

Engineering Reactions in Crystalline Solids: Photochemical Generation of Secondary and Tertiary Enol Radical Pairs from Crystalline Ketodiester

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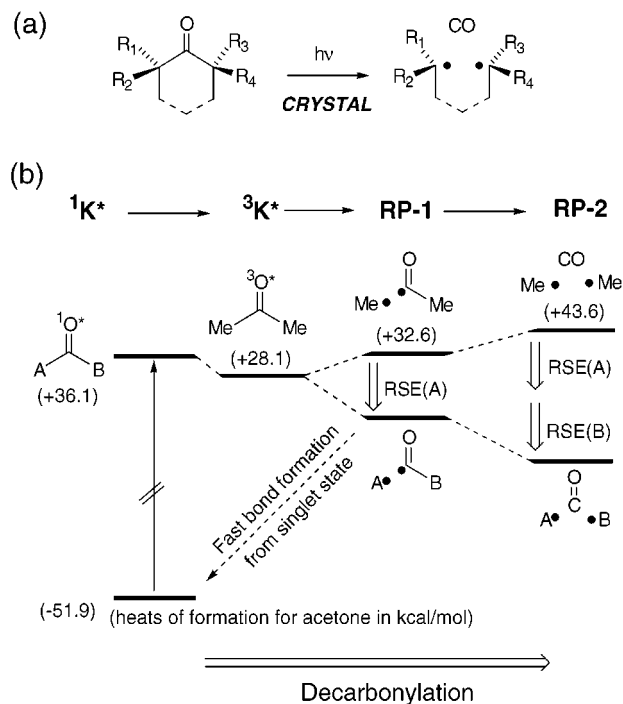
The photochemical decarbonylation of several crystalline 1,3-acetonedicarboxylates has been analyzed in solution and in the solid state. It is shown that the efficiency of the solid-state reaction depends on the stability of the intermediate acyl–alkyl and alkyl–alkyl radical pairs. Reactions proceeding through tertiary enol radicals are more efficient than reactions proceeding through secondary enol radical centers. Solid-state reactions that require the intermediacy of primary enol radicals do not occur. It is also shown that the selectivity of product formation in crystals depends on the structure of the reactant solid phase.

Introduction

Although reactions in crystals are severely restricted by the lack of external reagents and their limited molecular motion, they include some of the most impressive examples of reaction control and mechanistic insight.¹ An immediate challenge in the field of crystal chemistry comes from the need to carry out a wide range of reactions in a reliable manner to help develop qualitative models and rigorous theories. Some limitations come from the lack of additional reagents, low melting temperatures, and the unpredictability of packing arrangements for bimolecular reactions. To alleviate some of these problems, we have recently explored the use of crystalline compounds that are capable of forming high-energy species such as carbenes,² biradicals, and radical pairs.³ By taking advantage of their unimolecular reactions, we have analyzed the effect of crystals on their chemical reactivity,^{2,3} and the effects of reactivity on the structure and properties of crystals.^{2d,3c}

In search of general reaction models, we have recently suggested that photochemical decarbonylation of crystalline ketones may constitute a reliable entry to the

Scheme 1



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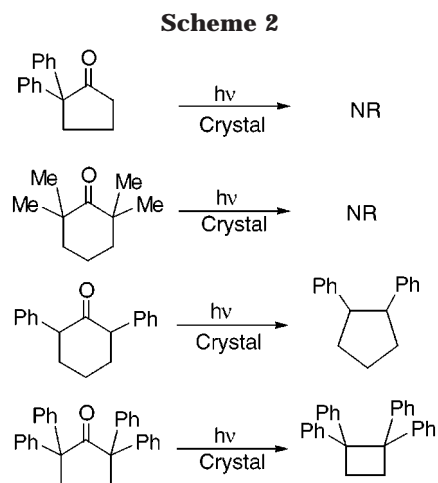
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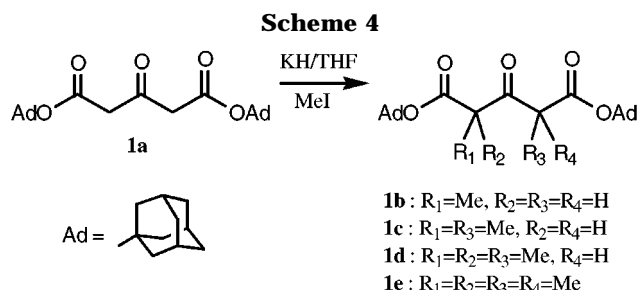
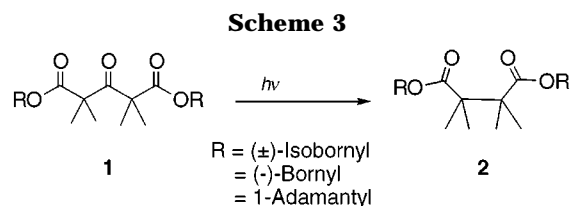
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been absorbed by the ground-state molecule. Reactions occur along the singlet (1K) and triplet (3K) excited states, which form an intermediate acyl-alkyl (**RP-1**) radical pair before proceeding to the target alkyl-alkyl radical pair (**RP-2**). It is known that α -cleavage occurs from singlet and triplet states with n,π^* electronic configuration. However, since regeneration of the starting ketone from the singlet state of **RP-1** should be exceedingly fast (Scheme 1, dotted arrow),³ reactions in crystals should be favored on the triplet manifold.

It is well known that the kinetics of the α -cleavage and decarbonylation reactions have a strong correlation with thermochemical parameters.⁴ It is also known that the thermochemistry of the two cleavage reactions is determined by excitation energies and the stability of the resulting radical centers.^{6a} We have proposed that substituents that lower the bond dissociation energies of the A-CO-B bonds, by increasing the stabilities of radicals A^\bullet and B^\bullet [RSE(A) and RSE(B)], may facilitate the solid-state reaction. In the case of triplet acetone, the α -cleavage and decarbonylation steps are endothermic by 4.5 and 11.0 kcal/mol, respectively, making the loss of CO the reaction-determining step (Scheme 1). Therefore, assuming that reactions in crystals must be thermoneutral or exothermic, and taking triplet acetone as a benchmark, we propose that decarbonylation should require substituents that can lower the BDE values of the two α -bonds by more than ~ 11.0 kcal/mol.⁷ In support of this proposal we have shown that crystalline ketones leading to secondary (ca. RSE ~ 6 kcal/mol) and tertiary (ca. RSE ~ 8.5 kcal/mol) radical centers fail to react in the solid state, even when they are able to react efficiently in solution and in the gas phase. While all the ketones in Scheme 2 react efficiently in solution, only those with phenyl substituents (RSE ~ 15 – 20 kcal/mol) on both α -carbons proceed through stabilized benzylic radicals and lead to products in the solid state.^{3,8}

Since the effects of substituents on bond dissociation energies can be obtained from thermochemical data, *it should be possible to predict the reactivity of a large*



number of crystalline ketones. To test this hypothesis we have just begun a systematic exploration of the effects of substituents on the relative efficiencies of solid-state reactions.⁹ While the α -cleavage (or Norrish type-I) and acyl decarbonylation reactions are well-established processes in solution, they have not been predictable in the solid state. In a recent communication we reported that photolysis of crystalline dialkyl 1,1,3,3-tetramethyl-1,3-acetonedicarboxylates yielded the corresponding succinates in high chemical yields (Scheme 3).¹⁰ On the basis of literature data, we estimated that an ester carbonyl and two methyl groups provide a RSE of ca. 12.3 kcal/mol.^{7,11} Given the high solid-state reaction efficiencies observed, it was of interest to determine the extent of alkyl substitution required for the solid-state reaction. In this paper, we report solution and solid-state results obtained with a set of diadamantyl-1,3-acetonedicarboxylates **1a**–**1e** with varying degree of α -methyl substituents (Scheme 4). We have found that reactions in crystals proceed with good to excellent efficiencies through secondary and tertiary enol radicals but not at all through primary enol radical pairs. It was also confirmed that radical reactions in the crystalline phase proceed with excellent chemoselectivities and sometimes with excellent chemical yields.

Results and Discussion

Preparation of Compounds 1a–e. The adamantyl group in compounds **1a**–**e** was chosen with the hope of obtaining crystalline compounds with suitable melting points. The unsubstituted ketodiester **1a** (Scheme 4) was prepared by transesterification of commercially available diethyl-1,3-acetonedicarboxylate with 1-adamantanol using a reported procedure.¹² We had previously noticed that **1a** exists as a mixture of tautomers (keto:enol = 8:1) in solution, but only the keto tautomer appeared to be present in the solid state.¹⁰ In the cases of ketones **1b**–**d**, we have established that only the keto form is present both in $CDCl_3$ and in crystals. The α -monomethyl keto-

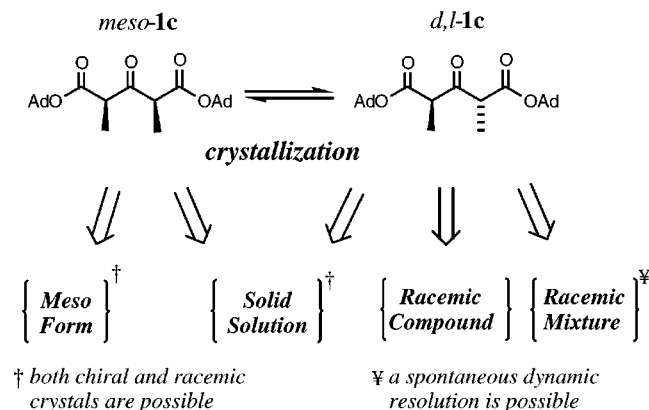
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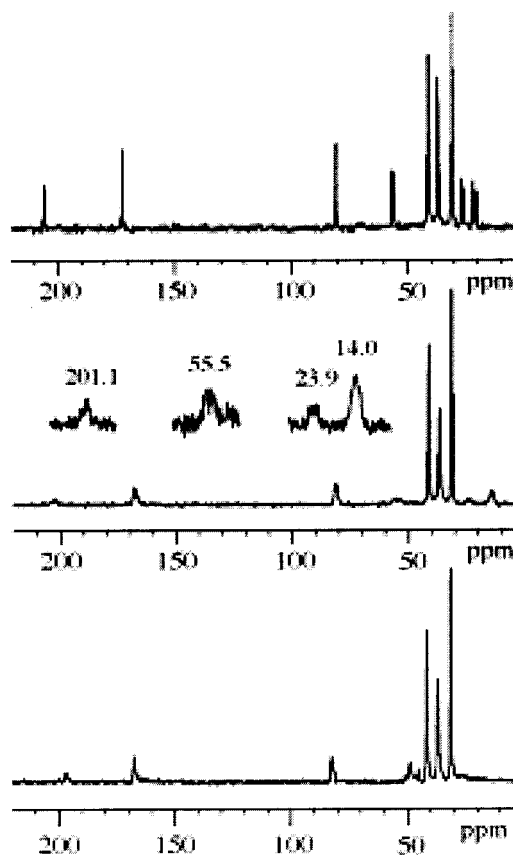
Table 1. Melting Points and Carbonyl Stretching Frequencies of Compounds 1a–e in Crystals

	mp (°C)	(C=O) FT-IR (cm ⁻¹)
1a ^a	67–69	1726, 1716 (sh)
1b	74–79	1738, 1732, 1709
1c ^b	55–59	1737, 1710
1d	93–95	1738, 1731, 1712
1e	165–167	1731, 1705

^a Weak bands were also observed at 3422 and 1647 cm⁻¹.^b Mixture of diastereomers.**Scheme 5**

diester **1b**, and the α,α' -dimethyl ketodiester *meso*- and *d,l*-**1c** were obtained as a mixture by reaction of **1a** with 1.5 equiv of KH and excess MeI at 0°C in THF. Compound **1b** was separated from the two diastereomers of **1c** by flash chromatography, each in ca. 35% isolated yield. The trimethyl compound **1d** was obtained in 90% yield under similar reaction conditions with 3 equiv of both KH and MeI. The synthesis of **1e** was accomplished with excess KH and MeI as reported in a previous paper.¹⁰

Crystallization and Characterization of the Keto-Form by FT-IR. To interpret the photochemical reactivity of crystalline diadamantyl ketodicarboxylates **1a–e** we first analyzed their crystallization properties and set out to determine the tautomeric form that is present in the solid state. As we had hoped, all of the adamantyl-substituted compounds used in this study turned out to be crystalline solids with melting points ranging from 55–59 °C to 165–167 °C (Table 1). Compounds **1a**, **1b**, **1d**, and **1e** were crystallized by slow solvent evaporation from hexane and diethyl ether mixtures (4:1) at ambient temperature. The mixture of *d,l* and *meso* isomers of ketodiester **1c** was crystallized in the same solvents at 0 °C. The presence of the keto form in the solid state was confirmed for all samples by FT-IR spectra obtained with microcrystalline samples in KBr matrices. The stretching frequency of the ester carbonyls in the solid state occurred between 1726 and 1738 cm⁻¹, and the corresponding signals for the ketones were found between 1705 and 1716 cm⁻¹ (Table 1). From the five ketodiester, samples of **1a** and mixtures of *d,l*- and *meso*-**1c** were particularly interesting. Samples of **1a** appeared to contain also the enol form, and crystals grown from samples of *meso*- and *d,l*-**1c** were interesting because of the possible epimerization and selective crystallization of one of the two diastereomers (Scheme 5). To determine the composition of their crystals we decided to analyze their solid state ¹³C NMR by cross polarization and magic angle spinning (CPMAS).

**Figure 1.** Solid-state ¹³C CPMAS NMR of compounds **1a** (bottom), **1c** (middle), and **1e** (top).

Analysis of Compounds 1a, 1c, and 1e by CPMAS ¹³C NMR. Given its crystallinity, high melting point, and the lack of enolizable hydrogens, we determined the ¹³C CPMAS NMR spectrum of compound **1e** as a standard for comparison with the spectra of **1a** and **1c**. As shown in Figure 1 (top), the solid-state spectrum of **1e** is remarkably sharp, with carbonyl signals at 205.6 and 172.3 ppm, assigned to the ketone and ester groups, respectively. Four signals corresponding to 10 adamantyl carbons at 80.5, 41.1, 36.7, and 30.8 ppm suggest a high average symmetry by rapid rotation about the 3-fold axis of the adamantyl moiety.¹³ Two signals corresponding to the quaternary α -carbons (56.6 and 55.6 ppm), and four signals corresponding to the methyl groups (26.7, 25.7, 21.7, and 20.3 ppm) indicate the lack of average mirror symmetry that is observed in the solution spectrum.

The spectra of compounds **1a** and **1c**, also shown in Figure 1, had significantly broader lines than that of the tetramethyl derivative. The presence of the enol form in crystals of **1a** was analyzed because of its possible impact on the solid-state photodecarbonylation reaction. Our attention to the enol form in **1a** was initially drawn by weak bands in the FT-IR spectrum that were centered at 3422 and 1647 cm⁻¹, which suggested the presence of O–H and a C=C functional groups. However, as illustrated in the bottom spectrum in Figure 1, only the keto form can be detected within the limits of the solid-state NMR experiments (ca. >90%). We believe that a small amount of enol may form upon preparation by mechanical grinding of the relatively low melting crystals

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of **1a** with the KBr salt. Although the solid-state spectrum of **1a** is somewhat broadened, it is consistent with a symmetric structure having two equivalent halves. Carbon resonances at 196 and 167 ppm are assigned to ketone and ester carbonyls, and a signal at 48 ppm is assigned to the α -carbons. As in the crystals of **1e**, an axially rotating adamantyl substituent in the solid is suggested by only four signals at 82, 41, 37, and 31 ppm for the 10 adamantyl carbons.

A detailed characterization of crystals of the α,α' -dimethyl compound **1c** was motivated by its rich stereochemical possibilities. Our initial attempts to isolate the two diastereomers of **1c** by chromatography were fruitless, suggesting that they equilibrate under conventional handling conditions. NMR experiments run with samples of **1c** with added pyridine increased the equilibrium concentration of the enol form in CDCl_3 from immeasurably small to ca. 10% and established that samples of **1c** were present at equilibrium in a 1:4 diastereomeric ratio. Methyl and methine signals of the major diastereomer, resonating at higher field in both ^1H and ^{13}C NMR spectra, are tentatively assigned to *d,l*-**1c** on the basis of conformational analysis with molecular mechanics and semiempirical AM1 calculations.¹⁴

The crystallization of **1c** may involve either or both diastereomers, and several crystal forms are possible (Scheme 5). Crystalline samples may exist as heterogeneous mixtures of various polymorphs, as a single polymorph of a given diastereomer, or as a solid solution with the two diastereomers in the same crystal lattice (Scheme 5).¹⁵ Crystals of the *meso* form may exist in chiral or racemic space groups,¹⁶ and crystals of the *d,l* form may be racemic or optically active. Substances that racemize under crystallization conditions can sometimes undergo a spontaneous dynamic resolution, where crystallization can resolve one of the equilibrating stereoisomers.¹⁷ Solid solutions may in principle occur within any of the crystal phases of the components.¹⁸ We had noticed that the melting point of the mixture of *d,l*- and *meso*-**1c** was relatively sharp (55–59 °C), suggesting the possibility of a single-crystal phase rather than a heterogeneous mixture. To distinguish between these two possibilities, we determined the composition of single crystals by rapid dissolution and ^1H NMR analysis in CDCl_3 . The results revealed a 1:4 ratio, such as was observed in solution under equilibrating conditions. While it is possible that equilibrium may be established within the time of ^1H NMR analysis, further evidence of a solid solution of the diastereomers was obtained by spectroscopic methods and thermal analysis. FT-IR spectra obtained with crystals of **1c** revealed only one broad ester band at 1736 cm^{-1} and one ketone signal at 1716 cm^{-1} (Table 1). This result is consistent with a single-crystal phase because it is not uncommon for polymorphs and crystals of

Table 2. Irradiation Times, Percent Conversion, and Product Distribution of Ketodiester 1a–e in Benzene and in Crystals^a

	media	time (h)	conv (%)	2a	2b	2c	2d	2e	3	4	5
1a	C_6H_6	4	tr	tr							
	crystal	4	~0	~0							
1b	C_6H_6	4	80	6	6	27			35 ^f	6	20
	crystal	4	17 ^b	0	10	50					40
1c^c	C_6H_6	4	86			54			27		0
	crystal	1.5	8 ^d	0	100	0					
1d	C_6H_6	4	94			6	19		7	63 ^f	4
	crystal	4	36			0	100 ^e	0			
1e	C_6H_6	4	100						20	45	35
	crystal	4	87						100		

^a Irradiations were carried out with a Hanovia medium-pressure mercury lamp using a 305 nm cutoff filter. Conversions were determined by gas chromatography using an external standard. Relative yields were determined by gas chromatography and are not calibrated. ^b Product was detected only when liquid was observed. ^c Mixture of the *meso* and *d,l* pair. ^d Crystals melted after 1.5 h or 10% conversion. ^e The selectivity decreased to **2c:2d:2e** = 5:90:5 after 45% conversion. ^f Mixture of acetate and propionate from **1b** and mixture of propionate and isobutyrate from **1d**.

stereoisomers to have resolvable signals.¹⁹ A differential scanning calorimetric (DSC) analysis is also consistent with a single crystalline phase. The DSC consists of a broad endothermic transition with a maximum at 59 °C, rather than two transitions, as would be expected for a two-phase mixture.²⁰ Finally, the CPMA ^{13}C NMR spectrum of **1c** (Figure 1, middle) was characterized by broad signals, as expected from the large chemical shift dispersion caused by the crystallographic disorder of a solid solution. Broad ketone and ester carbonyls are observed at 202 and 168 ppm. Quaternary α -carbons occurred at 55.5 ppm and broad methyl signals were observed at 23.85 and 13.98 ppm. Remarkably, the composition of the solid-state samples, determined from the intensity of the methyl signals is in complete agreement with the spectrum obtained in CDCl_3 after dissolution of the sample (see Supporting Information). Methyl signals corresponding to each of the two diastereomers integrate for a ratio of about 1:4. These results conclusively demonstrate that *meso*- and *d,l*-**1c** co-crystallize in a solid solution.

Photochemical Results in Benzene and in Crystals. To determine the effect of substituents on solid-state reactivity, we set out to analyze the relative reactivity of compounds **1a–1e** in solution and in the solid state. Since reactants in crystals tend to have access to fewer products than reactions in the liquid phase, changes in selectivities and specificities were taken as a measure of crystallinity to detect the involvement of liquid phases (melting) or defect sites. The results from irradiations in both reaction media are shown in Table 2. Listed in the table are the percent conversion and the chemoselectivity of product formation determined by gas chromatographic analysis. Irradiation of **1a–1e** in deoxygenated 10^{-3} M benzene solutions at ambient temperature for 4 h gave mixtures of succinates **2a–e**, acetates **3**,

(14) Force field (Sybyl) and semiempirical (AM1) analysis carried out with the Spartan program suggest that the lowest energy conformer of *d,l* form is more stable than that of the *meso* form by 0.99 and 0.80 kcal/mol, respectively: *Spartan*; Wavefunction, Inc. 18401 von Karman Ave., Suite 210, Irvine, CA 92715.

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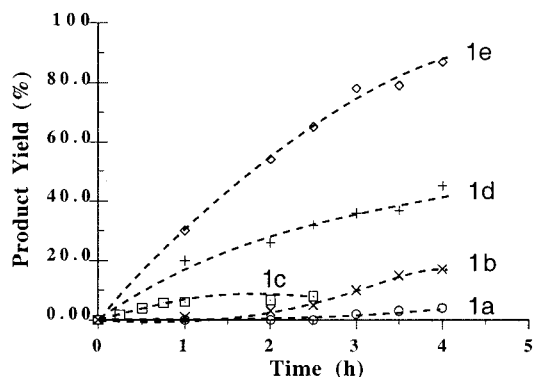


Figure 2. Yields of decarbonylation of ketones **1a–e** in the solid state as a function of irradiation time. Ketones **1a** and **1b** display sigmoidal behavior and begin to react after ~2 h. Mixtures of *meso*- and *d,l*-**1c** melted at ambient temperature after reaching about 10% conversion.

acrylates **4**, and diketodiester **5** (Scheme 6). Products **2–4** were identified by co-injection with authentic samples prepared independently. Compound **5** was only observed upon irradiation of **1b** and its assignment is based on MS data. The extent of reaction of **1a–e** in benzene varied from traces, in the case of **1a**, to more than 80% in the cases of **1b–e** (Table 2). Differences in solid-state reactivity were determined in side-by-side photolysis experiments with fine crystals of compounds **1a–e** (5 mg) over a 4 h period at ambient temperature (Figure 2). The extent of reaction for compounds **1a**, **1b**, **1c**, **1d**, and **1e** after 1 h at ambient temperature was 0%, 0%, 6%, 20%, and 30%, respectively. A plot of reaction yields as a function of irradiation time reflects the relative efficiencies of product formation while exposing phase changes or crystal melting. The sigmoidal plots (Figure 2) and the low reaction selectivities (Table 2) in the case of ketodiester **1a** and **1b** can be associated with reactions that occur at dislocations, high strain sites, and other product-induced crystal defects.²¹ The solid solutions of *meso*- and *d,l*-**1c** reacted rapidly and cleanly until melting occurred at about 10–12% conversion. This observation is consistent with a rapid decrease in the melting point of the four-component mixture consisting of two diastereomeric reactants and their products.²² In contrast, irradiation of **1d** and **1e** in the solid state proceeded very cleanly, with high chemo- and stereoselectivities, and to relatively high conversion values.

Reaction Efficiencies in Benzene and in Crystals.

A quantitative comparison of reaction efficiency in solution and in crystals is complicated by difficulties involved in the precise determination of the number of photons absorbed by the solid.²³ However, a qualitative analysis based on relative chemical efficiencies provides a reactivity ranking that can be correlated with the effects of substituents. The relative efficiencies of product formation in solution and in crystals are consistent with the effect of the environment on the α -cleavage and decar-

bonylation steps illustrated in the reaction mechanism of Scheme 6.⁶ The main differences between the two reaction media come from the severely limited motion and close proximity between radical centers in the solid state. The tight packing and rigidity in crystals may reduce the yields of the cleavage reactions, and the close proximity between radical centers may force the reversible formation of the ground-state ketone.

Reactions in solution occur through free radicals, and reactions in crystals through tightly “caged” radical pairs.²⁴ In either case, the reaction starts by photochemical excitation and is followed by fragmentation of the weakest α -bond (steps 1 and 2, Scheme 6). While formation of acyl–alkyl radical pairs RP-1 may occur from both singlet and triplet excited states, it is known that productive pathways for ¹RP-1 depend strongly on the viscosity of the medium. Rapid separation in nonviscous liquids produces free radicals, which have sufficiently long lifetimes to find reaction partners or to undergo unimolecular rearrangements. In contrast, singlet acyl–alkyl radical pairs (¹RP-1) that are formed within crystals are likely to revert to the ground-state ketone much faster than they can undergo any reaction. It is expected that the total reaction yields in liquids will be determined by the quantum yields of α -cleavage from both singlet and triplet manifolds. In contrast, reactions in crystals should depend on the quantum yields of triplet formation, the yield of triplet α -cleavage to generate a triplet acyl–alkyl radical pair, ³RP-1 (steps 1 and 2), and on the efficiency of the decarbonylation reaction to generate the alkyl–alkyl radical pair ³RP-2 (step 5, Scheme 6).

Assuming that formation of RP-2 is irreversible, the branching point that determines whether products can form in the solid state is given by the competition between step 5 relative to steps 3 and 4. It is well known that methyl substituents decrease the dissociation energy of the carbonyl– α -carbon bond in ketones, and increase the rate of decarbonylation reactions of acyl radicals.⁴ In contrast, it may be expected that the rates of intersystem crossing (step 3) of acyl–alkyl radicals pairs (³RP-1) in crystals should be similar for radicals with different methyl substituents.²⁵ Experimental²⁶ and computational²⁷ results indicate that a carbonyl group should have a radical stabilization energy of about 7–9 kcal/mol, which is slightly higher than that of an alkyl substituent but significantly lower than the more delocalized allyl radical. It is known that methyl substituents can lower the homolytic energies of the α -bonds by a combination of electronic and steric effects.^{7,28} The addition of a single methyl group, to form a secondary enol radical, is estimated to add about 6 kcal/mol stabilization energy,^{26,27} suggesting that the required ~11 kcal/mol

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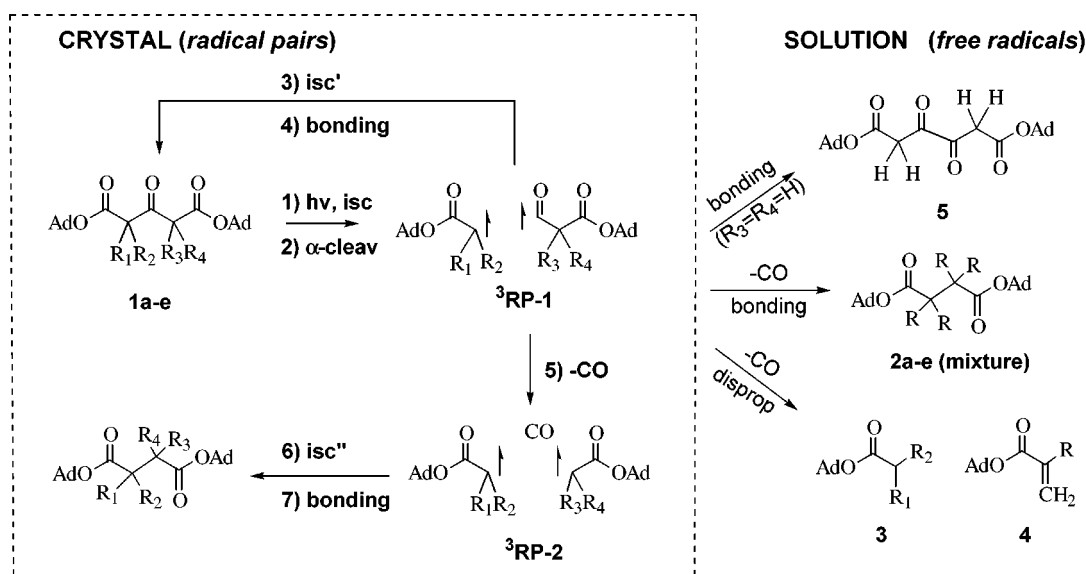
(25) Intersystem crossing in biradicals and radical pairs is primarily determined by distance and orientation-mediated spin-orbit coupling and by hyperfine interactions. These factors should be similar for radical pairs from ketones **1a–e**.

(26) (a) Solly, R. K.; Golden, D. M.; Benson, S. W. *Int. J. Chem. Kinet.* **1970**, *2*, 381. (b) King, K. D.; Golden, D. M.; Benson, S. W. *J. Am. Chem. Soc.* **1970**, *92*, 5541. (c) Calle, L. M.; Kana'an, A. S. *J. Chem. Thermodyn.* **1974**, *6*, 935.

(27) Parkinson, C. J.; Mayer, P. M.; Radom, L. *J. Chem. Soc., Perkin Trans. 2* **1999**, 2305–2313.

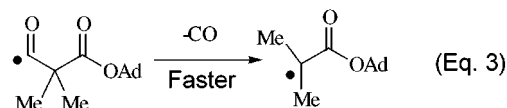
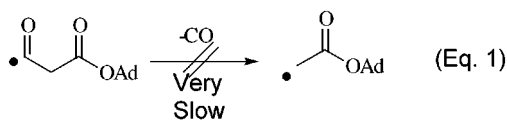
(28) Rüdhardt, C.; Beckhaus, H.-D. *Top. Curr. Chem.* **1985**, *130*, 1–22.

Scheme 6



that we have proposed for a solid-state reaction can be satisfied for secondary enol radicals (*vide supra*). Finally, unless there is a large strain relief, the additional stabilization of a third methyl group to form a tertiary radical center is expected to be relatively small, ca. 1–3 kcal/mol.

The results in Table 1 and Figure 2 qualitatively confirm the expected substituent effects on the solid-state reactions. Crystals of **1e**, with four α -methyl groups, react about twice as fast as crystals of **1d** that have only three. Ketone **1e** more than doubles the solid-state reactivity of **1c**, which has only one methyl group on each of the α -carbons. Compounds **1b** and **1a**, with at least one α -carbon having no methyl substituents, are both stable. A closer analysis of α, α' -dimethyl ketone **1c** and monomethyl ketone **1b** reveals that decarbonylation is essential for efficient solid-state reactions. Results in solution suggest both compounds undergo α -cleavage to give secondary enol radicals with similar efficiencies. However, while α -methyl acyl free radicals from **1c** decarbonylate efficiently to give another secondary enol (eq 2), free acyl radicals from **1b** are unable to decarbonylate (eq 1). Compound **1c** reacts in the solid state with modest efficiency to give the decarbonylation product **2c**, but compound **1b**, which is unable to decarbonylate, can only react in solution, in defect sites, and in the melt, to give a mixture of products that includes α -diketone **5**.



It is clear from results with compounds **1a–c** that radical-stabilizing substituents are needed at both sides

of the ketone group to facilitate both the α -cleavage and decarbonylation steps. Since it is expected that α -cleavage will occur preferentially at the side with the more substituted α -carbon, the more efficient solid-state reactivity of trimethyl ketone **1d** as compared to that of dimethyl ketone **1c** can be assigned to the more efficient α -cleavage of the former. Decarbonylation to give secondary enol radicals should be approximately the same for the two compounds. Analogously, α -cleavage to generate tertiary enol radicals in the cases of both **1d** and **1e** is likely to occur with similar quantum efficiencies. Therefore, the 2-fold increase in solid-state reactivity for **1e** as compared to that for **1d** is tentatively assigned to the more efficient decarbonylation step of the tetramethyl compound.

Reaction Selectivities. Differences in reaction selectivity in solution and in crystals reflect the much smaller configurational entropy of the crystalline solid state, as compared to that present in a fluid solution.²⁹ As indicated in Table 2, the selectivity of product formation in solution was generally low. Succinates **2b–e** form by statistical combination of enol free radicals formed after α -cleavage and decarbonylation. Unsymmetric ketones **1b** and **1d** give rise to two different enol radicals which combine to give three different products in solution. Meanwhile, symmetric ketones **1c** and **1e** give only one type of enol radical and only one combination product. Adamantyl acetates **3a–c**, and acrylates **4a, b** form only in solution by disproportionation of methyl-substituted enol radicals from compounds **1b–e**.

The photochemistry of **1b** was different from that of the other ketodiester and it was characterized by the efficient formation of the α -diketone **5**. The reaction mechanism involves efficient α -cleavage to give a secondary enol radical ($\text{MeCH}^{\bullet}\text{COEt}$) and a β -ethoxycarbonyl-acyl radical ($^{\bullet}\text{CO-CH}_2\text{COEt}$). Since the latter does not lose CO to give a primary enol radical, it reacts by random radical–radical combinations. Encounter and bond formation with the secondary enol regenerates the starting material, **1b**, a process that occurs with 50%

(29) Garcia-Garibay, M. A. *Curr. Opin. Solid State Material Sci.* **1998**, 3/4, 399–406.

probability but which goes undetected by product analysis. Reaction of the acyl radical with itself gives compound **5** with a similar probability as that of two enol radicals combining to give **2c** (about 25% each). Other compounds from this ketone are formed in solution in relatively minor quantities by radical–radical disproportionation. Interestingly, in contrast to solution photolyses, no radical disproportionation products were observed in reactions that proceeded when crystals melted. While the origin of this difference is not clear, it is possible that changes in chemoselectivity may reflect differences in viscosity between the two media

We have suggested that crystal rigidity limits the number of choices for each reactant, while crystal homogeneity restricts the number of reactant structures. The chemoselectivity induced by the crystalline phase is nearly ideal, with a clear preference for the combination of the intermediate enol radicals. The low selectivity for product formation in crystals of **1b** was correlated with sample melting, and no products were observed in the case of unsubstituted ketodiester **1a**. In contrast, compounds **1c–e** cleanly produced succinic esters **2c–e** by loss of carbon monoxide. The stereospecificity of the reaction in the case of mixed crystalline *meso*- and *d,l*-**1c** was reflected in the formation of *meso*- and *d,l*-**2c**. As in previous examples,³ we noticed that dissolution of reacted crystals gives rise to a vigorous gas evolution, indicating that CO gas remains trapped within the crystal lattice.

Conclusion

We have shown that the chemical efficiency of the photochemical decarbonylation of crystalline acetone-1,3-dicarboxylates correlates well with the stability of the intermediate radical species as determined by their α -methyl substituents. Photochemical experiments on the 1,3,5-tricarbonyl compounds were carried out after a careful characterization of the keto form by solid-state FT-IR, ¹³C CPMAS NMR, and DSC. The photochemical stability of diadamantyl 1,3-acetone-dicarboxylates **1a** and **1b** in solution and in crystals, at ambient temperature, indicates that the carbonyl of an ester group alone does not provide sufficient stabilization to the incipient enol radical for either α -cleavage or decarbonylation to occur. However, the reaction efficiency increases remarkably with increasing methyl substituents at the α , α' -positions of the diadamantyl ketodiester **1c–e**. We have also found that reactions in crystals proceed with very high chemoselectivity. While reactions in solvents include random radical–radical combinations and disproportionation, reactions in crystals proceed by combination of radical pairs formed from the same ketone (geminate radical pairs). Computational studies in progress in our group are aimed at providing a deeper insight into the energetics of these reactions, including the possible involvement of spin–spin interactions. We expect that high combination selectivities in crystals and a preference for highly substituted ketones as substrates may be useful in the synthesis of compounds with adjacent chiral tertiary and quaternary carbon–carbon bonds. To increase the scope of the solid state reaction we are currently investigating other radical stabilizing groups that may favor decarbonylation in the solid state.

Experimental Section

Materials. Commercial reagents of the highest purity available were used without further purification, and solvents were distilled over CaH₂. Gas chromatography (GC) was conducted on a 0.2 mm \times 25 m \times 0.11 μ m HP-1 (cross linked methyl silicone gum) capillary column. IR spectra were obtained with a Perkin-Elmer spectrometer either in KBr disks or as neat oils. ¹H and ¹³C NMR spectra were obtained with a Bruker ARX400 spectrometer in CDCl₃. Spectral data of compounds **1b–d** in CDCl₃ contained a 5–10% contribution of the enol forms. The spectra data described below are for the keto forms. High-resolution mass spectra were obtained by electron ionization. The syntheses of compounds **1a**, **1e**, **3c** and **4b** were reported previously.¹⁰

General Procedure for Photolysis in Benzene. Ketodiester **1a–e** were dissolved in anhydrous benzene (10⁻³ M), and 1 mL of each of these solutions was transferred to a dry Pyrex 7 mm internal diameter (i.d.) NMR tube. Each sample was deoxygenated by bubbling argon for 15 min. All five samples were placed at a similar distance from a medium-pressure Hg Hanovia lamp. After 4 h of irradiation, the samples were analyzed by GC, and products were identified by co-injections with the authentic samples.

General Procedure for Photolysis in the Solid State. Finely powdered solid samples of ketodiester **1a–e** (5 mg) were placed evenly between two microscope slides (which also acted as a $\lambda > 305$ nm filter) and placed at a similar distance from a medium-pressure Hg Hanovia lamp. During the course of irradiation, small amount of each compound was removed at various times, dissolved in diethyl ether, and analyzed by GC. Products were identified by co-injections with the authentic samples.

1,3-Dimethyl Diadamantyl-1,3-acetonedicarboxylate (1c) and 1-Methyl Diadamantyl-1,3-acetonedicarboxylate (1b). A round-bottom flask containing potassium hydride (0.10 g, 2.5 mmol) and THF (15 mL) was cooled to 0 °C in an ice bath. Compound **1a** (0.70 g, 1.7 mmol) in 2 mL of THF was added dropwise with stirring, and the resulting yellow solution was stirred for 30 min. An excess of MeI was added slowly into the reaction mixture, which was allowed to stir for 2 h at 0 °C. The reaction mixture was quenched with water and extracted with ethyl acetate three times. The organic layers were combined, washed with brine, and dried over anhydrous MgSO₄. Removal of solvent in vacuo gave a crude white solid. The crude product was purified by flash chromatography (hexane/ethyl acetate = 9:1) to give first 0.25 g (34%) of **1c** as a white solid (mixtures of *meso* and *d,l* forms), followed by 0.25 g (35%) of **1b** as a white solid.

Data for 1b. Mp 73–75 °C. ¹H NMR: δ 1.28 (d, $J = 7.2$ Hz, 3H), 1.64 (br, 12H), 2.09–2.10 (m, 12H), 2.15 (br, 6H), 3.44 (d, $J = 14.4$ Hz, 1H), 3.56 (d, $J = 14.4$ Hz, 1H), 3.60 (q, 1H). ¹³C NMR: δ 12.42, 30.70, 30.72, 35.94, 35.96, 41.02, 41.08, 41.09, 49.39, 53.63, 82.08, 82.12, 165.74, 168.63, 199.02. IR (KBr): 2913, 2849, 1738, 1732, 1709, 1455, 1245, 1183, 1064. EI HRMS: calcd for C₂₆H₃₆O₅ 428.2563, found 428.2552.

Data for 1c (mixture of diastereomers). Mp 55–59 °C. ¹H NMR: δ 1.26 (d, $J = 7.2$ Hz, 3H), 1.29 (d, $J = 7.2$ Hz, 3H), 1.61 (br, 12H), 2.04 (br, 12H), 2.06 (br, 6H), 2.07 (br, 6H), 3.63 (q, 1H), 3.77 (q, 1H). ¹³C NMR: δ 12.42, 13.29, 30.69, 35.93, 35.98, 40.99, 41.05, 41.08, 52.28, 53.19, 81.89, 82.08, 168.69, 168.84, 201.98, 202.8. IR (KBr): 2911, 2852, 1737, 1710, 1455, 1209, 1102, 1055. EI HRMS: calcd for C₂₇H₃₈O₅ 442.2719, found 442.2723.

1,1,3-Trimethyl Diadamantyl 1,3-acetonedicarboxylate (1d). A round-bottom flask containing potassium hydride (0.10 g, 2.5 mmol) and THF (8 mL) was cooled to 0 °C in an ice bath. Ketodiester **1a** (0.35 g, 0.84 mmol) in 1 mL of THF was added dropwise, and the resulting yellow solution was stirred for 30 min. An excess of MeI was added slowly into the reaction mixture, which was then stirred for an additional 2 h. The reaction mixture was quenched with water and extracted with EtOAc (three times). The organic layers were combined, washed with brine, and dried over anhydrous MgSO₄. The solvent was removed to give the crude product,

which was purified by flash chromatography (hexane/ethyl acetate = 9:1) to give 0.35 g white solid **1d** in 90% yield, mp 93–95 °C. ¹H NMR: δ 1.33 (s, 3H), 1.35 (d, *J* = 7.2 Hz, 3H), 1.41 (s, 3H), 1.65 (br, 12H), 2.07 (br, 12H), 2.16 (br, 6H), 3.75 (q, 1H). ¹³C NMR: δ 15.39, 21.93, 22.16, 30.79, 30.84, 36.05, 36.07, 41.09, 49.53, 57.21, 81.81, 81.99, 169.04, 172.06, 204.58. IR (KBr): 2914, 2853, 1738, 1731, 1712, 1455, 1251, 1156, 1054. EI HRMS: calcd for C₂₈H₄₀O₅ 456.2876, found 456.2860.

Diadamantyl Succinate (2a). To a solution of succinic anhydride (0.2 g, 2 mmol) in toluene was added 1-adamantanol (0.73 g, 4.8 mmol), followed by a catalytic amount of *p*-toluenesulfonic acid. The resulting mixture was heated to reflux with a Dean–Stark apparatus overnight. The reaction mixture was washed with 5% sodium bicarbonate and extracted with ethyl acetate (three times). The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and concentrated to give a crude white solid. Excess 1-adamantanol was removed by sublimation to give 0.69 g of diester **2a** in 89% yield. ¹H NMR: δ 1.60 (br, 12H), 2.05 (br, 12H), 2.10 (br, 6H), 2.42 (s, 4H). ¹³C NMR: δ 30.79, 36.17, 41.26, 44.98, 80.46, 171.35. IR (KBr): 2985, 2914, 1740, 1374, 1242, 1048. EI HRMS: calcd for C₂₄H₃₄O₄ 386.2457, found 386.2462.

Methyl Diadamantyl Succinate (2b). To a solution of methyl succinic acid (0.16 g, 1.2 mmol) in toluene was added 1-adamantanol (0.48 g, 3.1 mmol), followed by a catalytic amount of *p*-toluenesulfonic acid. The resulting mixture was heated to reflux with a Dean–Stark apparatus overnight. The reaction mixture was washed with 5% sodium bicarbonate and extracted with ethyl acetate (three times). The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and concentrated to give a crude white solid. Excess 1-adamantanol was removed by sublimation to give 0.43 g of diester **2b** in 90% yield. ¹H NMR: δ 1.07 (d, *J* = 7.2 Hz, 3H), 1.64 (br, 6H), 1.65 (br, 6H), 2.02 (br, 6H), 2.03 (br, 6H), 2.05 (br, 6H), 2.17 (dd, *J* = 14.4, 7.2 Hz, 1H), 2.50 (dd *J* = 14.4, 7.2 Hz, 1H), 2.62–2.68 (m, 1H). ¹³C NMR: δ 16.95, 30.68, 30.76, 36.14, 36.16, 36.95, 39.08, 41.17, 41.25, 80.20, 80.48, 170.91, 174.36. IR (KBr): 2910, 2851, 1729, 1455, 1276, 1170, 1056. EI HRMS: calcd for C₂₅H₃₆O₄ 400.2614, found 400.2604.

2,3-Dimethyl Diadamantyl Succinate (2c). To a solution of 2,3-dimethyl succinic acid (0.18 g, 1.2 mmol) in toluene was added 1-adamantanol (0.48 g, 3.1 mmol), followed by catalytic amount of *p*-toluenesulfonic acid. The resulting mixture was heated to reflux with a Dean–Stark apparatus overnight. The reaction mixture was washed with 5% sodium bicarbonate and extracted with ethyl acetate (three times). The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and concentrated to give a crude white solid. Excess 1-adamantanol was removed by sublimation to give 0.46 g of diester **2c** in 92% yield. ¹H NMR: δ 0.98 (d, *J* = 3.6 Hz, 3H), 1.03 (d, *J* = 3.6 Hz, 3H), 1.64 (br, 12H), 1.65 (br, 12H), 2.02 (br, 24H), 2.06 (br, 12H), 2.42–2.45 (m, 2H), 2.56–2.60 (m, 2H). ¹³C NMR: δ 13.26, 15.33, 30.79, 36.04, 36.18, 36.20, 41.13,

41.18, 41.22, 41.29, 42.51, 43.90, 80.24, 80.47, 173.89, 174.35. IR (KBr): 2912, 2852, 1728, 1455, 1245, 1053. EI HRMS: calcd for C₂₆H₃₈O₄ 414.2770, found 414.2774.

Adamantyl Acetate (3a). To a solution of 1-adamantanol (0.19 g, 1.2 mmol) in 4 mL of CH₂Cl₂ were added acetyl chloride (0.13 mL, 1.8 mmol) and pyridine (0.5 mL). The resulting solution was stirred overnight at room temperature. Aqueous sodium bicarbonate (5%) was added, and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and concentrated in vacuo to give 0.21 g of ester **3a** in 90% yield. ¹H NMR: δ 1.60 (br, 6H), 1.91 (s, 3H), 2.05 (br, 6H), 2.09 (br, 3H). ¹³C NMR: δ 22.60, 30.66, 36.06, 41.15, 80.19, 170.24. IR (neat): 2912, 2853, 1732, 1457, 1244, 1060. EI HRMS: calcd for C₁₂H₁₈O₂ 194.1307, found 194.1306.

Adamantyl Propionate (3b). To a solution of 1-adamantanol (0.24 g, 1.6 mmol) in CH₂Cl₂ (5 mL) were added propionyl chloride (0.3 mL) and pyridine (0.8 mL). The resulting solution was stirred overnight at room temperature. Aqueous sodium bicarbonate (5%) was added, and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and concentrated in vacuo to give 0.3 g of ester **3b** in 92% yield. ¹H NMR: δ 0.89 (t, 3H), 1.48 (br, 6H), 1.93 (br, 6H), 1.97 (br, 3H), 2.04 (q, 2H). ¹³C NMR: δ 9.07, 28.72, 30.65, 36.08, 41.18, 79.76, 173.49. IR (neat): 2913, 2858, 1731, 1242, 1196, 1057. EI HRMS: calcd for C₁₃H₂₀O₂ 208.1463, found 208.1459.

Adamantyl Acrylate (4a). To a solution of 1-adamantanol (0.18 g, 1.2 mmol) in CH₂Cl₂ (4 mL) were added acryloyl chloride (0.3 mL) and pyridine (0.5 mL). The resulting solution was stirred overnight at room temperature. Aqueous sodium bicarbonate (5%) was added, and the aqueous layer was extracted twice with diethyl ether. The combined organic layers were washed with brine, dried over anhydrous MgSO₄, and concentrated in vacuo to give 0.22 g of ester **4a** in 90% yield. ¹H NMR: δ 1.57 (br, 6H), 2.05 (br, 9H), 5.61 (dd, *J* = 1.6, 10.3 Hz, 1H), 5.91 (dd, *J* = 10.3, 17.3 Hz, 1H), 6.17 (dd, *J* = 1.6, 17.3 Hz, 1H). ¹³C NMR: δ 30.74, 36.07, 41.21, 80.39, 129.10, 130.38, 165.06. IR (neat): 2912, 2853, 1720, 1636, 1457, 1402, 1198, 1058. EI HRMS: calcd for C₁₃H₁₈O₂ 206.1307, found 206.1297.

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Supporting Information Available: Full ¹³C NMR spectra of all new compounds. This material is available free of charge via the Internet at <http://pubs.acs.org>.

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