

CHIRAL PROPIONATE ENOLATE EQUIVALENT FOR STEREOSELECTIVE ADDITIONS
TO SYMMETRICAL KETONES

Philip W. Ambler and Stephen G. Davies,*

The Dyson Perrins Laboratory, South Parks Road, Oxford, OX1 3QY.

Summary: The copper enolate derived from $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})(\text{PPh}_3)\text{COCH}_2\text{CH}_3$ reacts stereoselectively with symmetrical ketones to generate RR,SS- α -methyl- β -hydroxy acyl complexes which on decomplexation liberate the corresponding β -hydroxy acids.

In the preceding paper we have demonstrated that the E-aluminium and copper enolates derived from $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})(\text{PPh}_3)\text{COCH}_2\text{CH}_3$ 1 react stereoselectively with aldehydes to give α -methyl- β -hydroxy acyl complexes. In these reactions both the aluminium and copper enolates exhibit the same control over the stereochemistry at the α -centre relative to the chiral iron centre but complementary control over the β -centre and thus after decomplexation yield *threo*- and *erythro*- α -methyl- β -hydroxy acids respectively. The lithium enolate 2 derived from 1 showed little stereoselectivity at either the α or β centres on reaction with aldehydes. We report here that the copper enolate derived from 1 adds stereoselectively to symmetrical ketones (R_2CO) to produce the complexes RR,SS- $(\eta^5\text{-C}_5\text{H}_5)\text{Fe}(\text{CO})(\text{PPh}_3)\text{COCH}(\text{CH}_3)\text{-C}(\text{OH})\text{R}_2$ 3 which on decomplexation liberate the corresponding β -hydroxy acids 5.

Addition of symmetrical ketones to the lithium enolate 2 at -78°C shows little stereoselectivity and gives only low yields of the β -hydroxy acyl complexes 3 and 4 (Table), the major product being recovered starting acyl complex 1 arising from deprotonation of the ketones. Addition of SnCl_2 , ZnCl_2 or BF_3 to the lithium enolate 2 prior to addition of the ketones completely suppressed formation of 3 and 4 with only 1 being isolated. Addition of Et_2AlCl to 2, warming to -40°C (2 hrs) and subsequent addition of the ketones at -78°C gave high yields of 3 and 4 but little change in stereoselectivity compared to the lithium enolate 2. Addition of the lithium enolate 2 to 1 equivalent of anhydrous CuCN at -78°C and warming to -40°C for 2 hrs prior to addition of the ketones at -40°C showed a high stereoselective preference for formation of 3 together with good isolated yields (Table). The relative configuration of the α -centre to the iron centre was assigned as described previously.¹ The observed stereoselectivities can only be achieved with strictly 1 equivalent of CuCN and formation of the copper enolate appears to be suppressed if small amounts of free Ph_3P are present. Lower temperatures increase the stereoselectivities but are detrimental to the yields. The observed stereoselectivities correlate with the size of R in the ketones R_2CO ; the smaller the effective size of R the better the selectivity.

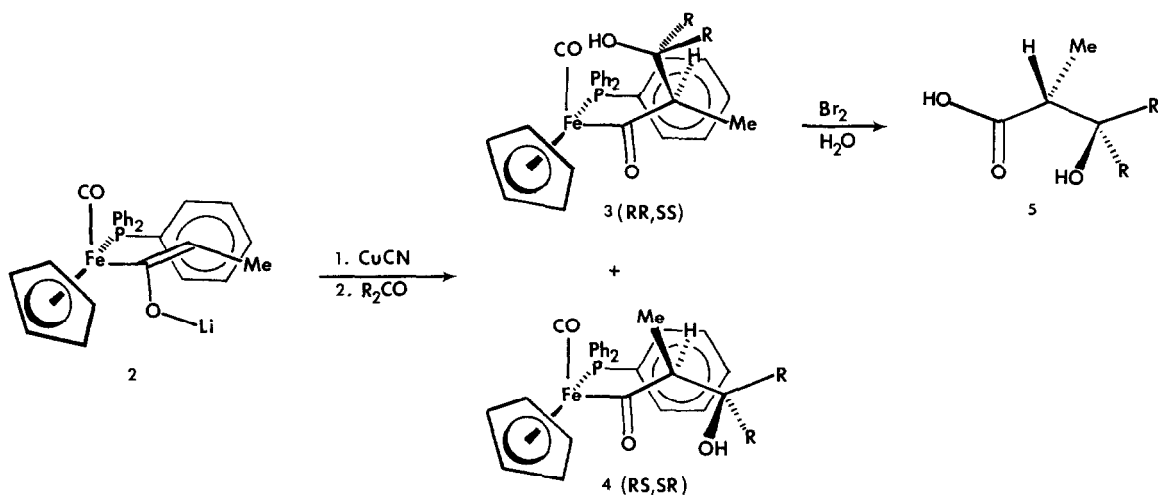

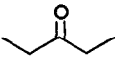


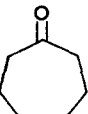


Table: Stereoselectivities (ratio $\underline{3}$: $\underline{4}$) observed in the addition of R_2CO to the lithium $\underline{2}$ and copper enolates derived from $(\eta^5-C_5H_5)Fe(CO)(PPh_3)COCH_2CH_3$ $\underline{1}$.

R_2CO					
Lithium enolate ($-78^\circ C$)	3 : 1	2 : 1	4 : 1	6 : 1	2 : 1
Copper enolate ($-40^\circ C$) (Yields [†])	> 40 : 1 (61%)	2 : 1 (35%)	> 60 : 1 (71%)	> 30 : 1 (84%)	10 : 1 (68%)

[†] isolated but unoptimised

Oxidative decomplexation as described previously generates the corresponding α -methyl- β -hydroxy acids $\underline{5}$ in good yields.² The stereoselective preference for formation of $\underline{3}$ rather than $\underline{4}$ is consistent with addition of the ketones to the unprotected face of the enolate in the anti (O^- to CO) conformation.³ The addition of these chiral propionate enolate equivalents to unsymmetrical ketones is currently under investigation.

References

1. S.G. Davies, I.M. Dordor, J.C. Walker and P. Warner, *Tetrahedron Letters*, 1984, 2709.
2. S.G. Davies, I.M. Dordor-Hedgecock, P. Warner, R.H. Jones and K. Prout, *J. Organometal. Chem.*, 1985, in press.
3. S.G. Davies and J.I. Seeman, *Tetrahedron Letters*, 1984, 1845.

(Received in UK 15 February 1985)