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ASYMMETRIC INDUCTION III. EFFECT OF THE *t*-BUTYL GROUP DIRECTLY BONDED TO THE CARBONYL

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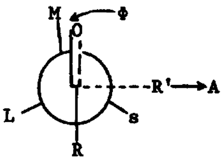
In order to establish the limits of applicability of our model of asymmetric induction[1], we began studies designed to probe initially the soundness of the assumptions upon which the model is based. Having commented[2] previously on the question of bond breaking and making at the transition state, we focus attention in this communication on a consequence of one of the basic assumptions of the model.

On the basis of little bond making and breaking at the transition state, structures 1 and 2 were chosen as the ones best representing the two minimum energy transition states leading to diastereomers A and B. The diastereomeric product ratio A/B was predicted from the relative magnitudes of $M \leftrightarrow O$ (1) *vs*. $L \leftrightarrow O$ (2) interactions. In *both* transition states the incoming group R' is nearest the smallest group s. In contrast, the corresponding transition states of the Cram model[3] are 3 and 4, whereby the incoming group R' is nearest the smallest group s in 3 and the



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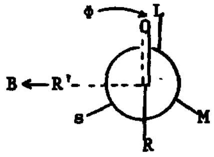

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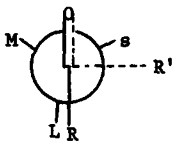
medium sized group M in 4. The diastereomeric product ratio A/B is, thus, primarily controlled by the relative magnitudes of R'↔s vs. R'↔M interactions*.



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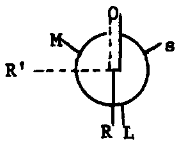

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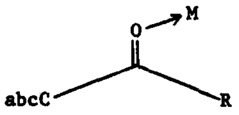
As pointed out[1], the model should apply only to cases where the complexed carbonyl compound has structure 5, as in such structures 1 and 2 best represent the minimum energy diastereomeric transition states. It should fail with systems in which 6 is more stable than 5, as in such



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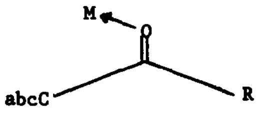

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*It is unfortunate that Felkin and his co-workers[4] misrepresented Cram's model and misconstrued ours. As pointed out above, Cram's model has the incoming group R' nearest s in one diastereomeric transition state and nearest M in the other, not nearest s in both transition states as represented by the authors[4]. Furthermore, the representation of the diastereomeric transition states in terms of eclipsing conformations (dihedralangle $\Phi=0°$ in 1 and 2) is done for convenience and does not imply that the dihedral angles are, or must be, zero. Indeed, these angles are not zero in many carbonyl compounds. For example, Φ is 0° in one conformer of propionaldehyde and 11° in the other[5]. The important feature of the model is the assumption that the dihedral angles of the transition states are similar to those of the uncomplexed carbonyl compound at the ground state, not that they are zero. Zero dihedral angles are probably the exception rather than the rule. By varying the dihedral angle Φ one does not necessarily construct different models.

TABLE I

DIASTEREOMERIC PRODUCT RATIOS FROM ADDITIONS TO $C_6H_5CH_3HC-COR$

NO.	SUBSTRATE	NUCLEOPHILE	SOLVENT	TEMP, C°	A/B[a]	$-\Delta\Delta G^{\ddagger}_{AB}$, KCAL/MOLE
1	$\Phi CH_3HC-COC(CH_3)_3$	$(CD_3)_3CLi$	Pentane	0°	>99/1	>2.5
2	$\Phi CH_3HC-COC(CH_3)_3$	CH_3MgBr	Ether	0°	97/3	1.9 ± 0.2
3	$\Phi CH_3HC-COC(CH_3)_3$	CH_3MgCl	Ether	0°	>99/1	>2.5
4	$\Phi CH_3HC-COC(CH_3)_3$	$(CH_3)_2CHLi$	Ether	-50°	>99/1	>2.5
5	$\Phi CH_3HC-COC(CH_3)_3$	$(CH_3)_2CHLi$	Pentane	0°	>99/1	>2.5
6	$\Phi CH_3HC-COC(CH_3)_3$	C_6H_5Li	Ether	0°	>99/1	>2.5
7	$\Phi CH_3HC-COC(CH_3)_3$	CH_3Li	Ether	0°	98/2	2.1 ± 0.3
8	$\Phi CH_3HC-COC(CH_3)_3$	CH_3Li	Pentane	35°	96/4	1.9 ± 0.2
9	$\Phi CH_3HC-COC(CH_3)_3$	$LiAlH_4$	Ether	0°	98/2	2.1 ± 0.3
10	$\Phi CH_3HC-COC(CH_3)_3$	$LiAlH_4$	Pentane	0°	97/3	1.9 ± 0.3
11	$\Phi CH_3HC-COCH(CH_3)_2$	$LiAlH_4$	Ether	0°	83/17	.85 ± .04
12	$\Phi CH_3HC-COCH(CH_3)_2$	CH_3Li	Ether	0°	95/5	1.6 ± .2
13	$\Phi CH_3HC-COCH(CH_3)_2$	C_6H_5Li	Ether	0°	93/7	1.4 ± .1
14	$\Phi CH_3HC-COCH_3$	$LiAlH_4$	Ether	25°	71/29[b]	.55
15	$\Phi CH_3HC-COCH_3$	$(CH_3)_2CHLi$	Ether	-52°	85/15	.75 ± .04
16	$\Phi CH_3HC-CHO$	CH_3Li	Ether	2°	78/22	.68 ± .04
17	$\Phi CH_3HC-CHO$	$(CH_3)_2CHLi$	Ether	-54°	87/13	.81 ± .05
18	$\Phi CH_3HC-CO\Phi$	$(CH_3)_2CHLi$	Ether	-36°	90/10	1.0 ± .1
19	$\Phi CH_3HC-CO\Phi$	$(CH_3)_2CHLi$	Pentane	36°	78/23	.76 ± .05

[a] The A isomer is the major isomer and assumed to be the one predicted by the model. Absolute configurations were carried out in the products of entries 9, 11 and 14. The results, to be communicated elsewhere, were consonant with the above assumption. Diastereomeric products A and B were determined both by NMR and gas chromatographic analyses.

[b] From D. J. Cram and F. A. Abd Elhafez, *J. Am. Chem. Soc.*, *74*, 5828 (1952).

systems the minimum energy transition states should be best represented by the conformations of the *anti* isomers of the derivatives of carbonyl compounds[7]. If so, the diastereomeric A/B ratios ought to be influenced by R'←→S *vs*. R'←→M interactions and, thus, be much greater than those predicted by our model. In essence, Cram's model rather than ours should represent best the two diastereomeric transition states.

To test the validity of the above arguments and assumptions we investigated systems in which *6* is more stable than *5*, *i.e.* those where R is *t*-butyl[7a]. The data are summarized in Table I.

Indeed the diastereomeric product ratios from additions to the *t*-butyl ketones (first 10 entries) are very high, whereas those obtained from additions to the remaining compounds are smaller and not very much different from the 0.6 kcal/mole value predicted from the model. We know of only one case, the reduction of 2,2-dimethyl-4-cyclohexyl-3-pentanone with lithium aluminum hydride, in which the diastereomeric product ratio is very small[4].

Acknowledgment:

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