to 1 mV. Looking into these unusual properties in detail is clearly desirable; however, this has been impeded by our inability to routinely prepare tips with the properties just described.

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Conformation–Reactivity Correlations in the Solid-State Photochemistry of Macrocyclic Diketones

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As part of a research program designed to investigate the crystalline-phase photochemistry of a wide variety of organic systems,[1] our interest in macrocyclic diketones was aroused by a paper reporting the crystal structure of the 18-membered-ring "diametric" diketone, cyclooctadecane-1,10-dione (**1b**, Scheme I).[2] This report indicated that **1b** has an intramolecular, six-membered cyclic C═O···H contact of 2.8 Å in the crystal that should allow for Norrish type II photoreaction[3] in this medium. Previous studies from our laboratory have shown that intramolecular hydrogen abstraction reactions in the solid state are feasible over C═O···H distances of approximately 3 Å or less.[4]

In the present communication, we report that diketone **1b** does in fact undergo Norrish type II photoreaction in the solid state. Two additional macrocyclic diketones were also investigated: the 16-membered analogue, cyclohexadecane-1,9-dione (**1a**), and the 22-membered compound, cyclododocosane-1,12-dione (**1c**);[5] each was analyzed crystallographically for the first time and photolyzed in the solid state. For comparison purposes, all three macrocyclic diketones were also irradiated in solution. Overall, the results provide valuable information on (1) the preferred conformations of the 16- and 22-membered-ring diametric diketones, (2) favorable six-membered transition state hydrogen atom abstraction distances, (3) the effect of molecular conformation on Norrish type II reactivity, and (4) novel crystal lattice medium effects in organic photochemistry.

The X-ray crystal structures of diketones **1a** and **1c**[6a] reveal that they too have close C═O···H_γ contacts that are favorable for type II photochemistry. Stereodiagrams showing the molecular conformations and closest C═O···H_γ contacts are given in Figure 1.[7] We note that diketone **1a** has the rectangular [3535] conformation predicted by Allinger, Gorden, and Profeta[8] and not the square [4444] structure predicted by Alvik, Borgen, and Dale.[9]

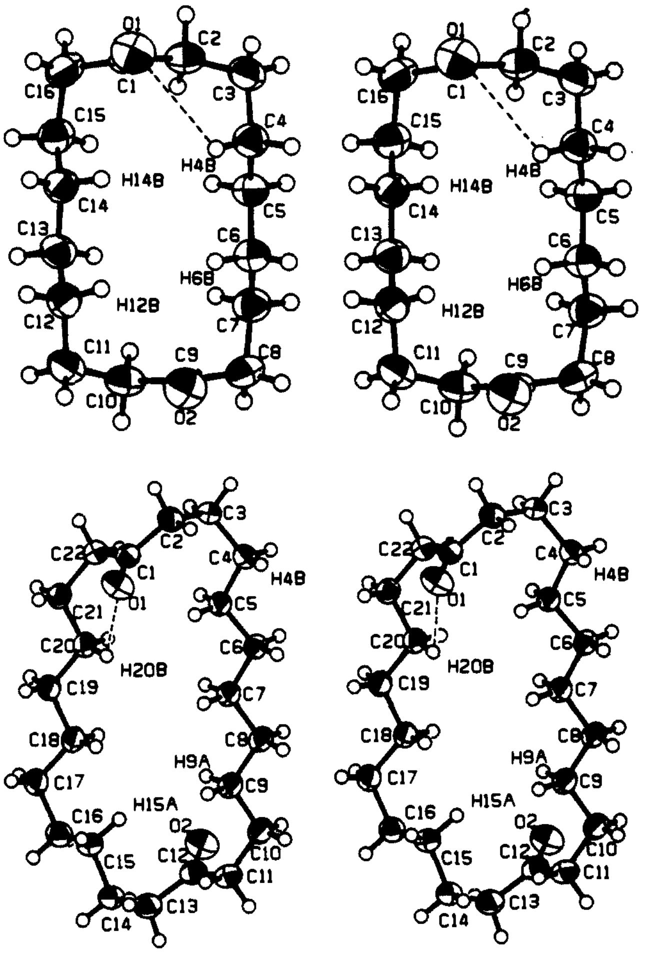
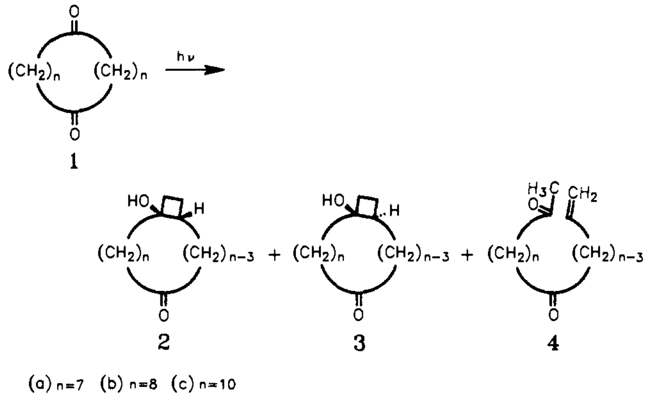


Figure 1. ORTEP stereodiagrams of diketones **1a** (top) and **1c** (bottom), showing 50% probability ellipsoids and atom labeling. The dotted lines indicate the shortest C═O···H_γ contacts (2.7 Å in each case).[7]

Scheme I



As outlined in Scheme I, irradiation of diketones **1a–c** to low conversions, both in the solid state and in solution, led to three photoproduct types: the *cis*- and *trans*-cyclobutanols **2a–c** and **3a–c** (type II cyclization)[3] and the ene–diones **4a–c** (type II elimination).[3] Eight of the nine photoproducts were isolated and fully characterized. The ninth, cyclobutanol **2b**, could never be completely freed of its isomer, **3b**, and was therefore analyzed spectroscopically as a mixture. There was some ambiguity in assigning the cyclobutanol ring junction stereochemistry, but this was overcome by obtaining the crystal structure of cyclobutanol **2a**.[6b] With the configuration of **2a** (and, by default, that of **3a**) known with certainty, NMR correlations enabled the remaining stereochemical assignments to be made confidently.

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(1) Scheffer, J. R.; Garcia-Garibay, M.; Nalamasu, O. In *Organic Photochemistry*; Padwa, A., Ed.; Marcel Dekker: New York, 1987; Vol. 8; pp 249–347.

(2) Allinger, N. L.; Gorden, B. J.; Newton, M. G.; Lauritsen-Norskov, L.; Profeta, S., Jr. *Tetrahedron* **1982**, *38*, 2905.

(3) Review: Wagner, P. J. In *Molecular Rearrangements in Ground and Excited States*; de Mayo, P., Ed.; Wiley-Interscience: New York, 1980; Chapter 20.

(4) Scheffer, J. R. In *Organic Solid Sate Chemistry*; Desiraju, G. R., Ed.; Elsevier: New York, 1987; Chapter 1.

(5) Compounds **1a–c** were prepared according to the procedure of Blomquist et al.: Blomquist, A. T.; Prager, J.; Wolinsky, J. *J. Am. Chem. Soc.* **1955**, *77*, 1804.

(6) (a) Diketone **1a**: $P\bar{1}$; a = 9.866 (1) Å, b = 14.923 (2) Å, c = 5.453 (1) Å; α = 95.03 (2)°, β = 90.42 (2)°, γ = 75.38 (1)°; Z = 2; R = 3.6%. Diketone **1c**: $P2_1/c$; a = 15.408 (1) Å, b = 5.508 (1) Å, c = 24.696 (1) Å; β = 99.662 (5)°; Z = 4; R = 4.7%. (b) Cyclobutanol **2a**: $P\bar{1}$; a = 9.784 (2) Å, b = 9.885 (3) Å, c = 9.580 (3) Å; α = 116.59 (2)°, β = 109.88 (2)°, γ = 95.91 (2)°; Z = 2; R = 3.8%.

(7) Only the closest C═O···H_γ contacts are given. In the case of **1a**, abstraction of H14B (2.9 Å), H12B (2.8 Å), or H6B (2.9 Å) is also possible (<3 Å). For **1c**, abstraction of H9A (2.8 Å) is also feasible.

(8) Allinger, N. L.; Gorden, B.; Profeta, S., Jr. *Tetrahedron* **1980**, *36*, 859.

(9) Alvik, T.; Borgen, G.; Dale, J. *Acta Chem. Scand.* **1972**, *26*, 1805.

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Table I. Photoproduct Percentages (Corrected for Detector Response and Extrapolated to 0% Conversion) as a Function of Reaction Medium and Temperature[a-c]

diketone	medium	temp, °C	% **2**	% **3**	% **4**
1a	crystal	20	89	10	1
	crystal	30	47	16	37
	crystal	40	17	20	63
	soln	20	22 (0.019)	35 (0.031)	43 (0.054)
	soln	40	19	30	51
1b	crystal	20	3	84	13
	soln	20	17 (0.015)[d]	42 (0.038)	41 (0.045)
1c	crystal	20	4	91	5
	soln	20	10 (0.009)[d]	34 (0.032)	56 (0.037)

[a] Quantum yields in parentheses. [b] The Pyrex-filtered output of a 450-W Hanovia medium-pressure mercury lamp was the light source in both the solid-state and the solution-phase (hexane) photolyses. At this wavelength, only the n,π^* absorption band (λ_{max} ca. 280 nm, ϵ = 60 for all three diketones in acetonitrile) was excited. The solid-state UV spectra were qualitatively similar to those measured in solution. [c] The range of conversion levels varied between 2% and 15%; over this range, the extrapolation to 0% conversion was linear. [d] Partial overlapping of peaks on GC makes these quantum yields and product percentages somewhat less precise.

Table I gives the product percentages resulting from Pyrex-filtered irradiation of diketones **1a-c** under various experimental conditions. We draw attention to three main trends that are evident in the data: (1) the proportion of type II cyclization (photoproducts **2** and **3**) is greater in the solid state than in solution; (2) the stereoselectivity of cyclobutanol formation increases in the solid state compared to solution; particularly striking is the *reversal* in cyclobutanol stereoselectivity observed in the case of diketone **1a**; and (3) for diketone **1a**, the solid-state photoproduct distribution (but not the solution-phase distribution) depends dramatically on the photolysis temperature.

The first two observations are explicable in terms of the well-established idea that solid-state chemical reactions tend to be topochemically controlled[10] and, in the case of unimolecular processes, conformation-specific.[11] Diketones **1a** and **1c** have very different conformations (Figure 1); the abstracting oxygen atoms and the *nonabstracted* γ-hydrogen atoms (which end up as the ring junction methine protons) are syn to one another in **1a** and anti in **1c** (and **1b**). Thus the process of hydrogen abstraction and cyclobutanol formation involving retention of configuration at both the carbonyl carbon and the γ-carbon leads, in a natural and topochemical fashion, to the cis-fused cyclobutanol **2a** from **1a** and to the trans-fused cyclobutanols **3c** and **3b** from **1c** and **1b**, respectively. This argument is valid regardless of which of the accessible γ-hydrogen atoms is abstracted in each case. Inspection of the packing diagrams does not reveal any obvious *inter*molecular contacts that might account for the stereoselectivities observed. In solution, reaction from other diketone conformers as well as possible conformational isomerization of the intermediate 1,4-biradicals leads to a greater degree of type II elimination plus a preference for formation of the presumably less strained cyclobutanols **3a-c** in each case.[12]

The dramatic change in the solid-state photoproduct percentages for diketone **1a** between 20 and 40 °C (Table I) deserves comment. This is due to a solid-solid phase transition that occurs in this temperature range, well below the melting point of 86 °C. This phase transition was first noted by Alvik, Borgen, and Dale,[9] who reported it as occurring at 28 °C; our own highly reproducible differential scanning calorimetry measurements indicate a transition temperature of 34 °C.[13] The nature of the high-temperature solid phase is under active investigation at the present time. From the photochemical results, however, it appears that this phase mimics the situation in solution to a considerable degree.

Acknowledgement is made to the donors of the Petroleum Research Fund, administered by the American Chemical Society, for partial support of this research. Financial support by the Natural Sciences and Engineering Research Council of Canada is also gratefully acknowledged.

Registry No. 1a, 31067-25-1; **1b**, 13747-10-9; **1c**, 38300-52-6; **2a**, 125735-63-9; **2b**, 125735-65-1; **2c**, 125735-67-3; **3a**, 125826-55-3; **3b**, 125826-56-4; **3c**, 125826-57-5; **4a**, 125735-64-0; **4b**, 125735-66-2; **4c**, 125735-68-4.

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[10] (a) Schmidt, G. M. J. *Pure Appl. Chem.* **1971**, *27*, 647. (b) Cohen, M. D. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 386.

[11] Ariel, S.; Evans, S.; Hwang, C.; Jay, J.; Scheffer, J. R.; Trotter, J.; Wong, Y.-F. *Tetrahedron Lett.* **1985**, *26*, 965.

[12] Quenching studies indicate that diketones **1a-c**, like other aliphatic ketones, undergo the Norrish type II reaction from both singlet and triplet excited states. Since it is well established that triplets generally cyclize to a greater extent than singlets,[3] part of the increased degree of cyclization observed in the solid state for compounds **1a-c** may stem from enhanced intersystem crossing in this medium relative to solution.

(13) An analogous phase transition was observed at 86 °C for diketone **1b** (mp 96 °C), and a similar (but less dramatic) variation in the solid-state photoproduct ratios above and below the transition point was found. No phase transition was detectable in the case of diketone **1c**, however.

Kinetic Effect of a Syn-Oriented Carboxylate on a Proximate Imidazole in Catalysis: A Model for the Histidine-Aspartate Couple in Enzymes

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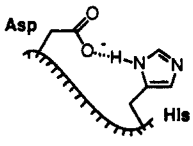
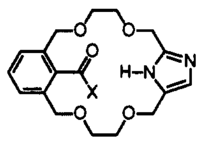
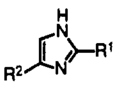
The catalytic dyad of histidine and aspartate (glutamate), known as the His-Asp couple (**1**), has been found in the active site of zinc-containing enzymes,[1a] glutathione reductase,[1b] phospholipase A_2,[1c] the serine proteases,[1d,e] malate and lactate dehydrogenase,[1f] and DNAse I,[1g] and possibly in ribonuclease T_1.[1h,i] In all but the zinc enzymes, the histidine residue has been proposed to act as a general acid/base[1] or, less frequently, as a nucleophile.[2] If convergent evolution has led to the presence of the His-Asp couple in these many enzymes, then the carboxylate must play an important structural and/or catalytic role.



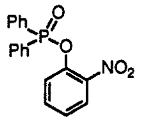
1



2: X = O⁻
3: X = NH_2



4: $R^1 = CH_2OCH_3$, $R^2 = CH_3$
5: $R^1 = CH_2CH_2OCH_3$, $R^2 = CH_3$
6: $R^1 = CH_2CH_3$, $R^2 = CH_3$



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The nature of this role is not known, but has been the subject of intense debate, particularly in the case of the serine proteases,[3]

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(1) (a) Christianson, D. W.; Alexander, R. S. *J. Am. Chem. Soc.* **1989**, *111*, 6412-6419. (b) Karplus, P. A.; Pai, E. F.; Schultz, G. E. *Eur. J. Biochem.* **1989**, *178*, 693-703. (c) Dijkstra, B. W.; Drenth, J.; Kalk, K. H. *Nature* (*London*) **1981**, *289*, 604-606. (d) Blow, D. M.; Birktoft, J. J.; Hartley, B. S. *Nature* (*London*) **1969**, *221*, 337-340. (e) Kraut, J. *Annu. Rev. Biochem.* **1977**, *46*, 331-358. (f) Birktoft, J. J.; Banaszak, L. J. *J. Biol. Chem.* **1983**, *258*, 472-482. (g) Suck, D.; Oefner, C. *Nature* (*London*) **1988**, *332*, 464-468. (h) Nishikawa, S.; Morioka, H.; Kim, H. J.; Fuchimura, K.; Tanaka, T.; Uesugi, S.; Hakoshima, T.; Tomita, K.; Ohtsuka, E.; Ikehara, M. *Biochemistry* **1987**, *26*, 8620-8624. (i) See, however: Mossakowska, D. E.; Nyberg, K.; Fersht, A. R. *Biochemistry* **1989**, *28*, 3843-3850.

(2) Hubbard, C. D.; Kirsch, J. F. *Biochemistry* **1972**, *11*, 2483-2493. Quinn, D. M.; Elrod, J. P.; Ardis, R.; Friesen, P.; Schowen, R. L. *J. Am. Chem. Soc.* **1980**, *102*, 5358-5365.