

CHIRAL HANDLE-INDUCED DIASTEREOSELECTIVITY IN AN ORGANIC PHOTOREARRANGEMENT:
SOLUTION VERSUS SOLID STATE RESULTS

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Abstract. The degree of asymmetric induction in the di- π -methane photorearrangement due to the presence of a remote chiral handle was found to vary with the nature and location of the chiral handle and with the medium in which the reaction was carried out.

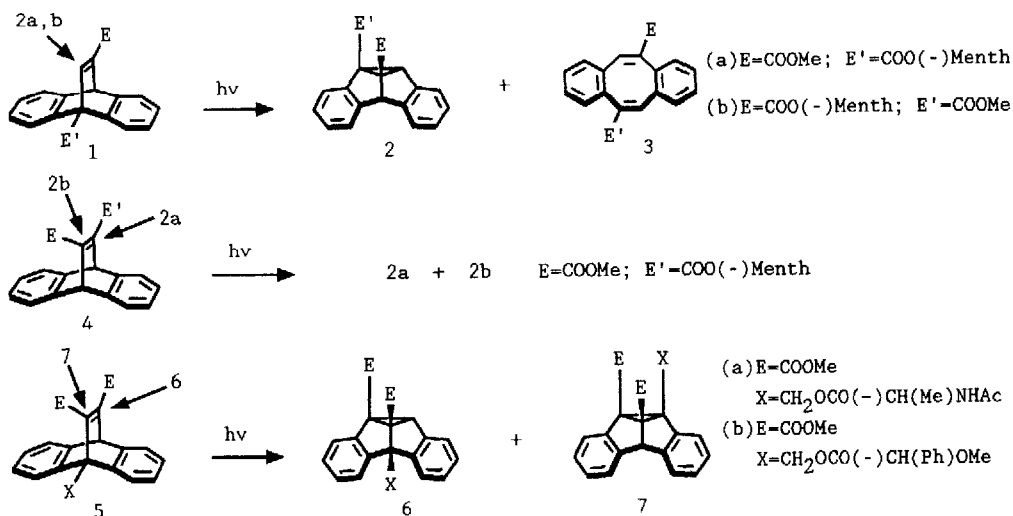
One of the central themes of organic chemistry has been the design of reactions that yield optically active products.¹ One approach to this goal is the introduction of a resolved chiral substituent (chiral handle) into the reactant. Ideally, during reaction this substituent induces formation of a new asymmetric center with a single chirality through differential steric effects in the diastereomeric transition states. For chemical reactions carried out in the solid state, the chiral handle exerts a second asymmetric influence that is not present in isotropic liquid solvents, namely it ensures the presence of a chiral environment for reaction through crystallization in a chiral space group.² By comparing the difference in asymmetric induction in the solid state and solution, the relative importance of the molecular versus the environmental effect for a given reaction may be determined. While various photoreactions have been investigated individually either in the crystalline² or the liquid³ phase from this point of view, a direct comparison of the diastereoselectivity of the same reaction in both media has never been made. In this communication we report the effect that placing a chiral handle at either a bridgehead or a vinyl position of dibenzobarrelene has on the diastereoselectivity of its di- π -methane photorearrangement⁴ in solution and the solid state.

Five compounds (1a, 1b, 4, 5a and 5b, Scheme 1) were investigated; each was synthesized in straightforward manner through Diels-Alder addition of the appropriate 9-substituted anthracene derivative to the corresponding acetylenic dienophile.⁵ Based on our own experience⁶ and that of others,⁷ it was anticipated that these compounds would undergo di- π -methane photorearrangement, both in solution and the solid state, to afford dibenzosemibullvalene derivatives with four new (but non-independent) chiral centers; each photoproduct is thus capable of being produced in two diastereomeric forms. The formation of a single regioisomer 2 in the case of compounds 1a and 1b was expected.⁷

Photolysis of dibenzobarrelene derivatives 1a, 1b, 5a and 5b in solution (benzene, acetonitrile) and in the solid state gave the results shown in Table 1. The di- π -methane products of photolysis of compounds 1a and 1b were shown to have the carbon skeleton 2 by transesterification to the corresponding known⁷ dimethyl diester. A second verification of their structure came from the finding that, as expected, all four were formed in the solution phase photolysis of the vinyl-substituted menthyl/methyl diester 4 (Scheme 1). This latter material proved to be an oil at room temperature, so that only its solution phase photochemistry was investigated (Table 1).

Direct irradiation of 1a and 1b in both media also afforded small amounts of the cyclooctatetraene derivative 3. NMR measurements of the photolysis mixtures indicated that 3 is formed in two diastereomeric forms with approximately the same selectivity as 2a (from 1a) and 2b (from 1b).⁸ Triplet-sensitized photolyses of 1a and 1b gave no 3, indicating that it is singlet-derived; no cyclooctatetraene-type photoproducts were formed in the case of compounds 4, 5a or 5b.

Scheme 1



In the case of compounds 5a and 5b, there is an opportunity to compare not only solution state versus solid state diastereoselectivity, but regioselectivity as well. Under all conditions, photoproduct 6 was the predominant regioisomer but was less dominant in the solid state than in solution. The reaction mixtures in these cases proved difficult to separate, so use was made of ¹H NMR spectroscopy for identification and quantification purposes. Photoproduct 6 could be differentiated from its regioisomer 7 on the basis of the chemical shifts of the non-aromatic methine protons. Cyclopropyl methine protons such as those present in 6a and 6b resonate typically at $\approx \delta$ 4.4, while the signals due to the doubly benzylic methine protons of 7a, 7b and related compounds are found characteristically at $\approx \delta$ 5.1. The chemical shifts of these resonances were found to be slightly different for each diastereomer. For example, the cyclopropyl methine hydrogens of diastereomers 6a and 6a' appeared at δ 4.36 and 4.38, and integration of these signals gave the diastereoselectivities reported in Table 1. In each case, the ratios were double checked by integration of a second pair of resonances (-NHC(=O)CH₃ for 6 and -OCH₃ for 7) and were reproducible to $\pm 5\%$ from run to run.

Several interesting conclusions can be drawn from the results presented in Table 1. First of all it is apparent that, in general, diastereoselectivity is higher in the solid state than

in solution. The two highest diastereoselectivities measured (2a:2a' - 20:80 and 7a:7a' - 24:08) were both observed in the crystalline state. There are, however, obvious exceptions to this rule, for example in the case of 6b and 6b', where the diastereoselectivity is actually slightly less in the solid state (49:31) than in solution (60:30). An attractive explanation for the variability of the diastereoselectivity ratios is that the molecular and environmental effects of the chiral substituents may either reinforce or oppose one another in the solid state. Depending on their relative magnitude, opposing effects could lead either to reduced or strongly reversed diastereoselectivity in the solid state compared to solution. An example of the latter situation is found in the case of photoproducts 2a and 2a', whose ratio changes from 60:40 in solution to 20:80 in the solid state.

Table 1. Photoproduct Ratios in the Solid State and Solution.^a

Reactant	Chiral Handle	2a:2a'		2b:2b'		6:6'		7:7'	
		Solid	Sol'n	Solid	Sol'n	Solid	Sol'n	Solid	Sol'n
1a	E' = COO(-)Menth ^b	20:80	60:40						
1b	E = COO(-)Menth ^b			50:50	50:50				
4	E' = COO(-)Menth ^b		39:17		22:22				
5a	X = CH ₂ OCO(-)CH(Me)NHAc ^c					32:36	47:38	24:08	08:07
5b	X = CH ₂ OCO(-)CH(Ph)OMe ^d					49:31	60:30	10:10	07:03

^aRatios determined at complete conversion in solution and $\leq 50\%$ in the solid state. No melting was observable in the solid state photolyses. ^bMenth = (1R,2S,5R)-(-)-Menthol ester; ^c(S)-(-)-N-Acetylalanine ester; ^d(R)-(-)- α -Methoxyphenylacetic acid ester.

A conclusion that may be drawn from the results for compounds 5a and 5b is that different chiral handles lead to different regioselectivities and diastereoselectivities, both in the solid state and solution. The effect of (non-chiral) substituents on di- π -methane regioselectivity has been documented previously in our laboratory,⁹ but the results reported in this communication represent the first examples of the effect of substituents on solid state versus solution di- π -methane diastereoselectivity. Regioselectivity changes were attributed⁹ to differential crystal packing arrangements around those portions of the reactant that are required to move most during the initial stages of reaction, i.e., the vinyl ester substituents. A similar interpretation is likely to be valid in the case of compounds 5a and 5b, but a detailed interpretation of the solid state structure-reactivity relationships involved must await X-ray crystal structure determinations that are not yet complete.

Finally, it is apparent that the location of the chiral handle in relation to the site of reaction (primarily a molecular rather than an environmental effect) has a strong influence on the diastereoselectivities observed. As can be seen from Scheme 1, in which the arrows indicate the locations of the vinyl carbon atoms involved in initial vinyl-benzo bridging,¹⁰ the nearer the chiral handle is to the reaction site, the more it influences diastereoselecti-

vity. This is most clearly seen in compounds 1a, 1b and 4, where the formation of photoproduct 2b is completely non-diastereoselective in contrast to the unequal distribution of diastereomers 2a and 2a'. The diminution of this effect in the case of compounds 5a and 5b is attributable to the fact that the chiral handles in these molecules are attached by four-bond "tethers" rather than the three-bond tethers present in adducts 1a, 1b and 4.

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5. Full synthetic details will be presented in a full paper. All new compounds reported in this communication exhibited spectra completely in accord with their assigned structures.

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10. Vinyl-benzo bridging refers to formation of a cyclopropyldicarbonyl diradical species by bonding between one of the vinyl carbon atoms and a neighboring aromatic carbon atom. While there is general agreement that this interaction precedes formation of the 1,3-biradical intermediate that leads to product, it is unclear whether cyclopropyldicarbonyl diradicals represent true minima on the di- π -methane rearrangement hypersurface. For leading references on the mechanism of the di- π -methane reaction, see reference 4 plus (a) L.A. Paquette and E. Bay, J. Org. Chem., 47, 4597 (1982); (b) W. Adam, M. Dorr, J. Kron and R.J. Rosenthal, J. Am. Chem. Soc., 109, 7074 (1987); (c) H.E. Zimmerman and A.P. Kamath, J. Am. Chem. Soc., 110, 900 (1988).

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