Engineering Reactions in Crystalline Solids: Predicting Photochemical Decarbonylation from Calculated Thermochemical Parameters

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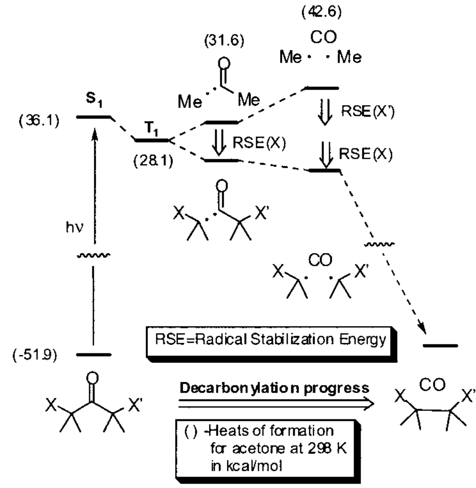
A detailed thermochemical analysis of the α-cleavage and decarbonylation reactions of acetone and several ketodiesters was carried out with the B3LYP/6-31G* density functional method. The heats of formation of several ground-state ketones and radicals were calculated at 298 K to determine bond dissociation energies (BDE) and radical stabilization energies (RSE) as a function of substituents. Results show that the radical-stabilizing abilities of the ketone substituents play a very important role on the thermodynamics of the α-cleavage and decarbonylation steps. An excellent correlation between calculated values and previous experimental observations suggests that photochemical α-cleavage and decarbonylation in crystals should be predictable from knowledge of excitation energies and the RSE of the substituent.

Introduction

Although reactions in crystals are significantly less common than reactions in the gas phase or in solution,[1] the degree of control exerted by the solid state is often comparable to that observed in enzymatic processes.[2,3] We have proposed that reactions in crystals can be designed in a reliable manner by taking advantage of high energy species capable of breaking weak bonds and making strong new ones despite severe structural constraints.[3−5]

Scheme 1



The photochemical decarbonylation of ketones by a Norrish type-I cleavage[6,7] is potentially a general reaction that may be exploited in material science and synthetic applications with many readily accessible crystalline precursors (Scheme 1).[5] The reaction involves the stepwise cleavage of two σ bonds to give an intermediate radical pair and occurs with a small amount of atomic and molecular displacement in the solid state. Although the homolytic cleavage of a sigma bond in ground-state ketones would require thermal energies that are incompatible with the integrity of low melting solids, photo-

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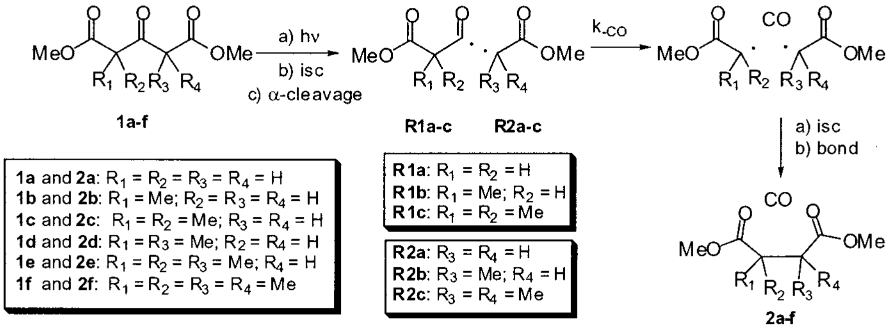
Scheme 2



chemical excitation provides the reacting ketone with ca. 70−80 kcal/mol of energy that may be directly channeled into the two sequential bond-breaking processes (Schemes 1 and 2). It is well-known that α-cleavage reactions in n,π^* ketones and decarbonylation of acyl radicals are symmetry-allowed processes with low activation barriers.[6a,7,8] Each of the two dissociation reaction rate constants depends on the stability of the resulting radicals[6,9] with an activation energy to reaction free energy relation such as that suggested by the Hammond postulate.[10] Exothermic α-cleavage reactions are fast enough to compete with deactivation of triplet excited states,[11] and exothermic decarbonylation of acyl radicals can be faster than recombination to the starting material,[9] even within the confines of the crystal lattice.[5] Taking acetone as a benchmark, we can estimate the extent of radical stabilization required by substituents X and X′ to make each cleavage step thermochemically favorable [Scheme 1, radical stabilization energies, RSE-(X) and RSE(X′)]. With ca. 79 kcal/mol in the triplet excited state,[12] the cleavage of a wide variety of σ bonds should be possible. In the case of acetone, α-cleavage and decarbonylation are endothermic by 3.5 and 11 kcal/mol, respectively.[13] Accordingly, α-cleavage in simple aliphatic ketones occurs with low quantum efficiency in solution and in the gas phase, but not at all in the solid state.[14] The formation of products in crystals requires efficient α-cleavage and decarbonylation reactions.[5] Given that decarbonylation is the product-formation-determining step, substituents that lower the bond dissociation energy (BDE) of the two α-bonds by ~11 kcal/mol or more (Scheme 1) should be needed to facilitate the solid-state reaction.

The predictive power of a simple thermochemical model (Scheme 1) can be tested and realized with the help of tabulated experimental data and/or by taking advantage of increasingly reliable computational chemistry. As a test of this hypothesis, we present here computational results with the B3LYP/6-31G* method that agree with experimental observations regarding the decarbonylation of ketodiesters **1a**−**f** (Scheme 2).[15,16] Recent experiments have shown that adamantyl ester analogues of **1a** and **1b** are photochemically stable in the solid state while the adamantyl ester analogues of **1d**−**f** yielded compounds **2d**−**f** with excellent selectivities. Although the enol form of the adamantyl analogues of **1a**,**b**,**d**−**e** can be observed in solution, solid-state ^{13}C CPMAS NMR and FT-IR revealed that they occur in crystals exclusively in the keto form.[16] As indicated in Scheme 2, the keto forms of these compounds are able to produce the α-carbonyl radicals **R2a**−**R2c**. Intermediates of this type are commonly referred to as enol radicals since they can exist formally as resonance-delocalized over the carbon and oxygen atoms. We found that reactions proceeding through tertiary enol radicals **R2c** (Scheme 1, $R_3 = R_4 = Me$) occur in crystals with higher efficiencies than reactions proceeding through their secondary analogues **R2b** ($R_3 = Me$, $R_4 = H$). We suggested that the lack of reactivity from ketodiesters **1a** and **1b** reflects the inefficient formation of the less stable primary enol radicals **R2a** ($R_1 = R_2 = H$) in the solid state. We report here an excellent correlation between the thermochemical values calculated here and our previous experimental observations. These results suggest the possibility of predicting the photoreactivity of a wide variety of crystalline ketones with reasonably inexpensive computational methods.

Approach

Bond dissociation and radical stabilization energies (BDE and RSE, respectively) were obtained from calculated thermochemical parameters in search of a correlation with experimental results. The definition of BDE is the enthalpy change of reaction I where the X−Y bond is broken and each of the elements retains one electron from the bond.[13]

$$X{-}Y \rightarrow X^{\bullet} + {}^{\bullet}Y \qquad (I)$$

The BDE can be calculated with eq 1, where $\Delta H_r(XY)$ is the enthalpy change of the dissociation of X−Y, $\Sigma\Delta H_{f(prod)}$ is the sum of the heats of formation of all the products in the reaction, and $\Sigma\Delta H_{f(react)}$ is the sum of the heat of formation of each reactant. Positive values of BDE

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[11] We have stressed that decarbonylation in crystals should be facilitated in triplet ketones that give rise to triplet acyl−alkyl radical pairs ($A^{\bullet}$ $^{\bullet}COB$). We assume that bond formation and return to the ground state from singlet radical pairs should be too fast as compared with decarbonylation.

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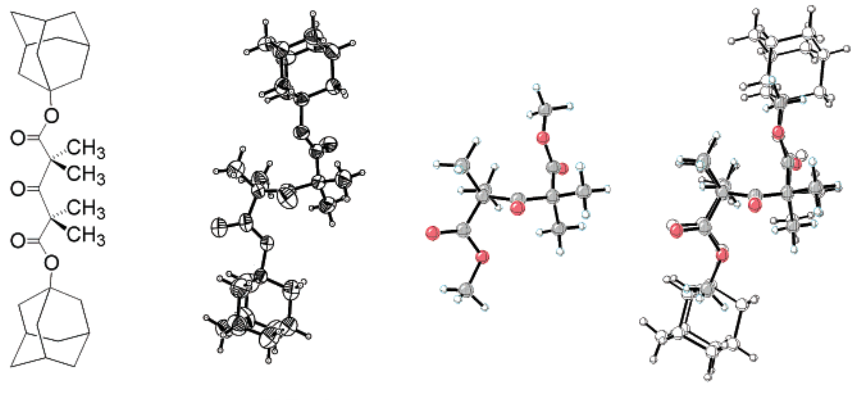
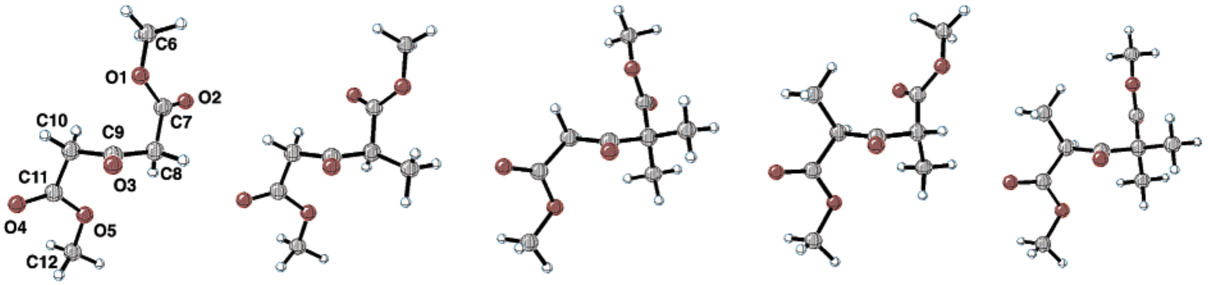


5 5 (X-Ray) 1f (B3LYP/6-31G*) Overlap 5 and 1f

Figure 1. X-ray structure of adamantyl ketodiester **5** and B3LYP/6-31G* structure of dimethyl ketodiester **1f**. Overlap of the two structures shows no significant differences.



1a 1b 1c 1d 1e

Figure 2. Optimized structures of ketodiesters **1a**−**e**. Optimizations were performed at the B3LYP/6-31G* level of theory.

that are larger than the triplet state energy should make the homolytic bond-breaking process highly improbable.

$$\mathrm{BDE(XY)} = \Delta H_r\mathrm{(XY)} = \Sigma\Delta \mathrm{H}_{\mathrm{f(prod)}} - \Sigma\Delta \mathrm{H}_{\mathrm{f(react)}} \quad (1)$$

The most generally accepted definition of the radical stabilization energy (RSE) of a substituent −X is the enthalpy change in the isodesmic reaction II:[17]

$$\mathrm{CH_3X} + {}^{\bullet}\mathrm{CH_3} \rightarrow {}^{\bullet}\mathrm{CH_2X} + \mathrm{CH_4} \qquad \mathrm{(II)}$$

Similar to the BDE, the RSE(X) can be calculated by eq 2:

$$\mathrm{RSE(X)} = \Delta_r H = \Sigma\Delta H_{\mathrm{f(prod)}} - \Sigma\Delta H_{\mathrm{f(react)}} \qquad (2)$$

This process describes the stability of the radical $^{\bullet}CH_2X$ relative to $^{\bullet}CH_3$ as the difference in the C−H BDE of CH_3X and CH_4. Large negative RSE(X) values reflect an increase in the stability of $^{\bullet}CH_2X$. In relation with Scheme 1, substituents with large RSE(X) are more likely to favor the α-cleavage (III) and decarbonylation (IV) steps.

$$\mathrm{XCH_2COCH_2X} \rightarrow \mathrm{XCH_2}^{\bullet} + {}^{\bullet}\mathrm{COCH_2X} \qquad \mathrm{(III)}$$

$$\mathrm{XCH_2}^{\bullet} + {}^{\bullet}\mathrm{COCH_2X} \rightarrow \mathrm{XCH_2}^{\bullet} + \mathrm{CO} + {}^{\bullet}\mathrm{CH_2X} \qquad \mathrm{(IV)}$$

Methods

Electronic structure optimizations and frequency calculations were carried out using the GAUSSIAN 98 suite of programs.[18] We have used density functional theory (DFT) based on Becke's three-parameter hybrid functional that incorporates a Slater and Hartree−Fock local exchange functional and other methods developed by Lee, Yang, and Parr (B3LYP)[19,20] with a polarization basis set developed by Pople (6-31G*).[21] This density functional method provides a good description of equilibrium geometries and an adequate account for reaction energetics at an affordable computational cost.

The coordinates of the **1f** analogue, diadamantyl 1,1,3,3-tetramethyl-1,3-acetonedicarboxylate **5**, were determined by X-ray diffraction analysis[22] to confirm the calculated structure of **1f** and to provide an initial structure for the optimization of compounds **1a**−**e** (see Figure 1). The adamantyl groups of the diesters used in previous studies were substituted with methyl groups in order to keep the functionality of the compound while decreasing the size of the molecule for computational cost purposes.

Previous studies have assessed several levels of theory and have shown that B3LYP/6-31G* generally yields good results for relatively large hydrocarbon molecules (such as the ones used in this study).[17] Figures 1 and 2 illustrate the structures

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[22] Ketodiester **5**: $C_{29}H_{42}O_5$, MW = 470.63, triclinic, space group $P\bar{1}$, $a = 6.4496(13)$ Å, $b = 10.477(2)$ Å, $c = 19.526(4)$ Å, $\alpha = 94.149(5)°$, $\beta = 95.894(4)°$, $\gamma = 97.053(4)°$, $V = 1287(4)$ Å^3, $Z = 2$, $\rho_{\mathrm{calcd}} = 1.204$ Mg/m^3, $F(000) = 512$, $\lambda = 0.710\ 73$ Å, $T = 293(2)$ K, crystal size 0.3 × 0.1 × 0.1 mm^3, max/min residual electron density 0.669 and −0.310 e Å^{-3}, R1 = 0.1004 ($I > 2\sigma I$) and wR2 = 0.2881.

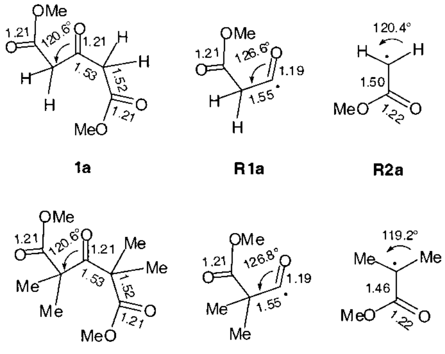


Figure 3. Selected structural parameters of ketodiesters **1a** and **1f** and their intermediate radical pairs.

Table 1. Calculated Standard Heats of Formation (kcal/mol) at 298 K (See Schemes 2 and 3 To Obtain the Structures of the Molecules Identified Numerically)

molecule	$\Delta H^\circ_{f\ 298\ \mathrm{K}}$ (calcd)[a]	$\Delta H^\circ_{f\ 298\ \mathrm{K}}$ (exptl)[b]	deviation (theory-exptl)
CO	−19.69	−26.4	6.71
CH_4	−19.20	−17.9 ± 0.1	−1.30
CH_3COCH_3	−49.56	−51.9 ± 0.2	2.34
CH_3CHO	−38.25	−41.0	2.75
$(CH_3)CH_2CHO$	−41.58		
$(CH_3)_2CHCHO$	−46.95		
$(CH_3)_3CCHO$	−51.52		
1a	−200.16		
1b	−205.37		
1c	−208.91		
1d	−209.19		
1e	−213.49		
1f	−213.07		
3a	−113.08		
3b	−118.17		
3c	−123.43		
4a	−95.28		
4b	−99.60		
4c	−103.44		

[a] Calculated from the B3LYP/6-31G* level of theory. [b] Experimental values from Curtiss et al. and references therein.[23]

Table 2. Calculated Standard Heats of Formation $\Delta H^\circ_{f\ 298\ \mathrm{K}}$ and Radical Stabilization Energies (RSE) in kcal/mol at 298 K (See Scheme 2 To Obtain the Structures of the Molecules Identified Numerically)

radical	$\Delta H^\circ_{f\ 298\ \mathrm{K}}$[a]	RSE
CH_3[b]*	33.78	0.0
CH_3CO[b]**	−2.20	−16.93
CH_3CH_2CO	−41.58	−17.42
$(CH_3)_2CHCO$	−46.95	−17.02
$(CH_3)_3CCO$	−51.52	−17.23
R1a	−76.58	−16.48
R1b	−81.60	−16.41
R1c	−87.17	−16.72
R2a	−51.20	−8.90
R2b	−61.69	−15.07
R2c	−70.25	−19.79

[a] This study, calculated from B3LYP/6-31G* level of theory. [b] Experimental values from Curtiss et al. and references therein:[23] * $\Delta H^\circ_{f\ 298\ \mathrm{K}}$ (CH_3) = 35.0 ± 0.1; ** $\Delta H^\circ_{f\ 298\ \mathrm{K}}$ (CH_3CO) = −2.4 ± 0.3.

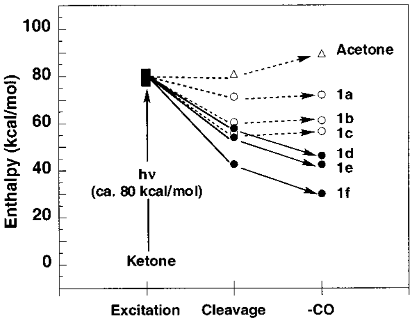
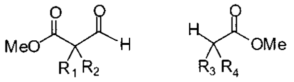


Figure 4. Calculated enthalpy changes upon electronic excitation (assumed at 79 ± 4 kcal/mol), α-cleavage, and decarbonylation of acetone and ketodiesters **1a**−**f**. Acetone and **1a** react in solution with very low quantum yields. Compounds **1b**−**f** react efficiently in solution. Compounds **1a** and **1b** are photostable in the solid state. Compound **1c** has not been investigated experimentally but is predicted to be reactive in solution and photostable in the solid state. Only **1d**−**f** (black dots and solid arrows) react efficiently in the solid state.[15,16]

Scheme 3



3a: $R_1 = R_2 = H$
3b: $R_1 = Me$; $R_2 = H$
3c: $R_1 = R_2 = Me$

4a: $R_3 = R_4 = H$
4b: $R_3 = Me$; $R_4 = H$
4c: $R_3 = R_4 = Me$

Table 3. Calculated Bond Dissociation Energies (BDE in kcal/mol) for the First and Second Homolytic Dissociations in the Decarbonylation of Acetone and the Ketodiesters (1a−f)

reactant	BDE-1	radicals (BDE-1)	BDE-2	radicals + CO (BDE-2)
CH_3COCH_3	81.14	CH_3, CH_3CO	9.58	$2CH_3$
1a	72.38	**R1a**, **R2a**	−1.02	2**R2a**
1b	67.10	**R1a**, **R2b**	−1.02	**R2a**, **R2b**
1c	62.08	**R1a**, **R2c**	−1.02	**R2a**, **R2c**
1d	65.90	**R1b**, **R2b**	−6.49	2**R2b**
1e	61.64	**R1b**, **R2c**	−6.49	**R2b**, **R2c**
1f	55.48	**R1c**, **R2c**	−9.48	2**R2c**

of the optimized ketodiesters. Selected structural parameters of ketodiesters **1a** and **1f** and of their intermediate radical pairs are shown in Figure 3. Table 1 shows the heat of formation for the molecules of interest and Table 2 shows the heat of formation for the radicals involved in the decarbonylation of acetone and ketodiesters **1a**−**f**. Heats of formation were obtained by using the method outlined by Curtiss et al.[23] Zero-point vibrational energies were scaled at the B3LYP/6-31G* to 0.9806, and thermal corrections to enthalpy were scaled to 0.9989.[24] The calculated values were relatively close to the experimental values for a set of standard molecules, with the exception of CO (Table 1). Due to the large deviation in $\Delta H^\circ_{f\ 298\ \mathrm{K}}$ for CO, the experimental value (−26.4 kcal/mol) was used for the calculation of the radical stabilization energy. Table 2 also contains the calculated values of the radical stabilization energy with respect to the methyl radical. Table 3 collects the calculated BDE values for α-cleavage from the ground-state ketone (BDE−1) and for decarbonylation from the acyl−alkyl radical pair (BDE-2). The standard heats of formation of aldehydes **3a**−**c** and methyl acetates **4a**−**c** (Scheme 3) were calculated to determine the RSE values for acyl radicals **R1a**−**R1c** and enol radicals **R2a**−**R2c** according to the isodesmic reaction II. The enthalpy changes calculated from values in Table 3, assuming that reaction starts with a triplet state excitation energy of 80 kcal/mol, are summarized graphically in Figure 4.

Results and Discussion

As illustrated in Figure 1, the X-ray structure of diadamantyl ketodiester **5** and the calculated structure of dimethyl ketodiester **1f** are in excellent agreement

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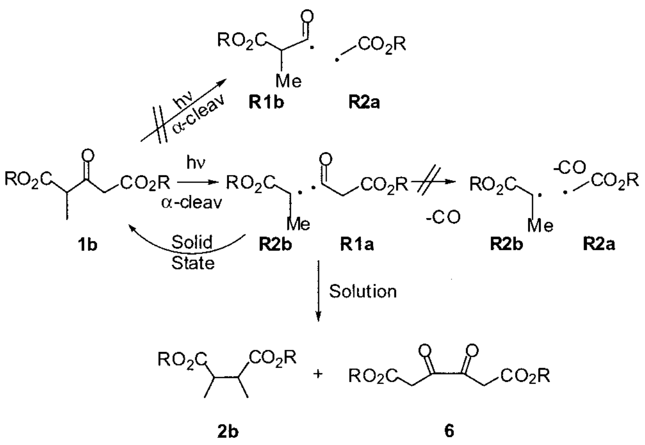
(overlap). It is known that the B3LYP/6-31G* level of theory yields ground-state structures that compare well to those obtained from experimental results, giving reasonable confidence in the calculated structures of ketodiesters **1a**−**e**. Structure and energy calculations in the case of acetone and the radicals included in this study compare well with values determined by experiment or with calculations carried out with higher levels of theory.

The calculated structures of compounds **1a**−**f** share similar ester conformations (Figure 2). The two ester groups are anti to each other and nearly orthogonal to the plane of the ketone. The dihedral angles O3−C9−C10−C11 and O3−C9−C8−C7, which describe the orientation of the ester groups in **1a**, have values of −83.7° and −114.39°, respectively (Figures 2 and 3). The three carbonyl groups in ketones **1a**−**f** adopt a conformation that optimizes intramolecular dipole−dipole interactions. One of the ester carbonyls is approximately anti to the ketone while the other adopts an angle that approaches 90°. Although some structural variations are observed in the series **1a**−**f**, their conformations are remarkably similar.

The structures of the intermediate radicals were also consistent with those expected for alkyl- and acyl-centered radicals. Enol radicals have the α-carbon and ester carbonyl groups coplanar, but there are no additional indications of electronic delocalization. Carbon-centered radical structures are suggested by the relatively small changes in the R_2C-CO_2R bond distances in going from ketones to enol radicals. This is illustrated in Figure 3 in the case of compounds **1a** and **1f**. The R_2C-CO_2R bond, which connects the ester group with the α-carbon in **1a**, changes insignificantly from the closed-shell ground-state molecule (1.52 Å) to the enol radical **R2a** (1.50 Å). The C═O bond distance in the ester carbonyl takes values of 1.21−1.22 Å in **1a**, **R2a**, and **R1a**. Furthermore, the addition of four α-methyl groups in **1f** causes relatively small structural changes as compared to those in the radicals derived from **1a**. While a smaller α-carbon to carbonyl-carbon bond distance of 1.46 Å may be taken as an indication of increased delocalization, the C═O distance in the ester group remains essentially unchanged as compared to the ketone (1.22 Å). The calculated structures of the acyl radicals are also consistent with those previously determined by experimental and computational methods.[25] All the structures are bent with C−C═O angles of ca. 126° and a short acyl C═O distance of 1.19 Å. With confidence on the calculated structures of the starting ketones and radical intermediates, we analyzed the energetics of the α-cleavage and decarbonylation reaction for acetone and ketodiesters **1a**−**f** in terms of eqs 1 and 3.

The enthalpy of the α-cleavage reaction can be estimated by subtracting the calculated BDE-1 (Table 3) from an excitation energy of ~80 kcal/mol assumed for the triplet excited state. Although this approximation may not be correct for ketones with all types of α-substituents, the spectroscopic triplet energies of a large number of aliphatic,[26] cyclic,[27] and α-phenyl[28] ketones are known to fall within a small range ($E_T \approx 79 \pm 4$ kcal/mol).[29] The enthalpy of the decarbonylation reaction is directly obtained from the calculated BDE-2 values. At a first approximation, it is assumed that spin−spin interactions do not affect the enthalpy of the solid state reaction. We also assume that energy variations due to structural differences between gas phase radicals and radicals trapped in crystals are relatively small. According to this simple model, the loss of carbon monoxide from crystalline acetone would be endothermic by 1.1 kcal/mol in the first step (α-cleavage) and by 9.6 kcal/mol in the second (decarbonylation). This estimation is in reasonably good agreement with experimental values of 3.5 and 11 kcal/mol, respectively.[13] These results, and those from compounds **1a**−**f**, are illustrated graphically in Figure 4 with the BDE for each step indicated by the vertical scale.

Scheme 4



With respect to compound **1a**, it is predicted that the enthalpy change for α-cleavage should be 9 kcal/mol lower than that of acetone (Figure 4). However, the enthalpy change for decarbonylation is exothermic by a modest −1.0 kcal/mol, which appears to be insufficient to favor decarbonylation over radical recombination in the solid state. Accordingly, compound **1a** reacted with low yields in benzene solution to give trace amounts of **2a** but did not react at all in the solid state. A similar result was obtained with compound **1b**. With one methyl group in the α-position the enthalpy change for the α-cleavage is more exothermic than that of **1a** (−12.9 kcal/mol). However, decarbonylation to give a primary enol radical is exothermic by only −1.0 kcal/mol. Although there are two possible routes for the initial α-cleavage of **1b**, radical pair **R2b** + **R1a** forms easier than **R2a** + **R1b** because of the radical-stabilizing effect of the methyl group in the α-position of **R2b** (Scheme 4). Solution products arise from combination of two secondary enol radicals **R2b** (product **2b**) and two acyl radicals **R1a** (product **6**) but no products from the primary enol

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[25] Experiments and calculations indicate that acyl radicals adopt a σ-type bent structure. Nimlos et al. have been suggested that the linear structure may be as much as 26.6 kcal/mol higher: (a) Chatgilialoglu, C.; Crich, D.; Komatsu, M.; Ryu, I. *Chem. Rev.* **1999**, *99*, 1991−2070. (b) Nimlos, M. R.; Soderquist, J. A.; Ellison, G. B. *J. Am. Chem. Soc.* **1989**, *111*, 7675−7681. (c) Yadav, J. S.; Goddard, J. D. *J. Chem. Phys.* **1986**, *84*, 2682−2690.

[26] (a) Borkman, R. F.; Kearns, D. R. *J. Chem. Phys.* **1966**, *44*, 945−949. (b) Naito, I.; Schnabel, W. *Bull. Chem. Soc. Jpn.* **1984**, *57*, 771−775.

[27] Yang, N.-C.; Shlod, D. M.; Neywick, C. V. *J. Chem. Soc., Chem. Commun.* **1976**, 727−728. (d) Uppili, S.; Marti, V.; Nilkolaus, A.; Jockush, S.; Adam, W.; Engel, P. S.; Turro, N. J.; Ramamurthy, V. *J. Am. Chem. Soc.* **2001**, *122*, 11025−11026.

[28] The triplet energy of α,α′-diphenylacetone and related compounds has been estimated to be ~79 kcal/mol: Engel, P. S. *J. Am. Chem. Soc.* **1970**, *92*, 6074−6076.

[29] The triplet energies of ketodiesters **1b**−**f** determined from phosphorescence spectra at 77 K in nonpolar glasses are slightly higher (2−4 kcal/mol) than that of acetone: Campos, L. M.; Garcia-Garibay, M. A. Unpublished results.

radical **R2a** (product **2a**) are observed because of the unfavorable decarbonylation of **R1a**. As expected from its unfavorable decarbonylation, crystals of **1b** are photostable.[16]

Although compound **1c** has not been studied experimentally, our calculations and our model predict that, like compound **1b**, reaction will proceed in solution but not in the solid state. Although the enthalpy change for α-cleavage to form the tertiary enol radical **R2c** and acyl radical **R1a** is favorable by −17.9 kcal/mol, decarbonylation of **R1a** to give the primary enol radical **R2a** is exothermic by only −1.0 kcal/mol. Thus, α-cleavage should occur in solution with high quantum efficiency to give products **2f** and **6** along with the starting material **1c**. However, without the diffusion of radicals, only the experimentally unobservable re-formation of **1c** should be possible in the solid state.

The adamantyl analogues of compounds **1d**−**f** are reactive in solution and in the solid state.[15,16] The solid-state reaction efficiencies increase in the order **1d** < **1e** < **1f** and decarbonylation occurs in high chemical yields to give succinate esters **2d**−**f**, respectively, as the only products (Scheme 2). An excellent correlation between solid-state reactivity and calculated energetics is evident by analysis of Figure 4. The reaction of **1d** proceeds through secondary enol radicals in each of the two homolytic steps and is the least efficient of the three. α-Cleavage is exothermic by −14.1 kcal/mol and decarbonylation by an additional −6.5 kcal/mol for a total of ca. −20.6 kcal/mol from the triplet excited state. In contrast, the α-cleavage reactions of compounds **1e** and **1f** produce tertiary enol radicals with enthalpy changes of −18.4, and −24.5 kcal/mol, respectively. Decarbonylation to produce secondary and tertiary enol radicals is exothermic by −6.5 and −9.5 kcal/mol, respectively, to give total exothermicities of −24.9 and −34.0 kcal/mol for **1e** and **1f** (Figure 4, Table 3).

The results in Table 3 and Figure 4 indicate that radical stabilizing abilities of the ketone substituents play an important role in the α-cleavage and decarbonylation steps. While the calculated BDE for acetone is 81.1 kcal/mol, the corresponding values for ketodiesters **1a**−**f** vary between 72.4 for **1a** to as low as 55.5 kcal/mol for **1f**. It is worth noting (Table 2) that the radical stabilization energies of all the acyl radicals investigated are essentially identical to RSE ≈ −17 ± 1 kcal/mol (Table 2). These results indicate that the ease of α-cleavage is primarily determined by the nature of the incipient alkyl radical centers. The calculated radical stabilization energies for primary, secondary and tertiary enol radicals (**R2a**−**R2c**), increase from −8.90 to −15.07 up to −19.79 kcal/mol, respectively. These values are in excellent agreement with expectations[15,16] that we previously formulated from published experimental[30] and computational data.[17]

Conclusions

The results obtained in this computational study are in excellent agreement with our experimental observations and support the hypothesis that calculated thermochemical parameters should help predict the solid-state reactivity of excited carbonyl compounds. As illustrated in Scheme 1, crystalline ketones with high excitation energies and exothermic bond cleavage processes should be reactive toward α-cleavage and decarbonylation reactions. Our hypothesis relies on the symmetry-allowed nature of these bond cleavage reactions, their early transition states and their low energy barriers. Our hypothesis is also consistent with the limited kinetic energies available in crystalline solids which may translate in reaction rate constants with relatively small temperature coefficients. The reliable formation of radical pairs and biradicals in crystals should open the doors for systematic mechanistic, kinetic and synthetic studies. Work in progress includes synthetic applications and the analysis of other radical-stabilizing substituents, such as α-cyano, α-vinyl, and α-ethynyl, as well as captodative radical stabilization patterns.

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Supporting Information Available: Stereoscopic views and X-ray data tables for compound **5**, Cartesian coordinates, energies (HF), and zero-point vibrational energies (ZPE) for all ketodiesters and radicals in this study. This material is available free of charge via the Internet at http://pubs.acs.org.

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