

Generation of Homochiral Quaternary Carbon Centres from (Vinylketenimine)tricarbonyliron(0) Complexes

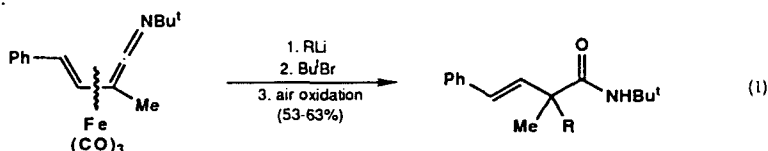
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Abstract: The first homochiral (vinylketenimine)tricarbonyliron(0) complexes have been formed. Nucleophilic attack occurs exclusively on their *exo* face and after an oxidative work-up homochiral β,γ -unsaturated carboxylic acids containing an α quaternary carbon centre are obtained.

We recently discovered that addition of alkyl-lithium reagents to (vinylketenimine)tricarbonyliron(0) complexes followed by an oxidative work-up gives β,γ -unsaturated amides containing an α quaternary centre (Equation (1)).¹

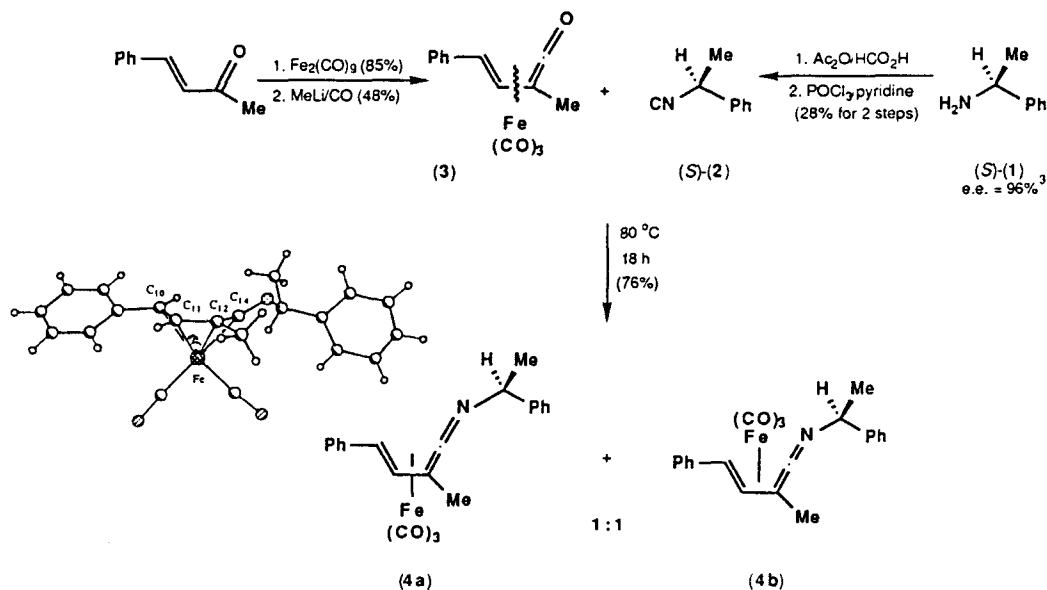


Due to the current interest in methods for constructing homochiral quaternary carbon atoms,² we were interested to determine whether or not this reactivity could be adapted to generate homochiral quaternary centres. We thus describe below: (a) formation of the first homochiral (vinylketenimine)tricarbonyliron(0) complexes, (b) experiments which reveal that nucleophilic attack on these complexes occurs stereospecifically at the *exo* face, and (c) experiments which demonstrate that nucleophilic addition to homochiral (vinylketenimine)tricarbonyliron(0) complexes may be used to generate homochiral quaternary centres.

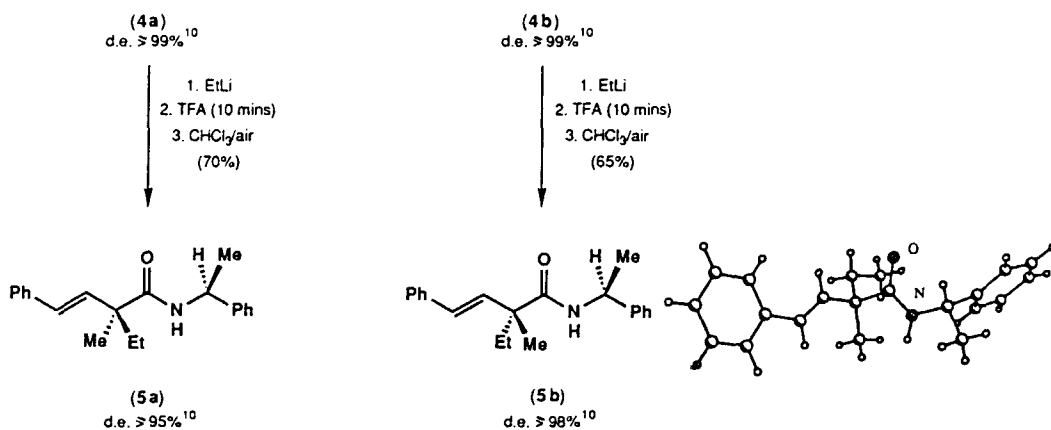
Commercial³ (*S*)-(-)- α -methylbenzylamine (**1**) was converted into (*S*)-(-)- α -methylbenzyl isonitrile (**2**) using a method which is reported to proceed without any loss of stereochemical integrity.⁴ The isonitrile (*S*)-(**2**) was subsequently heated with the racemic (vinylketene)tricarbonyliron(0) complex (**3**)^{5,6} in order to form the corresponding (vinylketenimine)tricarbonyliron(0) complex (**4**).^{7,6} Work-up gave a yellow viscous oil which was identified by ¹H n.m.r spectroscopy as a 1:1 mixture of the diastereoisomeric (vinylketenimine)tricarbonyliron(0) complexes (**4a**) and (**4b**). These were subsequently separated by column chromatography (SiO₂; 9:1, 40-60 petroleum ether:ethyl acetate) to give pure samples of the new compounds

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(4a) and (4b) which were fully characterised.⁸ The slower-moving diastereoisomer on the silica column was subjected to X-ray crystal structure analysis in order to determine its stereochemistry. The analysis revealed that the stereochemistry of this diastereoisomer was as depicted in (4a).⁹

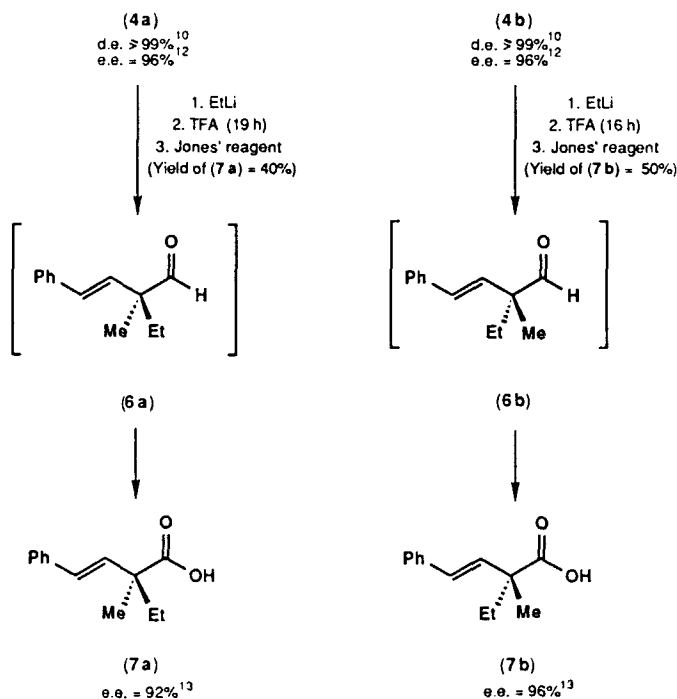


Ethyl-lithium was then added to a diastereoisomerically pure (d.e. $\geq 99\%$ ¹⁰) sample of (4a) in THF and stirred for 1 h at -78°C . The reaction mixture was quenched with trifluoroacetic acid, removed from the cooling bath, and stirred for 10 min. Aerial oxidation overnight in chloroform followed by filtration gave a light brown oil which according to 400 MHz ^1H n.m.r. analysis contained only one (d.e. $\geq 95\%$ ¹⁰) diastereoisomer of the β,γ -unsaturated amide (5). Addition of ethyl-lithium to a diastereoisomerically pure (d.e. $\geq 99\%$ ¹⁰) sample of (4b) followed by an identical work-up gave a crude product which contained a second single (d.e. \geq



98%¹⁰) diastereoisomer of the β,γ -unsaturated amide (5). The two crude products were purified by chromatography and fully characterised.⁸ An X-ray crystal structure analysis of the diastereoisomer derived from complex (4b) revealed that it had the structure indicated by (5b)⁹ and thus the β,γ -unsaturated amide derived from complex (4a) must have the structure depicted by (5a). These results demonstrate that nucleophilic attack on the (vinylketenimine)tricarbonyliron(0) complexes (4a) and (4b) occurs stereospecifically at the *exo* face *i.e.* the face not shielded by the tricarbonyliron(0) unit.

It was found that if the reaction mixture from the addition of ethyl-lithium to complex (4a) was stirred for 2 h at room temperature after quenching with TFA, then the yield of isolated amide dropped to 6%. It was accompanied however by a second compound which was isolated and identified as the aldehyde (6a) (34%). (The stereochemistry of (6a) was assigned initially by assuming that the ethyl-lithium had attacked the *exo* face of complex (4a).) Aldehyde (6a) proved to be unstable and so in subsequent experiments aldehydes (6a) and (6b) were not isolated but oxidised directly to the corresponding carboxylic acids. Thus complexes (4a) and (4b) were converted into the β,γ -unsaturated carboxylic acids (7a) and (7b)¹¹ respectively by adding ethyl-lithium to a solution of the appropriate complex in THF at -78 °C, stirring at -78 °C for 1 h, quenching with TFA, stirring at room temperature overnight, and finally oxidising the reaction mixture with Jones' reagent. The stereochemistry of carboxylic acids (7a) and (7b) was assigned initially by assuming *exo* attack on complexes (4a) and (4b) respectively.



Finally the enantiomeric purity of carboxylic acids (7a) and (7b) was measured. Prior to isolation and characterisation, crude (7a) and (7b) were reacted with (*S*)-(1) and the coupling reagent DCC. This converted acids (7a) and (7b) into amides (5a) and (5b) respectively thus confirming the absolute stereochemistry of (7a)

and (7b). Examination of the 400 MHz ^1H n.m.r. spectrum of the product mixtures revealed that in each case all the carboxylic acid had been consumed and the product amides (5a) and (5b) could both be detected in ratios of 95:5 and 3:97 respectively. Thus acids (7a) and (7b) are of high enantiomeric purity revealing that the optical activity of the (*S*)-(-)- α -methylbenzylamine (1) used initially to generate the isonitrile (2) is not lost during subsequent reactions but is transferred cleanly to the α quaternary centres of carboxylic acids (7a) and (7b).

Acknowledgements

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References and Notes

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7. (Vinylketene)tricarbonyliron(0) complexes are readily converted to (vinylketenimine)tricarbonyliron(0) complexes simply by heating them with an isonitrile, C.J. Richards and S.E. Thomas, *J. Chem. Soc., Chem. Commun.*, 1990, 307.
8. New compounds (4a), (4b), (5a), and (5b), all gave satisfactory spectroscopic (^1H n.m.r., ^{13}C n.m.r., i.r., m.s.) and microanalytical data. The diastereoisomeric complexes (4a) and (4b) gave distinctly different ^1H n.m.r. data as did the diastereoisomeric amides (5a) and (5b).
9. Crystal data: (4a), $\text{C}_{22}\text{H}_{19}\text{NO}_3\text{Fe}$, $M = 401.2$, monoclinic; $P2_1$, $a = 7.735(5)$, $b = 7.717(7)$, $c = 17.495(2)$ Å, $\beta = 98.4(6)^\circ$, $Z = 2$, Mo- $K\alpha$ radiation, $\lambda = 0.71073$ Å, $\mu = 7.5$ cm $^{-1}$. $R = 0.064$ for 1231 observed ($I/\sigma(I) \geq 2.0$) reflections ($R_w = 0.065$). Fe-C(10) 2.16(1), Fe-C(11) 2.09(1), Fe-C(12) 2.09(1), Fe-C(14) 2.00(1), C(10)-C(11) 1.39(2), C(11)-C(12) 1.37(2), C(12)-C(14) 1.41(2) Å. (5b) $\text{C}_{21}\text{H}_{25}\text{NO}$, $M = 307.4$, orthorhombic; $P2_12_12_1$, $a = 10.071(7)$, $b = 19.218(15)$, $c = 19.406(14)$ Å, $Z = 8$, $\mu = 0.6$ cm $^{-1}$. $R = 0.063$ for 1600 observed reflections ($R_w = 0.061$); all dimensions standard; two independent identical molecules.
10. Minor diastereoisomer not observed in 400 MHz ^1H n.m.r. spectrum. D.e. quoted is based on estimate of the detection limit in the spectrum and reflects the quality of the data.
11. W.G. Dauben, G. Lodder, and J.D. Robbins, *Nouv. J. Chim.*, 1977, **1**, 243.
12. Assuming no loss of optical activity in synthesis from (*S*)-(1).³
13. E.e. corrected to allow for enantiomeric impurity of (*S*)-(1).³