

Electronic Effects of Ring Substituents on Triplet Benzylic Biradicals

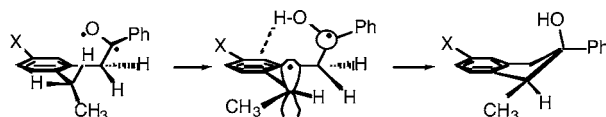
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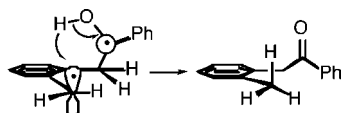
ABSTRACT



UV irradiation of α -(*o*-alkylphenyl)acetophenones with a methoxy or cyano substituent para to the *o*-alkyl group of the α -aryl ring has revealed that a methoxy group slightly increases the stereoselectivity but not the quantum yield of indanol formation, whereas a cyano group greatly lowers both diastereoselectivity and quantum efficiency, confirming the likelihood that hydrogen-bonding of the hydroxy group to the α -phenyl ring plays an important role in the cyclization of the photogenerated triplet 1,5-biradical intermediates.

When we first began studies of δ -hydrogen abstraction by excited ketones,¹ we were surprised to find a quantum yield of 100% for indanol formation from α -(*o*-tolyl)acetophenone, since quantum yields for product formation in photoreactions that proceed via a biradical intermediate often are quite low because of competing reversion of the biradical to ground-state reactant via intramolecular radical–radical reactions. In the case of the hydroxyl-substituted biradicals formed via hydrogen abstraction by a carbonyl, an internal disproportionation reaction occurs in which the remote benzyl radical site abstracts a hydrogen atom from the hydroxyl-substituted radical site, forming the original ketone (Scheme 1) and thus

Scheme 1

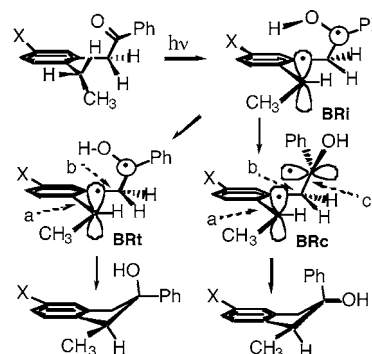


minimizing formation of distinct photoproducts.

A later study revealed remarkable diastereoselectivity in the photocyclization of α -(*o*-ethylphenyl)acetophenone: in hydrocarbon solvents a 95% preference for formation of the 3-methyl-2-phenyl-2-indanol isomer with the methyl and

phenyl groups trans, but in methanol only a 2:1 trans/cis ratio of isomers.² Computational study of the various minimum energy 1,5-biradical conformations (see the Supporting Information) indicated that the conformer that can most easily rotate to form the major product is significantly lower in energy than the conformer that is more likely to rotate into the minor product (see Scheme 2). This energy difference

Scheme 2

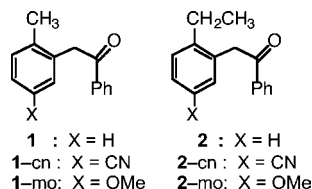


appeared to be due to hydrogen bonding of the biradical OH group to the α -phenyl ring, since rotation of the C–OH bond

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such that the O–H bond points away from the α -phenyl ring raises the conformer's energy close to that of the conformer that can form the cis indanol. Thus, the internal hydrogen bonding could be the source of the high stereoselectivity, whereas H-bonding to solvent alters selectivity. To test this notion further, we decided to study some α -(*o*-ethylphenyl)- and α -(*o*-tolyl)acetophenones with conjugating substituents on the α -aryl groups. We presumed that these substituents would alter the Lewis basicity of the α -aryl rings and thus, by altering the strength of any hydrogen bonding, also alter biradical behavior and product ratios.



Ring-substituted versions of α -tolyl- and α -(*o*-ethylphenyl)acetophenone, **1** and **2**, were synthesized by Pd(II)-catalyzed coupling of para-substituted *o*-bromoalkylbenzenes with acetophenone.³ Details of the syntheses of both of the substituted 2-bromoalkylbenzenes and the reactant ketones are included in the Supporting Information.

The four ring-substituted α -aryl ketones, 0.1 M in benzene-*d*₆ solutions containing varying amounts (or none) of a diene quencher, were irradiated at 313 nm in parallel with an actinometer. Measurements of product concentrations provided the quantum yield and triplet reactivity data in Table 1. The slopes of linear Stern–Volmer plots of quantum yields

Table 1. Kinetics of Photocyclization

ketone	Φ_{cyc}	$k_{\text{q}\tau}$, M ⁻¹	k_{H} , 10 ⁸ s ⁻¹
1 ^a	1.0	31.0	1.6
1-om	0.98	14.9	4.0
1-cn	0.34	53.0	0.1
2 ^a	0.64	5.4	10.8
2-om	0.61	2.5	23.6
2-cn	0.29	14.5	4.1

^a References 2 and 5.

as a function of quencher concentrations provided the $k_{\text{q}\tau}$ values from which k_{H} and $1/\tau$ values were derived, with k_{q} known to be 5×10^9 M⁻¹ s⁻¹.

The two substituents had the expected effect on reaction kinetics, the methoxy group speeding up δ -hydrogen abstraction (k_{H}) and the cyano group slowing it down, neither by large amounts. This behavior is in accord with the known charge-transfer nature of benzylic hydrogen abstraction by triplet ketones.⁴ Quantum yields depend on biradical behavior, and the large negative cyano effect suggests little OH hydrogen bonding to the α -phenyl ring, allowing the biradical

(3) Palucki, M.; Buchwald, S. L. *J. Am. Chem. Soc.* **1997**, *119*, 11108. Culkun, D. A.; Hartwig, J. F. *Acc. Chem. Res.* **2003**, *35*, 234.

(4) Wagner, P. J.; Truman, R. J.; Puchalski, A. E.; Wake, R. *J. Am. Chem. Soc.*, **1986**, *108*, 7727.

to undergo more reversion to reactant than cyclization to indanol. The methoxy group does not enhance quantum yields even though it should enhance benzyl radical basicity; a different electronic effect on biradical behavior may well be involved (see below).

To determine the stereoselectivity of cyclization, compounds **2-om** and **2-cn**, 0.1 M in benzene-*d*₆, were irradiated at 300–360 nm and different temperatures in sealed, deaerated NMR tubes. The only products from each ketone were two isomeric 2-indanols, easy to distinguish because of the 0.44 ppm difference in the chemical shifts of their methyl groups. Preparative-scale irradiation at higher concentrations followed by column chromatography provided isolation and identification of the two isomers.

Table 2 lists the variations in isomeric indanol ratios as a

Table 2. Indanol Isomer Ratios from **2-cn** and **2-om**

<i>T</i> , °C	% cis		% trans		trans/cis	ratio
	2-cn	2-om	2-cn	2-om	2-cn	2-om
0	9.9	4.5	89.3	95.5	9.0	21.
25	10.4	5.5	89.2	94.0	8.6	17.2
45	11.9	5.9	87.6	93.7	7.4	15.8
75	14.1	6.0	85.6	93.4	6.1	15.6

function of temperature and para-substituent X. Figure 1 contains Arrhenius plots of the trans/cis indanol ratios from

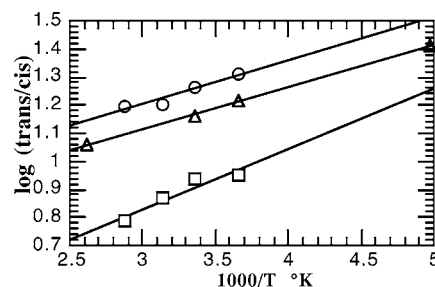


Figure 1. Temperature effects on trans/cis indanol ratios for **2** (Δ), **2-om** (\circ), and **2-cn** (\square).

2-cn, **2-om**, and **2**, the latter from an earlier paper.⁵ Table 3 lists the enthalpic and A-factor differences between cis and trans cyclization of the biradicals formed from the three

Table 3. Activation Parameters for Cyclization

ketone	$\Delta\Delta E^*$ (c–t) kcal/mol	$A_{\text{trans}}/A_{\text{cis}}^a$
2	0.67	4.5
2-mo	0.74	5.5
2-cn	1.00	1.5

^a Arrhenius preexponential factors: $\exp(\Delta S^\ddagger/R)$.

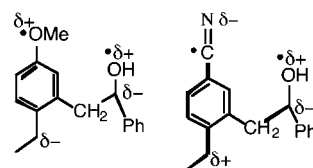
ketones. The two substituents clearly have dramatically opposite effects on stereoselectivity.

Scheme 2 displays the computed minimum energy biradical conformers involved in this cyclization process, with **BRT** able to undergo least motion radical coupling (rotations of bonds a and b) easier than the higher energy **BRC** (rotation of bond c also), as mentioned above. Our original study of temperature effects on the diastereoselectivity of photocyclization by **2**⁵ revealed that the large trans/cis indanol ratio is due to both enthalpic and entropic factors, which clearly affect both **2-om** and **2-cn** as well. The fact that there are both enthalpic and nonenthalpic cis/trans preferences is in accord with there being at least two separate biradical conformers that cyclize to diastereomers. We have suggested⁵ that the measured enthalpic differences most likely reflect the thermodynamically controlled proportions of separate biradical conformers as well as varied activation energies for the bond rotations that allow cyclization of different conformers to different isomers. The nonenthalpic differences probably reflect different alignments of the two singly occupied p orbitals in each of the biradical conformers that presumably cyclize to different isomers. In the world of ground states, intramolecular cyclization has a relatively fixed negative activation entropy whether stereoisomers are formed and regardless of reacting conformers with differing geometries. But in the world of triplet biradicals, the nonenthalpic spin-orbit induced conversion to singlet multiplicity required for product formation does depend on biradical geometry.⁶ With two biradical conformers, rates of direct intersystem crossing (isc) before cyclization would differ because of different distances between the two radical sites and different orientations of the singly occupied p orbitals. Rates of isc coupled with radical-radical coupling would differ as the two radical sites approach each other and as the p orbitals realign for σ -bond formation.

Ketone **2** displays a 670 cal enthalpic preference and a nearly 5:1 (28 eu) nonenthalpic (or entropic) preference for trans cyclization.³ Both the enthalpic and nonenthalpic trans preferences are slightly greater for **2-om**, perhaps indicating a small electron-donating effect by the methoxy group. The cyano group in **2-cn** has a larger electronic effect; the enthalpic trans preference is 50% greater than it is in **2**, whereas the nonenthalpic trans preference is only 1/3 that for **2**. The enthalpic increase may reflect diminution of OH H-bonding, which removes one impediment to the bond rotation required for cyclization, while the nonenthalpic decrease is likely due to partial electron withdrawal from the benzylic carbon.

There are two ways that the para substituents' electronic effects can affect biradical behavior. The simpler one is that the electron donor enhances the phenyl ring's basicity, thus favoring a large BRT/BRC ratio via OH H-bonding as suggested above, while the strong electron withdrawer reduces the ring's basicity and thus lowers the BRT/BRC ratio

by minimizing OH H-bonding. The differences among the



three reactants in quantum yields and stereoselectivity of cyclization could well be due largely to this effect. However, the substituents being para to the benzylic radical site adds a factor to biradical behavior that has not received much attention, namely the ionic effect of π conjugation. As Arnold and co-workers have reported,⁷ both *p*-methoxy- and *p*-cyanobenzyl radicals have delocalized spin, with the benzyl carbon becoming either somewhat negative or positive, respectively. With the spin density at the benzyl site of the biradical lowered, spin-orbit coupling could be very different from that for a simple 1,5-pentanedyl biradical. This could well explain why the nonenthalpic factor for **2-cn** displays the lowest trans/cis cyclization preference. Likewise, the lack of any increase in indanol quantum yield that could have been afforded by the methoxy group on **2-om** may be caused by the partial negative charge on each radical site discouraging radical-radical coupling.

A possible cause of the low diastereoselectivity for **2-cn** and the low quantum yields for **1-cn** and **2-cn** may be the π conjugation-induced opposite partial charges on the two benzylic carbons of the biradical intermediates. Salem's original analysis of biradical multiplicity and spin-orbit coupling⁶ suggested that opposite charges at the two radical sites would favor primarily singlet multiplicity and thus enhance the rate of cyclization by BRC and possibly enhance the rate of disproportionation by the no-longer hydrogen-bonding BRT. The low quantum yields may also result from k_H values being so low that significant CT quenching of the triplet ketones by solvent benzene⁸ can compete and lower the overall triplet lifetime, whereas triplet δ -hydrogen abstraction by ketones **1** and **2** is some three orders of magnitude faster than solvent quenching. In any event, these results tend to verify our belief that internal hydrogen bonding promotes both high quantum yields and diastereoselectivity in the photocyclization of α -aryl ketones via δ -hydrogen abstraction from ortho substituents on the α -aryl ring.

Finally, the significant effects that the two π -conjugating substituents had on 1,5-biradical intermediates suggest that additional studies, both experimental and computational, be performed on how such substituents can affect triplet biradical behavior.

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Supporting Information Available: Synthesis of reactant ketones, photochemical procedures, identification of indanol photoproducts, and computational methods. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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