Tetrahedron Letters,Vol.25,No.34,pp 3693-3696,1984 0040-4039/84 $3.00 + .00
Printed in Great Britain

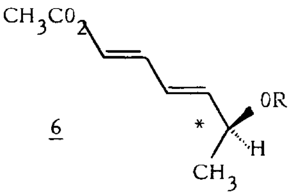
Enantioselective Synthesis of E,E Diene Alcohols and Ethers.

René Grée, Mohammed Laabassi, Paul Mosset and Robert Carrié *
Groupe de Recherche de Physicochimie Structurale, ERA 389, Université de Rennes I,
Campus de Beaulieu, 35042 RENNES, FRANCE.

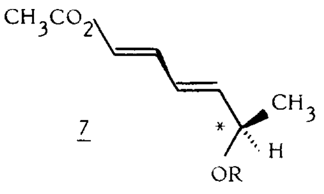
Summary : Starting from the readily accessible organometallic complex 1, the optically active dienes 6 and 7 have been prepared in high stereoisomeric (E,E > 95 %) and enantiomeric (e.e >95 %) purity.

Functionnalized dienes are versatile intermediates in organic synthesis, for instance in Diels-Alder (1) or carbene (2) reactions. Dienes bearing a chiral allylic carbon atom are not always easily prepared ; the main approaches include olefination procedures with optically active components ; either the aldehyde (3) or the phosphorus reagent (4) may contain the chiral center. The use of chiral butadiene iron tricarbonyl complexes offers an interesting alternative to such methodologies : starting from a very few chiral complexes, a large variety of optically active dienes can in principle be obtained.

The purpose of this letter is to describe our preliminary results in this area : using the readily accessible complexes (+) 1 or (-) 1 (5), the dienes 6 and 7 bearing alcohol or ether functions have been prepared in an high stereoisomeric (> 95 % E,E) and enantiomeric (> 95 % e.e) purity.



6

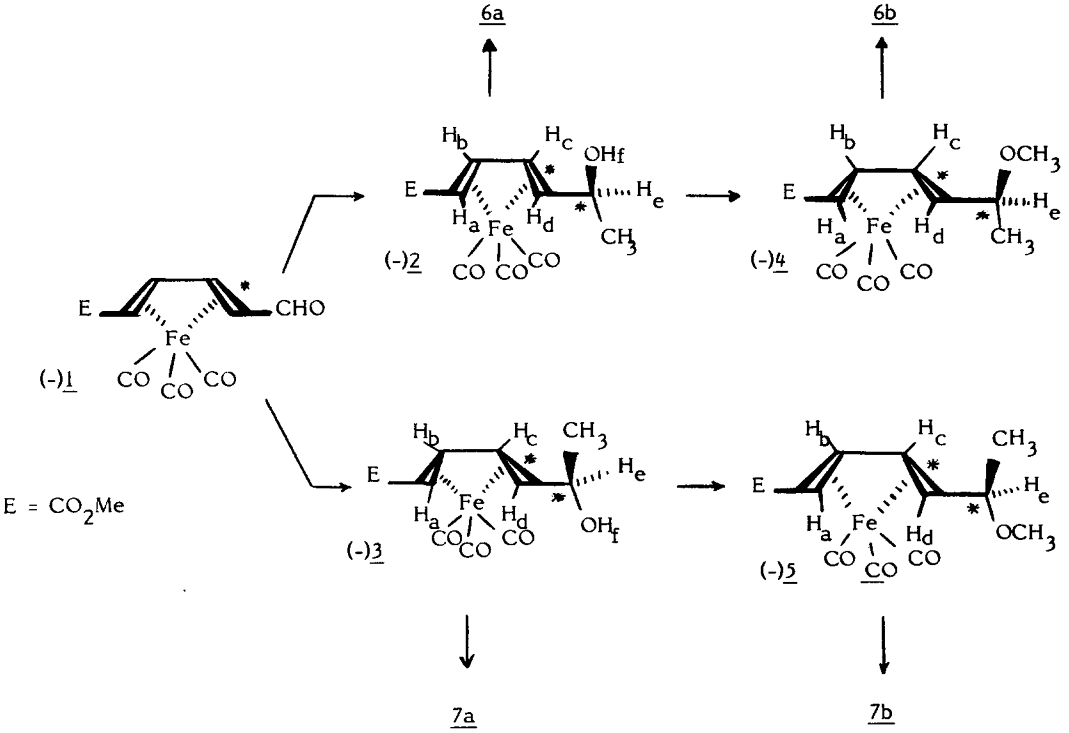


7

a: R = H
b: R = CH_3

The reaction of complex (-) 1 with CH_3MgI (THF, -15°, 80 % overall yield) gives a 2/1 mixture of alcohols (-) 2 and (-) 3 easily separated by chromatography (6). Their stereochemistry is established as follows :

- X-ray data on racemic $(\pm)$ 3 (7) allows an unambiguous assignment of the relative configuration of the carbon atoms, as indicated. It is in agreement with literature data concerning this "Ψ endo" type complex (8).



- The absolute configuration (IR, 4S) of the starting complex (-) 1 has been previously established by X-ray analysis (9). (-) 2 is then the (1R, 4S, 5S) derivative and (-) 3 the (1R, 4S, 5R).

Protection of the alcohol function [$HC(OCH_3)_3$ in CH_2Cl_2 with a catalytic amount of TsOH, 80 % yield] gives stereoselectively the corresponding ethers (-) 4 and (-) 5. This reaction occurs with retention of configuration as shown by comparison of X-ray data of racemic $(\pm)$ 5 with those of $(\pm)$ 3 (7). Decomplexation is best accomplished (yields > 90 %) by $Ce(NH_4)_2(NO_3)_6$ in CH_3OH at -15° (11) : (-) 2 gives 6a and (-) 4 yields 6b (12). Their (R) enantiomers 7a and 7b are obtained starting from (-) 3 and (-) 5 (13).

All these dienes are pure (> 95 %) E,E isomers by ^1H and ^{13}C NMR. The optical purity (e.e. >95 %) of alcohols 6a and 7a is easily established by NMR using $Eu(tfc)_3$ complexes (14). After correlation (15) and comparison of the optical rotations, a similar purity (e.e > 95 %) is obtained for ethers 6b and 7b.

These organometallic complexes thus provide an easy synthesis of functionnalized E,E dienes of known absolute configuration with an high optical purity. The synthesis of other dienes and the application of these chiral compounds in synthesis are currently under active investigation in our laboratory.

References and Notes

(1) For a few recent references : W. OPPOLZER, Angew. Chem. Int. Ed., 16, 10 (1977) ; G. BRIEGER and J.N. BENNETT, Chem. Rev., 80, 63 (1980) ; W.R. ROUSH, H.R. GILLIS and A.I. KO, J. Amer. Chem. Soc., 104, 2269 (1982) ; S.E. HALL and W.R. ROUSH, J. Org. Chem., 47, 4611 (1982) ; R.L. FUNK and W.E. ZELLER, J. Org. Chem., 47, 181 (1982).

(2) S. DANISHEFSKY, Acc. Chem. Res., 12, 66 (1979) ; T. HUDLICKY, F.J. KOSZYK, D.M. DOCHWAT and G.L. CANTRELL, J. Org. Chem., 46, 2911 (1981) ; T. HUDLICKY, D.B. REDDY, S. V. GOVINDAN, T. KULP, B. STILL and J.P. SHETH, J. Org. Chem., 48, 3422 (1983).

(3) E.J. COREY, A. MARFAT, G. GOTO and F. BRION, J. Amer. Chem. Soc., 102, 7984 (1980). K.C. NICOLAOU, D.P. PAPAHATJIS, D.A. CLAREMON and R.E. DOLLE III, J. Amer. Chem. Soc., 103, 6967 (1981) ; K.C. NICOLAOU, D.A. CLAREMON, D.P. PAPAHATJIS and R.L. MAGOLDA, J. Amer. Chem. Soc., 103, 6969 (1981) ; M. HIRAMA and M. UEI, J. Amer. Chem. Soc., 104, 4251 (1982) ; S.G. PYNE, M.J. HENSEL and P.L. FUCHS, J. Amer. Chem. Soc., 104, 5719 (1982) ; Y. GUINDON, R. ZAMBONI, C.K. LAU and J. ROKACH, Tetrahedron Lett., 23, 739 (1982) ; M.P. EDWARDS, S.V. LEY, S.G. LISTER and B.D. PALMER, J. Chem . Soc. Chem. Comm., 630 (1983) ; M.A. SUTTER and D. SEEBACH, Lieb. Ann. Chem., 939 (1983).

(4) E.J. COREY, H. NIWA and J. KNOLLE, J. Amer. Chem. Soc., 100, 1942 (1978) ; E.J. COREY, A. MARFAT and D.J. HOOVER, Tetrahedron Lett., 22, 1587 (1981) ; R.K. BOECKMAN Jr., J.J. NAPIER, E.W. THOMAS and R.I. SATO, J. Org. Chem., 48, 4152 (1983).

(5) A. MONPERT, J. MARTELLI, R. GRÉE and R. CARRIÉ, Tetrahedron Letters, 22, 1961 (1981).

(6) $Si0_2$, ether-light boiling petroleum ether 1/1 : (-) 2 : Rf = 0,18 ; $[\alpha]_D^{25}$ = -237° (MeOH), c = 0,071); (-) 3 Rf = 0,45 ; $[\alpha]_D^{25}$ = -210° (MeOH, c = 0,046).

2 : IR (Nujol, cm^{-1}) : 3450-3100 (broad) ; 2060 ; 1790 (broad) ; 1713 ; 1701. RMN ^1H (80 MHz, $CDCl_3$) δ : 5,80 (d.d.d ; J_{ab} = 7,8 ; J_{bc} = 4,8 and J_{bd} = 1 Hz ; H_b) ; 5,43 (d.d.d ; J_{cd} = 8,1 ; J_{ac} = 1 Hz ; H_c) ; 3,65 (s ; 3H ; $CO_2C\underline{H}_3$) ; 3,63 (d.d.q ; J_{de} = 7,5 ; J_{ef} = 4,2 ; H_e) ; 2,8 (d ; H_f) ; 1,37 (d ; J = 6,1 ; $C\underline{H}_3$) ; 1,30 (d.d.d ; H_d) ; 1,09 (d.d ; H_a).

3 : IR (Nujol, cm^{-1}) : 3460 (sharp) ; 2066 ; 2045 ; 1990 ; 1975 ; 1966 ; 1685. RMN ^1H (80 MHz, $CDCl_3$) δ 5,78 (d.d ; J_{ab} = 7,6 ; J_{bc} = 4,6 ; H_b) ; 5,37 (d.d ; J_{cd} = 8,4 ; H_c); 3,90 (d.d.q ; J_{de} = 6,0 ; J_{ef} = 3,8 ; H_e) ; 3,63 (s ; 3H ; $CO_2C\underline{H}_3$) ; 2,10 (d ; H_f) ; 1,38 (d.d ; H_d) ; 1,36 (d ; J = 6,0 ; CH_3) ; 0,95 (d ; H_a).

(7) L. TOUPET and J.C. MESSAGER, Acta Cryst. B, in press.

(8) J.E. MAHLER and R. PETTIT, J. Amer. Chem. Soc., 85, 3955 (1963) ; N.A. CLINTON and C.P. LILLYA, J. Amer. Chem. Soc., 92, 3058 (1970).

(9) A. MONPERT, J. MARTELLI, R. GRÉE and R. CARRIÉ, Nouv. J. Chim., 7, 345 (1983).

(10) (-) 4 : $[\alpha]_D^{25}$ = -230° (MeOH, c = 0,045) ; (-) 5 : $[\alpha]_D^{25}$ = -163° (MeOH, c = 0,012).
4 : IR (Nujol, cm^{-1}) : 2050 ; 1982 ; 1715 ; 1695. RMN ^1H (80 MHz, $CDCl_3$) ; 5,80 (d.d.d J_{ab} = 7,9 ; J_{bc} = 4,8 ; J_{bd} = 1 ; H_b) ; 5,41 (d.d ; J_{cd} = 8,3 ; H_c) ; 3,67 (s ; 3H ; CO_2CH_3) ; 3,32 (s ; 3H ; OCH_3) ; 3,16 (d.q ; J_{de} =6,0; H_e) ; 1,33 (d ; J = 5,9 ; CH_3) ; 1,23 (d.d ; H_d) ; 1,07 (d ; H_a).
5 : IR (Nujol, cm^{-1}) : 2050 ; 1992 ; 1705. RMN ^1H (80 MHz, $CDCl_3$) ; 5,78 (d.d.d ; J_{ab}= 7,6 ; J_{bc} = 4,8 ; J_{bd} = 0,9 ; H_b) ; 5,35 (d.d.d ; J_{cd} = 8,5 ; J_{ac} = 0,8 ; H_c) ; 3,67 (s ; 3H CO_2CH_3) ; 3,34 (s ; 3H ; OCH_3) ; 3,3-3,60 (m, 1H, H_e) ; 1,30 (d.d ; H_d) ; 1,29 (d ; J = 5,9 ; CH_3) ; 0,92 (d.d ; H_a).

(11) Other methods (Me_3NO, $FeCl_3$ for instance) give lower yields or less pure materials.

(12) 6a : $[\alpha]_D^{25}$ = +20° (MeOH, c = 0,014) ; 6b : $[\alpha]_D^{25}$ = -53° (MeOH, c = 0,087).
6a and 7a : IR (film, cm^{-1}) : 3420 ; 1708 (broad) ; 1644 ; 1615. RMN ^1H (80 MHz, $CDCl_3$): 7,26 (d.d ; J_{ab} = 15,4 ; J_{bc} = 9,0 ; H_b) ; 6,37 (d.d ; J_{cd} = 15,1 ; H_c) ; 6,11 (d.d ; J_{de} = 4,2; H_d) ; 5,85 (d ; H_a) ; 4,40 (d.q ; J_{de} = 4,2 ; H_e) ; 3,74 (s ; 3H ; CO_2CH_3) ; 3,5-2,50 (1H, broad, OH) ; 1,30 (d ; J = 6,4 ; CH_3).
6b and 7b : IR (film, cm^{-1}) : 1717 ; 1643 ; 1612. RMN ^1H (80 MHz, $CDCl_3$) : 7,23 (d.d; J_{ab} = 15,0 ; J_{bc} = 9,8 ; H_b) ; 6,29 (d.d ; J_{cd} = 14,8 ; H_c) ; 5,95 (d.d ; J_{de} = 6,2 ; H_d); 5,85 (d ; H_a) ; 3,83 (d.q; H_e) ; 3,75 (s ; 3H ; CO_2CH_3) ; 3,29 (s ; 3H ; OCH_3) ; 1,26 (d; J = 6,2 ; CH_3).

(13) Similar reactions have been performed starting from (+) 1 ; they gave 6 and 7 with the same stereo and enantiomeric purity.

(14) Racemic mixture 6a + 7a exhibits a strong splitting of Me signals in the presence of the Europium chiral shift reagent. Under the same conditions only one methyl doublet is observed for 6a ; the other being observed with 7a.

(15) Me_2SO_4, under phase transfer catalysis conditions (80 % yield), slightly modified (0°C, TBAI 2 % mol.) procedure from A. MERZ, Angew. Chem. Int. Ed., 12, 846 (1973).

(Received in France 11 May 1984)