

## Preliminary communication

---

### Optically active organometallic derivatives in asymmetric reactions: chiral aluminum 2-methylbutoxide in the reduction of methyl ethyl ketone

RITA MENICAGLI, G. PAOLO GIACOMELLI and LUCIANO LARDICCI

*Istituto di Chimica Organica, Facoltà di Scienze M.F.N., Università di Pisa, 56100 Pisa (Italy)*

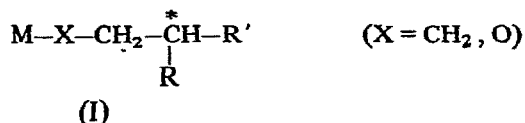
(Received January 16th, 1973)

#### SUMMARY

The ability of tris[(*S*)-2-methylbutoxy] aluminum to bring about asymmetric reduction of methyl ethyl ketone has been reinvestigated: only a low stereoselectivity has been observed.

---

Asymmetric reductions of carbonyl substrates have been carried out with optically active organometallic compounds of main group elements or their derivatives, in which the metal atom is still able to coordinate with the carbonyl group in a preliminary step of the reaction. While the stereoselectivity of the reduction using (I) ( $X = \text{CH}_2$ ) was clearly verified<sup>1,2</sup>, meaningful conclusions concerning the ability of (I) ( $X = \text{O}$ ) to bring about asymmetric reduction have not been achieved at least when  $M = \text{Al}$ <sup>3,4</sup>.



Baker and Linn<sup>3</sup> have observed the absence of asymmetric reduction in the reaction of some prochiral ketones with optically active aluminum 2-methylbutoxide but more recently<sup>4</sup> a high stereoselectivity was surprisingly found in Meerwein–Ponndorf–Verley (MPV) reduction of the methyl ethyl ketone using the same chiral aluminum alkoxide in (–) (*S*)-2-methyl-1-butanol. As the reaction is essentially reversible, its stereochemical course depends mainly on the reaction time, and a low extent of asymmetric reduction consequent upon equilibration phenomena should be expected. Moreover, the chiral center is not incorporated into the cyclic transition state invoked for the hydrogen transfer process<sup>1,2,5</sup>, and therefore the stereoselectivity of the reaction should not be so high<sup>1,2,4</sup>.

In order to verify the previous reported results<sup>3,4</sup> and to gain further information about the transfer of the diastereotopic hydrogens  $\beta$  to the aluminum atom<sup>2</sup> we have reduced methyl ethyl ketone with tris[(*S*)-2-methylbutoxy] aluminum according to the experimental method described by Yamashita<sup>4</sup>.

In a typical run 85 g (0.96 mole) of (–)(*S*)-2-methyl-1-butanol\* was added under nitrogen to 54 g (0.26 mole) of aluminum triisopropoxide (C. Erba, Milan) in a dried 250 ml-round-bottomed flask. The mixture was boiled under reflux for 3 h and isopropanol (47 g) was slowly distilled out through a Hempel column; excess of (–)(*S*)-2-methyl-1-butanol (15 g) was removed under reduced pressure to leave optically active tris[(*S*)-2-methylbutoxy] aluminum. The solid alkoxide was suspended in 16 g of (–)(*S*)-2-methyl-1-butanol\* and a solution of 55 g (0.76 mole) of methyl ethyl ketone in 51 g of (–)(*S*)-2-methyl-1-butanol\* was added dropwise to the heated reaction mixture.

After 3.5 h refluxing the solution was carefully distilled to give 70 g of a fraction, b.p. 114°, containing 2-butanol, (+)(*S*)-2-methylbutanal and unreacted ketone (by GLC analysis, 2m X 0.3 cm Carbowax 1500 on Chromosorb W column, room temperature). This mixture was separated by preparative GLC on 4m X 0.8 cm 20% EAS on Chromosorb W and 2m X 0.8 cm 20% BDS on Chromosorb W columns at 65° (C. Erba Fractovap P instrument) to give 7.2 g of 2-butanol, b.p. 99–100°,  $\alpha_D^{25} + 0.08^\circ$  ( $l = 1$ , neat). To check that the optical rotation did not arise from a trace of (+)(*S*)-2-methylbutanal in the alcohol, this sample was further purified by preparative GLC on 3m X 0.8 cm 20% Carbowax 20 M on Chromosorb P column at 60° (Perkin–Elmer F 21 instrument). The recovered alcohol (3.5 g) showed b.p. 99°,  $n_D^{25} 1.3951$ ,  $\alpha_{589}^{19.5} + 0.09^\circ$ ,  $\alpha_{436}^{19.5} + 0.19^\circ$ ,  $\alpha_{365}^{19.5} + 0.31^\circ$  ( $l = 1$ , neat) (Perkin–Elmer Model 141 polarimeter).

On the basis of the experimental data we must conclude:

- (i) that asymmetric reduction occurs<sup>4</sup>, but the optical purity of the recovered (*S*)-2-butanol is very low.
- (ii) the previous claim<sup>4</sup> of a high asymmetric reduction of methyl ethyl ketone by tris[(*S*)-2-methylbutoxy] aluminum is now shown to be erroneous. In our opinion it is possible that the high positive rotation of 2-butanol observed by Yamashita<sup>4</sup> arises from unseparated (+)(*S*)-2-methylbutanal formed in the reaction<sup>3</sup>.
- (iii) it is noteworthy that classical stereochemical models generally proposed for the MPV reaction transition state<sup>5</sup>, correctly predict the absolute configuration of the carbinol recovered, on the basis of the chirality of the aluminum alkoxide employed.

The present results, which are obviously connected with different reductive properties of alkoxide and alkyl groups in the organoaluminum derivatives (I), confirm the complex nature of the MPV reaction and suggest dynamic features and stereochemical requirements substantially different from those of alkyl reductions<sup>1,2</sup>.

\*  $[\alpha]_D^{25} - 5.76$  (neat).

## ACKNOWLEDGMENT

This work was partially supported by the Consiglio Nazionale delle Ricerche, Rome.

## REFERENCES

- 1 J.D. Morrison, D.L. Black and R.W. Ridgway, *Tetrahedron Letters*, (1968) 985; J.D. Morrison and R.W. Ridgway, *J. Amer. Chem. Soc.*, 91 (1969) 4601.
- 2 L. Lardicci, G.P. Giacomelli and R. Menicagli, *Tetrahedron Letters*, (1972) 687.
- 3 R.H. Baker and L.E. Linn, *J. Amer. Chem. Soc.*, 71 (1949) 1399.
- 4 S. Yamashita, *J. Organometal. Chem.*, 11 (1968) 377.
- 5 E.L. Eliel, *Stereochemistry of Carbon Compounds*, McGraw-Hill, New York, 1962, p. 72.