4324 J. Org. Chem. 1989, 54, 4324–4330

Latent Photochemical Hydrogen Abstraction Reactions Realized in Crystalline Media

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Received December 15, 1988

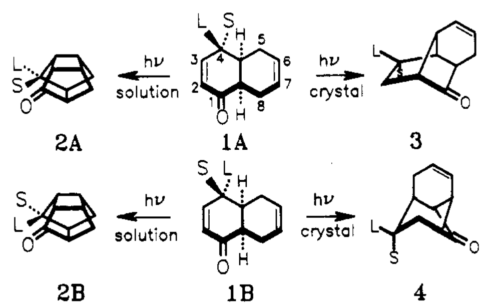
The photochemistry of four closely related compounds possessing the 2-cyclohexen-1-one chromophore has been investigated in solution as well as in the solid state. Each enone has two relatively low energy conformational isomers, one of which (A) is ideally arranged for hydrogen abstraction through a five-membered transition state, while the other (B) has a structure that favors hydrogen atom abstraction through a six-membered transition state. In solution, despite the fact that conformer A may predominate in the conformational equilibrium, all four enones give products resulting from the much faster six-membered transition state abstraction process. In the solid state, because each enone is frozen in its lower energy conformation, the process followed is conformation-specific. Two of the enones studied crystallize in conformation B and therefore give the same photoproducts as observed in solution. The other two enones crystallize in conformation A, and in these cases, the "latent" five-membered transition hydrogen abstraction process is realized.

Previous studies from our laboratory have established a clear picture of the structure–reactivity relationships involved when cis-fused bicyclic enones of general structure 1 (Scheme I) are photolyzed.[1] Regardless of the relative stereochemistry at C(4), irradiation in isotropic liquid media invariably leads to cage compounds (**2A**, **2B**) resulting from intramolecular [2 + 2] photocycloaddition. In contrast, photolysis of crystals of epimers **1A** and **1B** affords the tricyclic ketones **3** and **4**, respectively.

X-ray crystallographic studies revealed the reason for the different photochemical behavior of enones **1A** and **1B** in the solid state. The explanation is that, because of their epimeric relationship at C(4), compounds **1A** and **1B** crystallize in, and are restricted to, *different conformations*, and these conformations exhibit different photoreactivity. We have termed this "conformation-specific" photochemistry. In solution, on the other hand, compounds **1A** and **1B** are free to explore several conformations during their excited-state lifetimes. One of these, not present in the solid state, brings the C(2)–C(3) and C(6)–C(7) double bonds into proximity, and the ensuing rapid [2 + 2] cycloaddition forms cage compounds **2A** and **2B**.

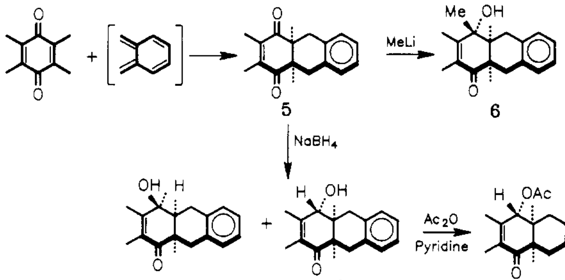
In the present paper we report the solution and solid-state photochemistry of four enones analogous to **1A** and **1B** in which the C(6)–C(7) double bond is part of a benzene ring. Although intramolecular [2 + 2] photocycloaddition reactions between aromatic and aliphatic double bonds are known,[2] we expected that this process would be sufficiently slow to allow alternative reaction pathways, such as those leading to compounds analogous to **3** and **4**, to be competitive in solution. This is exactly what was observed. In solution, irradiation of 6,7-benzannulated analogues of **1A** and **1B** invariably leads to cyclobutanone type photoproducts (e.g., **4**), whereas the crystalline-phase photochemistry is, as before, conformation-specific. Detailed crystallographic studies that support these conclusions are reported along with the photochemical results.

Scheme I



S = small group; L = large group; other substituents omitted for clarity

Scheme II



Preparation of Starting Materials. The four cis-fused tricyclic enones chosen for study were those having structures **6**–**9** shown in Scheme II. Their synthesis was straightforward once the conditions for the Diels–Alder reaction leading to enedione **5** had been worked out. The preparation of **5**, along with a number of additional *o*-quinodimethane/*p*-quinone Diels–Alder adducts, has been reported previously.[3] All four enones are crystalline solids, and for compounds **6**, **7**, and **9**, crystal and molecular structures have been determined by direct X-ray diffraction methods;[4] this also establishes their chemical structures and stereochemistries. Since **9** is derived from **8** by simple acetylation, the structure and stereochemistry of **8** are similarly established.

Results

Photochemical Studies. Scheme III summarizes the photochemical results, both in solution and the solid state. Three product types were formed, depending on the structure of the reactant photolyzed and the medium employed. Hemiacetal (HA) photoproducts were produced

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(1) Appel, W. K.; Jiang, Z. Q.; Scheffer, J. R.; Walsh, L. *J. Am. Chem. Soc.* **1983**, *105*, 5354.

(2) Kushner, A. S. *Tetrahedron Lett.* 1971, 3275.

(3) Askari, S.; Lee, S.; Perkins, R. R.; Scheffer, J. R. *Can. J. Chem.* **1985**, *63*, 3526.

(4) (a) Compound **6**: Ariel, S.; Trotter, J. *Acta Crystallogr.* **1987**, *C43*, 1100. (b) Compound **7**: Ariel, S.; Trotter, J. *Acta Crystallogr.* **1987**, *C43*, 959. (c) Compound **9**: Ariel, S.; Trotter, J. *Acta Crystallogr.* **1987**, *C43*, 1103.

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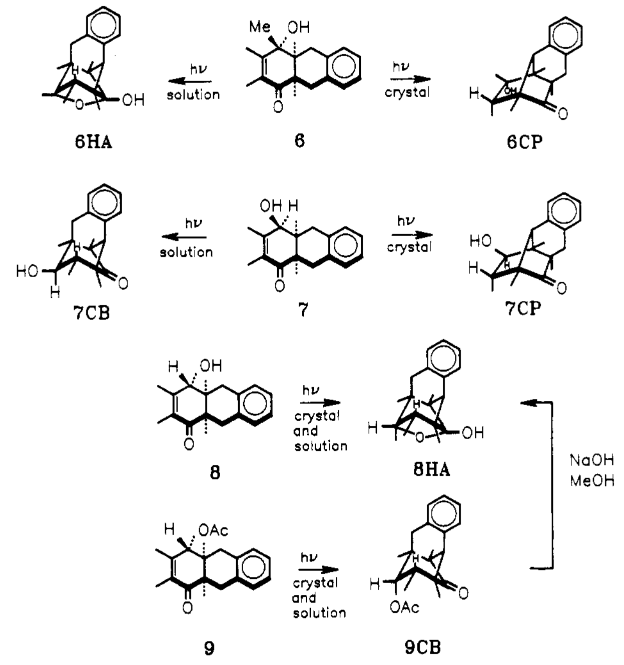
Scheme III

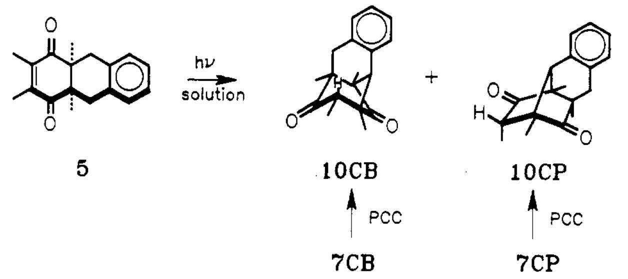


by solution irradiations of enone **6** and by solid-state and solution photolysis of **8**. Cyclopentanone (CP) type products were formed in the crystalline-phase irradiations of enones **6** and **7**, and cyclobutanone (CB) containing compounds resulted when enone **7** was photolyzed in solution and when **9** was irradiated in the solid state and solution. As is readily apparent from the structures of the photoproducts and from the conversion of cyclobutanone acetate **9CB** into hemiacetal **8HA** (Scheme III), hemiacetal photoproducts are derived from cyclobutanone photoproducts that have hydroxyl groups with the correct orientation for internal nucleophilic attack. Thus there are really only two basic carbon skeletons produced in this study, namely the tricyclo[5.3.0.0^{3,8}]decane ring system of photoproducts **6CP** and **7CP** and the tricyclo[6.2.0.0^{4,9}]decane carbon skeleton common to the other photoproducts. As we shall see, these two carbon skeletons are the result of two different primary photochemical processes that the reactants can undergo.

The solution irradiations were performed in acetonitrile with a 450-W Hanovia lamp fitted with a Pyrex filter sleeve. In the case of enones **8** and **9**, the chemical yields were near-quantitative; for enones **6** and **7**, yields were approximately 90%, and gas chromatography indicated the presence of approximately 10% of photoproducts **6CP** and **7CP**, respectively (the solid-state photoproducts). Identical results were obtained when the photolyses were carried out in the presence of the triplet energy sensitizers acetone or acetophenone. The quantum yield for the unsensitized photolysis of enone **8** in acetonitrile was found to be 0.04.

Solid-state photolyses were carried out in two ways: preliminary runs were conducted on KBr pellets, and the course of reaction was monitored by infrared spectroscopy. Larger scale runs were performed on pure polycrystalline samples sandwiched between 2 × 6 cm Pyrex plates packed and sealed under nitrogen in polyethylene bags. The light source for the solid-state irradiations was a 450-W Hanovia medium-pressure mercury lamp; in one or two runs, a nitrogen laser (337 nm) was used as the light source. This did not alter the photoproduct structures or ratios. Unless otherwise noted, all photochemistry was carried out at room temperature. At low conversions, the photoproducts indicated in Scheme III were the only products that could be detected by gas chromatography. However, above approximately 20% conversion, the crystals began to melt and other photoproducts began to appear. These were identified as the corresponding solution photoproducts on the basis of their gas chromatographic retention times. For example, at 23% conversion, enone **7** gave 21.5% of **7CP** and 1.5% of **7CB**; at 85% conversion, the **7CP**:**7CB** ratio was 80:5. Similarly, crystals of enone **6** underwent photolysis to a 23:1 = **6CP**:**6HA** mixture at 24% conversion; at 95% conversion, the ratio was 91:4.

Scheme IV



Photoproduct Structure Elucidation. The photoproduct structures were determined by spectroscopy coupled with conversion to compounds of known structure. Infrared spectroscopy was most useful in preliminarily establishing the ring system present. Four-membered ring ketones **7CB** and **9CB** exhibited characteristic carbonyl stretching absorptions in the 1750–1760-cm^{-1} region, and the five-membered ring ketones **6CP** and **7CP** showed carbonyl stretches near 1725 cm^{-1}; the hemiacetal type photoproducts **6HA** and **8HA** lacked any absorptions in the carbonyl region. All six photoproducts exhibited NMR spectra in accord with their structures. Particularly revealing was the presence in each case of a 3-proton (CH_3) doublet with a coupling constant of 7 Hz. This indicates the presence of the $C\mathit{H}CH_3$ structural unit in each photoproduct; the most likely mechanism by which this unit can be formed is through intramolecular hydrogen transfer to one of the carbon atoms of the α,β-unsaturated double bond.

The structures of photoproducts **7CB** and **7CP** were confirmed by oxidation to the corresponding diketones **10CB** and **10CP** (Scheme IV). Compounds **10CB** and **10CP** are formed when enedione **5** is photolyzed in solution; irradiation of crystals of enedione **5** leads exclusively to **10CB**.[5] Finally, the structure of hemiacetal **8HA** was confirmed by hydrolysis of acetate **9CB** using methanolic sodium hydroxide.

Crystallographic Studies. Three of the four enones investigated photochemically also had their crystal and molecular structures determined by single-crystal, direct-method X-ray diffraction studies.[4] Two of the enones (**6** and **7**) crystallized with similar conformations, which we term conformation A; the third enone, **9**, crystallized in a different conformation, which we call conformation B. Idealized conformational drawings of all three reactants are shown in Scheme V.

Conformations A and B represent energy minima for cis-fused enones of general structure **1**[1] as well as their benzannulated derivatives **6**, **7**, **9**, and, presumably **8**. In addition, the corresponding enediones (e.g. **5**) crystallize in similar conformations.[5] Both conformations A and B are characterized by flattened cyclohexenone rings cis-fused to half-chair benzocyclohexene rings; the torsion

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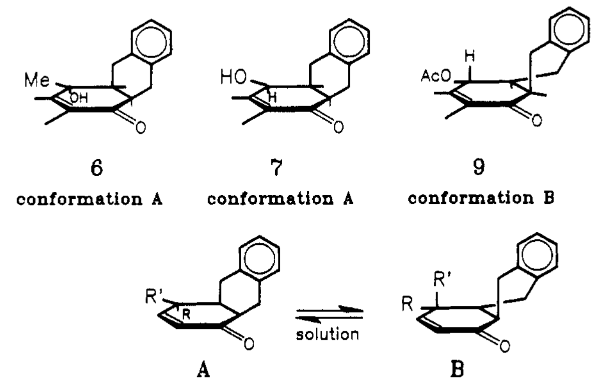
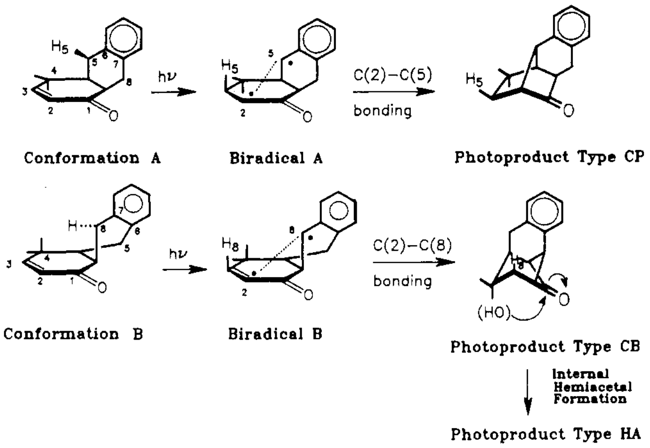
[5] Ariel, S.; Askari, S. H.; Scheffer, J. R.; Trotter, J.; Wireko, F. *J. Am. Chem. Soc.* 1987, *109*, 4623.

Scheme V



Scheme VI

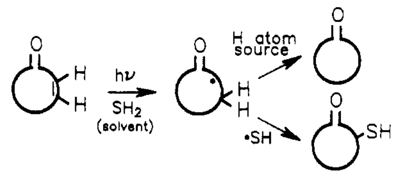


angles around the ring junction carbon–carbon bond are all close to 60° in both cases. For a given enone, conformers A and B bear a diastereomeric relationship and are in rapid equilibrium with one another in solution (Scheme V).[6] In the crystalline state, however, it is very rare that any but the lowest energy conformer is present.[7] This is the situation with enones **6**, **7**, and **9**; compounds **6** and **7** crystallize in conformation A because this places the bulkier substituent at C(4) (the methyl and hydroxyl groups, respectively) in the pseudoequatorial position. In contrast, enone **9** adopts conformation B in the solid state because this leads to the acetate group at C(4) being in the pseudoequatorial position. Without a doubt, enone **8**, which closely resembles **9** in structure and stereochemistry, also crystallizes in conformation B.

Discussion

Solid-State Photoreactivity. With the conformations of the four enones established by crystallography, the photochemical reaction mechanisms stand revealed (Scheme VI). Enones **6** and **7**, which exist in conformation A, react by intramolecular transfer of the endo hydrogen atom at C(5) to C(3), the β-carbon atom of the α,β-unsaturated double bond. This represents a rare example of a five-membered transition state hydrogen atom transfer between carbon atoms. After hydrogen transfer, the biradical produced (biradical A) undergoes C(2)–C(5) bond formation resulting in photoproducts of the CP type (**6CP** and **7CP**). As we shall see, both steps of the proposed reaction mechanism are geometrically feasible and are compatible with the severe restraints to motion present in the crystalline medium; that is, they are topochemically allowed.[8]

Scheme VII



Compounds **8** and **9**, which exist in conformation B in the crystal, undergo photoreaction involving a six-membered transition state hydrogen transfer. In this case it is the endo hydrogen atom at C(8) that lies over the C(2)–C(3) double bond, and transfer of this hydrogen to C(3) gives rise to biradical B (Scheme VI); closure of biradical B by C(2)–C(8) bonding then affords photoproducts of type CB. In the case of compound **8CB**, the stereochemistry at the hydroxyl-bearing carbon atom is such that internal hemiacetal formation is possible, and so the final product that is isolated has structure **8HA**. Conformation B reactivity, like that of conformation A, is characterized by a favorable geometric relationship between the reacting centers resulting in a least motion, topochemically allowed process.

Hydrogen abstraction reactions in which the abstracting atom is the β-carbon atom of an α,β-unsaturated ketone, while relatively rare, have ample literature precedent.[9] The preference for β- as opposed to α-abstraction is presumably dictated by formation of the more stable radical next to the carbonyl group, and in most cases studied, this species undergoes reaction with a second hydrogen atom donor to afford overall reduction of the C=C bond; alternatively, coupling with a solvent-derived radical leads to an α-substituted saturated ketone (Scheme VII). Our solid-state results can be seen to be the fully intramolecular version of this latter process.

The stereochemistry of intermolecular hydrogen transfer to the β-carbon atom of enones has been studied recently by Chan and Schuster[10] who found results consistent with reaction through a $(\pi,\pi^*)^3$ excited state that is pyramidal at the β-carbon. Pyramidalization was suggested to account for the difference in C=C photoreduction stereochemistry between the $(\pi,\pi^*)^3$ and $(n,\pi^*)^3$ excited states. In the latter case, the initial hydrogen transfer is to the enone oxygen atom, and the resulting radical, which is planar at the β-carbon, abstracts a second hydrogen at this atom to give a trans ring junction photoproduct. The fact that the $(\pi,\pi^*)^3$ state gives the same photoproduct with a cis ring junction led Chan and Schuster to suggest a different (pyramidal) β-carbon geometry in this case. It should be noted that Wiesner[11] was the first to suggest that the $(\pi,\pi^*)^3$ excited states of enones possess pyramidal β-carbon atoms. This idea was advanced to explain the stereochemistry of the [2 + 2] photocycloaddition reactions between enones and allenes. Although several cases are known that are consistent with this notion, there are some that are not,[12] and a recent ab initio SCF and CI study[13]

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[6] For NMR studies that establish such equilibria for symmetrically substituted enediones, see: (a) McDowell, C. A.; Naito, A.; Scheffer, J. R.; Wong, Y.-F. *Tetrahedon Lett.* **1981**, *22*, 4779. (b) Ariel, S.; Scheffer, J. R.; Trotter, J.; Wong. Y.-F. *Tetrahedron Lett.* **1983**, *24*, 4555.

[7] Dunitz, J. D. *X-Ray Analysis of the Structure of Organic Molecules*; Cornell University: Ithaca, 1979; Chapter 7.

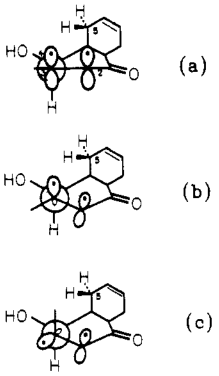
[8] (a) Cohen, M. D.; Schmidt, G. M. J. *J. Chem. Soc.* **1964**, 1996. (b) Cohen, M. D. *Angew. Chem., Int. Ed. Engl.* **1975**, *14*, 386.

[9] A compilation of the relevant literature is given in ref 1 (above), footnote 15.

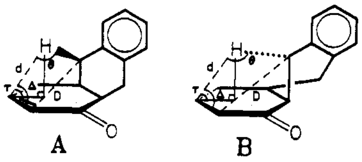
[10] Chan, A. C.; Schuster, D. I. *J. Am. Chem. Soc.* **1986**, *108*, 4561.

[11] (a) Wiesner, K. *Tetrahedron* **1975**, *31*, 1655. (b) Marini-Bettolo, G.; Sahoo, S. P.; Poulton, G. A.; Tsai, T. Y. R.; Wiesner, K. *Tetrahedron* **1980**, *36*, 719. (c) Blount, J. F.; Gray, G. D.; Atwal, K. S.; Tsai, T. Y. R.; Wiesner, K. *Tetrahedron Lett.* **1980**, 4413.

Scheme VIII



Scheme IX



concludes that, for acrolein, the β-carbon atom of the $(\pi,\pi^*)^3$ excited state remains planar.

Our results are consistent with either a planar or pyramidal β-carbon atom excited state geometry. Scheme VIII part a depicts conformation A in its planar (ground state) geometry, and part b shows the same material after twisting about the C=C bond and pyramidalization at the β-carbon atom; in both cases, the view is down the C(3)–C(4) bond. The main difference between these species is that C(2), and to a lesser extent C(1), have moved down during pyramidalization; C(3) remains fixed, and in both cases, the atomic orbital on C(3) is favorably disposed with respect to abstraction of the C(5) endo hydrogen atom. The pyramidalized excited state is actually somewhat less favorable for abstraction because the abstracting atomic orbital projects slightly away from H(5) relative to the planar situation. It should be pointed out that pyramidalization can also occur to give a species for which abstraction is impossible; this is depicted in Scheme VIII part c and need be considered no further.

Quantitative Structure–Reactivity Correlations. The crystal structure data permit quantitative assessment of the feasibility of the proposed mechanisms. With certain assumptions, both the hydrogen abstraction and the biradical coupling steps can be investigated. For the purposes of discussion, we define four geometric parameters that serve to characterize the reaction pathways. These are (1) d, the distance between the abstracting atom C(3) and the hydrogen being abstracted [H(5), conformation A or H(8), conformation B]; (2) τ, the angle formed between the C(3)···H(5) [or C(3)···H(8)] vector and its projection on the mean plane of the C(2)–C(3) double bond; (3) Δ, the C(2)–C(3)···H(5) [or C(2)–C(3)···H(8)] angle; (4) θ, the angle between the abstracting atom [C(3)], the hydrogen being abstracted, and the carbon to which the abstracted hydrogen is attached; (5) D, the C(5)···C(2) [or C(8)···C(2)] distance, i.e., the distance between the carbons that become bonded to one another in the final photoproducts. Scheme IX depicts these distances and angles for conformations A and B.

Table I. Crystal Structure Derived Geometric Data for Compounds 6, 7, and 9[a]

enone	d, Å	τ, deg	Δ, deg	θ, deg	D, Å
6	2.80	48	72	103	3.31
7	2.85	54	77	97	3.32
9	2.85	49	74	111	3.17

[a] See text for definition of d, τ, Δ, θ, and D.

The data are collected in Table I. Since, as mentioned above, C(3) does not appear to alter its position significantly upon pyramidalization, these ground-state data should be representative of both the planar and twisted excited-state conformations. An exception is the distance D. As depicted in Scheme VIII, D [the C(2)···C(5) distance] is expected to be somewhat greater for the twisted geometry (b) than for the planar enone (a). The biradical intermediate produced by hydrogen transfer is also pyramidal at C(3) and should therefore have a conformation similar to that of twisted conformation (b).

The hydrogen abstraction distances, d, collected in Table I fall within the range 2.82 ± 0.03 Å. Some time ago we suggested, based on extensive crystal structure–solid-state reactivity correlations, that, in general, hydrogen atom abstraction is feasible provided that the abstracting and abstracted atoms are not separated by more than the sum of their van der Waals radii.[5] While recent studies have raised the limit somewhat,[14] the values of d for enones **6**, **7**, and **9** fall well within the van der Waals radii sum of 2.90 Å for carbon and hydrogen. We have also pointed out recently that cyclization reactions of biradical intermediates are favorable when the radical centers are within the van der Waals radii sum of one another (3.40 Å in the case of two carbon atoms).[15] Assuming that the biradical intermediates have geometries that are similar to their ground-state precursors in the solid state, the values of D compiled in Table I can be seen to be consistent with this notion as well. Overall, the geometric data for compounds **6**, **7**, and **9** compare very favorably with those of other enones, enediones, and aromatic ketones whose solid-state photochemistry has been studied in our laboratory. More details on this aspect of the work can be found in two recent review articles.[14,15]

Solution-Phase Photoreactivity. We recall (Scheme III) that upon photolysis in solution all four enones give cyclobutanone type products, and that in two instances (enones **6** and **8**) the initially formed cyclobutanones undergo spontaneous internal hemiacetal formation owing to a favorable orientation between the hydroxyl group and the carbonyl group of the four-membered ring. From the solid-state studies discussed above, we know that cyclobutanone formation occurs uniquely from conformer B, and we thus conclude that in solution all four enones react preferentially from this conformation, even though in two cases (**6** and **7**) conformer A undoubtedly has a lower conformational energy and is therefore the major isomer present.

The general situation whereby conformational isomers react photochemically in solution to afford different products has been analyzed kinetically by Lewis, Johnson, and Johnson.[16] Two limiting conditions were defined: (1) conformational isomerization in the excited state is rapid relative to either rate-determining photochemical step, and (2) the photochemical rates are much faster than excit-

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(12) For a thorough discussion of Wiesner's proposal, see: (a) Weedon, A. C. In *Synthetic Organic Photochemistry*; Horspool, W. M., Ed.; Plenum: New York, 1984; pp 96–99 and 131–134. (b) Piers, E.; Abeysekera, B. F.; Herbert, D. J.; Suckling, I. D. *Can. J. Chem.* **1985**, *63*, 3418.

(13) Valenta, K.; Grein, F. *Can. J. Chem.* **1982**, *60*, 601.

(14) Scheffer, J. R. In *Organic Solid State Chemistry*; Desiraju, G. R., Ed.; Elsevier: Amsterdam, 1987; Chapter 1.

(15) Scheffer, J. R.; Trotter, J. *Rev. Chem. Int.* **1988**, *9*, 271.

(16) Lewis, F. D.; Johnson, R. W.; Johnson, D. E. *J. Am. Chem. Soc.* **1974**, *96*, 6090.

ed-state conformational isomerization. In the latter case, the final product ratio will depend on the excited-state conformer population (A* and B*), and since excitation is faster than molecular motion, also on the ground-state conformer distribution. Because, as discussed above, the major product is derived in two instances from the minor conformational isomer, we conclude that condition (1) applies in the case of compounds **6**–**9**. A similar conclusion was reached in our studies[1] on the nonbenzannulated enones of general structure **1** discussed in the introduction section. In this case the exclusive solution process consisted of intramolecular [2 + 2] photocycloaddition from a minor (eclipsed) conformer in which the two double bonds are close to one another and parallel.

As pointed out by Lewis et al.,[16] when condition (1) is met, the Curtin–Hammett principle applies, and the product ratio should depend only on the relative magnitude of the two rate-limiting photochemical steps. In analogy to other hydrogen abstraction initiated processes such as the Norrish type II reaction,[17] the rate-determining steps in the photoreactions of compounds **6**–**9** are likely to be the five-membered transition state (conformer A) and six-membered transition state (conformer B) hydrogen atom abstractions shown in Scheme VI. This analysis predicts, therefore, that the latter process (which leads to the major product in solution) is the faster. This conclusion is entirely consistent with the well known competitive advantage that γ-hydrogen atom abstraction has in the Norrish type II reaction.[17] Interestingly, the data in Table I suggest that there is no *geometric* advantage to six-membered transition state abstraction for enone **9**. We note also the possibility that reverse hydrogen atom abstraction (well established in the type II process[17]) could be influencing the photoproduct ratios. Return of biradical A (Scheme VI) to ground state enone faster than biradical B would favor formation of cyclobutanone type photoproducts as observed. There seems, however, to be no obvious reason why this should be the case. In any event the observation of small but significant amounts of CP photoproducts from enones **6** and **7** indicates that overall the two pathways are closely balanced.

Summary

The work reported in this paper demonstrates that organic molecules may possess latent reaction pathways that are realized when a chemical impetus (in this case, photoexcitation) is applied *in the solid state*. This situation arises when the liquid phase reaction is particularly rapid and occurs through a minor, high-energy conformational isomer. In the crystal, however, organic molecules nearly always adopt (and are restricted to) their more stable, lower energy conformations.[7] If (as is the case for enones **6** and **7**) this conformation happens to react differently from, and more slowly than, its higher energy (solution) isomer, new products will be observed in the solid. In other cases (such as enones **8** and **9**), the low energy conformer reacts *faster* than the high energy conformer. This leads to identical chemistry in the solid state and solution. The property of the solid state that is of primary importance in these photoreactions is its ability to restrict the interconversion of conformers A and B. Even at conversions as high as 20%, the photochemistry remains conformation-specific, thus ruling out conformational equilibration at reaction-caused defect sites. This implies that other highly viscous media should exert a similar effect, and such has indeed been found to be the case for a nonbenzannulated enone of type **1**.[18]

Experimental Section

General Methods. Melting points were determined on a Fisher-Johns hot stage apparatus and are uncorrected. Infrared (IR) spectra were determined on a Perkin-Elmer 710B instrument by using KBr disks and are reported as $\nu_{\max}$ in cm^{-1}. Proton nuclear magnetic resonance (NMR) spectra were recorded either on a Bruker WH-400 or Varian XL 300 instrument by using $CDCl_3$ as the solvent and Me_4Si as the internal standard. Signal positions are given in δ, and the multiplicities, integrated areas, coupling constants, and assignments are indicated in brackets. Mass spectra (MS) were recorded with a Kratos MS-50 instrument operating at 70 eV. Gas chromatography–mass spectrometry (GCMS) was carried out on Kratos MS-80RFA and Carlo Erba 4160 instruments by the departmental mass spectral service; the relative intensity of each ion is given in parentheses. Analytical gas chromatography (GC) was carried out on a Hewlett-Packard Model 5890 instrument by using a 15-m DB-1 capillary column with He as the carrier gas. Elemental analyses were carried out by the departmental microanalyst, P. Borda. Spectral grade solvents were used directly as obtained; others were purified by well-established procedures.[19] Photolyses were carried with a 450-W Hanovia medium-pressure mercury lamp, and in several instances, with a Molectron UV-22 pulsed nitrogen laser (λ = 337 nm, 330-mW average power). The liquid-phase samples were freed of oxygen by bubbling nitrogen through the solution for 1 h prior to photolysis. The crystalline samples, sandwiched between 2 × 6 cm Pyrex plates, were sealed under nitrogen in polyethylene bags using a heat-sealing device. Quantum yields were determined in a merry-go-round apparatus at 313 nm by using valerophenone actinometry. Nonadecane and tetradecane were used as internal standards for quantitative GC analysis.

Preparation of Enone 6. To a stirred solution of enedione **5**[3] (0.54 g, 2.0 mmol) in 20 mL of freshly distilled, anhydrous THF maintained under nitrogen, was added 0.88 g (2.0 mmol) of methyl lithium in ether solution. The resulting yellow reaction solution was stirred for 1 h at room temperature and then quenched with dilute, aqueous ammonium chloride. After extraction with ether (3 × 50 mL) and drying over sodium sulfate, ether was removed in vacuo to afford 0.52 g of white solid, which GC indicated to be a 4:1 mixture of two products. Recrystallization of this mixture from acetone gave 0.35 g (62%) of large, well-formed prisms of the major product, enone **6**: mp 171–172 °C; IR (KBr) 3498 (OH), 1655 (C=O), and 1635 (C=C) cm^{-1}; ^{1}H NMR CD_3OD) δ 7.17–6.92 (m, 4 H, Ar-H), 3.22 (d, 1 H, J = 18 Hz, benzylic H), 2.58 (m, 3 H, remaining benzylic H), 2.00 (s, 3 H, C(3)–CH_3, this peak was obscured by solvent in CD_3OD but was clearly visible in DMSO-d_6), 1.70 (s, 3 H, C(2)–CH_3), 1.36 (s, 3 H, CH_3), 1.26 (s, 3 H, CH_3), 1.06 (s, 3 H, CH_3); MS m/e (rel intensity) 284 (M^+, 15), 266 (17), 255 (8), 223 (30), 197 (8), 165 (12), 126 (42), 83 (100). Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.17; H, 8.58. Final proof of structure came from an X-ray crystal structure determination.[4a]

Preparation of Enones 7 and 8. To a stirred solution of enedione **5** (1.60 g, 6.0 mmol) in 20 mL of methanol and THF (19:1, v/v), maintained at 0 °C, was added 0.30 g (7.9 mmol) of solid sodium borohydride over a period of 5 min. After 20 min, the reaction was quenched with aqueous ammonium chloride solution. The resulting mixture was extracted with ether (2 × 50 mL), and the organic layers were combined and dried over sodium sulfate. Removal of solvent in vacuo afforded a colorless oil, which was purified by flash column chromatography[20] by using low-boiling petroleum ether–ethyl acetate (4:1, v/v). The compound corresponding to R_f = 0.66 on TLC was isolated and recrystallized from methylcyclohexane to afford colorless needles (0.89 g, 55%), identified as enone **8**: mp 162–163 °C; IR (KBr) 3484 (OH), 1651 (C=O), and 1629 (C=C) cm^{-1}; ^{1}H NMR ($CDCl_3$)

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δ 7.16–7.00 (m, 4 H, Ar-H), 4.31 (d, 1 H, *J* = 8 Hz, collapses to a singlet after D_2O exchange, C*H*OH), 3.10 (d, 1 H, *J* = 18 Hz, benzylic H), 3.05 (d, 1 H, *J* = 18 Hz, benzylic H), 2.56 (d, 1 H, *J* = 18 Hz, benzylic H), 2.44 (d, 1 H, *J* = 18 H, benzylic H), 1.99 (d, 1 H, *J* = 8 Hz, exchangeable, OH), 1.96 (s, 3 H, C(3)-CH_3), 1.82 (s, 3 H, C(2)-CH_3), 1.18 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3); UV λ_{max} (CH_3CN) 246 (ε 20 280), 328 (ε 87); MS *m/e* (rel intensity) 270 (M^+, 10), 252 (48), 237 (23), 225 (15), 209 (20), 166 (100), 141 (26), 112 (51), 104 (36). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 80.10; H, 8.40.

A second reduction product corresponding to R_f = 0.42 was isolated and recrystallized from low-boiling petroleum ether to afford 0.54 g (34%) of large, well-formed crystals, identified as enone **7**: mp 143–144 °C; IR (KBr) 3457 (OH), 1647 (C=O) and 1632 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.15–6.94 (m, 4 H, Ar-H), 4.42 (d, 1 H, *J* = 6 Hz, collapses to a singlet after D_2O exchange, C*H*-OH), 3.46 (d, 1 H, *J* = 18 Hz, benzylic H), 2.82 (d, 1 H, *J* = 18 Hz, benzylic H), 2.60 (d, 1 H, *J* = 18 Hz, benzylic H), 2.55 (d, 1 H, *J* = 18 Hz, benzylic H), 2.25 (d, 1 H, *J* = 6 Hz, exchangeable, OH), 2.00 (s, 3 H, C(3)-CH_3), 1.77 (s, 3 H, C(2)-CH_3), 1.16 (s, 3 H, CH_3), 1.14 (s, 3 H, CH_3); MS *m/e* (rel intensity) 270 (M^+, 3), 252 (100), 237 (46), 224 (17), 209 (62), 195 (12), 169 (28), 141 (22), 128 (28), 104 (24). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.91; H, 8.30. Final proof of structure came from an X-ray crystal structure determination.[4b]

Preparation of Enone 9. To a suspension of 50 mg (0.19 mmol) of enone **8** in 3 mL of acetic anhydride was added 0.9 mL of pyridine. After being at room temperature for 12 h, the reaction mixture was diluted with 20 mL of water and extracted with chloroform (3 × 5 mL). The combined organic layers were washed with concentrated HCl (3 × 3 mL), saturated $NaHCO_3$ solution (2 × 5 mL), and water (5 mL). After drying over sodium sulfate, chloroform was removed by rotary evaporation to afford a colorless solid, which was recrystallized from cyclohexane to afford 55 mg (93%) of large prisms, identified as enone–acetate **9**: mp 132–133 °C; IR (KBr) 1742 (acetate C=O), 1665 (enone C=O), 1641 (C=C) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.22–6.92 (m, 4 H, Ar-H), 5.65 (s, 1 H, C*H*-OAc), 3.25 (d, 1 H, *J* = 18 Hz, benzylic H), 2.57 (m, 3 H, benzylic H), 2.18 (s, 3 H, $COCH_3$), 1.83 (s, 6 H, C(2) and C(3)-CH_3), 1.23 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3); MS *m/e* (rel intensity) 312 (M^+, 9), 270 (10), 252 (100), 237 (45), 223 (17), 209 (57), 166 (64), 142 (12), 130 (21), 112 (61), 104 (16). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 77.10; H, 7.69. Final proof of structure came from an X-ray crystal structure determination.[4c]

Photolysis of Enone 6 in Solution. A solution of enone **6** (140 mg, 0.50 mmol) in 250 mL of acetonitrile was irradiated through Pyrex for 72 h by using a 450-W Hanovia lamp. GC analysis showed the formation of two products in 90% and 10% yield. Identical results were obtained when acetone was the photolysis solvent. The major product (TLC R_f = 0.28) was isolated by silica gel column chromatography with low-boiling petroleum ether–ethyl acetate (3:1, v/v) as the eluting solvent. Recrystallization from low-boiling petroleum ether afforded 80 mg (57%) of colorless crystals, identified as internal hemiacetal **6HA**: mp 127–128 °C; IR (KBr) 3326 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.23–6.94 (m, 4 H, Ar-H), 2.92 (s, 1 H, exchangeable, OH), 2.68 (fortuitous s, 2 H, benzylic CH_2), 2.64 (s, 1 H, benzylic CH), 1.50 (q, 1 H, *J* = 7 Hz, C*H*CH_3), 1.20 (s, 3 H, CH_3), 1.02 (s, 3 H, CH_3), 0.98 (s, 3 H, CH_3), 0.92 (s, 3 H, CH_3), 0.70 (d, 3 H, *J* = 7 Hz, CH_3); MS *m/e* (rel intensity) 284 (M^+, 36), 269 (14), 239 (100), 223 (35), 209 (12), 195 (11), 183 (13), 169 (28), 157 (78), 141 (35), 127 (31), 115 (22). Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.06; H, 8.61.

Preparative Photolysis of Enone 6 in the Solid State. An 80-mg polycrystalline sample of enone **6** was photolyzed with the 450-W lamp through Pyrex for 28 h. A GC analysis indicated a conversion of 90%. The major photoproduct, R_f = 0.59, was isolated by column chromatography as described above for the solution photolysis mixture. Recrystallization from methylcyclohexcane gave 40 mg (50%) of colorless crystals of material identified as keto alcohol **6CP**: mp 165–167 °C; IR (KBr) 3459 (OH), 1724 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.20–6.92 (m, 4 H, Ar-H), 2.74 (AB q, 2 H, *J* = 17 Hz, benzylic CH_2), 2.65 (s, 1 H, benzylic CH), 1.85 (q, 1 H, *J* = 7 Hz, C*H*CH_3), 1.44 (s, 3 H, CH_3), 1.36 (s, 3 H, CH_3), 1.06 (s, 1 H, exchangeable, OH), 1.00 (s, 3 H, CH_3), 0.94 (s, 3 H, CH_3), 0.90 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$); MS *m/e* (rel intensity) 284 (M^+, 100), 269 (13), 241 (44), 228 (37), 213 (85), 195 (27), 185 (18), 169 (27), 158 (60), 142 (45), 127 (40), 115 (27), 83 (36). Anal. Calcd for $C_{19}H_{24}O_2$: C, 80.24; H, 8.51. Found: C, 80.13; H, 8.45. There was no deuterium incorporation when this material was treated with CH_3ONa/CH_3OD. Small scale, analytical photolyses of enone **6** gave the results reported in the text.

Photolysis of Enone 7 in Solution. Irradiation (Pyrex) of enone **7** (150 mg, 0.55 mmol) was carried out in 250 mL of acetonitrile for 3.5 h. A GC analysis showed the formation of two products in a 92:8 ratio. Identical results were obtained when the photolysis was repeated in acetonitrile in the presence of a 10-fold molar excess of the triplet energy sensitizer acetophenone. Silica gel column chromatography of the reaction mixture by using low-boiling petroleum ether–ethyl acetate (3:1, v/v) as the eluting solvent allowed separation of the major photoproduct (R_f = 0.60), identified as hydroxycyclobutanone **7CB**: mp 99–100 °C; IR (KBr) 3496 (OH), 1747 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.24–7.00 (m, 4 H, Ar-H), 2.99 (m, 1 H, collapses to d, *J* = 10 Hz after deuterium exchange, C*H*OH), 2.91 (d, 1 H, *J* = 17 Hz, one of benzylic CH_2), 2.64 (m, 2 H, one of benzylic CH_2 plus benzylic CH), 1.50 (m, 1 H, C*H*CH_3), 1.44 (d, 1 H, *J* = 8 Hz, exchangeable, OH), 1.20 (s, 3 H, CH_3), 1.18 (s, 3 H, CH_3), 1.11 (s, 3 H, CH_3), 0.93 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$); MS *m/e* (rel intensity) 270 (M^+, 9), 242 (9), 227 (6), 209 (22), 194 (5), 169 (29), 157 (100), 142 (48), 128 (30), 115 (33). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.76; H, 8.21.

Preparative Photolysis of Enone 7 in the Solid State. Crystals of enone **7** (55 mg, 0.20 mmol) were sandwiched between two Pyrex glass plates and irradiated for 15 h with the 450-W Hanovia lamp. Two recrystallizations from methylcyclohexane gave 35 mg (64%) of a pure crystalline material, which was identified as keto alcohol **7CP**: mp 155–156 °C; IR (KBr) 3449 (OH), 1724 (C=O) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.19–6.56 (m, 4 H, Ar-H), 3.74 (m, 1 H, C*H*OH), 2.96 (s, 1 H, benzylic CH), 2.75 (AB q, 2 H, *J* = 17 Hz, benzylic CH_2), 1.85 (m, 1 H, C*H*CH_3), 1.77 (d, *J* = 4.5 Hz, exchangeable, OH), 1.03 (s, 6 H, 2 CH_3), 0.94 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$), 0.86 (s, 3 H, CH_3); MS *m/e* (rel intensity) 270 (M^+, 51), 252 (10), 237 (15), 224 (10), 209 (45), 195 (12), 179 (57), 169 (71), 157 (84), 156 (97), 142 (88), 141 (100), 128 (64), 115 (67), 91 (20). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.97; H, 8.35. Small-scale, analytical photolyses of enone **7** gave the results reported in the text.

Photolysis of Enone 8 in Solution and the Solid State. A solution of 200 mg (0.74 mmol) of enone **8** in 250 mL of acetonitrile was photolyzed for 2.5 h through Pyrex by using the Hanovia 450-W medium-pressure mercury lamp. Removal of solvent in vacuo followed by recrystallization of the solid residue from acetonitrile afforded 180 mg (90%) of colorless crystals, identified as internal hemiacetal **8HA**: mp 164–165 °C; IR (KBr) 3272 (OH) cm^{-1}; ^1H NMR ($CDCl_3$) δ 7.15–6.95 (m, 4 H, Ar-H), 3.48 (s, 1 H, C*H*O), 3.28 (s, 1 H, exchangeable, OH), 2.76 (AB q, 2 H, *J* = 17 Hz, benzylic CH_2), 2.64 (s, 1 H, benzylic CH), 1.58 (q, 1 H, *J* = 7 Hz, C*H*CH_3), 1.12 (s, 3 H, CH_3), 1.01 (s, 3 H, CH_3), 0.96 (s, 3 H, CH_3), 0.79 (d, 3 H, *J* = 7 Hz, CHC*H*$_3$); MS *m/e* (rel intensity) 270 (M^+, 8), 240 (3), 225 (12), 209 (21), 169 (30), 157 (100), 142 (43), 128 (21), 115 (27). Anal. Calcd for $C_{18}H_{22}O_2$: C, 79.96; H, 8.20. Found: C, 79.98; H, 8.31. Irradiation of 0.01 M acetonitrile solutions of enone **8** with the nitrogen laser (337 nm) at temperatures ranging from −40 to +56 °C gave **8HA** as the only product detectable by GC; laser irradiation of 0.01 M solutions of **8** containing 1.0 M acetophenone likewise afforded only **8HA**. Laser photolysis of KBr pellets containing crystalline **8** (2 mg in 50 mg of KBr) gave IR spectra identical with that of pure **8HA**; similar irradiation of crystals of **8** gave a single photoproduct identical with that formed in solution according to GC co-injection analysis.

Photolysis of Enone 9 in Solution and the Solid State. A solution of 20 mg (0.06 mmol) of enone **9** in 20 mL of acetonitrile was photolyzed for 2 h through Pyrex by using the 450-W Hanovia lamp. Removal of solvent in vacuo afforded an oil, which was purified by silica gel column chromatography by using low-boiling petroleum ether–ethyl acetate (4:1, v/v) as the eluting solvent. The material corresponding to R_f = 0.74 on TLC was isolated as a colorless oil (16 mg, 80%) and identified as cyclobutanone **9CB**:

IR (neat) 1764 (cyclobutanone C=O) and 1738 (acetate C=O) cm^{-1}; ^{1}H NMR (CDCl$_3$) δ 7.34–6.97 (m, 4 H, Ar-H), 4.90 (d, 1 H, J = 6 Hz, C*H*OAc), 2.82 (AB q, 2 H, J = 17 Hz, benzylic CH$_2$), 2.52 (s, 1 H, benzylic CH), 2.05 (m, 4 H, COC*H*$_3$ and C*H*CH$_3$), 1.16 (s, 3 H, CH$_3$), 1.14 (s, 3 H, CH$_3$), 1.03 (s, 3 H, CH$_3$), 0.73 (d, 3 H, J = 8 Hz, CHC*H*$_3$); MS *m/e* (rel intensity) 312 (M$^+$, 3), 270 (42), 225 (13), 209 (32), 169 (70), 157 (100), 142 (35), 128 (15), 113 (18). Anal. Calcd for $C_{20}H_{24}O_3$: C, 76.89; H, 7.74. Found: C, 76.84; H, 7.85.

Nitrogen laser irradiation of 0.01 M solutions of enone **9** in acetonitrile at temperatures ranging from −40 to +56 °C gave **9CB** as the only product detectable by GC. Laser photolysis of KBr pellets containing crystalline **9** gave IR spectra identical with that of **9CB**; similar irradiation of polycrystalline **9** gave a single product identical with that formed in solution as shown by GC co-injection analysis.

Interconversion of Photoproducts 9CB and 8HA. A stirred solution of cyclobutanone–acetate **9CB** (20 mg, 0.06 mmol) in 2 mL of methanol was treated with 1 mL of a 2% aqueous solution of sodium hydroxide for 3 h at room temperature. The reaction mixture was extracted with ether (2 × 3 mL), and the combined organic extracts were washed with water (2 × 2 mL) and then dried over sodium sulfate. The solvent was removed in vacuo to afford 16 mg (92%) of crystalline material whose melting point and IR spectrum were identical with those of internal hemiacetal **8HA** isolated from photolysis of enone **8**.

Oxidation of Photoproduct 7CP to the Known Compound 10CP. Keto alcohol **7CP** (40 mg, 1.5 mmol) was added to a solution of 48 mg (2.2 mmol) of pyridinium chlorochromate in 5 mL of freshly distilled anhydrous methylene chloride, and the resulting mixture was stirred at room temperature for 3.5 h under nitrogen. The mixture was extracted with three 10-mL portions of ether, and the combined organic extracts were filtered through Florisil in a sintered-glass funnel. Removal of solvent in vacuo gave an off-white solid, which was recrystallized from low-boiling petroleum ether to afford 35 mg (88%) of colorless crystals whose melting point and IR spectrum were identical with those of diketone **10CP** obtained from the low-temperature, solution-phase photolysis of enedione **5**.[5]

Oxidation of Photoproduct 7CB to the Known Compound 10CB. The procedure described above was repeated with 10 mg (0.04 mmol) of photoproduct **7CB** and 13 mg (0.05 mmol) of pyridinium chlorochromate. The crystalline product thus obtained (8 mg, 80%) proved to be exactly identical (melting point, IR) to photoproduct **10CB** obtained by photolysis of enedione **5** in the solid state or in solution at elevated temperatures.[5]

Acknowledgment. We thank the Natural Sciences and Engineering Research Council of Canada for financial support.

Synthesis of *N*-(Alkyloxy)pyridine-2(1*H*)-thiones: Alkylations of the Ambident Nucleophile Pyridine-2(1*H*)-thione *N*-Oxide and Attempted Isomerizations of 2-(Alkylthio)pyridine *N*-Oxide

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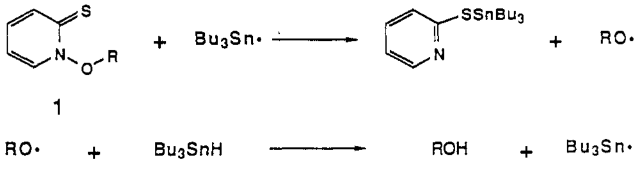
Received March 13, 1989

Two possible routes for the preparation of *N*-(alkyloxy)pyridine-2(1*H*)-thiones (**1**), namely, nucleophilic substitution of pyridine-2(1*H*)-thione *N*-oxide anion (**5**) and the thermal rearrangement of isomeric 2-(alkylthio)pyridine *N*-oxides (**6**), have been investigated. The ambident nucleophilic anion **5** undergoes both O- and S-alkylation upon treatment with alkyl bromides, chlorides, mesylates, or triflates; the regioselectivity is influenced by the temperature and the nature of the solvent, counterion, alkyl group, and leaving group. Details of the synthesis and characterization of a number of *N*-(alkyloxy)pyridine-2(1*H*)-thiones (**1**) (alkyl = *n*-propyl, *n*-butyl, benzyl, neopentyl, methoxymethyl, isopropyl, cyclopentyl, cyclohexyl, and *tert*-butyl) and 2-(alkylthio)pyridine *N*-oxides (**6**) (alkyl = *n*-propyl, *n*-butyl, and benzyl) are reported. Attempts to prepare **1** from the thermal rearrangement of **6** were unsuccessful, as **6** proved to be the thermodynamically stable isomer; the benzyl sulfide **1c** was converted into its isomer **6c** upon heating. Preliminary studies show that this rearrangement occurs in competition with N–O bond homolysis and appears to be catalyzed by molecular oxygen.

Introduction

Recently, we reported the use of *N*-(alkyloxy)pyridine-2(1*H*)-thiones (**1**) as sources of alkoxy radicals for mechanistic studies.[1,2] Reactions of **1** with an excess of tributylstannane, initiated either by heat and azobisisobutyronitrile or by irradiation with visible light, proceed in accordance with the radical chain mechanism shown in Scheme I. This manifold provides a suitable system for the measurement of the rates of rapid alkoxy radical rearrangements against the known rates of hydrogen abstraction from tributylstannane by alkoxy radicals.[3] The utility of this method has been demonstrated by the measurement of rate constants and Arrhenius parameters for the β-scission of the cyclopentyloxy radical.[2] The present work is concerned with the preparation of these novel alkoxy radical precursors.

Scheme I



Prior to the mechanistic studies cited above, the synthesis and reactivity of **1** had not been reported, but a very similar class of compounds, the *N*-(alkyloxy)pyridin-2-(1*H*)-ones (**2**), had been prepared and studied.[4-6] In early

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[3] (a) In ref 2 we used the estimated values of E_a = 1.83 ± 0.54 kcal/mol and $\log^{10} A$ = 9.70 ± 0.40 for the hydrogen abstraction from tributylstannane by the cyclopentyloxy radical. These estimates are in good agreement with the recent measurement of the corresponding Arrhenius parameters for the *tert*-butoxy radical: E_a = 1.1 ± 0.1 kcal/mol and $\log^{10} A$ = 9.5 ± 0.1.[3b] (b) Private communication with Dr. J. Lusztyk.

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