A novel decomplexation of π-allyltricarbonyliron lactone complexes using borohydride reagents: a new route to stereodefined acyclic 1,5-diols and 1,5,7-triols

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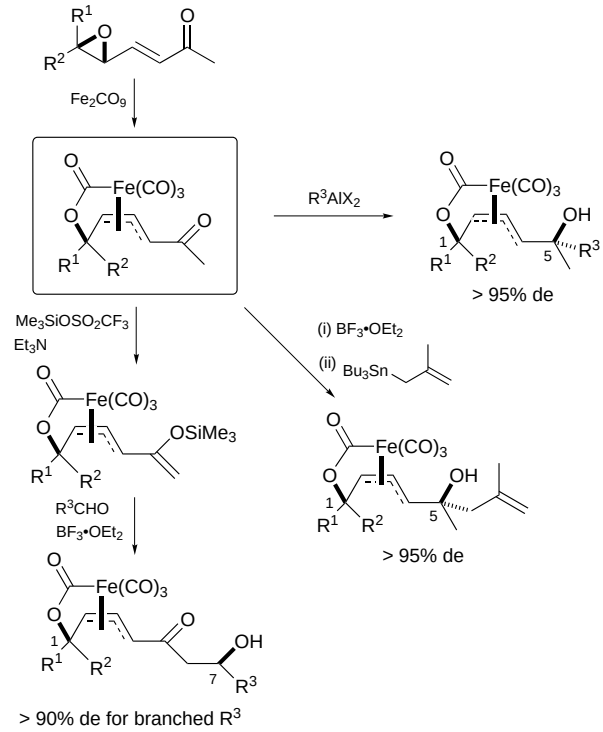
π-Allyltricarbonyliron lactone complexes undergo a highly stereoselective decomplexation reaction on treatment with sodium triacetoxyborohydride to afford acyclic alcohols in excellent yields.

Remote asymmetric induction in acyclic systems remains a challenging problem in contemporary organic synthesis. The use of a complexed transition metal as a temporary structural feature is a strategy which is finding increasing utility in addressing this problem.[1] The higher level of organisation and rigidity in such an organometallic system can allow the transfer of stereochemical information across distances of several atoms, for a variety of different bond forming reactions and functional group transformations.

We have previously shown that the use of a π-allyltricarbonyliron lactone complex as a scaffold affords excellent diastereoselectivity in the manipulation of a ketone group appended to the allyl unit (Scheme 1). Thus a 1,5 stereochemical relationship of oxygen functionalities may be established in a controlled manner by the addition of organoaluminium reagents[2] or allylstannanes[3] into the side-chain ketone. We have now also demonstrated high diastereocontrol in Mukaiyama aldol reactions of aldehydes with π-allyltricarbonyliron lactone complexes bearing a silyl enol ether functionality in the side-chain.[4] The products of these reactions have a 1,7 stereochemical relationship between the new chiral centre and the lactone tether.

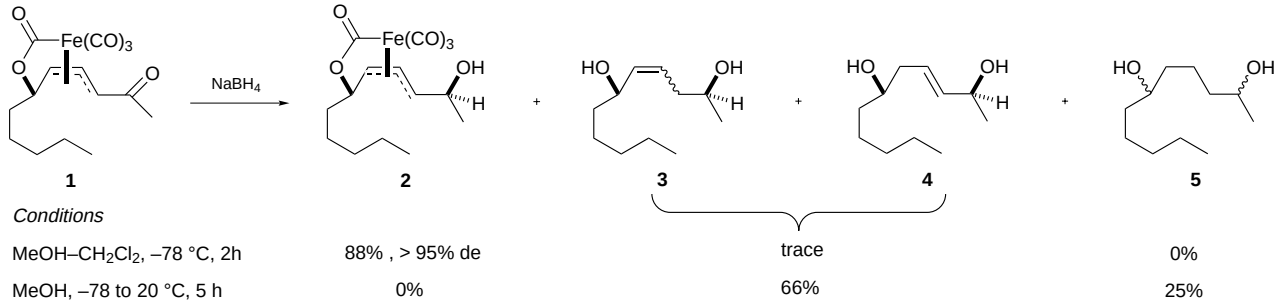
Existing methods for the removal of the iron carbonyl moiety are limited in scope.[5] Treatment with ceric ammonium nitrate leads to the stereoselective formation of β-lactones,[6] while δ-lactones can be accessed under exhaustive carbonylation conditions.[7,8] Treatment with barium hydroxide affords (η⁴-diene)tricarbonyliron complexes.[2b,7] We now report a new decomplexation reaction which effectively unwraps the carbon chain from the iron centre to reveal a linear molecule, with the chiral centre at the lactone tether preserved as a free alcohol and the side-chain functionality intact.

Our interest in hydride donors as potential decomplexing agents was initially aroused by the reaction between ketone **1** and sodium borohydride in 50% MeOH–CH_2Cl_2 at −78 °C.[9] After 1 h the ketone group was completely reduced to afford a single diastereoisomer of the corresponding secondary alcohol **2** in 88% yield. Over longer reaction times, however, the product began to react further and small quantities of chromatographically inseparable decomplexation products, tentatively assigned as **3** and **4**, could be isolated (Scheme 2).



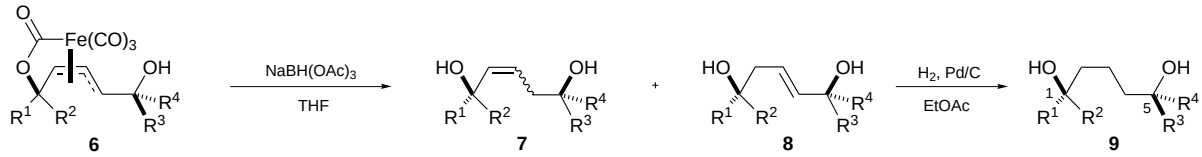
Scheme 1

In order to drive the decomplexation reaction to completion it was necessary to use a large excess of sodium borohydride, added portionwise to a methanolic solution of the diastereomerically pure secondary alcohol complex at room temperature. Under these conditions a further, saturated product **5** could be detected in the diol mixture (Scheme 2). Hydrogenation of the mixture afforded exclusively saturated diol, but with a diastereomeric excess of only 56%. These results indicate



Scheme 2

Table 1 Decomplexation of a range of functionalised π-allyltricarbonyliron lactone complexes using $NaBH(OAc)_3$



Complex	R^1	R^2	R^3	R^4	Yield of **9** (%)[a]	De (%)[b]
6a	C_5H_{11}	H	H	H	59	—
6b	C_5H_{11}	H	Ph	H	71	96
6c	Me	H	$(CH_2)_4OBn$	H	63	> 96
6d	H	C_5H_{11}	Me	H	82 (97)[c]	> 96
6e	H	C_5H_{11}	Me	Pr^n	52 (67)[c]	> 96
6f	H	C_5H_{11}	$CH_2CH(OH)Ph$	H	65[d] (87)[c]	> 96

[a] Isolated yield of **9** over two steps from **6**. [b] Diastereomeric excess of **9** determined by comparison of integrals in the 600 MHz ^1H NMR spectra. [c] Yield based on recovered starting material. [d] The OH at C-7 was lost during hydrogenation; see text.

that positional isomerisation of the double bonds in products **3** and **4** had taken place during decomplexation. Formation of the saturated product **5** could then be explained by initial iron carbonyl catalysed double bond isomerisation to form an enol,[10] followed by decomplexation and non-stereospecific borohydride reduction of the tautomeric ketone.

Extensive screening of different reducing systems revealed that decomplexation could be achieved without isomerisation using sodium triacetoxyborohydride in dry THF. A variety of different lactone complexes were exposed to these conditions and the results are shown in Table 1. In each case, the major component of the product mixture was *cis*-**7** which could generally be isolated by careful flash chromatography; the proportion of *cis*-**7** : (*trans*-**7** + **8**) was typically around 2 : 1. The products were combined and hydrogenated in order to facilitate characterisation and determination of the diastereomeric excesses.

In the case of the *syn* 5,7-diol complex **6f**, prepared by a Mukaiyama aldol reaction followed by stereoselective reduction of the C-5 ketone group,[4] the 1,5,7-triol decomplexation product *cis*-**7f** was isolated in 55% yield. After recombination with the other ene triol products and hydrogenation according to the standard procedure, however, a fully saturated 1,5-diol was obtained, which was formed by elimination of the C-7 hydroxy group during hydrogenation. This problem should be avoidable by variation of the hydrogenation conditions.

In summary, a new decomplexation reaction has been developed which allows removal of the iron carbonyl moiety from functionalised π-allyltricarbonyliron lactone complexes and conversion into functionalised alcohols without loss of stereochemical integrity. Application of this procedure to the nucleophilic adducts of ketone complexes constitutes an expedient route to stereodefined 1,5-diols, while application to the products of Mukaiyama aldol reactions allows access to stereodefined 1,5,7-triols. Studies on the mechanism of the decomplexation reaction and its utility in natural product synthesis will be published in due course.

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Footnote and References

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