

Hydroformylation of (+)(S)-3-Methylpent-1-ene

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In the hydroformylation of (+)(S)-3-methylpent-1-ene the extent of racemization of the synthesized dissymmetric aldehydes is shown to decrease with increasing pressure of carbon monoxide; the ratio of *erythro*- to *threo*-2,3-dimethylpentanal formed differs considerably from the diastereoisomeric equilibrium value.

Racemic 4-methylhexanal is shown to arise from racemic 3-methylpent-1-ene and therefore gives some indication of the relative rates of hydroformylation and isomerization of the olefinic substrate.

The secondary butyl group exerts, under conventional 'oxo' conditions, a weak asymmetric induction in the formation of 2,3-dimethylpentanal, probably connected to the steric requirements in the complex formation between the olefin and the cobalt catalyst.

MANY attempts have been made in recent years to determine the extent and the role of the isomerization of the olefin during the synthesis of aldehydes by hydroformylation.¹⁻⁴

In order to clarify further the influence of the migration of the double bond on the isomeric composition of the hydroformylation products, we have studied the hydroformylation of (+)(S)-3-methylpent-1-ene (I).

This olefin is a suitable substrate, since the eventual reversible migration of the double bond during the hydroformylation would cause racemization of the substrate from which, in turn, aldehydes of corresponding lower optical purity would be formed.

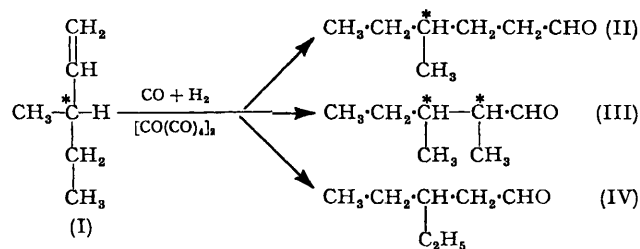
In a short communication we have already emphasized, on the basis of the optical purity of (+)(S)-4-methylhexanal (II) obtained from the hydroformylation of (I) under various conditions, that olefin racemization, and therefore double-bond migration is favoured by high temperatures and low partial pressures of carbon monoxide (p_{CO}).

Here we report a more complete investigation on the

influence of p_{CO} on the optical purity of (II) and on the olefinic double-bond migration rate; furthermore, the optical purity and the diastereoisomeric composition of 2,3-dimethylpentanal (III) have been determined and some stereochemical aspects of its formation are discussed.

RESULTS

The hydroformylation of (+)(S)-3-methylpent-1-ene occurs according to the Scheme:²



SCHEME

¹ M. Johnson, *J. Chem. Soc.*, 1963, 4859; *Chem. and Ind.*, 1963, 684.

² P. Pino, S. Pucci, and F. Piacenti, *Chem. and Ind.*, 1963, 294.

³ F. Piacenti, P. Pino, R. Lazzaroni, and M. Bianchi, *J. Chem. Soc. (C)*, 1966, 488.

⁴ Y. Takegami, Y. Watanabe, H. Masada, and C. Yokakawa, *Bull. Chem. Soc. Japan*, 1966, **39**, 1499.

TABLE 1

Hydroformylation of (+)(S)-3-methylpent-1-ene at various partial pressures of carbon monoxide; (+)(S)-3-methylpent-1-ene (5 g, optical purity 90%), [Co(CO)₄]₂ (0.150 g), benzene (50 ml), p_{H₂} 80 atm., temp. 100°

p _{co} (atm.)	Reaction time (min.)	% Conversion ^a	(+) (S)-4-Methylhexanal				3-Ethyl- pentanal (%)	2,3-Dimethyl- pentanal (%)
			(%)	Optical ^b purity (%)	Arising from isomerized (I) (%)	Arising from not isomerized (I) (%)		
2.2	320	75	81.9	23.1	74.3	25.7	11.8	6.3
5	250	77	83.5	33.4	62.8	37.2	10.7	5.8
12	150	82	89.9	65.0	27.8	72.2	7.0	3.1
33	260	88	90.0	80.0	11.1	88.9	6.6	3.4
63	280	86	91.0	86.2	4.2	95.8	5.6	3.4
102	360	88	92.2	88.2	2.0	98.0	4.5	3.3 ^c

^a Carbonyl compound, (equiv.)/olefin charged (moles) × 100. ^b On the basis that no racemization takes place in the oxidation of the aldehyde and esterification of the corresponding acid. ^c Optical purity of the (3S) asymmetric carbon atom: 89%.

The reaction rate also depends, as expected,³ on the carbon monoxide partial pressure and shows a maximum at ca. 10 atm. (Table 1).

The isomeric distribution of the reaction products was determined with the previously described technique.^{2,3}

The racemization encountered in the formation of (II) by hydroformylation of (I) has been calculated by comparing the optical purity of (II) * (Table 2) with that of the starting olefin.

TABLE 2

Optical purity of methyl (+)(S)-4-methylhexanoate obtained from (+)(S)-4-methylhexanal produced by hydroformylation of (+)(S)-3-methyl-1-pentene ([α]_D²⁰ +33.84, optical purity ^a 90%)

p _{CO} (atm.)	[α] _D ²⁰	Methyl (+)(S)-4-methyl- hexanoate	
		Optical purity ^b (%)	Racemization (%)
2.2	2.28	23.1	74.3
5	3.31	33.4	62.8
12	7.19	65.0	27.8
33	7.92	80.0	11.1
63	8.54	86.2	4.2
102	8.73	88.2	2.0

^a Calculated assuming for optically pure (+)(S)-3-methylpent-1-ene, [α]_D²⁰ +37.58 (P. Pino, F. Ciardelli, G. P. Lorenzi, and G. Montagnoli, *Makromol. Chem.*, 1963, **61**, 207). ^b Calculated assuming [α]_D²⁵ +9.9 for optically pure methyl ester of (+)(S)-4-methylhexanoic acid; a sample of this ester derived from (+)(S)-4-methylhexanoic acid having 93.6% optical purity had in fact [α]_D²⁵ +9.25. In the literature [α]_D²⁵ +10.1 is reported for the above optically pure ester (R. Rossi, P. Pino, F. Piacenti, L. Lardicci, and G. Del Bino *J. Org. Chem.*, 1967, **32**, 842).

Fractional distillation and gas-chromatographic techniques were used to separate the mixture of diastereoisomeric methyl 2,3-dimethylpentanoates from the other isomers.

N.m.r. spectroscopy⁷ was used to determine the composition of the resulting diastereoisomeric mixture while the optical purity of the asymmetric centre in positions 3 was determined by the method of Rossi and Pino.⁸

* The optical purity of (II) was determined by oxidizing the hydroformylation products with Ag₂O and separating the acids, as methyl esters; the optical purity of (II) was assumed to be identical to that of the corresponding methyl esters thus obtained. It has in fact been proved that no racemization is encountered in the oxidation of the aldehyde and esterification of the corresponding acid.^{5,6}

DISCUSSION

In agreement with previous findings² very little racemization occurred in the formation of (II) by hydroformylation of (I) at 100° and at a carbon monoxide pressure (p_{CO}) of 102 atm.

In various samples of the reaction mixture after 88% conversion of (I) under high p_{CO} (ca. 100 atm.) no isomeric olefins were detected by g.l.c.

With a pressure of carbon monoxide below 50 atm. the ratio between racemic and optically active compound (II) increased.

These data may be used to obtain information on the ratio between the rates of hydroformylation and isomerization of compound (I) with different pressures of carbon monoxide. In fact, since (+)(S)- (II) does not racemize under 'oxo' conditions racemic compound (II) must arise from racemic compound (I). The hydroformylation and the isomerization of compound (I) at constant p_{CO} and p_{H₂} can be considered as simultaneous reactions. Therefore, the ratio of racemic to optically active compound (II) arising from isomerization and hydroformylation of optically pure compound (I) allows an estimate to be made of the minimum ratio of the rates of these two reactions.

From the Figure it appears that the two rates are approximately equal at p_{CO} 6–8 atm. (under the conditions chosen) and that this ratio increases as the pressure of carbon monoxide is decreased. Since the hydroformylation rate increases when p_{CO} is decreased to 12 atm. this result confirms that the isomerization rate increases with a decrease in p_{CO} in the same pressure range.

The absence of racemization in the synthesis of 2,3-dimethylpentanal at a high pressure of carbon monoxide demonstrates that initial double-bond migration is not necessary in order to have the addition of a CHO group in position 2.

The ratio (40 : 1) of the amounts of (II) to (III) obtained in the hydroformylation of (I), under non-isomerizing conditions (high p_{CO}), is the same as the ratio

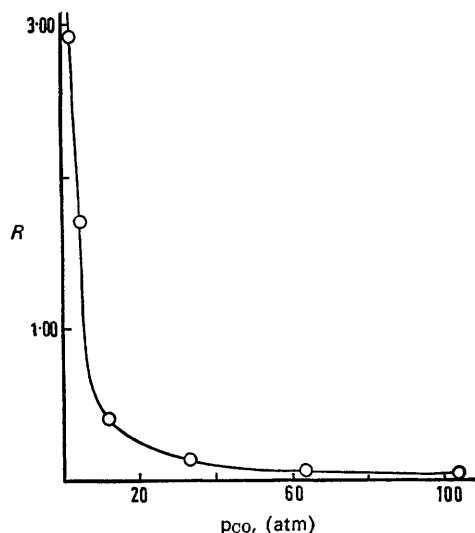
⁵ L. Lardicci, *Gazzetta*, 1961, **91**, 458.

⁶ R. Rossi, P. Pino, F. Piacenti, L. Lardicci, and G. del Bino, *Gazzetta*, 1967, **97**, 1194.

⁷ R. Rossi, *Gazzetta*, 1967, **97**, 1239.

⁸ R. Rossi and P. Pino, *Gazzetta*, 1968, **98**, 398.

of the hydroformylation reaction rates in the 1- and 2-positions. It is interesting to note that this value is much higher than those observed for the products of the hydroformylation of propene (*ca.* 4), 1-butene (*ca.* 3.9), pent-1-ene (*ca.* 5.4), and 4-methylpent-1-ene (*ca.* 8.9)³ in nonisomerizing conditions.



p_{CO} influence on the ratio (R) between racemic 4-methylhexanal and optically active (+)(S)-4-methylhexanal arising from optically pure (+)(S)-3-methyl-pent-1-ene

The above results confirm that the methyl branching near the double bond strongly affects the hydroformylation rate and hence the composition of the reaction product.

The presence of achiral (IV) among the products of the hydroformylation of (I) carried out under high p_{CO} in amounts larger than racemic (II) has been rather puzzling for a long time. In fact, at a high pressure of carbon monoxide if no isomerization of the olefin takes place and (IV) is produced only by addition of a formyl group to the double bond, no (IV) at all should be formed by hydroformylation of (I).

The recent finding⁹ that (R)-3-ethylhexanal obtained by hydroformylation of (+)(S)-3-methylhex-1-ene at a high pressure of carbon monoxide and 100° is optically active, suggests that the formation of most of the 3-ethylpentanal might be due to a direct insertion of the CHO group at a C-H bond of the methyl group in position 3.*

The diastereoisomeric mixture of the *erythro*- and *threo*-2,3-dimethylpentanal obtained at a high pressure of carbon monoxide was found to contain 66% of the *threo*-(2*R*,3*S*)-diastereoisomer, and 34% of *erythro*-(2*S*,3*R*)-diastereoisomer.

In order to check if this value corresponded to the

* In view of the recently reported finding of an increase in oxidation number of a metal atom by breaking a C-H bond,¹⁰⁻¹² we believe that this explanation is more likely than the alternative hypothesis of a migration of the double bond in the olefin cobalt carbonyl complex. In fact, in the case of (+)(S)-3-methylhex-1-ene⁹ the subsequent restoration of the tertiary carbon atom, which in this case is asymmetric, should take place with a rather improbable retention of configuration.

equilibrium ratio between the two diastereoisomers, the epimerization of 2,3-dimethylpentanal was investigated in dioxan-HCl-H₂O (Table 3). A ratio *erythro*:*threo*

TABLE 3

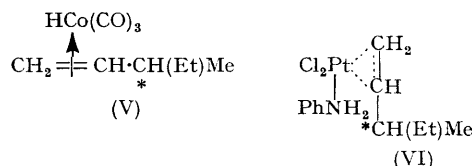
Hydrochloric acid-catalysed epimerization of 2,3-dimethylpentanal at 25°

Expt.	Initial composition		Solvent	Reaction time (days)	Final composition	
	% <i>erythro</i> ^a	% <i>threo</i>			% <i>erythro</i> ^a	% <i>threo</i>
1	49.5	50.5	CHCl ₃	6	49	51
2	67	33	dioxan + H ₂ O	30	44	56
3	67	33	dioxan + H ₂ O	180	45	55

^a Determined by n.m.r. (R. Rossi, *Gazzetta*, 1967, **97**, 1239).

of 45.5 : 55.5 was found in the equilibrium mixture. This value is considerably different from that (34 : 66) found for the ratio between the diastereoisomers of (III) arising from the hydroformylation of (I). The above difference is too large to be attributed to the different solvent and temperature used in the epimerization of 2,3-dimethylpentanal and in the hydroformylation of (+)(S)-3-methylpent-1-ene; thus, an asymmetric induction by the secondary butyl group on the hydroformylation in position 2 seems very likely.

Taking into account the accepted mechanism for the hydroformylation¹³ the asymmetric induction might arise either in the formation of the olefin-cobalt complex (V) or during the addition of the CHO group to the 2 position of the complexed olefin.



Since the asymmetric induction caused by the secondary butyl group on the carbon atom in the 2 position of 3-methylpent-1-ene has been found to be *ca.* 30% in the complex (VI),¹⁴ which can be taken as a suitable model of (V), we are inclined to think that the asymmetric induction takes place during the formation of (V).

EXPERIMENTAL

All b.p.s are uncorrected. G.l.c. analysis was performed on a Perkin-Elmer model F 11 instrument equipped with a 2-m column filled with polyethylene glycol (400) monostearate on Chromosorb W. The isomeric esters were separated by a Perkin-Elmer model F 20 preparative instrument using 5-m column filled with polyethylene glycol (400) monostearate. I.r. spectra were recorded on a Perkin-Elmer model 225 spectrophotometer. Rotations were

⁹ F. Piacenti, S. Pucci, M. Bianchi, R. Lazzaroni, and P. Pino, *J. Amer. Chem. Soc.*, 1968, **90**, 6847.

¹⁰ F. A. Manuel, *J. Org. Chem.*, 1962, **27**, 3941.

¹¹ G. Allegra, F. L. Giudice, G. Natta, U. Giannini, G. Fagherazzi, and P. Pino, *Chem. Comm.*, 1967, 1263.

¹² R. Cramer, *Accounts Chem. Res.*, 1968, **1**, 186.

¹³ R. F. Heck and D. S. Breslow, *J. Amer. Chem. Soc.*, 1961, **83**, 4023.

¹⁴ R. Lazzaroni, P. Salvadori, and P. Pino, *Chem. Comm.*, 1970, 1164.

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determined using a Perkin-Elmer 141 polarimeter with sensitivity of $\pm 0.005^\circ$, neat in a 1-dm tube, unless otherwise stated. The high-pressure equipment used is the same as described in previous papers.^{3,15}

Materials.—(+)(S)-3-Methylpent-1-ene (I), prepared as described by Pino *et al.*,¹⁶ had 90% optical purity. Octacarbonyldicobalt, prepared as described by Natta and Ercoli¹⁷ and crystallized from light petroleum, had m.p. 51.5° .

Racemization of (+)(S)-4-Methylhexanal and Subsequent Oxidation to the Corresponding Acid by Ag_2O .—A solution of (+)(S)-4-methylhexanal⁵ (3.5 g) ($[\alpha]_D^{20} +9.00$, optical purity 94.7%) and $[\text{Co}(\text{CO})_4]_2$ (0.160 g) in dioxan (20 ml) was heated at 145° for 1 h in a 125-ml autoclave under CO and H_2 (1:1; 160 atm). The solution was added, at 0° , to an aqueous suspension of Ag_2O prepared from AgNO_3 (11 g) and NaOH (5.2 g) in H_2O (131 ml). The mixture was stirred for 16 h at room temperature and 1 h at 40° and was then worked up. By distillation (+)(S)-4-methylhexanoic acid (2.5 g) was recovered (b.p. $115\text{--}116^\circ/18$ mm), $n_D^{20} 1.4248$, $[\alpha]_D^{25} +11.10$, optical purity 91%¹⁸ (racemization 3.8%).

Acid-catalysed Epimerization of 2,3-Dimethylpentanal.—A mixture of diastereoisomeric methyl 2,3-dimethylpentanoates ($n_D^{25} 1.4114$, *erythro:threo* = 67:33⁷) by reduction with LiAlH_4 and successive oxidation was converted into diastereoisomeric 2,3-dimethylpentanals (b.p. $91^\circ/152$ mm). The presence in the n.m.r. spectra of the aldehydes of bands analogous both in position and intensity to those of the spectra of the esters used to determine the *erythro:threo* ratio suggests that such a ratio has not changed in the mentioned reactions. Diastereoisomeric 2,3-dimethylpentanals (0.256 g) thus obtained were added to a mixture of H_2O (3 g) and (1 g) dioxan (0.603N with respect to hydrogen chloride). After 10 days at room temperature the n.m.r. spectrum changed no more and the mixture was oxidized with Ag_2O ; the resulting acids were esterified by diazomethane. Methyl 2,3-dimethylpentanoates thus obtained were purified by preparative gas-chromatography, the *erythro:threo* ratio being 45:55.

Reaction of (I) with CO and H_2 in the Presence of $[\text{Co}(\text{CO})_4]_2$.—In the autoclave, evacuated from air, containing octacarbonyldicobalt (0.350 g) a solution of (I) (15 g, 0.18 mol) in benzene (60 ml) was introduced by suction. Carbon monoxide was then introduced up to a pressure not to exceed, at reaction temperature, the desired p_{CO} value.

The autoclave was then rocked and heated up to 100° . After 20 min. carbon monoxide and then hydrogen were rapidly added to reach the desired gas composition (p_{CO} 90 atm, p_{H_2} 80 atm). Reaction commenced and the pressure was kept at the desired value $\pm 2\%$ by injection of a carbon monoxide-hydrogen mixture (1:1) from a high-pressure container.

When gas adsorption ceased the autoclave was rapidly cooled and the gases were discharged into a gasometer and analysed by the usual gas-volumetric techniques.

The carbonyl compounds present in the liquid product, determined according to Smith and Mitchell,¹⁹ were 0.16 equiv. (yield 89%).

The isomeric distribution of the aldehydes (II), (III), and (IV) in the crude was found to be, by g.l.c. analysis, 93:3:4.

Ag_2O Oxidation of the Reaction Products of (I) with CO and H_2 and Conversion of the Acids into Methyl esters.—The reaction products of (I) with carbon monoxide and hydrogen were oxidized by Ag_2O to the corresponding acids as described above. By distillation 19 g (0.146 mol, 81%) of acids were recovered: b.p. $114\text{--}116^\circ/18$ mm, $n_D^{20} 1.4240 = 1.4245$. Equiv. wt. 131.0.

The acids recovered from three such experiments (40 g) were treated in ether solution with CH_2N_2 in excess at 0° .

Besides small amounts of impurities, g.l.c. analysis indicated the presence of three compounds in the ratio 93.5:3.7:2.8 having retention times equal to those of methyl 4-methylhexanoate, methyl 3-ethylpentanoate, and methyl 2,3-dimethylpentanoate respectively.

The mixture of esters was distilled through a 90-cm column filled with glass helices and the liquid was separated into 15 fractions.

Fractions 1—10 (10 g), containing ca. 10% of methyl (—)(3S)-2,3-dimethylpentanoate, gave by preparative g.l.c. three fractions: the first fraction (0.800 g, $n_D^{25} 1.4117$, $[\alpha]_D^{25} -14.229$ (c 1.1216, ethyl ether), with the shortest retention time, contained methyl (—)(3S)-2,3-dimethylpentanoate (pure by g.l.c.), as shown by comparing its i.r. and n.m.r. spectra with those of an authentic sample.²⁰

From the n.m.r. spectrum⁷ the diastereoisomeric ratio of the mixture resulted $66 \pm 2\%$ *threo*, $34 \pm 2\%$ *erythro*.

The second fraction (0.800 g, $n_D^{25} 1.4129$), with intermediate retention time, was shown, by the same method, to contain methyl 3-ethylpentanoate,²¹ and the last one ($n_D^{25} 1.4177$, $[\alpha]_D^{25} +8.74$, o.p. 88.3%), with the highest retention time, methyl (+)(S)-4-methylhexanoate.⁵

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¹⁵ P. Pino, F. Piacenti, and P. P. Neggiani, *Chimica e Industria*, 1962, **44**, 1367.

¹⁶ P. Pino, L. Lardicci, and L. Centoni, *J. Org. Chem.*, 1959, **24**, 1399.

¹⁷ G. Natta and R. Ercoli, *Chimica e Industria*, 1952, **34**, 503.

¹⁸ L. Lardicci and P. Pino, *Gazzetta*, 1961, **91**, 441.

¹⁹ D. M. Smith and J. Mitchell, *Analyt. Chem.*, 1950, **22**, 750.

²⁰ P. A. Levene and R. E. Marker, *J. Biol. Chem.*, 1931, **91**, 405.

²¹ R. F. Kepner, S. Winstein, and G. Young, *J. Amer. Chem. Soc.*, 1949, **71**, 118.