Communications to the Editor

Crystal Lattice Control of a Unimolecular Photorearrangement. Divergent Behavior of a β,γ-Unsaturated Ketone in Solution and the Solid State

Sir:

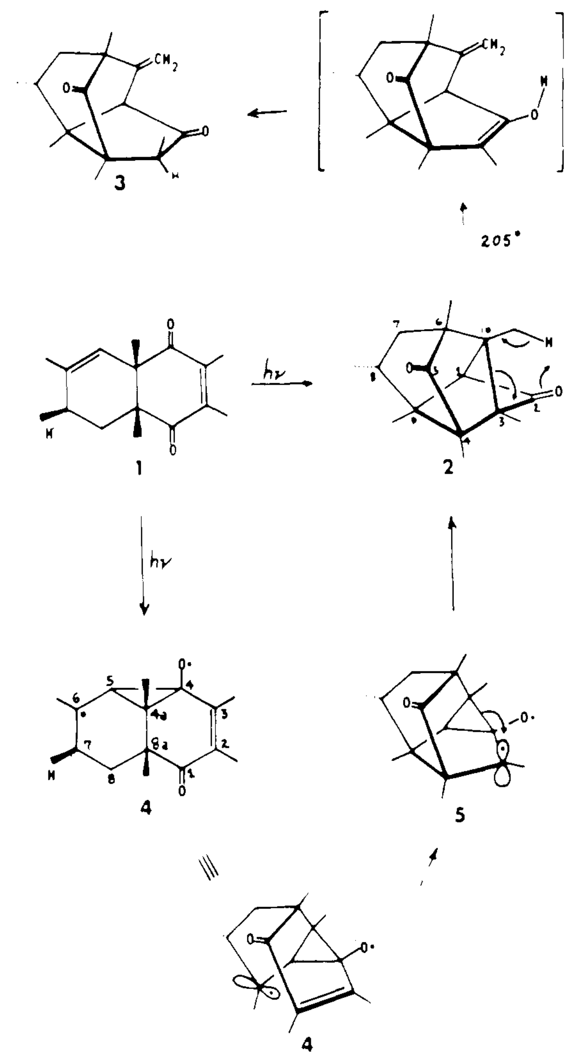
A major incentive for studying organic reactions in the solid state stems from the possibility of observing chemistry from a single conformation of a normally (solution, gas phase) conformationally mobile system. Coupled with the technique of X-ray crystallography, studies of this type present unparalleled opportunities for the construction of detailed unimolecular structure-reactivity relationships. In this regard, crystal lattice or topochemical control of *bimolecular* organic photochemical reactions (e.g., [2 + 2] photodimerizations[1,2]) as the result of intermolecular lattice-enforced proximity and orientation effects is well established. However the idea that lattice-imposed restrictions on atomic and molecular motions can also bring about complete *unimolecular* solid-state/solution reactivity differences has not yet been demonstrated.[3] In this paper we report the first example of such behavior. In addition to providing a unique (and synthetically useful) instance of intramolecular photoproduct control through phase change, the results are of interest crystallographically in that they further delineate the range of motions allowable in an organic solid-state process.

Both direct and benzophenone-sensitized irradiation (λ >340 nm) of 2,3,4aβ,6,7β,8aβ-hexamethyl-4a,7,8,8a-tetrahydro-1,4-naphthoquinone (**1**, Scheme I)[4] in either benzene or hexane solution gave rise to a single crystalline photoproduct, mp 114-114.5 °C, which could be isolated in >95% yield: IR (KBr) 1750 and 1778 (C═O) cm^{-1}; NMR ($CDCl_3$) δ 0.78 (s, 3 H), 0.85 (d, J = 6 Hz, 3 H), 0.92 (s, 3 H), 0.94 (s, 3 H), 0.99 (s, 3 H), 1.08 (s, 3 H), 1.20-1.85 (m, 3 H), 2.56 (s, 1 H); mass spectrum parent (70 eV) m/e 246.[5] Unequivocal evidence for the novel tetracyclic photoproduct structure **2** comes from a single-crystal X-ray structure determination, the details of which will be published separately.[6]

Sealed-tube thermolysis of diketone **2** at 205 °C gave rise to a 90% yield of the interesting *exo*-methylene compound **3**: mp 125-126 °C; IR (KBr) 1720 and 1735 (C═O) cm^{-1}; NMR ($CDCl_3$) δ 0.87 (d, J = 7 Hz, 3 H), 0.98 (s, 3 H), 1.01 (d, J = 6 Hz, 3 H), 1.11 (s, 3 H), 1.20 (s, 3 H), 1.22-1.34 (m, 1 H), 1.85-2.12 (m, 2 H), 2.34 (q, J = 7 Hz, 1 H, further split by long-range coupling, J = 1.5 Hz, exchangeable), 3.20 (d, J = 1.4 Hz, 1 H), 5.01 (dd, J = 14.5, 1.4 Hz, 2 H); UV (cyclohexane) λ_{max} 303 nm (ϵ 405), shoulder 312 nm (ϵ 385); mass spectrum parent (70 eV) m/e 246.[5,7] This rearrangement formally represents a particularly unusual example of a ketone to enol retro-ene process (arrows) of the type discussed by Conia.[8] The regioselectivity observed is in accord with cleavage of the longest cyclobutanone ring bond C_3-C_{10} = 1.594 (2), C_1-C_{10} = 1.582 (2) Å.

Turning next to the question of the mechanism of the photoconversion of **1** to **2**, the process shown in Scheme I appears feasible. Well-precedented[9] bridging of triplet excited β,γ-unsaturated ketone **1** gives biradical **4** which, rather than continuing along the normal oxadi-π-methane hypersurface, is diverted by the close proximity of an intramolecular carbon-carbon double bond. Carbon radical-olefinic bonding in **4** leads to biradical **5** which can rearrange to **2** via a stereoelectronically favored 1,2 shift of the cyclopropane ring bond which best overlaps with the p orbital at the migration terminus.[10]

Scheme I



Completely different results were obtained when β,γ-unsaturated ketone **1** was photolyzed in the solid state. Polycrystalline samples of **1**, mp 53.0-53.5 °C, were irradiated (λ >340 nm) to ~30% conversions in the apparatus previously described[2] and the temperature was maintained at −40 °C to ensure crystallinity of the two-component reaction mixture during photolysis.[11] Gas chromatographic analysis indicated the formation of essentially a single photoproduct, subsequently shown to have the structure **6** (Scheme II),[4] and this material could be isolated by silica gel column chromatography in ~65% yield based on unrecovered starting material.

Concomitant with the chemical studies, the X-ray crystal structure of starting diketone **1** was determined. Crystals of **1** are monoclinic, a = 6.865 (1), b = 16.043 (2), c = 13.166 (2) Å; β = 99.57 (1)°; Z = 4, space group $P2_1/c$. Diffractometer data provided 1862 observed reflections using Cu Kα radiation. The structure was determined by direct methods (symbolic addition procedure programmed by Long[12]) and refined by full-matrix least squares to the final R of 0.047 using

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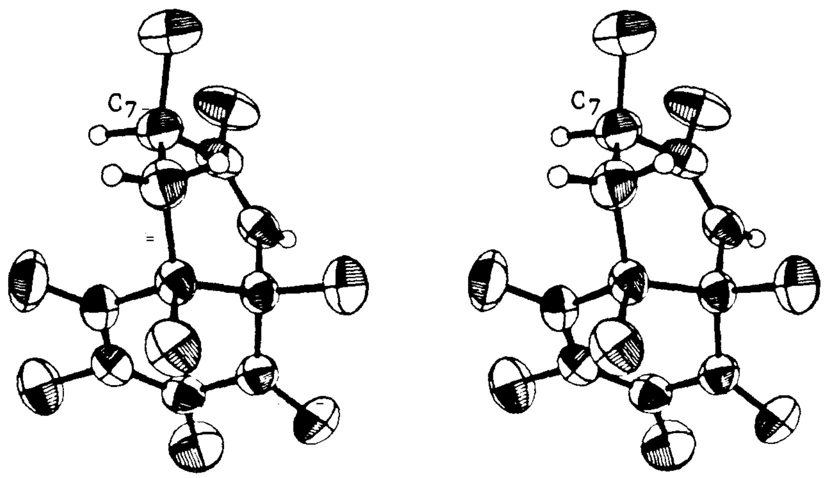
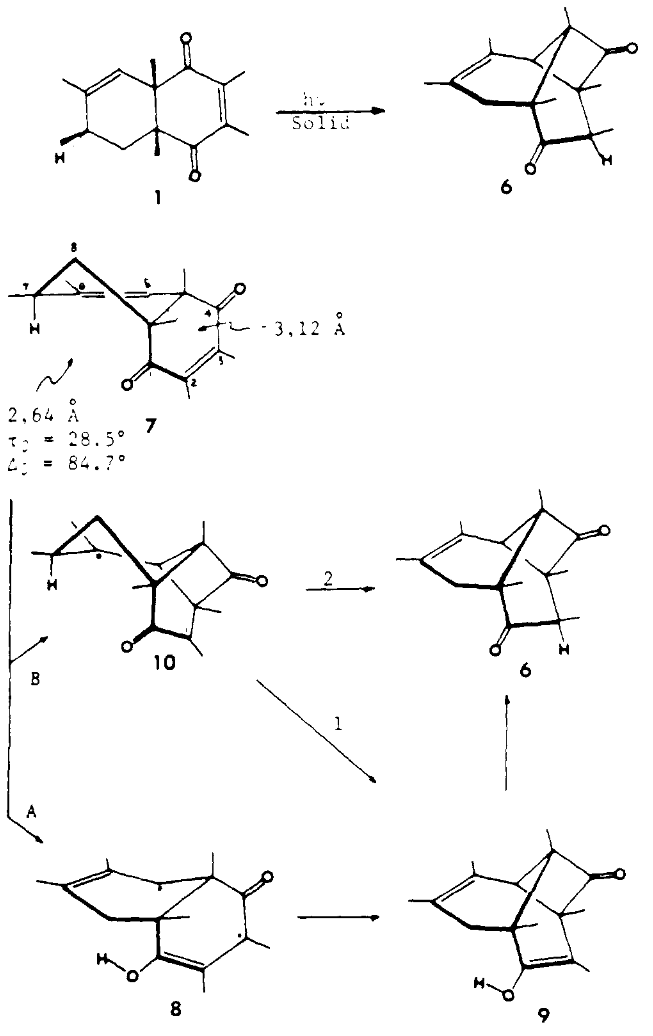


Figure 1. Stereodiagram of the conformation of β,γ-unsaturated ketone **1** in the solid state. The methyl hydrogen atoms are omitted for clarity.

Scheme II



absorption corrected data. Ansiotropic thermal parameters were used for C and O; H atoms were refined isotropically. The molecular structure is shown in Figure 1. Bond lengths and angles are normal and intermolecular contacts correspond to van der Waals interactions. A complete report of the crystallographic analysis will be published separately.[6]

As can be seen from Figure 1, tetrahydronaphthoquinone **1** adopts a solid-state conformation in which the cyclohexene ring is half chair-like and the methyl group at C_7 is pseudoequatorial rather than pseudoaxial. A key feature of this conformation (cf. structure **7**, Scheme II) is that the hydrogen atom at C_7 is pseudoaxial and in a position to be transferred to the ene-dione ring at some stage in the formation of photoproduct **6**. The mechanistic possibilities (which cannot presently be distinguished) include the following.

Initial γ-hydrogen abstraction of the C_7 hydrogen atom by oxygen gives biradical **8** (path A), which in turn collapses to **9**, the enol form of the final photoproduct **6**. The oxygen to hydrogen distance involved in this case is 2.64 Å, somewhat greater than the distances observed in our previous work on solid-state intramolecular hydrogen-atom abstractions (2.26 to 2.58 Å)[2], but still within the suggested[2] limit of the sum of the van der Waals radii for oxygen and hydrogen (2.72 Å). The angle τ_0 for **7**, essentially the degree to which the abstracted hydrogen is out of planarity with the mean plane of the abstracting carbonyl group, is 28.5°, considerably greater than the near-coplanar abstractions previously observed,[2] and the C_1 to oxygen to H_7 angle, Δ_0, is 84.7°, very similar to the values found previously.

We feel that, while these parameters admit of the possibility of initial hydrogen transfer, they certainly do not demand it, particularly since there is a possibility that the reactive excited state of **1** is $\pi,\pi^{*\,3}$ in nature.[13] A mechanism which is compatible with such an excited state involves the initial formation of biradical **10** via C_3 to C_5 bonding (path B).[14] The feasibility of this process is indicated by the fact that the p orbitals at C_3 and C_5 extend toward one another (angle 98°) with an internuclear distance of 3.12 Å, well below the sum of the van der Waals radii for carbon (3.40 Å). Once formed, biradical **10** can proceed to product by either (1) internal hydrogen transfer to oxygen generating enol **9** or (2) internal transfer of hydrogen to carbon forming photoproduct **6** directly. This latter pathway avoids the problem of having to suggest an intramolecular solid-state enol to ketone conversion with, presumably,[15] a very high activation energy.

Finally we turn to a discussion of the possible reasons for the solution/solid-state differences observed in the photochemistry of diene-dione **1**. In view of the likelihood that the solution and solid-state photoprocesses both originate from a common $\pi,\pi^{*\,3}$ excited state,[13] the simplest explanation at present appears to be that in the solid-state, crystal-lattice effects do not permit the relatively great atomic and molecular motions necessary for the formation of the normally favored solution photoproduct **2**, the result being that an alternative unimolecular process (formation of **6**), involving much less atomic and molecular movement, predominates. In terms of overall atomic motions, formation of **6** requires only the relatively minor processes of rehybridization of carbon atoms 2, 3, 5, and 7 plus a decrease in the C_3 to C_5 contact; the basic molecular shape remains constant throughout the transformation. On the other hand, the shape of solution photoproduct **2** bears little resemblance to that of its progenitor **1**, and is formed via a sequence of steps (cf. Scheme I), each of which requires substantial atomic motion and molecular deformation.

We are currently extending our studies on unimolecular solid-state photoprocesses in the hope of finding additional examples of this intriguing phenomenon.

Acknowledgment 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 National Research Council of Canada is also gratefully acknowledged.

References and Notes

(1) G. M. J. Schmidt, *Pure Appl. Chem.*, **27**, 647 (1971).
(2) J. R. Scheffer and A. A. Dzakpasu, *J. Am. Chem. Soc.*, **100**, 2163 (1978).
(3) Photoproduct ratios have been observed to vary in going from solution to the solid state as the result of changes in the conformational freedom of the biradical intermediates involved; the primary photochemical processes remained the same in each medium however. See, for example, ref 2 as well as G. Quinkert, T. Tabata, E. A. J. Hickman, and W. Dobrat, *Angew. Chem., Int. Ed. Engl.*, **10**, 199 (1971).
(4) For the preparation of **1** and the characterization of **6**, see J. R. Scheffer, K. S. Bhandari, R. E. Gayler, and R. A. Wostradowski, *J. Am. Chem. Soc.*, **97**, 2178 (1975).
(5) Satisfactory elemental analyses were obtained for all new compounds described.
(6) T. J. Greenhough and J. Trotter, manuscript in preparation.
(7) The stereochemistry at C_3, while not certain, is likely as shown owing to preferential protonation of the enol intermediate from the least hindered side. A second product of this reaction (~10%) can be detected by GLC and is very likely the epimer of **3** since it can be formed in the same 9:1 equilibrium ratio by treatment of **3** with base.
(8) J. M. Conia and P. LePerchec, *Synthesis*, 1 (1975).
(9) (a) S. S. Hixon, P. S. Mariano, and H. E. Zimmerman, *Chem. Rev.*, **73**, 531 (1973); (b) W. G. Dauben, G. Lodder, and J. Ipaktschi, *Fortschr. Chem. Forsch.*, **54**, 73 (1975); (c) K. N. Houk, *Chem. Rev.*, **76**, 1 (1976); (d) K. Schaffner, *Tetrahedron*, **32**, 641 (1976).
(10) A variation of this mechanism involves cleavage of the C_4-C_{4a} bond of **4** *prior* to C_2-C_6 bonding. A referee has pointed out that **2** can also be formally derived from 1 via initial C_2-C_6 bonding followed by 1,4-biradical cleavage and cyclization of the resulting ketene. Irradiation of **1** in methanol, however, affords no ketene-derived product; only **2** is produced.
(11) Irradiation of **1** at −25 to −30 °C in hexane gave results identical with those observed in solution at room temperature thus indicating that the solution/solid-state reactivity differences do not arise from the different temperatures employed.
(12) R. E. Long, Ph.D. Thesis, University of California at Los Angeles, 1965.
(13) We have previously provided experimental evidence and literature precedent for the assignment of the lowest triplet state of the 2,3-dimethylcyclohex-2-ene-1,4-dione chromophore as being $\pi \rightarrow \pi^*$ in nature; cf. J. R. Scheffer, B. M. Jennings, and J. P. Louwerens, *J. Am. Chem. Soc.*, **98**, 7040 (1976). The solution photochemistry of **1** also likely originates from this state since it shares a common first step (carbonyl carbon-vinyl bridging) with the π,π^* ^{3} derived oxadi-π-methane rearrangement. See J. C. Dalton, M. Shen, and J. J. Snyder, *ibid.*, **98**, 5023 (1976), and references cited therein.
(14) A mechanism involving initial C_7 hydrogen abstraction by C_2 appears unlikely owing to a large (3.83 Å) internuclear distance as well as unfavorable geometric factors.
(15) W. J. Bouma, D. Poppinger, and L. Radom, *J. Am. Chem. Soc.*, **99**, 6443 (1977). The intriguing possibility exists that the enol could be converted to ketone **6** in the solid state via an allowed photochemical process.

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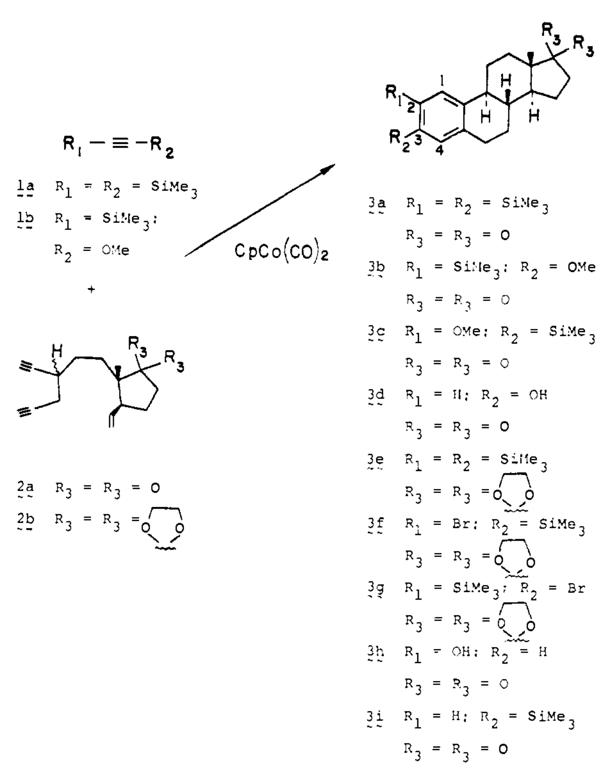
Received July 28, 1978

The Cobalt Way to *dl*-Estrone, a Highly Regiospecific Functionalization of 2,3-Bis(trimethylsilyl)estratrien-17-one

Sir:

The recent literature reveals several approaches to the A-ring aromatic steroid nucleus based on novel BC ring construction via intramolecular cycloadditions to *o*-xylylenes derived from benzocyclobutenes or other precursors.[1] None of these provides an efficient route to the female sex hormone estrone, a prime target in this class of compounds as a synthetic relay point to contraceptive drugs and a challenging structure on which to measure the utility of modern synthetic methodology.



We had recently described[1c] a transition metal catalyzed route to the series based on the cobalt-mediated cooligomerization[2] of bis(trimethylsilyl)acetylene (BTMSA, **1a**) with 1,5-hexadiyne **2a** which provided the one-step construction of rings ABC of the steroid nucleus with essentially complete chemo-, regio-, and stereospecificity. This method appeared to suffer from a lack of convenient methodology to convert the final silylated steroid **3a** into phenolic derivatives, for example the title compound **3d**. We report two solutions to this problem, the first based on the cobalt-catalyzed partially regiospecific cotrimerization of alkoxyacetylene **1b** with **2a** and the second on the highly regiospecific functionalization of bis silyl derivative **3a**.

Acetylene **1b**[3] (prepared from sodium methoxyacetylide generated in situ[4] and trimethylsilyl chloride in 62% yield) was considered a good candidate for cooligomerization with 1,5-hexadiynes since (similar to BTMSA[2]) it appeared to contain sufficient steric bulk to prevent efficient self-trimerization. However, when neat **1b** was cocyclized with 1,5-hexadiyne in the presence of catalytic amounts of $CpCo(CO)_2$ under the usual conditions,[2] a quantitative conversion of catalyst to a single, complexed cyclobutadiene isomer **5** was observed.[5,6] The latter is catalytically inert as evidenced by the recovery of starting diyne. Employment of a (optimum) ratio of **1b**:diyne of 4:1 in *n*-octane resulted in the formation of some **4** (15%)[5,6] before all of the cobalt had been removed as **5**. The assignment of structure **5** rests on spectral data,[6] particularly the characteristic molecular ion fragmentation pattern.[7] We noticed an improvement in the outcome of this cyclization when diyne **2a**[1c] was employed in the presence of larger than catalytic amounts of $CpCo(CO)_2$ (>20 mol %). Cooligomerization[2] of **1b** with