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Preliminary communication

Model studies for an organometallic route to *cis,trans*-dienols

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Abstract

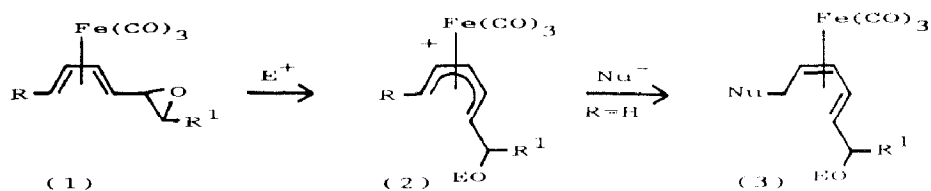
An ylide derived from trimethylsulphonium iodide was added to the tricarbonyliron complex of hexa-2,4-dienal to produce a mixture of diastomeric epoxides, which were partially converted into a cationic organoiron species by reaction with $\text{HBF}_4 \cdot \text{OEt}_2$.

The development of stereocontrolled syntheses of leukotrienes and hydroxy-eicosatetraenoic acids (HETEs) has recently received much attention [1]. In particular, the creation of versatile, stereoselective routes to the *cis,trans*-dienol portion offers an important challenge, since this sub-unit is common to both series of natural products. Organometallic methods have proved valuable in work addressing this problem because of the powerful stereocontrol effects normally available from reactions of this type. Palladium coupling reactions [2], cuprate chemistry [3], and diastereoselective alkylations of carbonyl groups adjacent to chiral tricarbonyliron complexes [4,5], have all been used, and a synthesis of the left-hand portion of leucotriene B₄ based on the use of stoichiometric iron complexes has recently been reported [6].

Our work in this area involves an approach (summarized in Scheme 1: R = H) in which the formation of the chiral centre at the alcohol position of the dienol would be achieved by the electrophilic opening of an epoxide of type **1** *. After rearrangement, the expected cisoid pentadienyl cation (**2**) would contain a suitably protected alcohol at the required position. This would then serve in a subsequent nucleophile addition step to introduce the left-hand portion of the molecule.

In view of the recent interest in the introduction of epoxides into organoiron complexes [5], and in the alkylation of pentadienyl cations related to HETE synthesis [7], we report here results of a model study designed to demonstrate

* During the preparation of this manuscript a review appeared (ref. 15) which draws attention to the difficulty of synthesizing such epoxides, and to the recent preparation of the first compounds of this general type (ref. 16).

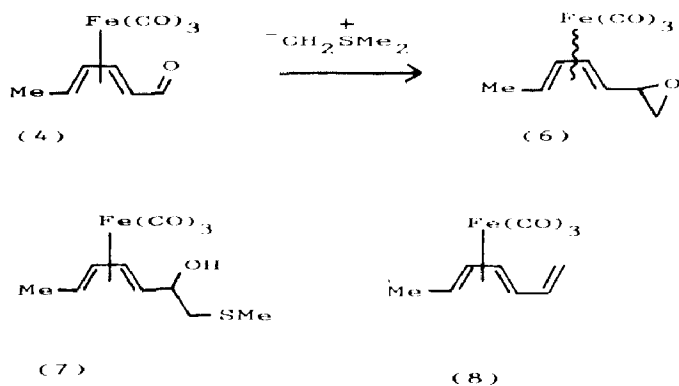


Scheme 1

transformations of the type required in our approach. We have initially employed a readily available series of compounds to explore access to the epoxide (6) from tricarbonyl(η^4 -hexa-2,4-dienal)iron(0) (4).

Epoxidation via nucleophilic addition of ylides [8–11] derived from alkylsulphonium or arsonium salts would be expected to provide a convenient method for the conversion of 4 into 6. Addition of the ylide formed from trimethylsulphonium iodide (5) by a procedure based on the method of Corey [9] was examined first. Deprotonation of 5 in THF with 1.1 equivalents of *t*-butyllithium at -40°C was followed by addition of the aldehyde 4 at -60°C . After 2 h, the mixture was allowed to warm to room temperature and then quenched with water. The required epoxide 6, 22% yield, was separated by chromatography from a minor product 7, 6% yield, which arose from a competing demethylation reaction.

The epoxide 6 was identified by ^1H NMR spectroscopy and chemical ionisation mass spectrometry ($M^+ + \text{H}$, 251.002; $\text{C}_{12}\text{H}_{11}\text{FeO}_4$ calcd.: 251.001). ^{13}C NMR spectroscopy revealed the presence of two diastereoisomers in the product: two pairs of signals at 72.6 ppm (d, $J(\text{CH})$ 147 Hz) and 71.7 ppm (d, $J(\text{CH})$ 144 Hz) and at 42.1 ppm (t, $J(\text{CH})$ 139 Hz) and 41.1 ppm (t, $J(\text{CH})$ 142 Hz) indicated that two epoxides had been isolated in roughly equal amounts. The lack of diastereoselectivity in the epoxidation reaction is surprising in view of the high degree of stereocontrol often observed [4,5] in nucleophile addition reactions at carbonyl groups adjacent to organometallic π -complexes. To examine further the selectivity of the reaction, the stereochemical homogeneity of 7 was also studied by ^{13}C NMR spectroscopy. This complex proved to be substantially a single stereoisomer, exhibiting the expected nine signals including resonances at 15.7 ppm (q, $J(\text{CH})$ 139 Hz) and 44.0 ppm (t, $J(\text{CH})$ 139 Hz), corresponding to the CH_2SMe group and at 70.5 ppm (d, $J(\text{CH})$ 144 Hz) corresponding to the CHOH position. Thus while both



diastereofaces of the aldehyde are available for reaction with the nucleophile, the rate of conversion of the intermediate adducts into **6** may depend on the relative stereochemistry of the complex. The yields of both products, however, are too low at present to allow this to be established with certainty.

In the search for improved yields and diastereoselectivity, methyldiphenylsulphonium PF_6^- was prepared by the method of Badet and Julia [10], and deprotonated by t-BuLi. Reaction of the resulting ylide with the aldehyde **4**, however, produced none of the required epoxide **6**. The use of an ylide derived from an arsonium salt was also examined. In this case, traces of an olefination product [12*], rather than a product of epoxidation, was observed, and a small quantity of the η^4 -triene complex **8** was isolated and identified from its ^1H NMR spectrum [13].

A preliminary study of the electrophilic opening of the epoxide **6** yielded encouraging results. In a pilot study employing Pearson's $\text{HBF}_4/\text{Ac}_2\text{O}$ conditions [14] for in-situ acetylation, the opening of **6** was followed by IR spectroscopy. Upon addition of $\text{HBF}_4 \cdot \text{OEt}_2/\text{Ac}_2\text{O}$ to a solution of **6** in Ac_2O at 0°C the neutral starting material ($\nu(\text{CO})$, 2046 and 1974 cm^{-1}) was partially converted into a cationic species with new bands at 2112 and 2079 cm^{-1} that are characteristic of cationic η^5 -tricarbonyliron complexes. No precipitation of the salt was observed, and transoid/cisoid structure of the cation could not be established from this experiment.

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* Reference number with asterisk indicates a note in the list of references.

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