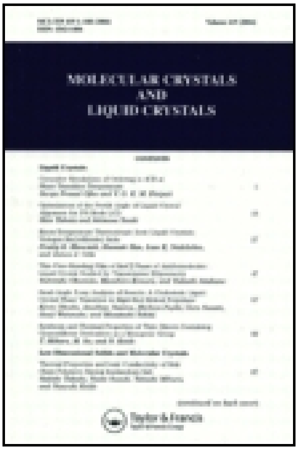

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STUDIES ON THE DI-π-METHANE PHOTOREARRANGEMENT IN THE SOLID STATE

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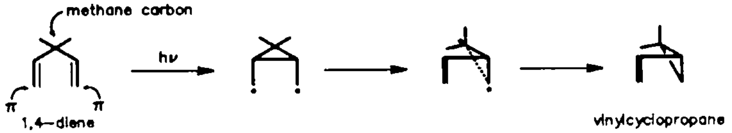
Abstract The solution and crystalline phase photochemistry of a number of dibenzobarrelene 11,12-diesters has been studied as a function of the nature of the ester alkyl substituents; results for both symmetrical ($CO_2R_1 = CO_2R_2$) and unsymmetrical ($CO_2R_1 \neq CO_2R_2$) compounds are reported. All compounds studied underwent smooth di-π-methane photorearrangement in the solid state to give dibenzosemibullvalene diesters. In the case of reactants having non-equivalent ester groups, two possible regioisomeric dibenzosemibullvalene products are possible, and the photoproduct ratios as a function of the reaction medium (solution vs solid state) are reported. The striking differences observed are interpreted on the basis of the crystal and molecular structures of the reactants and products. One of the symmetrical diesters investigated ($CO_2R_1 = CO_2R_2 = CO_2iPr$), which is achiral in solution, undergoes spontaneous resolution upon crystallization from the melt, affording material in the chiral space group $P2_12_12_1$. Irradiation of $P2_12_12_1$ conglomerates leads to

optically active dibenzosemibullvalene photoproduct in quantitative enantiomeric yield. This is the first example of an absolute asymmetric synthesis in a unimolecular chemical reaction.

INTRODUCTION

The di-π-methane reaction is one of the most general and thoroughly studied of all organic photorearrangements. Thanks largely to the efforts of Howard Zimmerman and his research group at the University of Wisconsin, the main photochemical and photophysical features of the process in isotropic liquid media are well established.[1] The reaction draws its name from the observation that organic molecules possessing two independent π systems separated by a saturated or "methane" carbon atom rearrange to vinylcyclopropane derivatives upon absorption of a photon of ultraviolet light. The process is illustrated figuratively in Scheme I for the simplest di-π-methane system, 1,4-pentadiene (1).

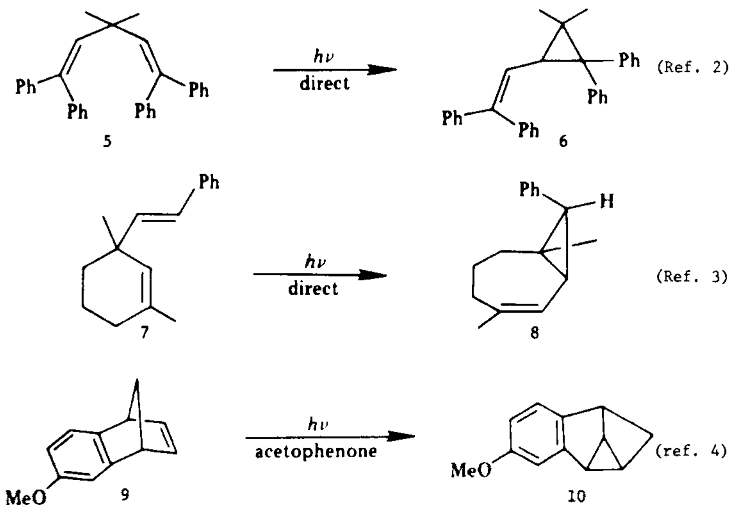


1 2 3 4

Scheme I. Figurative Representation of the Di-π-Methane Photorearrangement for 1,4-Pentadiene.

Scheme I also includes Zimmerman's suggested mechanism for the transformation,[1] which involves initial 2,4-bond formation to give biradical 2 followed by bond reorganization to yield biradical 3 and closure to vinylcyclopropane (4).

Scheme II shows some real-life examples of the di-π-methane photorearrangement drawn from the literature.

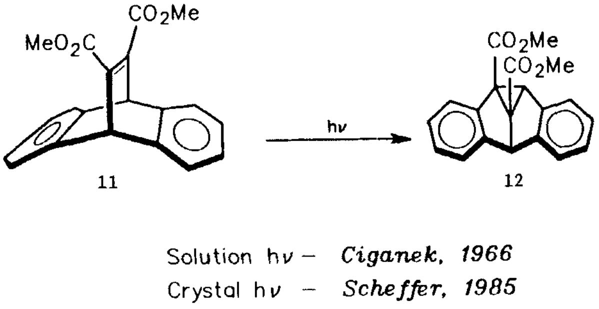


Scheme II. Literature Examples of the Di-π-Methane Photorearrangement.

Application of the simple three step mechanism outlined in Scheme I leads to the observed photoproduct in each case. We note that both aliphatic and aromatic π-bonds are capable of participating in the process.

RESULTS AND DISCUSSION

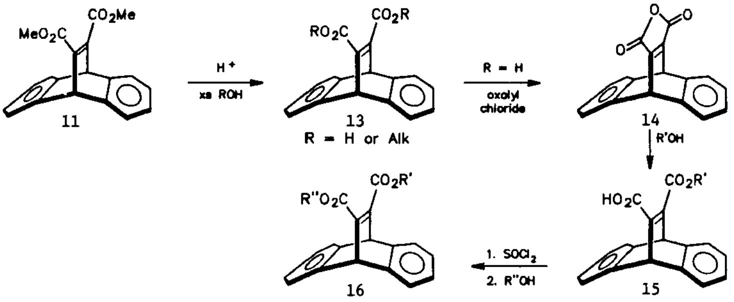
In the present paper, we report some of our results on the solution and crystalline phase photochemistry of certain dibenzobarrelene diester derivatives analogous to the anthracene-dimethylacetylene dicarboxylate Diels-Alder adduct **11** (Scheme III). Portions of this work have been published in a preliminary communication.[5] Ciganek[6] was the first to demonstrate the di-π-methane photorearrangement of compound 11 in solution, the product having the interesting dibenzosemibullvalene structure 12.



Scheme III. Di-π-Methane Photorearrangement of Dibenzobarrelene Diester 11.

We have investigated the photochemistry of a large number of analogues of diester 11, both those having identical ester substituents (13, Scheme IV) and those with non-identical ester groups (16).

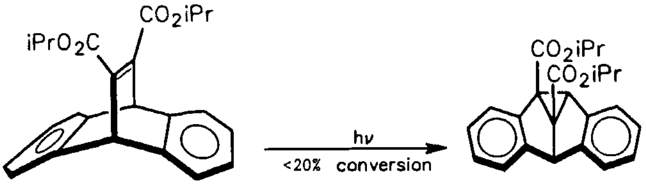
The preparation of these compounds was straightforward: as outlined in Scheme IV, the symmetric diesters 13 were synthesized by transesterification of the dimethyl diester 11, and the asymmetrically substituted diesters 16 were prepared through the anhydride 14[7] by ring opening to the acid/ester 15 followed by a second esterification reaction with a different alcohol.



Scheme IV. Synthesis of Starting Materials.

No previous solid state di-π-methane photorearrangements having been reported, our first task was to determine whether the process is feasible in the crystalline medium at all. A priori, it seemed possible that the transformation might be too sterically demanding to be topochemically allowed in the solid state. For example, the conversion of dimethyl diester 11 into photoproduct 12 appears to involve a substantial change in molecular shape and size that might be incompatible with the lattice restraints present. However, crystals of diester 11, mp 160-161°, were smoothly transformed into 12, the same product as formed in solution.

We then turned our attention to a number of other symmetric diesters. Due to space limitations, we shall discuss only one of these in this paper, namely the diisopropyl diester 17 (Scheme V). This material proved to be dimorphic. Recrystallization from ethanol affords large prisms with the achiral space group Pbca; recrystallization from cyclohexane gives Pbca crystals plus a dimorph having the chiral space group $P2_12_12_1$. This latter dimorph is obtained exclusively when crystals are grown from the melt.



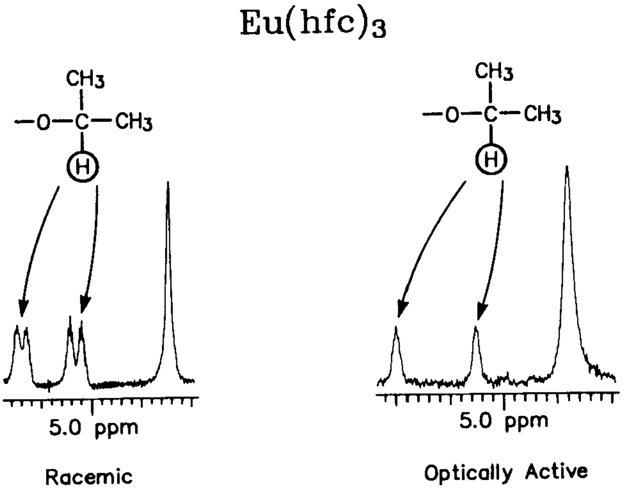
17 18

Photolysis Medium	Specific Rotation	ee
Solution	0	0
Pbca Crystal	0	0
$P2_12_12_1$ Crystal	24.2 ± 2.9°	100%

Scheme V. Irradiation of Diisopropyl Diester **17**.

NMR studies of compound **17** in solution show that it possesses average C_{2v} molecular symmetry. The crystal structure, however, demonstrates that in the solid state both dimorphs are composed of molecules that lack symmetry because the ester groups are frozen in non-C_{2v} orientations. Both enantiomers of the disymmetric conformation are present in equal amounts in the Pbca crystal resulting in a non-chiral space group. In the $P2_12_12_1$ case, however, only one of the two possible enantiomers is present, and the crystal is thus chiral. The crystallization process in the latter case thus constitutes a spontaneous resolution[8], a phenomenon that is probably much more common than is generally realized simply because most organic chemists do not have occasion to determine the space groups in which their compounds crystallize. Other examples of spontaneous resolution of one of two rapidly equilibrating enantiomers from solutions or melts are known,[9] the most thoroughly studied case being that of binaphthyl.[10]

The finding that diester **17** crystallizes in a chiral space group raised the intriguing possibility that its crystal chirality could be transformed into permanent molecular chirality in the expected photoproduct, diester **18**, which contains four chiral centers. Accordingly, large single crystals of each dimorph as well as solutions of diester **17** were photolyzed, and the product **18**, which was formed as expected, was analyzed for optical activity. This was done by dissolving the samples in chloroform and measuring their rotation at the sodium D line. The specific rotation was then calculated from the weight of the crystal and the percent conversion as determined by capillary gas chromatography. The unreacted starting material contributes nothing to the rotation because it immediately loses its chirality in solution. As summarized in Scheme V, only in the case of the $P2_12_12_1$ crystals was optical activity observed. Remarkably, NMR chiral shift reagent studies using $Eu(hfc)_3$ established that, within the limit of the method, the chiral crystals give the photoproduct **18** in quantitative enantiomeric excess. As shown in Scheme VI, the NMR analysis uti-

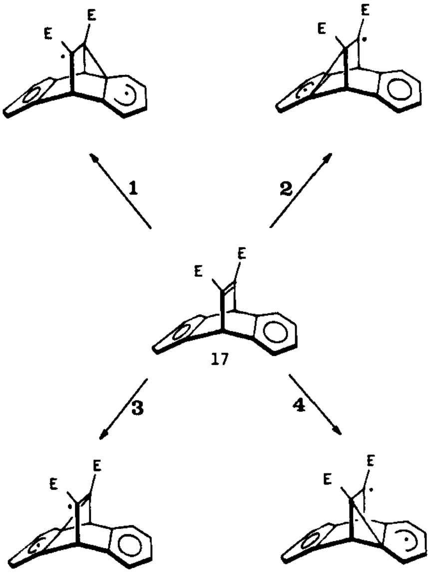


Scheme VI. NMR Chiral Shift Reagent Studies on Diester **18**.

lized the methine hydrogens of the chemically non-equivalent isopropyl groups of diester **18**. Four lines were observed for the racemate (solution photoproduct) in the presence of the chiral shift reagent, whereas only two lines were present in the spectrum of the photoproduct isolated from the chiral crystal irradiations.

It was of interest to determine whether the resolution that diester **17** undergoes upon crystallization from the melt is truly spontaneous, that is whether it gives a random (1:1) distribution of enantiomorphic crystals over a statistically significant number of runs. This was checked as follows: nine samples of the racemic (Pbca) modification of diester 17 were sealed in Pyrex tubes and heated for one hour at a temperature 20° above the melting point of 145-146°.[11] The tubes were cooled to approximately 120°, opened, and crystallization induced by pricking the contents with a rigorously cleaned needle. This provided diester 17 in its $P2_12_12_1$ modification in what appeared to be a polycrystalline mass. The tubes and their contents were then immediately irradiated using a nitrogen laser (337 nm) and the resulting mixtures dissolved in chloroform and analyzed by polarimetry. Four of the samples gave dextrorotatory photoproduct and five gave levorotatory material. From this we conclude that the resolution is indeed spontaneous and not caused by some adventitious chiral impurity. Interestingly, the specific rotations produced in these experiments were very similar to those obtained by photolyzing beautifully shaped single crystals of diester 17. This indicates that the polycrystalline mass obtained from the melt is of high optical purity.

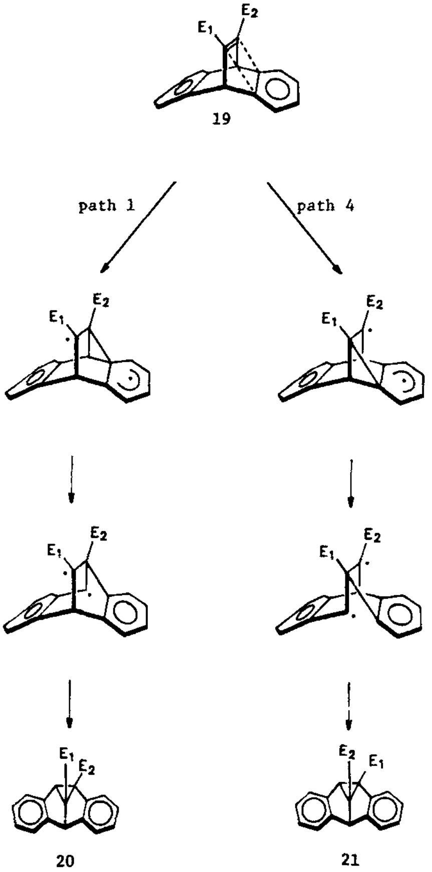
Our interpretation of these results in terms of mechanism is outlined in Scheme VII. Assuming the three step Zimmerman mechanism,[1] the first, product-determining step necessarily involves bond formation between one of the carbon atoms of the vinyl group and a nearby aromatic carbon atom (so-called vinyl-benzo bridging[1]). There are four vinyl-benzo bridging modes possible for the dibenzobarrelenes, and for symmetrically substituted reactants in an isotropic medium, all four pathways (1 - 4, Scheme VII) would be expected to occur with equal probability. This is not the case in the solid state, however. Here the fixed disymmetric conformation present as well as anisotropic medium effects may favor certain pathways over others, and in general, one would expect that bonding modes 1 - 4 would not be equally likely. This conclusion is supported by the



Scheme VII. Initial Bonding Possibilities in the Di-π-Methane Photorearrangement of Dibenzobarrelene Diesters.

photochemical results with the $P2_12_12_1$ crystals. Starting from a given enantiomer of the reactant, paths 1 and 2 lead to one photoproduct enantiomer, and paths 3 and 4 give the other. The fact that the reaction proceeds with 100% enantioselectivity in the crystalline phase indicates complete (1 + 2) versus (3 + 4) discrimination in this medium. It does not, however, tell us whether (1 + 2) is favored over (3 + 4) or vice versa, nor does it indicate the relative importance of path 1 versus path 2 or path 3 versus path 4.

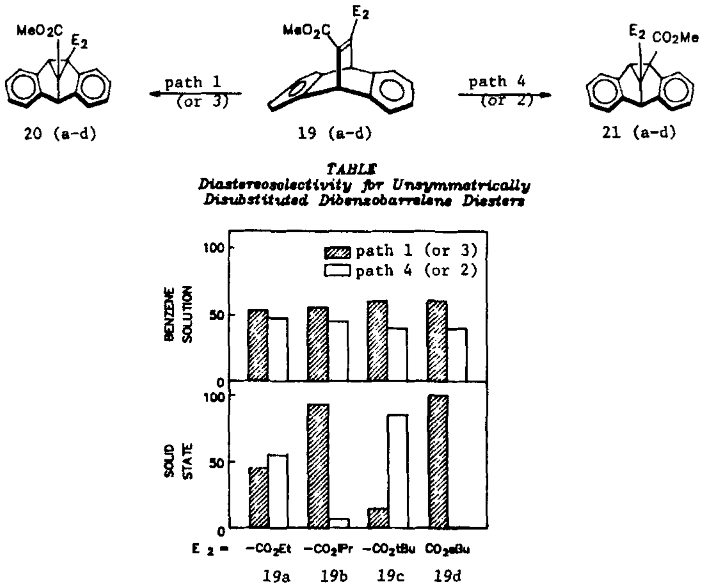
It is possible in principle to differentiate between pathways (1 + 2) and (3 + 4) by determining the absolute configuration of the reactant and correlating this with the absolute configuration of the photoproduct. Studies of this type are in progress in our laboratory. A second experiment that is capable of distinguishing between paths (1 + 3) and (2 + 4) involves the use of reactants in which the two ester groups are different (e.g., **19**, Scheme VIII). As shown, photolysis of compounds of this type can lead to two regioisomeric photoproducts, **20** and **21**. By combining these two approaches, that is by absolute configuration studies on unsymmetrically substituted diesters, the contribution from each of the four possible pathways in the solid state may be determined. With this in mind, we have investigated the photochemistry of a series of analogues of unsymmetrical diester **19**. The remainder of this article will describe some of our initial results in this area, and will specifically address the question of how the regioselectivity of the di-π-methane rearrangement changes as the reaction medium is altered from the isotropic liquid state to the crystalline phase. The compounds studied were diesters **19 a-d** (Scheme



Scheme VIII. Regioisomeric Products Possible by Photolysis of Unsymmetrically Substituted Diesters. To save space, only paths 1 and 4 are shown; pathways 2 and 3 would lead to the enantiomers of photoproducts 21 and 20, respectively.

IX) in which one of the carboxylate groups was held constant in the form of its methyl ester while the other was varied through the series ethyl, isopropyl, tert-butyl and sec-butyl. The general method of preparation of these compounds is outlined in Scheme IV. To date it has been possible to obtain the crystal structure of only the methyl/isopropyl diester **19b**. This material crystallizes in an achiral space group ($P\bar{1}$), thus precluding simultaneous determination of the reaction regio- and enantioselectivity as discussed above.

The differences observed in irradiating diesters **19 a-d** in the crystalline state and solution (benzene) are summarized in the Table in Scheme IX. The photoproduct ratios

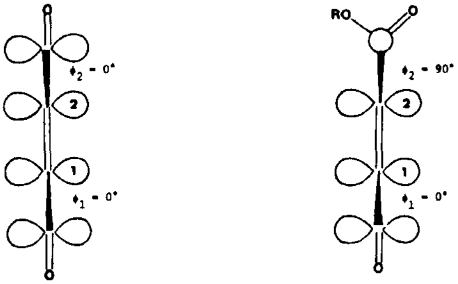


Scheme IX. Reaction Regioselectivity for Unsymmetrically Substituted Diesters.

were established as follows: compounds **20b** and **21b** were isolated by fractional crystallization from methylcyclohexane and their structures established by X-ray crystallography. NMR spectroscopy of these regioisomers revealed that the methyl resonance of **20b** appeared at a higher field (3.70 ppm) than that of **21b** (3.86 ppm), and this fact was used in determining the regiochemistry of the photoproducts from diesters **19a**, **19c** and **19d**. Overall, the results demonstrate a striking variation in reaction regioselectivity between the crystalline and solution media. Only the methyl/ethyl diester **19a** gave a photoproduct ratio that did not vary significantly with phase change. Interestingly, while there was a slight (but uniform) regiochemical preference for photoproducts **20 a-d** in solution (consistent with the preference for the smaller methyl ester group to occupy the sterically more congested apical position), such was not the case in the solid state, where the **20**:**21** ratio changed from 99:1 (compound **19d**) to 15:85 (compound **19c**).

There are at least two possible explanations that come to mind for the differences observed between the photoproduct ratios in the solid state and solution. The first is the possibility that in the solid state the crystal lattice may enforce different degrees of conjugation between the non-equivalent ester groups and the double bond between them. This would tend to favor initial benzo-vinyl bridging at the vinyl carbon atom that is <u>less</u> conjugated to its attached ester group. This is the carbon atom that would be expected to have the greater excited state odd-electron density, and bonding at this site would lead to formation of the more highly resonance stabilized biradical intermediate.[12] Such an effect would not be expected in solution, where the ester groups are free to adopt a conformation in which they are fully conjugated with the central double bond. Scheme X depicts the situation in terms of molecular structure. The angles ϕ_1 and ϕ_2 are defined as the dihedral

Top View of Ene-Dioate System



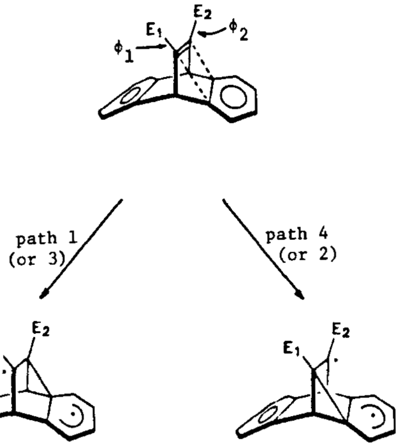
Initial bond formation equally likely at C_1 or C_2.

Initial bond formation favored at C_2: C_2 has radical character in the excited state; product radical more stable at C_1.

Scheme X. Possible Effect of Ene-Dioate Conjugation on Reaction Regioselectivity.

angles between the π-orbitals on the carbonyl carbons and the adjacent C=C bond π-orbitals; $\phi_1 = \phi_2 = 0°$ denotes the fully conjugated conformation.

For all the diesters whose crystal structures have been determined to date, both symmetrical and unsymmetrical, ϕ_1 and ϕ_2 are indeed different, and in general, both angles deviate substantially from 0°. The values of ϕ_1 and ϕ_2 for two unsymmetrically substituted diesters are given in Scheme XI along with the regioselectivities observed in the solid state. As can be seen, the major photoproduct in each case



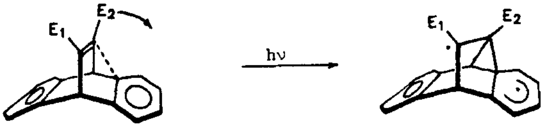
E_1	E_2	ϕ_1	ϕ_2	Predicted Pathway	Observed Pathway
CO_2Me	CO_2iPr	45°	37°	4	1 (93%)
CO_2sBu	CO_2iPr	70°	13°	4	1 (90%)[a]

[a] J.R. Scheffer and M. Garcia-Garibay, unpublished results.

Scheme XI. Predicted versus Observed Regioselectivities.

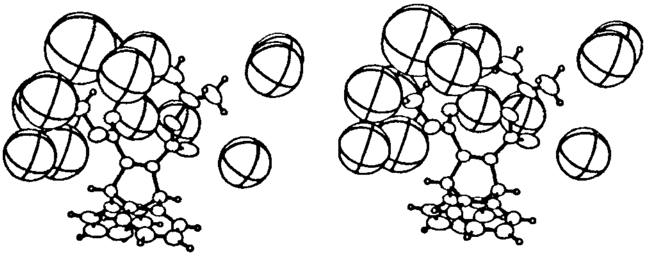
is formed through initial benzo-vinyl bridging at the more conjugated vinyl carbon atom. This is precisely the opposite of what would be expected based on the argument presented above. We thus tentatively conclude that excited state electron distribution and biradical stabilization differences brought about by conformational rigidity in the solid state are not controlling the reaction regioselectivities of diesters **19 a-d**.

A second explanation for the observed solid state regioselectivities involves the possibility that steric effects between the reacting molecule and its more or less stationary lattice neighbors may be the controlling factor. Such effects are absent in isotropic liquid solvent media, where the essentially random steric interactions between solute and solvent play little role in determining product structure. The basic idea is that the four non-equivalent reaction pathways in the solid state (refer to Scheme VII) may involve significantly different steric interactions with neighboring molecules. In particular, vinyl-benzo bridging involves substantial motion of the attached ester group (Scheme XII), and perhaps the regioselectivity can be related to differences in the free lattice space around each of the non-equivalent ester groups.



Scheme XII. Motions Involved in Vinyl-Benzo Bridging.

The packing difference around each of the ester groups of the methyl/isopropyl diester **19b** is depicted in Scheme XIII. The large spheres represent atoms from neighboring molecules at contact distances of less than 3.0 Å. Qualitatively, it is apparent that the methyl ester group is more tightly surrounded by neighboring atoms than is the isopropyl ester group, particularly in the directions the ester groups would have to move given the Zimmerman mechanism. This is consistent with initial benzo-vinyl bridging at the vinyl carbon bearing the sterically less encumbered isopro-

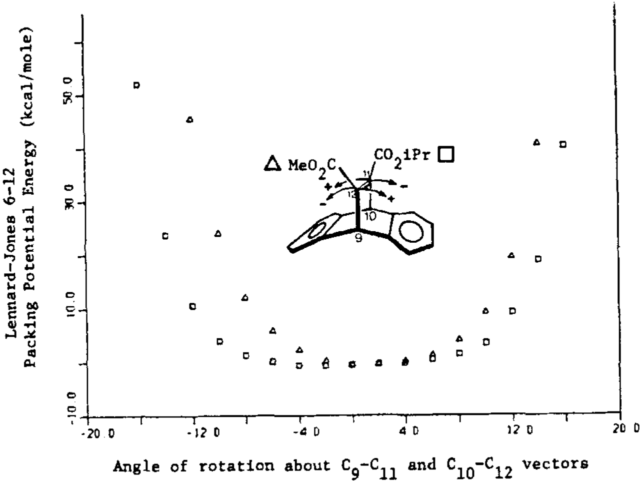


The large spheres represent contact atoms at d < 3 Å in the surrounding molecules.

Scheme XIII. Lattice Environment of COOMe versus COOiPr for Diester 19b.

pyl ester group; this is the pathway that leads to the observed major photoproduct 20b in the solid state.

In order to put these ideas on a more quantitative basis, the motions involved in initial benzo-vinyl bridging (cf., Scheme XII) were simulated using a locally written computer program,[13] and the resulting intermolecular steric repulsion energies calculated. The approach taken and the results are shown in Scheme XIV. Using the crystallographically derived coordinates for diester 19b as the starting point (0°), vinyl carbon atom 11 and its attached isopropyl ester group were displaced toward the nearby benzo carbon atoms on either side by rotation in 2° increments around the C_{10}-C_{12} vector. The (-) direction corresponds to path 1 and the (+) direction to path 3. Similar motions were applied to vinyl carbon atom 12 and its attached carbomethoxy group. In this case, pathway 2 is (-) and path 4 is (+), and the axis about which C_{12} was rotated corresponds to the C_9-C_{11}



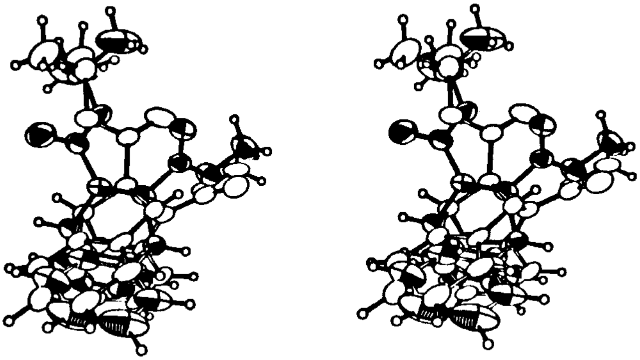
Scheme XIV. Simulated Energetics of Benzo-Vinyl Bridging for Diester **19b** in the Solid State.

vector. At each 2° interval, the non-bonded contacts involving the moving ester group were converted into non-bonded repulsion energies using the Lennard-Jones 6-12 potential function[14] and summed over all contacts. This leads to the repulsion energy versus angle of rotation plot shown in Scheme XIV. This plot clearly supports the qualitative conclusion reached earlier that initial bonding at the vinyl carbon atom bearing the isopropyl ester group (paths 1 and 3) is favored over bonding at the carbomethoxy-bearing vinyl position (paths 2 and 4). This result is in accord with the experimental facts. A further conclusion is that of the two lower energy pathways, 1 and 3, path 3 is favored. This conclusion is not presently amenable to experimental verification.

A final point of discussion in the present paper concerns our incorrect intuitive feeling that the di-π-methane photorearrangement might involve motions too drastic to be accommodated by the rigid crystalline medium. With accurate crystal structure data for diester **19b** and its two photoproducts, **20b** (major) and **21b** (minor), it is a simple matter using best molecular fit programs[15] to juxtapose the shape of the starting material with that of each of its photoproducts. Scheme XV shows this correlation in stereo.

Two points are evident from the correlations shown in Scheme XV. The first is that starting diester **19b** and its two photoproducts actually have rather similar overall shapes, and the second is that there is a significantly better fit between the reactant and the major solid state product, **20b**, than there is between the reactant and the minor photoproduct, **21b**. The measure of the fit is given by the square of the distances between corresponding atoms summed over all positions, $\Sigma\Delta^2$, which is 84.6 Å^2 for **19b**+**20b** and 132.8 Å^2 for **19b**+**21b**. It is intuitively reasonable that in a restricted environment such as the reaction cavity[16] of a crystalline solid, the product that most resembles the reactant in shape and size should be favored. The importance of this effect in the present instance, however, is still far from clear, one reason being that each of the photoproducts was recrystallized prior to determination of its crystal structure, thus allowing it to adopt a conformation different from that in which it is formed during the solid state photorearrangement.

19b + 20b



19b + 21b

Scheme XV. Stereodiagrams of the Best Molecular Fits between Diester **19b** and its Photoproducts **20b** and **21b**.

CONCLUDING REMARKS

One important point that emerges from the work described in this paper is that steric effects in the solid state are not as regular as they tend to be in solution. Most chemists would agree that, in solution, if a steric effect can be attributed to a substituent of moderate size, then increasing the bulk of the substituent should bring about a similar but larger steric effect. In the solid state, however, changing substituents (methyl for ethyl, etc.) often changes the packing arrangement completely, thus resulting in a totally different steric environment. This can be seen in the solid state regioselectivities reported in the table in Scheme IX, where replacing an isopropyl ester group in compound **19b** by a tert-butyl ester substituent (compound **19c**) causes a complete reversal in the **20**:**21** photoproduct ratios from 93:7 to 15:85. A more detailed understanding of this difference must await an X-ray crystal structure for diester **19c**, but it is interesting to note that the solid state **20c**:**21c** = 15:85 ratio has overcome an inherent solution phase 60:40 preference for photoproduct **20c**.

ACKNOWLEDGMENTS

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