

Combination vs. disproportionation in dialkyl biradicals. Selectivity reversal in a crystalline solid†

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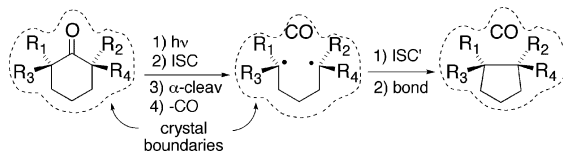
Received 11th January 2006, Accepted 31st March 2006

First published as an Advance Article on the web 18th April 2006

DOI: 10.1039/b603909j

While 1,6-biradicals produced by photodecarbonylation of dimethyl 11-oxodibenzo[*c,h*]bicyclo[4.4.1]undeca-3,8-diene-1,6-dicarboxylate (**1**) react exclusively by disproportionation in benzene solution, reactions in crystals lead to radical-radical combination reactions in almost quantitative yield.

Although photochemical reactions in crystals tend to proceed with high selectivity and specificity,¹ their limited predictability has prevented chemists from exploiting their potential. In recent years, we have shown that crystalline ketones with radical stabilizing substituents in the two α -positions can photodecarbonylate to form radical pairs and biradicals in a relatively efficient and reliable manner (Scheme 1).²

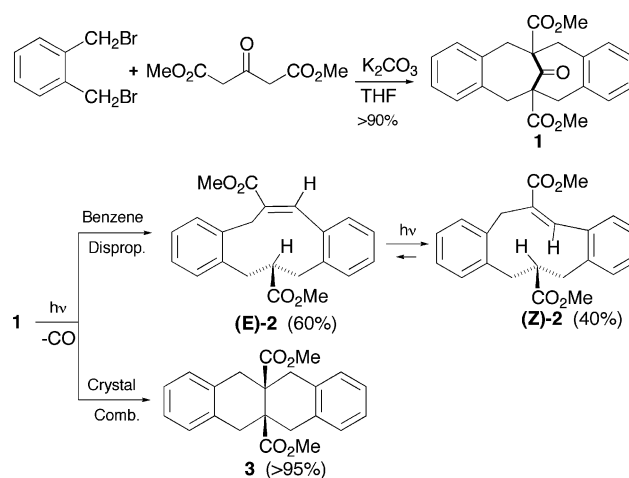


Scheme 1

Based on thermochemical arguments that consider the energy of the excited state and the energies of the two breaking sigma bonds, we have postulated that substituents with radical stabilizing energies (RSE) greater than *ca.* 12–15 kcal mol⁻¹ should react in the solid state.^{2,3} Our suggestion is based on the assumption that these RSE values are sufficient to render the excited state bond-cleavage reactions exothermic. In support of this postulate, we have shown that crystalline ketones with α -phenyl,⁴ α -carbonyl,⁵ α -vinyl,⁶ and α,α -dialkoxy-substituents⁷ with RSE > 12 kcal mol⁻¹ react efficiently when exposed to UV light. In addition, while radical pairs and biradicals formed in solution tend to give complex mixtures of combination and disproportionation products, reactions in crystals are highly selective.^{8,9} Examples involving hexasubstituted acyclic alkanones,⁵ cyclohexanones,^{6a,7,9,10} and cyclopentanones¹¹ illustrate an ideal selectivity for a stereospecific radical combination despite the steric repulsion arising during formation of a σ -bond between two bulky quaternary carbons. Recognizing the synthetic potential of this process, we have

recently applied it the total synthesis of the naturally product herbertenolide.¹²

As part of our continuing studies on the feasibility, selectivity and general scope of the solid state reaction, we decided to investigate the solid state photochemical reactivity of dimethyl 11-oxodibenzo[*c,h*]bicyclo[4.4.1]undeca-3,8-diene-1,6-dicarboxylate **1** and to compare its chemo- and stereoselectivity with those observed in solution.¹³ Our interest in compound **1** was motivated by its α,α -dicarboxylic ester substitution, which is expected to facilitate the solid state reaction,³ and by the fact that reaction in solution was shown to yield the macrocyclic cyclodecene isomers (*E*)-**2** and (*Z*)-**2** by disproportionation of an intermediate 1,6-cyclodecane biradical followed by photoequilibration (Scheme 2).¹³



Scheme 2

Samples of bicyclic ketodiester **1** were prepared as reported by Rodriguez and Lavoisier-Gallo^{14a} from α,α -dibromo-*ortho*-xylene and dimethyl-1,3-acetone-dicarboxylic acid (Scheme 2). As reported previously, photochemical experiments in benzene solution with $\lambda \geq 290$ nm (Pyrex filter) yielded the disproportionation products (*E*)-**2** : (*Z*)-**2** = 60 : 40 in a photostationary state.¹³ In contrast, experiments carried with powdered crystals of **1** grown from hexane revealed a very smooth solid-to-solid photochemical reaction, which provided the recombination product **3** as the only product in nearly quantitative yield.

Good quality crystals of **1**, (*Z*)-**2**, and **3**, obtained from hexane, were analyzed by single crystal X-ray diffraction.† The X-ray structure of ketone **1** (mp = 182–183 °C) was solved in the triclinic space group $P\bar{1}$ with two molecules per asymmetric unit, as a different polymorph than the one previously reported by Mataka and coworkers,^{13,14b} which crystallized from ethanol in

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† Financial support by the USA National Science Foundation is gratefully acknowledged.

the monoclinic space group $P2_1/c$ with only one molecule per asymmetric unit. The two molecules in the triclinic crystals are nearly identical to each other and may be described as having their two seven-membered rings in a chair-boat conformation (Fig. 1, top). The structure of **1** has an approximate mirror plane that cuts across the center of the two aromatic rings, and across the bridging ketone, with the two ester groups adopting a nearly parallel alignment. The X-ray structure of (*Z*)-**2** allowed us to confirm the (*Z*) configuration of the double bond, which had been previously suggested from chemical shift arguments, and the mechanistically expected (*endo*) relation of the methine hydrogen towards the transannular double (Fig. 1, bottom left). The crystal structure of (*Z*)-**2** was solved in the space group $C2/c$ with one molecule per asymmetric unit. The molecular structure of (*Z*)-**2** adopts a rectangular [2323] boat-boat-boat conformation¹⁵ with the two aromatic rings tilted in the same orientation. The X-ray structure of the recombination product **3** (mp = 109–111 °C) was solved in the space group $P2_1/c$ with one molecule per asymmetric unit. The molecular structure of **3** was characterized by the expected *cis*-ring junction of the dibenzo decaline,¹⁶ with the two fused 6-membered rings adopting twist-boat conformations. The ester groups adopt an antiparallel orientation with the carbonyl oxygens pointing towards the center of the structure. Notably, the shape of the recrystallized photoproduct **3** is very different from the structure of its crystalline precursor **1**.

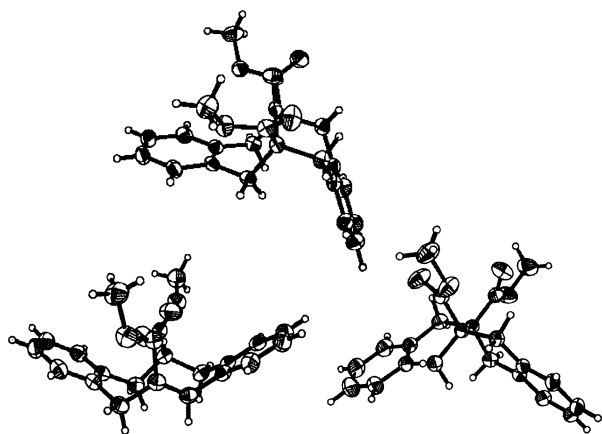
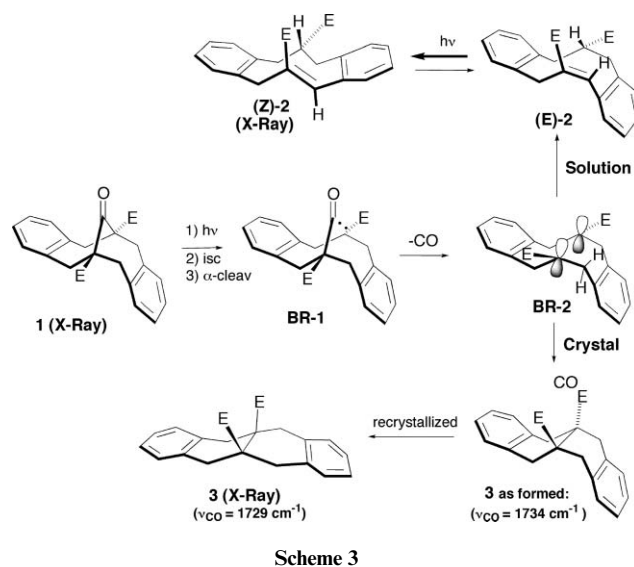


Fig. 1 Ortep diagrams at 50% probability from X-ray structures of ketodiester **1** (top), the secondary solution disproportionation photoproduct (*Z*)-**2** (bottom left), and the solid state combination product **3** (bottom right). The views in the figure approach the perspective shown by line formulas in Scheme 3.

The selectivity of the reaction in solution and in crystals can be understood by analysis of the reaction mechanism (Scheme 3).^{2,17,18} It is well known that ketone photodecarbonylation is a stepwise process involving: (1) electronic excitation into the ketone n,π^* excited state followed by intersystem crossing, (2) a Norrish type-I α -cleavage reaction to form an intermediate acyl-alkyl biradical **BR-1**, (3) the loss of CO to form the dialkyl biradical **BR-2**, and (4) the formation of products by either radical disproportionation [such as (*Z*)-**2** and (*E*)-**2**] or by radical combination (**3**) from the biradical singlet state.

One of the main differences between reactions in solution and in crystals is the limited conformational freedom experienced by



molecules in the solid state. In fact, reactions in crystals are known to occur under topochemical control, implying that they are least motion processes brought about by the structural organization present in the crystal lattice and the constraints for molecular motion.¹⁹ In the case of **1**, it is expected that α -cleavage, decarbonylation, and bond formation will proceed in such a way that the shape of the cavity corresponding to the starting ketone will be retained along the entire reaction coordinate. A preference for radical disproportionation over radical combination in solution may be the result of the high steric encumbrance expected during the bond-forming reaction to give **3**, along with the close proximity of a *trans*-annular hydrogen to the radical centers in **BR-2**. The formation of (*E*)-**2** as the primary photoproduct may be a sign of conformational memory in **BR-1** and **BR-2**. As illustrated in Scheme 3, the overall conformation of the ten-membered ring may be very similar in the ketone, in the two biradicals, and in (*E*)-**2**. The observed photo-equilibration of (*E*)-**2** and (*Z*)-**2** suggests that the two isomers have similar stabilities under the reaction conditions in solution.

Reactions in the solid state tend to prevent conformational isomerization and to favor products that retain the shape of the reactant. The exclusive formation of **3** suggests a least motion process, and a preference for reactions with small changes in shape and size. It is noteworthy that the stable conformation of the dibenzo-*cis*-decaline ring system in crystals of **3** has a more flattened and twisted structure than that expected when it forms in the crystal lattice of **1**. Searching for evidence of different conformation for the two solid samples we analyzed the FT-IR spectrum of “as-formed” and recrystallized samples of **3**. The two spectra are indeed very different. The spectrum of the “as-formed” diester has a strong band at 1734 cm^{-1} and two medium bands at 1234 , and 1205 cm^{-1} , which we assign to the C=O and C–O stretching modes of the two ester groups, respectively. The corresponding bands in the recrystallized samples occur at 1729 cm^{-1} for the C=O, and a single strong band at 1205 cm^{-1} for the C–O stretch. Many differences were also observed in the fingerprint region. Thermal analyses as a function of reaction progress by differential scanning calorimetry revealed a solid-to-solid reaction with a steady depression of the melting

point, broadening of the melting transition, but no indication of an eutectic. The lack of eutectic point indicates a solid-to-solid reaction that proceeds in a continuous phase, suggesting the formation of **3** in a metastable phase where product molecules retain the approximate shape and packing arrangement of the reactant.²⁰

In conclusion, with the radical stabilizing effects of the two α -ester groups, the photochemical reaction of ketone **1** in the crystalline solid state proceeds smoothly, with excellent chemical yields and with complete control of the reaction chemoselectivity. This and other recently published examples strongly suggest the synthetic potential of the solid state photodecarbonylation reaction as a reliable method to generate biradicals that have a large tendency to form bonds in a stereospecific manner between adjacent quaternary centers.

Notes and references

‡ Single crystals of compound **1** were obtained from hexane by slow solvent evaporation with samples obtained as described in ref. 14a. Single crystals of (*Z*)-**2** were obtained by selective crystallization from a mixture containing 60% (*Z*)-**2** and 40% of (*E*)-**2** from a photostationary state obtained by photolysis of ketone **1** in benzene with $\lambda > 290$ nm (Pyrex filter). Single crystals of **3** were obtained by slow solvent evaporation from hexane using a sample obtained by irradiation of **1** in the solid state with $\lambda > 290$ nm (Pyrex filter). *Crystal structure determinations.* 1,6-Dimethoxycarbonyl-11-oxodibenzo[*c,h*]bicyclo[4.4.1]undeca-3,8-diene **1**, C₂₃H₂₂O₅, *M* = 378.41, triclinic, space group *P1* (no. 2), *a* = 12.4283(9) Å, *b* = 12.4686(8) Å, *c* = 12.8462(9) Å, α = 85.951(2)°, β = 88.997(1)°, γ = 78.875(1)° *U* = 1948.4(2) Å³, *T* = 298 K, *Z* = 4, $\mu(\text{Mo-K}\alpha)$ = 0.09 mm⁻¹, 12879 reflections measured, 8970 unique (*R*_{int} = 0.0167) which were used in all calculations. *F*² refinement, *R*₁ = 0.044, *wR*(*F*₂) was 0.1284 (all data). 6,13-Dimethoxycarbonyl-(*Z*)-5,6,7,12-tetrahydrodibenzo[*a,f*]cyclohexene (*Z*)-**2**, C₂₂H₂₂O₄, *M* = 350.40, monoclinic, space group *C2/c* (no. 15), *a* = 25.049(3) Å, *b* = 11.381(1) Å, *c* = 14.777(1) Å, β = 117.603(2)°, *U* = 3733.2(7) Å³, *T* = 298 K, *Z* = 8, $\mu(\text{Mo-K}\alpha)$ = 0.085 mm⁻¹, 16369 reflections measured, 4536 unique (*R*_{int} = 0.0209) which were used in all calculations. *F*² refinement, *R*₁ = 0.049, *wR*(*F*₂) was 0.1607 (all data). 5*a*,11*a*-Dimethoxycarbonyl-*cis*-5,6,11,12-tetrahydronaphthacene **3**, C₂₂H₂₂O₄, *M* = 350.40, monoclinic, space group *P2₁/c* (no. 14), *a* = 14.816(1) Å, *b* = 14.899(1) Å, *c* = 8.3482(7) Å, β = 90.134(2)°, *U* = 1842.8(3) Å³, *T* = 298 K, *Z* = 4, $\mu(\text{Mo-K}\alpha)$ = 0.086 mm⁻¹, 16259 reflections measured, 4455 unique (*R*_{int} = 0.0477) which were used in all calculations. *F*² refinement, *R*₁ = 0.052, *wR*(*F*₂) was 0.1538 (all data). CCDC reference numbers 295161–295163 for **1**, (*Z*)-**2** and **3**, respectively. For crystallographic data in CIF or other electronic format see DOI: 10.1039/b603909j

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