622. *Reductions with Aluminium Alkoxides. Part III.* The Kinetics of the Racemization of Optically Active Alkoxides by their Corresponding Ketones.*

By L. M. Jackman and A. Killen Macbeth.

The existing evidence for a postulated mechanism of the reduction of carbonyl compounds by aluminium alkoxides is reviewed. The racemization of aluminium (+)-1-methylpropoxide and aluminium (+)-1-methylheptyloxide by butan-2-one and octan-2-one respectively has been followed polarimetrically under various conditions of concentration and temperature. The presence of *cyclo*hexylamine has been shown to retard the reaction. The kinetic interpretation of these results is discussed in the light of the postulated mechanism.

In view of the high specificity of the reaction, the mechanism of the Meerwein–Ponndorf–Verley reduction represents a peculiar problem. Various mechanisms have been proposed for it, the most feasible involving the initial co-ordination between the alkoxide and ketone, followed by the intramolecular transfer of hydrogen through a cyclic transition state. This type of mechanism, first proposed by Meerwein (*J. pr. Chem.*, 1936, **147**, 211), has since been adopted by other workers (Woodward, Wendler, and Brutschy, *J. Amer. Chem. Soc.*, 1945, **67**, 1425; Dewar, " Electronic Theory of Organic Chemistry," Oxford, 1949, p. 136; Jackman and Mills, *Nature*, 1949, **164**, 789). Hammett (" Physical Organic Chemistry," McGraw-Hill Book Co., New York, 1940, p. 352) also suggested co-ordination as the first step, but then assumed the hydrogen transfer to proceed intermolecularly. The two steps in the mechanism involving the cyclic transition state are represented as (1) and (2). Although there is little direct evidence for this mechanism, it is found adequately to explain all known facts concerning the reduction, and some of the more important of these are now summarized, the facts being dealt with in two classes, according to whether they are consequent upon the first or the second stage of the reaction.

The high specificity of the aluminium atom may be considered under the first heading. Although the alkoxides of aluminium are reducing agents *par excellence*, the alkoxides of other elements are also capable of functioning in such reversible reduction systems.

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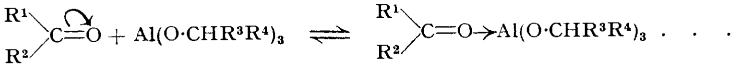
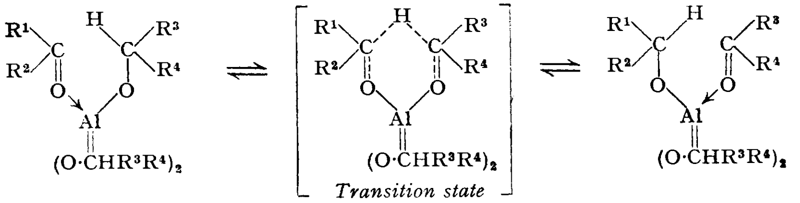
* Part II, *J.*, 1949, 2646.

Magnesium ethoxide (Meerwein and Schmidt, *Annalen*, 1925, **444**, 221), halogenomagnesium alkoxides (Meerwein and Schmidt, *loc. cit.*; Gomberg and Bachmann, *J. Amer. Chem. Soc.*, 1930, **52**, 4967; Shankland and Gomberg, *ibid.*, p. 4973; Bachmann and Kloetzel, *ibid.*, 1937, **59**, 2210), and boron alkoxides (Wuyts and Duquesne, *Bull. Soc. chim. Belg.*, 1939, **48**, 77; Kuivila, Slack, and Siiteri, *J. Amer. Chem. Soc.*, 1951, **73**, 123) have all been shown to bring about reduction but are all inferior to the aluminium derivatives in ease and scope of reduction. These elements all possess p-orbitals available for co-ordination. It is to be expected that the Group III elements might exhibit a greater tendency to co-ordinate,



$$R^1R^2C{=}O + Al(O{\cdot}CHR^3R^4)_3 \rightleftharpoons R^1R^2C{=}O{\rightarrow}Al(O{\cdot}CHR^3R^4)_3 \quad . \quad . \quad . \quad . \quad (1)$$



. (2)

thus explaining why aluminium is more effective than magnesium. Similarly, within Group III itself it might be expected that the first member, boron, in view of its greater co-ordinating ability, would be a more effective reducing agent than aluminium, whereas in fact the reverse is true and reductions of aldehydes with *iso*propyl borate require many hours' heating at 150°. The alkyls and fluoride of boron are strongly co-ordinating, but the alkoxides probably show no such tendency because of a highly effective overlap of the oxygen $2p_z$ orbital with the vacant $2p_z$ orbital of boron. Mulliken (*ibid.*, 1950, **72**, 4493) has recently calculated the overlap integrals for various heteropolar bonds involving first- and second-row elements, and it would appear that p_π-orbital overlap is less effective for elements of the second row. Although the type of bond considered above has not been dealt with by Mulliken, it is reasonable to suppose that they also follow this rule. The fact then that the $3p_\pi$–$2p_\pi$ bond in aluminium alkoxides is less effective than in the boron compounds would permit the formation of stronger $3p_\sigma$–$2p_\sigma$ bonds with a carbonyl oxygen atom. This concept of π-bonding, which has been termed "back co-ordination," is reflected in the absence of association of boric esters in solution (Sidgwick, "Chemical Elements and Their Compounds," Oxford, 1950, Vol. I, p. 387). It is significant that alkoxides of aluminium usually possess association factors of 3—5 in benzene solution (Robinson and Peake, *J. Phys. Chem.*, 1935, **39**, 1125; Ulich and Nespital, *Z. phys. Chem.*, 1933, **165**, 294). The marked difference in co-ordinating power and the relative π-bond formation of the oxy-compounds of aluminium and boron may be further gauged by results of certain *X*-ray crystallographic studies. The crystal of boric acid is found to consist of planes of molecules held together by hydrogen bonds (Zachariasen, *Z. Krist.*, 1934, **88**, 150) and the B–O distance is 1·35 Å, compared with 1·54 Å, the sum of the two covalent radii. The B–O distance corresponds to approximately one-third double-bond character in each of the three bonds and implies that boron has a complete octet. In analogous aluminium compounds, hydrargillite (Megaw, *ibid.*, 1934, **87**, 185) and diaspore (Ewing, *J. Chem. Phys.*, 1935, **3**, 203), the aluminium is found to be in the six-covalent state and the Al–O distance corresponds, within the somewhat large limits of experimental error, to the sum of the covalent radii. Electron-diffraction studies (Bauer and Beach, *J. Amer. Chem. Soc.*, 1941, **63**, 1394) show a similar shortening of the B–O distance in methyl borate, but unfortunately, values are not available for aluminium alkoxides. A similar difference between the compounds of boron and aluminium is well illustrated by the dipole moments of the halides in benzene solution (*Trans. Faraday Soc.*, 1934, **30**, Appendix). Boron trichloride has a zero dipole moment, indicating a planar configuration as a result of back co-ordination (Pauling, "Nature of the Chemical Bond," Cornell Univ. Press, New York, 1945, p. 238), but aluminium bromide is apparently non-planar, as it has a dipole moment of 4·89 D. Further evidence of the non-co-ordination of boron esters has been summarised by Yabroff, Branch, and Almquist (*J. Amer. Chem. Soc.*, 1933, **55**, 2935). Almost certainly, back co-ordination exists in the aluminium alkoxides, but to a lesser extent than in boron analogues. The difference in reducing power of the boron and aluminium compounds may then arise from their relative ability to co-ordinate with the carbonyl compounds.

In the light of the above discussion it would seem most unlikely that stable addition compounds with aluminium alkoxides would exist, other than in solution, except, perhaps, in the most favourable cases and under ideal conditions. A few examples can be quoted. Salts of the hypothetical acid $HAl(OR)_4$, in which the aluminium is in the four-covalent state, are well known, and it is significant that sodium aluminium ethoxide (Meerwein *et al.*, *loc. cit.*), and magnesium aluminium *iso*propoxide (Kulpinsky and Nord, *J. Org. Chem.*, 1943, **8**, 256) are devoid of reducing power. There are, of course, the various well-known chelate compounds which may be regarded as co-ordination compounds of phenoxides or alkoxides. The complexes with acetylacetone and 8-hydroxyquinoline are quite stable. These examples are all most favourable cases, and it is found that no co-ordination compounds of the type resulting from the simple union of two neutral molecules have been isolated. Chelinzev (*Bull. Soc. chim.*, 1924, **35**, 741) claims to have produced evidence, based on thermal data, for the existence of such compounds between iodomagnesium alkoxides and alcohols and ketones. It thus appears that aluminium alkoxides owe their specificity to their ability to co-ordinate with carbonyl compounds to a degree *sufficient* to permit the reaction to proceed at a measurable speed. Further evidence based on physical measurements will, however, be sought to confirm this point. In the Meerwein–Ponndorf reduction, then, the amphoteric aluminium alkoxides may be regarded as functioning as acids. With the realization of this fact, the formal analogy between this reaction and the base-catalysed Cannizzaro reaction disappears, and a similarity in mechanisms is no longer to be expected (cf. Verley, *ibid.*, 1927, **39**, 797; Waters, "The Chemistry of Free Radicals," 2nd edn., Oxford, 1948, p. 192). In addition to the alkoxides already discussed Meerwein (*loc. cit.*) has reported that benzaldehyde can be reduced in varying yields by the ethoxides of zirconium(IV), tin(IV), titanium(IV), antimony(V), and iron(III), and the ease of reduction appears to be in that order. All are inferior to aluminium ethoxide, although the zirconium derivative may be classed as a "good" reducing reagent. That these elements can exercise higher valencies as their ethoxides has been shown by Meerwein and Bersin (*Annalen*, 1929, **476**, 113), who prepared their "Alkoxosalze" with the alkoxides of Group I and II elements; *e.g.*, the compounds $[Zr(OEt)_6]HNa$, $[Ti(OBu)_6]HK$, and $[Sn(OEt)_6]K_2$ were prepared. Furthermore, the halides of zirconium, stannic tin, and titanium are known to form addition compounds with one or two molecules of ethers or ketones (Scagliarini and Tartarini, *Atti Accad. Lincei*, 1926, **4**, 318; Evard, *Compt. rend.*, 1933, **196**, 2007; Jantsch, *J. pr. Chem.*, 1927, **115**, 7).

Concerning the second step of the reduction, it has been stated elsewhere (Jackman and Mills, *loc. cit.*) that the path through the cyclic transition state is to be favoured because of the possibility of resonance in such a system, with an equivalent lowering of the activation energy. It was pointed out at the same time that models indicated the transition state to be favourable on steric grounds. There are certain experimental facts which also favour this mechanism. First, the fact that αβ-double bonds are not reduced was mentioned as a possible consequence of the cyclic transition state, as 1 : 4-addition would require a sterically less favourable eight-membered ring. This view has recently been confirmed by the work of Lutz and Gillespie (*J. Amer. Chem. Soc.*, 1950, **72**, 344). Perhaps more significant are the stereochemical results of the reductions of certain alkyl*cyclo*hexanones with various alkoxides (Jackman, Macbeth, and Mills, *J.*, 1949, 2641), which receive interpretation in the light of this mechanism. Similarly, the achievement of asymmetric syntheses in this reaction (Doering and Young, *J. Amer. Chem. Soc.*, 1950, **72**, 631; Jackman, Mills, and Shannon, *ibid.*, p. 4814), and the configurations of the predominent enantiomers, are consistent with the theory.*

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* McGowan (*Chem. and Ind.*, 1951, 601) has provided a very elegant confirmation of the postulated cyclic transition state.

In view of the nature of the above evidence, a kinetic study of the reaction seemed desirable in order to provide more precise confirmation. No investigation of the kinetics of the reduction has been reported, and there are certain problems which complicate such work. The reduction process may be considered as the establishment of an equilibrium between two oxidation–reduction systems (cf. Baker and Adkins, *ibid.*, 1940, **62**, 3305), and to follow the chemical change it is necessary, in the general case, to be able to estimate *one* alcohol or *one* ketone in the presence of the other alcohol or other ketone. The use of a light-absorption technique was given some consideration, as it was thought that with fluorenone–fluorenol as one of the systems the progress of the reaction might be followed. This idea was abandoned in preference to that reported below, for the kinetics of the equilibrium reaction were complicated by the formation of mixed alkoxides and the necessity of dealing with two competing reactions. The light-absorption method, however, may be capable of development, and could be useful as it offers a wider scope than the present method. The kinetic procedure now described consists of the measurement of the rate of racemization of an aluminium derivative of an optically active alcohol by the *corresponding* ketone. This method greatly simplifies the kinetics, as the possibility of the formation of mixed alkoxides no longer exists, and the actual rate process under consideration goes to completion unaffected by an opposing reaction. The chief disadvantage of this method is that it is confined to alkoxides of the few readily accessible alcohols which have their asymmetric centres at the hydroxylated carbon atoms and cannot undergo epimerization. Of these the active butan-2-ols and octan-2-ols are used here. The resolutions of the two alcohols (Ingersoll, " Organic Reactions," Vol. II, John Wiley, 1944, pp. 400, 403) give reasonably high yields and can be carried out quickly and on a fairly large scale. (—)-Aluminium 1-methylpropoxide (but-2-oxide) is prepared by the action of aluminium on the (+)-alcohol. This method is not available for aluminium 1-methylheptyloxide (octyl-2-oxide) as this alkoxide cannot readily be distilled nor can the crude product be purified by chromatography. The desired compound was eventually obtained in a pure state by the use of an alcohol-exchange reaction (cf. Baker and Lynn, *J. Amer. Chem. Soc.*, 1949, **71**, 1399) between the octanol and aluminium *tert.*-butoxide in toluene. The *tert.*-butanol may be removed, as it is formed, as its azeotrope with toluene. This alkoxide has the opposite sign of rotation to its parent alcohol. Attempts to carry out the exchange without a solvent failed to go to completion, and the resulting mixed alkoxide, when aluminium *iso*propoxide is used, exhibits an interesting mutarotation when its solution in benzene is treated with octan-2-one.

EXPERIMENTAL

*Methyl*cyclo*hexane.*—Commercial samples were shaken with one-tenth their volume of oleum for 2 hours. The hydrocarbon was decanted and washed with sodium hydroxide solution (5%) and then with water, until neutral to litmus. The product was dried ($MgSO_4$), fractionated over sodium, and stored over this metal. Spectroscopic analysis showed the complete absence of aromatic compounds.

Butan-2-one.—Commercial ethyl methyl ketone was purified by conversion into its bisulphite compound and fractionation of the regenerated ketone. The last traces of moisture were removed by prolonged storage over anhydrous copper sulphate.

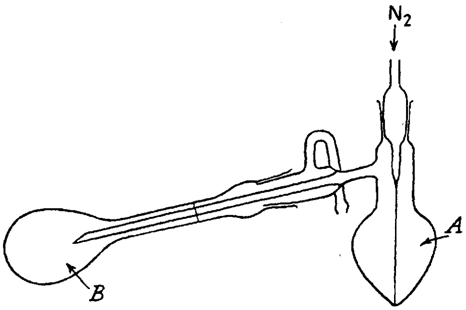
Octan-2-one.—A solution of sulphuric acid (96 ml.; *d* 1·83) in water (200 ml.) was added dropwise to a mechanically stirred mixture of octan-2-ol (130 g.), powdered potassium dichromate (195 g.), and water (800 ml.). The acid was added at such a rate as to keep the mixture at 60°. After the addition of the acid was complete, stirring was continued until the temperature fell to 25°. The oily layer was separated, and washed with water, sodium hydroxide solution (5%), and finally with water. The crude octan-2-one was added to a solution of semicarbazide (105 g.) and crystalline sodium acetate (130 g.) in water (500 ml.). Ethanol (350 ml.) was added to dissolve the ketone, and an immediate formation of the semicarbazone took place. The reaction mixture was set aside in a refrigerator overnight, and the crystalline material was filtered off and washed with 50% ethanol (100 ml.). After one recrystallisation from 50% ethanol the semicarbazone (132 g.) melted sharply at 122°. A solution of the semicarbazone in 5% sulphuric acid (3 equiv.) was steam-distilled. The distillate was extracted twice with ether and the extract dried ($MgSO_4$). After removal of the solvent the octan-2-one was distilled. The product

(88 g., 69% calc. on octan-2-ol), b. p. 64°/15 mm., was stored over anhydrous copper sulphate until required.

(+)-*Butan-2-ol.*—The resolution was carried out by Ingersoll's method (*loc. cit.*). The hydrolysis of the active hydrogen phthalate was modified slightly. A solution of (+)-1-methylpropyl hydrogen phthalate (65 g.) in 10% aqueous sodium hydroxide (290 ml.) was fractionated through a 60-cm. column (packed with beads) under a reflux ratio of 4 : 1. The water–butanol azeotrope, b. p. 86·5°/762 mm., distilled first and the fractionation was continued until the temperature of the distillate reached 100°. The distillate was shaken with anhydrous potassium carbonate (15 g.), and the aqueous layer removed. The alcohol was refluxed and distilled over freshly prepared calcium oxide. The last traces were removed from the calcium oxide by momentarily evacuating the system. The active alcohol (17·0 g.) had $[\alpha]_D^{22\cdot2}$ +10·65° homogenous. Residues from the resolution yielded samples of (−)-butan-2-ol with α_D as high as −4·18°, which were useful for preliminary experiments.

Aluminium (+)-1-*Methylpropoxide* (*But-2-oxide*).—Aluminium foil (3·65 g.) was treated with (+)-butan-2-ol (35 g.) and a few mg. of mercuric chloride. The mixture was refluxed until the foil had completely dissolved. The excess of alcohol was removed under reduced pressure in a stream of dry nitrogen. The alkoxide was distilled under reduced pressure into the flask *A* (Fig. 1) and from thence redistilled (b. p. 146—154°/0·55 mm.) into an accurately weighed 100-ml. graduated flask *B*. The use of this technique greatly minimized the risk of hydrolysis during the subsequent handling of the product. The aluminium (+)-but-2-oxide (32·246 g.) was then dissolved in methyl*cyclo*hexane and made up to 100 ml.

FIG. 1.



(+)- *and* (−)-*Octan-2-ol.*—Both optically active forms were obtained by Ingersoll's method (*loc. cit.*) and dried by refluxing over one-tenth of their weight of fresh calcium oxide.

Aluminium (±)-1-*Methylheptyloxide* (*Octyl-2-oxide*).—(*a*) Aluminium foil (1·0 g.) was treated with dry (±)-octan-2-ol (15 g.) and a few mg. of mercuric chloride. The mixture was heated in a heating mantle and a vigorous reaction ensured near the b. p. of the alcohol. Heating was continued until all the aluminium had dissolved (½ hour). The excess of alcohol was removed on a water-pump (b. p. 87°/17 mm.). Attempts to distil the alkoxide by ordinary techniques led to decomposition, but it could be distilled in a " short-path " still at 10^{-2} mm./240—250° (bath temp.). This method was slow and unsuitable for large-scale preparations.

The crude alkoxide prepared as above was probably substantially pure except for the presence of suspended impurities of undissolved metals. Long periods of centrifuging failed to remove these impurities, which must have been colloidal. Neutral alumina was prepared by permitting redistilled aluminium *iso*propoxide to hydrolyse spontaneously in a desiccator over water. The traces of moisture were removed at 700° in an electric furnace. This alumina was used in an attempted chromatography of the alkoxide in benzene, but the colloidal material was eluted as readily as the alkoxide.

(*b*) Aluminium *iso*propoxide (11·0 g.) was distilled under reduced pressure in the apparatus illustrated in Fig. 1. To the redistilled aluminium *iso*propoxide (9·80 g.) in the standard flask *B* was added dry (±)-octan-2-ol (24·69 g.). A dried boiling chip (0·05 g.) was added, the flask was fitted for distillation, and then heated in a bath at 120°, whereupon a liquid (6 ml.), b. p. 88—92°, distilled. The distillation was now continued at 9 mm. (bath temp. 130°), and a stream of dry nitrogen drawn through the residue. Finally, the system was evacuated to 10^{-2} mm. In this way a colourless viscous product (17·75 g.) was obtained. This compound was assayed for aluminium by the 8-hydroxyquinoline method (Found : Al, 7·35. Calc. for $C_{24}H_{51}O_3Al$: Al, 6·5%). It was concluded that some *iso*propoxy-residues still remained.

(*c*) Carefully purified aluminium *tert.*-butoxide (5·0 g.) was dissolved in a mixture of toluene (200 ml.) and (±)-octan-2-ol (9·0 g.). The solution was fractionated through a 30-cm. column packed with single-turn Fenske glass helices and fitted with a reflux divider. With a reflux ratio of 10 : 1, a toluene–*tert.*-butanol azeotrope, b. p. 81·5°/757 mm., was slowly removed. A further quantity (100 ml.) of toluene was taken off. The residue was cooled and rapidly transferred to a dry centrifuge cone and traces of turbidity were removed by centrifuging. Finally, the solvent and excess of octanol were removed by distillation in a current of dry nitrogen at 150°/0·1 mm. (bath temp.) (4 hours). The clear viscous liquid thus obtained was (±)-*aluminium* 1-*methylheptyloxide* (*octyl*-2-*oxide*) (Found : Al, 6·4. $C_{24}H_{51}O_3Al$ requires Al, 6·5%).

Aluminium (+)- *and* (−)-1-*Methylheptyloxide.*—An optically active mixed alkoxide was prepared by method (*b*). Samples of pure (+)- and (−)-alkoxides were obtained by method (*c*). It was noted that (+)-octan-2-ol, $[\alpha]_D^{15}$ +8·10° (homogeneous), yielded (−)-aluminium 1-methylheptyloxide, $[\alpha]_D^{30\cdot0}$ −8·52 (*c*, 12·8 in methyl*cyclo*hexane). Slight hydrolysis could therefore have a marked effect on the rotation of the alkoxide.

cyclo*Hexylamine.*—Commercial samples were fractionated over sodium through a short column of single-turn helices; b. p. 134°.

The Kinetic Method.—The polarimetric measurements were carried out on a Hilger Barfit polarimeter fitted with a 2-dm. jacketed brass tube of 9—10 ml. capacity with a side tube to facilitate filling. Sodium-*D* lines were used for all measurements. Water from a thermostat was circulated through the jacket of the tube, and the temperature of the effluent could be held to ±0·02°.

The ketone solutions were dispensed from a 5-ml. automatic microburette fitted with a 250-ml. reservoir and carefully protected from the atmosphere by " anhydrone " tubes. Samples of the alkoxide solutions were transferred in vacuum pipettes. All apparatus was dried before use by washing them with anhydrous ether, and evaporating the ether in a stream of dry air. It was found that the solutions could be introduced into the polarimeter tube within 1 minute and that equilibrium temperature was reached within 3 min., so the first reading could be made approximately 4 min. after the admixing.

Results.—(The standard deviation has been employed as the precision index throughout. Unless otherwise stated, methyl*cyclo*hexane is the solvent used for all experiments.)

For each experiment, the racemization process was found to obey, within certain limits, the general first-order equation

$$k = (1/2t) \ln \alpha_0/\alpha_t \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (3)$$

where α_0 and α_t are rotations at zero time and time *t* (seconds), respectively. The coefficient $\frac{1}{2}$ takes into account the fact that the racemization is complete when one-half of the alkoxide molecules have undergone inversion (cf. Hughes *et al.*, *J.*, 1935, 1526). For a process of this type it is possible to select any point during the reaction as an arbitrary zero. Table 1 gives the result of a characteristic experiment on the racemization of (+)-aluminium 1-methylpropoxide by butan-2-one; *k'* and *k''* are rate constants calculated by taking zero values at the beginning and at 6·9% completion respectively.

TABLE 1. *The variation of the rate constant with time for the racemization of* (+)-*aluminium* 1-*methylpropoxide* (0·6545M) *by butan-2-one* (0·360M).

t (min.)	α^{30}	$10^5k'$	$10^5k''$	*t* (min.)	α^{30}	$10^5k'$	$10^5k''$	*t* (min.)	α^{30}	$10^5k'$	$10^5k''$
8	+2·40°	—	—	51	+2·26°	1·43	—	124	+1·96°	1·56	1·60
11 [a]	2·42	—	—	57 [b]	2·235	1·44	—	139	1·90	1·59	1·65
17	2·41	0·55	—	64	2·20	1·50	1·90	154	1·84	1·59	1·67
21	2·40	0·68	—	73	2·16	1·53	1·79	167	1·79	1·61	1·69
26	2·38	0·93	—	82	2·13	1·49	1·60	195	1·69	1·63	1·69
31	2·35	1·23	—	89	2·10	1·52	1·62	211	1·65	1·59	1·65
37	2·33	1·21	—	100	2·05	1·55	1·67	242	1·555	1·59	1·66
41	2·31	1·30	—	106	2·025	1·57	1·68	269	1·49	1·59	1·58
46	2·285	1·36	—	115	1·99	1·57	1·67	298	1·41	1·59	1·58

[a] Denotes the zero for *k'*. [b] Denotes the zero for *k''*.

Fig. 2 shows the plot of log α_0/α_t against time for the first 13% of the reaction, and it is seen that a linear relationship only exists after an initial period of inconsistency. For this reason the rate constants for the various experiments have been calculated by selecting, as zero values, times at which the reaction has passed this initial period. As the accuracy of the rate constants depends, in part, on the precision of the zero measurements, three such values have been obtained for each experiment. In order to avoid the measurement of very small differences, reasonable intervals of time were allowed to elapse between the " zero " readings and the first t reading. Ten such t readings were made and then an arithmetic mean of all 30 rate constants thus calculated was computed and accepted as the rate constant for the particular experiment. After the reactions had proceeded past 50% completion, downward drifts in the rate constants were invariably observed. Readings were therefore confined to the first half of the reaction. The drift is almost certainly a consequence of a mesityl oxide type of condensation which is well known as a side reaction of the Meerwein–Ponndorf reduction (cf. Wayne and Adkins, *J. Amer. Chem. Soc.*, 1940, **62**, 3401). It is significant that the drift was found to occur earlier at higher ketone concentrations, which is consistent with the probable dependence of the rate of condensation on the *square* of the ketone concentration.

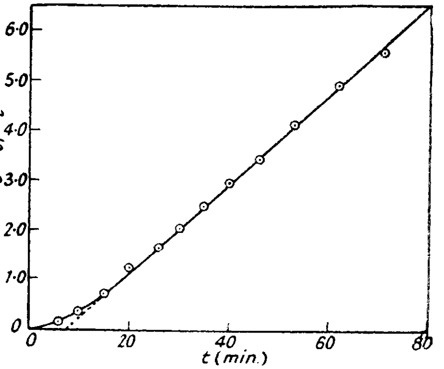
Table 2 indicates that the rate of racemization is dependent on the concentration of ketone and the rate equation now becomes

$$k_2 = (1/[\mathrm{B}]t) \ln \alpha_0/\alpha_t \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (4)$$

where [B] is the ketone concentration.

Similar results have been obtained for the system (−)-aluminium 1-methylheptyloxide–octan-2-one, although in this case the nature of the initial stage of the reaction differs from that of the (+)-aluminium 1-methylpropoxide experiments. Fig. 3 shows the plot of log α_0/α_t for the early part of a characteristic experiment. It is seen here that the rate of racemization appears to be greatest at the commencement of the reaction. Blank experiments, without ketone, showed no variation of rotation with time, and even the most vigorous drying of the ketone failed to alter the observed result. The results recorded in Table 3 show equation (4) to be obeyed for the racemization of constant concentrations of aluminium 1-methylheptyloxide. In both Figs. 2 and 3 only a part of that actual fraction of the reaction for which first-order kinetics was obeyed has been plotted. For the experiments with 1-methyl-propoxide and -heptyloxide the initial period of inconsistency extended over the first 7—9% and 15—20%, respectively, and in each case the rate equations have been based on at least 40% of the reaction subsequent to the initial period.

FIG. 2.



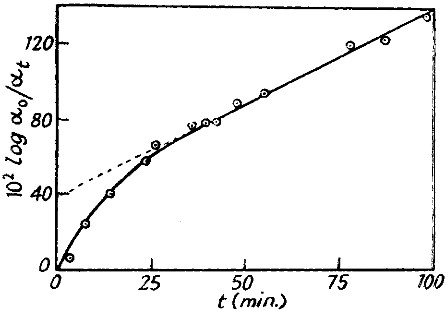


TABLE 2. *The effect of ketone concentration.*

(+)-Aluminium 1-methylpropoxide, 0·6545M; 30·00°.

Ketone molarity	0·180	0·240	0·300	0·360	0·420
$10^5 k_2$ (l. g.-mol.$^{-1}$ sec.$^{-1}$)	4·61 ± 0·10	4·59 ± 0·06	4·53 ± 0·11	4·60 ± 0·06	4·53 ± 0·11

TABLE 3. *The effect of ketone concentration.*

(+)-Aluminium 1-methylheptyloxide, 0·227M; 30·0°.

Ketone molarity	0·120	0·160	0·200	0·400
$10^5 k_2$ (l. g.-mol.$^{-1}$ sec.$^{-1}$)	8·90 ± 0·51	8·90 ± 0·42	9·25 ± 0·37	9·05 ± 0·68

Experiments with varying alkoxide concentration indicate that, in spite of the nature of equation (4), the absolute alkoxide concentration has a marked effect on the rate of racemization of (+)-aluminium 1-methylheptyloxide. The results obtained fit the general equation (5) over the limited range examined: [A] is the total alkoxide concentration. The closeness of fit

$$k' = ([\mathrm{A}]/[\mathrm{B}]t) \ln \alpha_0/\alpha_t \quad . \; . \; . \; . \; . \; . \; . \; . \; . \quad (5)$$

of this equation may be assessed from rate constants (Table 4) obtained at various concentrations of aluminium 1-methylheptyloxide. The theoretical significance of this unexpected observation that the kinetics of the racemization are of first order in ketone, but independent of alkoxide concentration, will be discussed later. Meanwhile, it is obvious that the Arrhenius equations must be based on this new equation (5). Similar results have been observed with (±)-aluminium 1-methylpropoxide in which the values 5·09 and 4·59 for 10^5k_2 (equation 4) were obtained for two experiments under identical conditions, with the exception of the alkoxide molarities, which were 0·627M and 0·654M, respectively.

TABLE 4. *The effect of alkoxide concentration.*

Octan-2-one concentration, 0·200M; 30·0°.

Alkoxide molarity	0·154	0·227	0·270	0·386
$10^5k'$, sec.$^{-1}$	2·20 ± 0·15	2·10 ± 0·08	2·16 ± 0·11	2·11 ± 0·08

Tables 5 (*a*) and (*b*) give the values of the rate constants at various temperatures for the racemization of (+)-aluminium 1-methylpropoxide and (−)-aluminium 1-methylheptyloxide, respectively.

TABLE 5. *The effect of temperature.*

(*a*) (+)-Aluminium 1-methylpropoxide, 0·6275M; butan-2-one, 0·240M.

Temp.	20·15°	22·60°	25·00°	27·00°	30·00°	33·75°
$10^5k'$ (sec.$^{-1}$)	1·20 ± 0·04	1·49 ± 0·09	1·95 ± 0·06	2·45 ± 0·03	3·20 ± 0·07	5·00 ± 0·11

(*b*) Aluminium 1-methylheptyloxide, 0·227M; octan-2-one, 0·220M.

Temp.	22·10°	25·00°	26·95°	30·00°	31·90°
$10^5k'$ (sec.$^{-1}$)	1·15 ± 0·08	1·44 ± 0·07	1·78 ± 0·16	2·10 ± 0·10	2·56 ± 0·26
	1·21 ± 0·04	1·40 ± 0·08	1·79 ± 0·11	—	2·16 ± 0·13
Grand means	1·20 ± 0·04	1·42 ± 0·11	1·79 ± 0·10	2·10 ± 0·10	2·22 ± 0·13

Calculations of the Arrhenius parameters from the data in Table 5 have been carried out by the method of "least squares" (Worthing and Geffner, "Treatment of Experimental Data," John Wiley, 1943, p. 240). In the treatment of the data in Table 5(*b*) the grand means were assigned weights equivalent to the inverse squares of their standard deviations and these weights were then included in the "least squares" calculations. The results are shown in equations (6) and (7) for the methylpropoxide and the methylheptyloxide, respectively:

$$k' = 1{\cdot}15(\pm 0{\cdot}05) \times 10^9 \mathrm{e}^{-18{,}800(\pm 960)/\boldsymbol{R}T} \quad . \; . \; . \; . \; . \; . \quad (6)$$

$$k' = 8{\cdot}22(\pm 2{\cdot}41) \times 10^4 \mathrm{e}^{13{,}400(\pm 2{,}900)/\boldsymbol{R}T} \quad . \; . \; . \; . \; . \; . \quad (7)$$

The larger errors in the case of (−)-aluminium 1-methylheptyloxide are a result of the numerically small observed rotations. The approximate entropies of activation at 30·0° have been calculated from equations (6), (7), and (8) (Glasstone, Laidler, and Eyring, "Theory of Rate Processes," McGraw-Hill Book Co., 1941, p. 417), by assuming a transmission coefficient of unity. These values are −18 and −38 E.U. for (+)-1-methylpropoxide and (−)-1-methylheptyloxide, respectively.

$$k = \mathrm{e}(\boldsymbol{k}T/\boldsymbol{h})\mathrm{e}^{\Delta S^{\ddagger}/\boldsymbol{R}}\,\mathrm{e}^{-\Delta E^{\ddagger}/\boldsymbol{R}T} \quad . \; . \; . \; . \; . \; . \; . \; . \quad (8)$$

The addition of *cyclo*hexylamine was shown to have a marked effect on the rate of racemization of (−)-aluminium 1-methylheptyloxide. At the same time, a reduction in the initial rotation of the alkoxide solutions was observed. Table 6 summarizes these results.

TABLE 6. *Effect of the addition of* cyclo*hexylamine.*

Aluminium 1-methylheptyloxide, 0·171M; octan-2-one, 0·151M.

Amine molarity	0	0·500	1·00
$\alpha_D^{30\cdot0}$ initial	−1·10°	−0·63°	−0·46°
$\alpha_D^{30\cdot0}$ at *ca.* 300 min.	−0·63°	−0·65°	−0·41°

TABLE 7. *Racemization of* (+)-*aluminium* 1-*methylheptyloxide by octan*-2-*one in benzene solution.*

Alkloxide molarity, 0·555 Ketone ,, 0·667				Alkoxide molarity, 0·555 Ketone ,, 0·800			
t (min.)	α^{13}	*t* (min.)	α^{13}	*t* (min.)	$\alpha^{14\cdot5}$	*t* (min.)	$\alpha^{14\cdot5}$
2	−0·20°	30	−1·25°	7	−1·14°	210	−1·075°
7	−0·45	41	−1·23	8	−1·29	289	−0·925
9	−0·88	132	−1·16	10·5	−1·34	402	−0·79
14	−1·17	339	−0·95	16	−1·36	800	−0·52
20	−1·23	1322	−0·40	81	−1·225		

The results of certain preliminary experiments utilizing impure aluminium 1-methylheptyloxide—preparation " (*b*) "—are recorded in Table 7. The results, which probably arise from the impure nature of the alkoxide, have no significance as far as the present investigation is concerned, but have been included as they represent a rather unusual case of mutarotation and indicate the complications which may arise in the study of more complex systems.

DISCUSSION

It has been observed that, for both examples examined, the rate of racemization is dependent on the ratio of the concentrations of the alkoxide and ketone, *i.e.*, on the factor [A]/[B] (cf. equation 5). This result appears to be consistent with the postulated mechanism provided the associated nature of aluminium alkoxides is borne in mind. If it is assumed that the rate of hydrogen transfer (step 2) is slow compared with the rate at which the initial equilibrium is attained, it follows that the rate of racemization (R) is given by equation (9). The concentration of optically active complex is determined by the result of the

$$R = k_1[(+)\text{-Complex}] \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad . \quad (9)$$

initial co-ordination equilibrium (step 1) which, however, is in competition with another equilibrium process, namely, the association of the aluminium alkoxide. The association reaction depends on the square or higher powers of the alkoxide concentration and may therefore be expected to compete more favourably at higher alkoxide concentrations. It is thus possible that changes in alkoxide concentration over the limited range examined have little or no effect on the concentration of the complex, the increased tendency for co-ordination being offset by the greatly increased tendency towards association. Equation (5) therefore becomes intelligible. It is possible that the observed initial inconsistencies (Figs. 2 and 3) are due to the establishment of the co-ordination and association equilibria.

The addition of a strong base to the reaction mixture introduces a third equilibrium, a process which is also competing for free alkoxide, and thus reduces the rate of racemization. Furthermore, the formation of a new optically active species, the alkoxide–amine complex, would be expected to have an effect on the initial rotation of the mixture. These conclusions are substantiated by the results recorded in Table 7. The amine greatly reduces the initial rotation, and further, this change is very rapid, indicating that the co-ordination reactions are fast. It is also seen from Table 7 that the racemization is almost completely inhibited by the addition of the amine. There are, however, several examples of successful reductions of amino-ketones (Lions *et al.*, *J. Proc. Roy. Soc. N.S. Wales*, 1939, **72**, 233, 280; Lutz *et al.*, *J. Amer. Chem. Soc.*, 1948, **70**, 2020; 1949, **71**, 478), although Lutz and his co-workers (*ibid.*, 1950, **72**, 4085; 1951, **73**, 1639) found that the Oppenauer oxidations of certain amino-alcohols do not proceed at measurable speeds. It is probable that racemization in the presence of *cyclo*hexylamine would occur more rapidly at 80°, the usual temperature at which the Meerwein–Ponndorf reduction is carried out. The basic strength of the amine must also be a critical factor.

It is surprising to find such large differences in both the energies and the entropies of activation of the two processes examined. If the above interpretation of the kinetics is correct, the experimental parameters will refer to complex combinations of the several factors:

$$\Delta E_{\text{obs.}} = \alpha + \Delta E^{\ddagger} \qquad \Delta S_{\text{obs.}} = \beta + \Delta S^{\ddagger}$$

Thus α and β may be interpreted as the heat and entropy of dilution of the alkoxide in a mixture of ketone and methyl*cyclo*hexane, while $\Delta E^{\ddagger}$ and $\Delta S^{\ddagger}$ refer to the hydrogen transfer through one configuration of the transition state. Experiments with ^{14}C-labelled ketones are being undertaken to examine the path through the other configuration.

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