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Stereoselectivity in *o*-Alkylphenyl Ketone Photochemistry: How Many *o*-Xylylenes Can One Ketone Form?

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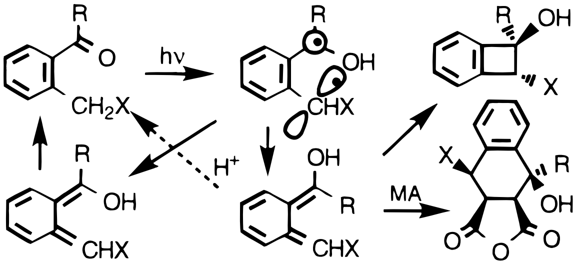
The photochemistry of *o*-alkylphenyl ketones[1,2] has maintained its fascination for over 35 years, since Yang and co-workers first reported that *o*-alkylbenzophenones undergo photoenolization to *o*-xylylenol[3] intermediates.[4,5] The ensuing decades have witnessed a host of mechanistic studies as well as synthetic utilization of the Diels−Alder adducts formed from the *o*-xylylenols. Although such products sometimes are formed stereoselectively, there does not seem to have been any general model developed for predicting stereoselectivity in these reactions. We describe several examples of photoenolization in which product structures vary in ways that substantiate our earlier suggestion[6] that the geometry of a twisted triplet *o*-xylylenol intermediate controls product selectivity.

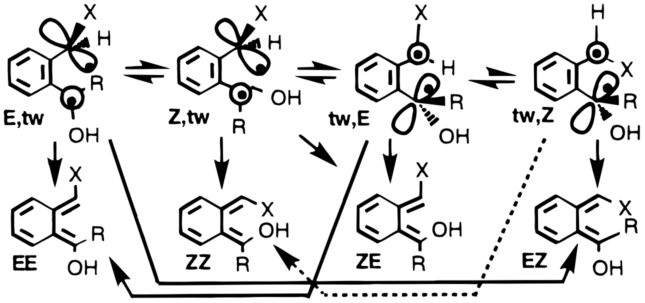
Scheme 1 summarizes the currently accepted[2] chronology of the various reactions that follow γ-hydrogen abstraction by *triplet o*-acylalkylbenzenes. The initial biradical is the triplet state of an *o*-xylylenol,[7] which decays to ground-state isomers with both *Z* and *E* configurations at the enol carbon.[8] The latter react rapidly with various dienophiles and O_2,[1,9] cyclize to benzocyclobutenols,[6,10] and undergo catalyzed reversion to reactant ketone.[4] The *Z* isomers usually undergo 1,5-sigmatropic return to the ground-state ketone so rapidly ($>10^6\ s^{-1}$) as to preclude participation in product formation.[8]

Scheme 1



Since most stable products are formed by stereospecific pericyclic reactions of the photogenerated *o*-xylylenols, stereochemistry must be determined by the structures of the available xylylenols. When $X \neq H$, four xylylenols are possible. Some attention[11,12] has been paid to such systems but not to the factors that determine which of the four are formed, except for a general supposition that the least congested *o*-xylylenol is formed preferentially. In contrast, we have suggested that product geometries are determined by the geometry of the lowest energy *triplet* xylylenol conformation. Scheme 2[6] depicts how triplet xylylenol geometry determines which of the four possible ground-state xylylenols are formed.[13] It is based on five premises about the triplet *o*-xylylenol: (1) Like a triplet 1,3-diene,[14] it is essentially a 1,4-biradical with one end twisted 90° and the other coplanar with the central ring. (2) It lives long enough for the initial **Z,tw**[15] geometry to equilibrate with other possible geometries via cooperative twisting of both ends. (3) Its lowest energy geometry has the end with the better conjugating substituents twisted, so that the less substituted end can benefit from conjugation with the central ring. (4) The end conjugated with the central ring has a preferred geometry with its larger substituent pointed out. (5) The twisted end rotates in both directions when collapsing to the ground state, like triplet alkenes. We find that both semiempirical and ab initio (6-31G*) geometry optimizations predict such a twisted triplet, which has been given limited previous theoretical consideration.[16]

Scheme 2



Our original use of Scheme 2 was to explain selective formation from *o*-ethylbenzophenone (oEtBP) of the benzocyclobutenol[6] that forms thermally only from the *EE* or *ZZ o*-xylylenols. With R = phenyl and X = methyl, **tw,E** should be the predominant biradical geometry. All calculations agree that it is 4 kcal/mol more stable than **tw,Z**, such that only the *EE* and *ZE* xylylenols should be formed, with only the former living long enough to cyclize. We also have confirmed the diastereoselectivity reported earlier[11] for the Diels−Alder adducts formed from oEtBP as that expected from an *EE* xylylenol.

To test the generality of Scheme 2, we have surveyed how substituents affect the products of *o*-alkylphenyl ketone photoreactions. When X = phenyl, the triplet xylylenol may exist in geometries with its CHX end twisted. For example, the triplet xylylenol from *o*-benzylbenzaldehyde (oBnBA) should exist predominantly in the **E,tw** and **Z,tw** geometries. The former should be preferred ($OH > H$); it would decay to both the *EE* and *EZ* xylylenols, which could each undergo endo cycloaddition with a dienophile. In fact, oBnBA does form two Diels−Alder adducts with maleic anhydride (MA).[12,17] Although one report

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(1) Sammes, P. G. *Tetrahedron* **1976**, *32*, 405−422.

(2) Wagner, P.; Park, B.-S. *Org. Photochem.* **1991**, *11*, 227.

(3) These *o*-xylylene derivatives generally have been called "photoenols", a nonspecific term that was not confusing originally. Now that several other forms of photoenolization are known, a term more specific to this particular photoreaction is required and we propose "*o*-xylylenol".

(4) Yang, N. C.; Rivas, C. *J. Am. Chem. Soc.* **1961**, *83*, 2213.

(5) Zwicker, E. F.; Grossweiner, L. I.; Yang, N. C. *J. Am. Chem. Soc.* **1963**, *85*, 2671.

(6) Wagner, P. J.; Subrahmanyam, D.; Park, B.-S. *J. Am. Chem. Soc.* **1991**, *113*, 709.

(7) Ullman, E. F.; Huffman, K. R.; Loy, M. *J. Am. Chem. Soc.* **1965**, *87*, 5417. Tchir, M. F.; Findlay, D. M. *J. Chem. Soc., Faraday Trans. 1* **1976**, *72*, 1096. Das, P. K.; Scaiano, J. C. *J. Photochem.* **1980**, *12*, 85.

(8) (a) Haag, R.; Wirz, J.; Wagner, P. J. *Helv. Chim. Acta* **1977**, *60*, 2595. (b) Das, P. K.; Encinas, M. V.; Small, R. D., Jr.; Scaiano, J. C. *J. Am. Chem. Soc.* **1979**, *101*, 6965.

(9) Porter, G.; Tchir, M. *J. Chem. Soc. A* **1971**, 3772.

(10) Kitaura, Y.; Matsuura, T. *Tatrahedron* **1971, *27*,** 1597.

(11) Pfau, M.; Combrisson, S.; Rowe, J. E.; Heindel, N. D. *Tetrahedron* **1978**, *34*, 3459.

(12) Arnold, B. J.; Mellows, S. M.; Sammes, P. G.; Wallace, T. W. *J. Chem. Soc., Perkin Trans. 1* **1974**, 401.

(13) The first *E* or *Z* refers to the OH-bearing carbon of the xylylenol.

(14) Hoffman, R. *Tetrahedron* **1966**, *22*, 521. Saltiel, J.; Townsend, D. E.; Sykes, A. *J. Am. Chem. Soc.* **1973**, *95*, 5968. Caldwell, R. A.; Singh, M. *J. Am. Chem. Soc.* **1982**, *104*, 6121.

(15) Our geometry notation for a triplet xylylenol starts with that for the planar ground state and then substitutes a "tw" for the first or second *E* or *Z*, depending on which carbon is twisted.

(16) (a) Baird, N. C. *J. Am. Chem. Soc.* **1972**, *94*, 4941. (b) Flynn, C. R.; Michl, J. *J. Am. Chem. Soc.* **1974**, *96*, 3280. (c) Sevin, A.; Bigot, B.; Pfau, M. *Helv. Chim. Acta* **1979**, *62*, 699. (d) Dannenberg, J. J.; Rayes, J. C. *J. Org. Chem.* **1983**, *48*, 4723.

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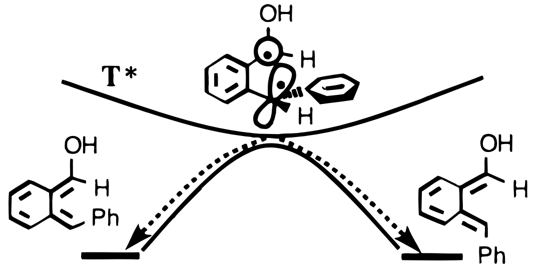
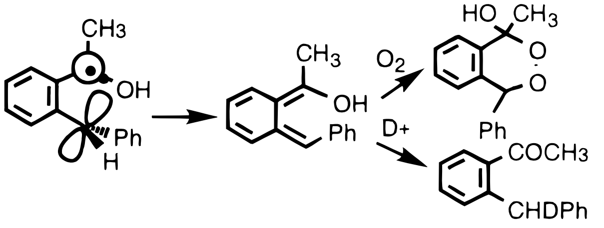
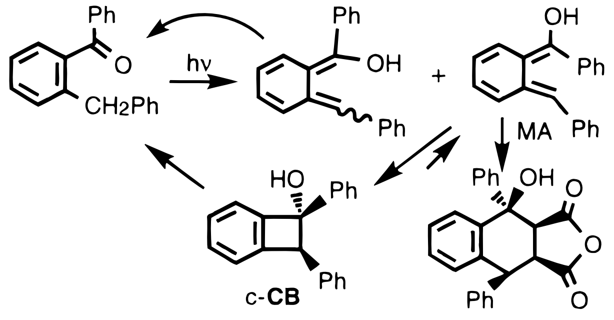


suggested that both endo and exo cycloadditions to a single xylylenol occur,[17] the evidence for only endo reaction directed by hydrogen bonding of the OH group to MA is compelling.[12] Moreover, oBnBA forms two sulfone adducts with SO_2.[18]

o-Benzylacetophenone (oBnAP) is reported to be unreactive when irradiated with several dienophiles.[19] We too find that it forms no products at all after extended irradiation in benzene, with or without added dienophiles. However, in methanol-d_4, it does undergo slow photoinduced H/D exchange of its benzylic protons. When irradiated in oxygen-saturated methanol, it forms a 50:50 mixture of two products with NMR spectra characteristic of cyclic peroxides, presumably by addition of oxygen to an *o*-xylylenol; these both gradually convert to *o*-acetylbenzophenone, their expected homolysis product.[20] Thus oBnAP does undergo γ-hydrogen abstraction to form a triplet *o*-xylylenol. Its initial **Z,tw** geometry should be its best, so only the *ZZ* and *ZE* *o*-xylylenols would be formed and they both should revert to oBnAP faster than they can cyclize or undergo Diels–Alder reaction. We surmise that hydrogen bonding of the enolic OH to methanol slows sigmatropic reversion to ketone[8] enough to allow some reaction with small reagents such as O_2 and protons. Internal H-bonding to the phenyl may produce the same effect in the sterically hindered *ZZ* isomer. We cannot distinguish between stepwise addition of oxygen to a single xylylenol and concerted addition to two xylylenols. We also note that electrocyclization of a dienol with OH pointed in should be quite slow.[21]

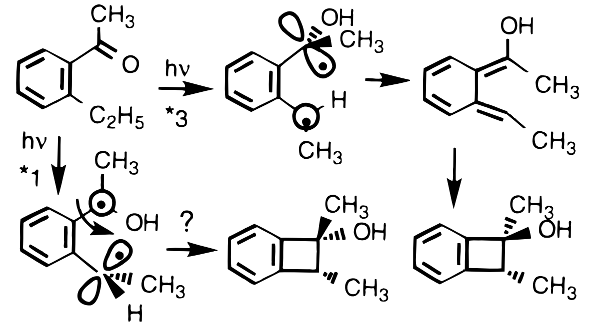


It has been reported that irradiation of *o*-benzylbenzophenone (oBnBP) in the presence of various dienophiles including MA produces only one Diels–Alder adduct from each; their configurations indicated endo cycloaddition to an *EE* xylylenol,[11] which has been assigned to long-lived yellow transients detected by flash spectroscopy.[5,9,22] We have reconfirmed that result and find that brief irradiation of oBnBP in several solvents converts it totally to the *cis*-benzocyclobutenol (*c*-CB), which is unusually labile thermally, so that its presence was missed in earlier studies.[4,22] With a phenyl at each end of the biradical triplet xylylenol, **Z,tw** and **tw,E** could be comparably populated geometries, such that the *ZZ*, *ZE*, and *EE* xylylenols all could be formed. Presumably only the latter lives long enough to be trapped and to cyclize.



The initial photoproducts from oBnBP undergo a variety of further reactions that are described separately.[23]

Since the disparate product distributions from the three *o*-acyldiphenylmethanes are entirely consistent with what is predicted by Scheme 2, this twisted triplet model appears to explain some unusual reactivity and to offer stereochemical predictability. Thus *o*-ethyl-α,α,α-trifluoroacetophenone forms only the *E*-benzocyclobutenol, as expected from a **tw,E** biradical. However, irradiation of *o*-ethylacetophenone (oEtAP) in benzene for several days produces a 3:1 *E*/*Z* ratio of benzocyclobutenols. With maleic anhydride present, two Diels–Alder adducts are formed in a 3:2 ratio. The assumptions about triplet xylylenol structure that work for the above cases would predict that only *ZE* and *EE* xylylenols be formed from the dominant **tw,E** geometry, with the former reverting entirely to ketone. Little, if any, *EZ* xylylenol should be formed, since its two precursor triplet xylylenol geometries **tw,Z** and **E,tw** each have an inward methyl group. Indeed, UHF 6-31G* calculations predict that the **E,tw** and **tw,Z** geometries lie, respectively, 2.5 and 3.4 kcal/mol higher than **tw,E**, as expected. Significant excited singlet hydrogen abstraction occurs in *o*-alkylacetophenones, most of which leads to direct quenching,[8a,24] which is undoubtedly responsible for the low product quantum yields from both oBnAP and oEtAP. Some produce a twisted singlet biradical, the fate of which is not readily predictable,[16c] but which could conceivably result in *EZ* xylylenol formation. Direct cyclization of a singlet biradical seems unlikely, given the lack of evidence for any cyclobutenol formation from oBnAP.



In summary, the selectivity of product formation from triplet *o*-acylalkylbenzenes seems to correlate with the predicted geometry of the lowest energy twisted triplet xylylenol conformer, but the full consequences of singlet reaction need further study. The long struggle to fully understand Yang's photoenolization is not yet over. For example, we find but cannot yet explain that α-(*o*-acylphenyl)acetic acid derivatives (esters and nitriles) are photoinert, forming neither benzocyclobutenols nor Diels–Alder adducts. The cause of this behavior may well be more electronic than geometric.

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