

ASYMMETRIC INDUCTION IN SIMPLE [2 + 2] PHOTOADDITIONS

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Abstract: Photochemical cycloaddition of cyclopentene with enone esters 1 containing different chiral auxiliaries yielded *anti* and *syn* adducts 2 and 3 in good yield and with moderate to high (79%) enantiomeric excesses.

Asymmetric induction in organic synthesis has received considerable attention in the last few years particularly as applied to such areas as the Diels-Alder and ene reactions, hydride reductions, alkylations, 1,2- and 1,4-additions to carbonyl systems, epoxidations, and catalytic processes.¹⁻⁶ But only the following few examples of asymmetric induction in photochemical cycloadditions have been reported: formation of oxetanes from optically active phenylglyoxylic acid ester,^{7,8} cycloadditions in chiral crystals,⁹ photoaddition of stilbene to optically active fumarates,¹⁰ and photoaddition of dicinnamate esters of optically active diols.¹¹ We wish to report our successful attempts at induction using simple substrates to form cyclobutane adducts which are potentially useful for the synthesis of several natural product carbon skeletons.

Irradiation (350 nm) of a toluene solution of excess cyclopentene with the optically active enone esters 1a-c gave in varying proportions the *cis-anti-cis* adducts 2a-c and the *cis-syn-cis* adducts 3a-c, respectively. Table 1 reports the adduct distribution for each of the irradiations and includes for comparison the result with the methyl ester 1d.¹² This table indicates that as the effective size of the R group increases from methyl to 8-phenylmenthyl, the proportion of adduct 2 decreases. Examination of the adduct 2 shows that the cyclopentane ring and the ester group are on the same face of the cyclobutane ring and as the size of the ester group is increased the steric interaction between these two moieties increases, whereas in 3 this interaction is not present. Thus by varying the size of the R group we have the capability of altering the proportions of adducts 2 and 3, a feature which could be of use in synthetic planning.

Table 1 Ratio of Photoadducts

<u>R</u>	<u>Adduct</u>	
	<u>2</u>	<u>3</u>
(-)-8-phenylmenthyl (<u>a</u>)	60%	40%
(-)-menthyl (<u>b</u>)	70	30
(-)-bornyl (<u>c</u>)	83	17
methyl (<u>d</u>)	90	10

Each of the adducts 2a-c and 3a-c are a mixture of two diastereomers because of the presence of the chiral auxiliary R. The proportions of the two diastereomers in 2a, for example, are a measure of the asymmetric induction in the photoaddition. Obviously, in the irradiation with the methyl ester 1d, both adducts 2d and 3d are racemic mixtures. Although the adducts 2 and 3 could be separated by chromatography,¹³ it was not possible to separate the diastereomeric mixtures of each adduct by tlc or hplc and furthermore ¹H and ¹³C nmr analysis of the mixtures did not always give conclusive results. Thus adducts 2 and 3 were separated by flash chromatography and converted to their methyl esters using vigorous saponification conditions (very hindered esters) followed by methylation with diazomethane. The enantiomeric



excess (e.e.) present in the methyl esters 2d derived from 2a-c and in 3d derived from 3a-c was then determined by ¹H nmr in the presence of a chiral lanthanide shift reagent¹⁴ (Table 2). For each entry, the rotation of the derived methyl ester was consistent with the e.e. value.

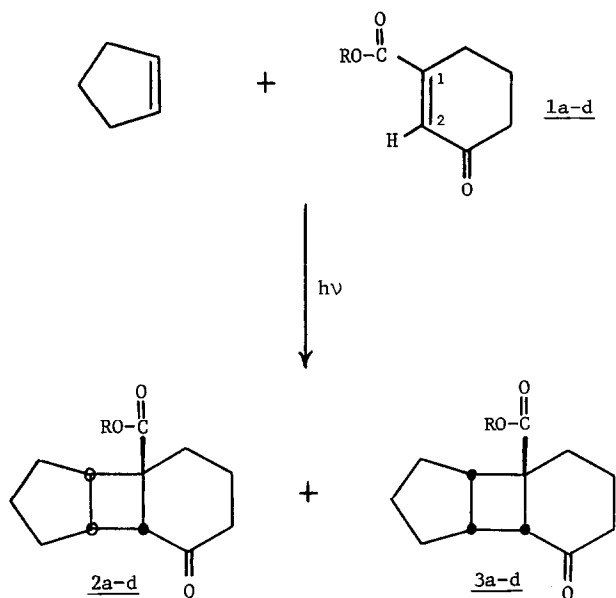
Table 2 Asymmetric Induction of Adducts as Determined from Derived Methyl Esters 2d and 3d

<u>Chiral Auxiliary, R</u>	<u>2</u>		<u>3</u>	
	<u>e.e.</u>	$[\alpha]_D^{20}$	<u>e.e.</u>	$[\alpha]_D^{20}$
(-)-8-phenylmenthyl (<u>a</u>)	30%	+31°	79%	+215°
(-)-menthyl (<u>b</u>)	18	+25°	25	+37°
(-)-bornyl (<u>c</u>)	4	+7°	-	-

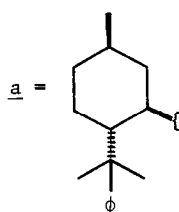
A number of conclusions may be drawn from the results recorded in Table 2. First, it is possible to obtain high asymmetric induction (e.g. 79% for 3a) in these simple mixed photoadditions yielding cyclobutane adducts. Secondly, of the three chiral auxiliaries used in this study, the 8-phenylmenthyl group was the most effective at promoting this diastereoselection process. This same group has been effective in similar studies of the Diels-Alder reaction¹⁵ and preferred conformations which block one face of the ester enophile have been proposed.^{4,16} We will withhold such speculation in this study until the absolute configurations of the major diastereomers in 2 and 3 have been determined.¹⁷ Thirdly, the induction process appears to be more effective in the formation of the *syn* adduct 3 rather than the *anti* adduct 2 (e.g. 79% vs. 30% for 3a vs. 2a).

Finally, we have shown that substantial asymmetric induction is possible in photoadditions which yield adducts with potential use in natural product synthesis. We intend to employ a related system in an approach to the synthesis of members of the capnellane family of tricyclopentanoid sesquiterpenoids. We have also shown that the chiral auxiliary may be used to alter the regioselectivity (*syn* vs. *anti* adducts) of the photoadditions as well as to control the degree of asymmetric induction. A detailed study of other factors which may influence these product ratios is now underway.

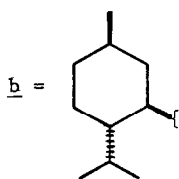
Scheme 1



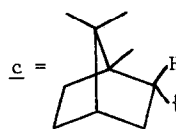
R group:



(-)-8-phenylmenthyl



(-)-menthyl



(-)-bornyl

d = CH₃

References and Notes

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12. Preparation of esters 1 and structural elucidation of adducts 2 and 3 will be published elsewhere. A single crystal X-ray analysis of 2d has been performed.
13. Adducts 3 were always less polar than 2 on silica gel chromatography with 10% ethyl acetate/petrol as solvent.
14. The shift reagent employed was tris[3-(heptafluoropropylhydroxymethylene)-d-camphorato], europium(III) and the areas of the two unequal methyl ester peaks were used to determine the e.e. values. Each entry in Table 2 is an average of at least two runs.
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17. It is noteworthy that in the nmr spectra of enone esters 1b and 1d the vinyl proton (H-2) appears at δ 6.72 and 6.60, respectively, while in 1a this proton is significantly shielded by the phenyl ring and appears at δ 6.15 ppm.

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