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EFFICIENT SOLID STATE PHOTOCYCLIZATION OF STERICALLY CONGESTED α-o-TOLYL KETONES DESPITE "POOR" GEOMETRIES FOR HYDROGEN ABSTRACTION

Peter J. Wagner* and Boli Zhou

Chemistry Department, Michigan State University, East Lansing, Michigan 48824

Abstract: *Several α-mesityl and α-(o-tolyl)acetophenones undergo photocyclization to 2-indanols almost quantitatively when irradiated as crystals, even those that undergo significant competing α-cleavage or 1,3-aryl shift in solution. The requisite triplet δ-hydrogen abstraction apparently can occur at what appears to be a "bad" geometry. One ketone, α-(o-tolyl)propiophenone, partially rearranges to the β-isomer, which arises from disproportionation of the radicals formed by initial α-cleavage.*

Recently we reported that the efficiency with which α-(o-tolyl)- and α-mesityl-acetophenones photocyclize to 2-indanols[1] is significantly reduced by other α-substituents.[2] The cyclization involves 1,5-biradicals formed by δ-hydrogen atom abstraction by the n,π^* ketone triplets. Scheme 1 summarizes the competing photoreactions of α-mesityl and α-(o-tolyl) acetophenones in benzene solution. We have now performed these reactions in the solid state and find high chemical yields of cyclization in all cases, together with one example of a novel rearrangement. The solid environment impedes the several reactions that compete in solution and strongly enhances the synthetic potential of this reaction. The rate constants measured for these sterically congested ketones in solution provide the first quantitative picture of the angular dependence of hydrogen atom abstraction and indicate that such reaction can occur at geometries far from "ideal".

Scheme 1

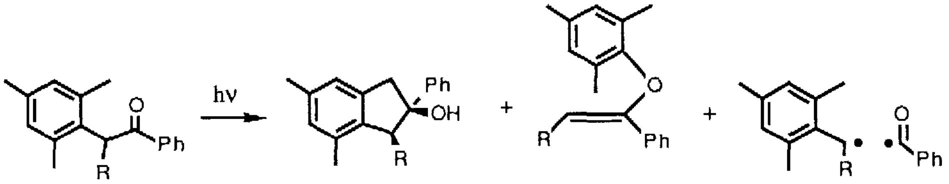


Table 1 contains photokinetic data for several ketones in benzene; its last column lists indanol yields obtained in the solid state. These were measured by irradiation of crystals of the reactants held in melting point tubes inside sealed, argon-saturated test tubes. High yields of indanol were found at both high and low conversion. For example, product ratios from **5** were the same at 23% and 70% conversion and the crystals had not "melted" during irradiation.

α-Substitution on **1** or **3** sharply reduces both the rate constant for triplet state δ-hydrogen abstraction and the overall quantum efficiency of cyclization in solution. We have already suggested without further elaboration that steric congestion impedes δ-hydrogen abstraction and thus facilitates the competing

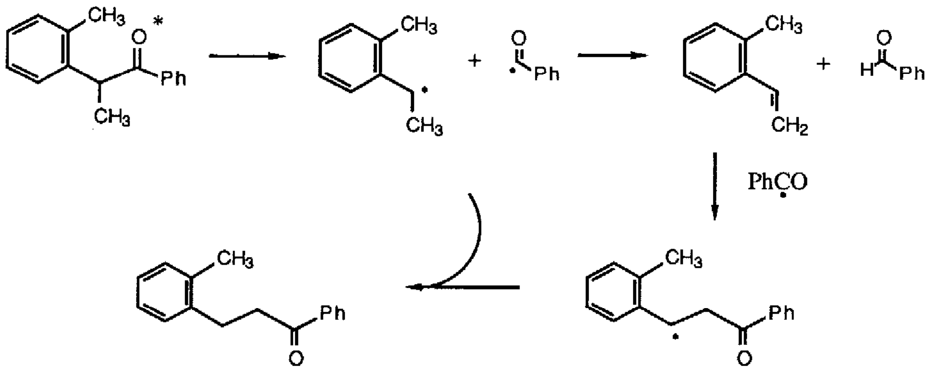
Table 1. Photokinetics of Ar-CH(R)-CO-Ph in benzene.

Ketone	Ar	R	$1/\tau^{a,b}$	Φ_{cyc}	$k_{\delta\text{-}H}^{b,c}$	Φ_{other}^{d}	% cyc (solid)
1	o-tolyl	H	1.6	1.0	1.6	0	100
2	o-tolyl	CH_3	0.5	0.05	0.025	0.28^{e}	67
3	mesityl	H	11.0	0.55	5.8	0	
4	mesityl	CH_3	2.9	0.24	0.7	0.03^{e+f}	100
5	mesityl	n-Pr	10.0	0.12	1.2	0.025^{e+f}	94
6	mesityl	Ph	50.0	0.03	0.6	0.024^{e+f}	100

[a] from Stern-Volmer quenching with conjugated dienes, $k_q = 6 \times 10^9\ M^{-1}\ s^{-1}$. [b] units of $10^8\ s^{-1}$.
[c] $k = \Phi_{cyc}/\tau$. [d] total of competing reactions. [e] yield of trapped benzaldehyde from α-cleavage. [f] enol ether.

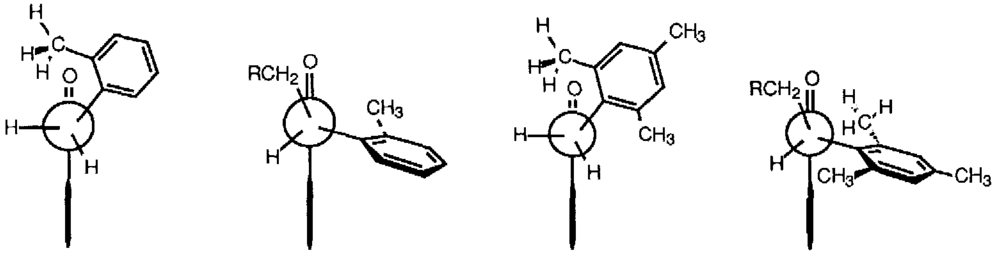
enol ether formation and radical cleavage reactions.[2] Both of these reactions are inhibited in the solid state. The former probably requires too much molecular motion within the crystal lattice. The latter occurs, but immobility forces the radicals to recombine, as observed for ketones adsorbed on silica.[3]

In the case of crystalline ketone **2**, benzaldehyde and β-(o-tolyl)propiophenone were formed in yields of 22% and 10%, respectively. In solution, the yield of the former is very small unless a good radical trap such as a thiol is present, and none of the latter is formed. The most likely mechanism for formation of these extra products involves disproportionation of the initial radical pair formed by triplet α-cleavage.[4] Presumably a later α-cleavage of a neighboring ketone produces a benzoyl radical that can then add to the styrene. Observation of these disproportionation products confirms that α-cleavage still occurs in the solid.



The fact that high yields of indanol are obtained in the solid means that the molecules exist in geometries that permit formation by δ-hydrogen abstraction of biradicals that can easily attain the geometry required for cyclization.[5] Scheme 2 shows for each ketone the lowest energy conformation that has a hydrogen within bonding distance of oxygen, as determined by MMPMI calculations.[6] The x-ray crystal structure of **5**[7] reveals a molecular geometry nearly identical to that calculated as having the lowest energy. This fact makes us confident that the calculations validly predict the most populated conformations of these molecules. The key conclusion is that the presence of a second substituent on the α-carbon forces the α-aryl group to twist away from the carbonyl, in contrast to the more eclipsed orientation in the simple α-aryl acetophenones **1** and **3**.

Scheme 2

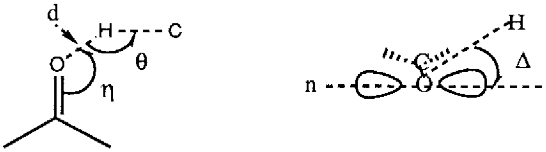


1 **2** **3** **4, 5**

There has been much interest in defining the "ideal" geometry for hydrogen atom abstraction by n,π* ketone triplets, as described by the parameters in Scheme 3.[5,8-12] It has been suggested that hydrogen atom abstraction by triplet ketones may depend strongly on the location of the hydrogen with respect to the long axis of the half-occupied n-orbital on oxygen.[8] Recent calculations[12] do suggest that the rate constant for hydrogen abstraction is maximum when the reacting C-H bond lies along the axis of the n orbital ($\Delta = 0°$). One of us has suggested[9] that the actual rate constant for hydrogen abstraction should be proportional to $\cos^2 \Delta$. Ketones **1** and **3** exist in geometries that are nearly ideal for δ-hydrogen abstraction. The lowered rate constants measured for those ketones containing an α-alkyl group must reflect the nonideal geometry that characterizes these ketones' stablest conformations: Δ is 61° in **5**; the other geometric parameters are less than ideal; and **2** also exists in an *unreactive* conformation with the benzylic methyl twisted 180° away from the carbonyl. We originally thought that the low solution rate constants reflected reaction arising from low equilibrium populations of "ideal" conformations.[2] However, we now know that **5** reacts efficiently in the solid from a quite nonideal geometry.[13] Reaction from this geometry produces a biradical almost ideally positioned for cyclization. These results strongly suggest that the low rate constants for δ-hydrogen abstraction by the sterically congested ketones in solution represent reaction occurring from the lowest energy "nonideal" conformations.

There have been a large number of experimental reports of efficient hydrogen atom abstraction in crystalline ketones with Δ values around 30°.[3] There have been a few positive[5] and a few negative[4] reports of ketones undergoing intramolecular triplet hydrogen abstraction with Δ ~90°. The differences may reflect variations in the range of Δ values that the flexibilities of the various molecular systems allow. The k_H value for **5** is 20% that for **3**. This factor compares well with $\cos^2 61° = 0.23$ Since the other key geometric parameters of Scheme 3 are quite similar for the two systems, these results provide the first quantitative confirmation that this basic excited state reaction displays the theoretical geometric dependence[14] on the electron density in the n orbital.

Scheme 3



ideal:	$\eta = 90°$	$\theta = 180°$	$\Delta = 0°$	$d < 2.5$ Å
5:	76°	119°	61°	2.7
3:	99°	125°	23°	2.8

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(7) Complete details will be provided in the full writeup. Schemes 2 and 3 include relevant geometric features. Excited state geometries undoubtedly differ slightly, but not so much as to change *relative* conformational energies significantly.

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