



Engineering reactions in crystals: *gem*-dialkoxy substitution enables the photodecarbonylation of crystalline 2-indanone

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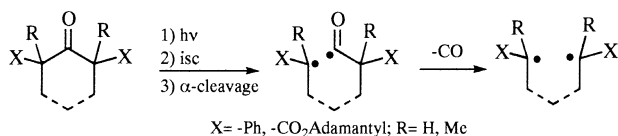
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Abstract—The photochemical reactivity of three 1,1,3,3-tetrasubstituted 2-indanones was investigated in solution and in crystals. While solution irradiation of tetramethyl-2-indanone **2** leads to 1-isopropenyl-2-isopropyl benzene **5** in high yield, crystals of **2** were completely inert. In contrast, samples of 1,3-bis(ethylenedioxy)-2-indanone **3** reacted efficiently in both media. While solution irradiation yielded benzocyclobutane **7** and *o*-xylylene **8**, only the former was formed in the solid state. Finally, the 1,3-bis-thioke-tal analog **4** reacted sluggishly in solution but not at all in the solid state. Differences in reactivity between the three indanones were analyzed in terms of radical stabilization effects and possible intramolecular quenching mechanisms. © 2002 Elsevier Science Ltd. All rights reserved.

Although many reactions in crystals proceed with remarkably high selectivity and specificity,¹ their limited predictability has prevented chemists from exploiting their potential in synthetic applications. With the purpose of identifying reliable solid state reactions, we have explored the use of compounds that form high-energy species such as carbenes,² biradicals, and radical pairs.³ We anticipate that highly reactive intermediates will break weak bonds and make new stronger ones despite having severely limited motion in the solid state.

To generate radical pairs and biradicals in crystals, we have analyzed the stepwise α -cleavage (Norris type-I reaction)⁴ and decarbonylation of triplet dialkyl ketones.^{3,5} We have shown that cyclic and open chain ketones with α,α' -diphenyl and α,α' -diester substituents can react smoothly in the solid state (Scheme 1). As the bond dissociation energies of the α -bonds are reduced by the α -substituents, the bond cleavage reactions become more exothermic from the triplet excited state.⁶



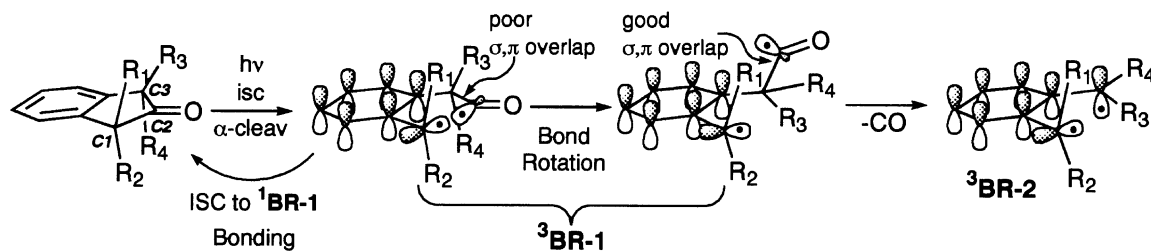
Scheme 1.

Keywords: solid state reactivity; α -cleavage; decarbonylation; radical stability; 2-indanones; benzyl radicals.

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The more exothermic these reactions, the earlier and lower their transition states, and the higher their rate constants and quantum efficiencies.^{4a,6,7}

In order to document the scope of the reaction, we have analyzed several α -substituents^{3,5} and potential quenching mechanisms that may prevent ketones from reacting in the solid state.⁸ With regard to the effect of α -phenyl groups, it is well known that conformational factors have a strong effect on the stability of benzylic radicals.⁹ Experimental¹⁰ and computational⁹ studies suggest that conformers with ideal overlap between the radical p-orbital and the aromatic π -system are 12.5 ± 1.5 kcal/mol lower in energy than those where the two groups are orthogonal. In this context, the solid state reactivity of 2-indanones is of significant interest. Although the carbonyl group of 2-indanones is formally α,α' -diaryl substituted, the perpendicular orientation between the σ -bonds undergoing cleavage (C1–C2 and C2–C3) and the aromatic π -system may deprive them of the benefits of benzylic stabilization (Scheme 2). However, the photochemical α -cleavage and decarbonylation reactions of several 2-indanones have been well documented in solution, suggesting that benzylic stabilization may not be essential in the first step.^{11,12} If formation of the acyl-alkyl triplet biradical ³BR-1 by α -cleavage also occurs in the solid state, differences in reactivity may arise from different radical stabilization during the decarbonylation step. If rotation about the C–C=O bond in ³BR-1 is hindered in the solid state, diminished benzylic stabilization may slow down the rate of decarbonylation to the extent that formation of

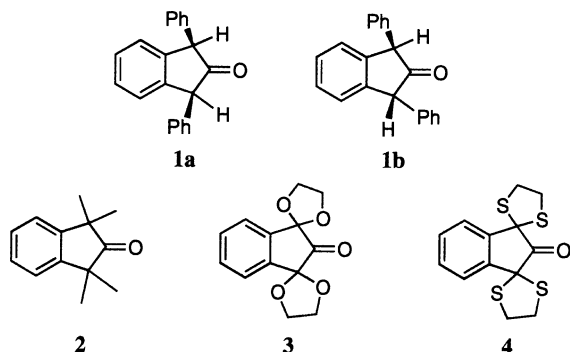


Scheme 2.

the triplet biradical ${}^3\text{BR-2}$ may not compete with intersystem crossing to the singlet acyl-alkyl biradical ${}^1\text{BR-1}$ which would undergo rapid bond-formation the ground state (Scheme 2).

In the absence of benzylic stabilization, the reactivity of 2-indanones in crystals should depend on the enabling effect of substituents R_1 – R_4 . Interestingly, *cis*- and *trans*-1,3-diphenyl-2-indanones **1a** and **1b** (Scheme 2) are known to give *cis*- and *trans*-diphenylbenzocyclobutanes stereoselectively upon irradiation in the solid state.¹³ While their crystals react efficiently, it is not known whether the indanone structure can facilitate the solid state reaction on its own, or whether the α -phenyl groups are required. In order to answer this question and to expand on our previous observations, we have analyzed the solution and solid state reactivity of 2-indanones **2**, **3** and **4** (Scheme 3).

Differences in reactivity between 2-indanones **2**, **3** and **4** should reflect the effects of *gem*-dialkyl, ketal, and thioketal substituents on the α -carbons. Since we have shown that alkyl groups alone do not enable decarbonylation in the solid state,³ results with the tetramethyl derivative **2** should reveal whether or not the indanone ring satisfies the required stabilization in the solid state. With compounds **3** and **4** we can examine whether the added effect of dialkoxy and dithioxy substituents can assist (or hinder) the reaction. Tetramethyl indanone **2** (mp = 75–76°C)¹² was prepared from 2-indanone by standard procedures. Compounds **3** and **4** were selected for their known crystallinity (mp = 115°C¹⁴ and mp = 197–198°C,¹⁵ respectively), simple preparation, and because of the potential radical stabilizing abilities of the *gem*-dialkoxy and *gem*-dithioxy groups.^{16–18}



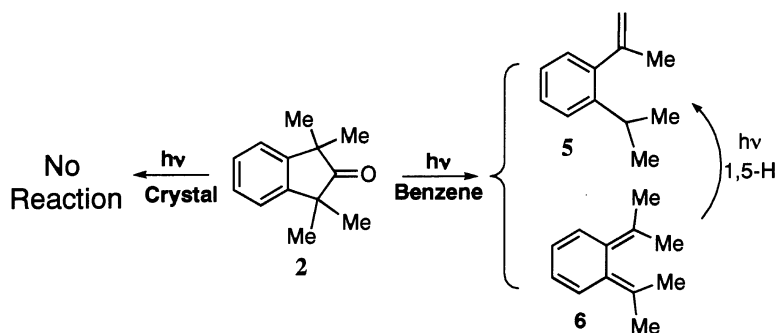
Scheme 3.

Solution- and solid-state photochemistry of 1,1,3,3-tetramethyl-2-indanone (2). As reported by Starr and Eastman,¹² the photoreaction of **2** proceeds in solution with high chemical efficiency to give 1-*iso*-propenyl-2-*iso*-propylbenzene **5** in 95% yield. However, it was shown that **5** originates (at least partially) from tetramethyl-*ortho*-xylylene **6** by a photochemical 1,5-H shift (Scheme 4).¹⁹ When crystals of **2** were irradiated at ambient temperature for 12 h, no trace of a reaction was observed.

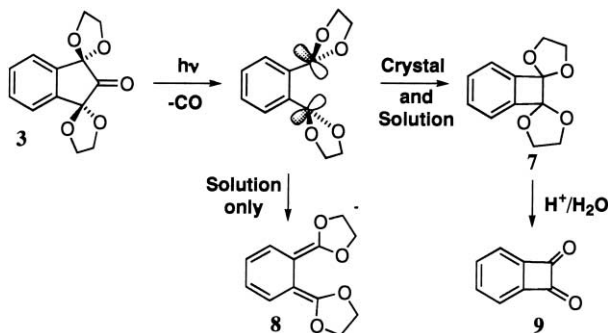
The lack of reactivity in the solid state may come from inefficient α -cleavage and/or decarbonylation steps. Although the absolute efficiency of solid state reactions is difficult to quantify, we have noticed that α -cleavage reactions that are efficient in solution can also be observed in the solid state.^{3,5} Based on that, we attribute the difference in photoreactivity between solution and the solid state to the restriction imposed by the rigid medium on rotation about the α,β -bond and its effects on decarbonylation (Scheme 2). Flash photolysis studies in solution by Scaiano and co-workers indicate that decarbonylation of ${}^3\text{BR-1}$ (R_1 – R_4 = Me) occurs in less than 10 ns. The dialkyl biradical ${}^3\text{BR-2}$ formed in this step goes on to products (**5** and **6**) with a time constant of 580 ns,^{11b,c} which is limited by intersystem crossing to the singlet state. In the absence of bond rotation, poor alignment between the aromatic π -system and the breaking C–CO bond should slow decarbonylation with respect to intersystem crossing, resulting in bond formation to regenerate the ground state starting material.

Solution- and solid-state photochemistry of 1,3-bis(ethylenedioxy)-2-indanone (3). The photochemical decarbonylation of 1,3-bis(ethylenedioxy)-2-indanone **3** was recently reported as a convenient way to prepare benzocyclobutanedione **9** (Scheme 5).¹⁴ Irradiation of **3** in THF was reported to yield 48% of bisketal **7**.¹⁴ We noticed that irradiation of **3** in benzene through a Pyrex filter produced a new UV–vis absorption band with a $\lambda_{\text{max}} = 420$ nm, which is a typical value for *o*-xylenes¹¹ (Fig. 1, dashed line). Continued photolysis of **3** led to disappearance of this band, as expected from the known photolabile nature of these species.¹¹

Although pure samples of **8** cannot be isolated due to their low steady state concentrations, NMR analysis of partially irradiated samples of **3** in d_6 -benzene gave clear evidence of benzocyclobutane **7** and xylylene **8**



Scheme 4.



Scheme 5.

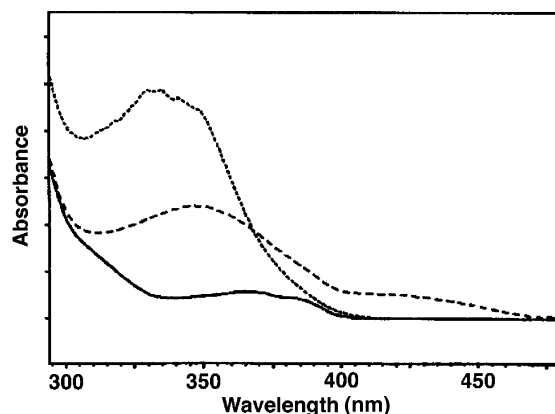


Figure 1. UV-vis spectra of 2-indanone **3** (—); spectra after 15 min (---), and 45 min (····) of irradiation, respectively. The transient absorption between 400 and 475 nm is assigned to *ortho*-xylylene **8**.

(Scheme 5). In addition to the signals of **7**, a doublet of triplets and a broad doublet assigned to *o*-xylylene **8** were observed at $\delta = 6.0$ and $\delta = 5.7$ ppm, respectively. Other signals present were attributed to secondary photoproducts of **8**. No olefinic protons were observed in the NMR spectrum when **3** was irradiated in the presence of maleic anhydride suggesting effective trapping of **8**. However, we established that reaction of **8** with maleic anhydride is photochemical as no reaction was observed after 5 days in the absence of light. The formation of the photolabile *o*-xylylene **8** and its secondary photoproducts may account for low yield of **7** in solution.¹⁴

Irradiation of pulverized crystals of bisketal **3** at room temperature with a Pyrex filter for 3 h afforded benzocyclobutane **7** as the only product after 25% conversion (Scheme 5). Longer irradiation under these conditions led to partial melting and formation of additional products. Photolysis at 0°C was sluggish with less than 5% formation of cyclobutane **7** after 10 h. The absence of *o*-xylylene **8** in the solid state is to be expected and is in agreement with results previously reported with **1a** and **1b**.¹³ While conversion of bisketal **3** to benzocyclobutane **7** involves only a small change in shape and volume, the formation of *o*-xylylene requires rotation of the two ketal units from nearly orthogonal to nearly co-planar with respect to the aromatic group. The crystalline environment should restrict such drastic motion.

Solution- and solid-state photochemistry of 1,3-bis(ethylenedithioxy)-2-indanone (4). To our knowledge, the photochemistry of bistioketal **4** has not been documented. The photochemical reactivity of **4** in solution was extremely sluggish and only complex mixtures were observed upon extended irradiation times. Crystals of **4** were completely stable at room temperature despite the potential radical stabilization endowed to the α -carbons by the thioketal substituents. We attribute the high photostability of **4** to intramolecular quenching. There are several reported examples of triplet ketone ${}^3n,\pi^*$ quenching by photoinduced electron transfer from thioethers.²⁰ In support of this hypothesis, we were able to quench the solution reactivity of the bisketal **3** with added 1,3-dithiane. A Stern–Volmer analysis that assumes diffusion-controlled quenching suggests an excited state lifetime of <4 ns, as expected for a highly reactive excited state.

Concluding remarks. The lack of solid state reactivity in tetramethyl indanone **2** suggests that the photodecarbonylation of **1a** and **1b** must be facilitated by the radical stabilizing abilities of the α -phenyl groups. The solid-state reactivity of bisketal **3** appears to be due to the *gem*-dialkoxy substituents rather than to benzylic stabilization by the indanone aryl group. These results indicate that *gem*-dialkoxy groups may enable decarbonylation of a wide variety of crystalline ketones, potentially allowing synthetic applications with suitable substrates. In contrast, the lack of reactivity of the bistioketal **4** is probably due to fast intramolecular

quenching. Additional examples and other functional groups are currently under investigation.

Acknowledgements

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