ASYMMETRIC INDUCTION IN MIXED [2 + 2] PHOTOADDITIONS.

EFFECT OF SOLVENT, ALKENE CONCENTRATION AND TEMPERATURE

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Abstract: In mixed [2 + 2] photoadditions with the chiral auxiliary in either the enone or the alkene component, it was found that changing the polarity of the solvent or the temperature of the irradiation had a marked effect on the extent of asymmetric induction.

In two previous Letters we reported that significant asymmetric inductions were achieved in mixed [2 + 2] cyclobutane-forming photoadditions when various chiral auxiliaries were attached to the enone component <u>1</u> (reaction 1)¹ or to the alkene component <u>4</u> (reaction 2).^{2,3} Inductions as high as 79% and 57% respectively, were achieved in the two studies with the (-)-8-phenylmenthyl group as the chiral auxiliary and toluene as the solvent. In this Letter we report the effect on the extent of asymmetric induction of changing (a) the polarity or acidity of the solvent in reactions (1) and (2), (b) the concentration of cyclopentene in reaction (1), and (c) the temperature of the irradiations.



In the reaction of <u>1</u> with cyclopentene, the major product is the <u>cis-anti-cis</u> adduct <u>2</u> and the minor product is the <u>cis-syn-cis</u> isomer <u>3</u>.¹ The d.e.'s (diasteromeric excesses) determined for the latter adduct <u>3</u> are generally quite high (Table 1) so our major goal in this investigation was to improve the d.e. of the major adduct <u>2</u>. Normally in mixed photoadditions the alkene component is in excess (5- to 20-fold) to minimize side reactions of the enone such as dimerization. In reaction (1) with toluene as solvent there was a significant increase in the d.e. of adduct <u>2</u> (30 to 49%) when the equivalents of cyclopentene were reduced from 20 to 1.5 (Table 1, entries 5 and 6). With methanol as solvent, there was a similar increase in the d.e. of <u>2</u> (37 to 51%) when the cyclopentene concentration was decreased (Table 1, entries 7 and 8). Clearly, at lower alkene concentrations there is greater face selectivity in the cycloaddition reaction.

The effect of solvent and acidity on the extent of asymmetric induction in reactions (1) and (2) was our primary interest in this study. Table 1 (entries 1, 2, 8, and 9) shows that there was a gradual improvement in the d.e. of adduct $\underline{2}$ as the H-bonding ability of the solvent was increased.⁴ The addition of Lewis acids such as $Ti(OPr^1)_4$ and Me_3SnC1 (entries 3 and 4) caused no significant increase in the d.e. but the use of acetic acid in a mixed solvent gave considerably higher d.e.'s (entries 10 and 11). The use of stronger acids such as trifluoroacetic acid resulted in decomposition of the starting material during the irradiation.

A similar investigation with reaction (2) indicated that the solvent had an even more dramatic effect on the d.e. of adduct 5. The highest d.e. was obtained with the solvent cyclohexane (Table 2, entry 1) and as the hydrogen bonding ability of the solvent was increased the d.e. got progressively lower. With trifluoroethanol as solvent, the major diastereomer possesses the 6S absolute configuration rather than 6R, which is the predominant diastereomer in the other solvents (Table 2). In concert with this trend, Table 2 also reveals that the chemical shift of the H-2 vinyl proton in enoate $\frac{4}{2}$ gradually moves downfield as the H-bonding ability of the solvent is increased.

To account for the solvent effects observed, we propose that in reactions (1) and (2) the face selectivity is high and that the d.e.'s are controlled primarily by the s-cis:s-trans ratio in the enoates 1 and 4. In an extreme case, one could argue that a system could exhibit 100% face selectivity but if the s-cis:s-trans ratio of the enoate was 1:1, the resultant d.e. would be zero. We suggest that as the H-bonding ability or the acidity of the solvent increases the percentage of the s-trans conformer in either 1 or 4 also increases.⁵ In reaction (2) the absolute configuration of the major diastereomer 5 is known to be 6R and thus we can infer that s-cis is the major reacting conformation of 4 (shown in reaction 2) in solvents such as cyclohexane.² As the H-bonding ability of the solvent increases the percentage of the s-trans conformer of 5 then has the 6S configuration (Table 2). Further, we suggest that in the s-trans conformer of 4, H-2 is deshielded by the phenyl substituent of the chiral auxiliary and as the percentage of this conformer increases in the more polar solvents, the chemical shift for that proton moves downfield (Table 2).⁶ By

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Entry	<u>Solvent</u>	Equivalents of Cyclopentene	d.e. of adduct 2 ^a	d.e. of adduct 3 ^a
1	cyclohexane	1.5	32%	-
2	CH ₂ C1 ₂	1.5	37	68%
3	$CH_2Cl_2 + Ti(OPr^{i})$ (2 equiv.)	1.5	37	67
4	CH ₂ Cl ₂ + Me ₃ SnCl (2 equiv.)	1.5	41	66
5	toluene	20	30	79
6	toluene	1.5	49	79
7	methanol	20	37	68
8	methanol	1.5	51	78
9	trifluoroethanol	1.5	56	78
10	5% HOAc/MeOH	1.5	63	-
11	95% HOAc/MeOH	1.5	68	76

Table 1 Solvent and Alkene Concentration Effects in Reaction (1)

^a The d.e.'s of <u>2</u> and <u>3</u> were determined by comparing the areas of the H-7 doublets and the carbinyl multiplets (in the 8-phenylmenthyl group) in the ¹H nmr spectra of the diastereomeric mixtures.

Table 2 Solvent Effects in Reaction (2)

Entry	Solvent	d.e. of adduct 5 ^a	abs. config. of major diastereomer	<u>δ(ppm) of</u> <u>H-2 in 4</u>
1	cyclohexane	62 %	6R	6.12
2	CH2C12	52	6R	6.18
3	toluene	56	6R	6.22
4	methanol	30	6R	6.45
5	trifluoroethanol	12	68	6.89

^a The d.e.'s of 5 were determined as previously reported.²

analogy, in reaction (1) the major reacting conformation of <u>1</u> is s-<u>trans</u> (shown in equation 1) even in cyclohexane and in the better H-bonding solvents or in acidic media the percentage of this conformer increases and consequently the d.e. of adduct <u>2</u> also increases.⁷

Table 3 indicates that when the temperature of reactions (1) and (2) was lowered from 10° to -60° C, the d.e.'s for adducts 2 and 5, respectively, improved significantly. A study conducted by another group with components similar to those employed in reaction (1) showed no difference in the d.e.'s of an adduct obtained at 23° vs. -40° C, 3° while in an investigation of a Diels-Alder reaction it was reported that the d.e.'s of the adduct were significantly enhanced as the reaction temperature was lowered.⁸ The data in Table 3 suggest that as the temperature of the enoate solutions is lowered the percentage of the more stable conformers (s-trans for 1 and s-cis for 4) is enhanced and the d.e.'s of the resultant adducts are increased. A 13 C study of dienones showed that there is a shift towards the more stable conformer as the temperature is lowered.⁹

		Table 3 D.e.'s o	Adducts 2 and 5 at 10° vs. -60° C		D.e.'s ^a at	
	Reaction	Enoate	Solvent	Adduct	10 ⁰ C	-60°C
	(1) ^b	<u>1</u>	methanol	2	51%	68%
	(2)	<u>4</u>	toluene	<u>5</u>	56	74
a	Determined a	s described in Tables 1 a	and 2. ^b With 1.5	equivalents of cycl	opentene.	

In conclusion, we have presented evidence to suggest that an important factor in determining the extent of asymmetric induction in these [2 + 2] photoadditions is the position of the s-<u>cis</u>:s-<u>trans</u> conformational equilibrium in the enoate containing the chiral auxiliary.

We have shown also that the position of this equilibrium may be shifted, and consequently the d.e. of the resultant photoadduct changed, by varying the H-bonding ability or acidity of the solvent or by lowering the temperature of the irradiation.

References and Notes

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