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EPOXIDE SYNTHESIS IN THE BUTADIENE-IRON TRICARBONYL SERIES

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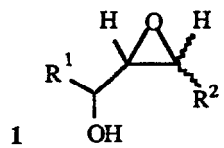
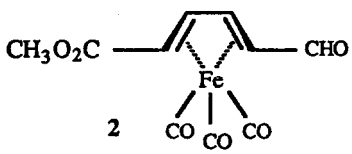
Abstract : The synthesis of functionalized epoxide-alcohols **8** to **11** is reported. The Sharpless procedure [TBHP- $VO(acac)_2$] is fully compatible with the presence of an organoiron complex.

The epoxide-alcohols which possess the general structure **1** (R^1 and R^2 being alkyl, alkenyl or alkynyl groups) are versatile intermediates in natural products synthesis including sex attractants, carbohydrates and leukotrienes [1]. Compounds of type **1** in which R^1 (or R^2) is a butadiene-iron tricarbonyl moiety are presently unknown.



1

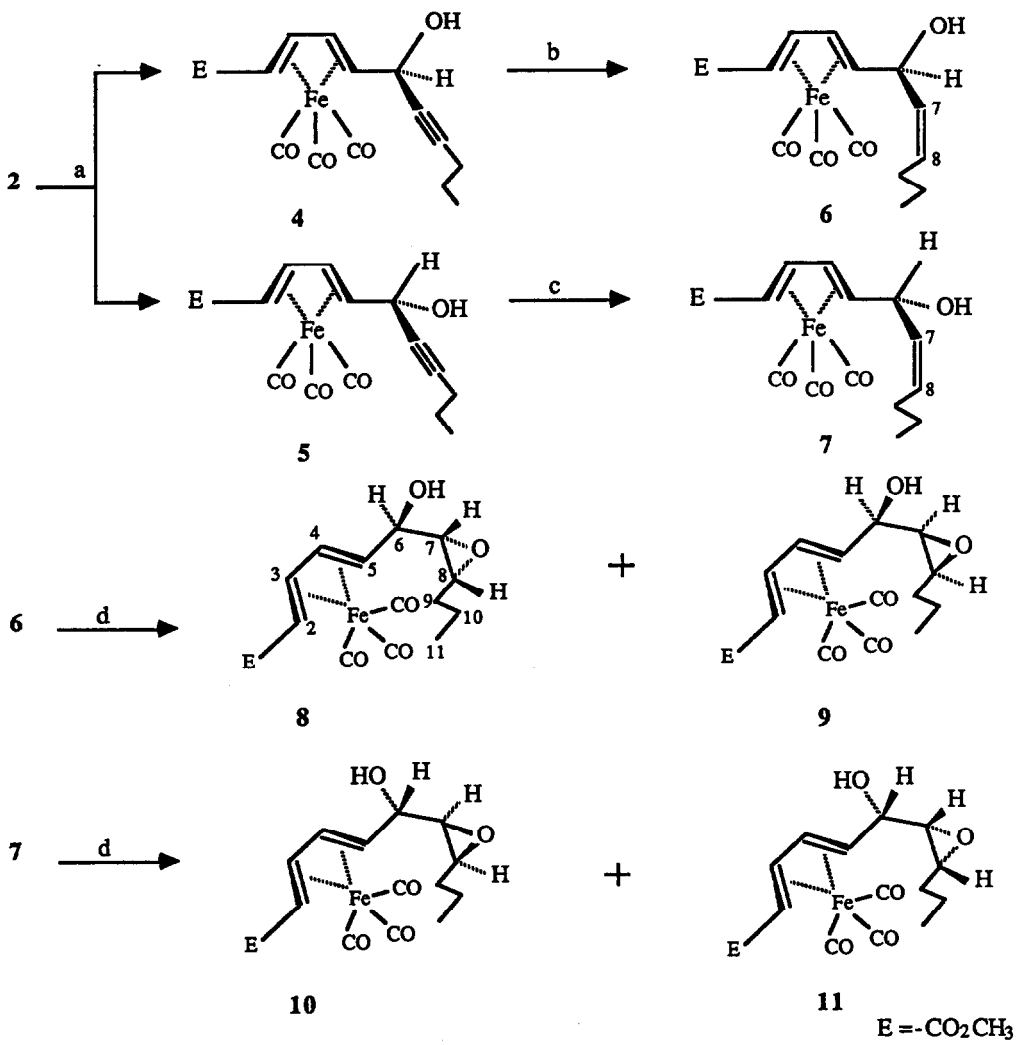


2

Such compounds would be of interest for several reasons : the bulky organometallic complex could afford major changes in the reactivity at the epoxide-alcohol part of the molecule ; these derivatives, bearing a functionnalized dienyl chain in a protected and possibly in a chiral form, furthermore appear as useful models for the preparation of several oxygenated fatty acid metabolites such as for instance diHETES [2], Lipoxins [3] or their analogs.

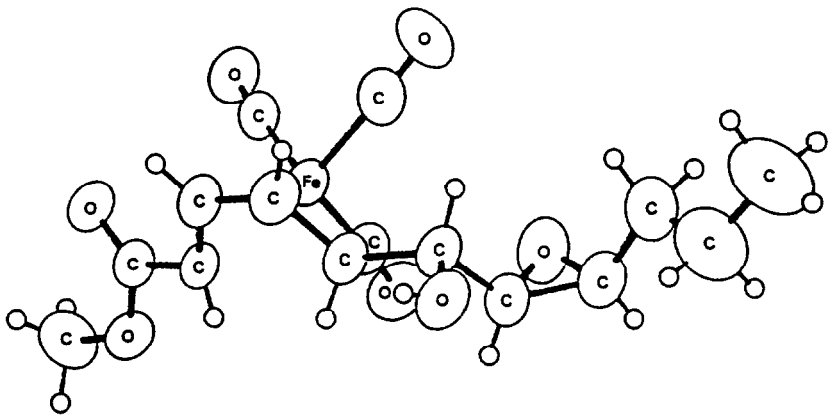
To the best of our knowledge, there is only one example of a compound bearing in the same molecule both a butadiene-iron-tricarbonyl moiety and an epoxide [4]. The purpose of this Letter is thus first to confirm that the Sharpless procedure [5] [6] [TBHP + $VO(acac)_2$] can be used, without decomplexation, for the epoxidation of *molecules bearing an organoiron moiety* [7] and then, to study the diastereoselectivity of the reaction on simple acyclic models.
The complex **2** appears as a good starting material since it is bifunctionnal and easily accessible even in chiral form [8]. The synthesis of epoxides **8** to **11** is described in Scheme 1. The reaction of pentynyllithium **3** with **2** yields a 7/3 mixture of the alcohols **4** and **5** easily separated by chromatography [9] (96 % overall yield). The major and more polar diastereoisomer **4** is assigned the ψ-exo [8] configuration in agreement with litterature data on this type of complex [10] [11]. These rather unstable alkynes are partially reduced on a palladium catalyst in deoxygenated methanol, under normal temperature and pressure conditions, to give respectively the corresponding alkenes **6** and **7** [12]. In agreement with previous work [13] the ψ-endo derivative **5** is found to be much more reactive ; in addition, saturated compounds are not obtained during this reduction step.

Scheme 1



a) **2** (1.07 mM), **3** (1.78 mM), anh. THF (7 cm^3), -80°C, 30 min. ; b) **4** (0.16 mM), Pd 5 % C (5 mg), CH_3OH (4 cm^3), room temp., 7 h, 98 % ; c) **5** (0.16 mM), Pd 10 % C (20 mg), CH_3OH (4 cm^3), room temp., 20 min, 85 % ; d) **6** or **7** (0,1 mM), $VO(acac)_2$ (1µM), anh. toluene (1.3 cm^3), tBuOOH (0.2 mM), room temp., **6** (43 h), **7** (30 h).

The hydroxyalkenes **6** and **7**, by reaction with the tBuOOH-$VO(acac)_2$ reagent, give respectively two readily separable mixtures of the epoxide-alcohols **8** and **9** [14] (**8/9** = 3/2 ; 85 % overall yield) and **10** and **11** [15] (**10/11** = 3/2 ; 78 % yield) without any significant decomplexation. The stereochemistry of the erythro derivative **9** has been established unambiguously by X-Ray crystallography [16], as shown in Scheme 2.



Scheme 2

In the case of **10** and **11**, the stereochemistry has been attributed only by analogy of their NMR data with those of **8** and **9** respectively ; particularly relevant are the J_{56} values : 4.7 and 4.9 for **8** and **10** compared to 7.6 and 8.5 in the case of **9** and **11**. The protons H_5 are also shielded (~ 0.1 ppm), in the threo isomers **8** and **10**.
The major diastereoisomer is then threo, in accordance with the selectivity already found by Sharpless in the epoxidation of Z olefins [6]. According to the proposed mechanism this preference could be due to a strong interaction between the propyl chain and the bulky butadiene-iron-tricarbonyl substituent in the transition state leading to the erythro derivative [6].

We are currently studying the synthetic potentialities of these epoxide-alcohols, especially in the field of icosanoids.

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7 - Notice that organoiron derivatives are commonly decomplexed using oxidizing reagents and also that TBHP itself is known to be sensitive to certain metal salts like those of iron [4] !

8 - A. MONPERT, J. MARTELLI, R. GREE and R. CARRIE, Tetrahedron Lett., 1981, 22, 1961.

9 - All new compounds have spectral data (IR, NMR, MS) in full agreement with the proposed structures. The chromatographic separation of **4** and **5** is performed by medium pressure liquid chromatography on silica gel using a 4/6 mixture of hexane and ether ; **4** : Rf = 0.21 and **5** Rf = 0.44.

10 - N.A. CLINTON and C.P. LILLYA, J. Amer. Chem. Soc., 1970, 92, 3058.

11 - P.E. RILEY and R.E. DAVIS, Act. Cryst, 1976, B32, 381 ; J.C. MESSAGER and L. TOUPET, Act. Cryst., 1986, B42, 371.

12 - The Z stereochemistry of the double bond has been established by ^{1}H-NMR : J_{78} = 11.7 Hz in the case of **6** and 11.0 Hz for **7**.

13 - P. MOSSET, Docteur-Ingenieur Thesis, University of Rennes, 1984.

14 - **8** (oil) ; IR (film ; ν cm^{-1}) : 3440 (broad, OH) ; 2060, 1980 (C≡O) ; 1712 (C=O). ^{1}H-NMR (300 MHz ; $CDCl_3$, δ p.p.m., J_{HZ}) : 5.90 (d.d.d. ; J_{23} = 8.1 ; J_{34} = 5.1 ; J_{35} = 0.9 ; H_3) ; 5.70 (d.d. ; J_{45} = 8.6 ; H_4) ; 3.80 (s ; 3H ; -0CH_3) ; 3.70 - 3.50 (m ; 1H ; H_6) ; 3.15 (d.t., J_{89} = 7.6 ; J_{78} = 4.2 ; H_8) ; 3.05 (d ; -OH ; J = 3.3) ; 2.98 (d.d. ; J_{76} = 7.7 ; H_7) ; 1.70 - 1.40 (m ; 4H ; H_9, H_{10}) ; 1.15 (d.d. ; J_{56} = 4.7 ; H_5) ; 1.02 (d. ; H_2) ; 1.00 (t. ; 3H ; J = 7.1 ; H_{11}) .

9 (F = 94°C) ; IR (film ; ν cm^{-1}) : 3400 (broad, OH) ; 2060, 1980 (C≡O) ; 1680 (C=O). ^{1}H-NMR (300 MHz ; $CDCl_3$, δ p.p.m., J_{HZ}) : 5.88 (d.d.d. ; J_{23} = 8.1 ; J_{34} = 5.1 ; J_{35} = 0.9 ; H_3) ; 5.50 (d.d.d. ; J_{45} = 8.3 ; J_{42} = 0.8 ; H_4) ; 3.69 (s ; 3H ; -OCH_3) ; 3.45 (d.t. ; J_{56} = J_{67} = 7.6 ; J = 3.4 ; H_6) ; 3.20 - 3.00 (m ; 1H ; H_8) ; 2.95 (d.d. ; J_{78} = 4.0 ; H_7) ; 2.05 (d. ; J = 3.4 ; -OH) ; 1.70 - 1.50 (m ; 4H ; H_9, H_{10}) ; 1.25 (t. ; H_5) ; 1.10 (d.d. ; H_2) ; 0.95 (t. ; 3H ; J = 7.0 ; H_{11}).
Separation by chromatography on silica gel using a 4/6 mixture of hexane and ether containing 1 % of ammonia ; **8** ; Rf = 0.39 ; **9** ; Rf : 0.21.

15 - **10** (oil) ; IR (film ; ν cm^{-1}) : 3440 (broad, OH) ; 2060, 1980 (C≡O) ; 1720 (C=O). ^{1}H-NMR (300 MHz ; $CDCl_3$, δ p.p.m., J_{HZ}) : 5.85 (d.d. ; J_{23} = 7.3 ; J_{34} = 4.9 ; H_3) ; 5.50 (d.d. ; J_{45} = 7.9 ; H_4) ; 3.80 - 3.60 (m ; H_6) ; 3.67 (s ; 3H ; -OCH_3) ; 3.20 - 3.00 (m ; H_8) ; 2.90 (d.d. ; J_{67} = 7.3 ; J_{78} = 3.2 ; H_7) ; 2.30 (d. ; J = 2.6 ; -OH) ; 1.60 - 1.40 (m ; 4H ; H_9, H_{10}) ; 1.15 (d.d. ; J_{56} = 4.9 ; H_5) ; 1.00 (t ; 3H ; J = 6.7 ; H_{11}) ; 0.95 (d. ; H_2).

11 (oil) ; IR (film ; ν cm^{-1}) : 3460 (broad, OH) ; 2070, 2000 (C≡O) ; 1720 (C=O). ^{1}H-NMR (300 MHz ; $CDCl_3$, δ p.p.m., J_{HZ}) : 5.88 (d.d. ; J_{23} = 7.9 ; J_{34} = 4.9 ; H_3) ; 5.48 (d.d. ; J_{45} = 8.5 ; H_4) ; 3.68 (s ; 3H ; -OCH_3) ; 3.55 - 3.35 (m ; H_6) ; 3.16 - 2.96 (m ; H_8) ; 2.90 (d.d. ; J_{76} = 7.3 ; J_{78} = 3.0 ; H_7) ; 1.65 - 1.45 (m ; 4H ; H_9, H_{10}) ; 1.35 (t ; J_{56} = J_{45} = 8.5 ; H_5) ; 1.05 (d. ; H_2) ; 1.00 (t ; 3H ; J = 7.3 ; H_{11}). Separation by chromatography as before ; **10** ; Rf = 0.64 ; **11** : Rf = 0.50.

16 - "Atomic coordinates for this structure have been deposited with the Cambridge Crystallographic Centre. The coordinates can be obtained on request from the Director, Cambridge Crystallographic Data Centre, University Chemical Laboratory, Lensfield Road, Cambridge CB2 1EW, UK".
Fe $C_{15}O_7H_{18}$: Mr = 732.4, Triclinic, P1, Z = 4, a = 11.346 (6), b = 13.534 (9), c = 14.001 (7) Å, α = 65.96 (5), β = 65.99 (5), γ = 90.01 (5)° ; v = 1757.9 (6) Å^3, d_c = 1.38 Mg m^{-3}, μ = 7.82 cm^{-1}. Structure solved with a Patterson map. Full-matrix refinement gives R = 0.062, R_w = 0.057.

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