Stereoselective Synthesis of Quaternary Carbon Centres

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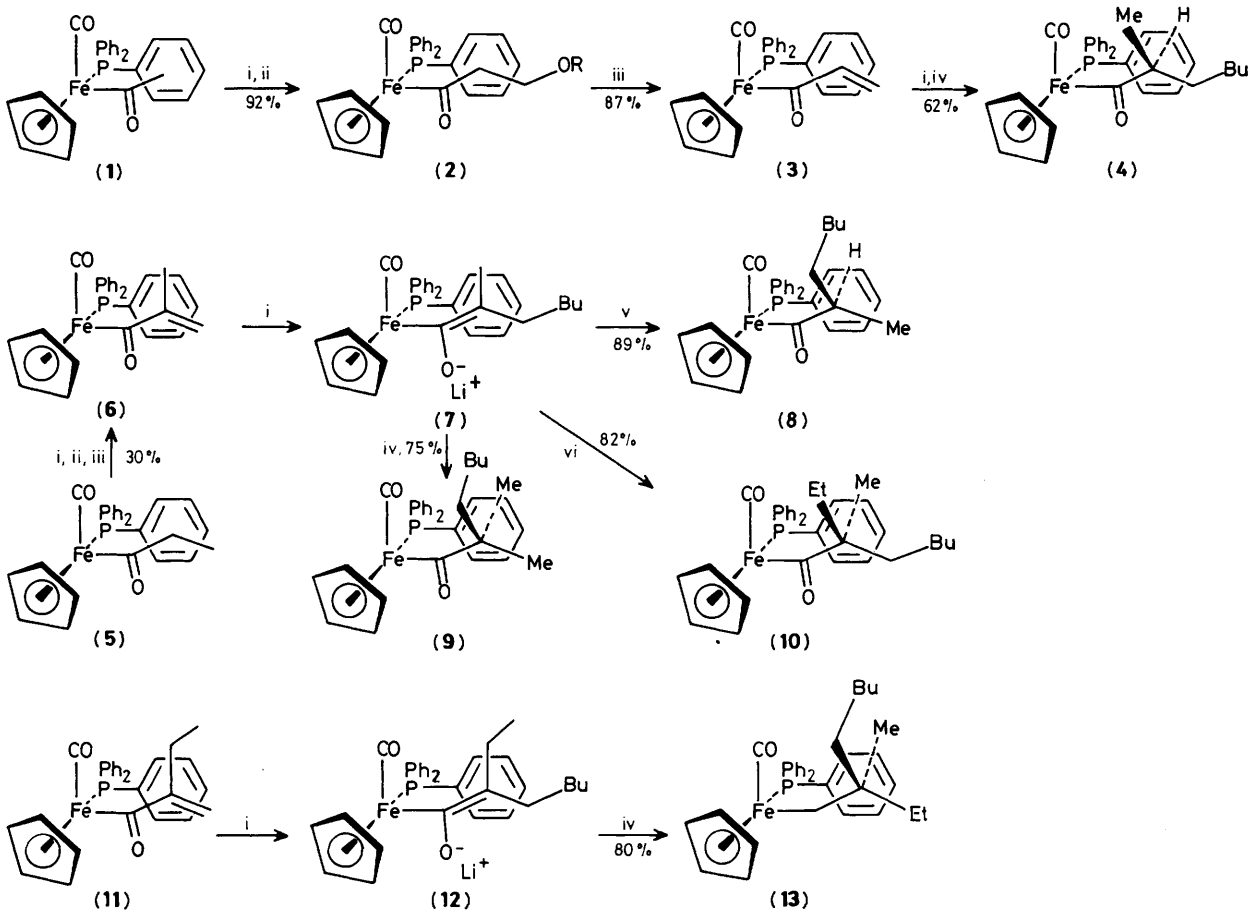
α-Alkyl-α,β-unsaturated acyl ligands attached to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ undergo Michael additions to generate the corresponding *E*-enolates which on alkylation produce quaternary carbon centres stereoselectively.

Highly stereoselective elaborations of tertiary carbon centres can be achieved by alkylation of enolates derived from acyl ligands ($COCH_2R$) attached to the chiral auxiliary $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$.[1,2] However this methodology is not directly applicable to the synthesis of quaternary carbon centres because α,α-disubstituted acyl ligands are not enolisable by strong base. Although quaternary carbon centres are a common feature of many natural products, few methods applicable to their asymmetric synthesis are available.[3] We describe here the formation, *via* Michael additions to α-substituted-α,β-unsaturated acyl ligands, of geometrically pure α,α-disubstituted enolates attached to $[(\eta^5\text{-}C_5H_5)Fe(CO)(PPh_3)]$ and their subsequent alkylations to generate, stereoselectively, quaternary carbon centres.

Alkylation of the acetyl complex (**1**) with chloromethyl alkyl ethers gives the β-alkoxy complexes (**2**) which undergo sodium hydride-induced elimination of alcohol, as described previously, to generate the α,β-unsaturated acyl complex (**3**).[4] Complex (**3**) undergoes a Michael addition reaction with n-butyl-lithium to generate an enolate which on methylation gives (**4**) as a single diastereoisomer identified as (*RS,SR*) by the methyl doublet at δ 1.01 in its ^1H (300 MHz) n.m.r. spectrum.[5] In complex (**4**) the configuration of the α chiral centre relative to the iron centre arises from methylation of the unhindered face of the intermediate *E*-enolate[1] which in turn must arise from Michael addition to (**3**) in the *cisoid* conformation.[2] The α-methyl-α,β-unsaturated acyl complex (**6**) is readily prepared as above from the ethyl acyl complex (**5**). Complex (**6**) also undergoes a Michael addition reaction with n-butyl-lithium to give, after quenching with methanol, (*RR,SS*)-(**8**) as a single diastereoisomer [methyl doublet at δ 0.18 in its ^1H (300 MHz) n.m.r. spectrum[5]], *i.e.* the alternative diastereoisomer to (**4**). The stereoselective formation of (**8**) is consistent with Michael addition to the *cisoid* conformation of (**6**) generating the *E*-enolate (**7**) which then undergoes protonation onto the unhindered face.

The possibility of utilising enolate (**7**) for the elaboration of quaternary carbon centres was demonstrated by the addition of methyl iodide which generated the α-*gem*-dimethyl acyl complex (**9**). Addition of ethyl iodide to (**7**) gave (**10**) as a single diastereoisomer. The relative configurations of the iron and new quaternary carbon centre in (**10**) were assigned as (*RS,SR*) by analogy with protonation giving (**8**) *i.e.* the result of ethylation of the *E*-enolate (**7**) from the unhindered face. The alternative (*RR,SS*) diastereoisomer (**13**) was prepared by addition of n-butyl-lithium to (**11**) followed by methylation of the *E*-enolate (**12**) thus formed.

The stereoselectivities of all the reactions described herein



Reagents: i, Bu^{n}Li, tetrahydrofuran (THF), −78 °C; ii, $ClCH_2OR$ (R = Me, menthyl), −40 °C; iii, NaH, THF, 50 °C; iv, MeI, −78 °C; v, MeOH, −100 °C; vi, EtI, −78 °C.

are extremely high since no crossover products between the diastereoisomeric pairs (**4**)/(**8**) and (**10**)/(**13**) could be detected in the crude reaction products by either ^1H (300 MHz) or ^{13}C (62.9 MHz) n.m.r. spectroscopy.

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