Tetrahedron, 1967, Vol. 23, pp. 205 to 214. Pergamon Press Ltd. Printed in Northern Ireland

THE STEREOCHEMISTRY AND RATE OF REDUCTION OF SUBSTITUTED CYCLOHEXANONES WITH DIBORANE

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(*Received* 23 *May* 1966)

Abstract—3-Methyl-cyclohexanone and *cis* and *trans*-dimethylcyclohexanone-3,4-dicarboxylate yield on reduction with diborane mostly the equatorial alcohol, whereas dihydroisophorone gives mostly the axial isomer. Hindered alkoxyboranes give with dihydroisophorone the more of the axial isomer the larger the reducing agent. The rate of the reaction is first order in ketone and three halves order in diborane. In presence of boron-trifluoroide more axial isomer is obtained and the rate is first order in diborane. A two step reaction is assumed.

DIBORANE addition to double bonds is strongly directed by an ester group in position 4 in the cyclohexane ring.[1] The stereochemical course of the addition of diborane to a C=O bond in cyclohexanones having a carboxylate function on the ring seemed to us of interest. It was found by Henbest[2] and Kwart[3] that substituents at position 4 of cyclohexanones give on reduction with sodium borohydride the higher amount of *cis* products the higher the electronegativity of the substituent. These effects are expected to be more pronounced in the reduction with diborane in view of the mechanism of this reaction which is assumed[4] to proceed through the formation of a complex between borane and the ketone with subsequent intramolecular hydride transfer from boron to carbon. This reaction should therefore not be sensitive to steric hinderance and polar and potential energy effects only should be operative.

The reduction of 4-t-butylcyclohexanone with diborane was shown[5] to give the alcohol containing 92% of the *trans* isomer, a result consistent with the assumption that the more stable isomer should be formed. Also 2-methylcyclohexanone yielded in this reaction mostly the *trans* product,[6] which is the more stable one. These studied compounds belong however to a group of ketones that obey on reduction with metal hydrides the "product development control" rule.[7] Systems which yield on other reduction products of "kinetic approach control" were not studied. The reduction of hindered ketones with diborane could be a valid test for the intramolecular character of the hydride transfer. The appraisal of steric effects and comparison with results of reduction of cyclohexanones containing a carboxylate substituent could also permit to assess the importance of polar effects in this reaction.

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[1] J. Klein, E. Dunkelblum and D. Avrahami, in press.

[2] H. Henbest and M. G. Combe, *Tetrahedron Letters* 404 (1961).

[3] H. Kwart and T. Takeshita, *J. Amer. Chem. Soc.* **84**, 2833 (1962).

[4] H. C. Brown, *Hydroboration*. W. A. Benjamin, New York (1962).

[5] W. M. Jones, *J. Amer. Chem. Soc.* **82**, 2528 (1960).

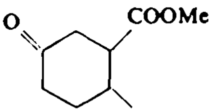
[6] H. C. Brown and D. B. Bigley, *J. Amer. Chem. Soc.* **83**, 3166 (1961).

[7] W. G. Dauben, G. J. Fonken and D. S. Noyce, *J. Amer. Chem. Soc.* **78**, 2579 (1956).

A stereochemical study of the diborane reduction of a series of cyclohexanones, having alkyl and carboxylate substituents was made and the rate of this reaction was measured, after it was apparent that the stereochemical results are not in agreement with expectations. Dihydroisophorone was chosen as the hindered ketone whose reaction with diborane was studied in view of the thorough study[8] carried out on the reduction of this compound with metal hydrides.

RESULTS

The steric course of the reduction with diborane of *cis*-I and *trans*-II 4-oxocyclohexane 1,2-dicarboxylic acid dimethyl ester, of 3-methylcyclohexanone III and dihydroisophorone IV are given in Table 1.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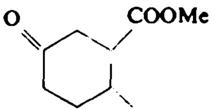
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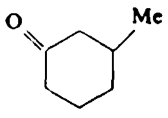
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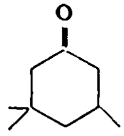
IV

TABLE 1. REDUCTION WITH DIBORANE[a]

Ketone	Catalyst	% of *cis* alcohol	% of *trans* alcohol	Yield[b]
I	—	80	20	60
I	BF_3Et_2O	85	15	50
II	—	80	20	70
II	BF_3Et_2O	85	15	70
III	—	88	12	[c]
III	BF_3Et_2O	80	20	[c]
IV	—	34	66	61
IV	BF_3Et_2O	15	85	70
IV[d]	—	34	66	[c]
IV[e]	—	37	63	[c]

[a] All reactions in tetrahydrofuran, at room temp, ½ hr.
[b] Isolated and distilled product.
[c] The product was not isolated, but ratios determined by GLC.
[d] 1 hr reaction at 60°.
[e] 1 hr reaction in boiling diglyme.

The product obtained is the more stable alcohol in the case of unhindered ketones. Dihydroisophorone IV however yielded mostly the less stable isomer. Carboxylate groupings had no visible influence. Addition of BF_3-etherate to the reaction mixture raised the amount of the less stable axial alcohol in all ketones studied; hindered, unhindered or containing a carboxylate group. Heating the product of the reaction of dihydroisophorone with diborane in diglyme does not change the ratio of the isomers.

In Table 2 are recorded the steric results of the reduction of IV with dimethoxyborane and with diisopropoxyborane obtained from diborane and the corresponding alcohols. Dimethoxyborane reduces the ketone slower than diborane and yields even a larger amount of the axial alcohol. This trend is maintained with diisopropoxyborane, which gives still a larger amount of the *trans* isomer.

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[8] H. Haubenstock and E. L. Eliel, *J. Amer. Chem. Soc.* **84**, 2363 2368 (1962).

TABLE 2. REDUCTION OF DIHYDROISOPHORONE WITH DIALKOXYBORANES[a] AT 0°

Dialkoxy-borane	Time of reaction hr	% of *cis* alcohol	% of *trans* alcohol	Yield
$(CH_3O)_2BH$	1	25	75	45
$(CH_3O)_2BH$	4	25	75	60
$(CH_3O)_2BH$	20	28	72	87
$(CH_3O)_2BH$[b]	1	25	75	100
$[(CH_3)_2CHO]_2BH$	4	20	80	15
$[(CH_3)_2CHO]_2BH$	20	20	80	65
$[(CH_3)_2CHO]_2BH$[b]	1	20	80	35

[a] Mole of dialkoxyborane per mole of ketone.

[b] 4·5 moles of dialkoxyborane per mole of ketone.

The rates of the reduction of I, II, III and IV with diborane were measured in tetrahydrofuran spectrophotometrically and the results are recorded in Table 3. An excess of diborane was used.

TABLE 3. RATES OF REDUCTION OF KETONES WITH DIBORANE

Ketone	conc. (M) Ketone	conc. (M) Diborane	τ sec	1/sec k_1	(1/sec)(l./mole)$^{\frac{1}{2}}$ k	k average
Cyclohexanone	$12·5 \times 10^{-3}$	$43·5 \times 10^{-3}$	13	$5·3 \times 10^{-2}$	5·9	
Cyclohexanone	$12·5 \times 10^{-3}$	87×10^{-3}	4·5	$15·5 \times 10^{-2}$	6·0	6·0
I	$12·5 \times 10^{-3}$	$43·5 \times 10^{-3}$	23	$3·0 \times 10^{-2}$	3·3	
I	$12·5 \times 10^{-3}$	87×10^{-3}	9	$7·7 \times 10^{-2}$	3·0	3·1
II	$12·5 \times 10^{-3}$	$43·5 \times 10^{-3}$	31	$2·2 \times 10^{-2}$	2·5	
II	$12·5 \times 10^{-3}$	87×10^{-3}	10	$6·9 \times 10^{-2}$	2·7	
II	$12·5 \times 10^{-3}$	$130·5 \times 10^{-3}$	5	$13·9 \times 10^{-2}$	2·9	2·7
III	$12·5 \times 10^{-3}$	$33·5 \times 10^{-3}$	53	$1·3 \times 10^{-2}$	1·4	
III	$12·5 \times 10^{-3}$	67×10^{-3}	19	$2·3 \times 10^{-2}$	1·3	
III	$12·5 \times 10^{-3}$	134×10^{-3}	7	$9·8 \times 10^{-2}$	1·3	1·3
IV	$12·5 \times 10^{-3}$	$43·5 \times 10^{-3}$	70	$1·0 \times 10^{-2}$	1·1	
IV	$12·5 \times 10^{-3}$	87×10^{-3}	23	$3·1 \times 10^{-2}$	1·2	
IV	$12·5 \times 10^{-3}$	25×10^{-3}	192	$3·6 \times 10^{-3}$	1·0	
IV	$12·5 \times 10^{-3}$	50×10^{-3}	64	$1·1 \times 10^{-2}$	1·0	
IV	$12·5 \times 10^{-3}$	75×10^{-3}	29	$2·4 \times 10^{-2}$	1·1	
IV	$12·5 \times 10^{-3}$	100×10^{-3}	21	$3·3 \times 10^{-2}$	1·1	
IV	$12·5 \times 10^{-3}$	150×10^{-3}	10	$6·9 \times 10^{-2}$	1·2	1·1

Examples of the recorded optical density *vs.* time curves are shown in Fig. 1 for IV. The half-life period was found graphically by (1) where

$$\tau = t(d/2) - t(d) \tag{1}$$

$t(d)$ and $t(d/2)$ are the intervals from the beginning of the reaction, where the optical density after the second interval is half of the optical density of the first one. The half-life period was constant in each run and the reaction is first order in ketone. The pseudo first order constant was found by

$$k_1 = \ln 2/\tau \tag{2}$$

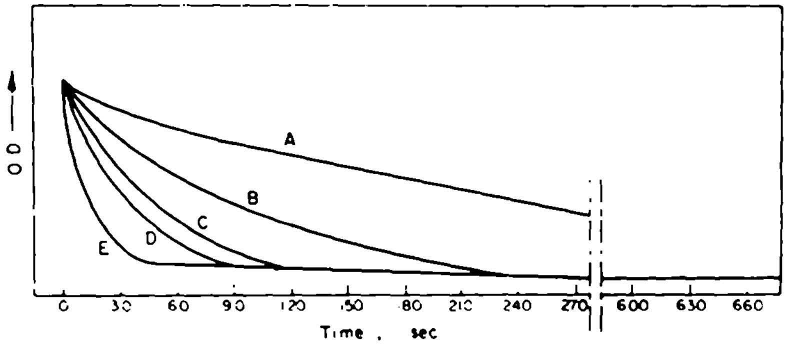

FIG. 1. Rate of reduction of dihydroisophorone with diborane. Concentration of the ketone $12{\cdot}5 \times 10^{-3}$M, concentration of diborane: A—25×10^{-3}; B—50×10^{-3}; C—75×10^{-3}; D—100×10^{-3}; E—150×10^{-3}M.

However, τ changed when the diborane concentration is changed. The rate dependence was not first order in diborane or borane, but of one and a half. The rate constant k was calculated from (3),

$$k_1 = k\,[\text{Diborane}]_t^{3/2} \tag{3}$$

$$\frac{-\text{d}\,[\text{Ketone}]_t}{\text{d}t} = k\,[\text{Ketone}]_t\,[\text{Diborane}]_t^{3/2} \tag{4}$$

On Fig. 2 are recorded the log k_1 vs. log $[B_2H_6]$. The points are on a straight line with the slope of $\frac{3}{2}$. The point recorded at log $[B_2H_6] = 0$ is the average k from Table 3.

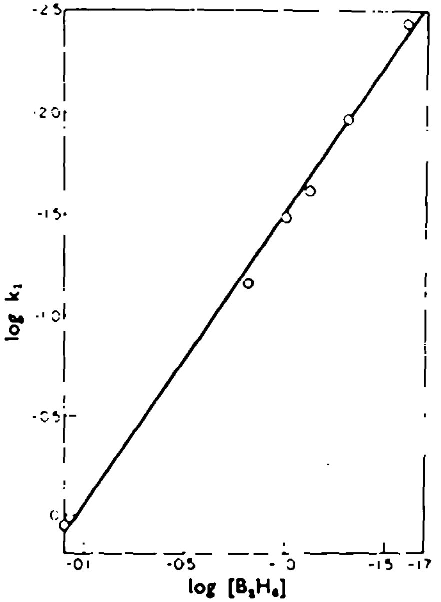

FIG. 2. Dependence of the rate of reduction of dihydroisophorone on diborane concentrations.

Addition of BF_3-etherate enchanced the rate of the reaction. The data of the catalysed reactions are given in Table 4.

TABLE 4. REDUCTION OF DIHYDROISOPHORONE WITH DIBORANE IN PRESENCE OF BORON-TRIFLUORIDE

Total conc. of diborane M	Total conc. of BF_3 M	τ sec	k_1 1/sec	k_3 (l/sec)(l/mole)$^{\frac{1}{2}}$	k_3' (l/sec)(l/mole)$^{\frac{1}{2}}$
$42{\cdot}5 \times 10^{-3}$	$8{\cdot}3 \times 10^{-3}$	29	$2{\cdot}4 \times 10^{-2}$	40·7	27·5
85×10^{-3}	$8{\cdot}3 \times 10^{-3}$	10	$6{\cdot}9 \times 10^{-2}$	59·1	27·5
$42{\cdot}5 \times 10^{-3}$	$41{\cdot}5 \times 10^{-3}$	18	$3{\cdot}8 \times 10^{-2}$	16·1	22·7
$63{\cdot}5 \times 10^{-3}$	$41{\cdot}5 \times 10^{-3}$	11	$6{\cdot}3 \times 10^{-2}$	17·2	22·7
85×10^{-3}	$41{\cdot}5 \times 10^{-3}$	8	$8{\cdot}6 \times 10^{-2}$	16·8	22·7
$33{\cdot}5 \times 10^{-3}$	$8{\cdot}3 \times 10^{-3}$	41	$1{\cdot}7 \times 10^{-2}$	33·3	27·5
67×10^{-3}	$8{\cdot}3 \times 10^{-3}$	16	$4{\cdot}3 \times 10^{-2}$	43	27·5
$33{\cdot}5 \times 10^{-3}$	$4{\cdot}15 \times 10^{-3}$	46	$1{\cdot}5 \times 10^{-2}$	59·7	22
$33{\cdot}5 \times 10^{-3}$	$8{\cdot}3 \times 10^{-3}$	41	$1{\cdot}7 \times 10^{-2}$	37·0	27·5
$33{\cdot}5 \times 10^{-3}$	$16{\cdot}6 \times 10^{-3}$	30	$2{\cdot}3 \times 10^{-2}$	29·3	24
$33{\cdot}5 \times 10^{-3}$	$33{\cdot}2 \times 10^{-3}$	20	$3{\cdot}4 \times 10^{-2}$	24·6	24·3
$33{\cdot}5 \times 10^{-3}$	$66{\cdot}4 \times 10^{-3}$	14	$4{\cdot}9 \times 10^{-2}$	19·2	19
$47{\cdot}5 \times 10^{-3}$	$4{\cdot}15 \times 10^{-3}$	30	$2{\cdot}3 \times 10^{-2}$	59·3	22
$95{\cdot}0 \times 10^{-3}$	$4{\cdot}15 \times 10^{-3}$	11	$6{\cdot}3 \times 10^{-2}$	78·1	22
$47{\cdot}5 \times 10^{-3}$	$20{\cdot}75 \times 10^{-3}$	19	$3{\cdot}6 \times 10^{-2}$	25·1	25·9
$95{\cdot}0 \times 10^{-3}$	$20{\cdot}75 \times 10^{-3}$	8	$8{\cdot}6 \times 10^{-2}$	27·3	25·9

* The concentration of the ketone was $6{\cdot}25 \times 10^{-3}$ M. The solvent was tetrahydrofuran.

At low concentration of boron trifluoride, the reaction is of three halves order in diborane, but with increasing concentration of the catalyst the order in diborane drops until it almost reaches one at high concentration of the catalyst. Typical optical density curves at high and constant boron trifluoride and varying diborane concentrations are recorded in Fig. 3.

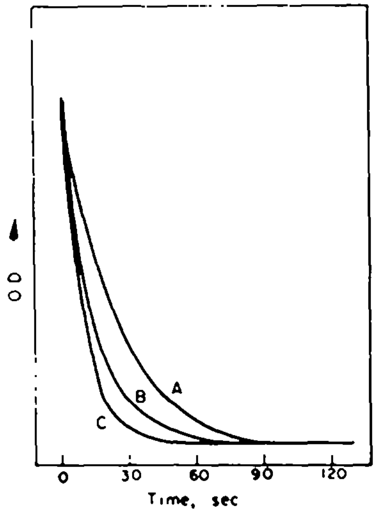

FIG. 3. Rates of boron trifluoride catalysed reduction of dihydroisophorone. Conc. of BF_3: $41{\cdot}5 \times 10^{-3}$M. Conc. of IV: $6{\cdot}25 \times 10^{-3}$M. Conc. of diborane: A—$42{\cdot}5 \times 10^{-3}$; B—$63{\cdot}5 \times 10^{-3}$; C—$85 \times 10^{-3}$M.

The reduction of dihydroisophorone is first order in the ketone also in the presence of boron trifluoride (5).

$$\frac{-\mathrm{d}\,[\text{ketone}]_t}{\mathrm{d}t} = k_2\,[\text{ketone}]_t \tag{5}$$

The reduction can therefore be regarded as a composite one, consisting of two parallel reactions, one catalysed and one uncatalysed as in (6).

$$\begin{aligned}\frac{-\mathrm{d}\,[\text{ketone}]_t}{\mathrm{d}t} &= k_2\,[\text{ketone}]_t = k\,[\text{ketone}]_t\,[\text{diborane}]_t^{3/2}\\ &+ k_3\,[\text{ketone}]_t[\text{diborane}]_t\,[\mathrm{BF_3}]_t\end{aligned} \tag{6}$$

However, the rate of the reduction was not of any determined order in boron trifluoride Moreover the "constant" k_3 was not constant.

DISCUSSION

The kinetic results of the reduction of the studied ketones with diborane can be explained by a mechanism involving a fast equilibrium between the ketone, borane and their complex (8) followed by (9) a slow attack of diborane on this complex.

$$\mathrm{B_2H_6} \rightleftharpoons 2\mathrm{BH_3} \tag{7}$$

$$\text{ketone} + \mathrm{BH_3} \rightleftharpoons \text{ketone}\cdot\mathrm{BH_3} \tag{8}$$

$$\text{ketone}\cdot\mathrm{BH_3} + \mathrm{B_2H_6} \longrightarrow \text{products} \tag{9}$$

This mechanism is not only consistent with the first order reaction in ketone and three halves order in diborane but is also compatible with the stereochemical results. These results follow the expected course of formation of the more stable isomer only in the case of unhindered ketones. The reduction of a hindered ketone yields the less stable isomer as in the reduction with metal hydrides. The product of this reaction is kinetically controlled, since heating of the reaction mixture even in the presence of excess ketone does not change the ratio of the isomers in favor of the more stable one.[9]

An intramolecular hydride transfer does not seem compatible with these results. The intermolecular rate determining step is also consistent with the influence of the bulk of the reducing agent on the steric course of the reaction. The increase of the amount of the product of "kinetic approach control" with the bulk of the dialkoxyboranes supports this picture. In an intramolecular hydride transfer a larger amount of the more stable product is expected from the complex with larger groups attached to boron. Our results are also consistent with Brown's results on the influence of the bulk of the alkyls in dialkylboranes on the amount of *cis* product in the reduction of 2-methylcyclohexanone.

The higher amount of the axial alcohol obtained in the dialkoxyboranes reductions relatively to the amount obtained with diborane prove that the dialkoxyboranes are involved directly in the reduction and that this reaction is not preceded by their disproportionation to diborane and trialkoxyboranes.

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[9] Haubenstock[10] has found that in diisobutylaluminium hydride reductions there is isomerization in presence of excess ketone.

[10] H. Haubenstock, *J. Org. Chem.* **28**, 2772 (1963).

The influence of added boron trifluoride on the rate and stereochemistry of the reduction is also in agreement with this mechanism. The gradual change of the order of the reaction in diborane from one and a half to one on addition of increasing amounts of boron trifluoride is explained by the intervention of a competing two-step reaction, consisting of a fast equilibrium between the ketone, boron trifluoride and their complex (10) and then a slow attack of this complex by diborane (11).

$$\text{ketone} + \text{BF}_3 \rightleftharpoons \text{ketone}\cdot\text{BF}_3 \tag{10}$$

$$\text{ketone}\cdot\text{BF}_3 + \text{B}_2\text{H}_6 \longrightarrow \text{products} \tag{11}$$

It is expected that boron trifluoride is a more strongly complexing agent than borane. The complex with boron trifluoride will be also probably more polarized and therefore its reaction with diborane faster than of the ketone–borane complex. The enchanced rate of the reduction is expected to be accompanied by an increase of the amount of the axial *trans* alcohol in the product of reduction of dihydroisophorone, since the transition state should be on the reaction coordinate nearer to the starting material than in the case of the uncatalysed reaction. For this reason the axial–axial interaction between a methyl and the forming hydroxyl should be less pronounced and the formation of the axial product more favored than in the uncatalysed reaction. This is in fact observed.

A comparison of the rate of reduction of the substituted cyclohexanones does not show a uniform trend connected with the polarity of the substituents. Thus, introduction of methyl or carboxylate groups, which cannot interact with the attacking species, both slow down the rate. This effect is probably caused by a different step of the reaction in each case. A methyl group will probably shift the equilibrium (8) to the right, but should slow down the following step (9); on the other side, it can be expected that equilibrium (8) will be shifted to the left in the presence of a carboxylate group in the molecule, but step (9) should be faster than in the case of parent compound. The possibility that the small retardation factors of all substituents are due to steric and not electronic effects, seems to us not to be in agreement with the greater rate of reaction of the *cis*-diester I (one axial substituent) relatively to the *trans*-diester II (equatorial substituents only).

At high concentrations of boron trifluoride the reduction is almost first order in diborane. It can therefore be assumed that the reaction proceeds almost exclusively by way of (10) and (11) and the rate can be expressed by (12).

$$\begin{aligned} \frac{-\mathrm{d}\,[\text{ketone}]}{\mathrm{d}t} &= k_3\,[\text{ketone}]_t\,[\text{BF}_3]_t\,[\text{diborane}]_t \\ &= k_3^0\,[\text{ketone}\cdot\text{BF}_3]\,[\text{diborane}]_t \end{aligned} \tag{12}$$

Where $[\text{BF}_3]$ is the concentration of boron trifluoride uncomplexed by the ketone and $[\text{BF}_3]_t$ is the total concentration of this catalyst and k_3^0 is a true constant. This constant k_3^0 and also the constant K of the equilibrium (13) can be obtained from the reaction rates at high and

$$K = \frac{[\text{ketone}\cdot\text{BF}_3]}{[\text{BF}_3]\,[\text{ketone}]} \tag{13}$$

changing concentrations of boron trifluoride. By assuming that $[\text{BF}_3] = [\text{BF}_3]_t$ at these concentrations and by algebraic transformation of (12) and (13) the relation (14) can be obtained.

$$\frac{1}{k_3} = \frac{1}{k_3{}^0 K} + \frac{[BF_3]_t}{k_3{}^0} \tag{14}$$

A plot of $1/k_3$ against $[BF_3]_t$ gives at high concentration of boron trifluoride a straight line (Fig. 4), whose slope is $1/k_3{}^0$ and intercept $1/k_3{}^0K$. It is found in this manner $K = 12{\cdot}9$ l./mole and $k_3{}^0 = 2{\cdot}8$ l./mole. sec. The constant $k_3{}^0$ thus obtained will be somewhat higher than the real one, since abstraction was made of the uncatalytical reaction.

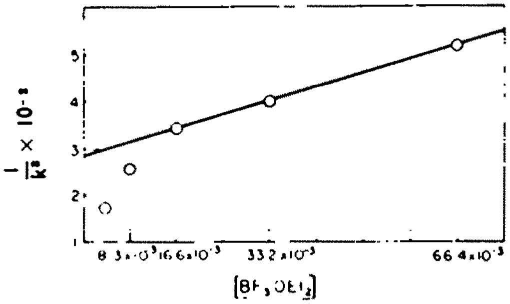
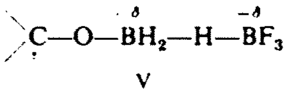


Fig. 4.

The change in k_3 cannot be explained by equilibrium (13). This is shown by a recalculation of k_3 using $K{\cdot}k_3{}^0$ and relations (12) and (13). The values of k_3 so obtained are called $k_3{}^c$ and given in Table 4. They are constant, if one takes in account the approximations used, and smaller than k_3 obtained from (6) except at very high concentrations of $[BF_3]$. The difference between k_3 and $k_3{}^c$ is particularly high at low concentrations of boron trifluoride. This difference is even increased, when the concentrations of the ketone and catalyst are kept constant, (which leaves $k_3{}^c$ identical) but the diborane concentration is increased. Moreover, the reaction at lower concentrations of boron trifluoride, although faster than in its absence remains still of the order one and a half in diborane. It seems therefore that the addition of this catalyst not only causes the appearance of a parallel reaction first order in diborane, but catalyses also the reaction, which is of the order one and a half in diborane. The nature of this effect is not clear. The possibility, that boron trifluoride forms a complex with diborane, which is more reactive than diborane in hydride transfer reactions does not seem plausible on electronic considerations. It is more probable that this catalyst solvates the ketone-borane complex, apparently the borane end of it, which is more electron rich and by so doing disperses the negative charge formed on this end during the reaction. A new complex V may be the reaction intermediate.



$$>C-O-\overset{\delta}{B}H_2-H-\overset{-\delta}{B}F_3$$

V

The possibility that a fluorodiborane $(FBH_2)_2$ formed by disproportionation between diborane and boron trifluoride is the reducing species can also not be eliminated now.

It is interesting that diborane is the reducing species. It is known that diborane introduced into tetrahydrofuran is converted into the borane–tetrahydrofuran complex, as evidenced by the dependence of its solubility on pressure.[11] Only small amounts of diborane are expected to be present in equilibrium with the complex, and accordingly its reactivity should be much higher. This suggests, that the high reactivity of diborane in ether solvents is not connected with its dissociation and formation of borane–ether complexes. This is also supported by the fact, that diethyl ether does not form a borane–ether complex in appreciable amounts, and reactions in this ether proceed easier than in hydrocarbon solvents. The role of ethers in these reactions consists apparently in solvating the moiety of diborane which remains after the hydride transfer.

It is interesting that disiamylborane dimer is the active species in olefin hydroboration.[12] Disiamylborane however exists in tetrahydrofuran as the dimer.

Preliminary experiments have shown that the reaction of olefins with diborane are first order in diborane. This study is continued.

EXPERIMENTAL

Starting materials. Cyclohexanone and 3-methylcyclohexanone were commercial products, redistilled at 151–152° and 95°/25 mm respectively. Dihydroisophoron was obtained by catalytic hydrogenation of commercial isophorone and distillation at 80–82°/22 mm.

Diester I was prepared by oxidation of 4-*trans*-hydroxy-*cis*-1,2-cyclohexane dicarboxylic acid dimethyl ester.[1] To a soln of 10·5 g of the hydroxydiester in 100 ml acetone, cooled to 0°, there was added dropwise and with stirring a soln of 2·6 g CrO_3 and 4 g H_2SO_4 in 10 ml water. After 30 min stirring, EtOH was added until a green coloration appeared, the soln filtered and concentrated *in vacuo*. The residue was poured on 50 ml water, and the soln extracted several times with ether. Evaporation of the ether soln left 7·5 g of a residue that was purified by passing through a column of 100 g alumina and elution with benzene containing 10% of $CHCl_3$. Distillation yielded 5 g b.p. 140–142°/2 mm. (Found: C, 56·8; H, 6·8. Calc. for $C_{10}H_{14}O_5$: C, 56·1; H, 6·5%.)

Diester II was obtained from the corresponding alcohol[1] by two consecutive oxidations as above. It was obtained in 50% yield, b.p. 126–128°/1 mm, m.p. 34-35°. (Found: C, 55·8; H, 6·6. Calc. for $C_{10}H_{14}O_5$: C, 56·1; H, 6·5%.) GLC on Apiezon L showed that these ketones were free of the hydroxy compounds.

Stereochemical studies. All ketones, except the diesters I and II were reduced in the following manner: A soln of 0·005–0·01 moles of diborane in tetrahydrofuran (THF) was added during a few min to a soln of 0·01–0·02 mole of the ketone in THF at 0°. The reaction mixture was left at room temp for 30 min, excess diborane destroyed by careful addition of several drops of water, and 10% NaOHaq was added to make the soln alkaline. The solvent was then removed *in vacuo* and the residue extracted several times with ether. The product was either isolated by distillation or analysed and its amount estimated directly by GLC. In BF_3 catalysed reactions an amount of $BF_3 \cdot Et_2O$ equimolecular to the ketone was added.

The keto diesters (0·01 mole; 2·1 g) were dissolved in 5 ml THF and were reduced as above with 10 ml of a 0·7 molar soln of diborane in the same solvent. Then, 5 ml of water were added carefully, followed by 2 ml 10% NaOHaq and 4 ml 30% H_2O_2. The soln was stirred for 10 min, cooled, acidified to pH 1 with H_2SO_4 and treated with diazomethane in ether until a persistent yellow coloration, to re-esterify the carboxyl groups. The ether layer was separated, the aqueous layer extracted several times with ether and the product distilled.

All products were analysed on a 7-ft column of neopentylglycol succinate 20% on Chromosorb W, with the exception of the 3-methylcyclohexanols which were analysed on a column of 15-ft of diglycerol 10% on Chromosorb P.

The reference alcohols corresponding to 3-methylcyclohexanone and dihydroisophorone were not prepared separately but calibration of peaks of the gas chromatograms were carried out using mixtures

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[11] J. R. Elliott, W. L. Roth, D. F. Roedel and F. M. Boldebuk, *J. Amer. Chem. Soc.* **74**, 5211 (1952).

[12] H. C. Brown and A. W. Moerikofer, *J. Amer. Chem. Soc.* **83**, 3417 (1961).

formed in LAH reductions of the first[13] and the second[8] ketone and the ratio of isomers known from the lit.[8,13] The alcohols formed in the reduction of the ketodiesters I and II were prepared and characterized.[1]

Kinetic measurements. The rate of reduction of the ketones with diborane was followed spectrophotometrically at 285 mμ in THF soln at 25° using a Uvispec Hilger Spectrophotometer with the Gilford Absorbance Indicator (Model 220), adapted by Perlmutter-Hayman and Wolff[14] to the measurement of fast reactions. In each experiment, 0·075 ml of the soln of the ketone in anhydrous THF were added with the aid of a rapid mixing syringe to a diborane soln in the same solvent, containing the appropriate amount of BF_3-etherate (in cases when the catalysis was studied). The total amount of soln was 3 ml. Each experiment was repeated at least three times in the same conditions. The τ were evaluated in the central portion of the curve, several times for each curve. The spread of the τ was not more than 10% for the slow end 15% for the fast reactions.

Acknowledgement—We are grateful to Mr. Wolff for his help in carrying out the rate measurements.

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[14] B. Perlmutter-Hayman and M. A. Wolff, *Israel J. Chem.* 3, 155 (1965).