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ELECTROPHILIC VINYLOGOUS DIENYL π-COMPLEXES: A NOVEL APPROACH TO THE STEREOCONTROLLED PREPARATION OF POLYENES

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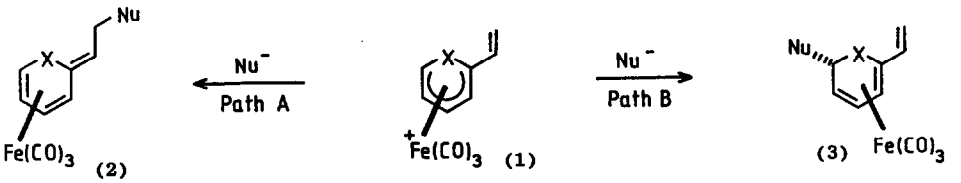
Abstract: Vinyl substituted cyclohexadienyl π-complexes have been prepared from η^4-trienol complexes. Regiocontrol of nucleophile addition depends on the nature of the reagent. Inclusion of a 2-OMe substituent on the η^5-dienyl portion promotes reliable reaction of the trienyl system at C-7.

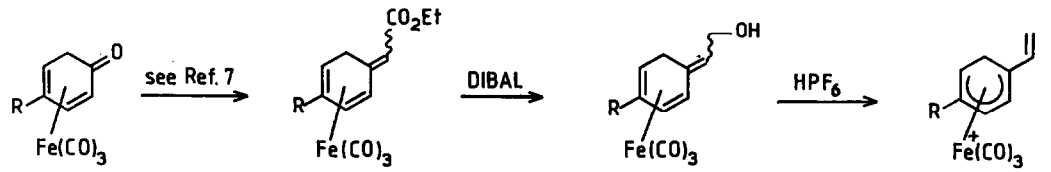
When stoichiometric π-complexes are employed in organic synthesis, it is important that the metal centre is used repeatedly in a series of steps.[1] Improved versatility in synthetic applications would be achieved, if the transition metal control centre could relay its effects to remote locations, since the influence of the metal can then be liberated from the restriction of its position of attachment to the organic ligand. Whilst remote stereodirecting effects of the required type have been demonstrated in neutral stoichiometric organochromium complexes,[2] the use, in this way, of more powerful electrophiles stabilized by tricarbonyliron complexes, has not been examined, despite the increasing importance of organoiron complexes as intermediates in total synthesis.[3]



Scheme 1 : (a) X = CH_2 ; (b) X = H,H

We describe here the first preparation of cationic vinylogous cyclohexadienyl complexes [(1-5)η-trienyl complexes][4] and an investigation that explores the regiocontrol of their reactions with nucleophites. Although nucleophile addition to cationic η^5-dienyl complexes can occur at any of the carbons bound to the metal,[5] reaction at C-1 or C-5 is normal for cyclohexadienyl complexes of $Fe(CO)_3$. In the case of (1a,b), attack at C-7 was also anticipated in view of conjugate addition processes known for other organometallic complexes.[2,6] The first stage of our investigations has examined the competition between nucleophile addition at the two termini of the π-system, paths A and B in Scheme 1.

The required complex (1a), was obtained from (5)[7] by reduction with DIBAL and reaction of the resulting E/Z mixture of neutral η^4-trienol complexes (6) with aqueous HPF_6 in acetic anhydride. The cation (1a) was purified by trituration with ether and, following addition of water, was precipitated in 63% yield for the two steps as a non-hydroscopic yellow powder.[8]



(4) R = H
(7) R = OMe

(5) R = H
(8) R = OMe

(6) R = H
(9) R = OMe

(1a) R = H
(10) R = OMe

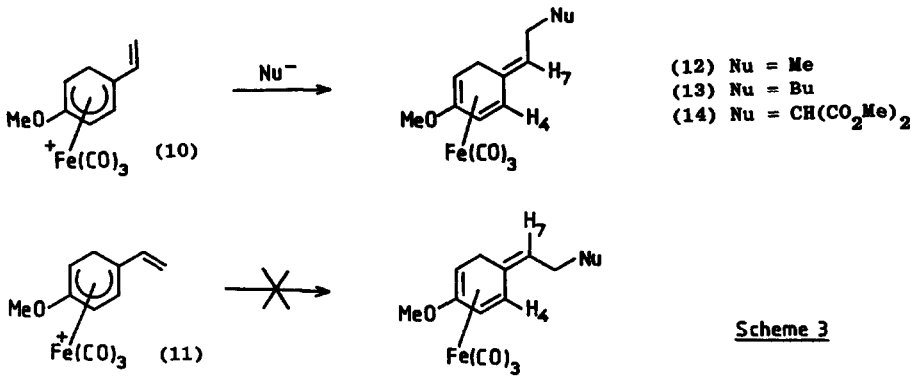
Scheme 2

Results of nucleophile addition to (1a) are summarized in the Table. These data show that either Path A or Path B can be selected, depending on the choice of nucleophile. Cuprate addition proceeded predominantly by Path A. In contrast, borohydride, cyanide and malonate anions preferred Path B. Thus products of either type (2a) or type (3a) are accessible depending on the nature of the nucleophile employed.

TABLE: Reactions of cations (1a) and (10)

Substrate	Nucleophile	Path A	Path B	Major Product	Yield
(1a)	$NaBH_4$	< 1	>99	(3a): $X=CH_2$, Nu=H	70%
(1a)	Me_2CuLi	80	20	(2a): $X=CH_2$, Nu=Me	60%
(1a)	Bu_2CuLi	87	13	(2a): $X=CH_2$, Nu=Bu	72%
(1a)	NaCN	< 1	>99	(3a): $X=CH_2$, Nu=CN	66%
(1a)	$NaCH(CO_2Me)_2$	< 1	>99	(3a): $X=CH_2$, $Nu=CH(CO_2Me)_2$	73%
(10)	Me_2CuLi	>99	< 1	(12): Nu=Me	73%
(10)	Bu_2CuLi	>99	< 1	(13): Nu=Bu	60%
(10)	$NaCH(CO_2Me)_2$	>99	< 1	(14): $Nu=CH(CO_2Me)_2$	73%

In order to enhance the conjugate mode of addition (Path A), a directing group is required to de-activate C-1 in reactions with nucleophiles. The C-2 methoxy substituted complex (10) was selected for study in an attempt to employ the powerful C-5 directing influence of the OMe substituent[9] to force nucleophile addition to the far end of the trienyl π-system. The complex (10) was obtained following the same procedure that was used for (1a) (Scheme 2: (7) to (8), 81%, (8) to (9) to (10) 66%), starting from the known dienone complex (7).[10]



Scheme 3

The results of reactions of (10) with nucleophiles are shown in the Table. In this case, all reagents added by path A, with reaction occurring exclusively at the uncomplexed end of the π-system. Even in the case of malonate addition, which, without the methoxy substituent, followed only Path B, a regioselective reaction occurred. The conjugate adduct (14) was the sole product obtained with the directing group in place. These results show that deactivation of C-1 by the C-2 OMe substituent is sufficient in these complexes to promote reliable nucleophile addition at C-7. It is also notable that no C-5 addition products were obtained, despite the normal tendency of C-5 substituted 2-methoxydienyl complexes to react at this position, forming compounds with quaternary centres.[9] In the case of (10), this would have produced a complex with a vinyl ($CH{=}CH_2$) substituent that would have been easily detected in NMR spectra.

Examination by high field NMR showed that the products obtained from (10) were similar to complexes of type (2a), suggesting that the vinylogous dienyl complexes had both reacted in the same conformation (see Scheme 3), in all the cases where C-7 addition had occurred. For the product (12), an n.O.e. study was undertaken to determine the stereochemistry about the $\Delta_{6,7}$ double bond, and so identify the nature of the more reactive conformation of the electrophile. An 11% enhancement was observed between H-4 and H-7, indicating these two atoms to be in close proximity, as shown in structure (12). In view of the similarity of NMR spectra obtained with all the C-7 adducts, this E stereochemistry can be provisionally assigned to both series of products, (2a) and (12)-(14).

Conclusions

When the natural directing effect of the vinyl substituent is allowed to operate freely, selective nucleophile addition at either the free (Path A) or the bound (Path B) terminus of the π-system can be obtained by the judicious choice of nucleophilic reagents. Alternatively, other directing groups on the dienyl cation can be employed to overcome the influence of the vinyl group, so improving the range of nucleophiles suited to Path A addition, and, in the case of 2-OMe substitution, ensuring complete regio-control.

Acyclic vinylogous dienyl complexes of type (1b) will be attractive as intermediates for the synthesis of lipoxins,[11,12] provided Path A addition can be followed. The effect of directing groups on the η^5-dienyl portion of cationic acyclic η^5-trienyl complexes is currently under investigation. At the present stage, however, we have demonstrated that addition by Path A in the cyclic series occurs in the conformation (10) rather than (11), as is required for the formation of the EZE polyene stereochemistry needed for the construction of the first three alkene linkages in lipoxin B.

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