Table I. Enantiomeric Excess and Correlation of Guest and Host Chirality in (+)-Tri-*o*-thymotide Clathrate Crystals^a

guest	type	host: guest^b	guest, % ee^c	guest confign
2-chlorobutane (**1a**)	cage	2:1	32^d	(*S*)-(+)
2-bromobutane (**1b**)	cage	2:1	34^d	(*S*)-(+)
2-chlorooctane (**1c**)	channel	2.6:1	4^e	(*S*)-(+)^e
2-bromooctane (**1d**)	channel	2.7:1	4^e	(*S*)-(+)^e
2-bromononane (**1e**)	channel	3:1	5^e	(*S*)^e
2-bromododecane (**1f**)	channel	3.8:1	5^e	(*S*)^e
trans-2,3-dimethylthiirane (**2a**)	cage	2:1	30^f	(*S*,*S*)-(−)^f
trans-2,3-dimethyloxirane (**2b**)	cage	2:1	47^f	(*S*,*S*)-(−)^f
propylene oxide (**3**)	cage	2:1	5	(*R*)-(+)^f
2-methyltetrahydrofuran (**4**)	cage	2:1	2^f	(*S*)-(+)^g
methyl methanesulfinate (**5**)	cage	2:1	15^h	(*R*)-(+)^h

^{a} With the exception of **3**, all chirality correlations rest on clathrates with excess *R* guest and with excess *S* guest, although only one TOT–guest pair is given. ^{b} Determined from crystal cell constants and measured density, VPC, and NMR analysis. ^{c} Maximum error limit, ±10% of value for ee $>10\%$; for smaller ee, maximum absolute error ±1%. ^{d} Polarimetric measurement, based on $[\alpha]_D$ 37° for **1a** and 34° for **1b**; limit of error for **1a** may exceed 10% [D. D. Davis and F. R. Jensen, *J. Org. Chem.*, **35**, 10 (1970)]. ^{e} Guest converted, through inversion of configuration, into the corresponding amino compound by treatment with ethanolic ammonia. VPC analysis of *N*-trifluoroacetyl derivatives on chiral phase gives ee as well as configuration: B. Feibush and E. Gil-Av, *J. Gas Chromatogr.*, 257 (1967); S. Weinstein, B. Feibush, and E. Gil-Av, *J. Chromatogr.*, **126**, 97 (1976). ^{f} VPC analysis on chiral phase was kindly performed by Professor V. Schurig and co-workers;[8,9] guest configuration was established by comparison with authentic optically active guests prepared independently. ^{g} Polarimetric measurement of guest in chloroform at 6328 Å in a microcell (100-μL volume); cf. D. Gagnaire and A. Butt, *Bull. Soc. Chim. Fr.*, 312 (1961). ^{h} Polarimetric measurement and NMR analysis using tris(dicampholylmethanato-d_2)-europium(III): M. D. McCreary, D. W. Lewis, D. L. Wernick, and G. M. Whitesides, *J. Am. Chem. Soc.*, **96**, 1038 (1974). Guest configuration assignment was made by analogy to ref 1g.

rate have been prepared, they may be crushed and used to seed subsequent crystallizations to give polycrystalline material having an optical purity of 80–90% of that in a single crystal. Secondly, crystallization of TOT from partially resolved material yields clathrates which contain guests having appreciably enhanced optical purity over that of the starting material.[12]

Acknowledgments. We are grateful to Dr. G. Tsoucaris for his interest and support and to Professor H. Kagan for kindly providing facilities where part of this work was performed. We thank Professor E. Gil-Av, Dr. S. Weinstein, R. Charles, and M. Lachmi for advice and discussions and for the columns used to separate the enantiomeric N-TFA-2-aminoalkanes. We are indebted to Professor V. Schurig and W. Bürkle, for the analyses of guests **2–4** and for fruitful discussions. Chiral Eu(III) reagent was very kindly provided by Professor G. M. Whitesides. TOT was synthesized by Mrs. A. Jacob; we thank her and Mme F. Villain for technical assistance. This research received support from the CNRS (as part of ATP No. 2662 on "Chiral Structures" with the NCRD, Jerusalem) and the Israel Academy of Sciences.

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(4) Although almost all of the TOT clathrates reported thus far belong to one of these two (chiral) types, TOT clathrates having achiral crystal structures have recently been prepared and characterized;[5] the choice of clathrate structure depends primarily on the nature of the guest.

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(12) The last two points may also be of interest in connection with speculations on the abiotic origin and amplification of optical activity.

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Crystal Lattice Control of Unimolecular Photorearrangements. Differences in Cyclohexenone Photochemistry in Solution and the Solid State. Solution Results

Sir:

We have recently demonstrated in the case of a β,γ-unsaturated ketone[1] that irradiation in the solid state leads to results different from those observed in solution owing to the fact that the molecular distortions and deformations necessary for the solution rearrangement process are too great to be permitted by the molecular rigidity of the crystal lattice. As a result, alternative least motion unimolecular processes occur in the latter medium. Implicit in these results was the assumption that reaction occurs from the same ketone conformational isomer in solution as in the solid state.

In this and the following paper,[2] we report an example of a second way in which crystal lattice restraints can affect unimolecular photoreactivity, namely by limiting reaction to one stable conformational isomer of a given substrate in contrast to the liquid phase where a minor higher energy conformational isomer is the reacting species. The class of molecules we have chosen to study possesses the basic tetrahydro-1,4-naphthoquinol structure common to compounds **2** and **3** (Scheme I). We first describe the solution photochemistry of several of these compounds, and in the following paper[2] we compare and

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Scheme I

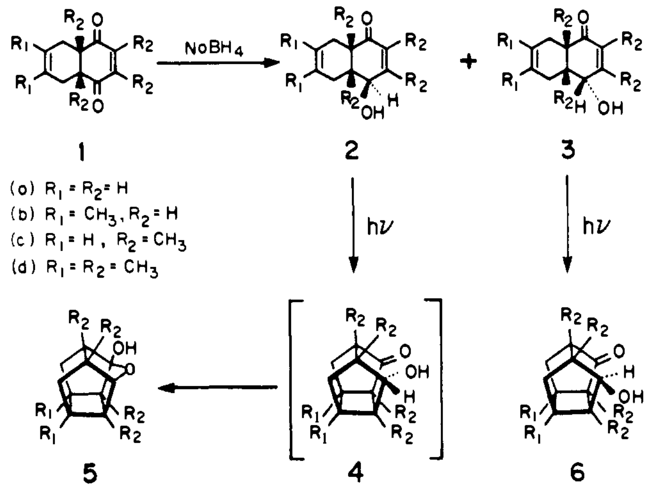


Table I. Relative Amounts of Hydroxycyclohexenones **2** and **3** Produced in Sodium Borohydride Reduction of Tetrahydronaphthoquinones **1a–1d**[a]

tetrahydronaphthoquinones	β-OH product, % (mp, °C)	α-OH product, % (mp, °C)
1a ($R_1 = R_2 = H$)	**2a,** not formed	**3a,** 79 (128–128.5)
1b ($R_1 = CH_3$; $R_2 = H$)	**2b,** not formed	**3b,** 65 (122–122.5)
1c ($R_1 = H$; $R_2 = CH_3$)	**2c,** 63 (118.5–119)	**3c,** 31 (115–116)
1d ($R_1 = R_2 = CH_3$)	**2d,** 50 (170.5–171)	**3d,** 35 (136.5–137.5)

[a] Isolated yields.

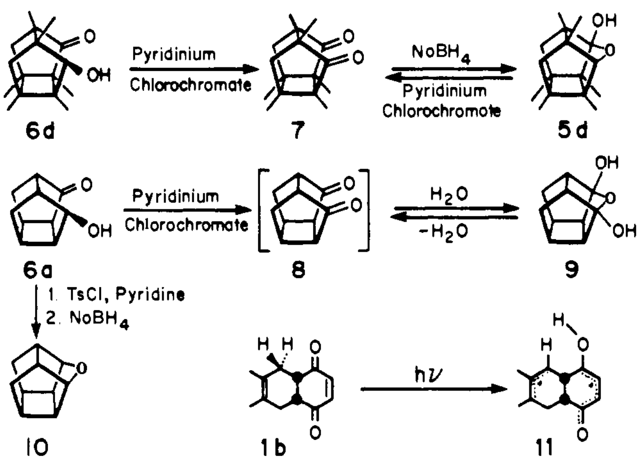
contrast the photoreactivity observed for these same systems in the solid state.

Sodium borohydride reduction of the readily available[3] tetrahydro-1,4-naphthoquinones **1a–d** leads in good yield to the corresponding epimeric hydroxycyclohexenones **2** and **3**. Table I summarizes the relative amounts of **2** and **3** produced in each case. The stereochemistry of each hydroxycyclohexenone was assigned either on the basis of an X-ray crystal structure determination[2] (compounds **2c, 2d,** and **3d**) or on the basis of the inability of its photoproduct to take part in internal hemiacetal formation (vide infra, compounds **3a, 3b,** and **3c**).[4] The predominant stereochemistry of reduction for each of the tetrahydro-1,4-naphthoquinones **1a–1d** is in accord with Baldwin's "approach vector analysis" concept.[5]

Both direct and benzophenone-sensitized irradiation (λ >330 nm) of benzene solutions of hydroxycyclohexenones **2c, 2d,** and **3a–d** afforded high yields of intramolecular [2 + 2] cycloaddition products having the tetracyclo-[5.3.0.0^{2,6}.0^{4,9}]decane ring skeleton (**5** and **6**). Substrates **3a–d** gave the keto alcohols **6a–d,** while compounds **2c** and **2d** yielded the hemiacetals **5c** and **5d.**[4] The latter are undoubtedly formed via the intermediacy of keto alcohols **4c** and **4d** which could not be isolated.

The cage photoproduct structural assignments were further verified by the transformations shown in Scheme II. Oxidation of keto alcohol **6d** led quantitatively to the corresponding symmetrical diketone **7** whose ^{13}C NMR showed the expected eight signals and which, upon reduction with sodium borohydride, gave hemiacetal **5d.** Oxidation of **5d** with pyridinium chlorochromate also gave **7,** however in considerably reduced yield. A similar series of interconversions was established for photoproducts **5c** and **6c.** In the case of keto alcohol **6a,** oxidation led to a product which we formulate as the diketone hydrate **9.** Attempted dehydration of **9** under a variety of conditions led to ketonic material which, however, could not be successfully purified and characterized as **8** owing to its extreme moisture sensitivity.[6] Finally, tosylation of keto alcohol **6a** followed by sodium borohydride reduction gave the interesting cyclic ether **10** whose ^{13}C NMR spectrum (five signals) was again indicative of a plane of symmetry. The chemistry observed in the case of photoproduct **6b** exactly paralleled that described above for **6a.**

Scheme II



The present photochemical results, aside from their obvious synthetic utility in the preparation of novel small-ring compounds, are of considerable interest and significance for two additional reasons. (1) They are completely different from the results that we obtain when irradiation is carried out in the solid state. We defer a discussion of this aspect of our findings to the paper which follows.[2] (2) They are also totally different from the results observed when the parent tetrahydro-1,4-naphthoquinone systems **1a–d** are photolyzed.[7] For example, irradiation of **1b,** both in solution[7a,b] and in the solid state,[7c] leads to products best formulated as arising from biradical **11** produced by intramolecular β-hydrogen abstraction by oxygen.[8] There appear to be at least two possible reasons for this. First of all, the carbonyl group of biradical **11** undoubtedly exerts a stabilizing influence on this species and hence facilitates hydrogen abstraction, and, secondly, the 2-ene-1,4-dione moiety of **1** is a better electron acceptor than the enone chromophore of substrates **2** and **3** which, it could be argued, indicates that a charge-transfer interaction between the cyclohexene double bond and the excited ene-dione system is required for subsequent β-hydrogen transfer.[9]

One further consideration which emerges from our previous solid-state work on systems of general structure **1**[7c] and from the X-ray crystal structure data on compound **3d** to be presented in the following paper[2] is that there is very little difference between the carbonyl oxygen to β-hydrogen atom interatomic distances and angles in these substrates in their preferred conformations in the solid state. This indicates that variations in these parameters are unlikely to be the source of the photochemical reactivity differences which are observed between the ene-dione system of **1** on the one hand and the enone chromophore of **3d** on the other.

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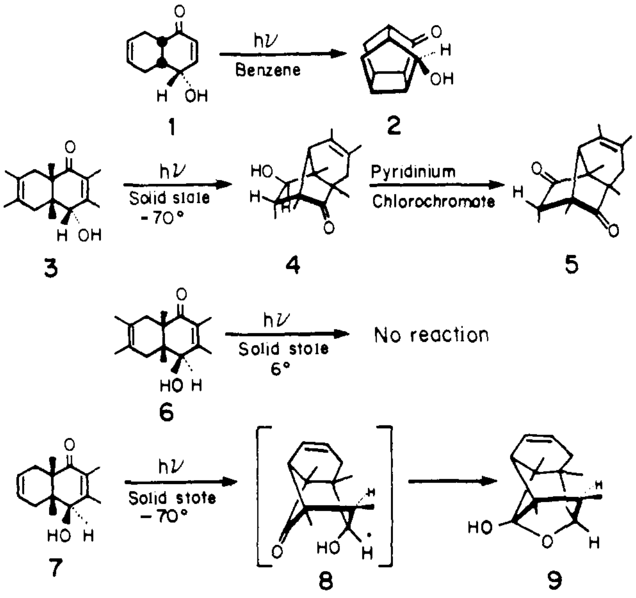
Crystal Lattice Control of Unimolecular Photorearrangements. Differences in Cyclohexenone Photochemistry in Solution and the Solid State. Solid-State Results

Sir:

In the preceding communication[1] we outlined the solution phase photochemistry of 4aβ,5,8,8aβ-tetrahydro-1-naphthoquin-4α-ol (**1**, Scheme I) and five of its substituted analogues. This consisted, in every case, of intramolecular [2 + 2] photocycloaddition to yield the corresponding tetracyclo[5.3.0.0^{2,6}.0^{4,9}]decane derivatives (e.g., **2**). In this paper we describe the different results obtained when three of these same tetrahydronaphthoquinols were irradiated in the solid state. In addition, we report the crystal and molecular structure of each of the three substrates as determined by single crystal X-ray diffraction methods. These studies establish that the solid phase photoreactions are crystal lattice-controlled, least motion processes and lead to the novel conclusion that the solid state/solution reactivity differences are the result of reaction from different conformational isomers in the two media.

The compounds studied were the tetrahydronaphthoquinols **3**, **6**, and **7** prepared via sodium borohydride reduction of the corresponding ene-diones.[1] Irradiation[2] (λ >330 nm) of polycrystalline samples of these substrates led to the results outlined in Scheme I, that is formation of photoproducts **4** and **9** from **3** and **7** respectively and no reaction in the case of tetrahydronaphthoquinol **6**. Accompanying products **4** and **9** were traces (<5%) of the corresponding intramolecular [2 + 2] solution photoproducts.[1] We attribute their formation to reaction at defect sites and/or regions of local melting. Photoisomer **4** was identified by oxidation (pyridinium chlorochromate, 95%) to the known[3] diketone **5**. The relative stereochemistry of **4** at the hydroxyl-bearing carbon atom and the adjacent center follows from a vicinal coupling constant of 4 Hz. Photoproduct **9** was identified by a single crystal, direct method X-ray structure determination, current R = 0.082.[4] It is undoubtedly formed by cyclization of the keto-alcohol **8** which could not be isolated. Evidence which indicates that this hemiacetal formation occurs even in the solid state comes from experiments involving irradiation of potassium bromide pellets of **7**. Infrared spectra of the irradiated pellet at various intervals showed only peaks due to **7** and **9**; no absorptions corresponding to the cyclobutanone carbonyl stretching frequency (ca. 1780 cm^{-1}) were observed.

Scheme I



1 **2** **3** **4** **5** **6** **7** **8** **9**

The X-ray crystal structures[4] of starting substrates **3** (R = 0.043), **6** (R = 0.041), and **7** (current R = 0.048) showed that all three adopt conformations which can be approximately described as consisting of a half-chair cyclohexene ring cis-fused to a second half-chair cyclohexenone moiety. There are two non-equivalent ring flipped conformations of this type for each substrate, one in which the hydroxyl group is pseudoequatorial and one in which it is pseudoaxial. The crystallographic results show that the conformation with the hydroxyl group pseudoequatorial is present exclusively in each case. Figure 1 shows a computer drawn stereodiagram of this conformation for substrate **3**.

The result of this conformational preference is that substrates **6** and **7** (hydroxyl group syn to bridgehead methyls)

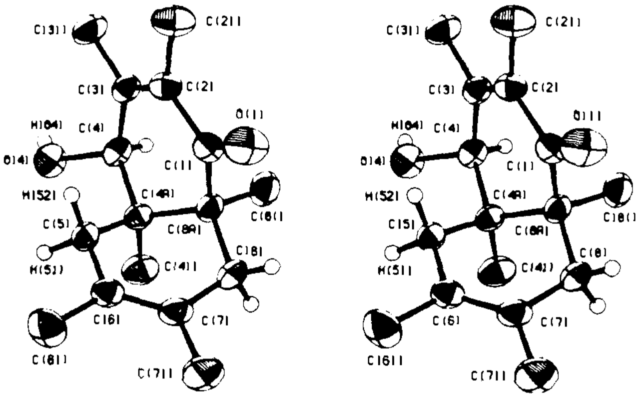


Figure 1. Stereodiagram of the conformation of tetrahydro-1,4-naphthoquinol 3 in the solid state. The methyl hydrogen atoms are omitted for clarity.