

## Reduction of Some Ketones using Sulphurated Sodium Borohydride (NaBH<sub>2</sub>S<sub>3</sub>): Kinetics and Mechanism

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Rates of sulphurated sodium borohydride (NaBH<sub>2</sub>S<sub>3</sub>) reduction of some ketones (acetone, acetophenones, benzophenones, and fluorenone) in tetrahydrofuran have been measured. Results for the two series (acetophenones and benzophenones) studied fit the Hammett equation with high  $\rho^+$  values (+2.531 for acetophenones and +1.982 for benzophenones) thus suggesting that BH<sub>2</sub>S<sub>3</sub><sup>-</sup> ion is a moderately strong nucleophile. Thermodynamic parameters have been evaluated and a suitable mechanism for these reactions has been proposed.

SULPHURATED borohydrides show selective properties as reducing and sulphurating agents that are of great interest in synthetic chemistry. The reduction of several organic functional groups with sulphurated sodium borohydride (NaBH<sub>2</sub>S<sub>3</sub>) has been recently studied extensively by Lalancette *et al.*<sup>1-4</sup> However, no kinetic investigation has yet been made of these interesting reactions even though the mechanisms of reductions of carbonyl groups using reducing agents such as sodium borohydride,<sup>5-13</sup> cyanohydrinborate ion,<sup>14</sup> and morpholine-borane<sup>15</sup> have been studied extensively. The present investigation deals with the kinetics and mechanism of reduction of some ketones using sulphurated sodium borohydride.

### RESULTS AND DISCUSSION

**Order of Reaction.**—Table I gives the second-order rate constants for reactions of NaBH<sub>2</sub>S<sub>3</sub> with acetone, acetophenone, benzophenone, and fluorenone at different concentrations of the substrate and NaBH<sub>2</sub>S<sub>3</sub>. Reactions were carried out in tetrahydrofuran (THF) with equal concentrations of the ketone and NaBH<sub>2</sub>S<sub>3</sub> in order to prevent the formation of sulphurated products as shown by Lalancette *et al.*<sup>3</sup> Constancy in the values of  $k_2$  (Table I) and the linearity of second-order plots observed for over 80% of the reaction indicate that the reaction in each case is second order.

**Effect of Substituents.**—The effect of suitably positioned substituents in acetophenone and benzophenone has been studied in detail. Reductions were carried out in THF under second-order conditions (with equal concentrations of ketone and NaBH<sub>2</sub>S<sub>3</sub>). Table 2 gives the second-order rate constants for the reduction of these compounds at four different temperatures. The reaction is inhibited by electron-supplying substituents and facilitated by electron-withdrawing groups. Hammett treatment (Figure 1) of the data, using  $\sigma^+$  constants (taken from ref. 16), yields  $\rho^+$  values of +2.513 ( $r$  0.992,  $s$  0.081) and

+1.982 ( $r$  0.996,  $s$  0.074) for acetophenones and benzophenones respectively. The fairly large positive  $\rho^+$  values suggest that BH<sub>2</sub>S<sub>3</sub><sup>-</sup> is a moderately strong nucleophile and that a fairly polar transition complex,

TABLE I

Second-order rate constants for the reaction of sulphurated sodium borohydride (NaBH<sub>2</sub>S<sub>3</sub>) with some selected ketones in tetrahydrofuran at 25°

Compound	Initial concentration of compound (M)	Initial concentration of NaBH <sub>2</sub> S <sub>3</sub> (M)	10 <sup>3</sup> $k_2$ /1 mol <sup>-1</sup> s <sup>-1</sup>
Acetone	0.012 04	0.012 02	44.2
	0.024 06	0.024 04	45.0
	0.036 10	0.036 06	44.6
	0.048 02	0.048 08	45.4
	0.060 08	0.060 10	44.8
		Mean value	44.8
Acetophenone	0.012 08	0.012 02	10.2
	0.024 16	0.024 04	10.6
	0.036 24	0.036 06	10.5
	0.048 06	0.048 08	10.1
	0.060 08	0.060 10	10.6
		Mean value	10.4
Benzophenone	0.010 48	0.010 44	6.18
	0.020 86	0.020 88	6.32
	0.031 30	0.031 32	6.26
	0.041 80	0.041 76	6.30
	0.062 68	0.062 64	6.19
		Mean value	6.25
Fluorenone	0.010 42	0.010 44	58.4
	0.020 90	0.020 88	57.0
	0.031 33	0.031 32	57.8
	0.041 80	0.041 76	57.2
			Mean value

involving the formation of a C-H bond, is likely, as observed in the case of borohydride (NaBH<sub>4</sub>) reduction of ketones.<sup>5-13</sup> The Hammett relationship was also tested using  $\sigma$  constants, and the  $\rho$  values are +2.657 ( $r$  0.963,  $s$  0.299) for acetophenones and +2.099 ( $r$

<sup>1</sup> J. M. Lalancette, A. Freche, and R. Monteaux, *Canad. J. Chem.*, 1968, **46**, 2754.

<sup>2</sup> J. M. Lalancette and A. Freche, *Canad. J. Chem.*, 1969, **47**, 739.

<sup>3</sup> J. M. Lalancette and A. Freche, *Canad. J. Chem.*, 1970, **48**, 2366.

<sup>4</sup> J. M. Lalancette, A. Freche, J. R. Brindle, and M. Laliberte, *Synthesis*, 1972, **10**, 526 and references cited therein.

<sup>5</sup> H. C. Brown and B. C. Subba Rao, *J. Amer. Chem. Soc.*, 1955, **77**, 3164.

<sup>6</sup> H. C. Brown, O. H. Wheeler, and K. Ichikawa, *Tetrahedron*, 1957, **1**, 214.

<sup>7</sup> H. C. Brown and K. Ichikawa, *Tetrahedron*, 1957, **1**, 221.

<sup>8</sup> G. G. Smith and R. P. Bayer, *Tetrahedron*, 1962, **18**, 323.

<sup>9</sup> H. C. Brown, R. Bernheimer, and K. J. Morgan, *J. Amer. Chem. Soc.*, 1965, **87**, 1280.

<sup>10</sup> J. A. Parry and K. D. Warren, *J. Chem. Soc.*, 1965, 4049.

<sup>11</sup> K. D. Warren and J. R. Yandle, *J. Chem. Soc.*, 1965, 5518.

<sup>12</sup> K. Bowden and M. Hardy, *Tetrahedron*, 1966, **22**, 1169.

<sup>13</sup> G. T. Bruce, A. R. Cooksey, and K. J. Morgan, *J.C.S. Perkin II*, 1975, 551.

<sup>14</sup> R. F. Borch, M. D. Bernstein, and H. D. Durst, *J. Amer. Chem. Soc.*, 1971, **93**, 2897.

<sup>15</sup> T. C. Wolfe and H. C. Kelly, *J.C.S. Perkin II*, 1973, 1948 and references cited therein.

0.974,  $s$  0.348) for benzophenones. The better correlations with  $\sigma^+$  values<sup>16</sup> clearly indicate that the transition state is stabilized by resonance in these reactions

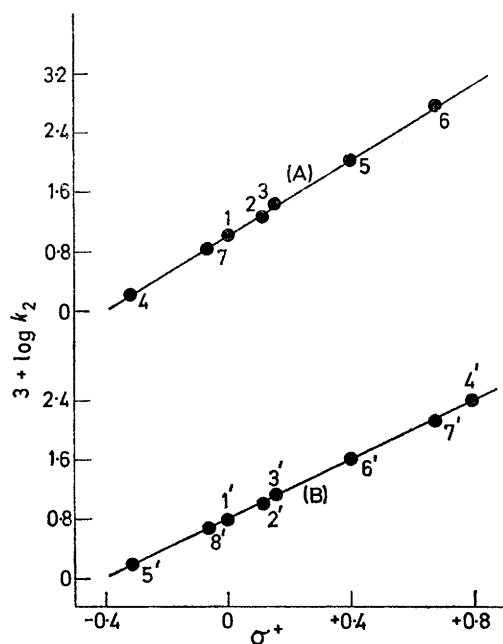


FIGURE 1 Hammett plots for acetophenones (A) and benzophenones (B) at 25° in THF. For key, see Table 2

and  $+M$  substituents such as halogens are fully conjugated with the reaction centre. In the absence of specific information about the geometry of the  $\text{BH}_2\text{S}_3^-$  ion,

greater steric inhibition of resonance by the unsubstituted phenyl ring in benzophenones, compared with the corresponding acetophenones.

**Temperature Dependence and Thermodynamic Parameters.**—The temperature dependence of these reduction reactions in the temperature range 20–40° is brought out in Table 2. From Arrhenius plots ( $\log k_2$  versus  $1/T$ ) which are all linear, the activation energies ( $E_a$ ), the heats ( $\Delta H^\ddagger$ ) and entropies ( $\Delta S^\ddagger$ ) of activation have been evaluated in the usual way and appear in Table 3. The expected increase in Arrhenius energy of activation with decrease in  $k_2$  is observed and  $-\Delta S^\ddagger$  increases as  $E_a$  decreases. The entropy of activation is in the range  $-27$  to  $-40$  cal mol<sup>-1</sup> K<sup>-1</sup> which is of the order of magnitude expected for a bimolecular reaction.

**Mechanism.**—The following are the experimental facts established by Lalancette *et al.*<sup>3</sup> for the reduction of ketones using  $\text{NaBH}_2\text{S}_3$ . (1) Low temperature leads to very high yields of the corresponding alcohols without any undesirable side reactions. Even in the case of sterically hindered ketones, the yield of alcohols remained high when an equimolar ratio of reductant and carbonyl was used. (2) The first step in the course of these reduction reactions must be a hydride shift, as shown by reduction with deuteriated sulphurated sodium borohydride ( $\text{NaBD}_2\text{S}_3$ ). With this reagent, using 1,3-diphenylacetone as substrate, the corresponding alcohol incorporated deuterium at C-2. The asymmetrical borate ester formed in the first step must be subject to spontaneous disproportionation by reacting with another molecule of ketone to form a symmetrical ester. The

TABLE 2

Second-order rate constants for the  $\text{NaBH}_2\text{S}_3$  reduction of acetophenones and benzophenones in THF at four different temperatures

	Compound	$10^3 k_2 / \text{l mol}^{-1} \text{s}^{-1}$				$\sigma^+$
		20°	25°	30°	40°	
1	Acetophenone	7.77	10.40	13.50	21.80	0
2	<i>p</i> -Chloroacetophenone	14.80	18.80	24.00	37.20	+0.114
3	<i>p</i> -Bromoacetophenone	21.40	26.50	34.30	51.30	+0.150
4	<i>p</i> -Methylacetophenone	1.23	1.68	2.35	3.99	-0.311
5	<i>m</i> -Chloroacetophenone	83.20	101.00	123.00	174.00	+0.399
6	<i>m</i> -Nitroacetophenone	447.00	526.00	620.00	832.00	+0.674
7	<i>m</i> -Methylacetophenone	5.22	6.89	9.12	14.70	-0.066
1'	Benzophenone	4.47	6.25	8.62	16.30	0
2'	<i>p</i> -Chlorobenzophenone	7.33	9.98	13.50	23.90	+0.114
3'	<i>p</i> -Bromobenzophenone	9.85	13.30	17.70	30.90	+0.150
4'	<i>p</i> -Nitrobenzophenone	197.00	237.00	285.00	400.00	+0.790
5'	<i>p</i> -Methylbenzophenone	1.10	1.58	2.28	4.50	-0.311
6'	<i>m</i> -Chlorobenzophenone	30.20	38.50	49.00	78.20	+0.399
7'	<i>m</i> -Nitrobenzophenone	100.00	126.00	159.00	240.00	+0.674
8'	<i>m</i> -Methylbenzophenone	3.35	4.68	6.46	12.10	-0.066

Each value of  $k_2$  was obtained as the mean of at least four different concentrations as in Table 1.

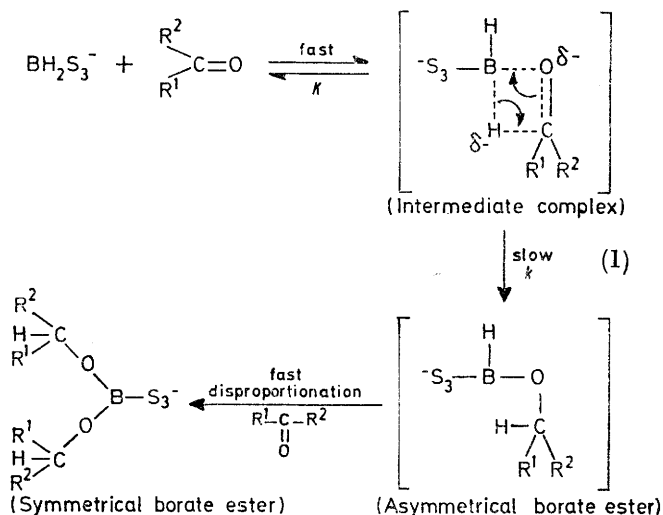
little can be said about the nucleophilicity or driving force for the observed resonance conjugation in  $\text{BH}_2\text{S}_3^-$  reductions, unobserved in  $\text{BH}_4^-$  reductions. The stability of the transition state is also reflected in the free energy ( $\Delta G^\ddagger$ ) values (refer to Tables 4 and 5). The lesser value of  $\rho^+$  for the benzophenones may be attributed to

<sup>16</sup> H. C. Brown and Y. Okamoto, *J. Amer. Chem. Soc.*, 1958, **80**, 4979.

symmetrical ester was isolated very easily by light petroleum extraction.

Taking into consideration the above observations of Lalancette *et al.*,<sup>3</sup> and the present kinetic data showing that (1) the reaction of  $\text{NaBH}_2\text{S}_3$  with ketones to form alcohols follows second-order kinetics and (2) the high value of  $\rho^+$  suggests that  $\text{BH}_2\text{S}_3^-$  is a moderately strong nucleophile, we can postulate mechanism (I) for the

reduction to explain all the experimental observations. This mechanistic scheme involves the hydride shift as the slow rate-determining step.



The reaction is assumed to proceed *via* the formation of an intermediate complex in order to explain the formation of the asymmetrical and symmetrical borate esters but at present, there is no experimental evidence for the

assumption of an intermediate complex. Thus, the observed rate constants ( $k_2$ ) represent the product of an equilibrium constant  $K$  for the association of  $\text{BH}_2\text{S}_3^-$  ion and the ketone and the rate constant  $k$  ( $k_2 = kK$ ) for the subsequent transfer of a hydride ion to the carbonyl group. The observed  $\rho^+$  values and calculated thermodynamic activation parameters are also composite. This hypothesis of an intermediate complex has already been invoked for the analogous sodium borohydride<sup>5-13</sup> reductions without direct kinetic evidence.

*Comparison with Other Systems.*—The rate constants at 25°, the relative rates, and derived thermodynamic data for some selected ketones are summarised in Table 4. The trend is almost the same as observed for the sodium borohydride reduction of ketones. The decrease in rate from acetone to acetophenone to benzophenone is in accord with greater steric requirements of the phenyl groups and their ability to conjugate with the carbonyl group and reduce their sensitivity to attack by nucleophilic reagents. The high reactivity of fluorenone in this series can be attributed to the perfectly planar nature of this molecule which reduces steric effects considerably.

*Comparison of Rate Constants and Thermodynamic Data for  $\text{NaBH}_4$  and  $\text{NaBH}_2\text{S}_3$  Reductions in THF.*—Rates were also compared with sodium borohydride ( $\text{NaBH}_4$ ) reductions for some ketones (acetone, acetophenone,

TABLE 3

Thermodynamic parameters for the  $\text{NaBH}_2\text{S}_3$  reduction of acetophenones and benzophenones at 25°

Compound	$10^3 k_2 / \text{l mol}^{-1} \text{s}^{-1}$	$E_a / \text{kcal mol}^{-1}$ ( $\pm 0.2$ )	$\Delta H^\ddagger / \text{kcal mol}^{-1}$ ( $\pm 0.2$ )	$-\Delta S^\ddagger / \text{cal mol}^{-1} \text{K}^{-1}$ ( $\pm 0.5$ )	$\log A$ ( $\pm 0.15$ )
1	10.40	9.6	9.0	35.4	5.05
2	18.80	9.0	8.4	36.3	4.87
3	26.50	8.7	8.1	36.6	4.80
4	1.68	11.4	10.8	33.0	5.58
5	101.00	7.2	6.6	39.0	4.28
6	526.00	6.0	5.4	39.7	4.12
7	6.89	10.0	9.4	34.9	5.16
1'	6.25	11.4	10.8	30.4	6.15
2'	9.98	10.8	10.2	31.5	5.91
3'	13.30	10.4	9.8	32.3	5.74
4'	237.00	6.5	5.9	39.6	4.14
5'	1.58	13.0	12.4	27.8	6.72
6'	38.5	9.0	8.4	34.9	5.18
7'	126.00	8.0	7.4	35.9	4.96
8'	4.68	11.6	11.0	30.3	6.17

TABLE 4

Kinetic data for the  $\text{NaBH}_2\text{S}_3$  reduction of some selected ketones in THF at 25°

Compound	$10^3 k_2 / \text{l mol}^{-1} \text{s}^{-1}$	Relative rate	$E_a / \text{kcal mol}^{-1}$ ( $\pm 0.2$ )	$\Delta H^\ddagger / \text{kcal mol}^{-1}$ ( $\pm 0.2$ )	$-\Delta S^\ddagger / \text{cal mol}^{-1} \text{K}^{-1}$ ( $\pm 0.5$ )	$\Delta G^\ddagger / \text{kcal mol}^{-1}$ ( $\pm 0.1$ )
Acetone	44.80	1.000	7.5	6.9	39.6	18.7
Acetophenone	10.40	0.232	9.6	9.0	35.4	19.6
Benzophenone	6.25	0.140	11.4	10.8	30.4	19.9
Fluorenone	57.60	1.285	8.5	7.9	35.7	18.6

TABLE 5

Rate constants and thermodynamic data for  $\text{NaBH}_4$  reduction in THF at 25°

Compound	$10^3 k_2 / \text{l mol}^{-1} \text{s}^{-1}$	$E_a / \text{kcal mol}^{-1}$ ( $\pm 0.2$ )	$-\Delta S^\ddagger / \text{cal mol}^{-1} \text{K}^{-1}$ ( $\pm 0.5$ )	$\Delta G^\ddagger / \text{kcal mol}^{-1}$ ( $\pm 0.1$ )
Acetone	7.92	9.2	37.3	19.7
Acetophenone	2.50	12.0	32.2	21.0
Benzophenone	2.02	13.4	28.0	21.2
Fluorenone	10.40	11.2	30.1	19.5

benzophenone, and fluorenone). The rate constants with calculated thermodynamic data for  $\text{NaBH}_4$  reduction in THF at  $25^\circ$  are presented in Table 5. The rates are considerably faster for  $\text{NaBH}_2\text{S}_3$  reductions and also the thermodynamic parameters differ significantly. A comparison of Tables 5 and 4 reveals this fact. The significant and consistent difference in rate ( $k_2$ ) for each ketone can be attributed to a more positive  $\Delta G^\ddagger$  for the  $\text{NaBH}_4$  relative to the  $\text{NaBH}_2\text{S}_3$  reduction which in turn reflects a more stable transition state (relative to reactants) in the case of the  $\text{NaBH}_2\text{S}_3$ . The increased rate of reaction in THF compared to that in isopropyl alcohol for  $\text{BH}_4^-$  reduction of ketones<sup>5-13</sup> may be due to the ion pairing in THF, because of its low dielectric constant, which stabilizes the transition state. Much

two series are  $496.8^\circ$  ( $r = 0.992$ ) and  $286.8^\circ$  ( $r = 0.990$ ) for acetophenones and benzophenones respectively. The difference in the  $\beta$  values for these two series may be attributed to the observed difference in the values of  $\rho^\ddagger$  since isokinetic temperature ( $\beta$ ) and reaction constant ( $\rho^\ddagger$ ) are interdependent.<sup>18</sup> According to Leffler,<sup>17</sup> the fact that the isokinetic temperature, in each case, is more than  $240^\circ$  higher than the experimental temperatures ( $20\text{--}40^\circ$ ) makes the isokinetic relationship valid for these two series. The correlations obtained for these two series were tested and found genuine by applying Exner's criteria.<sup>18</sup> However, current views<sup>19-21</sup> do not attach much physical meaning to the isokinetic temperature, since a linear correlation in equation (2) is usually a necessary condition for the validity of the Hammett equation.

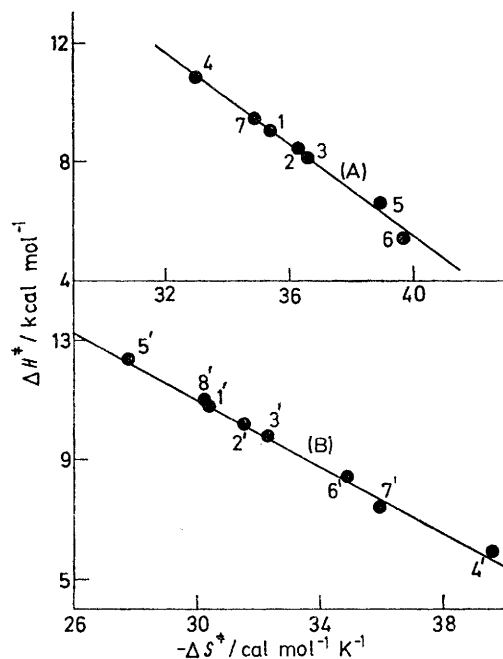


FIGURE 2  $\Delta H^\ddagger$  versus  $-\Delta S^\ddagger$  for acetophenones (A) and benzophenones (B). For key, see Table 2

cannot be said about this effect in  $\text{BH}_2\text{S}_3^-$  reduction since no comparison can be made inasmuch as the present experimental work was restricted to THF. (For reasons, refer to Experimental section.)

**Energy-Entropy Relationship.**—With regard to heats and entropies of activation, it has been pointed out by Leffler<sup>17</sup> that the two variables are correlated by equation (2) where  $\beta$  is known as the isokinetic temperature.

$$\Delta H^\ddagger = \Delta H_0^\ddagger + \beta \Delta S^\ddagger \quad (2)$$

Figure 2 gives the least square isokinetic plots ( $\Delta H^\ddagger$  versus  $-\Delta S^\ddagger$ ) for the reduction of acetophenones (Figure 2A) and benzophenones (Figure 2B) using  $\text{BH}_2\text{S}_3^-$ . The isokinetic temperatures obtained for these

#### EXPERIMENTAL

Sulphurated sodium borohydride ( $\text{NaBH}_2\text{S}_3$ ) was prepared from a mixture of sodium borohydride (3.78 g, 0.10 mol) and sulphur (9.60 g, 0.30 mol) in THF (20 ml) at  $25^\circ$  as reported in the literature.<sup>1,22</sup> In order to remove trace amounts of unchanged  $\text{NaBH}_4$ , the crude  $\text{NaBH}_2\text{S}_3$  was washed at least ten times with light petroleum, each time shaking the flask vigorously. The washed  $\text{NaBH}_2\text{S}_3$  sample was kept overnight in an excess of light petroleum under an atmosphere of nitrogen so as to ensure the complete removal of unchanged materials. The solid product was dried under vacuum at room temperature and such a sample was found to be spectroscopically pure.<sup>22</sup>

Estimation of  $\text{NaBH}_2\text{S}_3$  was done using excess of potassium iodate. The reaction between  $\text{NaBH}_2\text{S}_3$  and potassium iodate is fast and instantaneous in neutral medium unlike in alkaline medium<sup>22</sup> and the stoichiometry of this reaction is 1 : 1 in both cases. Also, such a large quantity of iodate is not required (since the reaction in neutral medium is very fast) as is reported for alkaline medium.

**Rate Measurements.**—All reactions were carried out in pure THF since  $\text{NaBH}_2\text{S}_3$  is highly stable in this solvent. Also, other solvents such as methanol or isopropyl alcohol cannot be used for kinetic measurements since  $\text{NaBH}_2\text{S}_3$  is known to react with alcohols.<sup>1</sup> Analytical reagent grade THF (Fisher Scientific Co.) was distilled, b.p.  $66^\circ$ , and dried before use. All the ketones used for the present investigation were of analytical reagent grade (Eastman Kodak, Fisher Scientific, and Aldrich Chemical). A solution of  $\text{NaBH}_2\text{S}_3$  in THF (50 ml; 0.02–0.14M) was mixed with a solution of the ketone in THF (50 ml; 0.02–0.14M) at the reaction temperature, solutions being thermostatted for at least 2 h prior to mixing. At appropriate times, portions (5 ml) were withdrawn and quenched in a known amount of potassium iodate (20 ml; 0.025–0.15M) containing potassium iodide (10 ml; 10%) solution. To the quenched solution, dilute sulphuric acid (10 ml; 6N) was added and the iodine liberated titrated against standardized sodium thiosulphate. Concentration of the unchanged  $\text{NaBH}_2\text{S}_3$  in each sample was determined from the concentration of the iodate consumed.

Rate constants were calculated from the second-order

<sup>17</sup> J. E. Leffler, *J. Org. Chem.*, 1955, **20**, 1202.

<sup>18</sup> O. Exner, *Coll. Czech. Chem. Comm.*, 1964, **29**, 1094.

<sup>19</sup> J. E. Leffler, *J. Org. Chem.*, 1966, **31**, 533.

<sup>20</sup> O. Exner, *Coll. Czech. Chem. Comm.*, 1972, **37**, 1425.

<sup>21</sup> O. Exner and V. Beranek, *Coll. Czech. Chem. Comm.*, 1973, **38**, 781.

<sup>22</sup> V. M. Sadagopa Ramanujam and N. M. Trieff, *Analyst*, 1975, **100**, 655.

rate equation for equimolar concentrations of reactants. Rate constants were all reproducible within the limits of experimental error ( $\pm 4\%$ ).

*Product Analysis*—Products were analysed in the case of some typical ketones such as fluoren-9-one, *m*-nitroacetophenone, and *m*-chloro-, *p*-nitro-, *p*-bromo-, and *p*-methylbenzophenone. To a solution of  $\text{NaBH}_2\text{S}_3$  (0.02 mol) in THF (50 ml) was added the ketone (0.02 mol), the reaction being allowed to go to completion at 40°. The mixture was then hydrolysed by adding hydrochloric acid (50 ml; 10%) and the alcohol formed extracted with chloroform. The

alcohol was further purified by recrystallization with methanol or ethanol. Yield of the alcohol in each case was found to be almost quantitative ( $> 90\%$ ). Identification of the alcohols was made by comparing their m.p.s with the values reported in the literature. Also, mixed m.p. determination with an authentic sample of the alcohol in each case showed no depression.

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