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REVERSAL OF DIASTEREOSELECTIVITY IN PROTONATION OF CHIRAL PHOTODIENOLS

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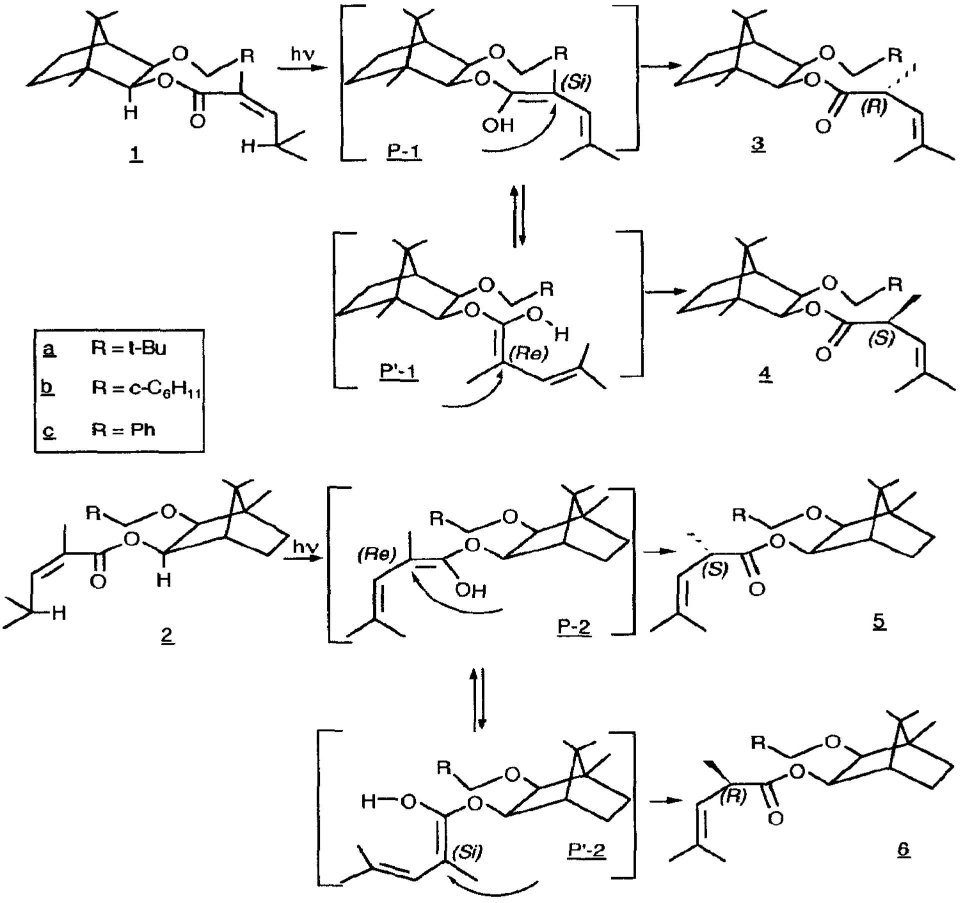
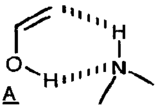
Abstract : *The configuration of the new asymmetric center created in the photodeconjugation of an α-substituted α,β-unsaturated ester derived from exo, exo-benzyloxybornanol depends on the structure of the achiral species used as the catalyst of the protonation of the* ***intermediate*** *dienol. Thus, the ratio of the deconjugated diastereoisomers varies from 91/9 to 37/63.*

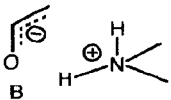
Irradiation of α-substituted conjugated esters in the presence of small quantities of optically pure Nor-ephedrine derivatives has been shown to produce deconjugated esters with enantioselectivities up to 70%[1]. A study of the effect of substituents either on the ester or on the inductor indicated that chiral recognition did not involve strong steric interactions between the alkoxy part of the ester and the aminoalcohol[2]. When esters of chiral alcohols were irradiated in the absence of chiral inductors, deconjugated isomers were produced with poor diastereoselectivities, except for esters of very hindered alcohols such as 1a and 2a[3]. The photodeconjugation of (R)-2-octyl or (R)-2-bornyl esters which are slightly crowded, in the presence of (+) or (-) ephedrine, created a new asymmetric center whose configuration was determined by the structure of the inductor, while under the same conditions, the new asymmetric center of hindered esters proceeded by a protonation from the less hindered side of the dienolic intermediate P-1 and P-2 whose formation and geometry were deduced from the favoured conformation of the starting material[4] and the mechanism of photoenolisation[3,5].

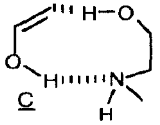
Taking into account these observations, the study of the photodeconjugation of 1b, 1c, 2b and 2c also prepared from (+) camphor has been undertaken to determine the influence of the substituents of the alkoxy side-chain on the diastereoselective step. We now report that an apparent protonation from the most hindered side can be the dominant process when the deconjugation is carried out in the presence of aminoalcohols.

From the results summarized in the table, it appears that methanol, secondary amines (runs 1, 4, 5, 11 and 12), and even an aminoalcohol (run 15) provided protonation mainly from the less hindered side of P-1 and P-2 as previously observed from 1a and 2a[3]. Catalysis of the tautomerism dienol/deconjugated ester by amines could be explained by transition states A or


hν
(Si)
OH
P-1
1
3
(R)
P'-1
(Re)
4
(S)
a R = t-Bu
b R = c-C6H11
c R = Ph
2
hν
(Re)
OH
P-2
5
(S)
P'-2
(Si)
6
(R)
H
O
R


A


B


C

B[6] and best rationalized by a 9-membered transition state C[2] in the presence of aminoalcohols.

The use of (+) or (-) ephedrine (runs 2, 3, 6, 7, 13 and 14) instead of methanol or amines often provided a large decrease and sometimes an inversion of the diastereoselectivity. These results can not be explained in considering only the cyclic transition state C previously proposed to rationalize the enantiodifferentiations obtained from achiral esters[2]. Indeed, no increase of diastereoselectivity was observed when a synergistic effect was expected for C (runs 3, 7 and 13). Obviously, the inversion of stereoselectivity can not be attributed to an antagonistic effect since the use of an achiral aminoalcohol (run 8) rather than (+) ephedrine (run 6) provided a similar result. The inversion of diastereoselectivity was limited to catalysis by an aminoalcohol: when the hydroxy group of the catalyst was replaced by a methoxy group the effect was suppressed (runs 6 and 10, 8 and 9). Furthermore, since the inversion was exclusively attained from 1c and 2c, the participation of the phenyl group of the alkoxy side-chain seems to be involved. An intramolecular hydrogen bonding between hydroxyl and phenyl groups[7] might

Table : Irradiation at λ = 254 nm of deoxygenated solutions of 1b, 1c, 2b and 2c in hexane (a) ($c=10^{-2}$M) containing AH (0.1 equiv.)

Run	SM	AH	t°C	Ratio[10] 3 : 4 or 5 : 6	Yield %
1	1b	i.Pr_2NH	-60	3 : 4 90 : 10	64
2	"	(+) ephedrine	-50	52 : 48	65
3	"	(-) ephedrine	-60	53 : 47	69
4	1c	(a)	-40	84 : 6	83
5	"	i.Pr_2NH (b)	-40	91 : 9	75
6	"	(+) ephedrine	-40	14 : 86	61
7	"	(-) ephedrine	-40	52 : 48	48
8	"	$PhCH_2NH(CH_2)_2OH$	-60	37 : 63	51
9	"	$PhCH_2NH(CH_2)_2OMe$	-65	50 : 50	46
10	"	(+) O-methyl-ephedrine	-65	48 : 52	56
11	2b	i.Pr_2NH	-60	5 : 6 94 : 6	71
12	2c	i.Pr_2NH	-40	88 : 12	35
13	"	(+) ephedrine	-40	79 : 21	40
14	"	(-) ephedrine	-60	39 : 61	64
15	"	$PhCH_2NH(CH_2)_2OH$	-55	73 : 27	62
16	"	$PhCH_2NH(CH_2)_2OMe$	-65	74 : 26	71

(a) In run 4, methanol was used as solvent.

(b) Similar results were obtained in using dicyclohexylamine, 2 equiv. of i.Pr_2NH or a mixture of iPr_2NH and MeOH. Lower d.e. have been observed in using diethylamine, dibutylamine or benzylethylamine.

increase, under particular conditions, the proportions of the conformers P'-1 and P'-2 with the *Re* and *Si* faces respectively becoming more accessible to the aminoalcohols. The protonation from apparently the most hindered face of P-1 or P-2 could also result from an intermolecular hydrogen bond[8] of the aminoalcohol with the phenyl group of the schielding chain.

We have also to point out the large influence of the bridgehead methyl group[9] as soon as crowded protic species were used as catalysts. Indeed, a diastereoselective protonation by N-benzyl-2-methoxyethylamine was only observed in the absence of such a group on the front face (compare runs 9 and 16). Similarly, the approach from the front side of P-2 by N-benzylethanolamine was not precluded and the usual selectivity was observed (run 15).

In conclusion, it appears that the discrimination between the two diastereofaces of a given photodienol by achiral species can be sometimes greatly influenced by the nature of these species.

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