A Low-Pressure System for Producing Normal Aldehydes by Hydroformylation of α Olefins[1]

R. L. PRUETT AND J. A. SMITH

Research and Development Department, Union Carbide Corporation, Chemicals and Plastics, South Charleston, West Virginia 25303

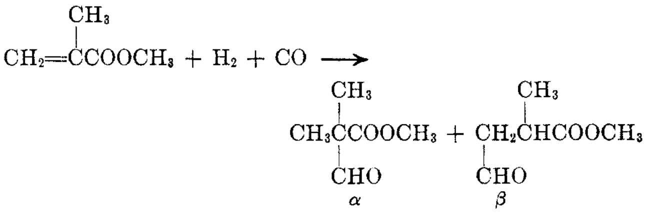
Received June 4, 1968

A new process is described for producing predominately normal aldehydes from α olefins with high efficiencies. The process consists of a rhodium-catalyzed, low-pressure hydroformylation in the presence of significant quantities of certain phosphorus ligands. The effect of various reaction parameters on the ratio of *n*- *vs.* isoaldehyde is reported. The results are consistent with a proposed mechanism which involves as the active catalyst a pentacoordinate rhodium complex, such as tris(triphenyl phosphite)rhodium carbonyl hydride, $[(C_6H_5O)_3P]_3Rh(CO)H$. Both trialkyl and triaryl phosphites are effective ligands. Of particular significance are the effects obtained by substituting electron-withdrawing and electron-donating groups in the *ortho* and *para* positions of the triaryl phosphites.

The hydroformylation of α olefins is successfully accomplished with cobalt catalysts at temperatures above about 100° and at pressures upward of 100 atm of synthesis gas. In general, aldehydes are obtained which may result from attachment of the carbonyl group at any of the positions on the carbon chain.[2] This is brought about by concomitant isomerization of the olefin and subsequent hydroformylation of the resulting internal olefin, in addition to the hydroformylation of the contained α olefin.[3] A number of experimental factors have been found which affect the distribution of the various aldehydes in the final product. Examples are pressure, temperature, solvent and H_2:CO ratios in the gas feed, among others. Piacenti and coworkers[4] demonstrated the effect of H_2:CO gas composition on the hydroformylation of pent-1-ene. Reaction of this olefin with 80 atm of hydrogen and 90 atm of carbon monoxide, at 100° and in the presence of cobalt carbonyl, produced *n*-hexanal, 2-methylpentanal, and 2-ethylbutanal in 76.8, 14.7, and 2.5% yields, respectively. Reaction under the same conditions of temperature and catalyst concentration, but with 80 atm of hydrogen and only 2.5 atm of carbon monoxide, produced these materials in 54.7, 24.3 and 3.7% yields. This work, along with other, leads to the conclusion that higher percentages of linear aldehydes are obtained at higher carbon monoxide partial pressures, in the cobalt-catalyzed reaction.

The metal catalyst has a marked effect upon the product distribution. It is known that rhodium is an extremely active catalyst for the hydroformylation of olefins.[5] It also was reported to produce an aldehyde product which contained predominately branched-chain isomers. Under our experimental conditions, the product produced by hydroformylation of oct-1-ene with rhodium catalyst at 70° and 2500 psi of 1:1 H_2:CO consisted of approximately equal amounts of *n*-nonanal and isomeric C_9 aldehydes.

Falbe and Huppes[6] have examined factors which affect the rhodium-catalyzed hydroformylation of methyl methacrylate. The direction of addition to the α,β-double bond was affected by temperature (low temperatures gave α, high temperature β) and by the addition of tributylphosphine to the catalyst system (more α).



$$\mathrm{CH_2{=}\overset{\displaystyle CH_3}{\overset{|}{C}}COOCH_3 + H_2 + CO \longrightarrow \underset{\alpha}{CH_3\underset{\displaystyle CHO}{\overset{\displaystyle CH_3}{C}}COOCH_3} + \underset{\beta}{\underset{\displaystyle CHO}{CH_2}\overset{\displaystyle CH_3}{C}HCOOCH_3}}$$

The hydroformylation of pent-1-ene with a rhodium carbonyl tri-*n*-butylphosphine complex catalyst at a temperature of 195° and total pressure of 450 psi has been reported by Slaugh and Mullineaux.[7] These workers obtained an aldehyde mixture which consisted of 72.1% *n*-hexanal and 27.9% branched-chain isomers. This result is similar to that of Osborn, Wilkinson, and Young,[8] who obtained a 70–20 product mixture with the use of a rhodium chloride–triphenylphosphine complex, and also similar to a result obtained in this investigation, *i.e.*, a 69–31 product percentage from the use of a rhodium–carbonyl–triphenyl phosphite complex.

Results and Discussion

We have found that under certain critical combinations of reaction parameters, very high percentages of linear aldehydes are obtained from the rhodium-catalyzed hydroformylation of α olefins. A typical example of conditions and results is temperature, 80°;

$$\underset{1\ \mathrm{mol}}{\text{oct-1-ene}} + \mathrm{CO} + \mathrm{H_2} \longrightarrow \underset{80\%}{n\text{-nonanal}} + \underset{13.3\%}{\text{isononanals}}$$

pressure of 1:1 H_2:CO, 80–100 psig; catalyst, 15 g of 5% Rh/C and 15 g $P(OC_6H_5)_3$; solvent, toluene. It should be emphasized that this set of experimental conditions, and many of those disclosed in the follow-

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[1] Presented, in part, at the 154th National Meeting of the American Chemical Society, Chicago, Ill., Sept 1967.

[2] This statement does not always apply to tetrasubstituted olefins [A. J. M. Keulemans, A. Kwantis, and Th. van Bavel, *Rec. Trav. Chim. Pays-Bas*, **67**, 298 (1948)], but since the olefins of this investigation are terminal, there is no contradiction.

[3] M. Johnson, *J. Chem. Soc.*, 4859 (1963).

[4] F. Piacenti, P. Pino, R. Lazzaroni, and M. Bianchi, *J. Chem. Soc., C*, 486 (1966).

[5] V. L. Hughes, U. S. Patent 2,880,241 (March 31, 1959).

[6] J. Falbe and N. Huppes, *Brennstoff-Chem.*, **48**, 46 (1967).

[7] L. H. Slaugh and R. D. Mullineaux, U. S. Patent 3,239,566 (March 8, 1966).

[8] J. A. Osborn, G. Wilkinson, and J. F. Young, *Chem. Commun.*, 17 (1965).

ing tables, are not necessarily optimum for making linear aldehydes. The intent of the experiments was to determine the effects of varying reaction conditions, and to relate these effects with a mechanistic model. It should also be noted that, although the examples described in this paper utilize rhodium on carbon as the metal catalyst source, the actual method of introduction is relatively unimportant. In any case the metal which dissolves is the actual catalyst; the rhodium on carbon was chosen for the sake of convenience. Preformed $HRh(CO)(PPh_3)_3$ acted in an identical manner; in this case a homogeneous, yellow solution was maintained throughout the reaction.

The product distribution was highly dependent on the total pressure of 1:1 H_2:CO gas. Some results are shown in Table I.

TABLE I
HYDROFORMYLATION OF OCT-1-ENE AT VARIOUS PRESSURES[a]

Psig (1:1 H_2:CO)	Reaction time, min	% aldehyde which is straight chain[b]
80–100	50	86
280–300	20	80
560–600	25	74
2500	25	69

[a] Octene (112 g), 5% Rh/C (15 g), triphenyl phosphite (15 g), toluene (200 ml), temperature 90°. [b] In these experiments, as well as those cited in tables following, the percentages are accurate to within 1%.

Even more striking are the results obtained with methyl methacrylate. The work of Falbe and Huppes[6] has demonstrated the controlled addition to the α-carbon atom with the catalyst system rhodium–tri-*n*-butylphosphine and with high pressure of hydrogen and carbon monoxide. The effects of incrementally lowering the pressure are shown in Table II.

TABLE II
HYDROFORMYLATION OF METHYL METHACRYLATE AT VARIOUS PRESSURES[a]

Psig (1:1 H_2:CO)	Reaction time, min	Ratio of β:α
2500		0.3:1[b]
450–470	180	2.0:1
220–240	124	5.2:1
110–114	110	24:1

[a] Methyl methacrylate (29.3 g), 5% Rh/C (1.3 g), triphenyl phosphite (1.2 g), toluene (146 g), temperature 100–110°. [b] The catalyst concentration was slightly different in this particular case, but not sufficiently so as to change the results.

Even at a low total pressure, variances in the partial pressures of the hydrogen and carbon monoxide from a ratio of 1:3 to a ratio of 3:1 produced significant changes in the product composition; the aldehyde produced was 79% straight chain in the former case and 90% in the latter.

The product distribution was also sensitive to the concentration of phosphorus ligand, although the effect leveled off at higher ligand concentrations. The results obtained by varying this reaction parameter are given in Table III.

All the prior discussion has been directed toward the effects of variables on the product composition with the use of a single phosphorus ligand, triphenyl phosphite.

TABLE III
HYDROFORMYLATION OF OCT-1-ENE WITH VARYING CONCENTRATIONS OF LIGAND[a]

$P(OC_6H_5)_3$, g	Reaction time, min	% aldehyde which is straight chain
0[b]	180	31
5.0	30	74
15.0	50	86
30.0	35	87
60.0	65	89

[a] Octene (112 g), 5% Rh/C (15 g), toluene (200 ml), temperature 90°, pressure 80–100 psig of 1:1 H_2:CO. [b] In the absence of phosphorus ligand, the reaction would not proceed at the cited conditions of temperature and pressure; slightly more severe conditions were required.

It was expected that changes in the nature of the phosphorus compound would also affect the results obtained, and this was proved to be the case.

The nature of the P(III) ligand was changed in two ways. The electronegativity of the group attached to P was changed; this would be expected to change the σ donor and π acceptor qualities of the phosphorus atom. The bulkiness of the phenyl groups in triphenyl phosphite was changed by attaching various groups in the *ortho* position(s); this would be expected to change the steric requirements of the R_3P ligand. The pronounced changes in products obtained in this manner are shown in Table IV.

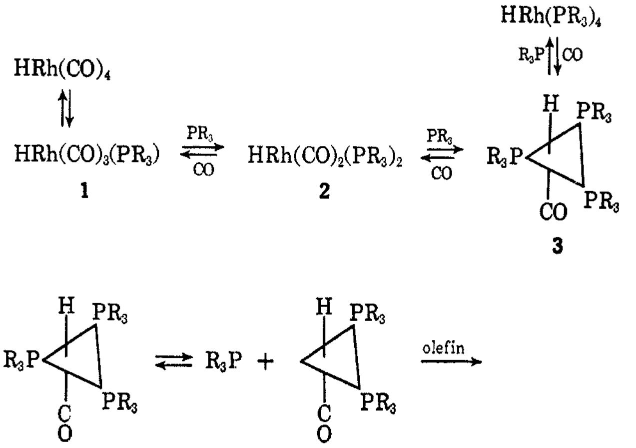
TABLE IV
HYDROFORMYLATION OF OCT-1-ENE WITH VARIOUS TRISUBSTITUTED PHOSPHORUS LIGANDS[a]

Nature of R in R_3P	Temp, °C	Reaction time, min	% aldehyde which is straight chain
n-Butyl	90	225	71
Phenyl	90	35	82
n-Butoxy	110	60	81
Phenoxy	90	50	86
o-Methylphenoxy	90	52	78
o,o-Dimethylphenoxy	90	80	47
o-Phenylphenoxy	90	95	52
p-Phenylphenoxy	90	70	85
p-Chlorophenoxy	90	55	93
p-Methoxyphenoxy	90	270	83

[a] Octene (112 g), toluene (200 ml), 5% Rh/C (10 g), R_3P (0.05 mol), pressure 80–100 psig of 1:1 H_2:CO.

In view of the effects produced by changes in the reaction conditions, as noted in the preceding discussion, it seems clear that the product composition bears a direct relationship with the ability of the phosphorus ligand to compete successfully with carbon monoxide in a multisubstituted species.

In solution, all species of type **1**–**2**–**3** probably exist. The one which predominates is determined by carbon monoxide concentration (pressure), ligand concentration, and the nature of R_3P. High pressures of CO would result in a trend **3** → **2** → **1** whereas raising the relative concentration of R_3P would cause the opposite shift, **1** → **2** → **3**. The trend toward **3** would be favored if R_3P has good back-bonding ability, thus being able to prevent excess charge build-up on the Rh(I) atom. This explains the large difference between trialkylphosphine and triaryl phosphites. In those cases involving heavy steric interference, as exemplified by tris(*o*-methylphenyl) phosphite, tris(*o*,*o*-dimethylphenyl) phosphite, and tris(*o*-phenylphenyl) phosphite, species **3** is in all probability nonexistent. Species **2** may even be open to question in such cases.

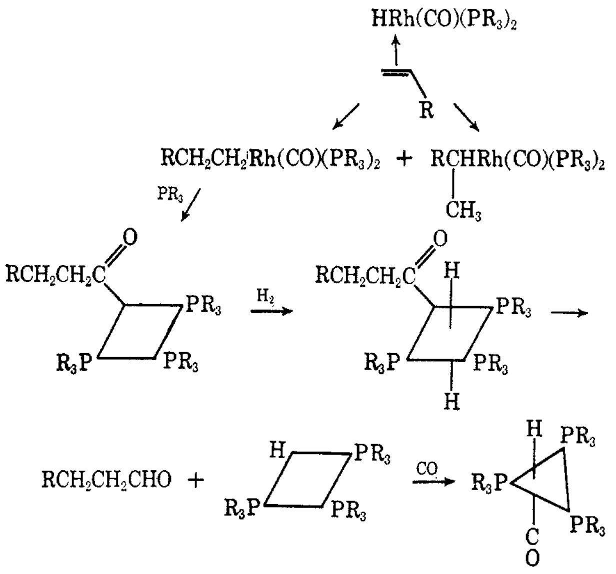


It is further theorized that each species results in an individual reaction rate and a characteristic product distribution. The most significant one, probably **3**, gives a predominance of straight-chain aldehyde. The indications are that steric crowding is mainly responsible for the linear predominance, although electronic interactions may play a slight role.

Attempts were made to characterize species **1** and **2**. Species **3**, in which R = Ph, is a well-defined compound[9] and was useful as a catalyst in the present investigation. Subjecting **3** to simulated reaction conditions (100 psig 1:1 H_2:CO at 80° in cyclohexanone solvent) in the presence of incrementally decreasing amounts of triphenylphosphine caused a strengthening of the carbonyl ir absorption band(s) and shifted them to shorter wavelengths. The CO absorption band of the complex is weak at 1926 cm^{-1}. Heating as outlined above, in the presence of triphenylphosphine concentrations of 10–20 wt % in cyclohexanone, produced a strong doublet absorption at 1930–1960 cm^{-1}. A further decrease in concentration to 5–10 wt % triphenylphosphine resulted in a solution with a strong principal absorption at 1980 cm^{-1}. Both the increase in intensity and direction of shift are consistent with a change in species from **3** toward **1**.

The mechanism postulated for cobalt-catalyzed hydroformylations,[10] with some slight modifications, is reasonable for the pathway of this series of reactions (Scheme I).

SCHEME I



The critical step, as concerns the relative amounts of *n*- and isoaldehydes formed, is the rearrangement of the π-bonded olefin to the σ-bonded *n*- or isoalkyl (step 3 above).

Falbe[11] has attributed the lower selectivity of rhodium, as compared to cobalt, to the larger size of the rhodium. This lessens the steric crowding of the individual ligands surrounding the central atom. However, as each carbon monoxide is successively replaced by the bulky P(III) ligand, the steric crowding and competition increases sharply. Thus even the hydroformylation of the strongly polarized methyl methacrylate, which is electronically controlled under normal circumstances, becomes sterically controlled in the presence of excess triphenyl phosphite. The tremendous reaction rate obtained in the rhodium-catalyzed hydroformylation, also attributed by Falbe to the lack of steric crowding around the larger rhodium atom, is also partially neutralized by excess phosphorus ligand.

Experimental Section

Materials.—Triphenyl phosphite and tributyl phosphite were used as purchased from Matheson Coleman and Bell. Triphenylphosphine and tributylphosphine were purchased from Carlisle Chemical Co. The tributylphosphine was redistilled under nitrogen before use. The triaryl phosphites were prepared by reaction of phosphorous trichloride with the appropriate substituted phenol in ether with N,N-dimethylaniline as the hydrogen chloride acceptor, as reported previously.[12] The crude triaryl phosphites were purified by vacuum distillation or by recrystallization, as appropriate. Such purification was necessary as the presence of amine hydrochloride has a deleterious effect on the reaction. Oct-1-ene was used as purchased from Phillips Petroleum Co. ("pure" grade).

General Procedure for Hydroformylations.—A 3-l. autoclave was charged with octene in toluene and with the appropriate amount of P(III) ligand and rhodium catalyst. The autoclave was sealed, placed in a rocking heater (American Instrument Co.), and flushed with carbon monoxide to remove the contained air. Hydrogen and carbon monoxide were added to give the desired pressure. Rocking was started and heat applied. The temperature was controlled at the desired temperature (usually 90°); reaction began at 75° in most cases. When the pressure had dropped to the lower limit of the desired range (80 psig in the 80–100-psig experiments), rocking was stopped while equal pressures of hydrogen and carbon monoxide were added in sufficient quantity to reach the upper pressure limit.

This same procedure has been conducted in a glass Fisher-Porter apparatus, with the contents being stirred magnetically. Thus the hydroformylation reaction may now be adapted to ordinary laboratory procedures, and it provides a very convenient

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[9] (a) S. S. Bath and L. Vaska, *J. Amer. Chem. Soc.*, **85**, 3500 (1963); (b) S. J. LaPlaca and J. A. Ibers, *ibid.*, **85**, 3501 (1963).

[10] (a) R. F. Heck and D. S. Breslow, *ibid.*, **83**, 4023 (1961); (b) R. F. Heck, *Advan. Organometal. Chem.*, **4**, 243 (1966).

[11] J. Falbe, "Synthesen mit Kohlenmonoxide," Springer-Verlag, Berlin, 1967, p 4 ff.

[12] A. E. Arbuzov, G. Kamai, and L. V. Nesterov, *Chem. Abstr.*, **51**, 5720*f* (1957).

method for preparation of terminal aldehydes, from which acids, alcohols, amines, and other derivatives may easily be derived.

Analysis of Products. A. From Methyl Methacrylate.—The two aldehydes, methyl α-formyl isobutyrate and the corresponding β-formyl isomer, were separated by distillation in a 3-ft spinning band column. The former distilled at 50–53° (6–8 mm), the latter at 60–63° (7 mm). The α-isomer was characterized by a singlet aldehydic hydrogen at 9.7 ppm (relative to tetramethylsilane, spectrum obtained on a Varian A-60). The β isomer was characterized by a triplet at 9.8 ppm.

After the original separation and identification of the individual constituents, which provided authentic samples of both forms, most subsequent analyses were made directly on the crude reaction mixture, by vpc techniques. A Barber–Colman Model 20 instrument fitted with a hydrogen flame detector was used, with a 200-ft capillary column coated with Dow-Corning 550 silicone fluid, at an oven temperature of 100°. The α isomer was eluted first; aldehyde ratios were determined directly by the areas under the respective peaks. Aldehyde yields were determined by distillation in a few cases, although loss by polymerization was always encountered. A representative yield is 74% with <5% loss to methyl isobutyrate.

B. From Oct-1-ene.—As in the previous case, distillation was used to provide authentic reference samples of nonanals. The linear isomer distilled at 100° (37 mm), the isononanal(s) distilled a few degrees lower but pure samples of the latter were never obtained. The linear aldehyde was characterized by the triplet nmr absorption at 9.77 ppm; samples rich in α-methyloctanal showed a doublet at 9.65 in addition to the triplet.

In the earliest work, vpc analyses were made on the Barber–Colman Model 20 instrument fitted with the column and detector described in the previous section. At 100°, all of the individual isomeric aldehydes present were resolved. In cases in which the yield of *n*-aldehyde was comparatively low, as in the first example of Table III, three compounds were eluted rapidly in succession followed by the fourth after an appreciable time interval. The fourth peak was identified as being that for *n*-nonanal and in all likelihood the third was 2-methyloctanal, with the other two being 2-ethylheptanal and 2-propylhexanal.

For convenience sake, most analyses were conducted with the use of a Varian Aerograph Series 202 instrument. The column was 0.25 in. × 5 ft, packed with 20% Carbowax 20M on Gas Chrom P 60/80. The oven temperature was 160°, programmed to 225° after elution of hydrocarbon. This gave a rapid determination; all isoaldehydes were under one peak, which was followed immediately by the peak for the linear aldehyde.

The major by-product of the reaction is formed by isomerization of oct-1-ene to oct-2-ene. In a typical case the yield of *n*-nonanal was 80%, of 2-methyloctanal 13%, and 7% oct-2-ene. In the experiments involving methyl methacrylate, the major by-product was the hydrogenation product. In all cases the yields of aldehydes were in the range of 72–84%.

Registry No.—Oct-1-ene, 111-66-0; tris(triphenyl phosphite)rhodium carbonyl hydride, 18346-73-1; methyl methacrylate, 80-62-6.

The Enamine Chemistry of 2,3,4,6,7,12-Hexahydroindolo[2,3-*a*]quinolizine. I. Reaction with α,β-Unsaturated Aldehydes and Ketones[1]

Robert N. Schut, Frederick E. Ward, and T. J. Leipzig

Therapeutics Research Division, Miles Laboratories, Inc., Elkhart, Indiana

Received June 4, 1968

The reaction of 2,3,4,6,7,12-hexahydroindolo[2,3-*a*]quinolizine (2) with various electrophilic olefins has been investigated. With acrolein, the pentacyclic system **4a** is formed. Methyl vinyl ketone, on the other hand, undergoes cycloaddition to give the pentacyclic system **13**.

Our interest in the synthesis of compounds structurally related to the indole alkaloids eburnamine (**1a**) and vincamine (**1b**) led us to investigate the reaction of 2,3,4,6,7,12-hexahydroindolo[2,3-*a*]quinolizine (**2**) with various electrophilic agents. In this paper, we wish to describe the results of the reaction of compound **2** with acrolein and methyl vinyl ketone.

It was expected that compound **2** would behave like an enamine derived from a cyclic ketone and reaction would take place at C_1 of the quinolizine system. After the initial 1,4 addition to an electrophilic olefin, the charge on the transient species is dissipated either by proton transfer and generation of a substituted enamine or by cycloaddition.[2] However, in the case of compound **2**, the indole nitrogen could react with the carbonyl group of the intermediate substituted enamine to form a pentacyclic system. In a similar situation, Wenkert and coworkers[3] reported that the intermediate obtained by addition of ethyl iodoacetate to the indole-enamine **3** cyclized on heating to give (after hydrogenation) epieburnamonine (**1c**).

The addition of acrolein to **2** in tetrahydrofuran–benzene solution was slightly exothermic; the product which precipitated in 82% yield was a monoadduct. It has been demonstrated that the reaction of enamines with acrolein can lead to aminodihydropyrans[4,5] (*cf.* compound **5**); however, the infrared spectrum of the adduct showed OH but no indole N–H or carbonyl absorption while the ultraviolet spectrum exhibited a maximum at 315 mμ characteristic of the conjugated system in 2,3,4,6,7,12-hexahydroindolo[2,3-*a*]quinolizines.[6] Thus it was apparent that the indole nitrogen had interacted with the aldehyde function to give the pentacyclic system **4a** wherein the newly formed ring is seven membered. Analogous results were obtained when crotonaldehyde or methacrolein were substituted for acrolein (compounds **4b** and **4c**) (Chart I).

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[1] Presented in part at the First International Congress of Heterocyclic Chemistry, Albuquerque, N. M., June 12, 1967.

[2] For a review of the reactions of enamines with electrophilic olefins, see J. Szmuszkovics, *Advan. Org. Chem.*, **4**, 27 (1963).

[3] E. Wenkert and B. Wickberg, *J. Amer. Chem. Soc.*, **87**, 1580 (1965).

[4] G. Optiz and I. Löschmann, *Angew. Chem.*, **72**, 523 (1960).

[5] R. N. Schut and T. M. H. Liu, *J. Org. Chem.*, **30**, 2845 (1965).

[6] (a) H. Zinnes, R. A. Comes, and J. Shavel, Jr., *J. Org. Chem.*, **30**, 105 (1965); (b) R. N. Schut and T. J. Leipzig, *J. Heterocycl. Chem.*, **3**, 101 (1966).