Tetrahedron Letters, Vol. 33, No. 9, pp. 1173-1176, 1992
Printed in Great Britain

0040-4039/92 $3.00 + .00
Pergamon Press plc

Optically Active Organoiron Complexes in Synthesis. An Enantioface Selective 3-Hydroxypropionate-2,3-Dication Equivalent

Kai-Hsuan Chu, Weiguo Zhen, Xiao-Ya Zhu, Myron Rosenblum*

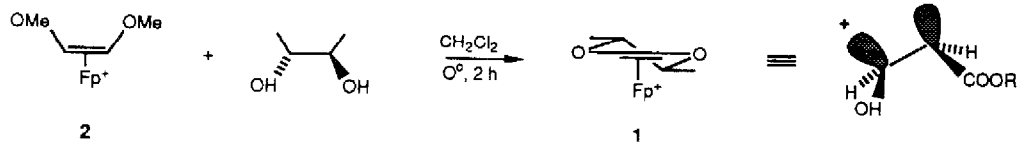
Department of Chemistry, Brandeis University, Waltham, MA 02254

Key Words: enantioface; 3-hydroxypropionate; sitophilate; organoiron; dication

Abstract: *The use of organoiron complexes 8 and 9 as chiral 3-hydroxypropionate-2,3-dication equivalents is illustrated by a sequence of transformations involving successive addition of nucleophiles to these cations, followed by redox promoted carboxylation to give 2R,3S-methyl 3-hydroxypentanoate and ent-sitophilate.*

The activation of transition metal coordinated centers of unsaturation to nucleophilic attack constitutes a pervasive theme in organometallic chemistry with important synthetic implications[1]. When the substrate in these reactions is an optically active metal-ene or -enyl complex, in which the metal is enantiofacially coordinated to the ligand, asymmetric synthesis becomes possible[2].

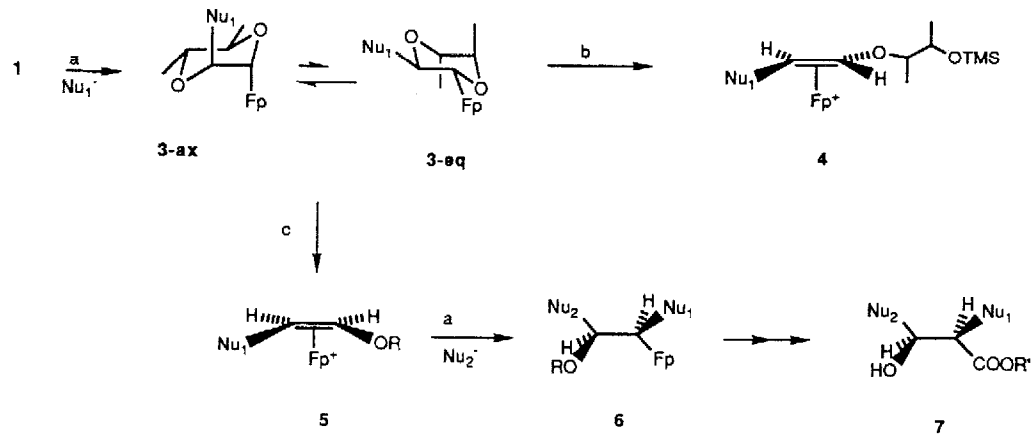
We recently reported the preparation of complex **1** from Fp(η^2-1,2-dimethoxyethylene)BF_4 **2** by exchange etherification with (R,R)-butane-2,3-diol[3]. We now show how such complexes may be used as *syn*-3-hydroxypropionate-2,3-dication equivalents.



2 **1**

The addition of both carbon and heteronuclear nucleophiles to **1** has been observed to occur with high regioselectivity to give optically pure adducts **3-ax**[3,4]. Ring opening of these adducts in the presence of TMS triflate, which proceeds through the minor conformer **3-eq**[5], affords the *trans*-vinyl ether complexes **4**, as the kinetic product at low temperatures. When this reaction is carried out with protic acids in the presence of an alcohol, the thermodynamically preferred *cis*-vinyl ether complex **5** is obtained, through sequential ring opening and *trans*-etherification. Since **5** has also been observed to add nucleophiles regioselectively at the carbon center bearing the ether function, and the resulting (alkyl)Fp complexes **6** are in principle transformable[6] to carboxylic acid derivatives with retention of configuration, complexes such as **1** may serve as enantioface selective 3-hydroxypropionate-2,3-

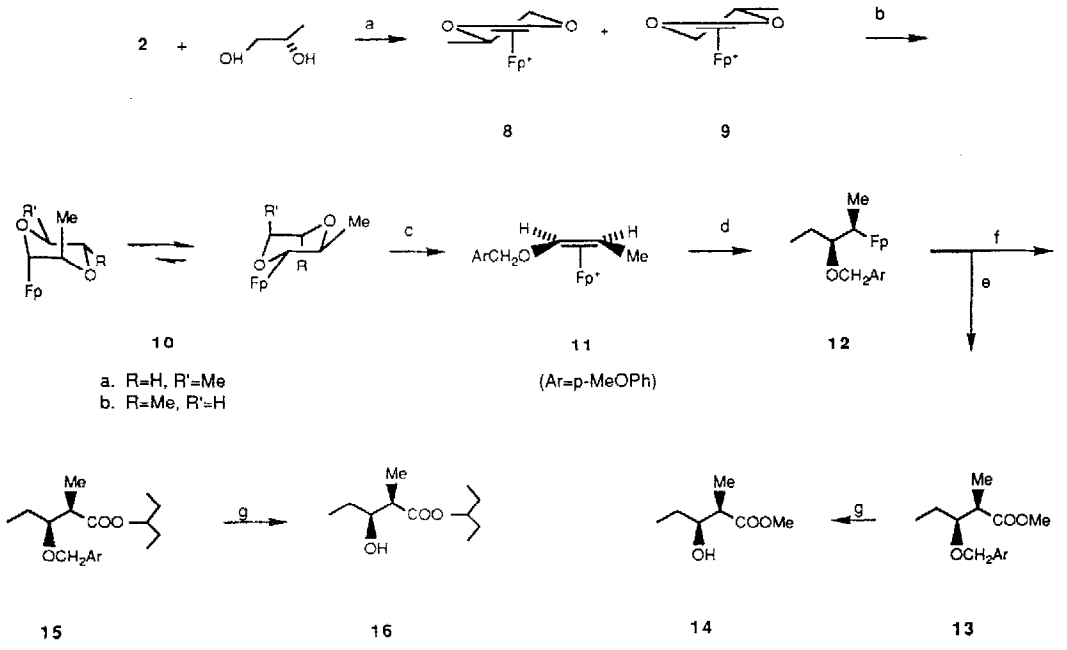
dication equivalents. We now illustrate the use of this sequence for the synthesis of 2,3-disubstituted 3-hydroxypropionates **7**.



a. THF, -78°, 1 h. b. TMS triflate, CH_2Cl_2-Et_2O, -78°, 10 m. c. $HBF_4{\cdot}Et_2O$, Et_2O, -78°; ROH, 0°.

Since both enantiomeric forms of propane-1,2-diol are readily available[7], we have turned to the use of this glycol for the preparation of analogs of **1**. Exchange etherification of Fp(η^2-1,2-dimethoxyethylene)BF_4 with (S)-propanediol gives a mixture of diastereomers **8** and **9**. These are separable by crystallization from cold methylene chloride, but in synthetic practice this is unnecessary since the absolute configuration at the two chiral olefinic carbon centers in **8** and **9** are identical. The addition of nucleophile to these cationic complexes, which proceeds through a chair transition state, is identically regioselective for each isomer, and consequently yields adducts with the same absolute configuration at the two newly created tetrahedral centers.

Thus, reaction of **9** or a mixture of diastereomers **8** and **9**, with lithium dimethylcuprate gave **10a** or **10a,b** (89%), and these were converted to the optically active vinyl ether complex **11**[8] (81%) by acid promoted ring opening followed by alcohol exchange with p-methoxybenzyl alcohol. Conversion of **11** to (2R,3S)-methyl-2-methyl-3-p-methoxybenzyloxypentanoate **13**[9] is readily achieved, without isolation of intermediates, through successive treatment with ethyl Grignard, followed by oxidation of the (alkyl)Fp intermediate **12** in the presence of methanol. The sequence of steps, **8,9** → **10** → **11** → **12** → **13** may also be conveniently carried out without purification of intermediates (35% overall). Deprotection of **13** with DDQ[10] gave the methyl ester **14**[11] (60%). When oxidation of **13** with ceric ammonium nitrate is carried out in the presence of 3-pentanol, the ester **15** is obtained (15%). Deprotection of **15** with DDQ yields *ent*-sitophilate **16**[12] (52%), the enantiomer of the granary weevil aggregation pheromone[13].



a. CH_2Cl_2, 0°, 6.5 h. b. $LiMe_2Cu$, Et_3N, THF, -78°, 3 h. c. HBF_4, Et_2O, CH_2Cl_2, -78°, 0.5 h. ; p-$MeOPhCH_2OH$, CH_2Cl_2, 0°, 10 h. d. EtMgBr, Et_3N, THF, -78°, 1 h. e. $Ce(NH_4)_2(NO_3)_6$, NaOAc, CO, THF-MeOH, -78° to 25°, 2 h. f. 3-pentanol, THF, NaOAc, CO, $Ce(NH_4)_2(NO_3)_6$, -78° to 25°, 2 h. g. DDQ, CH_2Cl_2, 25°, 10 m.

Further examination of these transformation with a view to using this sequence for the preparation of either *syn*- or *anti*-diastereomeric ß-hydroxyesters is projected.

Acknowledgement. This research was supported by a grant from the National Institutes of Health (GM-37067), which is gratefully acknowledged.

References

1. Collman, J. P.; Hegedus, L. S.; Norton, J. R.; Finke, R. G. *Principles and Applications of Organotransition Metal Chemistry*; University Science Books: Mill Valley, CA, 1987; Chapter 7.

2. Birch, A. J.; Raverty, W. D.; Stephenson, G. R. *J. Org. Chem.* **1981**, *46*, 5166. Bandara, B. M. R.; Birch, A. J.; Kelly, L. F.; Kfhor, T. C. *Tetrahedron Lett.* **1983**, *24*, 2491. Bandara, B. M. R.; Birch, A. J.;Kelly, L. F. *J. Org. Chem.* **1984**, *49*, 2496. Birch, A. J.; Kelly, L. F. *J. Org. Chem.* **1985**, *50*, 712. Panunzi, A.; DeRenzi, A.; Paiaro, G. *Inorg. Chim. Acta* **1967**, *1*, 475. Bosnich, B.; Mackenzie, P. B. *Pure and Appl. Chem.* **1982**, *54*, 189. Faller, J. W.; Chao, K.-H. *J. Am. Chem. Soc.* **1983**, *105*, 3893. Faller, J. W.; Chao, K.-H. *Organometallics* **1984**, *3*, 927. Trost, B. M.;

Dietsche, T. J. *J. Am. Chem. Soc.* **1973**, *95*, 8200. Trost, B. M.; Strege, P. E. *J. Am. Chem. Soc.* **1977**, *99*, 1649. Panunzi, A.; DeRenzi, A.; Paiaro, G. *J. Am. Chem. Soc.* **1970**, *92*, 3488. Salvadori, P.; Lazzaroni, R.; Merlino, S. *J. Chem. Soc., Chem. Commun.* **1974**, 435. Faller, J. W.; Linebarrier, D. *Organometallics* **1988** *7*, 1670.

3. Turnbull, M. M.; Foxman, B. M.; Rosenblum, M *Organometallics*, **1988**, *7*, 200.

4. Chu, K.-H.; Foxman, B. M.; Rosenblum, M.; Zhu, X.-Y. *Organometallics* **1990**, *9*, 3010.

5. Erlacher, H. A.; Turnbull, M. M.; Chu, K.-H, Rosenblum, M. *J. Org. Chem.* **1989**, *54*, 3012.

6. Nicholas, K. M.; Rosenblum, M. *J. Am. Chem. Soc.*, **1973**, *95*, 4449. Wong, P. K.; Madhavarao, M.; Marten, D. F.; Rosenblum, M. *J. Am. Chem. Soc.* **1977**, *99*, 2823. For migratory non redox promoted insertion, see Bock, P. l.; Boschetto, D. J.; Rasmussen, J. R.; Demers, J. P.; Whitesides, G. M. *J. Am. Chem. Soc.* **1974**, *96*, 2814.

7. Available from Aldrich Chemical Company, Milwaukee, Wi. Also prepared by Lithium aluminum hydride reduction of S- or R-lactate. Gombos, J.; Haslinger, E.; Schmidt, U. *Chem. Ber.*, **1976**, *109*, 2645. The R-isomer is also available by fermentation of glucose with bakers yeast: Levene, P. A.; Waltl, A. *Org. synthesis*, Coll. Vol. 2, p.545, or by enzymatic reduction of hydroxy acetone: Lee, L. G.; Whitesides, G. M. *J. Org. Chem.* **1986**, *51*, 25. Simon, S. E.; Whitesides, G. M.; Cameron, D. C.; Weitz, D. J.; Cooney, C. L. *J. Org. Chem.* **1987**, *52*, 4042.

8. ^{1}H NMR (CD_3NO_2) δ 7.81 (d, 1, J=4.4, O-C*H*=), 7.46 (d, 2, J=8.6, Ar*H*),7.02 (d, 2, J=8.6, Ar*H*), 5.51 (s, 5, Cp), 5.37 (d, 1, J=11.3, OCH*H*), 5.31 (d, 1, J=11.3, OCH*H*) 3.84 (s, 3, OCH_3), 3.65 (dq, 1, J=4.4, 6.2, CH_3CH=), 1.65 (d, 3, J=6.31 CH_3). Anal. Calcd. for $C_{18}H_{19}O_4FeBF_4$: C, 48.91; H, 4.33. Found: C, 48.76; H, 4.12. CD (CH_2Cl_2, -30°) $\Delta\varepsilon_{435}$=-1.17 $M^{-1}cm^{-1}$, $\Delta\varepsilon_{365}$=+1.96 $M^{-1}cm^{-1}$.

9. ^{1}H NMR ($CDCl_3$) δ 7.25 (d, 2, J=8.72, Ar*H*), 6.87 (d, 2, J=8.72, Ar*H*), 4.45 (bs, 1, PhCH_2), 4.46 (bs, 1, PhCH_2), 3.79 (s, 3, PhOCH_3), 3.66 (s, 3, CO_2CH_3) 3.64 (m, 1, OC*H*), 2.66 (dq, 1, J=5.67, 7.08, CH_3CH), 1.57 (m, 2, CH_3CH_2), 1.20 (d, 3, J=7.2, CH_3CH), 0.93 (t, 3, J=7.43, CH_2CH_3) $[\alpha]_D^{25}$ = -5.46° (0.25, $CHCl_3$). Chiral shift reagent experiments, using Eu(HFP)$_3$ with racemic **13** prepared from racemic **11**, and with optically active **13**, show that the optical purity of (-)**13** is greater than 99%.

10. Oikawa, Y.; Yoshioka, T.; Yonemitsu, O. *Tetrahedron Lett.* **1982**, *23*, 885.

11. ^{1}H NMR ($CDCl_3$) δ 3.80 (m, 1, OC*H*), 3.71 (s, 3, CO_2CH_3), 2.55 (dq, 1, J=7.20, 3.60, C*H*CO_2), 2.47 (d, 1, J=4.8, CHO*H*), 1.45 (m, 2, CH_2CH_3), 1.18 (d, 3, J=7.2, CHCH_3), 0.97 (t, 3, J=7.5, CH_2CH_3). $[\alpha]_D^{25}$= -2.70° (0.65, $CHCl_3$). ^{13}C NMR ($CDCl_3$) δ 176.6 (CO_2CH_3), 73.2 (*C*HOH), 51.8 (CO_2CH_3), 43.8 (*C*HCO_2CH_3), 26.7 (CH_2CH_3), 10.5 (CH*C*H$_3$), 10.4 (CH_2CH_3), identical with the ^{13}C NMR data reported by C. H. Heathcock, M. C. Pirrung, J. E. Sohn, *J. Org. Chem.* **1979**, *44*, 4294.

12. Identical by ^{1}H and ^{13}C NMR with the product reported in ref. 13b.

13. a. Phillips, J. K.; Miller, S. P. F.; Andersen, J. F.; Fales, H. M.; Burkholder, W. E. *Tetrahedron Lett.*, **1987**, *29*, 6145. b. Chong, J. M. *Tetrahedron*, **1989**, *45*, 623.

(Received in USA 3 December 1991)