

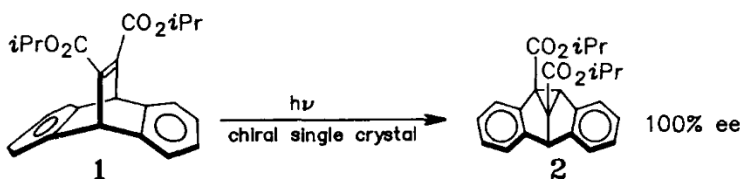
GENERATION OF OPTICAL ACTIVITY THROUGH SOLID STATE REACTION OF A RACEMIC MIXTURE THAT CRYSTALLIZES IN A CHIRAL SPACE GROUP

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Abstract. Because of disorder in the sec-butyl group, the photoreactive isopropyl/(R,S)-sec-butyl diester **3** is able to crystallize as a racemic solid solution in the chiral space group $P2_12_12_1$. Irradiation of single crystals of this material leads to products of high optical purity (80% ee). An accompanying process of kinetic resolution leaves the recovered starting material enriched in one of its enantiomers.

The synthesis of optically active compounds from racemic starting materials requires conditions that cause the two enantiomers to react at different rates. This is usually brought about through the influence of an external chiral agent that exerts different diastereomeric interactions in the transition states. However, prochiral compounds that crystallize in chiral space groups have asymmetric environments in their own crystal lattices and may react in the solid state to give optically active products without the need for other chiral reagents.¹ An example comes from our studies on the solid state di- π -methane rearrangement of dibenzobarrelene diesters. We have reported recently that photolysis of chiral single crystals of diisopropyl diester **1** leads to quantitative enantiomeric yields of dibenzosemibullvalene **2** (Scheme I).² In the present communication we report the generation of optically active products by solid state photoreaction of a racemic sec-butyl ester **3** (Scheme II), where both enantiomers are present in crystals of chiral space group $P2_12_12_1$.

SCHEME I

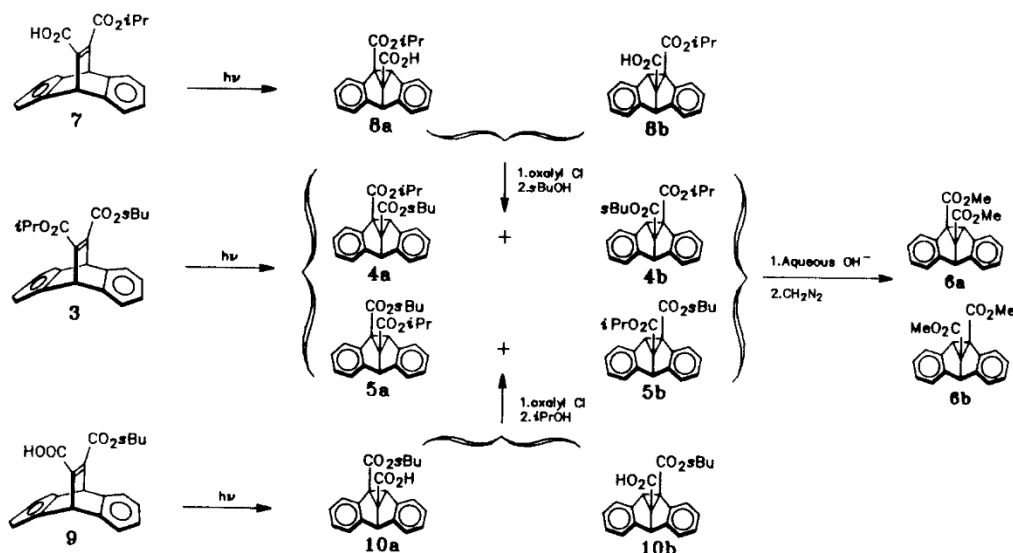


Compound **3** was prepared from the anhydride of the anthracene-acetylenedicarboxylic acid Diels-Alder adduct by reaction with isopropyl alcohol followed by esterification with either racemic (R,S)- or optically pure (S)-(+)-sec-butanol.³ Samples from each preparation were recrystallized from several solvents with no indication of polymorphism. The (R,S)- and (S)-(+)-sec-butyl-containing crystals exhibited markedly different melting points (122-124 and

133-135 ° C, respectively), but had identical morphologies and FTIR spectra. Preliminary X-ray diffraction analysis indicates that both materials are isostructural with **1** and crystallize in the chiral space group $P2_12_12_1$ with disorder in the sec-butyl group.⁴ It is precisely this disorder, which is well known for sec-butyl groups,⁵ that allows the racemic material to adopt a chiral space group.⁶

Di- π -methane photorearrangement of mixed diester **3** can give rise to four diastereomeric products that can be designated as **4** or **5** 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 (Scheme II). Although a tentative identification of photoproducts **4a**, **4b**, **5a** and **5b** could be made through a combination of 400 MHz NMR spectroscopy and capillary gas chromatography,⁷ in this communication we report only the 4:5 (regioisomeric) and **a**:**b** (enantiomeric) ratios, which were established unequivocally.

SCHEME II



Authentic samples of compounds **4a**, **4b**, **5a** and **5b** were synthesized independently as follows (Scheme II): the acid/esters **7** and **9** were prepared from the corresponding anhydride³ and photolyzed in acetonitrile to afford the dibenzosemibullvalene derivatives **8** and **10**.⁸ Esterification of **8** and **10** with the appropriate alcohol gave **4a/4b** and **5a/5b**, respectively, and gas chromatographic analysis of these mixtures established the retention times and permitted the

overall 4:5 product ratio to be determined in the photochemical runs. The a:b ratio was determined by complete hydrolysis of the photoproduct mixture and re-esterification with diazomethane to yield enantiomers 6a and 6b; the enantiomeric excess in this mixture was measured by ^1H NMR at 300 MHz using the chiral shift reagent $\text{Eu}(\text{hfc})_3$ (Aldrich).

The irradiations were conveniently carried out at room temperature using a pulsed nitrogen laser (337 nm). Single crystals of both (R,S)-sec-butyl-3 and (S)-(+)-sec-butyl-3 were photolyzed; conversions were kept below 25%. Each material was also photolyzed as a 0.1 M solution in benzene. The results from all four irradiations are summarized in Table I.

TABLE I. PHOTOPRODUCT DISTRIBUTION AND ENANTIOMERIC EXCESS AS A FUNCTION OF PHOTOLYSIS MEDIUM AND SEC-BUTYL CONFIGURATION.

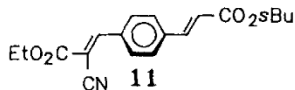
Reactant Structure	Photolysis Medium	4:5	a:b ^a
(S)-(+)-sec-butyl-3	solution	55:45	51:49
	single crystal	90:10	90:10
(R,S)-sec-butyl-3	solution	55:45	50:50
	single crystal	62:38	90:10

^aDextrorotatory enantiomer predominates; absolute configuration unknown.

The results show that no chiral selectivity occurred in the solution photorearrangement of racemic 3 (as expected) and that there is a very slight preference for regioisomer 4. Similar regioselectivity was observed for optically active 3 in solution, and in this case the "chiral handle" exerted a slight asymmetric induction. The solid state results were quite different. In both cases the solid state environment led to a dramatic increase in the formation of one substituted dibenzosemibullvalene configuration over the other (80% ee). Interestingly, the solid state rearrangements proceed with different regioselectivity, no doubt the result of packing differences between (R,S)-sec-butyl-3 and (S)-(+)-sec-butyl-3.⁹

The data in Table I raise the possibility that in the solid state photorearrangement of racemic 3, one enantiomer is reacting more rapidly than the other. If this is so, then the recovered starting material should be enriched in the slower-reacting enantiomer. This was verified experimentally. In the crystals examined (all from the same batch), the recovered starting material contained an excess of (S)-(+)-sec-butyl-3. From the specific rotation of this sample, we could conclude that the rate difference between enantiomers is approximately two-fold.

The results reported in this communication have a direct precedent in the pioneering work of Addadi and Lahav on the solid state [2+2] photocycloaddition reactions of diacrylate



derivative 11.¹⁰ This material also crystallizes in a chiral space group (P1) containing both enantiomers. Irradiation of crystals of 11 led to optically active dimers, trimers and oligomers, the optical purities of which varied from 0 to 100% depending on the R/S composition of the sample photolyzed.

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1. For a review on absolute asymmetric synthesis in solid state chemistry, see B.S. Green, M. Lahav and D. Rabinovich, Acc. Chem. Res., **12**, 191 (1979).

2. S.V. Evans, M. Garcia-Garibay, N. Omkaram, J.R. Scheffer, J. Trotter and F. Wireko, J. Am. Chem. Soc., **108**, 5648 (1986).

3. All new compounds described gave satisfactory elemental analyses and exhibited spectra completely in accord with their assigned structures. The anthracene-acetylenedicarboxylic acid Diels-Alder adduct anhydride was prepared by the method of O. Diels and K. Alder, Justus Liebigs Ann. Chem., **486**, 191 (1931).

4. (R,S)-sec-butyl-3: $P2_12_12_1$; $a = 8.4624(9)$, $b = 11.8705(11)$, $c = 21.6788(11)$ Å; $Z = 4$; $R = 10.1\%$. (S)-(+)-sec-butyl-3: $P2_12_12_1$; $a = 8.4936(7)$, $b = 11.9210(8)$, $c = 21.6691(12)$ Å; $Z = 4$; $R = 9.2\%$.

5. B.S. Green, R. Arad-Yellin and M. Cohen in "Topics in Stereochemistry," E.L. Eliel, S.H. Wilen and N.L. Allinger, Eds., Wiley Interscience, New York, vol. 16, 1986, pp. 146-147.

6. The possibility that isopropyl/(R,S)-sec-butyl-3 had undergone spontaneous resolution during recrystallization was investigated by measuring the rotation of solutions of chiral single crystals of this material. Several crystals had indeed undergone partial resolution with enantiomeric excesses of 5-15%. In no instance, however, was the extent of spontaneous resolution sufficient to account for the photoproduct optical activity.

7. J.R. Scheffer and M. Garcia-Garibay, unpublished results.

8. Approximately 10% of the alternative regioisomers were formed in each photolysis. The structure of the major photoproduct **8** (and, by analogy, that of **10**) was determined by conversion to the corresponding crystalline isopropyl/methyl diester whose X-ray crystal structure has been determined, J. Trotter and F. Wireko, unpublished results.

9. Medium- and packing-dependent regioselectivity differences are generally observed for the solid state di- π -methane photorearrangements of mixed dibenzobarrelene diesters, J.R. Scheffer and M. Garcia-Garibay, manuscript in preparation.

10. L. Addadi and M. Lahav, J. Am. Chem. Soc., **101**, 2152 (1979) and references cited therein.

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