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ASYMMETRIC INDUCTION IN MIXED [2 + 2] PHOTOADDITIONS EMPLOYING A CHIRAL AUXILIARY IN THE ALKENE COMPONENT

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Abstract: Asymmetric induction was achieved in the photoaddition of 3-methyl-2-cyclohexenone to optically active enoates 1a-c and the absolute configuration of the major adduct was determined.

In a previous communication we reported observing up to 79% π-face selectivity in the [2 + 2] photoaddition of cyclopentene to enones containing an optically active ester substituent.[1] In this letter we report our results of mixed [2 + 2] photoadditions where the chiral auxiliary is attached to the alkene component rather than the enone.

Irradiation at 350 nm of a toluene solution of excess 3-methyl-2-cyclohexenone with the chiral enoates 1a-c gave the *cis-anti-cis*, head-to-head adducts as inseparable mixtures of diastereomers 2a-c and 3a-c, respectively.[2] Photoaddition of achiral 1d was also performed to provide a racemic mixture of adducts 2d and 3d, which was used as a check in the asymmetric induction determinations. The diastereomeric excess (d.e., % of 2 minus % of 3) was determined for the irradiations with 1a-c using ^{1}H nmr[3] and the results are reported in Table 1.

Conversion of diastereomeric adduct mixtures 2a-c and 3a-c to 4 resulted in loss of the chiral auxiliary and formation of the lactone as an unequal mixture of enantiomers. This reduction and spontaneous lactonization was effected in high yield with $NaBH_4$ in refluxing dry methanol (1.5 hrs. for 2b,c/3b,c, 3 hrs. for 2a/3a).[4] The fact that 2 and 3 yielded lactone 4 by initial attack of hydride from the less hindered face of the cyclohexanone ring confirmed the regio- and stereochemistry proposed for these adducts. The lactones 4 obtained from each reduction were purified by preparative gc[5] to separate them cleanly from the chiral auxiliaries and the enantiomeric excess (e.e.) was determined by ^{1}H nmr in the presence of a chiral solvating agent (CSA).[6,7] Table 1 indicates there is excellent agreement between the d.e. values of the adducts and the e.e. values of the lactones for all three chiral auxiliaries. The specific rotations obtained for the lactones (Table 1) were also consistent with the e.e. values assuming a linear relationship between the two. From these results it is clear that 8-phenylmenthyl is the most effective of the three groups in achieving these asymmetric inductions. This was also the case in our previous study where the chiral auxiliary was attached to the enone.[1]

Table 1 Asymmetric Induction in Adducts 2a-c/3a-c and Lactone 4

chiral auxiliary, R	d.e. of adducts[a]	e.e. of 4[b]	4, $[\alpha]_D^{20}$ ($CHCl_3$)
(-)-8-phenylmenthyl (a)	56%	57%	+138°
(-)-menthyl (b)	13	12	+26°
(-)-bornyl (c)	19	18	+46°

[a] % of 2 minus % of 3. [b] % of (+)-4 minus % of (-)-4.

We wished to determine the absolute configuration of the major enantiomer in lactone 4 as this would indicate the preferred reacting conformation of enoates 1 during the photoaddition. Since the γ-lactone moiety in 4 is essentially planar and no other basic sites are present in the molecule, it would be expected to coordinate with the CSA to form a two-point solvate[8,9] as depicted in 5 for the 3R,8R-enantiomer. This arrangement implies that the α-hydrogen on C(8) would be shielded by the aromatic anthryl system while the β-proton on C(3) would be deshielded by the CF_3 group.[9] Examination of the 400 MHz ^1H spectra of lactones 4 (derived from 2a-c/3a-c mixtures) in the presence of the CSA showed the H(8) signal of the major enantiomer appeared upfield (δ 2.46, shielded) and the H(3) resonance appeared downfield (δ 4.64, deshielded) relative to the smaller signals at δ 2.52 and 4.60, respectively, for the minor enantiomer. This analysis established that the major (+)-enantiomer of 4 must have the 3R,8R-configuration and thus the major adduct must have the absolute configuration depicted for 2 in Scheme 1. Therefore, enoates 1a-c must possess C(α)-*re*-face directing ability in the photoaddition step. By analogy to the conformations proposed for the 8-phenylmenthyl acrylates in the Diels-Alder[10] and the 1,4-addition reactions,[11] we assumed enoate 1a would adopt the conformation shown in 6. The *syn*-planar orientation of the carbinol hydrogen (e.g. H(1') in 1a) and the carbonyl group in 1a-c was confirmed by aromatic solvent induced shift (ASIS) studies,[12] in that the carbinol hydrogen experienced a deshielding effect in all three compounds.[13] Conformation 6 shows that in the *s-trans* enoate 1a the phenyl ring sterically blocks the C(α)-*si*-face[14] and consequently the photoaddition is directed predominantly to the C(α)-*re*-face to give adduct 2a, which upon reduction gives (+)-4 lactone.

In conclusion, we have shown that moderate asymmetric induction is possible in photoadditions where the chiral auxiliary is attached to the alkene (enoate) component. We have also determined the absolute configuration of the major enantiomer of a lactone derived from the photoadducts and thus were able to suggest the preferred conformation of the chiral enoate in the photoaddition step. The results outlined in this study and in our previous report[1] should provide insights which will be useful in designing systems that yield even higher photoinductions.

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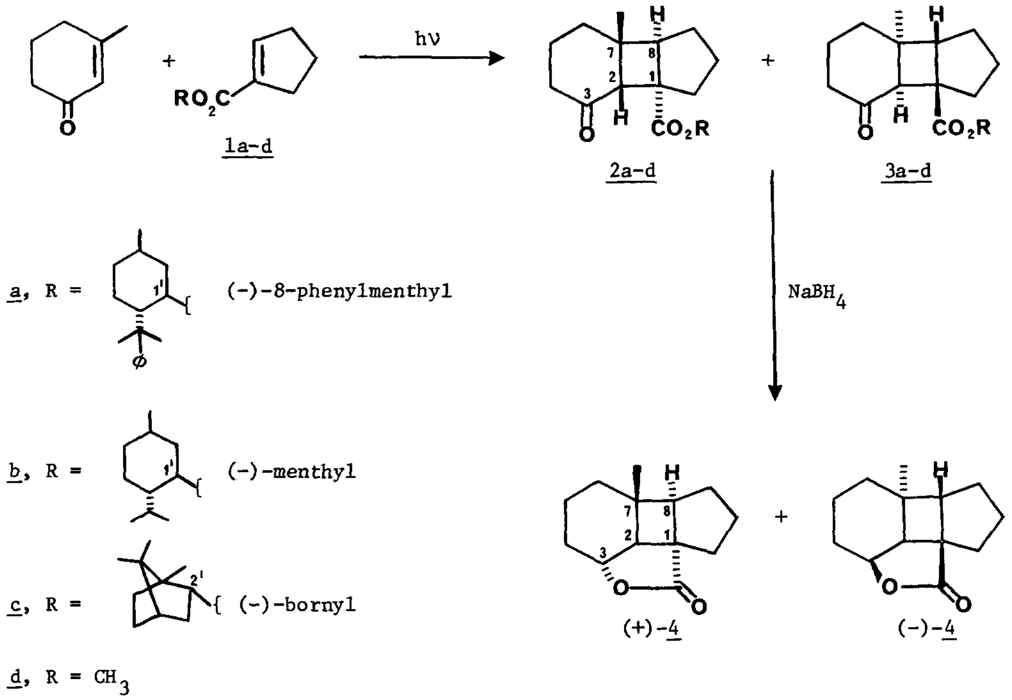
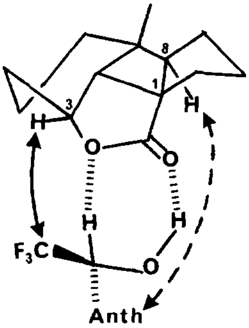
Scheme 1



(+)-4 : CSA Complex



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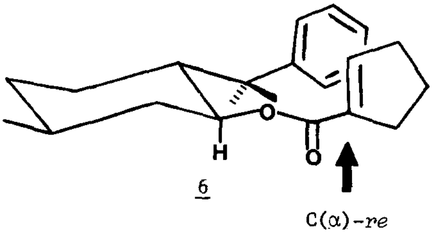
Conformation of 1a



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References and Notes

1. G.L. Lange, C. Decicco, S.L. Tan, and G. Chamberlain, *Tetrahedron Lett.*, 26, 0000 (1985).
2. Combined yields of the adducts based on reacted 1 were 2a/3a 51%, 2b/3b 54% and 2c/3c 57%.
3. The d.e.'s for adducts 2a/3a and 2c/3c were determined by measuring the unequal areas of the signals ($\delta\sim4.8$) for H(1') and H(2'), respectively. For 2b/3b, the d.e. was determined from the areas of the H(8) doublets ($\delta\sim2.65$).
4. In contrast, the reduction of 2d/3d, which does not contain a bulky chiral auxiliary, was effected at room temperature in 1.5 hrs.
5. A 6 ft. x 0.25 in. 20% OV 210 column operating at 200° was used for these separations. The retention time for 4 was 10.8 min.
6. W.H. Pirkle and D.J. Hoover in *Topics in Stereochemistry*, Vol. 13, Eds. N.L. Allinger, E.L. Eliel, and S.H. Wilen, Wiley-Interscience, New York, N.Y., 1982, p. 263.
7. The CSA used was (S)-(+)-2,2,2-trifluoro-1-(9-anthryl)ethanol. The areas of the unequal doublets for H(8) were used to determine the e.e. values. All samples were run in CCl_4 at 400 MHz. with 3 molar equivalents of the CSA.
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12. J.D. Connolly and R. McCrindle, *Chem. Ind.*, 379 (1965).
13. The ASIS values $[\delta(C_6D_6) - \delta(CDCl_3)]$ determined for the carbinol hydrogen in 1a, 1b, and 1c were $\Delta\delta$ +0.27, +0.23, and +0.22 ppm, respectively.
14. The vinyl proton of enoates 1b-d appeared at δ 6.75, 6.77, and 6.78 respectively, while in 1a this proton was significantly shielded by the phenyl group and appeared at δ 6.22 in $CDCl_3$ solvent.

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