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Competition between Cyclization, Cleavage, and Reverse Hydrogen Transfer in 1,4-Hydroxybiradicals: Crystal Structure–Solid State Reactivity Correlations

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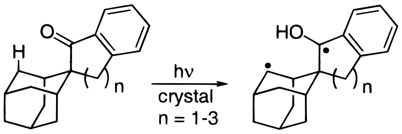
ABSTRACT



To provide experimental evidence on the relationship between stucture and reactivity in 1,4-hydroxybiradical intermediates, the Norrish type II photochemistry of a homologous series of spirobenzoyladamantane derivatives was investigated in the crystalline state and the outcome correlated with the structures of the compounds as determined by X-ray crystallography. The results provide an unusually detailed and compelling picture of the geometric factors responsible for the partitioning of these reactive intermediates among cleavage, cyclization, and reverse hydrogen transfer.

The idealized and widely accepted model of 1,4-biradical reactivity visualizes cleavage as occurring from either *gauche* or *anti* conformers in which there is overlap of the breaking σ bond with both half-occupied p-orbitals, whereas cyclization takes place exclusively from *gauche* conformers in which there is poor orbital alignment for cleavage.[1] What this picture lacks is detail. For example, what degree of orbital overlap is required for cleavage, and how close and in what orientation should the radical centers be to one another for cyclization to occur?

Our approach to answering these and related questions has been to make use of the organic crystalline state. We have shown that by low conversion irradiation of crystalline ketones capable of undergoing the Norrish type II hydrogen atom abstraction reaction, it is possible to generate and observe the behavior of the corresponding 1,4-hydroxybiradicals as "guests" inside the parent ketone lattice.[2] Because it is likely that hydrogen transfer occurs in the solid state with very little motion of the associated heavy atoms,[3,4] the

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(1) (a) Wagner, P. J. In *CRC Handbook of Organic Photochemistry and Photobiology*; Horspool, W. M., Song, P.-S., Eds.; CRC Press: Boca Raton, FL, 1995; Chapter 38. (b) Scaiano, J. C.; Lissi, E. A.; Encina, M. V. *Rev. Chem. Intermed.* **1978**, *2*, 139.

(2) Ariel, S.; Ramamurthy, V.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1983**, *105*, 6959.

(3) Gudmundsdottir, A. D.; Lewis, T. J.; Randall, L. H.; Scheffer, J. R.; Rettig, S. J.; Trotter, J.; Wu, C.-H. *J. Am. Chem. Soc.* **1996**, *118*, 6167.

(4) Leibovitch, M.; Olovsson, G.; Scheffer, J. R.; Trotter, J. *J. Am. Chem. Soc.* **1998**, *120*, 12755.

(5) (a) Because the biradicals are conformationally locked in the solid state, this approach avoids the thorny problem of conformation-dependent T_1 to S_1 intersystem crossing being the controlling factor determining biradical reactivity as suggested by Scaiano.[1b] (b) For an experimental structure−reactivity study of a carbene generated in the crystalline state, see: Keating, A. E.; Shin, S. H.; Houk, K. N.; Garcia-Garibay, M. A. *J. Am. Chem. Soc.* **1997**, *119*, 1474. For *theoretical* approaches to understanding 1,4-biradical behavior, see: (c) Hoffmann, R.; Swaminathan, S.; Odell, B. G.; Gleiter, R. *J. Am. Chem. Soc.* **1970**, *92*, 7091. (d) Borden, W. T.; Davidson, E. R. *J. Am. Chem. Soc.* **1980**, *102*, 5409. (e) Doubleday, C., Jr. *J. Am. Chem. Soc.* **1993**, *115*, 11968.

(6) Spiroketones **1**−**3** were synthesized via either standard Friedel−Crafts (**1**, **2**) or ring-closing metathesis reactions (**3**). All new starting materials and photoproducts described in the present paper gave spectroscopic data and elemental analyses completely in accord with their assigned structures. Details will be provided in a subsequent full paper.

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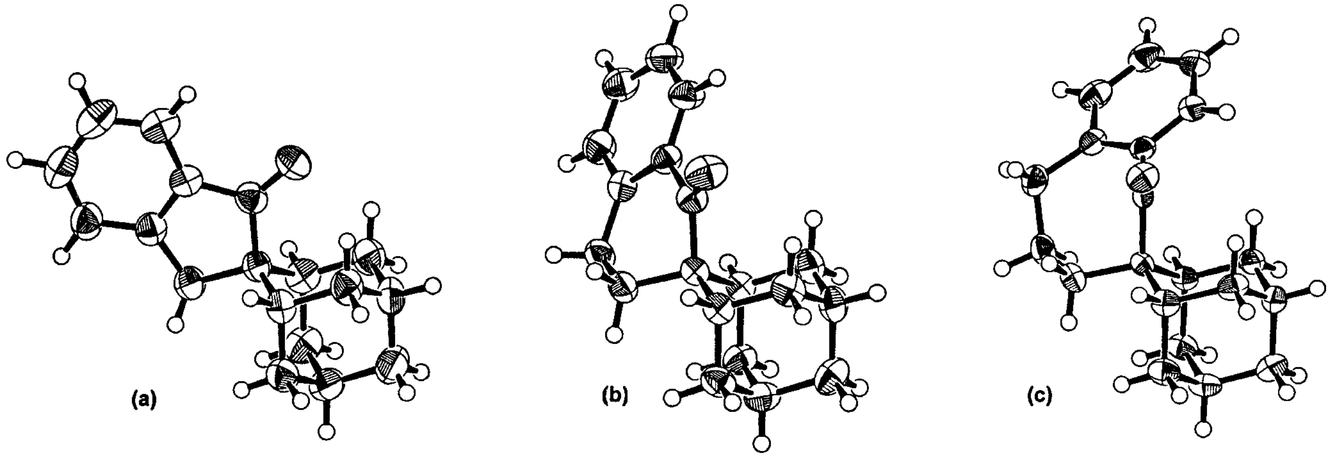
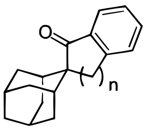


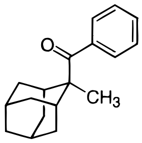
Figure 1. ORTEP diagrams for ketones **1** (a), **2** (b), and **3** (c).

structures of the biradicals can be inferred from a knowledge of the crystal structures of the parent ketones, and this allows *experimental* structure−reactivity relationships to be established for these elusive species.[5]

The compounds chosen for study in the present instance were the spiroketones **1**−**3**.[6] Included for comparison purposes is the nonspiro analogue **4** investigated previously.[4] By varying the number of methylene units in the carbonyl-containing ring from 1 to 3, the geometry of the 1,4-biradicals produced by γ-hydrogen atom abstraction could be altered, and these structural changes (as determined by X-ray crystallography of the parent ketones) were correlated with the solid state chemical behavior of these species as deduced from product studies. The results of this investigation provide an unusually detailed and compelling picture of the geometric factors responsible for the cyclization, cleavage, and reverse hydrogen transfer of 1,4-hydroxybiradicals.



1 n = 1
2 n = 2
3 n = 3



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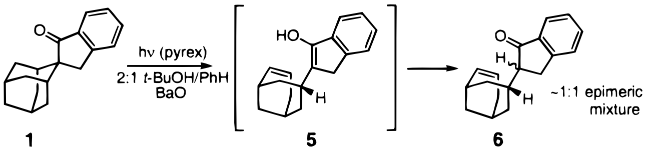
The X-ray crystal structures of ketones **1**−**3** were successfully determined[7] and, along with the crystal structure of compound **4** determined previously,[4] showed that the carbonyl group of ketone **1** is only 9° out of planarity with the plane bisecting the adamantane ring, whereas as the geometric restraints are reduced in ketones **2**, **3**, and **4**, this angle increases to 59°, 80°, and 86°, respectively (Figure 1). As we shall see, this is the key structural difference influencing biradical behavior in these systems.

Photolysis of ketone **1** in both the solid state and solution leads exclusively to products derived from Norrish type II cleavage. Irradiation (Pyrex, 4 h, ambient temperature) of **1** in 2:1 *tert*-butyl alcohol/benzene with anhydrous BaO leads to formation of enol **5** (Scheme 1). This enol has been observed by ^{1}H NMR[8] and is readily converted to its two epimeric ketone tautomers, **6**, on workup or on prolonged standing at room temperature. If the photolysis is carried out in a solvent that contains trace amounts of trifluoroacetic acid or ammonia, tautomerization of **5** occurs in situ, and only products derived from photolysis of **6** are observed.[9] Irradiation of crystals of ketone **1** to low conversions led to formation of **6** as the sole product. At higher conversions, secondary photolysis of **6** predominates, as in solution.

Scheme 1



In contrast to the reactivity of the five-membered ring spiroketone **1**, no photoproducts could be detected when the six-membered ring analogue **2** was irradiated (Pyrex filter, 2:1 *tert*-butyl alcohol/benzene). This lack of observed reactivity may be explained by efficient back abstraction of the hydroxyl hydrogen atom in the intermediate 1,4-biradi-

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(7) Ketone **1**: $P2_1/c$; $a = 6.7952(6)$ Å, $b = 6.7557(8)$ Å, $c = 28.909(3)$ Å; $\beta = 92.94(1)°$; $Z = 4$; $R = 5.3\%$. Ketone **2**: $C2/c$; $a = 17.788(2)$ Å, $b = 12.827(2)$ Å, $c = 12.960(1)$ Å; $\beta = 104.178°$; $Z = 8$, $R = 4.9\%$. Ketone **3**: $P\bar{1}$; $a = 10.898(4)$ Å, $b = 11.213(2)$ Å, $c = 7.218(6)$ Å; $\alpha = 99.52(3)°$, $\beta = 109.01(4)°$, $\gamma = 62.27(2)°$; $Z = 2$; $R = 4.8\%$.

(8) Photolysis (Pyrex, 0°, 4 h) of ketone **1** in CD_3CN gives rise to new signals at δ 6.32 (s, enol OH), 5.87 (m, vinyl H), and 5.50 (m, vinyl H). These signals disappear on addition of catalytic amounts of trifluoroacetic acid and are replaced by the four vinylic signals of the epimers of photoproduct **6**.

(9) Compounds **6** undergo efficient Norrish type II cleavage to afford 1-indanone (isolated) and bicyclo[3.3.1]nona-2,6-diene and bicyclo[3.3.1]-nona-2,7-diene (both observed by GC-MS).

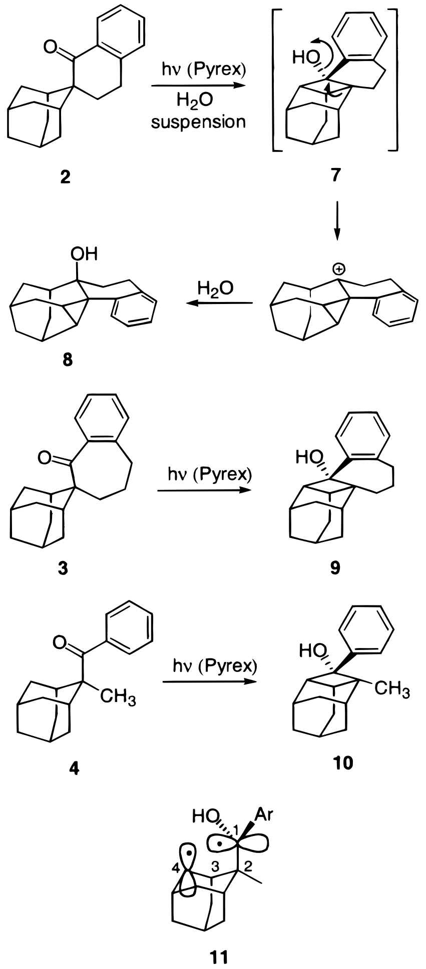
cal.[10] Evidence for this interpretation comes from the fact that irradiation of ketone **2** in 2:1 *t*-BuOD/benzene or 7% D_2O in acetonitrile leads to deuterium incorporation at the γ-positions;[11] ^2H NMR analysis of the deuterated photoproduct was consistent with exchange of only the axial γ-hydrogens on the adamantane ring.[12] Analogous exchange processes are surprisingly rare in Norrish/Yang type II photochemistry.[13]

As in solution, irradiation of crystalline samples of ketone **2** crushed between two Pyrex plates led to no detectable reaction. However, photolysis of ground crystals of **2** suspended in water containing a trace of added surfactant (sodium dodecyl sulfonate) led to the formation of rearranged alcohol **8** (Scheme 2) whose structure was confirmed by X-ray crystallography.[14] This product can arise via formation of the expected strained cyclobutanol **7** followed by a cyclobutyl to cyclopropylcarbinyl cation rearrangement. The nature of the difference in solid state reactivities (anhydrous versus water suspension) is not clear at this time but likely involves interactions between water and the ketone molecules on the solid surface.[15]

Irradiation of ketone **3** in both the solid state and solution led exclusively to the Yang cyclization (cyclobutanol) product **9** (Scheme 2), whose structure was confirmed by X-ray crystallography.[16] An analogous cyclobutanol (**10**), is formed in the solution and solid state photochemistry of the nonspiro ketone **4**.[4]

The geometry of the 1,4-biradical intermediates in these photoreactions may be characterized by three torsion angles as defined with reference to structure **11** in Scheme 2. Assuming that the hybridization of the radical centers is sp^2, we define φ_1 as the dihedral angle between the C_2-C_3 σ bond and the p-orbital lobe on C_1 with which it most nearly overlaps; φ_4 is defined as the analogous angle involving the C_2-C_3 σ bond and the most favorably oriented p-orbital lobe on C_4. The third angle is given the symbol ψ and refers to the $C_1-C_2-C_3-C_4$ torsion angle. In the present instance, this angle is fixed at 63 ± 1° (gauche) owing to the rigid adamantane carbon skeleton. Finally, we define D as the distance in angstroms between C_1 and C_4. The values of φ_1, φ_4, ψ, and D, taken from the X-ray crystal structures of ketones **1**−**4**, are given in Table 1. The angles φ_1 and φ_4 are also presented as cos φ_1 and cos φ_4, because these functions are proportional to the overlap between a $2p_z$ atomic orbital and an adjacent σ type orbital[17] and provide a more intuitive picture of the geometric relationships involved.

Scheme 2



As mentioned above, biradical cleavage is expected to be best when there is complete overlap between the orbitals of

Table 1. Geometric Data for Biradicals **1**−**4**

BR	φ_1 (deg)	cos φ_1	φ_4 (deg)	cos φ_4	ψ (deg)	D (Å)	reactn[a]
1[b]	−21	0.93	29	0.87	−64	3.03	CL
	40	0.77	−30	0.87	62	3.08	
2	−87	0.05	31	0.86	−63	3.07	*c*
3	70	0.34	30	0.87	−62	3.02	CY
4	66	0.41	30	0.87	−63	3.02	CY

[a] CL = cleavage; CY = cyclization. [b] See footnote 18. [c] Unreactive in solid state and solution; products derived from cyclization isolated only when solid state reaction is carried out in a water suspension.

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[10] Wagner, P. J.; Kochevar, I. E.; Kemppainen, A. E. *J. Am. Chem. Soc.* **1972**, *94*, 7489.

[11] For example, irradiation of ketone **2** in 2:1 *t*-BuOD/benzene for 29 h led to a 50% recovery of starting material after chromatography, which consisted of **2**-d_0 (48%), **2**-d_1 (42%), and **2**-d_2 (10%) as determined by mass spectrometry (31% overall deuteration assuming two exchangeable γ-hydrogen atoms).

[12] One peak at δ 2.20 (2:1 $CH_3OH-C_6H_6$) was observed in the proton-decoupled ^2H spectrum. This corresponds to a 2H doublet in the ^1H NMR spectrum which is produced by hydrogens on a carbon γ to the carbonyl carbon.

[13] Attempts to observe such exchange in γ,γ-d_2-nonaphenone were unsuccessful. See: Wagner, P. J.; Kelso, P. A.; Kemppainen, A. E.; McGrath, J. M.; Schott, H. N.; Zepp, R. G. *J. Am. Chem. Soc.* **1971**, *94*, 7506. For an example in which photoinduced H/D exchange occurs at the δ-position of a ketone as the result of reversible hydrogen atom abstraction, see: Hu, S.; Neckers, D. C. *J. Chem. Soc., Perkin Trans. 2* **1999**, 1771.

[14] Photoproduct **8**: $P\bar{1}$; a = 19.871(3) Å, b = 24.676(4) Å, c = 13.000(1) Å; α = 99.87(1)°, β = 101.20(1)°, γ = 109.14(1)°; Z = 16; R = 5.04%.

[15] The suspended crystals become fluffy as the reaction proceeds. This may result from the photoproduct sloughing off, thus exposing a new crystal surface to the water.

[16] Photoproduct **9**: $P2_1/c$; a = 8.763(3) Å, b = 14.060(5) Å, c = 11.890(2) Å; β = 90.51(2)°; Z = 4; R = 4.5%.

[17] Burdett, J. K. *Molecular Shapes*; Wiley-Interscience: New York, 1980; p 6.

the central σ bond and the two p-orbitals (i.e., $\varphi_1 = \varphi_4 = 0°$ and $\cos \varphi_1 = \cos \varphi_4 = 1$).[1] Inspection of Table 1 reveals that none of the four biradicals generated in the present study has this ideal geometry, but that the biradical derived from ketone **1** is close, with $\cos \varphi_1$ lying between 77% and 93% of the ideal value and $\cos \varphi_4$ at 87% of maximum.[18] This is significant, as ketone **1** is the only one of the four ketones to undergo type II cleavage. The biradicals derived from ketones **3** and **4**, in which overlap is very good on one side and poor on the other, prefer cyclization to cleavage. The behavior of the biradical derived from ketone **2** is unique. In solution, and presumably in the anhydrous solid state as well, it undergoes reverse hydrogen atom transfer to regenerate starting material. Only when the solid state photolysis is carried out in a water suspension is a cyclization-derived product observed. We discuss this result further in the next paragraph, but note at this point that the failure of biradical **2** to cleave is consistent with its poor geometry for this process, which is the worst of the four compounds studied. Overall, therefore, we conclude that while perfect orbital overlap is not required for cleavage, it should at least be very good and should involve both p-orbitals. The data clearly indicate that excellent overlap on one side and poor overlap on the other does not lead to cleavage.

Having dealt with the structural features that favor 1,4-hydroxybiradical cleavage, it is equally important to focus on the geometric factors that favor cyclization. Intuitively, it makes sense that Yang photocyclization will be favored when the radical-containing carbon atoms C_1 and C_4 are close to one another, probably ≤ 3.40 Å, which is the sum of the van der Waals radii for two carbon atoms. Table 1 reveals that the 1,4-biradicals generated in this study all have D values well under 3.40 Å. We must also take into consideration the *directionality* of the p-orbitals on C_1 and C_4, i.e., how well these orbitals overlap. Maximum overlap occurs when the p-orbital on C_1 is pointing directly at the top lobe of the orbital on C_4, i.e., when the C_1 orbital is parallel to the C_2-C_4 vector. The crystal structure data reveal that ketone **1** deviates from this ideal geometry by 52−69°[18] and that the corresponding deviation from ideality in ketones **2**, **3,** and **4** is 59°, 39°, and 32°, respectively. Thus, biradical **1**, which has the most favorable geometry for cleavage, has the least favorable geometry for cyclization, and it is hardly surprising that cleavage dominates completely in this case. Biradical **2** has a geometry that is imperfect for both cleavage and cyclization, and this is probably a major factor in the preference of this species for reverse hydrogen transfer in solution and the anhydrous solid state. The high strain energy of the cyclobutanol in this case (**7**) is undoubtedly a contributing factor as well.

In summary, the photochemical reactivity displayed by the benzoyladamantane system is exquisitely sensitive to the geometry of the intermediate 1,4-hydroxybiradicals, with cleavage predominating when the radical-containing orbitals overlap poorly with one another and well with the central carbon−carbon bond (ketone **1**). In contrast, Yang photocyclization takes over for biradicals that are reasonably well aligned for closure and poorly aligned for cleavage (ketones **3** and **4**), and in perhaps the most interesting case of all, reverse hydrogen transfer dominates for the biradical in which both cleavage and cyclization are geometrically disadvantaged (ketone **2**).

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[18] This analysis is based on identifying which of the two possible γ-hydrogen atoms is abstracted. This is clear in the case of ketones **2**−**4**, where one hydrogen is much closer to the ketone oxygen than the other, but for compound **1**, the two hydrogens are nearly equidistant (2.33 Å as opposed to 2.36 Å). Because it is not clear which hydrogen is abstracted, both sets of data are presented.