Hydroformylation of Unsaturated Dicarboxylic Esters with Rhodium Containing Catalysts**

László Kollár, Giambattista Consiglio, and Piero Pino*

Abstract: The regioselectivity observed in carbonyl-rhodium catalyzed hydroformylation of dimethyl itaconate (**1a**), which leads to the preferential formation of dimethyl 2-(formylmethyl)-butandioate (**3a**) is completely reversed by the modification of the catalyst with phosphanes resulting in the formation of dimethyl 2-formyl-2-methyl-butandioate (**2a**). Only the hydrogenation reaction was observed under «oxo» conditions for the isomeric dimethyl mesaconate (**1b**) or dimethyl citraconate (**1c**). A low enantioface discrimination involving the same face both for hydrogenation and hydroformylation is found in the reaction of **1a** using the chiral ligand (*R,R*)-2,2-dimethyl-4,5-(diphenylphosphinomethyl)-1,3-dioxolane (DIOP).

Despite its potential synthetic interest there is only one short report in the literature, to the best of our knowledge, on the hydroformylation of itaconic acid derivatives. Using octacarbonyldicobalt as the catalyst precursor in the hydroformylation of diethyl itaconate the formation of dimethyl 2-(formylmethyl)-butandioate was reported with moderate yields (56%)[1].

We have investigated the hydroformylation of dimethyl itaconate (**1a**) and some related compounds (**1b**, **1c**; see Scheme 1) using nonchiral and chiral[2] rhodium catalytic systems. The results are reported in Table 1. The hydroformylation products (**2a** and **3a**) were identified by ^{1}H-NMR, IR, and mass spectroscopy after their separation by fractional distillation from the reaction mixture.

Using $Rh_4(CO)_{12}$ as the catalyst precursor for the hydroformylation of **1a**, the selectivity to aldehydes is about 42%. Addition of PPh_3, or of the bisphosphane DIOP (P:Rh = 4), as well as the use of $RhH(CO)(PPh_3)_3$ results in a slightly higher chemoselectivity (about 50%). A more effective improvement of the chemoselectivity (to more than 82%) is observed by the addition of DIOP to the $RhH(CO)(PPh_3)_3$ catalyst precursor. The use of a $[Rh(CO)_2Cl]_2$/DIOP (P:Rh = 4) catalyst precursor causes a low selectivity towards the formation of aldehydes (35%) which is improved to 50% when 5 equivalents of NEt_3 (with respect to Rh) has been added to the catalytic system, as expected[3].

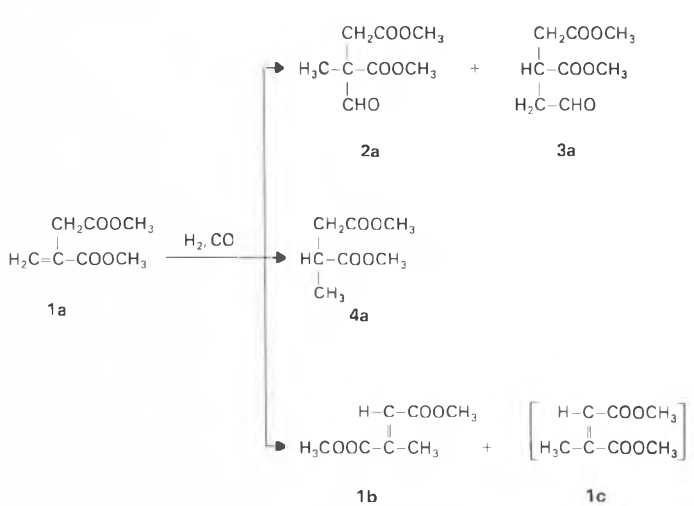
As it has been found for other α,β-unsaturated esters[4] using $Rh_4(CO)_{12}$ as the catalyst precursor, the less branched isomer (**3a**) is preferentially formed (80%). When triphenylphosphane was added to the above catalytic system or $RhH(CO)(PPh_3)_3$ was used as the catalyst precursor more than 80% of the more branched isomer (**2a**) was formed. This change in regioselectivity closely resembles that observed when methyl methacrylate is the substrate. In this case formylation at the unsubstituted methylene carbon atom results in 79% selectivity when $Rh_4(CO)_{12}$ was used as catalyst precursor and in 11% selectivity for the corresponding triphenylphosphane modified catalytic system[4].

Addition of DIOP both to $Rh_4(CO)_{12}$ or $RhH(CO)(PPh_3)_3$ improves regioselectivity towards the formation of **2a** to about 95%. Surprisingly, when $[Rh(CO)_2Cl]_2$ is used as the catalyst precursor in the presence of DIOP, an equimolar amount of the two aldehydic products (**2a** and **3a**) is formed. Addition of NEt_3 to this system (N:Rh = 5) restores the high regioselectivity towards formylation at the disubstituted methylene carbon atom.

Under the reaction conditions used and in contrast to the results obtained in the hydroformylation of methyl methacrylate with similar catalytic systems the hydroformylation of **1a** is always accompanied by competing hydrogenation to **4a**, and to a lower extent, in most cases by isomerization to **1b**. Under hydroformylation conditions **1b** and **1c** (the possible isomerization products of **1a**) are practically only hydrogenated, **1b** reacting faster than **1c**; for both substrates the hydrogenation rate is much lower than for **1a**. Therefore in the hydroformylation of **1a**, the hydrogenated product **4a** should form in part via isomerization to **1b**. The isomerization reaction of **1a** to the *trans*-isomer **1b** is in general faster than the hydrogenation of **1b** as shown by the presence of **1b** in the reaction products.

The use of the chiral ligand DIOP results in asymmetric hydroformylation and hydrogenation of the substrate (Table 1). The enantiomeric excess of the reaction products has been determined by ^{1}H-NMR spectroscopy in the presence of $Eu(dcm)_3$ [tris(dicampholylmethanato)europium(III)] as the chiral shift reagent. The relationship between sign of the optical rotation and absolute configuration for dimethyl 2-formyl-2-methyl-butandioate (**2a**) and for dimethyl 2-(formylmethyl)-butandioate (**3a**) has been determined through decarbonylation (Scheme 2) to di-

Scheme 1



* *Correspondence:* Prof. Dr. P. Pino
Technisch-chemisches Laboratorium
Eidgenössische Technische Hochschule Zürich
ETH-Zentrum, Universitätstrasse 6
CH-8092 Zürich

** *Acknowledgement:* This work was supported by the Schweizerischer Nationalfonds zur Förderung der wissenschaftlichen Forschung (grant No 2.301-0.81).

Table 1. Rhodium-catalyzed hydroformylation of the isomers **1a**, **1b**, and **1c** [a].

Substrate	Catalyst Precursor	Reaction time [h]	Conversion [%] [b]				Enantiomeric excess [%] (absolute configuration)		
			2a	**3a**	**4a**	**1b**	**2a**	**3a**	**4a**
1a	$Rh_4(CO)_{12}$	17	8	34	58	0			
1a	$Rh_4(CO)_{12}$ + 16 PPh_3	7	42	9	45	4			
1a	$Rh_4(CO)_{12}$ + 8 DIOP	6	43	3	40	6	8.3(*S*)	[e]	1.1(*S*)[f]
1a	$RhH(CO)(PPh_3)_3$	8	37	8	41	9			
1a	$RhH(CO)(PPh_3)_3$ + 2 DIOP	6	73	4	10	6	9.1(*S*)	[e]	0
1a	$[Rh(CO)_2Cl]_2$ + 4 DIOP	18	15	20	47	15	6.6(*S*)	1.3(*S*)[f]	0.3(*S*)[f]
1a	$[Rh(CO)_2Cl]_2$ + 4 DIOP [c]	17	43	5	44	6	7.2(*S*)	[e]	0
1b	$[Rh(CO)_2Cl]_2$ + 4 DIOP	205	2	≤ 0.5	97	0.5	[c]	[e]	0.4(*S*)[f]
1c	$[Rh(CO)_2Cl]_2$ + 4 DIOP	190	4	0.5	71	0 [d]	[e]	[e]	21.9(*R*)[f]

[a] Reaction conditions: $p_{CO} = p_{H_2}$ = 40 bar; 100 °C; 35 mL toluene; Rh/substrate = 1/2000.
[b] (mol product)/(mol initial substrate) × 100; the conversion was in all cases higher than 92%, with the exeption of **1c** where it was 77%.
[c] Et_3N added; Et_3N/Rh = 5.
[d] 23% of nonconverted substrate **1c** was present in the reaction mixture.
[e] Not determined.
[f] Optical purity determined from optical rotation.

methyl methylsuccinate (**4a**) under the assumption of retention of configuration during the decarbonylation reaction [5,6]. The hydrogenation product is also optically active; in the case of **1a** the prevailing antipode of dimethyl methylsuccinate and the hydroformylation products arise from the same enantioface of the olefine (Scheme 3). The asymmetric induction in the hydroformylation of **1a** is very low and comparable with that observed when nonfunctionalized vinylidene olefins are used as the substrate [2]. As far as enantioselectivity in hydrogenation is concerned, the enantioface discrimination is also low compared to the hydrogenation of the same substrate with chiral bisphosphane-rhodium catalytic systems [7]. However, under the reaction conditions used **1a** is partially isomerized to **1b** and probably also to **1c**, which by hydrogenation prevailingly generates the enantiomer opposite to that arising directly from **1a** (Table 1). Therefore a larger asymmetric induction can be assumed to occur in the «direct» hydrogenation of **1a** to **4a**.

Experimental

Carbon monoxide was prepared by decomposition of formic acid; its purity was higher than 99.5% by GC analysis. Hydrogen was a product of Sauerstoff- und Wasserstoffwerke AG, Luzern, with a purity ≥ 99.5%. Hexane and toluene (Fluka products) were purified through distillation over Na-K-alloy under nitrogen. $HRh(CO)(PPh_3)_3$ (Fluka product *purum*) was used without further purification. (*R,R*)-DIOP was prepared according to the known literature method [8].

The NMR analyses were recorded on a Bruker AM 300 WB spectrometer using tetramethylsilane as the internal standard.

In a typical experiment the solution of 9.4 mg (0.0125 mmol) $Rh_4(CO)_{12}$ and 49.8 mg (0.1 mmol) (−)-DIOP in 35 mL toluene was transferred under nitrogen into a 150 mL stainless-steel autoclave containing 15.8 g (100 mmol) of **1a**. The autoclave was pressurized to 80 bar total pressure ($CO:H_2$=1:1) and put into an oil bath with continual agitation by an arm shaker. After the reaction the autoclave was cooled to room temperature and vented; then the solution was removed and immediately analyzed by gas chromatography.

Dimethyl methylbutanedioate (**4a**): The pure hydrogenated derivative of **1a** was separated by fractional destillation at 28 °C/0.1 torr. For the determination of the optical purity the optical rotation value $[\alpha]_D^{20}$ = +6.44° (*R*) (neat) and the density ϱ_4^{20} = 1.076 g/cm³ were used [9]. – ^{1}H-NMR ($CDCl_3$): 3.56 (s, 3H, OCH_3), 3.55 (s, 3H, OCH_3), 2.81 (m, 1H, C*H*CH_3), 2.65 (dd, 1H, C*H*^{a}H^b$COOCH_3$, *J* = 16.4, 7.1 Hz), 2.23 (dd, 1H, CH^a*H*^{b}$COOCH_3$, *J* = 16.4, 6.7 Hz), 1.14 (d, 3H, CH_3, *J* = 7.1 Hz).

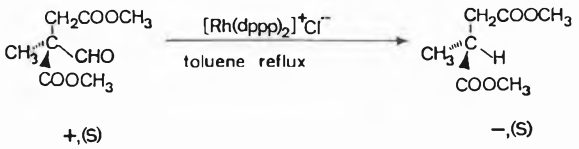
Dimethyl 2-formyl-2-methyl-butanedioate (**2a**): The hydroformylation products of **1a** were separated by fractional distillation at 44–46 °C/0.1 torr. The enantiomeric excess of **2a** was determined by ^{1}H-NMR shift technique using $Eu(dcm)_3$ as the chiral shift reagent on the basis of the signal of the formyl group. For sample having $[\alpha]_D^{20}$ = +0.551° (neat, ϱ_4^{20} = 1.180 g/cm³) 9.1% *ee* was found. – ^{1}H-NMR ($CDCl_3$): 9.93 (s, 1H, CHO), 3.80 (s, 3H, OCH_3), 3.67 (s, 3H, OCH_3), 2.89 (s, 2H, C*H*$_2$$COOCH_3$), 1.38 (s, 3H, CH_3). – The absolute configuration of **2a** was determined by homogeneous catalytic decarbonylation using $[Rh(dppp)_2]Cl$ (dppp = 1,3-bis(diphenylphosphino)propane) as a catalyst [5]. The solution of 48.2 mg (0.05 mmol) rhodium complex and 2.7 g (14.4 mmol) hydroformylation product in 30 mL toluene was refluxed under nitrogen for 2 days. The decarbonylation of (+)-**2a** ($[\alpha]_D^{20}$ = +0.551°, neat) resulted in (−)-**4a** ($[\alpha]_D^{20}$ = −0.420°, neat) having therefore prevailing (*S*) absolute configuration [9].

Dimethyl 2-(formylmethyl)-butandioate (**3a**): After separation of **3a** by fractional destillation at 54–56 °C/0.1 torr, the enantiomeric excess was determined by ^{1}H-NMR shift technique using $Eu(dcm)_3$ as the chiral shift reagent on the basis of the signals of the CHO and OCH_3 groups. A sample having $[\alpha]_D^{20}$ = +0.051° (neat, ϱ_4^{20} = 1.18 g/cm³) shows *ee* ≈ 1%. The optical purity determined assuming for the optically pure (*R*)-**3a** $[\alpha]_D^{20}$ = +3.81° (neat) is 1.3% [6]. – ^{1}H-NMR ($CDCl_3$): 9.77 (t, 1H, CHO, *J* = 0.8 Hz), 3.71 (s, 3H, OCH_3), 3.69 (s, 3H, OCH_3), 3.28 (m, 1H, C*H*CH_2), 2.85 (m, 2H, C*H*$_2$$COOCH_3$), 2.69 (m, 2H, C*H*$_2$CHO).

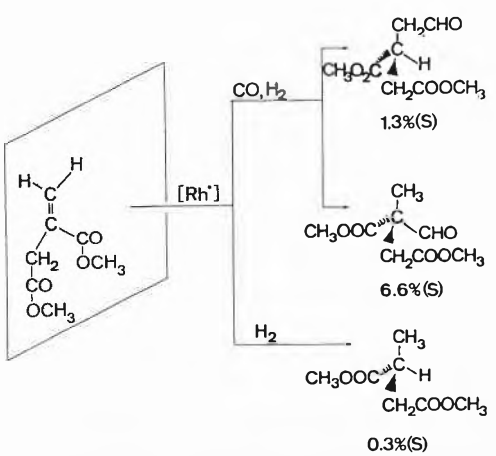
Dimethyl mesaconate (**1b**): From the hydroformylation products a mixture of **1b** and **4a** (4:6) was separated by distillation. **1b** was identified using GC-MS and ^{1}H-NMR. – ^{1}H-NMR ($CDCl_3$): 6.78 (q, 1H, CH, *J* = 1.55 Hz), 3.81 (s, 3H, OCH_3), 3.78 (s, 3H, OCH_3), 2.30 (d, 3H, CH_3, *J* = 1.55 Hz).

Received: November 6, 1986 [FC 88]

Scheme 2



Scheme 3



[1] H.J. Hagemeyer, D.C. Hull, US-Pat. 2 610 203 (1952).
[2] G. Consiglio, P. Pino, *Top. Curr. Chem. 105* (1982) 77.
[3] D. Evans, J.A. Osborn, G. Wilkinson, *J. Chem. Soc. A* (1968) 3133.
[4] J. Falbe, N. Huppes, *Brennst. Chem. 48* (1966) 46; M. Tanaka, T. Hayashi, I. Ogata, *Bull. Chem. Soc. Jpn. 50* (1977) 2351.
[5] D.H. Doughty, L.H. Pignolet, *J. Am. Chem. Soc. 100* (1978) 7083.
[6] L. Kollár, G. Consiglio, P. Pino, unpublished results.
[7] I. Ojima, T. Kogure, N. Yoda, *J. Org. Chem. 45* (1980) 4728; W.C. Christophel, B.A. Vineyard, *J. Am. Chem. Soc. 101* (1979) 4406.
[8] B.A. Murer, J.M. Brown, P.A. Chaloner, P.N. Nicholson, D. Parker, *Synthesis* (1979) 350; H.B. Kagan, T.P. Dang, *J. Am. Chem. Soc. 94* (1972) 6429.
[9] E. Berner, R. Leonardsen, *Liebigs Ann. Chem. 538* (1939) 14; R. Rossi, P. Diversi, G. Ingrosso, *Gazz. Chim. Ital. 98* (1968) 1391.