Asymmetric Synthesis of α-Amino-acids from Diastereomeric Metal–Imine Complexes

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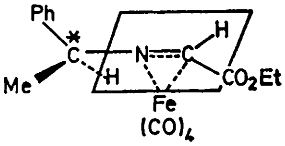
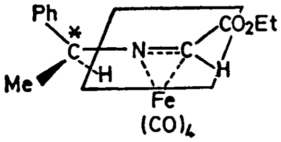
Summary A new route to optically active α-amino-acids has been achieved by treating halogen compounds with iron(0) and nickel(0) diastereomeric complexes of α-methylbenzyliminoglyoxylic acid ethyl ester.

THE π-bonding ability of the C=N double bond of α-methylbenzyliminoglyoxylic acid ethyl ester on several transition metals has been described recently.[1] We report here further reactions of the iron carbonyl–imine complex $Fe(CO)_4(Ph\overset{*}{C}HMe\text{-}N{=}CHCO_2Et)$.

When each enantiomer of the glyoxylic imine (obtained by reaction of D- or L-α-methylbenzylamine on ethyl glyoxylate) is treated overnight in benzene at room temperature with enneacarbonyldi-iron, a mixture of the two predictable diastereomeric complexes is obtained. In the case of the D-(−)-imine, their structures are (A) and (B). We isolated (A) and (B) as optically pure products by t.l.c. (eluting agent, benzene). Their relative abundance is A:B *ca.* 10:90.



(A)



(B)

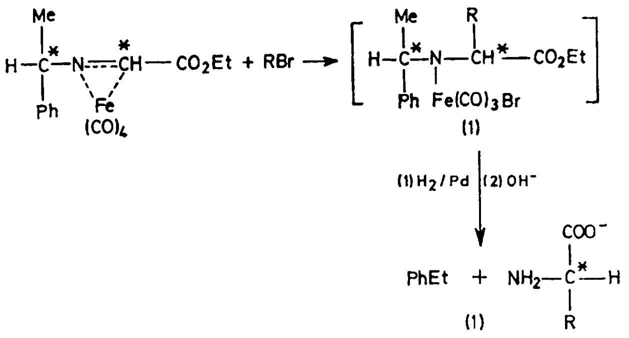
The $[\alpha]_D^{25}$ values of starting materials and iron diastereomeric complexes are as shown in the Table. The complexing behaviour of the glyoxylic imine parallels that of olefins.[2]

Optical activity of the diastereomers

	α-Methylbenzylamine[a]	Imine[a]	$Fe(CO)_4$(imine)[b] (A)	(B)
D	−39·2°	−53·5°	+780°	+268°
L	+39·0°	+53·1°	−845°	−254°

[a] Measured as a pure liquid. [b] Measured as 0·2% solution in C_6H_6.

By treating an excess of benzyl bromide (6 mmol) [R = $PhCH_2$, reaction (1)] with an ethanolic solution of the iron–imine complex (0·6 mmol) at 35 °C for a few hours, hydrogenating the resulting homogeneous red solution with palladium on charcoal, and working up the product,[3] phenylalanine (0·32 mol) is recovered. Starting from the most abundant diastereomer originating from the L-(+)-imine, D-(+)-phenylalanine is recovered (chem. yield 53%, opt. activity 77%). Similarly, L-(−)-phenylalanine is prepared from the D-(−)-imine. The optical yield is dependent on the reaction temperature, only the racemate being obtained at 80 °C (chem. yield 100%).



The same reaction takes place on mixing $Fe_2(CO)_9$, the imine, and benzyl bromide in ethanolic solution. The chemical and optical yields are, respectively, 15 and 55% under these conditions.

Anisyl bromide ($R = MeOC_6H_4CH_2$) affords *O*-methyltyrosine (chem. yield 28%, opt. yield 95%). Ethyl bromoacetate ($R = CH_2CO_2Et$) leads to aspartic acid (chem. yield 24%, opt. yield 78%). In contrast with the preceeding examples, we were unable to isolate significant amounts of alanine from methyl iodide. However, treatment of the iron complex with acetyl chloride (R = Ac) in benzene gives, apart from threonine, the less expected alanine, probably originating from the decarbonylation of an intermediate acyl complex. The factors governing the threonine: alanine ratio are under study.

Some other metal–imine complexes were treated with halogen compounds. When, for example, bis-(1,5-cyclooctadiene)nickel is treated in ethereal solution with the iminoglyoxylic ester, a paramagnetic, air-sensitive complex is obtained, which analyses for $Ni_4(imine)_4O_4$. Treatment with benzyl bromide, at room temperature in ethanolic solution, results readily in the formation of a mixture of α-amino-acids, including phenylalanine.

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