Diastereoselective addition reactions of allylstannanes to carbonyl groups in the side-chain of π-allyltricarbonyliron lactone complexes

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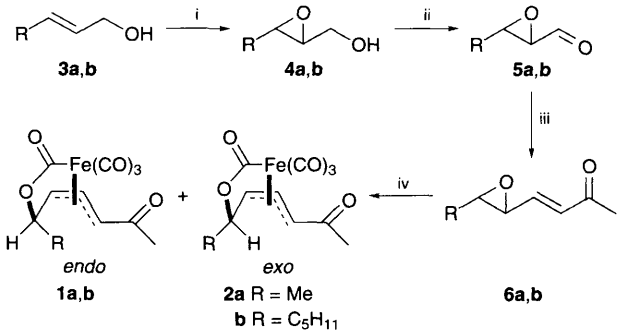
Lewis acid-mediated addition of allylstannanes to ketones adjacent to the allyl system of π-allyltricarbonyliron lactone complexes generates the corresponding homoallylic tertiary alcohols with excellent diastereocontrol.

We recently reported that tertiary alcohols could be generated in good yield and with excellent stereocontrol by the addition of alkenyl, aryl, alkynyl and various alkyl aluminium reagents to ketone groups in the side-chain of π-allyltricarbonyliron lactone complexes.[1] The allylation of these ketones would represent an important complement to the groups already transferred. We reasoned that allylstannanes, in the presence of a Lewis acid, would be sufficiently reactive to add to the ketone group α- to the allyl system of π-allyltricarbonyliron lactone complexes. Although the stereoselective allylation of aldehydes with allyl tin reagents has been thoroughly investigated,[2] the corresponding reaction with ketones is appreciably less well documented.[3] Here we report that the highly diastereoselective addition of a wide variety of allylstannanes to Lewis acid-activated ketones in the side-chain of π-allyltricarbonyliron lactone complexes generates the S_E2' homoallylic alcohol products in good to excellent yield.

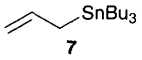
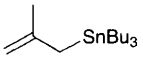
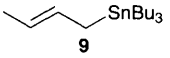
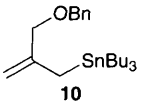
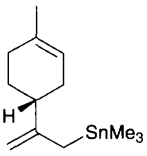
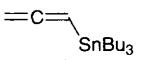
Work has concentrated on additions to the *endo*- and *exo*-methyl ketone complexes **1** and **2** respectively. These are accessed in a four step sequence outlined in Scheme 1. Two sets of complexes have been synthesised differing in the substituent at the oxy-end of the allyl system: a methyl group in set **a** and a pentyl group in set **b** (Scheme 1). Starting from the appropriate allylic alcohol **3**, a directed epoxidation using either the $VO(acac)_2$/*tert*-butylhydroperoxide (TBHP) or $Ti(OPr^i)_4$–TBHP systems afforded the corresponding epoxy alcohol **4** which was oxidised to the aldehyde **5** using pyridinium dichromate or *in situ*-generated Collins' reagent. Homologation using the commercially available,† stabilised ylide 1-triphenylphosphoranylidenepropan-2-one in a Wittig reaction, proceeded smoothly to the epoxy enone **6** with good control of the double bond geometry [$E:Z > 20:1$ as determined by ^{1}H NMR (200 MHz)]. Treatment of **6** with $Fe_2(CO)_9$ in THF furnished the *endo*- and *exo*-complexes **1** and **2** respectively, which were readily separable by flash column chromatography.



Scheme 1 *Reagents and conditions for R = Me*: i, $Ti(OPr^i)_4$, Bu^tOOH (3 mol dm^{-3} in isooctane), 3 Å powdered molecular sieves, CH_2Cl_2, 0 °C, 2 h, 42%; ii, Pyridinium dichromate, 3 Å powdered molecular sieves, CH_2Cl_2, 17 h. Product not isolated; iii, $MeC(O)CH{=}PPh_3$, CH_2Cl_2, 0 °C, 3 h, 10% over 2 steps; iv, $Fe_2(CO)_9$, THF, 1.5 h, 35% (**1a**), 10% (**2a**). *Reagents and conditions for R = C_5H_{11}*: i, $VO(acac)_2$, Bu^tOOH (3 mol dm^{-3} in isooctane), 4 Å powdered molecular sieves, CH_2Cl_2, 0 °C, 1.5 h, 73%; ii, pyridine, CrO_3 Celite, CH_2Cl_2, 0 °C to room temp., 1 h, 80%; iii, $Me_3C(O)CH{=}PPh_3$, CH_2Cl_2, 0 °C, 2 h, 70%; iv, $Fe_2(CO)_9$, THF, 2.5 h, 67% (**1b**), 15% (**2b**).

A number of allylstannanes were synthesised according to standard literature procedures and gave moderate to excellent yields of product when added into the ketone (Table 1). In the case of stannanes **7**,† **8**[4] and **10**,[5] with both *exo*- and *endo*-complexes only one diastereoisomeric product could be observed by ^{1}H NMR (500 MHz), 95% de is thus a conservative estimate for the selectivity of the reaction. With crotyltributylstannane **9**,[6] two products, inseparable by flash column chromatography, were obtained in a 1:1 mixture. This is consistent with the addition reaction proceeding through an open transition state. Thus, whilst selectivity in forming the tertiary alcohol centre is maintained, no control is exerted over the adjacent stereocentre. With (*R*)-limonene trimethylallylstannane **11**,[7] two inseparable products were also obtained, corresponding to the addition of a homochiral stannane with racemic ketone. Allenyltributylstannane **12**[8] reacted slower than the majority of the allylstannanes and, probably as a consequence, gave a number of products: in addition to the

Table 1 Diastereoselective addition reactions to racemic π-allyltricarbonyliron lactone complexes

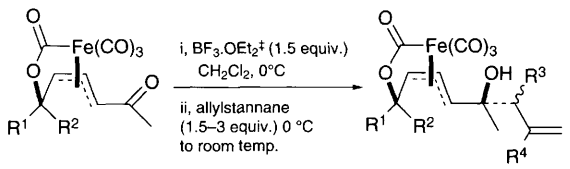
Complex	Allylstannane	Product	Yield (%)	de (%)
1a	 **7**	**13**	76	>95
1b		**14**	84	>95
2a		**15**	81	95
2b		**16**	76	>95
1a	 **8**	**17**	90	>95
1b		**18**	57	>95
1b	 **9**	**21**	65	>95
1a	 **10**	**19, 20**	20, 20	>95
1b	 **11**	**22, 23**	45, 45	>95
1a	 **12**	**24, 13**	47, 4	95

single homoprop-2-ynylic alcohol, the secondary alcohol reduction product, possibly formed by a β-hydride transfer was obtained (35%), as was a very small amount of homoallylic alcohol **13**. No allenylic alcohol was observed.

The relative stereochemical outcome of the reaction has been established by comparison of the ^{1}H NMR (500 MHz) data of the hydrogenated product from the homoallylic alcohol **13** with the addition product **25** obtained from adding tripropylaluminium into the ketone (Scheme 2). The propyl product derived from both routes proved identical thus suggesting that the allylstannane nucleophile adds opposite to the bulky tricarbonyliron moiety *via* the *s-cis* conformer in a similar fashion to organoaluminium reagents (Fig. 1).[1]

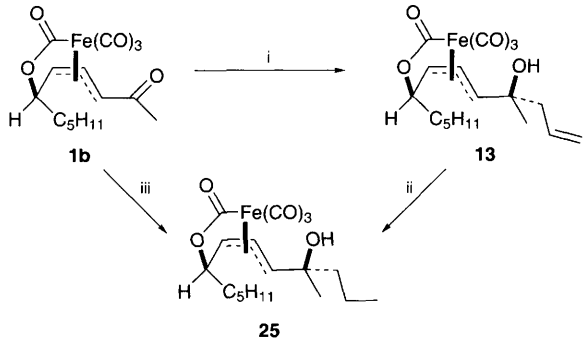
The *endo*-addition products can be converted into the corresponding *E,E*-dienes *via* a high yielding, two step procedure (Scheme 3). Stereoselective decarboxylation to the η^4-diene tricarbonyliron complex **26** proceeded readily upon treatment of **13** with $Ba(OH)_2$.[9] Subsequent decomplexation with alkaline H_2O_2 proceeded rapidly without loss of stereochemical integrity to release the *E,E*-diene **27** in good yield.[10] Other decomplexation routes[11] and further functionalisation of the side-chain unit are presently under investigation.

In conclusion, the highly diastereoselective addition of allylstannanes into the ketone of π-allyltricarbonyliron lactone complexes provides a useful route to diastereoisomerically pure



1a R^1 = H, R^2 = Me
b R^1 = H, R^2 = C_5H_{11}
2a R^1 = Me, R^2 = H
b R^1 = C_5H_{11}, R^2 = H

13 R^1 = H, R^2 = Me, R^3 = H, R^4 = H
14 R^1 = H, R^2 = C_5H_{11}, R^3 = H, R^4 = H
15 R^1 = Me, R^2 = H, R^3 = H, R^4 = H
16 R^1 = C_5H_{11}, R^2 = H, R^3 = H, R^4 = H
17 R^1 = H, R^2 = Me, R^3 = H, R^4 = Me
18 R^1 = H, R^2 = C_5H_{11}, R^3 = H, R^4 = Me
19,20 R^1 = H, R^2 = Me, R^3 = Me, R^4 = H
21 R^1 = H, R^2 = C_5H_{11}, R^3 = H, R^4 = CH_2OBn
22,23 R^1 = H, R^2 = C_5H_{11}, R^3 = H, R^4 = (1'*R*)-4'-methylcyclohex-3'-enyl
24 R^1 = H, R^2 = Me, R^3 = H, R^4 = –(CCH)



Scheme 2 *Reagents and conditions*: i, BF_3·OEt_2, CH_2Cl_2, 0 °C, then allyltributylstannane, 0 °C, 3 h, 84%; H_2, Pd/C, EtOAc, 2.5 h, 70%; iii, Pr_3Al (1 mol dm^{-3} in toluene, CH_2Cl_2, −78 °C to room temp., 2 h, 6% (90% reduction product)

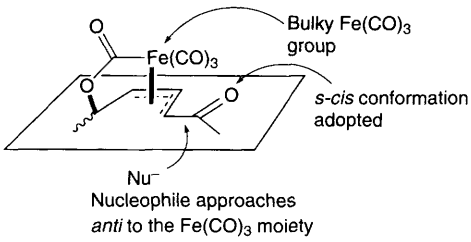
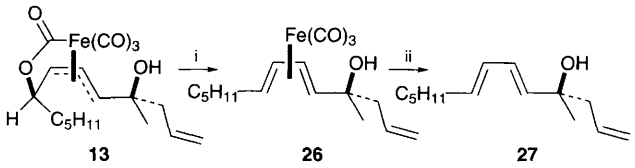


Fig. 1 Origins of the diastereoselectivity in the addition of nucleophiles to π-allyltricarbonyliron lactone complexes



Scheme 3 *Reagents and conditions*: i, $Ba(OH)_2$ (saturated aqueous solution), MeOH, 20 min, 85%; ii, H_2O_2, NaOH, MeOH, 0 °C, 25 min, 72%

homoallylic alcohols. Furthermore, use of the Sharpless asymmetric epoxidation protocol[12] potentially allows access to homochiral iron complexes and hence to enantiomerically enriched homoallylic alcohols. The tricarbonyliron lactone tether provides a source of 1,5-asymmetric induction of chirality in the formation of the new stereogenic centre.

We thank the EPSRC, Zeneca Pharmaceuticals and Trinity College Isaac Newton Trust bursary award scheme (L. R. C.) and the BP endowment and Ciba Geigy Research Fellowship (S. V. L.) for generously funding this work.

Footnotes

† Commercially available from Aldrich Chemical Company, Inc.
‡ $BF{\cdot}OEt_2$ proved to be the most effective Lewis acid.

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Received, 11th December 1995; Com. 5/08051G