Asymmetric Reduction of Ketones by using Complexes of Lithium Tetrahydridoaluminate(III) with 1,4:3,6-Dianhydro-D-mannitol and 1,3:4,6-Di-*O*-benzylidene-D-mannitol

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The use of chiral diols each containing a two-fold axis of symmetry to achieve asymmetric reductions of some ketones with metal hydrides is described. The symmetry of these complexes simplifies interpretation of the observed enantioselectivity.

SINCE the original conception of asymmetric synthesis [1] there have been many examples involving carbohydrate derivatives [2,3] and the use of a carbohydrate diol to influence reductions with lithium tetrahydridoaluminate(III) has given marked enantioselectivity.[4] Rationalisation of the results of such asymmetric reductions is complicated by many factors [5] including the presence, in the proposed diolatodihydridoaluminate(III) ion, of two available hydrogen atoms which display different stereoselectivity in their reactions with ketones.

The two available hydrogen atoms in a diolatodihydridoaluminate(III) ion derived from an asymmetric diol are diastereotopic,[6] whereas those in the complex ion derived from a chiral diol containing a two-fold axis of symmetry (C_2 axis) will be stereochemically equivalent.[6,†]

Therefore the use of chiral diols which contain a C_2 axis in asymmetric reductions should simplify interpretation of the results. We now report the first use of two such diols, namely 1,4:3,6-dianhydro-D-mannitol and 1,3:4,6-di-*O*-benzylidene-D-mannitol, in asymmetric reductions of some ketones. Both diols are readily available in one step from D-mannitol.

The 1,4:3,6-dianhydro-D-mannitolatodihydridoaluminate(III) complex was formed by addition with stirring of a solution of the diol (25 mmol) in dry ether to a clear standardised solution of the hydride (25 mmol) in dry ether. These conditions have been previously shown to give maximum stereoselectivity.[8] This complex was used to reduce a number of ketones. In each case the resulting secondary alcohol was isolated and its purity checked by g.l.c. The optical rotation was measured and compared with maximum values reported in the literature.[8] The enantioselectivity of the reduction in each case is expressed as (observed rotation × 100)/(maximum rotation), but it is recognised that there is not necessarily a linear relationship between observed optical rotation and enantiomeric composition.[9]

The reduction of methyl phenyl ketone (25 mmol) with the complex (25 mmol) gave 1-phenylethanol in 70% yield with 5.3% enantioselectivity in favour of the *S*-isomer. When the experiment was repeated with a 2 : 1 molecular ratio of ketone to reducing complex, the same product was obtained in a 75% yield with 4.7% enantioselectivity in favour of the *S*-isomer. Thus a similar result was obtained when one or both of the available hydrogen atoms was used. This observation was also borne out in the reduction of ethyl phenyl ketone. The remainder of the ketones were reduced by using a 2 : 1 molecular ratio of ketone to reducing agent and these results are shown in Table 1.

TABLE 1

Asymmetric reductions with 1,4:3,6-dianhydro-D-mannitolatodihydridoaluminate(III)

	Secondary alcohol			
		[α]D (°)		
Ketone	Yield (%)	Obs.	Max.[a]	Selectivity (%*S*)
Methyl phenyl ketone	75	−1.96	+42.8 (*R*)	4.7 [b]
	70	−2.30		5.3 [c]
Ethyl phenyl ketone	77	−1.03	−27.7 (*S*)	3.7 [b]
	60	−1.13		4.1 [c]
3,3-Dimethylbutan-2-one	41	+0.20	+7.8 (*S*)	2.5 [b]
4,4-Dimethylpentan-2-one	40	+0.39	+24.8 (*S*)	1.6 [b]
4-Methylpentan-2-one	65	+0.29	+20.5 (*S*)	1.4 [b]
Pentan-2-one	37	+0.15	+13.7 (*S*)	1.1 [b]

[a] Values for maximum rotation and configuration taken from ref. 8. [b] Ketone : reducing complex, 2 : 1. [c] Ketone : reducing complex, 1 : 1.

The enantioselectivity is less marked than the best results previously reported.[4] Generally higher selectivities were observed in the reduction of alkyl aryl ketones than with dialkyl ketones. Of the dialkyl ketones the highest selectivity was observed with 3,3-dimethylbutan-2-one. In each case examined the *S*-enantiomer of the secondary alcohol was formed preferentially.

A very low enantioselectivity (0.06% excess of the *S*-enantiomer) was observed when 1,4:3,6-dianhydro-D-mannitol was added as a powder to a clear solution of lithium tetrahydridoaluminate(III) in ether and the mixture was used to reduce methyl phenyl ketone. In all subsequent experiments, solutions of this and other diols were used.

† The stereochemical relationship between the available hydrogen atoms in these complexes is analogous to the relationship between the methylene protons at position 2 in 1,3-dioxepans, which may adopt conformations with or without C_2 axes.[7] In the former case the hydrogen atoms will be equivalent, and in the latter they appear at any instant to be diastereotopic, but pseudorotation of the ring should ensure that the time-averaged environments of the hydrogens will be equivalent on the time scale of a chemical reaction.

[1] E. Fischer, *Ber.*, 1894, **27**, 3231.
[2] J. D. Morrison and H. S. Mosher, 'Asymmetric Organic Reactions,' Prentice-Hall, New Jersey, 1971.
[3] T. D. Inch, *Adv. Carbohydrate Chem.*, 1972, **27**, 191.
[4] S. R. Landor, B. J. Miller, and A. R. Tatchell, *J. Chem. Soc.* (*C*), 1967, 197.
[5] O. Cervinka and O. Belovsky, *Coll. Czech. Chem. Comm.*, 1967, **32**, 3897.
[6] K. Mislow and M. Raban, *Topics Stereochem.*, 1967, **1**, 1.
[7] T. B. Grindley, J. F. Stoddart, and W. A. Szarek, *J. Chem. Soc.* (*B*), 1969, 172; J. F. Stoddart and W. A. Szarek, *ibid.*, 1971, 437.
[8] S. R. Landor, B. J. Miller, and A. R. Tatchell, *J. Chem. Soc.* (*C*), 1966, 2280.
[9] A. Horeau, *Tetrahedron Letters*, 1963, 3121.

When 1,4:3,6-dianhydro-D-mannitol was added to an aqueous solution of sodium tetrahydridoborate(III), approximately two moles of hydrogen gas per mole of diol were evolved, suggesting the formation of a 1,4:3,6-dianhydro-D-mannitolatodihydridoborate(III) complex. When this solution was used to reduce methyl phenyl ketone, the resulting 1-phenylethanol had a low positive rotation, indicating the formation of excess of the *R*-enantiomer (0.4%). When a similar reduction was performed on 3,3-dimethylbutan-2-one, racemic 3,3-dimethylbutan-2-ol was obtained.

When sodium tetrahydridoborate(III) was treated with 1,4:3,6-dianhydro-D-mannitol in bis-(2-methoxyethyl) ether as solvent two moles of hydrogen gas per mole of diol were evolved, again suggesting formation of a complex. When this solution was used to reduce methyl phenyl ketone the 1-phenylethanol obtained had a low negative rotation indicating 0.8% excess of the *S*-enantiomer. Thus in both solvents the enantioselectivity in reductions with sodium diolatodihydridoborate(III) was lower than that observed with the corresponding aluminate(III) complex in dry ether.

Another class of compounds which fall into the category of chiral diols containing a C_2 axis are the 1,3:4,6-diacetals of D-mannitol, and the potential use of these in asymmetric reductions was next explored. Because of its ease of preparation, the dibenzylidene acetal was chosen for further study. This compound has been made in 12% yield by direct treatment of D-mannitol with benzaldehyde in dimethyl sulphoxide. In our hands a similar reaction with *NN*-dimethylformamide as solvent gave the diacetal in 43% yield. The compound had a m.p. *ca.* 40 °C higher than the reported value,[10] but the optical rotation and n.m.r. and chromatographic data were similar. The compound described here gave a di-*O*-*p*-tolylsulphonyl derivative, confirming that it was a diacetal, and when methylated gave a di-*O*-methyl derivative with properties very similar to those reported previously.[10] Furthermore, benzylation and then hydrolysis gave the known 2,5-di-*O*-benzyl-D-mannitol, showing that the original acetal was indeed 1,3:4,6-di-*O*-benzylidene-D-mannitol. Dimorphic behaviour of benzylidene acetals has been described [11] and this may be another example.

Because of the low solubility of 1,3:4,6-di-*O*-benzylidene-D-mannitol in ether, the complex of this diol with lithium tetrahydridoaluminate(III) was made by addition of a solution of the diol in tetrahydrofuran to a clear, standardised solution of the metal hydride in dry ether. This was used to reduce ketones essentially as described above and the results of these reductions are summarised in Table 2.

Again the highest selectivities were observed with the alkyl aryl ketones, both of which gave more of the *S*-enantiomer of the secondary alsohol, whereas dialkyl ketones gave products in which the *R*-enantiomer predominated. This difference between aromatic and aliphatic ketones was not observed when the complex derived from 1,4:3,6-dianhydro-D-mannitol was used, but has been observed in asymmetric reductions influenced by (—)-quinine.[5]

TABLE 2

Asymmetric reductions with 1,3:4,6-di-*O*-benzylidene-D-mannitolatodihydridoaluminate(III)

	Secondary alcohol				
		$[\alpha]_D$ (°)			
Ketone	Yield (%)	obs.	max. [a]	Selectivity (%)	Main isomer
Methyl phenyl ketone	69	−4.174	+42.8 (*R*)	9.8 [b]	*S*
		−5.046		11.8 [b]	*S*
Ethyl phenyl ketone	62	−1.512	−27.7 (*S*)	5.6 [b]	*S*
3,3-Dimethylbutan-2-one	39	−0.298	+7.8 (*S*)	3.8 [b]	*R*
4-Methylpentan-2-one	48	−0.298	+20.5 (*S*)	1.5 [b]	*R*

[a,b] As Table 1.

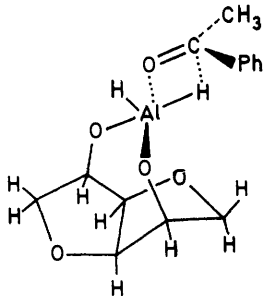

FIGURE 1

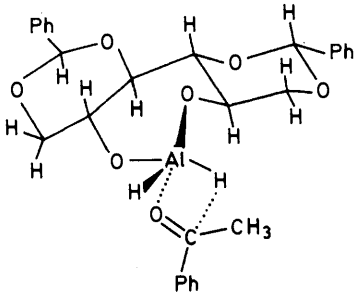

FIGURE 2

Possible transition state models for the reduction of methyl phenyl ketone by chiral diolatodihydridoaluminate(II) complexes

In previous work with chiral hydride complexes the greatest enantioselectivity in reduction of methyl phenyl ketone was observed when a reagent prepared by adding lithium tetrahydridoaluminate(III) (58 mmol) to a chiral diol (25 mmol) and then adding dry ethanol (110 mmol) was used. It was implied [4] that these conditions give optimum concentration of a 1 : 1 : 1 complex of ethanol, diol, and aluminium hydride *in solution* although simple consideration of the number of moles of reagent does not support this contention. When a similar experiment was performed with 1,3:4,6-di-*O*-benzylidene-D-mannitol as the diol, the enantioselectivity in reduction of methyl

[10] H. B. Sinclair, *Carbohydrate Res.*, 1970, **12**, 150.
[11] B. Dobinson, A. B. Foster, and M. Stacey, *Tetrahedron Letters*, 1958, 1.

phenyl ketone was similar to that observed in the absence of ethanol.

The selective formation of *S*-alcohols implies introduction of hydrogen onto the *re*-face of the carbonyl group. To take reduction of methyl phenyl ketone as an example, the observed enantioselectivity is consistent with approach of the reacting species as shown in Figures 1 and 2, in which the carbonyl oxygen atom is arranged near the aluminium atom, allowing a four-membered transition state model as previously proposed in discussion of reduction of ketones.[12] In both cases the less bulky group is placed in the more hindered position, closer to the diol molecule, and the more bulky phenyl group projects away from the diol ligand.

In contrast to the preferential formation of *S*-alcohols from alkyl aryl ketones, reduction of dialkyl ketones with the complex derived from 1,3:4,6-*O*-benzylidene-D-mannitol gave *R*-alcohols preferentially. The transition state model in Figure 2 cannot be used to explain this observation, and the different behaviour with aromatic and aliphatic groups suggests that factors other than steric bulk may be important. Further experiments aimed at clarifying the situation are in progress.

EXPERIMENTAL

Pyridine was distilled (b.p. 114—116°) from phosphorus pentaoxide and stored over potassium hydroxide. Ether was dried over sodium wire. Tetrahydrofuran was dried over calcium hydride and distilled (b.p. 64—66°) immediately before use. Bis-(2-methoxyethyl) ether was refluxed with calcium hydride, distilled (b.p. 160—162°), and stored over calcium hydride. Ethanol was dried with magnesium.[13] Reaction mixtures were examined by t.l.c. on silica gel (Merck 7731), with use of a vanillin–sulphuric acid spray.[14] Analytical g.l.c. was performed with a Pye Argon chromatograph [β-ionisation detector; gas flow 60 ml min^{-1}; 4 ft columns containing 10% Carbowax (at 100 °C for alkanols) or 10% polyethylene glycol adipate (at 150 °C for arylalkanols) on Celite]. I.r. spectra were measured with a Pye Unicam SP 200 G instrument for liquid films or Nujol mulls. N.m.r. spectra were recorded at 100 MHz with a Perkin-Elmer R14 instrument (internal Me_4Si standard). Optical rotations were determined at 21 °C with a Perkin-Elmer 141 automatic polarimeter (1 dm cell), with pure liquid samples unless otherwise stated. Standard ethereal solutions of lithium tetrahydridoaluminate(III) were prepared by stirring the hydride (10 g) in dry ether (400 ml) for 3 h under nitrogen, then decanting the settled solution. The resulting clear solution was stored under dry nitrogen and standardised with iodine.[15]

1,4:3,6-*Dianhydro*-D-*mannitol*.—This compound was prepared according to the literature procedure,[16] and was sublimed (75 °C at 1.5 mmHg); yield 23%, m.p. 87—88°, $[\alpha]_D$ +62.2° (*c* 1.03 in $CHCl_3$) {lit.,[17] m.p. 86.7—89.5°, $[\alpha]_D$ +62.2° (in $CHCl_3$)}.

Reduction of Ketones with Lithium 1,4:3,6-*dianhydro*-D-*mannitolatodihydridoaluminate*(III).—(*a*) A solution of 1,4:3,6-dianhydro-D-mannitol (3.65 g, 25 mmol) in dry ether (250 ml) was added with stirring to a measured volume of a standardised solution of lithium tetrahydridoaluminate(III) (25 mmol) in dry ether under nitrogen. The mixture was heated under reflux for 0.5 h and then methyl phenyl ketone (3.0 g, 25 mmol) in dry ether (50 ml) was added. After a further 2 h at this temperature, water (15 ml) was added, and the mixture was filtered through a Celite pad. Evaporation of the filtrate and distillation of the residue gave 1-phenylethanol (2.1 g, 70%), b.p. 98—102° at 15 mmHg, $[\alpha]_D$ −2.3°, homogeneous by g.l.c.

(*b*) Experiment (*a*) was repeated under similar conditions but with methyl phenyl ketone (6.0 g, 50 mmol). This gave 1-phenylethanol (4.5 g, 75%), b.p. 98—102° at 15 mmHg, $[\alpha]_D$ −1.96°, homogeneous by g.l.c.

(*c*) Experiment (*a*) was repeated under similar conditions but the mannitol derivative (3.65 g, 25 mmol) was added as a solid. The mixture was heated under reflux for 1 h before addition of methyl phenyl ketone (6.0 g, 50 mmol). The mixture was then treated as described in (*a*) to give 1-phenylethanol (5.0 g, 84%), b.p. 98—102° at 15 mmHg, $[\alpha]_D$ −0.025°, homogeneous by g.l.c.

(*d*) The experiment was repeated under the same conditions as (*a*) or (*b*) with a number of ketones. In each case the product was isolated as described in (*a*) and shown to be homogeneous by g.l.c. The results of these experiments are summarised in Table 1.

Reduction of Ketones with Sodium 1,4:3,6-*Dianhydro*-D-*mannitolatodihydridoborate*(III).—(*a*) A solution of sodium tetrahydridoborate(III) (0.76 g, 20 mmol) in water (10 ml) was placed in a flask connected to a gas burette. Hydrogen was evolved at 70 ml h^{-1}. A solution of 1,4:3,6-dianhydro-D-mannitol (0.73 g, 5 mmol) in water (10 ml) was added, and hydrogen (275 ml, 11 mmol) was evolved. In the following experiments a 10% excess of sodium tetrahydridoborate(III) was used to allow for decomposition.

(*b*) Methyl phenyl ketone (5.5 g, 46 mmol) in tetrahydrofuran (20 ml) was added to a stirred solution of sodium 1,4:3,6-dianhydro-D-mannitolatodihydridoborate(III) (25 mmol) in water (25 ml) and the mixture was stirred overnight. The solvents were evaporated off under reduced pressure and the residue was partitioned between ether (50 ml) and water (50 ml). The ether layer was washed with water (20 ml), dried ($MgSO_4$), and distilled to give 1-phenylethanol (3.0 g, 55%), $[\alpha]_D$ +0.271°. This was shown by g.l.c. to contain 1,4:3,6-dianhydro-D-mannitol. Chromatography on silica gel (20 g) and distillation (b.p. 98—102° at 15 mmHg) gave chromatographically homogeneous 1-phenylethanol, $[\alpha]_D$ +0.155°.

(*c*) Experiment (*b*) was repeated to give 1-phenylethanol, $[\alpha]_D$ +0.180°.

(*d*) A solution of 1,4:3,6-dianhydro-D-mannitol (3.65 g, 25 mmol) in bis-(2-methoxyethyl) ether (50 ml) was added to sodium tetrahydridoborate(III) (1.04 g, 27.5 mmol) in the same solvent (30 ml). Hydrogen (1 120 ml, 50 mmol) was evolved, then methyl phenyl ketone (5.5 mmol) was added and the mixture was stirred at room temperature for 5 h. Saturated aqueous ammonium chloride (50 ml) was added and the mixture steam distilled. The distillate was extracted with ether (2 × 50 ml); the combined extract was dried ($MgSO_4$) and distilled to give 1-phenylethanol, b.p. 85—90°

[12] *E.g.* see E. Toromanoff, *Topics Stereochem.*, 1967, **2**, 157.
[13] A. L. Vogel, ' Practical Organic Chemistry,' 3rd edn., Longmans, London, 1957, p. 167.
[14] D. Waldi, ' Chromatography,' 2nd edn., E. Merck A.G., Darmstadt, p. 30.
[15] H. Felkin, *Bull. Soc. chim. France*, 1951, **18**, 347.
[16] R. Montgomery and L. F. Wiggins, *J. Chem. Soc.*, 1948, 2204.
[17] H. G. Fletcher, jun., and R. M. Geopp, jun., *J. Amer. Chem. Soc.*, 1945, **67**, 1042.

at 14 mmHg, $[\alpha]_D$ −0.328°. G.l.c. indicated traces of bis-(2-methoxyethyl) ether and methyl phenyl ketone in the product.

(*e*) The experiment was performed essentially as in (*a*) but with 3,3-dimethylbutan-2-one (4.0 g, 40 mmol) to give 3,3-dimethylbutan-2-ol, b.p. 118°, $[\alpha]_D$ 0°, homogeneous by g.l.c.

1,3:4,6-*Di*-O-*benzylidene*-D-*mannitol*.—Concentrated sulphuric acid (20 ml) was added to a solution of D-mannitol (100 g) and benzaldehyde (120 ml) in *NN*-dimethylformamide (300 ml). The mixture was left at room temperature for 3 days and then poured into ice–water (3 l) containing potassium carbonate (30 g) and light petroleum (b.p. 60—80°; 500 ml). The mixture was stirred vigorously and a white solid was obtained as the ice melted. The solid was filtered off, washed with light petroleum (b.p. 60—80°), then extracted with boiling chloroform (2 × 200 ml). The residue was recrystallised from methanol to give the *product* (86 g, 42%), m.p. 192—193°, $[\alpha]_D$ −9.1° (*c* 1.06 in Me_2CO) {lit.,[10] m.p. 146—149°, $[\alpha]_D$ −7.0° (in Me_2CO)}, τ [$(CD_3)_2SO$] 2.5 (10 H, m, aromatic), 4.40 (2 H, s, PhC*H*), 4.65 (2 H, d, OH), and 5.7—6.6 (8 H, m, hexitol chain) (Found: C, 67.0; H, 5.9. $C_{20}H_{22}O_6$ requires C, 67.05; H, 6.2%).

1,3:4,6-*Di*-O-*benzylidene*-2,5-*di*-O-p-*tolylsulphonyl*-D-*mannitol*.—A solution of toluene-*p*-sulphonyl chloride (1.5 g) in pyridine (10 ml) was slowly added to a solution of 1,3:4,6-di-*O*-benzylidene-D-mannitol (0.5 g) in pyridine (5 ml) at 0 °C. The mixture was kept at 0 °C overnight and then water (5 drops) was added over 3 min to destroy the excess of toluene-*p*-sulphonyl chloride, and the solution was poured into ice–water (50 ml). The solution was extracted with chloroform (2 × 50 ml), and the combined extract was washed with water, dried ($MgSO_4$), and concentrated under reduced pressure. The *product* was recrystallised from benzene–light petroleum (b.p. 60—80°) and then from ethanol; yield 0.24 g (23%), m.p. 117—120°, $[\alpha]_D$ −25.8° (*c* 1.04 in $CHCl_3$), τ [$(CD_3)_2SO$] 2.1—2.65 (18 H, m, aromatic), 4.70 (2 H, s, PhC*H*), 5.5—6.1 (8 H, m, hexitol chain), and 6.70 (6 H, s, ArCH_3) (Found: C, 61.0; H, 5.3; S, 9.9. $C_{34}H_{34}O_{10}S_2$ requires C, 61.2; H, 5.2; S, 9.6%).

1,3:4,6-*Di*-O-*benzylidene*-2,5-*di*-O-*methyl*-D-*mannitol*.—Sodium hydride (0.28 g) was added to a solution of 1,3:4,6-di-*O*-benzylidene-D-mannitol (1.0 g) in *NN*-dimethylformamide (40 ml) at 0 °C. After 1 h, iodomethane (3.0 ml) was added slowly and the mixture was stirred overnight. Methanol (7 ml) was then added, and after a further 2 h the mixture was evaporated to dryness. The residue was partitioned between chloroform (50 ml) and water (50 ml). The chloroform layer was washed with water (3 × 50 ml), dried ($MgSO_4$), and concentrated under reduced pressure to give the *product* (0.91 g, 84%), m.p. 146—146.5° (from ethanol), $[\alpha]_D$ −25.4° (*c* 0.84 in Me_2CO) {lit.,[10] m.p. 144—145.5°, $[\alpha]_D$ −22° (in Me_2CO)} (Found: C, 68.1; H, 6.5. $C_{22}H_{26}O_6$ requires C, 68.4; H, 6.8%).

2,5-*Di*-O-*benzyl*-1,3:4,6-*di*-O-*benzylidene*-D-*mannitol*.—1,3:4,6-Di-*O*-benzylidene-D-mannitol (10 g) was dissolved in benzyl chloride (64 ml) and powdered potassium hydroxide (37 g) was added. The mixture was heated at 130—140 °C for 3 h with stirring, then cooled, and water (200 ml) was added. The mixture was extracted with chloroform (2 × 100 ml) and the combined extracts were washed with water (2 × 100 ml), dried ($MgSO_4$), and evaporated at 100 °C and 1 mmHg. The residue was stored at −15 °C overnight to give a solid *product*, which was recrystallised from light petroleum (b.p. 60—80°); yield 13.0 g (87%), m.p. 102—103°, $[\alpha]_D$ −36.6° (*c* 1.0 in $CHCl_3$), τ ($CDCl_3$) 2.8 (20 H, m, aromatic), 4.65 (2 H, s, PhC*H*), 5.47 (4 H, s, PhCH_2), and 5.64—6.40 (8 H, m, hexitol chain) (Found: C, 75.5; H, 6.5. $C_{34}H_{34}O_6$ requires C, 75.8; H, 6.35%).

2,5-*Di*-O-*benzyl*-D-*mannitol*.— 2,5-Di-*O*-benzyl-1,3:4,6-di-*O*-benzylidene-D-mannitol (3 g) was dissolved in ethanol (50 ml) and water (11 ml), and N-hydrochloric acid (3.5 ml) was added. The solution was heated under reflux for 8 h; t.l.c. in carbon tetrachloride–ethyl acetate (4 : 1) then showed that all the starting material had reacted. Barium carbonate was added to neutralise the solution; evaporation then left a solid which was extracted with hot ethyl acetate (2 × 50 ml). The extract was evaporated to a solid, which was recrystallised from ethyl acetate to give the product (1.0 g, 50%), m.p. 116—117°, $[\alpha]_D$ −7.7° (*c* 1.01 in EtOH) {lit.,[11] m.p. 119—120°, $[\alpha]_D$ −7° (in EtOH)}, τ [$(CD_3)_2SO$] 2.7 (10 H, m, aromatic), 5.41 (4 H, q, PhCH_2), and 5.85—6.60 (8 H, m, hexitol chain).

Reduction of Ketones with Lithium 1,3:4,6-*Di*-O-*benzylidene*-D-*mannitolatodihydridoaluminate*(III).—(*a*) A solution of 1,3:4,6-di-*O*-benzylidene-D-mannitol (5.0 g, 14 mmol) in dry tetrahydrofuran (100 ml) was added to a measured volume of a standardised solution of lithium tetrahydridoaluminate(III) (14 mmol). The mixture was heated under reflux for 0.5 h and then methyl phenyl ketone (3.3 g, 28 mmol) in dry ether (10 ml) was added. After 2 h at this temperature, the mixture was cooled and water (15 ml) was added. The mixture was filtered and the organic solvents were removed by evaporation under reduced pressure. The resulting aqueous layer was extracted with hot benzene (2 × 50 ml); the benzene layer was cooled and light petroleum (b.p. 60—80°; 300 ml) was added to crystallise most of the 1,3:4,6-di-*O*-benzylidene-D-mannitol, which was filtered off. The filtrate was concentrated and the residue distilled to give 1-phenylethanol (2.3 g, 69%), b.p. 98—102° at 15 mmHg, $[\alpha]_D$ −4.174°, homogeneous by g.l.c.

(*b*) A solution of 1,3:4,6-di-*O*-benzylidene-D-mannitol (8.95 g, 25 mmol) in dry tetrahydrofuran (100 ml) was added to a standardised solution of lithium tetrahydridoaluminate(III) (50 mmol) in dry ether. The mixture was heated under reflux for 1 h and then dry ethanol (5.06 g, 110 mmol) in dry ether (30 ml) was added. The heating was continued for 1 h and methyl phenyl ketone (3.0 g, 25 mmol) in dry ether (20 ml) was added. The reaction was continued as in (*a*) to give 1-phenylethanol (1.9 g, 63%), b.p. 98—102° at 15 mmHg, $[\alpha]_D$ −4.463°, homogeneous by g.l.c.

(*c*) A number of other ketones were reduced under the conditions described in (*a*); the results are summarised in Table 2.

We thank the S.R.C. for a studentship (to P. S.).

[6/1276 *Received*, 1*st July*, 1976]