

ASYMMETRIC INDUCTION. II. ON THE EXTENT OF BOND BREAKING AND MAKING IN THE
TRANSITION STATES OF SOME ADDITIONS TO CARBONYLS

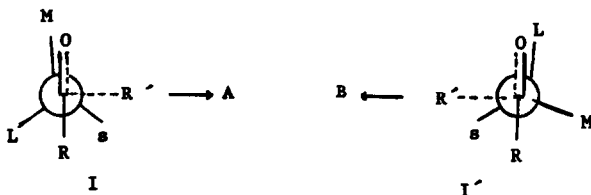
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(Received in USA 28 July 1967)

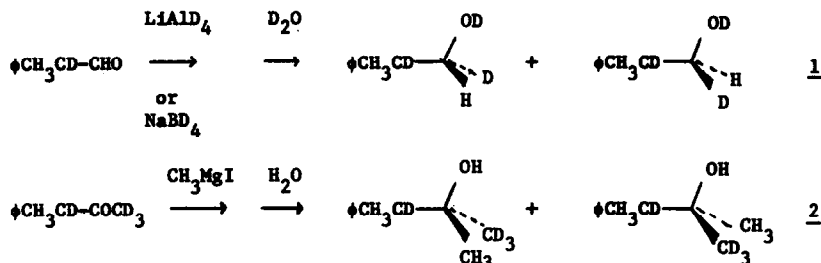
The recently proposed (1) empirical model of asymmetric induction was based on the assumption that little bond breaking and making marks the diastereomeric transition states that control product stereospecificity. Thus, diastereomeric product ratios A/B were predicted with moderate success from the relative magnitudes of M - O (I) vs. L - O (I') interactions. It



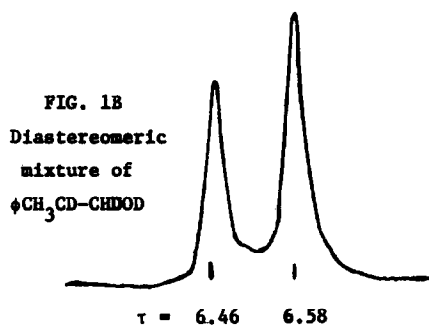
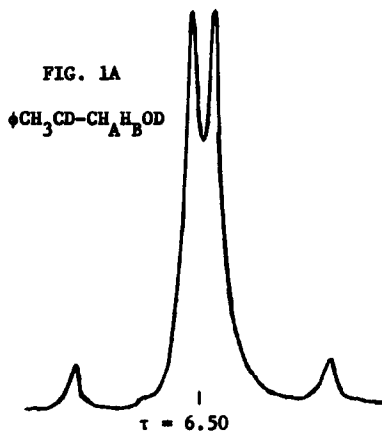
was pointed out (1) that discrepancies between predicted and experimental ratios ought to be expected in cases where extensive bond breaking and making has occurred in the transition state, as the experimental ratios in such cases would be influenced by the relative stabilities of A and B.

A simple probe into the validity of the assumption, as pertinent data on the relative stabilities of diastereomeric products are scarce, is the study of reactions leading to diastereomers whose structures and relative stabilities are a priori known to be practically the same. This condition is fulfilled when R and R' are isotopically related to each other. In such reactions, the diastereomeric product ratio A/B should decrease as the extent of bond breaking and making increases, and approach unity in the extreme case of complete bond breaking and making (2). The problem of determining the diastereomeric product ratios becomes trivial, as groups R, or R', are diastereotopically (3) related in A and B and therefore distinguishable by nmr.

The results of reactions 1 and 2 will now be presented (4). FIG. 1A shows the AB



part ($J_{AB} = 10.6$ cps; $\Delta\nu_{AB} = 7.2$ cps) of the nmr spectrum of neat liquid 2-phenyl-1-propanol-



0,2- d_2 ; FIG. 1B shows the corresponding section of the spectrum of the diastereomeric product mixture from reaction 1. The ratio A/B reported in TABLE I corresponds to the integrated area ratio of the two signals (5) at τ 6.58 and 6.46. The corresponding product ratio from reaction 2 was analogously calculated from the signals of the diastereotopically related methyl groups (6).

In discussing the data summarized in TABLE I, we wish to comment first on the temperature independence of the experimental $\Delta\Delta G_{AB}^\ddagger$ values. It was pointed out (1) that $\Delta\Delta S_{AB}^\ddagger$ contributions to $\Delta\Delta G_{AB}^\ddagger$ will limit the usefulness of the model, as it does not make allowances for such contributions. The present results, and those already available (7), constitute reassuring evidence that in the cases where the model applies $\Delta\Delta H_{AB}^\ddagger$ controls $\Delta\Delta G_{AB}^\ddagger$.

With respect to the question of bond breaking and making in the transition states of the reactions pertinent to the problem, the limited number of the results permits only tentative conclusions to be drawn. From the magnitude and close agreement of the experimental $\Delta\Delta G_{AB}^\ddagger$ value of entry 2 (TABLE I) with that of entry 1 and with the calculated $\Delta\Delta G_{AB}^\ddagger$ value, it may be concluded, as previously suggested (1), that the transition state of Grignard additions to carbonyls occurs very early in the reaction coordinate. The considerably smaller, however, $\Delta\Delta G_{AB}^\ddagger$ values of entries 4 and 5, when compared to the calculated and to that of entry 3, indicate extensive bond breaking and making in the transition states of the reactions of aldehydes with

TABLE I
DIASTEREOMERIC PRODUCT RATIOS FROM 1, 2 AND RELATED REACTIONS.

No.	Substrate	Nucleophile	Solvent	Temp, °C	A/B ^a	$\Delta\Delta G_{AB}^{\ddagger}$, exp. ^b	$\Delta\Delta G_{AB}^{\ddagger}$, calc. ^{b,c}
1	$\phi\text{CH}_2\text{CH-CHO}$	CH_3MgI	Ether	25	67/33 ^d	-0.41	-0.60
2	$\phi\text{CH}_2\text{CD-COCD}_3$	"	"	"	75/25	- .65	- .60
	"	"	"	-55	82/18	- .64	- .60
3	$\phi\text{CH}_2\text{CH-COCH}_3$	LiAlH_4	"	25	71/29 ^d	- .55	- .60
4	$\phi\text{CH}_2\text{CD-CBO}$	LiAlD_4	"	"	58/42	- .19	- .60
	"	"	"	-57	60/40	- .18	- .60
5	"	NaBD_4	THF	66	55/45	- .14	- .60
	"	"	"	0	57/43	- .15	- .60
6	"	"	<i>i</i> -PrOH	25	63/37	- .32	- .50 ^e
	"	"	"	-64	70/30	- .35	- .50 ^e

^a See ref. 5 ^b $\Delta\Delta G_{AB}^{\ddagger} = \Delta G_A^{\ddagger} - \Delta G_B^{\ddagger}$ in Kcal./mole. ^c See ref. 1 ^d From D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, 74, 5828 (1952). ^e As pointed out in ref. 1 the values involving the phenyl group are solvent dependent and decrease with increase of solvent dielectric constant. This value was estimated from the dielectric constant of 2-propanol.

lithium aluminum deuteride and sodium borodeuteride. Other conclusions, such as the relationship between steric effects and extent of bond breaking and making, that may be entertained from the present results, must await further experimentation.

Acknowledgment. We thank the Petroleum Research Fund, administered by the American Chemical Society, for financial support (Grant 2722-A1,4).

References

1. G. J. Karabatsos, *J. Am. Chem. Soc.*, 89, 3167 (1967),

2. Although the products are more or less energetically equivalent, the transition states leading to them are not quite so, because R' is still partially bonded to other groups.
3. The terms enantiotopic and diastereotopic, whose use we strongly recommend, have been introduced by K. Mislow and M. Raban, "Topics in Stereochemistry", Vol. 1, N.L. Allinger and E. L. Eliel, Eds., John Wiley and Sons, Inc., New York, N. Y., 1967, Ch. 1.
4. Deuterium instead of hydrogen was used on the asymmetric carbon in order to simplify the nmr spectra.
5. Absolute configurations of diastereomers A and B have not, as yet, been determined. We have tentatively assumed that the major diastereomer is the one predicted by the model.
6. The diastereotopic methyl groups were indistinguishable in neat liquid solutions of the compound. They were distinguishable in acetone, DMSO, DMF, pyridine, acetonitrile, cyclohexane and carbon tetrachloride. In these solvents their chemical shifts differed by 3.4 to 1.2 cps.
7. Y. Gault and H. Felkin, Bull. Soc. Chim., 1342 (1960).