Tetrahedron: Asymmetry Vol. 3, No. 3, pp. 375-376, 1992
Printed in Great Britain

0957-4166/92 $3.00+.00
Pergamon Press plc

Enzymatic Generation of Planar Chirality in the (Arene)tricarbonylchromium Series

Bernard Malézieux
Gérard Jaouen*

Ecole Nationale Supérieure de Chimie, 11 Rue Pierre et Marie Curie, 75321 Cedex 05, France

Jacques Salaün

Laboratoire des Carbocycles, Institut de Chimie Moleculaire d'Orsay, Université de Paris-Sud, Bâtiment 420, 91405 Orsay Cédex, France

James A.S. Howell*
Michael G. Palin

Chemistry Department, Keele University, Keele, Staffordshire, ST5 5BG, Great Britain

Patrick McArdle
Margaret O'Gara
Desmond Cunningham

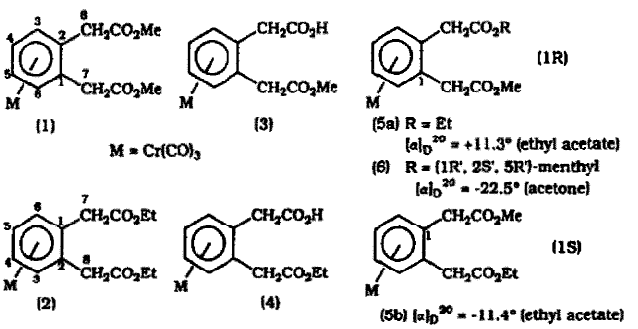
Chemistry Department, University College, Galway, Ireland

(*Received* 6 *February* 1992)

Abstract: Hydrolysis using pig liver esterase of the meso diesters [ortho-$C_6H_4(CH_2CO_2R)_2$]-$Cr(CO)_3$ (R = Me,Et) yields the half ester in good yield and high enantiomeric excess.

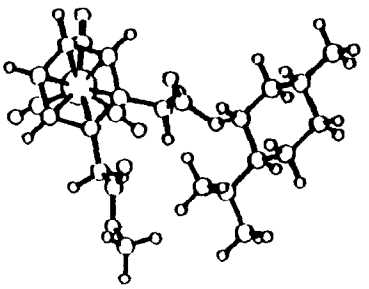
The ability of enzymes or stoichiometric reagents to differentiate enantiotopic groups in meso or prochiral compounds provides an excellent entry into asymmetric synthesis. (Arene)tricarbonylchromium complexes continue to attract interest as intermediates for enantioselective synthesis, and through enzymatic methods have been applied to the kinetic resolution of several chiral ortho and meta substituted complexes[1], the enzymatic *generation* of metallocenic planar chirality remains virtually unexplored[2]. We wish to report here the first examples of enzymatic generation of planar chirality in benchrotrenic compounds.

Controlled hydrolyses of the diesters (1) and (2) using pig liver esterase proceed cleanly with consumption of one mole of sodium hydroxide to provide the half esters (3) and (4) in high yield. Of limited solution stability, (3) and (4) were converted into the enantiomeric asymmetric diesters (5a,b) by treatment with the appropriate chloroformate[3,4]. Analysis by chiral HPLC of (5a,b) reveals enantiomeric excess values of 94 and 99% respectively by comparison with racemic samples.



A crystal structure determination[6] of the menthyl derivative (6) prepared from (3) establishes the absolute configuration of (5a) as (1R). Hydrolysis of the pro (S) substituent resulting from the molecular dipole created by the strongly electron withdrawing $Cr(CO)_3$ moiety is consistent with previous postulates regarding the action of pig liver esterase in purely organic systems[7].

This reaction, which can be carried out on a scale of several grams, thus provides an unprecedented example of an enantiogenic reaction in the new area of bioorganometallic chemistry[8]. Other examples of such reactions are currently under investigation.



(6)

REFERENCES AND NOTES

1. (a) Yamazaki, Y., Hosono, K. *Tetrahedron Lett.*, 1990, 31, 3895; (b) Top, S., Jaouen, G., Baldoli, C., del Buttero, P., Maiorana, S. *J. Organomet. Chem.*, 1991, 413, 125.
2. Only one example with poorer e.e. exists in the ferrocene series: Yamazaki, Y., Hosono, K. *Tetrahedron Lett.*, 1988, 29, 5719.
3. Complexes (1) and (2) were prepared from the free ligands and $Cr(CO)_6$ using standard procedures[5]. Pig liver esterase (1.3 g, Sigma L8251) was added as a powder to a solution of (1) (1g) in 10 ml of a 90:10 water/methanol mixture previously adjusted to pH 7.2 with 2 M NaOH. The pH was maintained at 7.2 during hydrolysis by addition of 2M NaOH from an automatic burette. After cessation of reaction at half-hydrolysis, the solution was acidified with 0.1M HCl and extracted with ethyl acetate to give (3) as a yellow oil (0.8 g, 85%). The diester (5a) was prepared by dissolution of (3) in THF followed by sequential addition at −10 °C of NEt_3 (1.2 equivalents) and ethyl chloroformate (1 equivalent) followed by purification by flash chromatography. Complexes (4), (5b) and (6) were prepared similarly by hydrolysis and subsequent reaction with methyl chloroformate and (−)-menthyl chloroformate respectively. Racemic samples of (5a,b) were prepared via non-enzymatic hydrolysis of (1) and (2) with exactly one mole of KOH. Optical purities of (5a,b) were determined using a Chiralcel O.J. column on a Beckman System Gold apparatus.
   Nmr data (200 MHz) (C_6D_6): (1) $H_{3/6}$ 4.51(m), $H_{4/5}$ 4.29(m), $H_{7/8}$ 2.69, 3.12 (dd, J = 16.2), CH_3 3.23(s); (2) $H_{3/6}$ 4.66(m), $H_{4/5}$ 4.42(m), $H_{7/8}$ 2.80, 3.20 (dd, J = 16.1), CH_2CH_3, 3.89(q) 0.95 (t, J = 7.1); (5a,b) $H_{3/6}$ 4.57(m), $H_{4/5}$ 4.32(m), $H_{7/8}$ 3.16, 2.75 (dd, J = 16.1), 3.16, 2.73 (dd, J = 16.1),CH_3 3.26(s), CH_2CH_3 3.86(q), 0.93 (t, J = 7.1); (6) $H_{3/6}$ 4.56(m), $H_{4/5}$ 4.32(m), $H_{7/8}$ 2.77, 3.11 (dd, J = 16.2), 2.88, 3.28 (dd, J = 16.4), CH_3 3.30(s), menthyl OCH 4.78(m), CH_3 0.76 (d, J = 6.5), $CH(\underline{CH_3})_2$ 0.89, 0.92 (dd, J = 7.0), CH and ring 0.7–2.0(m). Additional well defined resonances due to $H_{7/8}$ are seen in (6) prepared from racemic (3); no kinetic resolution occurs on reaction of (3) with excess (−)-menthyl chloroformate over long reaction times.
4. Precedents exist for facile CO_2 elimination from the presumed carbonic anhydride intermediate in cases where an electron withdrawing group is beta to the carbonyl: Windholz, T.B. *J. Org. Chem.*, 1960, 25, 1703.
5. Mahaffy, C.A.L., Pauson, P.L. *Inorg. Synth.*, 1979, 19, 154.
6. Data were obtained on an Enraf-Nonius CAD4F diffractometer using a Mo-Kα radiation (λ = 0.7093Å). Data were corrected for Lorentz and polarization effects but not for absorption. The structures were solved by direct methods and refined by full matrix least squares. Crystal data for (6): $C_{24}H_{30}CrO_7$, M = 482.49, orthorhombic, space group $P2_12_12_1$, a = 7.612, b = 12.425, c = 25.487 Å, U = 2410.5 Å^3, F(000) = 1016, D_c = 1.33 g cm^{-3}, unique reflections 3764, reflections with $I>3\sigma(I)$ 2926, R = 0.0946, R_w = 0.0795.
7. Mohr, P., Waespe-Sarcevic, N., Tamm, C., Gawronska, K., Gawronska, J.K. *Helv. Chim. Acta*, 1983, 66, 2501.
8. Ryabov, A.D. *Angew. Chem., Int. Ed. Eng.*, 1991, 30, 931 and references therein.