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THE REGIOSELECTIVITY AND STEREOSELECTIVITY OF THE PHOTOREARRANGEMENT OF 3-METHOXY-4-METHOXYCARBONYL-4-METHYL-2,5-CYCLOHEXADIEN-1-ONE

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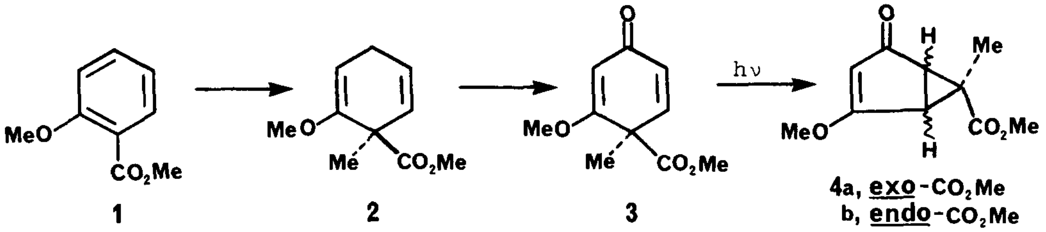
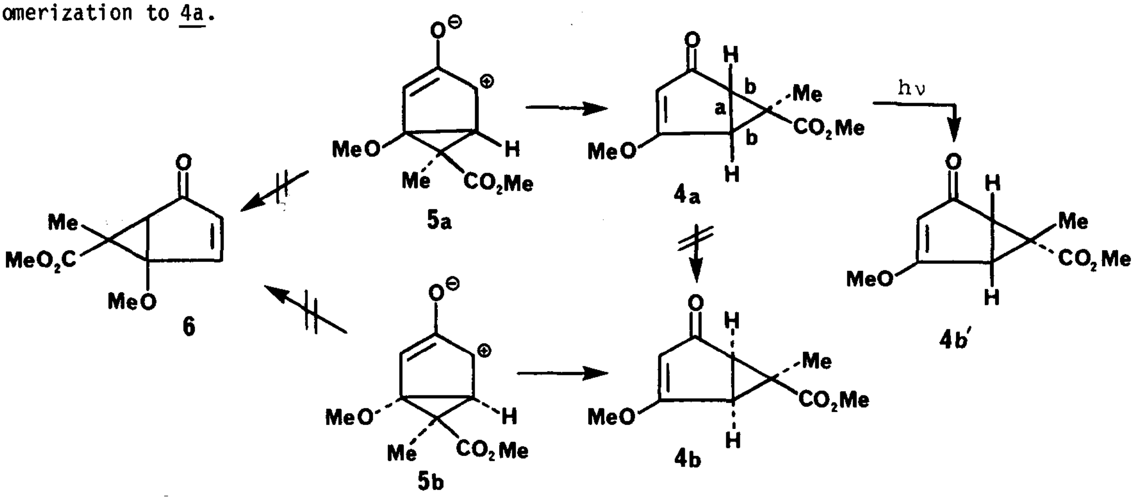
Summary: The photochemistry of racemic and enantiomerically pure 3-methoxy-4-methoxycarbonyl-4-methyl-2,5-cyclohexadien-1-one (3) is discussed.

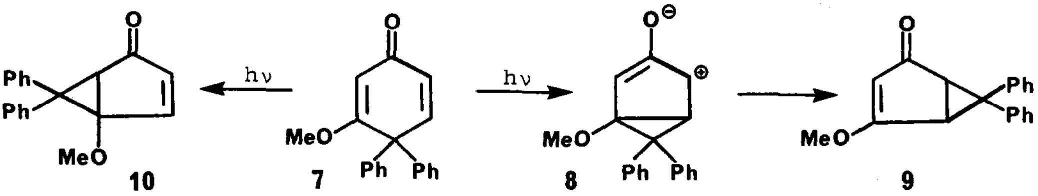
We wish to report that 3-methoxy-4-methoxycarbonyl-4-methyl-2,5-cyclohexadien-1-one (3) undergoes regiospecific photorearrangement to bicyclo[3.1.0]hex-3-en-2-one diastereoisomers 4a and 4b. Furthermore, we show that 1) enantiomerically pure 3 suffers photoracemization during photolysis at 366 nm, 2) bicyclohexenone 4a photoisomerizes to 4b' by external cyclopropane bond (b) cleavage, and 3) bicyclohexenones 4a and 4b do not photorevert to starting 2,5-cyclohexadienone 3 under the photolysis conditions used in these experiments. These observations underscore the importance of substituent effects on the generally accepted mechanisms for 2,5-cyclohexadienone and bicyclo[3.1.0]hexenone photorearrangements.[1]



Cyclohexadiene 2 is prepared by Birch reduction-alkylation of 1,[2] and 2 is converted to racemic 2,5-cyclohexadienone 3 by allylic oxidation with pyridinium dichromate (PDC) in refluxing chloroform solution.[3,4] Irradiation of 3 in deareated benzene solution with 366 nm light[5] produces a diastereoisomeric mixture of bicyclo[3.1.0]hexenones 4a and 4b. Continued irradiation (366 nm) of the mixture of 4a and 4b results in photoisomerization of 4a to give predominately the endo-methoxycarbonyl diastereoisomer 4b (95%),[6] unreacted 4a, and a trace of phenolic products. On the other hand, irradiation of 4b did not result in detectable photoisomerization to 4a.



We assume that zwitterions 5a and 5b are intermediates in the conversion of 3 to 4a and 4b.[1] Subsequent rearrangements of 5a and 5b apparently occur regiospecifically to give 4a and 4b, but not 6. These observations contrast with those of Zimmerman and Pasteris pertaining to photorearrangements of 3-methoxy-4,4-diphenyl-2,5-cyclohexadien-1-one (7) to a regioisomeric mixture of 9 and 10 (1.4:1).[7] In a separate experiment, zwitterion 8 (prepared by a non-photochemical technique) was found to rearrange exclusively to 9. Zimmerman suggested that rearrangement of 7 to 10 occurs from "an electronically excited (triplet) bridged species" distinct from 8. Our studies with 3 and several other 3-methoxy-4-methoxycarbonyl and 3-methoxy-4-cyano-2,5-cyclohexadien-1-ones demonstrate that photorearrangements of these compounds *occur exclusively to give the type 4 bicyclohexenone.*[8]



Rodgers and Hart[9] have reported that the stereoselectivity of photorearrangements of 2,5-cyclohexadienones to bicyclo[3.1.0]hexenones is dependent upon steric factors at C(3), C(4), and

C(5). Photointerconversion of bicyclohexenones was not reported in the Rodgers and Hart study. Both the Zimmerman and Schuster research groups have demonstrated that bicyclohexenone epimers do not interconvert under a variety of photochemical conditions.[10] Thus, photoisomerization of 4a to 4b appears to be without precedent, although the photosensitized epimerization of the structurally related bicyclo[3.1.0]hex-2-ene-6-*endo*-carboxylic acid and its methyl ester has been found to occur by cleavage of the external cyclopropyl bond.[11]

We have investigated the mechanism of bicyclohexenone formation and rearrangement by irradiation of enantiomerically pure 3 (absolute configuration as shown). This material was prepared by utilization of our recently reported method for performing an enantioselective Birch reductive alkylation.[12] The enantiomeric purities of 3 ($[\alpha]_D^{24}$ -7.14°; 8.56×10^{-2}M in MeOH) and derived bicyclohexenones 4a and 4b were determined by use of the chiral ^{1}H NMR shift reagent tris[3-((heptafluoropropyl)hydroxymethylene)-*d*-camphorato]europium(III), *i.e.*, Eu(hfc)$_3$.

After 20% photoconversion of 3, recovered 3 (silica gel flash chromatography) was found to be a 5:1 mixture of enantiomers, while 4a and 4b ($[\alpha]_D^{25}$ +205°) were each obtained as a 5:1 mixture of enantiomers (fortuitous equivalent enantiomeric distribution). Complete photorearrangement of 3 produced 4a ($[\alpha]_D^{23}$ -130°; 3:1 mixture of enantiomers) and nearly racemic 4b ($[\alpha]_D^{31}$ + 14.0°). Finally, irradiation of the 3:1 enantiomeric mixture of 4a (isolated by silica gel flash chromatography) provided a 1:3 enantiomeric mixture of 4b and 4b' ($[\alpha]_D^{23}$ -106°; 50% conversion of 4a), but recovered 4a had not lost optical activity.

These results emphatically demonstrate that 1) there is a pathway for return of the excited state of 3 and/or zwitterion 5 to starting 2,5-cyclohexadienone 3 that involves cleavage of one or both of the ring bonds to C(4),[13] 2) both diastereoisomeric zwitterions 5a and 5b are produced by photorearrangement of 3; 5a and 5b presumably rearrange to 4a and 4b by the Zimmerman "slither" mechanism,[1] 3) the photochemical conversion of 4a into 4b' occurs by external cyclopropane bond (b) cleavage; 4a does not undergo internal cyclopropane bond (a) cleavage to give 4b, and 4) the pathway for conversion of 4a into 4b' does not include a detectable shunt to starting 2,5-cyclohexadienone 3.[14]

A noteworthy feature of the photorearrangement of 3 is the excellent photochemical stability of the photoproduct 4b. In contrast to the reactivity of other bicyclo[3.1.0]hexenones,[1] 4b does not easily photorearrange to phenols at 366 nm (*vide supra*). We expect that substrates of type 4b will be useful intermediates for organic synthesis.[15] Bicyclohexenone 4b (and analogs)[8] can be prepared in three laboratory steps from methyl *o*-methoxybenzoate with excellent regiochemical and diastereochemical control. Preservation of configuration at C(4) in 3 is not possible at this time, but future studies of substituent effects on the photorearrangement of 2,5-cyclohexadienones may reveal a suitable control element.

Acknowledgment. This work was supported by the National Science Foundation (CHE83-19474).

References and Notes

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3. (a) Corey, E. J.; Schmidt, G. *Tetrahedron Lett.* 1979, 399. (b) Bonadies, F.; Di Fabio, R. *J. Org. Chem.* 1984, 49, 1647.

4. Satisfactory combustion analyses were obtained for all new compounds.

5. A Hanovia 450-W medium pressure Mercury-arc lamp in a Pyrex immersion well fitted with Corning color filters 0-25 and 7-54 was employed as the 366 nm light source.

6. Stereochemistry in 4a and 4b is assigned by ^{1}H NMR spectral data and comparisons to an analog of 4b, for which an X-ray structure determination has been performed.

7. Zimmerman, H. E.; Pasteris, R. J. *J. Org. Chem.* 1980, 45, 4876.

8. A more complete study of substituent effects will be published in the full account.

9. Rodgers, T. R.; Hart, H. *Tetrahedron Lett.* 1969, 4845 and references cited therein.

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12. (a) Schultz, A. G.; Sundararaman, P. *Tetrahedron Lett.* 1984, 25, 4591. (b) Schultz, A. G.; Sundararaman, P.; Macielag, M.; Lavieri, F. P.; Welch, M. *Tetrahedron Lett.* 1985, 26, 4575. (c) For a synthetic application, see Schultz, A. G.; Puig, S. *J. Org. Chem.* 1985, 50, 915.

13. For a demonstration of zwitterion return to starting 2,5-cyclohexadienone by a kinetic analysis, see Schuster, D. I.; Liu, K.-C. *Tetrahedron* 1981, 37, 3329.

14. The consequences of various cyclopropane bond cleavages in bicyclo[3.1.0]hexenone photochemistry are discussed in reference 1a, p. 192.

15. Recent synthetic applications from our laboratory include (a) Schultz, A. G.; Myong, S. O.; Puig, S. *Tetrahedron Lett.* 1984, 25, 1011. (b) Schultz; A. G.; Puig, S.; Wang, Y. *J. Chem. Soc., Chem. Commun.* 1985, 785.

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