

Asymmetric Hydride Reduction using a Chiral Aluminium Reagent Modified by a Crowned 2,2'-Dihydroxy-1,1'-binaphthyl

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The chiral aluminium hydride reagent **6** modified by a crowned 2,2'-dihydroxy-1,1'-binaphthyl **4** was found to exhibit high enantiomeric face selectivity towards a variety of prochiral carbonyl compounds including aliphatic ketones.

Increasing interest has been centred on asymmetric hydride reduction of prochiral ketones using a chiral aluminium reagent incorporating axially chiral modifiers.¹ However, in all cases reported, the chiral aluminium reagents have been found to exhibit a high enantiomeric face selectivity so far as α,β -unsaturated carbonyl systems. We now found that the crowned 2,2'-dihydroxy-1,1'-binaphthyl **4** is an excellent chiral modifier in asymmetric LiAlH_4 reduction toward a variety of prochiral ketones including aliphatic ketones.*

Condensation of (+)-(*S*)-3,3'-bis(hydroxymethyl)-2,2'-dihydroxy-1,1'-binaphthyl **1**³ with (-)-(*S*)-2,2'-bis(5-tosyloxy-3-oxapentyloxy)-1,1'-binaphthyl **2**³ [Bu^tOK -tetrahydrofuran (THF)] afforded the (*S,S*)-(-)-crown ether **3**[†] {m.p. 206–207 °C, 27% yield, $[\alpha]_D^{23} -76$ (CHCl_3)}, whose demethylation⁴ [EtSNa , dimethylformamide, 100 °C, 3 h] produced (-)-(*S,S*)-dihydroxy crown ether **4** {m.p. 192–193 °C, 65% yield, $[\alpha]_D^{23} -61$ (CHCl_3); δ (CDCl_3) δ 7.08–7.95 (m, ArH, 2 H), 4.85 (d, *J* 11, ArCH_2 , 2 H), 4.55 (d, *J* 11, ArCH_2 , 2 H), 5.05 (s, OH, 2 H), 3.93 (m, CH_2O , 4 H) and 3.36 (m, CH_2O , 12 H)}.⁵

Following the previously described procedure,¹ an asymmetric hydride reduction of prochiral ketones **5** was carried out. To a THF solution (1 mol dm^{-3}) of LiAlH_4 (6 mmol) under a nitrogen atmosphere was added ethanol in THF (2.0 ml dm^{-3} ; 6 mmol) at 0 °C. Then (+)-(*S,S*)-**4** in THF (0.2 mol dm^{-3} ; 6 mmol) was added at 0 °C and the mixture was stirred at room temperature for 2 h. The resulting chiral reagent **6** was cooled to 0 °C and to this reagent was added THF solution (1 mol dm^{-3}) of the prochiral ketone **5** (2.0 mmol). The mixture was stirred at

Table 1 Asymmetric hydride reduction of prochiral carbonyl compounds **5** with (*S,S*)-**6**^a

Substrate (R^1COR^2)	Conditions		Alcohol 7		Enantiomeric excess (%) (Config. ^a)
	Temp. (°C)	Time (h)	Isolated yield (%)	$[\alpha]_D^{23}$ / (c, solvent)	
$\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{Me}$	0	24	76	-38.3 (1.45, C_5H_{10})	89 (<i>S</i>) ^b
	-40	48	54	-37.5 (1.21, C_5H_{10})	87 (<i>S</i>) ^b
$\text{R}^1 = \text{Ph}$, $\text{R}^2 = \text{CH}_2\text{Ph}$	0	24	77	+50.8 (1.55, EtOH)	91 (<i>S</i>) ^c
	-40	48	52	+49.7 (1.10, EtOH)	89 (<i>S</i>) ^c
$\text{R}^1 = \text{CH}_2\text{Ph}$, $\text{R}^2 = \text{Me}$	0	24	75	+36.8 (1.88, C_6H_6)	88 (<i>S</i>) ^d
	0	24	78	+17.4 (2.21, EtOH)	85 (<i>S</i>) ^e

^a The reaction was carried out as described in text. ^b Based on $[\alpha]_D^{21} -43.1$ (C_5H_{10}) (ref. 6). ^c Based on $[\alpha]_D^{18} +55.9$ (EtOH) (ref. 7). ^d Based on $[\alpha]_D^{20} +41.8$ (C_6H_6) (ref. 8). ^e Based on $[\alpha]_D^{20} +20.5$ (EtOH) (ref. 8).

this temperature for 24 h and then quenched by the addition of HCl (2 mol dm^{-3}) at 0 °C. Extractive work-up with ether followed by evaporative distillation afforded the results summarized in Table 1.[§]

Inspection of Table 1 reveals the following: (a) the chiral hydride reagent **6** exhibits a high enantiomeric face selectivity towards both aromatic and aliphatic ketones at 0 °C and (b) the products **7** invariably have the *S*-configuration.

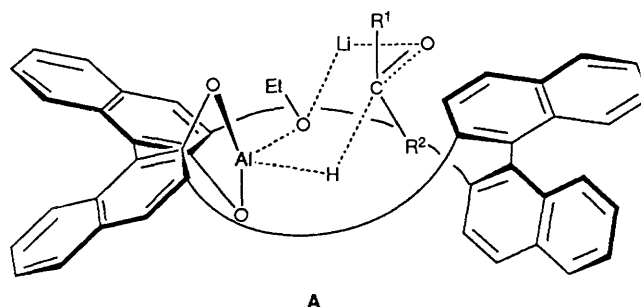
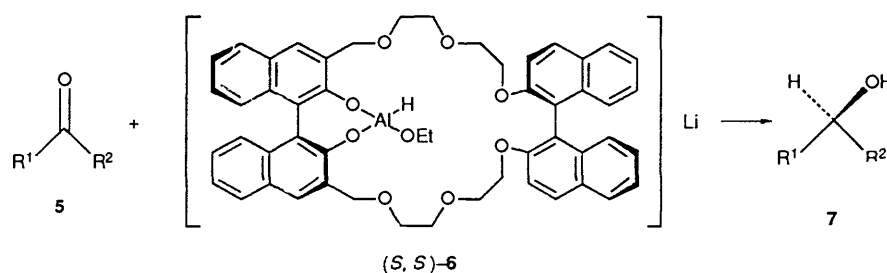
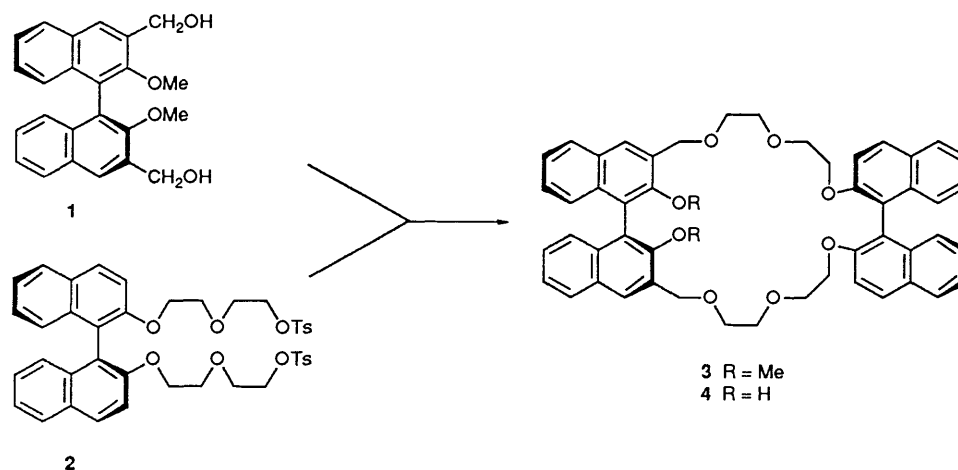
The configuration of the alcohol **7** formed by the reduction with chiral hydride reagent **6** is dependent upon the configuration of the six-membered, chelating transition state **A**.⁹ Inspection of Corey–Pauling–Koltun (CPK) space-filling molecular models suggests that the ether bridge with a chiral

* The highly enantioselective borane reduction of aliphatic ketones catalysed by oxazaborolidines has been reported by Corey and his group.²

† Satisfactory analytical and spectroscopic data have been obtained for all new compounds.

‡ Throughout $[\alpha]_D$ values are recorded in $10^{-1} \text{ deg cm}^2 \text{ g}^{-1}$.

§ The chiral modifier **4** was recovered without any noticeable loss in yield and optical purity.



binaphthyl unit plays an important role in enantiomeric face selectivity. The diastereoisomeric transition state A on steric grounds would appear to be more stable and the sterically hindered group (R^1) should occupy the axial position in the transition state, in accord with the observed enantioselectivity.

References

- 1 R. Noyori, I. Tomino and Y. Tanimoto, *J. Am. Chem. Soc.*, 1979, **101**, 3129; R. Noyori, I. Tomino and M. Nishizawa, *J. Am. Chem. Soc.*, 1979, **101**, 5843; N. Nishizawa and R. Noyori, *Tetrahedron Lett.*, 1980, 2821; 1981, 247; K. Yamamoto, H. Fukushima and M. Nakazaki, *J. Chem. Soc., Chem. Commun.*, 1984, 1490; H. Suda, S. Kanoh, M. Umeda, M. Ikka and M. Motori, *Chem. Lett.*, 1984, 899.
- 2 E. J. Corey, R. K. Bakshi and S. Shibata, *J. Am. Chem. Soc.*, 1987, **109**, 5551.
- 3 E. P. Kyba, W. G. Gokel, F. de Jong, K. Koba, L. R. Sousa, M. G. Siegel, L. Kaplan, G. D. Y. Sogah and D. J. Cram, *J. Org. Chem.*, 1977, **42**, 4173.
- 4 G. I. Feutrill and R. N. Mirrington, *Tetrahedron Lett.*, 1970, 1327.
- 5 Presented in part at the 61th Annual Meeting of the Chemical Society of Japan, March 29, 1991, Abstracts II, p. 1135.
- 6 A. W. Burgstahler, D. E. Walker, Jr., J. P. Kuebrich and R. L. Schowen, *J. Org. Chem.*, 1972, **37**, 1272.
- 7 G. Berti, F. Bothari, P. L. Farrarini and B. Haccchia, *J. Org. Chem.*, 1965, **30**, 4091.
- 8 R. H. Pickard and J. Kenyon, *J. Chem. Soc.*, 1911, 45; 1914, 1115.
- 9 E. C. Ashby and J. R. Boone, *J. Org. Chem.*, 1976, **41**, 2890, 5524.

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