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DIFFERENCES IN PHOTOCHEMICAL REACTIVITY OF 9,10-ETHENOANTHRACENE DERIVATIVES IN LIQUID AND CRYSTALLINE MEDIA

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Contents

1. INTRODUCTION

Is there anyone who is not struck by the beauty of crystals? They rank among the most valuable of mankind's material possessions and are regarded by some as possessing mystical powers that can influence human health and behavior. Scientists are not immune to this fascination with crystals, and the history of chemistry, biochemistry and physics is replete with studies of the structural and physical properties of crystalline materials ranging from metals to biological macromolecules. Surprisingly, however, until the early 1960s, when the late Gerhard Schmidt and his collaborators at the Weizmann Institute of Science began their now famous work on the solid state cinnamic acid photodimerizations,[1] the chemical reactivity of crystals had been largely overlooked, owing perhaps to the feeling that because of strong packing forces, molecules in crystals lie in deep potential wells that make reaction difficult. Such is not necessarily the case. There is an increasing body of experimental evidence that molecular and even ionic crystals can undergo a wide range of chemical reactions

involving a surprising degree of molecular motion. In the present article, we summarize some recent results from our laboratory that illustrate this point.

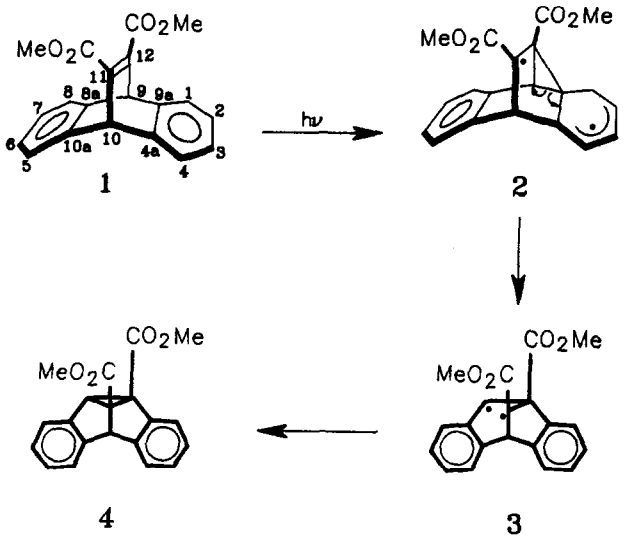
Our interest has been in delineating the differences in photochemical behavior between organic compounds in their pure crystalline states and when dissolved in organic solvents. What are the objectives of such research? We believe that such studies provide a fundamentally new way of investigating chemical reactivity. Each crystal offers a unique reaction environment with its own peculiar combination of steric and electronic properties, and because of the remarkable diversity of molecular organization present in organic crystals, there is an almost limitless variety of reaction media in which to study chemical processes. It is frequently found that molecules in crystals behave completely differently from their solution phase counterparts. New reactions are observed that offer new possibilities for organic synthesis. Furthermore, through X-ray crystallography and solid state spectroscopic techniques such as magic angle spinning C-13 NMR, one obtains a detailed picture of the structure of the reactants and their surroundings immediately prior to reaction. Such information allows the construction of structure-reactivity relationships in organic chemistry with a precision that is not possible in any other medium. Fuelled to a considerable extent by the explosive growth of interest in the field of materials science, solid state organic chemistry has experienced a vigorous renaissance, and many review articles, monographs, book chapters and symposia-in-print dealing with this subject have appeared in recent years.[1-26] The interested reader is referred to these articles for background information, as it is beyond the scope of the present article to review the field.

2. DI-π-METHANE PHOTOREACTIVITY OF 9,10-ETHENOANTHRACENE DERIVATIVES.

2.1. Background and Initial Studies

9,10-Ethenoanthracene (or "dibenzobarrelene") derivatives are readily prepared by the Diels-Alder addition of acetylenic dienophiles across the 9,10-positions of anthracene.[27] Ciganek[28] was the first to study the photochemistry of this class of compound in solution. He showed, for example, that irradiation of the dimethyl acetylenedicarboxylate adduct 1 in isotropic liquid phases leads to a product having the interesting "dibenzosemibullvalene" structure 4 (Scheme 1), a reaction that is now recognized as belonging to a very general type of process termed the di-π-methane photorearrangement.[29] The mechanism in the case of ethenoanthracene derivative 1 (and by extension, all ethenoanthracenes) is thought to involve (a) initial bonding between positions 9a and 12 ("vinyl-benzo bridging") to afford the 1,4-biradical 2, (b) cyclopropane ring cleavage to give 1,3-biradical 3 and (c) 1,3-biradical closure to form 4. The overall 1 → 3 transformation represents a 1,2-aryl shift, and the question of whether biradical 2 is a true intermediate in this process, or is simply a non-minimum energy point on the 1,2-shift reaction hypersurface, is still unclear;[30] we include it for ease in visualizing the mechanistic possibilities. Scheme 1 depicts only one of the possible pathways leading to photoproduct 4 (path I). In the case of 1, it is readily apparent

that there are three additional pathways (II-IV) for a total mechanistic degeneracy of four, paths I and II leading to one enantiomer of 4, and paths III and IV giving the other.



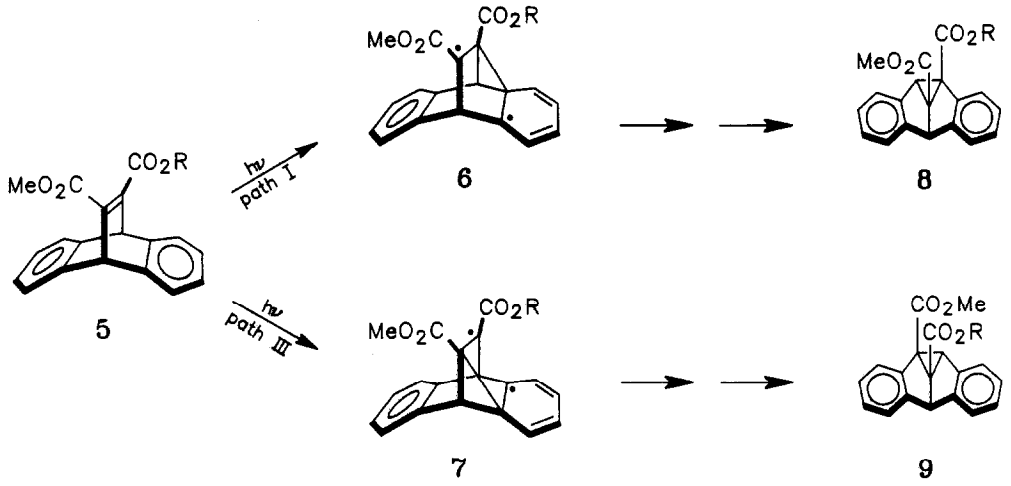
Path I : Initial 9a–12 bonding
Path II : Initial 10a–11 bonding
Path III: Initial 4a–11 bonding
Path IV: Initial 8a–12 bonding

Scheme 1

No previous solid state di-π-methane photorearrangement having been reported when we started this work, our first task was to determine whether the process is feasible in the crystalline phase at all. A priori, it seemed that the transformation might involve too great a change in molecular shape and size to be topochemically allowed. However, crystals of diester 1, mp 160-161°C, were smoothly transformed into 4 upon photolysis,[31] and some five years later, after having studied several dozen examples, we have yet to encounter an ethenoanthracene derivative that is photochemically unreactive in the solid state.

2.2. Regioselectivity

As depicted in Scheme 2, 9,10-ethenoanthracene derivatives bearing different substituents on the vinyl double bond can give two regioisomeric di-π-methane photoproducts. Benzo-vinyl bridging at C(12) leads to isomer **8** whereas initial bridging at C(11) affords **9**. To save space, only paths I and III are shown; pathways IV and II would lead to the enantiomers of photoproducts **8** and **9**, respectively. The 9,10-ethenoanthracene system thus offers the



(a) R=Et; (b) R=*i*Pr; (c) R=(±)*s*Bu; (d)R=*t*Bu

Scheme 2

opportunity of investigating the regioselectivity of the di-π-methane photorearrangement as a function of the reaction medium, a study that should tell us much about the forces that govern chemical reactivity in crystals. Our initial efforts in this area involved the mixed diesters **5a-d** shown in Scheme 2, in which the methyl ester substituent was held constant while the second ester group on the bridging double bond was varied from ethyl to tert-butyl.[32]

As expected, there was little difference in regioselectivity in solution, although there was a slight but uniform preference in all four cases for formation of the regioisomer in which the smaller ester group occupies the less hindered apical position of the

dibenzosemibullvalene ring system, i.e., photoproduct **8**. In contrast, the **8**:**9** ratios from photolyses carried out in the crystalline phase were not uniform and varied from 99:1 (compound **5c**) to 15:85 (compound **5d**). The solid state and solution phase product ratios are summarized in Table 1.

Two explanations were considered for the solid state results.[32] The first was that the preference for formation of the intermediate biradicals leading to photoproducts **8** and **9** depends on which ester group is better oriented by the crystal lattice for radical stabilization by resonance, i.e., on which ester substituent is more nearly coplanar with the vinyl double bond. While some unsymmetrical diesters we have studied conform to this reactivity pattern, others do not, and this leads to the general conclusion that differential biradical stabilization brought about by conformational rigidity in the crystal is not the factor that controls solid state regioselectivity.

Table 1. Solution vs Crystalline Phase Regioselectivity for Unsymmetrical Diesters

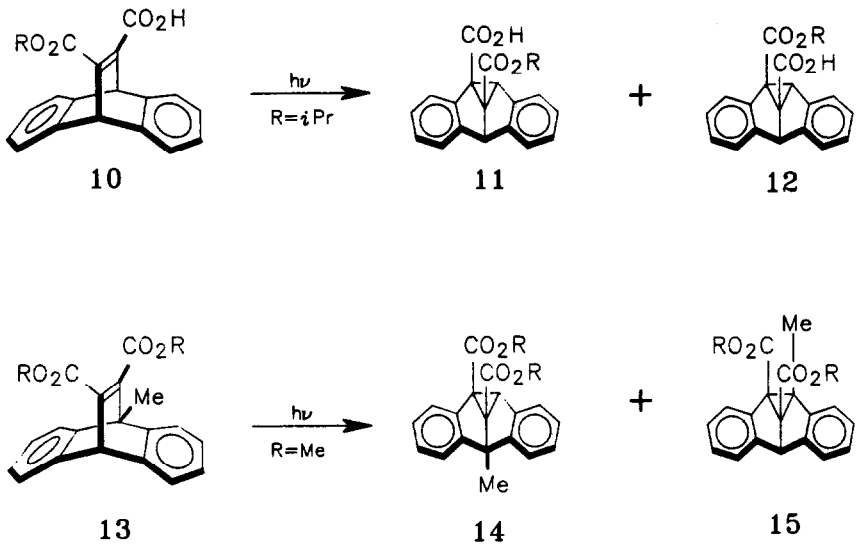
Diester	mp (°C)	**8**:**9** Ratio	
		Benzene	Crystal
5a	104-106	53:47	45:55
5b	124-125	55:45	93:7
5c	95-97	60:40	99:1
5d	128-129	60:40	15:85

The second explanation involves the possibility that steric effects between the reacting molecule and its lattice neighbors may be responsible for the solid state regioselectivities. The concept of a bimolecular steric effect on a unimolecular process is unimaginable in solution, where the random steric interactions between solute and solvent have no influence on unimolecular reaction selectivity. Reasoning from an inspection of molecular models that it is the ester substituent attached to the bridging vinyl carbon atom that moves most during the initial stages of reaction and is therefore most likely to suffer an unfavorable steric interaction with its lattice neighbors, we calculated the sum of the intermolecular non-bonded repulsion energies resulting from a computer simulation of these motions.[33] This was carried out by converting the non-bonded contacts developed between the atoms of the moving ester substituent and the atoms of the surrounding, stationary crystal lattice into repulsion energies by using the Lennard-Jones 6-12 potential function and then summing over all the contacts. In the case of compound **5b**, the only compound in the **5a-d** series for which we were able to obtain an X-ray crystal structure, the calculations showed that it is more expensive in terms of repulsion energy to move the CO_2Me substituent than the CO_2iPr substituent, a

finding that is in accord with the experimental results. We shall see other examples in the pages that follow where such an approach is able to rationalize the experimental results in the solid state. An important point that emerges from the regioselectivity work is that substituent effects in the solid state are not as regular as they tend to be in solution. Exchanging one substituent for another often results in a completely different packing arrangement and steric environment in the crystal, and this can lead, as we have seen for diesters **5a-d**, to very different chemical behavior for closely related compounds.

Other substituents may be tested against one another for their effect on di-π-methane regioselectivity exactly as described above, and in one such study we investigated a carboxylic acid group versus an ester group (compound **10**, Scheme 3).[34] Interestingly, the photochemical results obtained in the solid state once again proved to be very different from those observed in solution. In dilute benzene solutions, photoproduct **11** predominated (**11**:**12** = 83:17), whereas in the crystalline state there was a nearly complete preference for regioisomer **12** (**11**:**12** = 5:95). We attribute this to a difference in hydrogen bonding that exists in solution and in the crystal. In the latter medium, there is strong intermolecular hydrogen bonding between carboxylic acid groups, and we suggest that this "anchors" the carboxylic acid group and hinders the motions necessary for initial bonding at the vinyl carbon atom to which the carboxylic acid group is attached. As a result, bonding at the other vinyl carbon atom (whose substituent is not anchored) and formation of photoproduct **12** is favored in the crystal. Infrared studies showed that in benzene solution there is a concentration-dependent competition between inter- and intramolecular hydrogen bonding, and it appears that the latter situation presents conditions favorable for formation of photoproduct **11** (partial positive charge on the carboxylic acid-bearing vinyl carbon atom as a result of internal proton transfer to the carbonyl oxygen atom of the ester group). In accordance with this picture, it was found that as the proportion of cyclic dimer was increased in benzene by increasing the reactant concentration, the proportion of the solid state photoproduct **12** increased.[34]

If, as suggested above, crystal packing effects control di-π-methane regioselectivity in the solid state, then it follows that regioselectivity may be different at the surface of a crystal compared to the bulk. We have documented exactly such an effect.[35] The compound studied was the 9-methylethenoanthracene derivative **13** shown in Scheme 3. In this case unequal substitution at positions 9 and 10 leads to two possible di-π-methane regioisomers (**14** and **15**). By increasing the surface area of a crystalline sample of this material through grinding, it was found that the regioselectivity of its di-π-methane photorearrangement was significantly decreased compared that observed in large, carefully grown single crystals (**14**:**15** = 12:82 before grinding and 35:62 after grinding). A second indication that surface regioselectivity in this case is less than that characteristic of the bulk comes from the following experiment: a single crystal of **13** that had been irradiated to approximately 1% conversion was washed with three small portions of diethyl ether, in which the starting



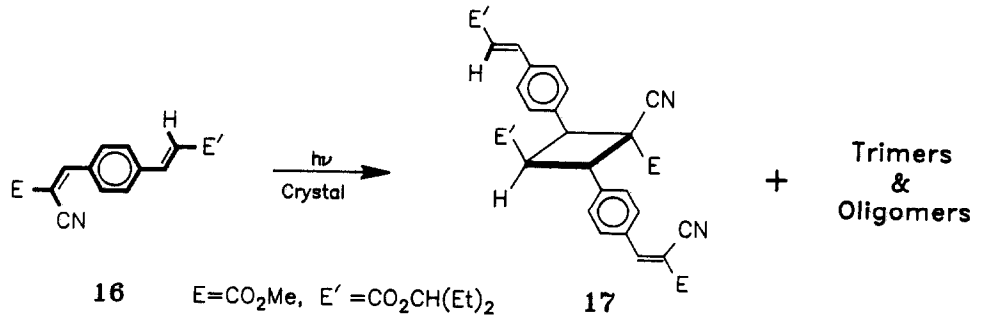
Scheme 3

material is sparingly soluble and the photolysis mixture is moderately soluble. Gas chromatographic analysis showed that the 14:15 ratio decreased with successive washings in the following way: 18:64 (30% conversion) to 10:79 (7% conversion) to 6.5:87 (3% conversion). These results illustrate the point that investigations of crystal photoreactivity should be conducted on samples of widely differing surface area, and where bulk reactivity is desired, photolysis wavelengths near the absorption tail should be used; a simple Beer-Lambert calculation reveals that for crystals that absorb strongly at the photolysis wavelength, most of the incident radiation will be absorbed near the surface.

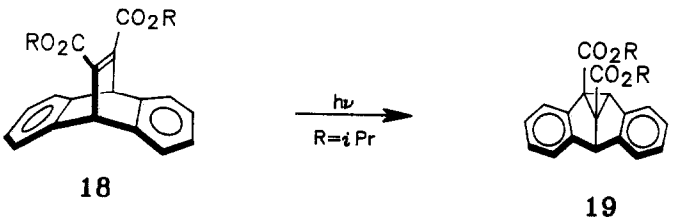
2.3. Absolute Asymmetric Induction

Absolute asymmetric synthesis is defined as an asymmetric synthesis carried out in a closed system in the absence of any external chiral inducing agents.[36] It is a process unique to the crystalline phase, and its first stage consists of the spontaneous crystallization of an achiral reactant in a chiral space group.[37] The second stage of the process involves a solid state chemical reaction, often photochemical in nature, that transforms the crystalline reactant into a product possessing permanent molecular chirality. In such cases, the enantiomeric excess in which the product is formed is a direct measure of the asymmetric induction by the chiral matrix. At the time our work in this area was initiated, the only known absolute asymmetric syntheses were those reported by a group at the Weizmann Institute of Science who were studying the bimolecular reactions of chiral crystals, primarily lattice-

controlled [2+2] photocycloadditions.[38] The most thoroughly studied example was that of the achiral diacrylate derivative **16** (Scheme 4), which crystallizes spontaneously in the chiral space group $P2_1$.[36] Irradiation of single crystals of this material gave optically active dimers, trimers and higher oligomers, and in fourteen separate trials the dimers were found to be formed in enantiomeric excesses ranging from 44-100%, the average being 67%; nine of the runs gave a predominance of (+)-**17** and five gave predominantly (-)-**17**.



16 E=CO_2Me, E′ =$CO_2CH(Et)_2$ **17**



18 **19**

Scheme 4

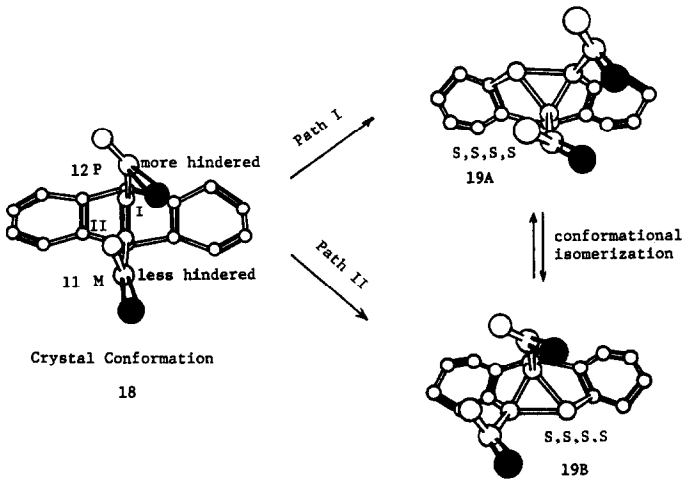
Our initial work in this area centered around the 9,10-ethenoanthracene derivative **18** (Scheme 4), which is readily prepared by transesterification of Diels-Alder adduct **1**.[39] This compound proved to be dimorphic: recrystallization from ethanol afforded prisms with the achiral space group Pbca and recrystallization from hexane gave the Pbca modification plus crystals in the chiral space group $P2_12_12_1$. We later found that the $P2_12_12_1$ space group is the exclusive result of growing crystals from the melt. X-ray crystallography revealed that both dimorphs crystallize in asymmetric conformations, but only the $P2_12_12_1$ crystals are chiral; the Pbca crystals are racemic (enantiomeric conformations related by crystal symmetry). The finding that ethenoanthracene derivative **18** crystallizes in two space groups, one chiral and the other achiral, afforded a unique opportunity to study the different effects

that these two fundamentally different packing modes exert on the chemical reactivity of the same substance. In addition, the expected photoproduct, **19**, possesses four chiral centers, thus raising the possibility of an absolute asymmetric photorearrangement.

Large (20-85 mg) crystals of each dimorph were irradiated by using a nitrogen laser (337 nm); parallel photolyses were conducted in benzene solution. At 337 nm, only the tail of the ene-dioate absorption is excited ($\epsilon < 10$). The optical activity produced in each photolysis was determined by dissolving the sample in chloroform and measuring its rotation at the sodium D line. The unreacted starting material contributes nothing to the rotation because it is achiral in solution. The results showed that only in the case of the $P2_12_12_1$ crystals was optical activity developed. Remarkably, NMR chiral shift reagent studies using $Eu(hfc)_3$ established that, within the limits of the method, the chiral crystals give photoproduct **19** in quantitative enantiomeric excess. In nine separate runs, four gave dextrorotatory photoproduct and five gave levorotatory material - results that are consistent with a truly spontaneous (i.e., random) resolution upon crystallization.

What do these results tell us about the mechanism of the di-π-methane photoreaction of the $P2_12_12_1$ crystal modification? Recalling from Section 2.1 that of the four possible reaction pathways (cf. Scheme 1), paths I and II lead to one enantiomer and paths III and IV give the other, we can say that the solid state reaction occurs with complete discrimination between pathways [I+II] and [III+IV]. The results do not, however, tell us whether [I+II] is favored over [III+IV] or vice versa, nor do they indicate the relative importance of I versus II or III versus IV.

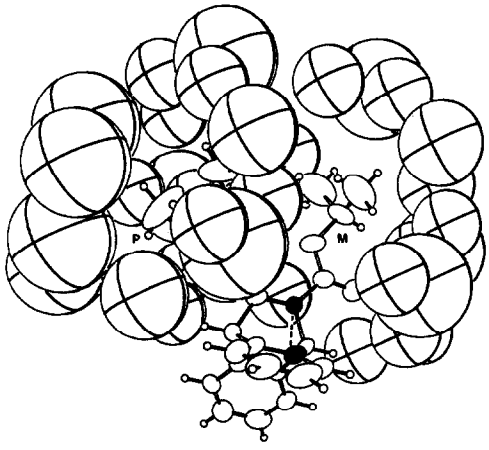
In principle, it is possible to differentiate between pathways (I+II) and (III+IV) by determining the absolute configuration of the molecules in a given $P2_12_12_1$ crystal and correlating this with the absolute configuration of the photoproduct generated by irradiation of that same crystal. We have recently reported the successful completion of such a study.[40] Thus a fragment of a large (55 mg) crystal of **18** ($P2_12_12_1$ modification) was subjected to X-ray crystal structure analysis taking account of anomalous dispersion.[41] This showed that the crystal studied contained molecules with the 11M,12P absolute configuration. The designation 11M,12P for **18** focuses on the site of disymmetry in the molecule (the ester groups) and uses the conformational chirality formalism for assigning absolute configuration.[42] In this approach, one determines the smallest torsion angle between the groups of highest priority attached to each end of the single bond about which the conformation is to be specified. A (+) torsion angle is designated P (plus) and a (-) torsion angle is termed M (minus). In the case of diester **18**, the axes to be considered are the single bonds joining the C=C and CO_2R substituents, and the groups of highest priority are the carbonyl oxygen atom at one end and the vinyl carbon at the other. Concomitant with the absolute configuration studies on diester **18**, the remaining crystal fragment was photolyzed and shown to give levorotatory **19**, and anomalous dispersion X-ray crystallography of this material indicated that it had the S,S,S,S configuration. Ball and stick drawings of both the reactant and photoproduct absolute configurations are given in Scheme 5. The dark circles indicate the oxygen atoms of the C=O groups.



Crystal Conformation

18

Crystal Conformation

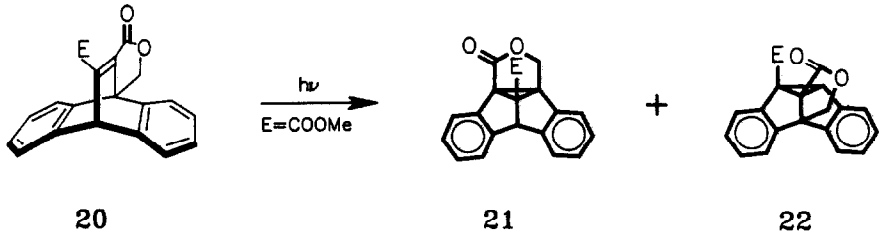


Lattice environment of compound **18** showing van der Waals radii of the atoms from neighboring molecules at d ≤ 3.0 Å. The largest spheres represent carbon atoms, intermediate sized spheres are oxygen atoms and the smallest spheres indicate hydrogen atoms. The dotted line joining the two dark atoms corresponds to path II benzo-vinyl bridging (see text).

Scheme 5

The first conclusion to be drawn from the results is that pathways I and/or II are followed; pathways III and/or IV would have given the R,R,R,R,-(+) photoproduct. Inspection of Scheme 5 reveals a possible reason for this enantioselectivity. The conformation of ethenoanthracene derivative **18** predicts that for pathways I and II, the bulky ester groups will move away from one another during initial vinyl-benzo bridging. In contrast, paths III and IV would involve severe clashing of the ester groups as they are forced toward each other during the initial stages of reaction; as a result, pathways I and/or II should be preferred kinetically. As mentioned above, the stereochemical results do not allow a distinction to be made between paths I and II, but we can speculate about their relative importance. We believe that path II is favored over path I. Two pieces of evidence lead to this tentative conclusion. First, the $P2_12_12_1$ packing diagram reveals that the 11M ester group, which is attached to the vinyl carbon atom involved in path II, is in a much freer lattice environment than its path I counterpart and therefore experiences less topochemical restriction of its movement during reaction. A packing diagram depicting the difference in local packing density around each of the ester groups of compound **18** is shown in Scheme 5. This qualitative conclusion is supported quantitatively by intermolecular non-bonded repulsion energy calculations of the type discussed earlier in connection with the regioselectivity studies.[43] Second, if we assume that the ester groups retain their original conformations during reaction, pathway II produces the final product directly in its crystal conformation **19B** (Scheme 5); in contrast, topochemical reaction via path I would lead to the unobserved conformer **19A**, which MM2 calculations reveal to be of higher energy. It is, of course, by no means clear that conformational energy and preferred pathway are related.

Recently we were fortunate to discover an unsymmetrically substituted ethenoanthracene derivative that, while itself achiral, crystallizes spontaneously in a chiral space group.[44] Such a compound permits us to probe the interesting question of whether, in an absolute asymmetric rearrangement that is capable of giving two regioisomeric photoproducts, each product will be formed in the same enantiomeric excess. The answer, at least in the case of compound **20** (Scheme 6), is no. Photolysis of crystals of this material (space group $P2_12_12_1$) afforded an 87:13 mixture of products **21** and **22**, the optical purities of which were determined by chiral shift reagent NMR spectroscopy. This showed that photoproduct **22** is formed in high enantiomeric excess and that its regioisomer **21** is racemic. In four separate trials at -20°C, the enantiomeric excesses for compound **22** were (+)-70%, (+)-74%, (-)-100% and (-)-100%. The accuracy of the ee determinations is estimated to be ca. ±3%. The interpretation of these results in terms of the crystal structure of ethenoanthracene derivative **20** is similar to that advanced to explain the solid state photochemistry of diester **18**, namely topochemical restriction of the vinyl-benzo bridging process leading to certain enantiomers but not others. Although we believe we have identified the specific contacts responsible for the high enantioselectivity observed in the formation of photoproduct **22**,[44] this has not been verified by absolute configuration correlation studies as in the case of the compound **18**.



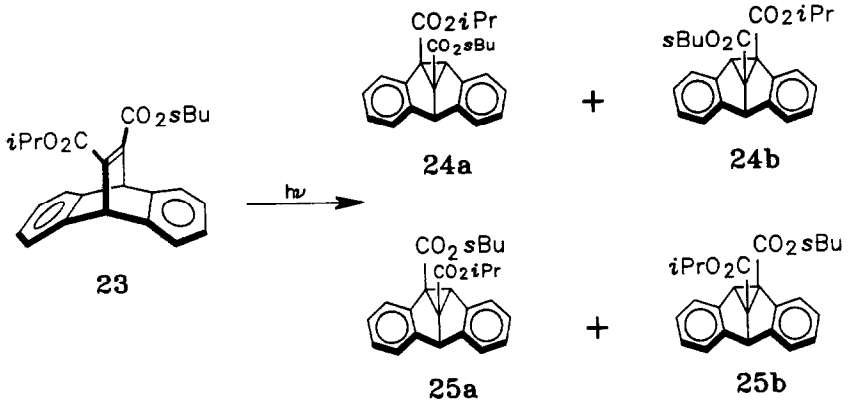
20 21 22

Scheme 6

2.4. Chiral Handle-Induced Asymmetric Induction

It has been recognized for some time that results such as those described above for compounds **18** and **20**, in which there is an enantioselective solid state chemical reaction of an achiral compound that crystallizes in a chiral space group, provide not only a plausible explanation for the prebiotic origin of optical activity, but also an attractive method of asymmetric synthesis.[45] The problem with using such an approach for organic synthesis is, of course, that spontaneous crystallization of achiral molecules in chiral space groups coupled with solid state reactivity that generates chirality is extremely rare.[39,44,46-49] In contrast, chiral space groups are obligatory for optically active compounds, and we therefore turned our attention to a study of the solid state photochemistry of ethenoanthracene derivatives bearing resolved chiral handles. An interesting aspect of this work is that for chemical reactions carried out in the solid state, the chiral handle exerts an asymmetric influence that is not present in isotropic liquid solvents such as benzene or acetonitrile, namely it ensures the presence of a chiral environment for reaction through crystallization in a chiral space group. Thus, by comparing the difference in asymmetric induction in the solid state and solution, the relative importance of the intrinsic versus the environmental effect of the chiral handle on a given reaction may be determined.

This was first done in the ethenoanthracene series for the unsymmetrical diester derivative **23**, in which one of the ester alkyl substituents was (S)-sec-butyl and the other was isopropyl (Scheme 7).[50] Di-π-methane photorearrangement of mixed diester **23** can give rise to four diastereomeric products that can be designated as **24** or **25** by the relative position of the two ester groups, and as **a** or **b** on the basis of the configuration of the substituted dibenzosemibullvalene ring system. Without going into detail, it was found possible to determine accurately both the 24:25 and **a**:**b** ratios for the solid state and solution photolyses.[50] Both ratios were near unity in solution (as expected), but in the solid state, high regioselectivity (24:25 = 9:1) and enantioselectivity (**a**:**b** = 9:1) was observed.

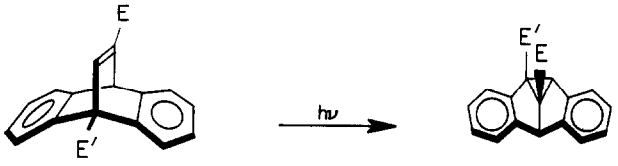


Scheme 7

Crystallographically, diester 23 is isostructural with diisopropyl diester **18** and crystallizes in space group $P2_12_12_1$ with disorder in the sec-butyl group. Interestingly, the racemic form of 23, i.e., the compound in which the sec-butyl group is (R,S), also crystallizes in $P2_12_12_1$, and the photochemistry of this material in solution and in the solid state was investigated.[50] The solid state enantioselectivity remained high (**a**:**b** = 9:1), but the regioselectivity was diminished to **24**:**25** = 3:2, a result we attribute to packing differences between the optically active and racemic material. These packing differences are clearly indicated by an 11° difference in melting point between the two forms, but owing to the disorder present in the sec-butyl group, the exact source of the solid state regioselectivity differences could not be pinpointed crystallographically. We note that the conversion of racemic 23 into optically active products constitutes a somewhat different form of absolute asymmetric synthesis. This aspect of the work has direct analogy in the work of Addadi and Lahav on racemic ethyl 2-cyano-3-(p-sec-butyl-3'-(E)-propenoate)phenyl-(E)-propenoate.[51] This material also crystallizes with disorder in the sec-butyl group in a chiral space group (P1) containing both enantiomers, and irradiation of these crystals led to optically active dimers, trimers and oligomers, the optical purities of which varied from 0-100% depending on the R/S composition of the sample photolyzed.

In a related study, the dibenzobarrelene derivatives **26a** and **26b** (Scheme 8), in which the chiral handle is an ester substituent derived from naturally occurring (-)-menthol, were prepared and photolyzed in the solid state and solution.[52] For both compounds, di-π-methane photorearrangement gives only the regioisomer shown owing to preferential initial bonding at

the unsubstituted vinyl carbon atom (more stable biradical intermediate). Two diastereomers are possible in each case, and it was found that the diastereoselectivity changed from 60:40 in solution to 20:80 in the solid state for compound **26a**, but remained at 50:50 in both media



26 **27**

(a) E = CO_2Me; E′ = CO_2(−)−menthyl

(b) E = CO_2(−)−menthyl; E′ = CO_2Me

Scheme 8

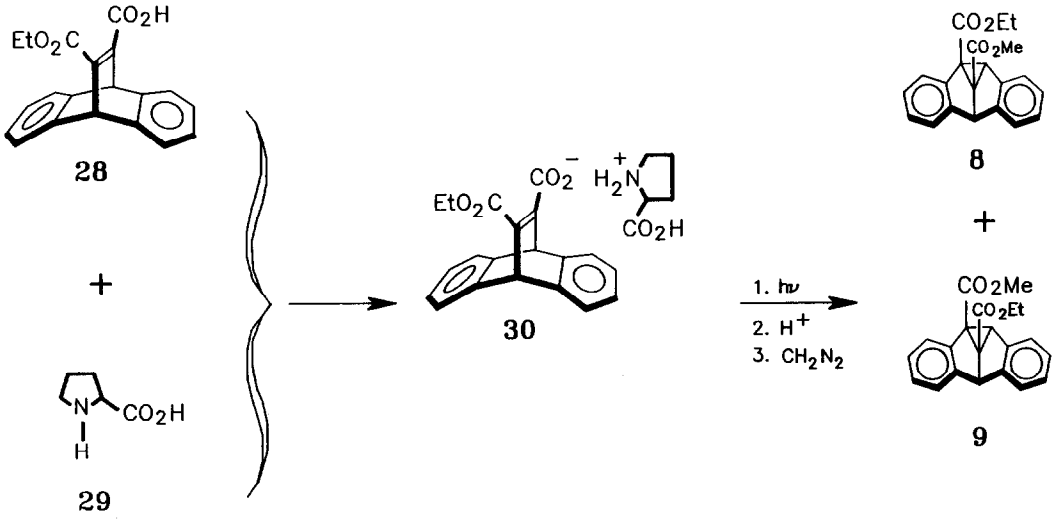
for **26b**. As before,[50] these results were interpreted in terms of an intrinsic asymmetric inductive effect of the chiral handle, which is exhibited both in solution and the solid state, and an environmental effect, which is present only in the latter medium and is due to the presence of a chiral crystal lattice. We suggest that these effects may either reinforce or oppose one another, the latter situation apparently being the case for compound **26a**, where the diastereoselectivity is reversed in the solid state compared to solution. The lack of diastereoselectivity observed for dibenzobarrelene derivative **26b** in solution is attributable to the greater distance in this compound between the site of reaction and the chiral handle. The non-diastereoselective photoreaction of **26b** in the solid state illustrates clearly that the asymmetric inductive power of a chiral organic crystal lattice need not be high.

2.5. Ethenoanthracene Carboxylate Salts

In seeking a more general approach to utilizing crystal chirality in asymmetric synthesis, it occurred to us that achiral compounds containing carboxylic acid groups could be forced into chiral space groups by formation of salts with optically active amines, for example, brucine, strychnine and other classical resolving agents. Provided that the carboxylate-containing portions of such salts undergo chemical processes that generate at least one new chiral center, reaction (in our case, di-π-methane photorearrangement) of the salts in the solid state followed by esterification of the products would lead to mixtures whose enantiomeric excesses provide a measure of the extent of asymmetric induction by the crystalline medium. Such an approach has the added advantages that (1) liquid carboxylic

acids can be investigated owing to the fact that their salts will almost certainly be solid, and (2) the strong lattice forces present in ionic crystals may help to bring about topotactic (single crystal-to-single crystal) behavior with attendant high chemical yields. It is only fair to point out that strong lattice forces may also translate into reduced solid state chemical reactivity. To date, however, we have not found this to be the case, and a paper outlining our initial findings in this area has been published recently.[53]

The compound studied was the acid-ester **28** (Scheme 9), synthesized by treatment of the corresponding anhydride[54] with ethanol. Salts of **28** with various optically active amines were prepared by mixing equimolar quantities of acid and base in ethanol or ether and filtering the resulting precipitate. Best results were obtained with the amino acid proline (**29**) as base, and these will be described in some detail. The proline salt **30** (ca. 100 mg) was irradiated (450 W Hanovia medium pressure mercury lamp) as a white powder sandwiched between two Pyrex microscope slides and sealed in a polyethylene bag; highest enantiomeric excesses were obtained at temperatures of -40°C, and conversions were kept below 20%. The reaction mixture was acidified, treated with excess diazomethane to produce the corresponding methyl/ethyl diesters, and then subjected to silica gel column chromatography. This afforded the known (cf. Scheme 2) photoproducts **8** and **9** as a mixture whose regioisomeric and enantiomeric composition was determined by 400 MHz NMR spectroscopy.



Scheme 9

Compound **9** was the major (ca. 90%) regioisomer in every case. This is the same regioselectivity as observed for a closely related sodium carboxylate salt photolyzed in aqueous solution,[34] a result attributable to preferential benzo-vinyl bridging at the carboxylate salt-bearing vinyl carbon atom so as to locate the resulting radical at the more favorable ester-bearing vinyl position. With regard to the solid state enantioselectivities, it was found that only one of the two regioisomeric photoproducts (**9**) is produced in optically active form.[53] When R-(+)-proline was used, the (-) enantiomer of compound **9** was formed in 80% ee, and when S-(-)-proline was employed, the (+) enantiomer predominated (76% ee). These results predict that the use of racemic proline should lead to racemic **9**, and this was found to be the case. Interestingly, photolysis of the optically active salts in ethanol solution also gave racemic products, thus highlighting the role of the chiral crystal lattice as the factor responsible for the enantioselectivity. Owing to a lack of crystal structure data (the salts are white powders), the lattice effects responsible for this outcome are unknown at present. Overall, however, the results are encouraging, and we are currently screening additional optically active amines in the hope of improving the optical yields. We are also extending the procedure in the opposite sense, that is, to salts of prochiral, photoreactive amines with optically active carboxylic acids. Finally, we point out that the natural, two-component nature of salts raises the possibility of using the counterion, not only as a chiral auxiliary as above, but as a sensitizer, quencher, heavy atom, trapping agent or the like. Such experiments, which require intimate contact between two different chemical substances, have seldom been carried out in the solid state because the addition of extra components to the crystalline medium necessarily disrupts the lattice regularity that is responsible for the unique reactivity in the first place.

3. CYCLOOCTATETRAENE FORMATION

The solution phase photochemistry of 9,10-ethenoanthracene itself (compound **31**, Scheme 10) is multiplicity-dependent. Irradiation of this material in the presence of triplet-energy sensitizers leads to dibenzosemibullvalene (**32**),[28] whereas direct irradiation (i.e., irradiation in the absence of triplet energy sensitizers) affords mainly dibenzocyclooctatetraene (**33**).[55,56] We recently demonstrated that this same multiplicity dependence is also present in the solid state photochemistry of 9,10-ethenoanthracene.[57]

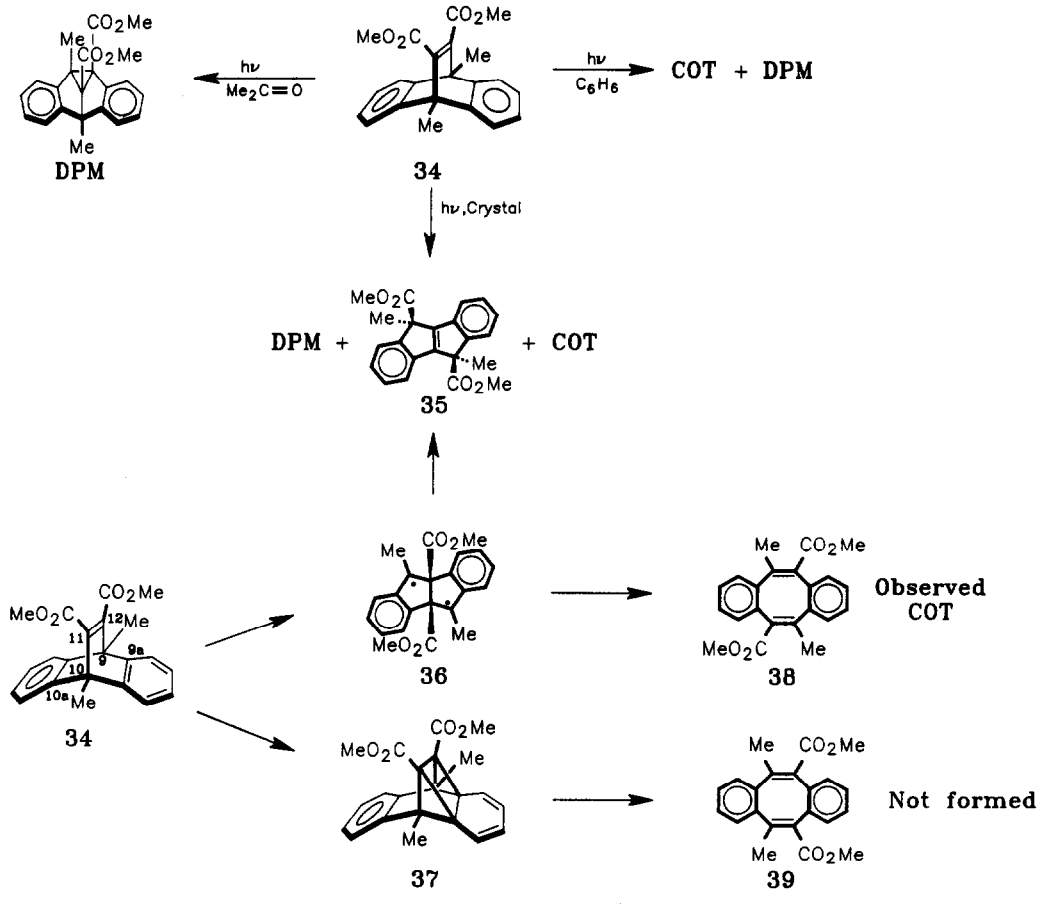
For most of the 9,10-ethenoanthracene derivatives discussed in Section 2, which have ester substituents attached to the vinyl double bond, direct irradiation leads, as we have seen, to triplet (di-π-methane) reactivity, a result that is presumably due to rapid intersystem crossing of the initially formed singlet excited state. Recently, however, we have discovered some ethenoanthracene derivatives in which cyclooctatetraene (COT) formation from S_1 is competitive with intersystem crossing, and the remainder of this article will be devoted to this subject.

33 31 32

Scheme 10

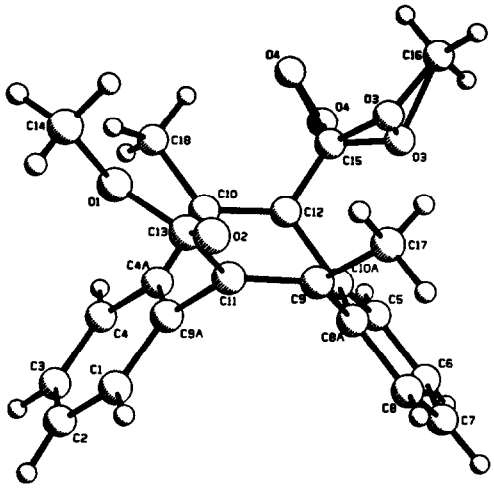
Thus for example we found[58] that direct irradiation of the tetrasubstituted etheno-anthracene derivative 34 (Scheme 11) in solution led to two photoproducts, a COT derivative and a di-π-methane (DPM) product (ratio ca. 1:1). In accordance with expectation, triplet-sensitized photolysis of 34 gave only DPM material, spectroscopic characterization of which indicated the normal structure shown. In contrast to the solution phase results, photolysis of compound 34 in the solid state afforded mainly the unexpected and unusual rearrangement product 35 (structure established by X-ray crystallography); small amounts of the COT and DPM products were also formed in the crystal irradiations.

It seems likely that the mechanism by which diester 35 is formed involves sequential carbomethoxy group migration in the bis-benzylic biradical 36 (Scheme 11). This mechanism rationalizes the stereochemistry of 35 (1,2-ester migration with participation of the ester carbonyl groups), and such migrations, while rare, do have literature precedent.[59] The origin of biradical 36 presents an interesting mechanistic problem. Its formation involves, at least formally, C(9a)···C(12) and C(10a)···C(11) double benzo-vinyl bridging followed by cleavage of bonds C(9)-C(9a) and C(10)-C(10a). Extended Huckel calculations by Zimmerman et al.[60] indicate that a non-concerted version of this process is most likely. The probable intermediacy of 1,4-biradical 36 suggested that it might also be involved in COT formation through fragmentation of the central bond, a common reaction of such species. Of particular note is that such a process generates a COT derivative (compound 38) with C_2 symmetry. In contrast, the commonly accepted mechanism for COT formation, which is based on labeling studies with monobenzobarrelene derivatives and related compounds,[61-64] involves initial intramolecular [2+2] cycloaddition followed by thermal reorganization of the resulting cage compound 37 (Scheme 11), a process that predicts the formation of dibenzocyclo-octatetraenes with C_s or mirror symmetry (compound 39). In order to resolve the question of the structure of the COT



Scheme 11

photoproduct in this case, a single-crystal X-ray diffraction study was undertaken. The results of this study unambiguously establish that the COT has the unexpected, fragmentation labeling pattern of structure **38**; Scheme 12 shows a PLUTO drawing of the molecular structure of this material.

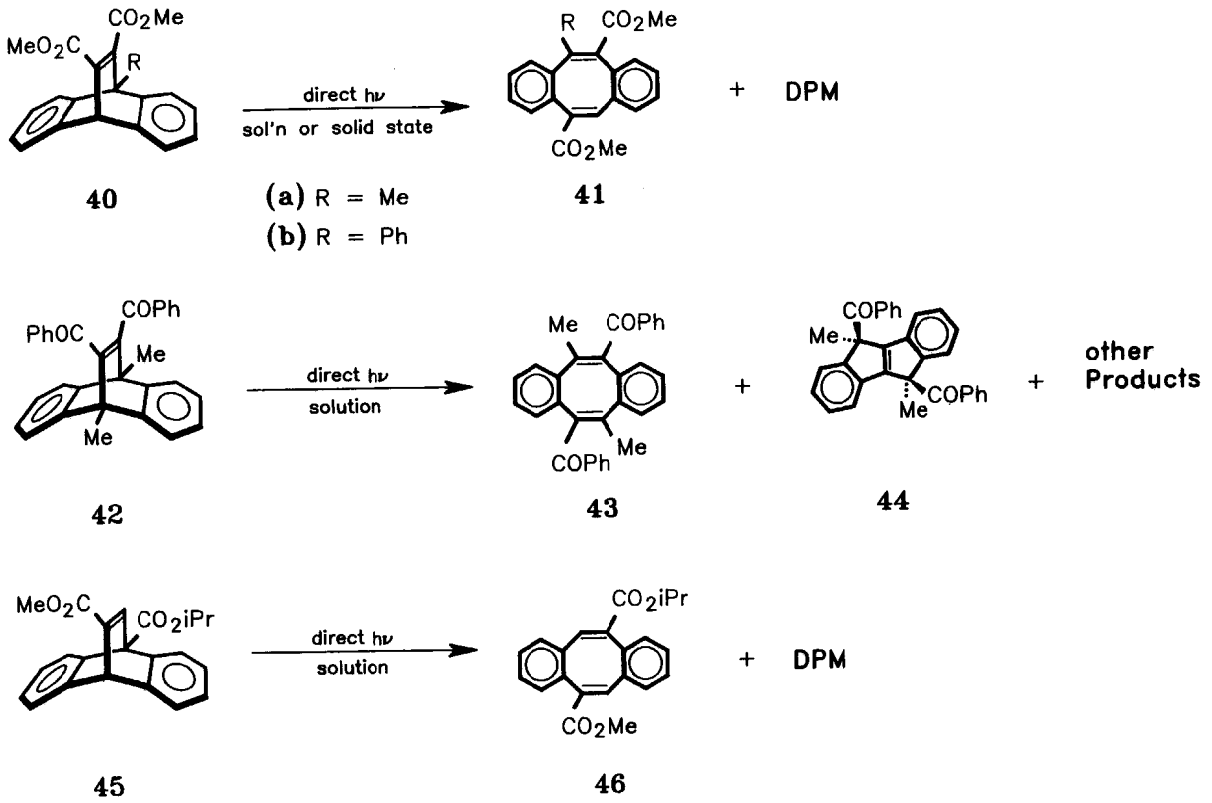


Molecular structure of COT **38** as determined by X-ray crystallography. Note disorder in ester substituent attached to C(12).

Scheme 12

To test the generality of these results, the photochemistry of the trisubstituted ethenoanthracenes **40a** and **40b** (Scheme 13) was investigated.[58] In each case, both in the solid state and solution, the COT formed was that derived from 1,4-biradical fragmentation rather than [2+2] photocycloaddition. In neither case, however, was a photoproduct analogous to diester **35** isolated. A further example of unexpected COT formation is found in the work of M.V. George et al. Originally assigned the [2+2]-derived structure,[65] the COT formed by solution phase photolysis of ethenoanthracene derivative **42** has recently been shown by X-ray crystallography to have the fragmentation-derived structure **43** (Scheme 13).[66] Interestingly, one of the other photoproducts formed in this reaction, compound **44**, was found to have a structure analogous to the double migration product **35**.[66] One might ask whether <u>all</u> ethenoanthracenes give fragmentation-derived COT photoproducts. They do not. X-ray data clearly indicate that the COT from disubstituted ethenoanthracene derivative **45** (Scheme 13) is of the [2+2] type (structure **46**).[58]

What factors control the competition between formation of [2+2]-derived and fragmentation-derived COTs? While it is clear that more examples are needed before a definitive conclusion can be reached, the results to date suggest that the degree of


CO2Me
MeO2C
R
direct hν
sol'n or solid state
R CO2Me
CO2Me
+ DPM
40
(a) R = Me
(b) R = Ph
41
COPh
PhOC
Me
Me
direct hν
solution
Me COPh
COPh Me
COPh
Me
COPh
Me
+
+ other Products
42
43
44
MeO2C
CO2iPr
direct hν
solution
CO2iPr
CO2Me
+ DPM
45
46

Scheme 13

substitution at positions 9, 10, 11 and 12 is an important factor. The reluctance of compounds that are tri- or tetrasubstituted at these positions to engage in intramolecular [2+2] photocycloaddition can be attributed reasonably to steric factors. This, coupled with the additional stability afforded the intermediate 1,4-biradical (e.g., **36**) by the substituents originally at C(9) and C(10), plausibly rationalizes the unexpected singlet excited state behavior of compounds **34**, **40a**, **40b** and **42**.

4. CONCLUDING REMARKS

Ethenoanthracene derivatives have proved to be extremely valuable models for probing the effects that the organic crystalline state exerts on chemical reactivity. With rare exceptions, the molecules are beautifully crystalline, easy to prepare and undergo interesting solid state chemistry. Significantly, the synthesis of a large number of closely related analogues has permitted the establishment of trends; this is important in establishing the ground rules for what is still a relatively undeveloped field.

We close this review with a look to the future. Imagine an experimental technique by which stereodiagrams of the starting materials, intermediates and products in a chemical reaction can be recorded in real time - a technique that is capable of providing a step-by-step visualization of organic reaction mechanisms. Sound fanciful? Such experiments may be feasible in the not-too-distant future through the application of synchrotron source X-ray crystallography[67] to chemical reactions that occur in the organic crystalline phase. For this reason, among many other more immediate reasons such as its direct relevance to the field of materials science, the study of chemical processes that take place in solids is an important and worthwhile undertaking.

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