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ASYMMETRIC SYNTHESIS BY CHIRAL RUTHENIUM COMPLEXES

III *. REGIOSELECTIVITY AND ASYMMETRIC INDUCTION IN CATALYTIC HYDROGENATION OF α, β-UNSATURATED DICARBOXYLIC ACIDS

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Summary

The homogeneous catalytic hydrogenation of citraconic and mesaconic acids in the presence of $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ gives, in addition to (—)(*S*)-methylsuccinic acid, a mixture of γ-lactones in ratios which depend on the substrate and the reaction temperature. An exceptionally high regioselectivity is obtained in the hydrogenation at 120°C of the more hindered carboxyl group of mesaconic acid.

Introduction

Ruthenium complexes have recently been found to catalyze efficiently the homogeneous hydrogenation of several unsaturated functional groups [1—3]. When the complexes contain optically active ligands they can be used as catalysts for asymmetric hydrogenation of a number of prochiral unsaturated substrates such as olefins, ketones, oximes, unsaturated carboxylic acids [4—8]. The ability of $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ to bring about the asymmetric hydrogenation of

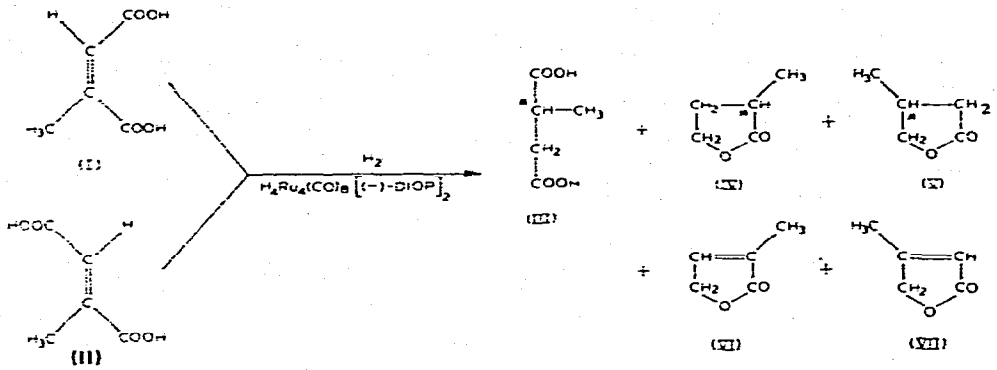
* Part II, see ref. 8.

carbon—carbon double bonds of α,β-unsaturated dicarboxylic acids has recently been reported [8].

Results and discussion

Citraconic acid (I) (see Scheme 1) in toluene/diethyl ether solution reacts

SCHEME 1



with hydrogen at 120°C in the presence of $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ giving (−)(*S*)-methylsuccinic acid (III) as main reaction product (83% yield, 1.1% optical purity). The by-products (17%) are γ-lactones IV, V, VI and VII (Scheme 1) formed in 1.9, 3.5, 8.7 and 2.9% yield, respectively. The regioselectivity in the catalytic reduction of the less hindered carboxyl group, defined as the ratio (IV + VI)/(IV + V + VI + VII) was 62%. This result is in line with that reported by Morand and Kayser [2] for the homogeneous reduction of 2,2-dimethylsuccinic anhydride in the presence of mononuclear ruthenium complexes.

Mesaconic acid (II) under the same conditions gives, besides (−)(*S*)-III (88.7% yield, 8% optical purity), a mixture of IV and V in 0.3 and 11.0% yield respectively. Thus in this case the formation of the saturated γ-lactones is practically regiospecific (97%); the more hindered of the two carboxyl groups is almost exclusively hydrogenated. The γ-lactone V shows the same chirality (*S*)- as (−)(*S*)-methylsuccinic acid formed simultaneously but in lower optical purity (3.2%).

When the catalytic reduction of II is carried out at 170°C γ-lactones IV and V, in the ratio 1/1.4 (72% yield), are the main products.

The different regioselectivity found in the reduction of I and II to lactones (see Table 1) rules out the formation, as a common intermediate, of an unsaturated cyclic anhydride which could arise by *trans—cis* isomerization. Even methylsuccinic acid III cannot be considered a precursor of lactones IV and V in the reduction of mesaconic acid since the hydrogenation of III at 120°C gave a mixture of the two γ-lactones in very different ratios (1/1.2 as against 1/37).

Furthermore the difference in the optical purities, found for III and V from II and the exceptionally high regioselectivity in the reduction of the more hindered carboxyl group suggest that more than one mechanism is operative under these conditions. In the hydrogenation of citraconic acid the regioselectivity observed is an indication that the main reaction path involves unsaturated γ-lactones VI

TABLE 1

HYDROGENATION OF DICARBOXYLIC ACIDS

Substrate 22 mmol; solvent toluene—diethyl ether (2/1) 30 ml; $H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ 0.0909 mmol; $p(H_2)$ 130 atm at 20°C; reaction time 22 h.

Substrate	T (°C)	Yield (%)				
		III	IV [a]	V [a]	VI [a]	VII [a]
Citraconic acid (I)	120	83.0	1.9	3.5	8.7	2.9
Mesaconic acid (II)	120	88.7	0.3	11.0	0.0	0.0
Methylsuccinic acid (III)	120	94.5	2.5	3.0	—	—
Methylsuccinic acid (III)	170	38.0	30.0	42.0	—	—

[a] (IV) α-methyl-γ-butyrolactone; (V) β-methyl-γ-butyrolactone; (VI) α-methyl-$\Delta^{\alpha,\beta}$-butenolide; (VII) β-methyl-$\Delta^{\alpha,\beta}$-butenolide.

and VII formed by preferential reduction of the less hindered carboxyl group.

In our opinion the different steric arrangement of the carboxyl groups around the double bond in I and II plays a fundamental role in determining the extent of asymmetric induction in the hydrogenation of the double bond, as shown by the differing optical purity of (—)(*S*)-methylsuccinic acid obtained from I and II (1.1 and 8.1%, respectively).

We believe that even the regioselectivity in the reduction of the carboxyl group is affected by the steric arrangement of the carboxyl groups. Thus acids I and II may act differently as bidentate ligands; the first may coordinate through both carboxyl groups while the second may preferentially coordinate with the catalyst through the carbon—carbon double bond and one of the carboxyl groups.

It is clear that diphosphine-substituted ruthenium carbonyl hydride clusters may be used as convenient catalysts for the homogeneous reduction of free carboxyl groups even in the presence of carbon—carbon double bonds.

Experimental

GLC analyses were performed on a Perkin—Elmer F30 instrument; preparative GLC separations were performed on a Perkin—Elmer F21 apparatus; NMR spectra were recorded on a Perkin—Elmer R32 spectrometer; the mass spectra were recorded with a Perkin—Elmer 270B spectrometer; the rotatory powers were measured with a Perkin—Elmer 241 polarimeter; IR spectra were recorded with a Perkin—Elmer 225 instrument;

Materials

Citraconic acid, mesaconic acid and (*R*)(*S*)-methylsuccinic acid were Merck—Schuchardt products.

$H_4Ru_4(CO)_8[(-)\text{-DIOP}]_2$ was prepared as previously described [8].

Hydrogenation of substrates

Hydrogenations were carried out by the procedure previously described [8]. Conversions were determined on the crude products by GLC analysis, after

esterification of the acids with diazomethane, using 2 m columns packed with Ucon oil LB 550 X (15%) on Chromosorb W (85%).

Analysis and identification of products from hydrogenation of:

(a) Citraconic acid. Citraconic acid was quantitatively converted; in addition to methylsuccinic acid (83%), 4 products were formed in 1.9, 3.5, 8.7 and 2.9% yields, respectively (GLC).

The product mixture was treated with a 5% $NaHCO_3$ water solution with vigorous stirring at room temperature. (—)(*S*)-Methylsuccinic acid was recovered from the aqueous layer by the usual procedure ($[\alpha]_D^{25} - 0.19$; *c* 5.0 ethanol; 11% optical purity [9]). The organic layer was concentrated by distillation at reduced pressure and submitted to preparative GLC separation using 3 m packed columns (15% Ucon oil LB 550 X on Chromosorb A, 110°C).

The mass spectrum of the product formed in 1.9% yield showed a molecular peak at *m/e* 100, and IR and NMR spectra identical to those of α-methyl-γ-butyrolactone (IV) [10,11]. The product formed in 3.5% yield showed a mass spectrum with a molecular peak at *m/e* 100, an IR spectrum identical to that reported by Seidel et al. [10] for β-methyl-γ-butyrolactone (V) and a consistent NMR spectrum (int. TMS, solvent C_6D_6, $Eu(DPM)_3$): δ (ppm) 1.15 (d, 3 H, $\underline{CH_3}CH$), 2.85 (sextet, 1 H, $CH_3\underline{C}H$), 4.02 (m, 2 H, CH_2CO), 4.71 (m, 2 H, CH_2O). The product formed in 8.7% yield showed a molecular peak at *m/e* 98, and IR and NMR spectra identical to those reported for α-methyl-$\Delta^{\alpha,\beta}$-butenolide (VI) [12, 13]. The product formed in 2.9% yield showed a molecular peak at *m/e* 98, and IR and NMR spectra identical to those reported for β-methyl-$\Delta^{\alpha,\beta}$-butenolide (VII) [12,13].

(b) Mesaconic acid. Mesaconic acid was quantitatively converted: two products were present (0.3 and 11.0% yield) besides methylsuccinic acid (88.7%, $[\alpha]_D^{25} - 1.38$; *c* 4.5 ethanol; 8.1% optical purity [9]).

Work-up as described for citraconic acid gave two products, which were identified as α-methyl-γ-butyrolactone (IV) and β-methyl-γ-butyrolactone (V). (V) showed $[\alpha]_D^{25} - 0.46°$ (*c* 1.96, pentane).

Determination of the optical purity of V by oxidation of (+)(R)-2-hydroxy-4-methyltetrahydrofuran

(+)(*R*)-2-Hydroxy-4-methyltetrahydrofuran (2.15 g) ($\alpha_D^{25}(l = 1) + 2.44°$ neat, 6.4% optical purity [14]) was added during 30 min to a well stirred mixture of 5.8 g of Ag_2O and 1.2 g of NaOH in water (30 ml) at room temperature. Stirring was maintained for 24 h. The solids were filtered off and the alkaline solution was washed with diethyl ether, acidified, and extracted with diethyl ether. The ethereal solution was dried (Na_2SO_4), the solvent evaporated, and the residue distilled under reduced pressure. Pure (+)(*R*)-(V) was obtained in 85% yield (b.p. 80°C/100 mmHg, α_D^{25} ($l = 1$) + 1.28° neat, optical purity 6.4%). On this basis V obtained by hydrogenation of II has (*S*) configuration and an optical purity of 3.2%.

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