Lifetimes of 1,5-Biradicals Formed from Triplet *o*-Alkoxy Ketones

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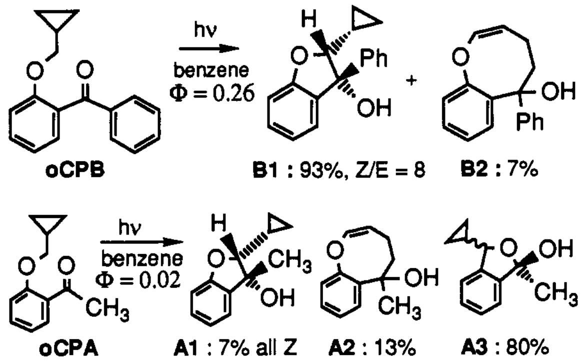
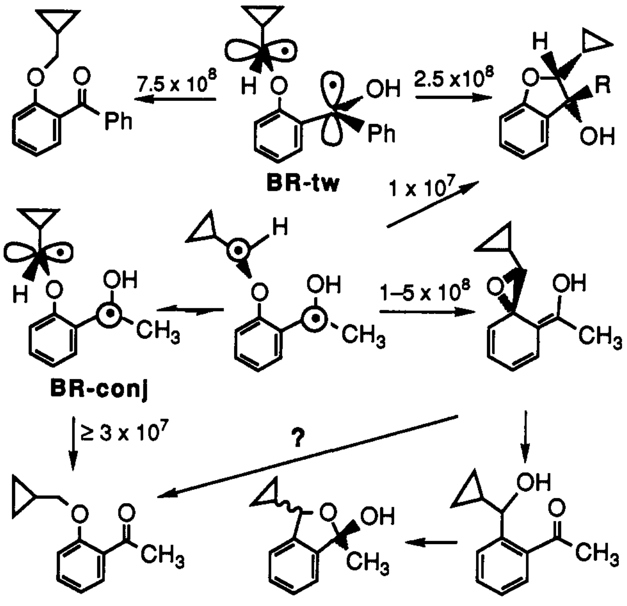
There has been intense interest over the past decade in the factors that determine the lifetimes of triplet-generated biradicals.[1] Although some researchers have suggested that rates of intersystem crossing (isc) determine both lifetimes and product distributions, most workers interpret product ratios in terms of differential barriers to chemical reaction. One particularly intriguing phenomenon is the large acceleration of 1,4-biradical decay caused by an oxygen atom between the two radical sites.[2] We have reported that the same effect occurs in the 1,5-biradicals formed by triplet-state δ-hydrogen abstraction in *o*-alkoxyphenyl ketones.[3] The products formed from such ketones differ dramatically for acetophenones and benzophenones, an effect that we have ascribed to different conformational freedoms of the biradicals.[3–5] We have now estimated the lifetimes of these biradicals by incorporating a cyclopropylmethyl radical clock[6,7] into the ketones and find that the acetophenone- and benzophenone-derived biradicals have comparable lifetimes despite forming different products.

We describe here the behavior of *o*-(cyclopropylmethoxy)-benzophenone and -acetophenone,[8] which undergo the photochemistry shown in Scheme I. Like other *o*-alkoxybenzophenones, **oCPB** cyclizes mainly to epimeric benzfuranols.[3,9] The acetophenone **oCPA** also forms some benzfuranol, but its major product is the hemiketal of an *o*-acetylbenzyl alcohol, which is thought to be formed by biradical rearrangement *via* a spiroepoxide.[3–5] We have independently prepared such *o*-acetylbenzyl alcohols and confirmed that they exist chiefly as hemiketals. Both ketones also form a *cis*-benzocyclooctenol[10] that reveals radical cyclopropylmethyl rearrangement occurring before cyclization. Direct NMR analysis of reaction mixtures indicated material balances ≥95% for **oCPA** and ≥90% for **oCPB**.[11]

Scheme I



Scheme II



Other biradicals undergoing cyclopropylmethyl rearrangements form cyclization and/or disproportionation products with both cis and trans double bonds,[7,12] as expected.[13] Thus, the initial 1,5-biradicals from **oCPB** and **oCPA** should each open to two 1,8-biradicals. The absence of products with trans double bonds suggests that the 1,8-biradicals with a trans double bond cannot cyclize or disproportionate and instead revert to the original 1,5-biradicals.

Scheme II portrays the competing reaction rates of both 1,5-biradicals, as deduced from the observed product ratios and an assumed identical rate constant for the cyclopropylmethyl rearrangement in both. The most recent measurement of the rate constant for opening of cyclopropylethyl radicals, the closest model for these 1,5-biradicals, is 7×10^7 s^{-1}.[14] With a trans/cis ratio of 2.2,[13] a rate constant of 2×10^7 s^{-1} best describes opening of the 1,5-biradicals to the 1,8-biradical precursors of *cis*-cyclooctenols **A2** and **B2**. Given this number and the assumption that the 26% quantum yield reflects 74% biradical disproportionation, the product ratios indicate a "normal" biradical decay rate of 1×10^9 s^{-1} for **oCPB**, every bit as fast as estimated by flash kinetics studies.[3] Since the lowest triplet of **oCPA** is π,π^*, its low quantum yield is partially due to slow triplet-state hydrogen

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[8] The ketones were prepared by simple S_N2 displacements on cyclopropylmethyl chloride by *o*-acylphenoxide ions.

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[10] Products were isolated by preparative HPLC. (*Z*)-**A1**: IR 3603 cm^{-1}; ^{1}H-NMR (C_6D_6) δ 0.15 (m, 1 H), 0.30–0.50 (m, 3 H), 1.15 (m, 1 H), 1.30 (s, 3 H), 3.23 (d, J = 2.7 Hz, 1 H), 6.77 (td, J = 7.4, 1.0 Hz, 1 H), 6.84 (dt, J = 7.8, 0.8 Hz, 1 H), 7.025 (td, J = 7.8, 1.5 Hz, 1 H), 7.14 (dd, J = 7.4, 1.5 Hz, 1 H). **A2**: IR 3600 cm^{-1}; ^{1}H-NMR δ 1.50 (s, 3 H), 1.66 (br s), 1.73–1.79 (m, 2 H), 1.83 (ddd, J = 15, 8, 4 Hz, 1 H), 2.40 (ddd, J = 15, 9, 4 Hz, 1 H), 4.85 (ddd, J = 6.6, 6.0, 4.8 Hz, 1 H), 6.38 (dt, J = 6.0, 2.0 Hz, 1 H), 6.90 (m, 1 H), 6.99 (m, 2 H), 7.71 (m, 1 H). **A3** (~1:1 *Z*/*E*): IR 3600, 1690 (w) cm^{-1}; ^{1}H-NMR δ 0.2–0.5 (m, 4 H), 0.8–1.0 (m, 1 H), 1.68 (s, 1.5 H), 1.75 (s, 1.5 H), 4.31 (d, J = 7.7 Hz, 1/2 H), 4.47 (d, J = 8.0 Hz, 1/2 H), 7.0–7.3 (m, 4 H). **B2** was identified by the two vinyl peaks at 4.6 and 6.4 ppm in the NMR spectrum of the reaction mixture.

[11] The yield of **B1** drops at high conversion; such benzofuranols are known to be photolabile.[9] The hemiketal was observed to undergo facile air oxidation to *o*-acetylphenyl cyclopropyl ketone, in agreement with our original findings on *o*-(benzyloxy)acetophenone.[4]

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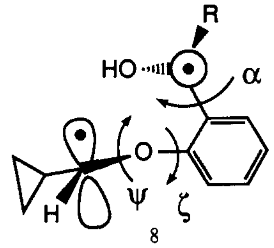
Scheme III



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Preferred Geometries

R	α	ζ	ψ	BT
Me	0°	120°	180°	**conj**
Ph	35°	125°	180°	**tw**

abstraction.[3] Additional inefficiency must derive from some combination of increased reversion of 1,5-biradicals and probable reversion of spiroepoxide to starting ketone. Given the uncertainty about how much the suspected spiroepoxide can partially revert to reactant as well as form **A3**, the total biradical decay rate is calculated to be $2\text{–}6 \times 10^8$ s^{-1}, with the higher value most likely. Despite this uncertainty, the low rate constant estimated for **A1** formation must be close to correct, since it is similar to the cyclization rates of the biradicals formed from α-(*o*-tolyl)acetophenones, which have geometries similar to that of the biradical from **oCPA**.[15]

What determines the rates in Scheme II? The radical clock establishes that indanol formation by the acetophenone-derived biradical is only 1/25 as fast and that spirocyclization/rearrangement becomes at least half as fast as cyclization by the benzophenone-derived biradical. Cyclization of the **oCPA**-derived biradical to a spiroepoxide has a rate that makes the total rate of decay similar for both biradicals. Is this lifetime similarity coincidental or does it indicate a common isc pathway? Griesbeck[16] has expanded upon Scaiano's suggestion of isc-based product ratios by correlating products with certain geometries suspected to be required for isc, specifically ones with the two singly-occupied p orbitals orthogonal to each other,[17] with product ratios being determined by the relative energies of these "isc geometries".

Given the short biradical lifetimes and the strong preference for a single benzfuranol isomer as product, it is tempting to speculate that the biradicals may be too short-lived to rotate out of their nascent geometries. We have rejected this possibility for two reasons: (1) the biradicals are formed in a high energy geometry,[3,4] so that rotation to more stable forms should be very rapid, and (2) *Z* and *E* products are formed almost equally in alcohol solvents.[3] Thus, our analysis is based on the assumption that the biradicals approach conformational equilibrium before decaying. Scheme III outlines the preferred geometries of our two biradicals, as estimated by AM1 semiempirical calculations[18] and as suggested by the stereoselective cyclization of such biradicals observed by Kirmse.[19] These calculations support our attribution of the different product partitioning for **BR-conj** and **BR-tw** to a large difference in the extent of conjugation of the hemipinacol radical site with the central benzene ring,[4] different products requiring different conformations.

The calculations reveal that neither cyclization mode can occur from a minimum energy conformation. Both require that ζ twist to 90° or less. Spiroepoxide formation requires that ψ twist to 90°, which the calculations suggest costs 2 kcal/mol. For **BR-conj**, such motion is sufficient; for **BR-tw**, additional energy is required to bring α close to 0°; so fewer molecules can assume the proper geometry and the observed rate for spirocyclization is low.[20] Benzfuranol formation requires a significant increase in α. For **BR-tw**, a 60° twist costs only 2 kcal/mol. For **BR-conj**, rotation of 30° in either direction costs only 1 kcal, but rotation to 60° results in a 5 kcal/mol energy increase. It is this barrier that apparently inhibits cyclization of **BR-conj** to benzfuranol, the 25-fold rate difference indicating a 2.0 kcal $\Delta\Delta G^{*}$.

Does isc occur in the lowest energy biradical conformations *before* they rotate into geometries required for product formation or is it coupled with bond formation after such rotations? The similarity of both the biradical lifetimes and geometries would seem to be strong evidence for the former scenario. In that case these results would be compelling evidence for small barriers to product formation *after isc*.[15] In both minimum energy biradical geometries, which are not dissimilar, the two half-occupied p orbitals are nearly perpendicular to each other. If this orthogonality alone were sufficient to induce isc, the similar lifetimes would need no further explanation. However, without further barriers to product formation, there should be no significant differences in product ratios. The vastly different product partitioning, which clearly reflects different barriers to rotation around bonds α and ψ, indicates that additional differentiation must occur.

Since the actual rotational barriers for **BR-tw** and **BR-conj** to reach their different product forming geometries appear to be very similar (~3–4 kcal/mol), it remains possible that product formation induces isc and that the similar lifetimes are coincidental. The 2- to 5-fold difference in isc rates could be related to different degrees of orbital overlap in the conformations necessary for the two different modes of cyclization; it is such overlap that provides the spin-orbit coupling and the surface crossing required for rapid isc.[15,21] The rotation about α and ψ required for benzfuranol formation allows the two nearly orthogonal p orbitals to develop strong overlap. Rotation about ζ and ψ, as required for spirocyclization, allows one p orbital to develop weaker overlap with the partial spin density at a carbon ortho to the hemipinacol radical site.[15,21]

In summary, orbital orthogonality alone does not explain product ratios. Whenever isc occurs, product ratios clearly are determined by differential barriers to reaction.

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