximum at 325 nm on the shoulder of a broader peak of similar intensity centred near 300 nm. Time evolution of the spectrum (taken at 2, 3, 5 and 9 μs) with and without the radical quenchers 2,2,6,6-tetramethylpiperidin-1-oxyl (TEMPO) or O_2 indicated that this spectrum arose from a single species which, since benzyl and diphenylmethyl radicals have sharp absorption maxima at 317 and 329 nm, respectively, we can safely assign as (**1a**).



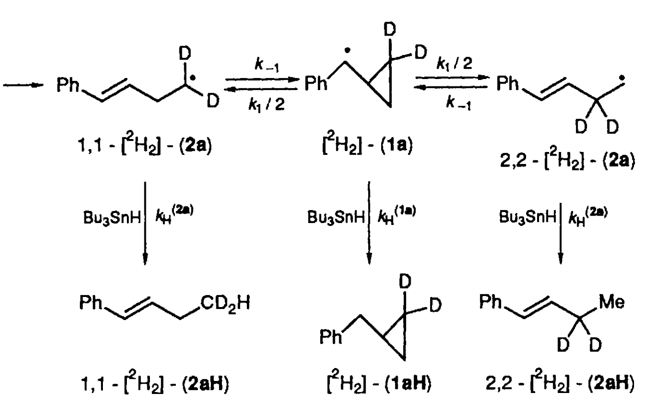
Scheme 1



Scheme 2

Rapid pseudo-first-order growth of the 325 nm absorption (measured rate constant, k_A, 4.4×10^{6} mol^{-1} dm^{3} s^{-1} at 18 °C in benzene) was followed, in the absence of radical quenching agents, by its slow second-order decay, a decay which had a *ca.* seven-fold longer life-time[†] than that of the species monitored by Masnovi *et al.*[1] Addition of the radical scavenger TEMPO in small increments (5 × 2 mM) produced more rapid decay of (**1a**) which now followed (pseudo) first-order kinetics (see Scheme 2). The experimental first-order decay rate constant, $k_{\mathrm{exptl.}}$, increased linearly with [TEMPO], *i.e.* $k_{\mathrm{exptl}} = k_0 + k_T[\mathrm{TEMPO}]$,[4] and the 18 °C data gave k_T values of 3.1 (±0.2) × 10^{7} mol^{-1} dm^{3} s^{-1} in benzene and 7.8 (±0.8) × 10^{7} mol^{-1} dm^{3} s^{-1} in hexane.[5] The magnitudes of k_T and of the solvent effect are consistent with previous measurements for benzylic radicals, *e.g.*, $k_T^{\mathrm{PhCMe_2}} = 11 \times 10^{7}$ mol^{-1} dm^{3} s^{-1} in hexane and k_T^{benzyl} (hexane)/k_T^{benzyl} (benzene) = 2.3.[5] LC-MS analysis[6] of the spent TEMPO-quenching reaction mixture indicated that only one trialkylhydroxylamine was produced, the nitroxide-trapped unrearranged species (**1aT**).[‡]

Photolysis of di-t-butyl peroxide with α-cyclopropyltoluene in cyclopropane at −80 °C in a Varian E104 EPR spectrometer using microwave levels of *ca.* 0.2 mW afforded a spectrum too complex for an unambiguous detailed analysis but which was clearly that of a benzylic radical with one α-hydrogen (a^{H} 16 Gauss) having typical couplings[7] to the aryl hydrogens together with small couplings to cyclopropyl ring hydrogens, *i.e.*, (**1a**).[§] Certainly the spectrum was not due to (**2a**). Photolysis of the same reactants in benzene at 20 °C also afforded a weak EPR spectrum which can again be assigned to (**1a**). The absence of EPR signal due to (**2a**) at both temperatures indicates that if (**1a**) undergoes irreversible ring-opening it does so very slowly indeed!



Scheme 3

To study the ring-closure of (**2a**), we treated 1-iodo-4-phenylbut-3-ene with Bu$^n{}_3$SnH (1.1 mol equiv.) and di-t-butyl hyponitrite as radical initiator (0.05 mol equiv., see Scheme 3). At 42 °C the ratio of ring-open to ring-closed products did not vary significantly with the stannane concentration, *i.e.*, [(**2aH**)]/[(**1aH**)] = 8.8 (±0.4) (GC). Similar treatment of 1,1-dideuterio-1-iodo-4-phenylbut-3-ene afforded the same ratio of ring-opened to ring-closed products by GC but the degree of deuterium label scrambling (measured by ^{2}H NMR analysis) varied with the stannane concentration: $[\mathrm{Bu^n{}_3SnH}]_{\mathrm{initial}}$ = 0.15, 0.40, 1.0, and 1.8 M afforded [1,1-[^{2}H$_2$]-(**2aH**)]/[2,2-[^{2}H$_2$]-(**2aH**)] = 1.03, 1.12, 1.33, and 1.55 (±0.06), respectively. Thus, with the assumption that the deuterium label has no kinetic effect, the usual kinetic analysis[8] of Scheme 3 and the appropriate hydrogen transfer rate constant ($k_H^{(2a)} = k_H^{1°\text{-alkyl}} = 3.4 \times 10^{6}$ mol^{-1} dm^{3} s^{-1} at 42 °C)[9] give a vinyl migration rate constant of 6×10^{6} s^{-1} and, thus, a ring-closure rate constant, k_{-1}, 1.2×10^{7} s^{-1} at 42 °C.

The preponderance of ring-opened products, in spite of the above LFP and EPR evidence that (**1a**) is the thermodynamically preferred form, indicates that (benzylic) (**1a**) is much less reactive than (1°-alkyl) (**2a**) towards the stannane ($k_H^{(2a)} >> k_H^{(1a)}$ in Scheme 3). This selectivity for (**2a**) over (**1a**) is congruent with available k_H data, *i.e.*,[9,10] $k_H^{\mathrm{alkyl}}/k_H^{\mathrm{benzyl}} = 80$ at 25 °C.[¶]

In conclusion, evidence presented here indicates that cyclopropylbenzyl radicals undergo reversible ring-opening at ordinary temperatures with the ring-closed form being thermodynamically preferred. We suggest that the reported first-order components of Masnovi *et al.*'s[1] pulse radiolysis decay traces probably arose from fragmentation of initial radical anions[11] (which absorb strongly at the monitored wavelengths[1,11]) and that the residual or *persistent* absorptions they observed may have arisen from real cyclopropylbenzyl radicals which decayed more slowly and by second-order processes. The lack of observable ring-opening in (**1a**), except in stannane where trapping selectivity strongly favours the ring-open product, casts doubt on calibrations and mechanis-

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[†] Second-order kinetics were indicated by the excellent second-order curve fitting (correlation coefficient $<r> = 0.9991$ for 44 points) and by variation of the decay rate with laser intensity. When a first-order decay curve was fitted to the initial 30% decrease in the 325 nm absorption, a rate constant of 4×10^{4} s^{-1} was obtained. Masnovi *et al.* reported 2.7×10^{5} s^{-1}.

[‡] Identified by co-injection of authentic material which was prepared by heating a benzene solution of di-t-butyl hyponitrite (a thermal source of Bu^{t}O$^•$), α-cyclopropyltoluene, and excess TEMPO (*ca.* 0.02 M) at 45 °C for 18 h followed by flash chromatography. ^{1}H NMR (CCl$_3$D) δ 0.2 (m, 2H), 0.4 (m, 2H), 0.8—1.4 (m, 19H), 4.25 (d, 1H, *J* 10 Hz), 7.2 (m, 5H).

[§] Couplings within (**1a**) should afford an EPR spectrum with 648 lines! Computer simulation with the following coupling constants (based on data in ref. 7) gives a reasonable match with the spectrum observed at −80 °C: $a^{\mathrm{H}\alpha} = 16.3$, $a^{\mathrm{H}ortho} = 5.2$, $a^{\mathrm{H}meta} = 1.8$, $a^{\mathrm{H}para} = 6.2$, $a^{\mathrm{H}\beta} = 2.5$, $a^{\mathrm{H}\gamma syn} = 2.0$, and $a^{\mathrm{H}\gamma anti} = 3.0$ Gauss. Saturation of the EPR spectrum above a relatively low microwave power is a characteristic of benzylic radicals. By contrast, (**2a**) would have a simple primary radical spectrum (nine lines) which would not be so readily saturated.

[¶] The value of k_1 cannot be reliably determined from the stannane product data because $k_H^{(1a)}$ is not known. However, by assuming $k_H^{(2a)}/k_H^{(1a)} = k_H^{\mathrm{alkyl}}/k_H^{\mathrm{benzyl}} = 80$, one may calculate, $k_1 = k_{-1}(k_H^{(1a)}/k_H^{(2a)})[(\mathbf{2aH})]/[(\mathbf{1aH})] = 0.11\,k_{-1} = 1.3 \times 10^{6}$ s^{-1} at 42 °C.

tic inferences which have relied on ring-opening of the phenyl group stabilized cyclopropylcarbinyl radicals as clocks.[1,12,13]||

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|| Substituents X and Y in Scheme 1 may alter the position of equilibrium through their radical-stabilizing and non-bonding interactions [*e.g.*, destabilization of (**1**) from interaction of X with the *ortho* hydrogens]. However, except in extreme cases (such as a very bulky X group), it seems most unlikely that these effects would make ring-opening (**1**) → (**2**) irreversible under LFP or radiolysis conditions.