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(14) Prepared ($(EtO)_2P(O)CH_2SPh$, bp 145–150 °C (0.1 mmHg)) from triethyl phosphite and chloromethyl phenyl sulfide (Arbusow reaction). For a recent preparation of chloromethyl phenyl sulfide, see B. M. Trost and R. A. Kunz, *J. Org. Chem.*, **39**, 2648 (1974).
(15) A 2:3 mixture of *cis*- and *trans*-vinyl sulfides **16** was obtained when the aldehyde **15** was treated with triphenylphosphinephenylmercaptomethylene in Me_2SO at 25°.
(16) The yield, as well as the ratio of the epimeric aldehydes **17a,b** was not affected when a cis–trans mixture of the sulfide **16**[15] was subjected to the cyclization reaction.
(17) For NMR spectrum δ H values of this compound, see Table in Supplementary material.

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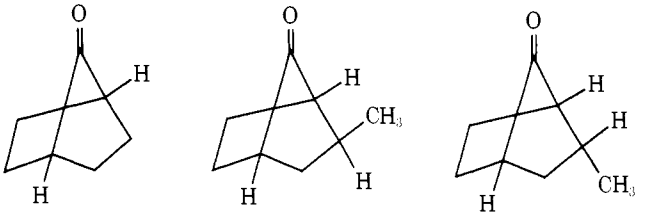
Evidence against Product Development Control as an Important Factor in the Reduction of Ketones by Simple and Complex Metal Hydrides

Sir:

All mechanisms concerning the stereoselective addition or reduction of ketones assume that the entering group approaches the carbonyl carbon on a line perpendicular to the plane of the carbonyl group so that maximum orbital overlap is achieved in the transition state. Dauben and co-workers[1] coined the terms "steric approach control" and "product development control" and suggested that these factors are important in determining the stereochemistry of $LiAlH_4$ reduction of cyclohexanones. Steric approach control implies an early, reactant-like transition state in which the entering group approaches the least-hindered side of the ketone. Product development control implies a late, product-like transition state in which the observed isomer ratio reflects the stability of the product.

Eliel and co-workers[2-5] have cast doubt on the importance of product development control by studying competitive rate experiments involving $LiAlH_4$ and 3,3,5-trimethylcyclohexanone. They have shown that an axial methyl group in the 3 and/or 5 position retards the rate of axial attack compared to 4-*tert*-butycyclohexanone, whereas the rate of equatorial attack remains essentially the same. This observation is not consistent with that predicted by product development control in which an axial methyl substituent would be expected to retard equatorial attack. However, in cyclohexanones other influential factors can be involved, such as torsional strain,[6] compression effect,[7] and conformational changes.[8] We would like to report reduction studies of a model ketone system in which the above mentioned effects are nonexistent so that steric approach control and product development control can be evaluated independently of these other effects.

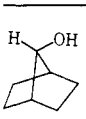
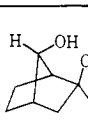
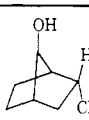
The ketone, 7-norbornanone (I), exhibits bridgehead hydrogen atoms in the 1 and 4 positions which eclipse the carbonyl group in the 7 position. This unique feature, unlike that of the 2,6-diequatorial hydrogens in cyclohexanone which lie 4–5° below the plane of the carbonyl group, eliminates torsional strain or compression effect as a complicating factor in evaluating stereochemical data obtained from this system. The fact that I is a rigid bicyclic system further eliminates conformational changes in the substrate as a further complicating factor. It is clear then the validity of the concept of product development control involving the reaction of $LiAlH_4$ with ketones can be more rigorously tested using this system.



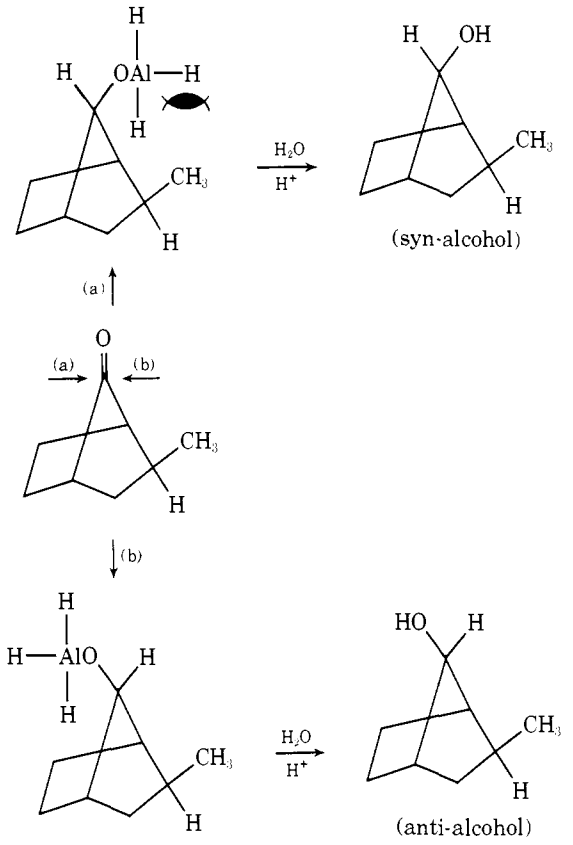
I II III

The reaction of $LiAlH_4$ with I should produce the corresponding alcohol at twice the rate that $LiAlH_4$ reacts with II to produce the syn-alcohol, provided that product development control is not important in this reaction. If product development control is important, then of course, the rate of attack on II to produce the syn-alcohol should be decreased due to the effect of the 2-*exo*-methyl group on the developing transition state (product development control). Whether or not the 2-*exo*-methyl group is sufficiently bulky to exert a valid test for product development control can of course be evaluated by comparing the syn-anti alcohol ratio when $LiAlH_4$ is allowed to react with II. If the 2-*exo*-methyl group exerts a significant steric effect in this system then significally less anti-alcohol should be produced compared

Table I. Reaction of $LiAlH_4$ and AlH_3 with Ketones I, II, and III in Ether and Tetrahydrofuran[a]

Run	Reducing agent	Solvent	Ratio[b] hydride:ketone I	II	III	Recovered Ketone (%)[c] I	II	III	Products (%)[d] 			Mass Bllance
1	$LiAlH_4$	Et_2O	6	–	–	0	–	–	95.0	–	–	95.0
2	$LiAlH_4$	Et_2O	–	6	–	–	0	–	–	93.7	–	93.7
3	$LiAlH_4$	Et_2O	–	–	6	–	–	0	–	–	92.2	92.2
4	$LiAlH_4$	Et_2O	0.25	0.25	–	60.6	80.4	–	27.5	13.9	–	91.2
5	$LiAlH_4$	Et_2O	0.25	–	0.25	70.8	–	71.8	20.1	–	20.8	91.8
6	$LiAlH_4$	Et_2O	–	0.25	0.25	–	74.3	59.0	–	14.2	28.9	88.2
7	$LiAlH_4$	Et_2O	0.11	0.11	0.11	69.3	81.7	71.8	20.6	11.2	19.7	91.4
8	$LiAlH_4$	THF	–	6	–	–	–	–	–	94.3	–	94.3
9	$LiAlH_4$	THF	–	0.25	0.25	–	78.6	61.7	–	14.9	29.1	92.0
10	$LiAlH_4$	Et_2O	–	0.22	0.11	–	168.8	72.6	–	21.3	22.0	94.9
11	$LiAlH_4$	Et_2O	–	0.16	0.04	–	325.5	81.7	–	31.2	15.8	90.8
12	$LiAlH_4$	Et_2O	–	0.04	0.16	–	89.3	321.7	–	4.1	35.7	90.2
13	AlH_3	THF	–	6	–	–	–	–	–	96.3	–	96.3
14	AlH_3	THF	–	0.25	0.25	–	70.9	62.7	–	15.8	30.4	90.0

[a] The hydride was added to 0.032 mmol of ketone at 25° for 2 h. [b] Hydride:ketone = 6 is equivalent to $LiAlH_4$:ketone mole ratio of 1.5:1. [c] Percent of each ketone recovered based on 100% relative to the hydride added. [d] Percent of each product based on 100% relative to the amount of hydride added.



to the syn-alcohol. In order to test perturbations on the carbonyl group other than the steric effect exerted by the 2-*exo*-methyl group, the reaction of $LiAlH_4$ with the 2-*endo*-methyl compound III was studied. If only the steric effect of the 2-*exo*-methyl group is significant, then the reaction of $LiAlH_4$ with III to produce both the syn- and anti-alcohol should proceed at the same rate as the reaction of $LiAlH_4$ with I and at twice the rate compared to the formation of the *syn*-2-*exo*-methyl alcohol.

Table I shows that reaction of $LiAlH_4$ with II produces only the syn-alcohol as a result of anti attack with respect to the 2-*exo*-methyl group. This shows that the 2-*exo*-methyl group exerts a significant steric effect with respect to attack at the 7-keto group since no anti-alcohol is observed. When I and II were admixed in equimolar portions with an insufficient amount of $LiAlH_4$, the alcohol products of I and II were produced in a 2:1 ratio indicating no noticeable product development control. Reaction of I and III in equimolar portions with an insufficient amount of $LiAlH_4$ produced the corresponding alcohols in 1:1 ratio showing that the 2-methyl group has no effect on the rate of reaction of the 7-keto group except when it is in the exo position. Admixture of II and III in equimolar ratio produced the corresponding alcohols in a 1:2 ratio and admixture of I, II, and III in equimolar ratio produced the corresponding alcohols in a 2:1:2 ratio when allowed to react with an insufficient amount of $LiAlH_4$, supporting the conclusion that anti attack on II takes place at the same rate as attack from either side of the carbonyl on I and III and indicating that the 2-*exo*-methyl group, although exerting a signicant steric effect, does not affect the formation of the syn-alcohol of II. Further experiments in THF, at different stoichiometries and experiments using AlH_3 as the reducing agent, simply provide further evidence for the above conclusions.

The synthesis of I was accomplished by using the procedure of Gassman and Pape.[9] Compounds II and III were prepared by following the method outlined by Lightner and Jackman.[10]

The reductions of I, II, and III were carried out under identical conditions. According to GLC and ^{13}C NMR, I and II gave only one reduction product, whereas III gave both the syn- and anti-alcohols. By comparing GLC and ^{13}C NMR, it was substantiated that the lone reduction product of II was the syn-alcohol. The syn-alcohol IV was allowed to equilibrate under Meerwein-Ponndorf conditions. The anti-alcohol V was formed almost exclusively except for a trace of the syn-alcohol. Also ketone II produced only the anti-alcohol V when allowed to react with aluminum isopropoxide and isopropyl alcohol thus establishing the anti-alcohol V as the thermodynamic isomer.

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Alkane Elimination in Mass Spectrometry. A Counterpart to the McLafferty Rearrangement

Sir:

We report a primary fragmentation of simple ketones, alcohols, and amines which can be the most facile reaction at low energy. In spite of the detailed attention[1] accorded the primary fragmentations of these functional groups over the past 20 years, this process has, in a situation reminiscent of the emperor's clothes,[2] not been commented upon.[3] The reaction is alkane elimination from the molecular ion.

Consider the mass spectrum[1a] of diisopropyl ketone which shows, as the fourth most abundant fragment ion, a peak at *m/e* 70 ($C_4H_6O^{\cdot+}$ [4]). The origin of this ion directly and exclusively[5] from the molecular ion of the ketone is shown by the accelerating voltage scan[6,7] of Figure 1a. The metastable peak confirms the transition (1).

$$C_3H_7COC_3H_7^{\cdot+} \rightarrow C_3H_6CO^{\cdot+} + C_3H_8 \qquad (1)$$

A scan of the mass-analyzed ion kinetic energy (MIKE) spectrum[8] of the molecular ion of diisopropyl ketone, shown in Figure 1b, confirms that on the time scale of this experiment, alkane elimination is the major primary fragmentation (>95%). The MIKE spectrum taken at higher collision gas pressures shows the well-known α-cleavage reaction leading to acylium ion formation. (The base peak in the mass spectrum is also due to this reaction.) Alkane elimination competes poorly with alkyl radical loss in these higher