Chiral Recognition in the Michael Addition Reaction between Lithium *N*-3,4-Dimethoxybenzyl-α-methylbenzylamide and the Chiral Iron Crotonoyl Complex [(C_5H_5)Fe(CO)(PPh_3)(COCH=CHMe)]

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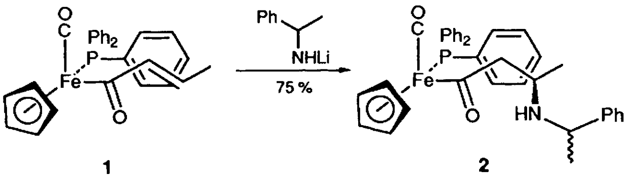
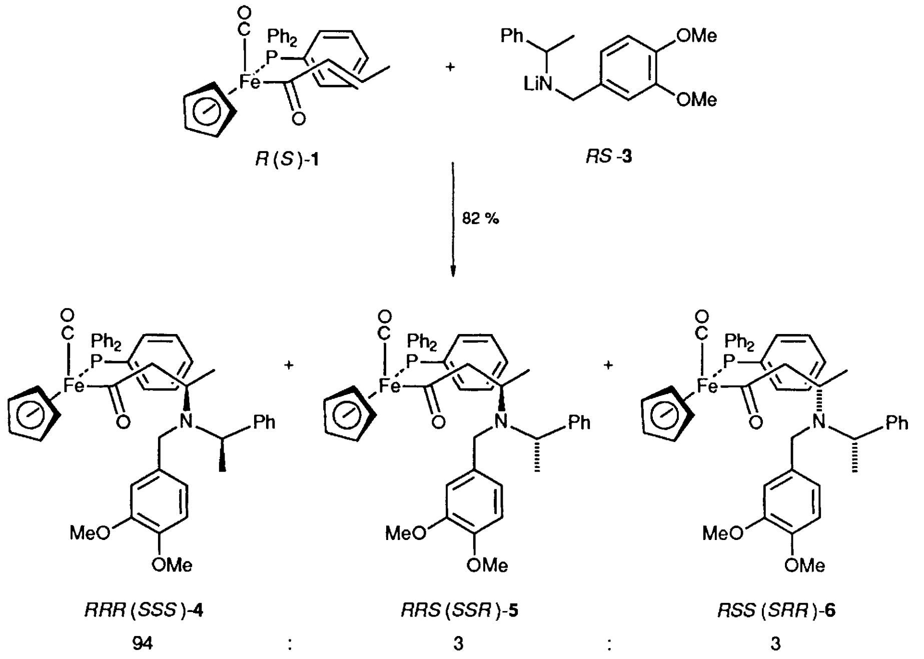
Chiral recognition in the Michael addition reaction between lithium *N*-3,4-dimethoxybenzyl-α-methylbenzylamide and the chiral iron crotonoyl complex [(C_5H_5)Fe(CO)(PPh_3)(COCH=CHMe)] (matched pair *R* + *R*, *S* = 15) allows the kinetic resolution of the latter.

We have previously demonstrated the stereoselective addition of lithium amides to α,β-unsaturated acyl ligands attached to the chiral iron auxiliary [(C_5H_5)Fe(CO)(PPh_3)] for the asymmetric synthesis of β-amino acids and β-lactams.[1,2] We report herein a high degree of chiral recognition in the Michael addition reaction between lithium amides derived from α-methylbenzylamine and the chiral iron crotonoyl complex **1**.

Treatment of the racemic iron crotonoyl complex **1**[3] with excess of racemic lithium α-methylbenzylamide gave a 1 : 1 mixture of the two diastereoisomers **2** consistent with the expected complete stereocontrol by the iron in the formation of the β-chiral centre, but with no discrimination by the iron chiral auxiliary between the enantiomers of lithium α-methyl-



1 **2**



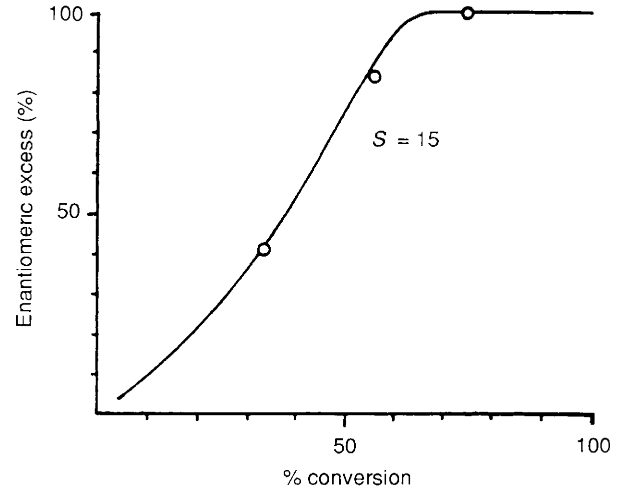


Fig. 1 Enantiomeric excess of recovered acryloyl complex **1** *vs*. % conversion for the reaction between racemic **1** and excess homochiral (*R*)-**3** (——, calculated for a stereoselectivity factor[7] of 15; ○, experimental values)

benzylamide. Although formation of the β-centre is nominally under the influence of two auxiliaries, the iron and the α-methyl benzylamine, the dominance of the iron auxiliary is not surprising given the known very poor control exerted by α-methylbenzylamine in Michael reactions.[4–6]

Addition of excess of the lithium amide **3**, derived from racemic *N*-3,4-dimethoxybenzyl-α-methylbenzylamine, to racemic **1** gave only three of the four possible product diastereoisomers in the ratio 94:3:3. These products were identified as (*RRR,SSS*)-**4**, (*RRS,SSR*)-**5** and (*RSS,SRR*)-**6** respectively by reaction of homochiral (*R*)-**1** and (*S*)-**1** with homochiral (*R*)-**3**. The former reaction gave (*RRR*)-**4** (90%) as a single diastereoisomer (>100:1) whereas the latter gave a 1:1 mixture (55%) of (*SSR*)-**5** and (*SRR*)-**6**.

Monitoring yield against equivalents of lithium amide (25%, 0.5 equiv.; 50%, 1 equiv.; >90%, 2 equiv.) indicated a stoichiometry of 1:2 for complex **1** : amide **3** for these Michael additions. Furthermore the above results indicate a 15:1 rate difference between the matched [(*R*)-**1** + (*R*)-**3**] and mismatched [(*S*)-**1** + (*R*)-**3**] pairs. This rate difference was confirmed by a kinetic resolution of racemic **1** by homochiral (*R*)-**3** (Fig. 1). Thus at 75% conversion recovered crotonoyl complex **1** was found to be essentially homochiral.

The exact mechanism of this chirality recognition remains to be determined, but the stoichiometry implies the intermediacy of an aggregate $(\mathbf{1} + 2 \times \mathbf{3})_n$. Furthermore the consistency of the results for the racemic and homochiral series implies that the reactive aggregates in the racemic case must be homo- not hetero-chiral.

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References

1 S. G. Davies, J. Dupont and R. J. C. Easton, *Tetrahedron Asymmetry*, 1990, **1**, 279.
2 S. G. Davies, I. M. Dordor-Hedgecock, K. H. Sutton, J. C. Walker, R. H. Jones and K. Prout, *Tetrahedron*, 1986, **42**, 5123.
3 S. G. Davies, R. J. C. Easton, J. C. Walker and P. Warner, *Tetrahedron*, 1986, **42**, 175.
4 R. Kinas, K. Pankiewicz, W. J. Stec, P. B. Farmer, A. B. Foster and M. Jarman, *J. Org. Chem.*, 1977, **42**, 1650.
5 M. Furukawa, T. Okawara and Y. Terawaki, *Chem. Pharm. Bull.*, 1977, **25**, 1319.
6 J. d'Angelo and J. Maddaluno, *J. Am. Chem. Soc.*, 1986, **108**, 8112.
7 H. B. Kagan and J. C. Fiaud, *Topics Stereochem.*, 1988, **18**, 249.