

Preliminary communication

SYNTHESIS OF ENANTIOMERICALLY PURE 2-METHOXY-5-METHYL-CYCLOHEXADIENYLTRICARBONYLIRON HEXAFLUOROPHOSPHATE [(2-MeO-5-MeC₆H₅)Fe(CO)₃]PF₆

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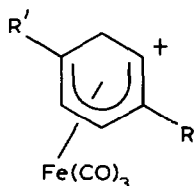
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(Received February 7th, 1983)

Summary

Enantiomerically pure (+)-[(2-MeO-5-Me-cyclo-C₆H₅)Fe(CO)₃]PF₆ may be prepared from (+)-[(2-MeO-cyclo-C₆H₆)Fe(CO)₃]PF₆ by conversion into phosphonium salt followed by Wittig reaction with formaldehyde and protonation with HPF₆.

The utility of [η^5 -cyclo-C₆H₇)Fe(CO)₃]⁺ salts in organic synthesis has been amply demonstrated by the work of Birch and coworkers [1] and the recent work of Pearson [2a,b] has shown how such complexes (notably the 2-methoxy and 2-methoxy-5-methyl derivatives 1a and 1b) may be used as precursors for the synthesis of several natural products. One potential advantage of their use is that reactions using enantiomerically pure samples of 1a or 1b should provide the opportunity for enantioselective syntheses of products derived from them by nucleophilic attack at C(5).



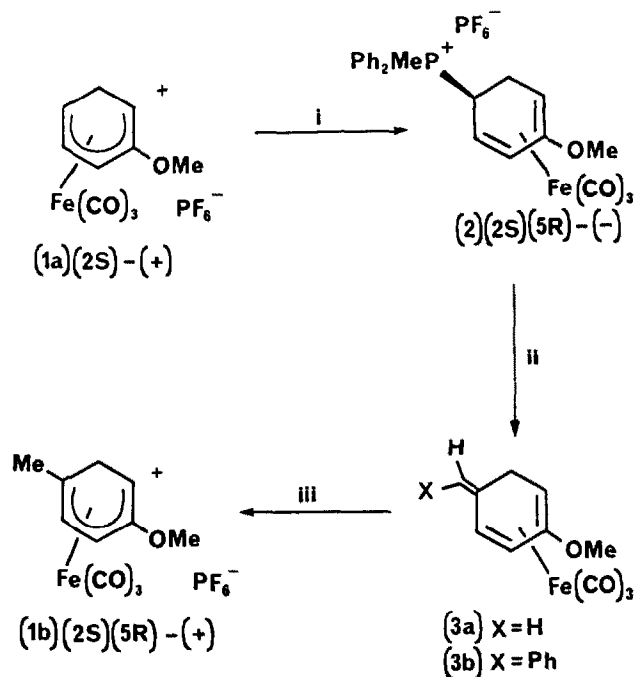
(1a) R = OMe, R' = H

(1b) R = OMe, R' = Me

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We recently described [3] the synthesis on a gram scale of enantiomerically pure samples of (+) and (-)-1a via chromatographic separation of their diastereoisomeric menthyl ethers, and we now report the conversion of enantiomerically pure 1a into 1b using the Wittig method recently reported by Lewis et al. [4].

Treatment of pure 1a ((2*S*)(+); $[\alpha]_D +120^\circ$) [5] with PPh_2Me (Scheme 1) provides an essentially quantitative yield of the phosphonium salt 2 ((2*S*)(5*R*)(-); $[\alpha]_D -93^\circ$) which on treatment with butyllithium followed by reaction with anhydrous formaldehyde yields the 5-methylenecyclohexa-1,3-diene complex 3a; protonation of 3a using aqueous HPF_6 yields enantiomerically pure 1b ((2*S*)(5*R*)(+); $[\alpha]_D +134^\circ$) in approximately 40% yield based on 1a. Complex 3a decomposes slowly in the solid state, and has been characterized spectroscopically by comparison with the completely stable phenyl derivative 3b obtained from the Wittig reaction using benzaldehyde [7]. Other than 3a, all complexes gave satisfactory analytical and spectroscopic data. The protonation is reversible, and 3a may be easily regenerated on treatment of 1b with Et_2NPr^i .



SCHEME 1. Reaction conditions: i. PPh_2Me , CH_2Cl_2 ; RT; ii. BuLi , THF, -50°C , followed by addition of XCHO ; iii. HPF_6 (75% aqueous), Et_2O ; RT.

The absolute configurations shown in Scheme 1 can be written with confidence, as the configurations of both 1a and 1b have been determined by conversion of enantiomerically enriched samples (ca. 10%) obtained from asymmetric complexation procedures into natural products of known configuration [8]. Most recently, a pure sample of the (2*R*)(5*S*)(-) isomer of 1b was obtained by fractional crystallization of an enantiomerically enriched sample of 1b obtained by asymmetric complexation [6]. Our method offers the advantages of providing both enantiomers by a route which is simpler overall, and which is potential-

ly extensible to the synthesis of other enantiomerically pure complexes. This is an area we are currently exploring.

We thank the SERC for a Studentship (M.J.T.).

References

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- 2 (a) A.J. Pearson, *Trans. Met. Chem.*, **6** (1981) 67; (b) A.J. Pearson, *Accts. Chem. Res.*, **13** (1980) 463.
- 3 J.A.S. Howell, M.J. Thomas, *J. Chem. Soc. Dalton*, in press.
- 4 P. Hackett, B.F.G. Johnson, J. Lewis, G. Jaouen, *J. Chem. Soc. Dalton*, (1982) 1247.
- 5 Rotations for **1a** and **1b** were measured in acetonitrile; the rotation of **2** was measured in acetone.
- 6 A rotation of -136° has been reported for the (2*R*)(5*S*)-isomer; G.R. Stephenson, *Aust. J. Chem.*, **34** (1981) 2339.
- 7 Complex **3b** is isolated as a 9/1 mixture of isomers differing in the orientation of the phenyl group; the major isomer is tentatively assigned the structure shown in Scheme 1. Protonation of **3b** yields 2-methoxy-5-benzylcyclohexadienylnitriccarbonyliron hexafluorophosphate.
- 8 A.J. Birch, W.D. Raverty, G.R. Stephenson, *J. Org. Chem.*, **46** (1981) 5166.