

Latent chemical behavior revealed in the crystalline state: novel photochemistry of a *cis*-9-decalyl aryl ketone

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The case of a ketone whose photochemistry in solution is markedly different from that observed in the crystalline state is reported.

Molecules in crystals may be thought of as residing in reaction cavities whose walls are composed of the neighboring molecules in the lattice.^{1,2} When the central molecule in this ensemble is caused to react in some way, for example by UV irradiation, the cavities often restrict certain reaction pathways and allow others, thus generally leading to a reduced number of products compared to reactions carried out in more forgiving fluid media. In some cases, the pathway favored in solution is topochemically forbidden in the solid state (*i.e.* prevented by lattice restraints), and when this is the case, less topochemically demanding reactions leading to new products take over.³ To put it another way, organic (and inorganic) molecules can be thought of as having *latent reactivity* that is expressed only when they are caused to react in the crystalline state; by restricting chemistry to fluid media, these new reactions would be missed. In the present communication we report an example of this type of behavior in the photochemistry of a *cis*-9-decalyl aryl ketone.

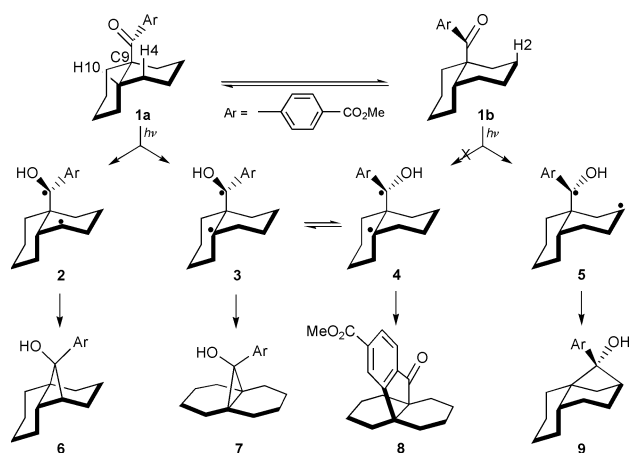
The molecule in question is *cis*-9-decalyl *p*-carbomethoxyphenyl ketone (**1**), mp 85–86 °C (Scheme 1).⁴ Irradiation of acetonitrile solutions of this compound (145 mg, 100% conversion) through Pyrex afforded cyclobutanols **6** (47%) and **9** (47%) along with 6% of cyclopentanone **8**. In contrast, when crystals of ketone **1** were irradiated (Pyrex, –20 °C to minimize melting, 76 mg, 100% conversion), the product mixture consisted of cyclobutanol **6** (81%) and the novel cyclopropanol derivative **7** (19%). The structure and stereochemistry of each photoproduct were deduced from FTIR, HRMS, 1D, 2D and NOE difference NMR, and microanalysis. The structures of compounds **6** and **8** were also verified by single crystal X-ray diffraction studies.[†]

What is responsible for the remarkable difference in product structure and distribution in going from solution to the solid state? To help answer this question, the X-ray crystal structure

of ketone **1** was determined (Fig. 1).[†] This conformation, which is depicted by structure **1a** in Scheme 1, clearly indicates that the ketone oxygen atom is directed toward hydrogen atoms H4 (2.55 Å) and H10 (2.38 Å). This is significant, because these are the very hydrogen atoms abstracted in the first step of the formation of solid state photoproducts **6** and **7**, respectively. Abstraction of H4 takes place through a 6-membered transition state and leads to 1,4-hydroxybiradical **2**, whose closure occurs with retention of configuration at the carbonyl carbon affording cyclobutanol **6**.⁵ Abstraction of H10, on the other hand, is a relatively rare 5-membered transition state process that produces 1,3-biradical **3** leading to cyclopropanol **7**.⁶ Both biradical closure processes are similar in that they occur without the need for any large molecular motions, *i.e.* they are not topochemically restricted by the confines of the solid state reaction cavity.⁷

Biradicals **2** and **3** are presumably formed in acetonitrile as well, and indeed, photoproduct **6** is a major product in this medium. Cyclopropanol **7** is not formed in solution, however, its place being taken by cyclopentanone **8**. The reason for this difference, we suggest, is that ring closure of biradical **3** to cyclopropanol **7** is slow (ring strain), and in solution, rotation of biradical **3** about the C9 to carbonyl carbon bond to form biradical **4** is faster. This places the aromatic ring in proximity to the radical at C10, and radical coupling of **4** at the *ortho* position followed by tautomerization and oxidation leads to cyclopentanone **8**.⁸ Why, then, is no photoproduct **8** formed in the solid state? The simple reason is that the required rotation about the C9 to carbonyl carbon bond in biradical **3** is topochemically restricted in the crystal. The aromatic ring would have to sweep through a large volume of space—a motion prohibited by the solid state reaction cavity.

A final point concerns the formation of cyclobutanol **9** in solution but not in the solid state. Formation of this photoproduct necessarily involves abstraction of H2, and this is not possible in the crystal because the C=O...H2 abstraction



Scheme 1

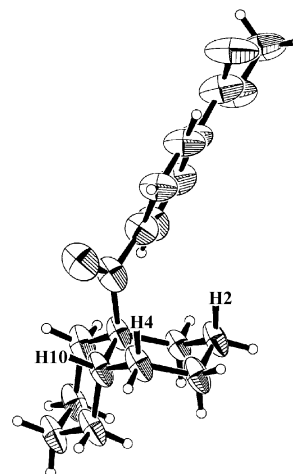


Fig. 1 ORTEP drawing of conformer **1a**

distance in conformer **1a** is too great (3.47 Å).⁹ In solution, on the other hand, ketone **1** can adopt alternative low energy conformations that permit abstraction of H2. Molecular mechanics calculations (Hyperchem MM+ and MacroModel MM3*) show that ketone **1** has two lowest energy conformations that differ in energy by only 0.1 kcal mol⁻¹. One of these is **1a**, the conformation adopted in the crystal, and the other is **1b**, in which abstraction of H2 (2.40 Å) is favored geometrically over abstraction of H4 (3.22 Å) or H10 (3.83 Å). We therefore postulate that cyclobutanol **9** is formed in solution from conformer **1b** via abstraction of H2 (6-membered transition state) followed by closure of the resulting 1,4-hydroxybiradical **5**.¹⁰

In summary, the latent solid state photochemical behavior of ketone **1** is manifested by the formation of cyclopropanol **7**, a product not observed in solution. Similarly, irradiation of ketone **1** in solution leads to two new photoproducts (**8** and **9**) not observed in the solid state. These reactivity differences can be explained on the basis of the conformational freedom (or lack thereof) that the reactants and intermediates experience in the two media.

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Notes and references

† *Crystal data*: **1**: C₁₉H₂₄O₃, *M* = 300.40, monoclinic, *a* = 13.881(5), *b* = 6.362(2), *c* = 18.197(8) Å, β = 97.77(4), *V* = 1591(1) Å³, *T* = 293 K, space group *P*2₁/*a* (no. 14), *Z* = 4, μ (Mo-K α) = 0.083 mm⁻¹, 2611 reflections measured, 2503 unique (*R*_{int} = 0.03), final *R*(*F*²) = 0.062 ($\geq 2\sigma$). The achiral space group in this case precludes solid state asymmetric induction studies.

6: C₁₉H₂₄O₃, *M* = 300.40, triclinic, *a* = 8.8083(3), *b* = 17.365(7), *c* = 6.182(2) Å, α = 90.99(3), β = 109.53(3), γ = 79.04(3)°, *V* = 801.9(5) Å³, *T* = 293 K, space group *P*1̄ (no. 2), *Z* = 2, μ (Cu-K α) = 0.659 mm⁻¹, 3515 reflections measured, 3263 unique (*R*_{int} = 0.02), final *R*(*F*) = 0.060 ($\geq 3\sigma$).

8: C₁₉H₂₂O₃, *M* = 298.38, monoclinic, *a* = 11.209(1), *b* = 10.149(1), *c* = 7.5641(8) Å, β = 70.368(9), *V* = 810.5(2) Å³, *T* = 293 K, space group *P*2₁ (no. 4), *Z* = 2, μ (Cu-K α) = 0.651 mm⁻¹, 1884 reflections measured, 1805 unique (*R*_{int} = 0.05), final *R*(*F*) = 0.041 ($\geq 3\sigma$). The absolute structure was not determined.

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- 9 For a discussion of the geometric requirements for intramolecular hydrogen atom transfer in the solid state, see H. Ihmels and J. R. Scheffer, *Tetrahedron*, 1999, **55**, 885.
- 10 Formation of biradical **4** from conformer **1b** is impossible owing to the long C=O...H₁₀ distance involved (3.83 Å).⁹