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STEREOSELECTIVE PREPARATION OF β-AMINO-ACYL IRON COMPLEXES FOR β-LACTAM SYNTHESIS

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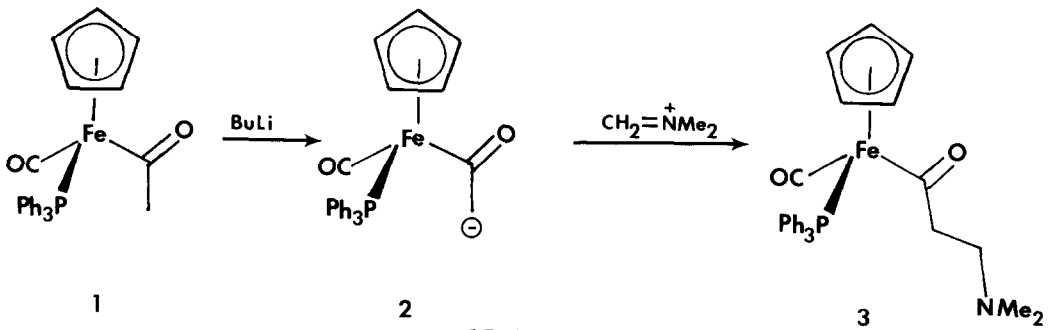
Abstract: The enolate derived from $[(\eta^5\text{-}C_5H_5)Fe(PPh_3)(CO)(COCH_3)]$ and n-butyl lithium reacts stereoselectively with imines to yield β-amino-acyl complexes which on oxidation give β-lactams.

The possibility of forming β-lactams via transition metal mediated reactions has been realised for some time.[1-4] Each of the reported routes is however very limited with respect to the substituents that can be tolerated. Furthermore the possibility of the asymmetric synthesis of β-lactams via such reactions remains to be demonstrated. An essential feature of all the above methods is the decomplexation of a β-amino-alkyl or acyl ligand.

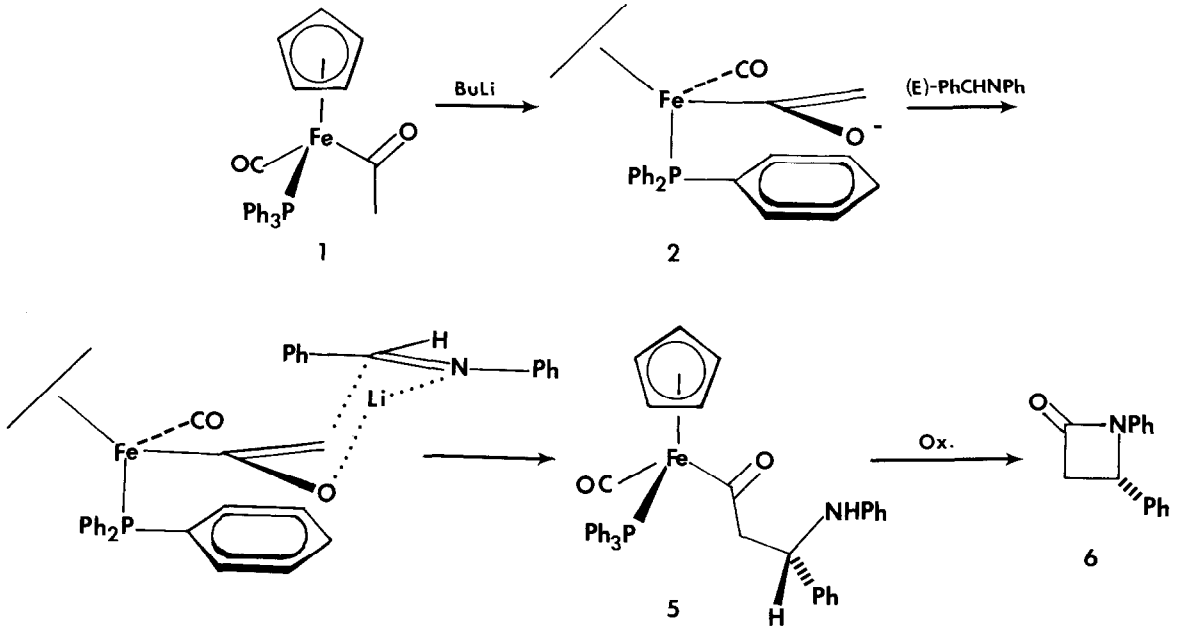
We have recently described the elaboration of iron acyl ligands via the reaction of the enolate 2, derived from the acetyl complex $(\eta^5\text{-}C_5H_5)Fe(PPh_3)(CO)(COCH_3)$ 1, and suitable electrophiles.[5] We report here that the enolate 2 is sufficiently nucleophilic to react with imines and that the resulting β-amino-acyl complexes are formed stereoselectively. Oxidative decomplexation of these β-amino-acyl complexes yields β-lactams.

The ready availability of imines (from amines and aldehydes/ketones) makes them attractive starting materials for β-lactam synthesis. Treatment of the iron acetyl complex 1 with n-butyl lithium at -78°C generates the enolate 2 which reacts with Eschenmoser's salt ($CH_2{=}NMe_2^+$) to give the β-(dimethylamino)-acyl complex 3.[6] Anion 2 is also sufficiently nucleophilic to react with the imine (E)-PhCH=NPh 4 at -78°C to give after methanolic work-up the β-amino-acyl complex 5. This latter reaction proceeds with high stereoselectivity (>98%); only one diastereoisomer being observable by 500 MHz ^1H n.m.r. spectroscopy.[7] This high stereoselectivity was lost when the temperature of the reaction was raised. Oxidation of 5 with ceric ammonium nitrate or cupric chloride gave the known β-lactam 6.



1 2 3

The assigned stereochemistry of diastereomer 5 is consistent with the Zimmerman cyclic transition state model for aldol condensations[8] and with the addition occurring onto the unhindered face of the enolate 2.[5,9]



This stereoselective elaboration of β-amino-acyl ligands from imines, combined with known procedures for the resolution of 1[10] will allow the development of efficient asymmetric syntheses of β-lactams.[11]

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6. All new complexes gave satisfactory elemental analyses.
7. 500 MHz n.m.r. data for the β-amino-acyl ligand of complex 5; ($CDCl_3$) δ 4.30 (1H,dd, J=3.3, 8.2 Hz, Hβ); 3.40 (1H,dd,J=8.2,15.9 Hz,Hα); 2.92 (1H,dd,J=3.3,15.9 Hz,Hα).
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11. A simultaneous independent study by Liebeskind et.al. has yielded similar results to those reported here. We thank Professor L.S. Liebeskind for communicating his results to us prior to publication.

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