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HYDROFORMYLATION OF NITROGEN-CONTAINING CYCLIC OLEFINS VIA "in-situ" RHODIUM-PHOSPHINE CATALYSTS

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Summary

Hydroformylation of nitrogen-containing cyclic olefins (*N*-substituted nortropidines, *N*-methyl-1,2,3,6-tetrahydropyridine (THP)) with rhodium-PR_3 catalysts prepared "in situ" is reported. The nortropidines reacted rapidly when either trialkyl- or triaryl-type phosphines were used, and the regioselectivities were not significantly influenced by the nature of the phosphine. With the less basic THP the rates and selectivities were generally lower, and were influenced by the phosphine ligand and by the presence of added bases such as Et_3N.

Introduction

Hydroformylation of various substrates with rhodium-phosphine catalysts have been described [1–3]. Nitrogen bases, especially tertiary amines have been found to be effective additives in these reactions [4–7], but their influence has not been studied systematically, and this is especially the case for the hydroformylation of cyclic olefins containing nitrogen.

Stille et al. [8] observed great selectivities and high rates in hydroformylation of *N*-acyl-2-pyrroline with $HRh(CO)(PPh_3)_3$ as catalyst. Evans and co-workers [9] examined the oxo-synthesis of several *N*-containing heterocyclic substrates with $HRh(CO)(PPh_3)_3$ as catalyst, and determined regio- and stereoselectivities as well as the extent of side-reactions and their dependence on the reaction conditions. We have also studied some of these compounds [10]. Our catalysts were prepared "in situ" from suitable precursors, and phosphines of various structures were chosen on the basis of previous studies [11–14] on stereoselective hydrogenation of nitrogen-containing cyclic ketones which revealed the decisive role of phosphine basicity and the influence of basic additives on the formation of the active mono- and dihydrido-rhodium species. The present investigation was aimed at providing some evidence of the value of these catalytic systems in selective hydroformylation reactions.

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Results and discussion

Hydroformylation of tropidine ($pK_a = 10.2$) and nortropidine derivatives with rhodium-phosphine catalysts prepared "in situ" occurs readily in benzene solution under the conditions specified in Table 1. The regio- and stereoselectivities are rather high, and the major products are 3-substituted equatorial aldehydes. Parallel and subsequent reactions are negligible. The regioselectivity is only slightly influenced by changing the phosphine ligand from the highly basic PBu_3 to PPh_3, and addition of Et_3N ($pK_a = 10.3$) does not alter the product distribution in accord with our earlier observation on hydrogenation of tropinone where the strongly basic substrate played a role equivalent to that of Et_3N [12]. We assume that abstraction of HCl from carbonylated rhodium-phosphine-chloro complexes under hydroformylation conditions occurs very easily independent from the nature of the phosphine ligand and that monohydrido-rhodium-carbonyl-phosphine complexes are the active catalysts. Replacement of the *N*-methyl group in tropidine by bulky substituents only slightly influences the selectivity. In a detailed study of hydroformylation of tropidine the phosphine ligands were varied over a wide range of Tolman's electronic parameters [15] and steric requirements [16] (Table 2). Phosphines of low cone angle form the active monohydrido-carbonyl-phosphine complexes mentioned earlier. With bulky but basic ligands no significant change in R_s value is detected suggesting the same type of active catalysts are involved, but, as expected, the rates are lower. Catalysts formed from bulky phosphines of low basicity (run 6, 7 in Table 2) promote reduction of aldehydes and formation of cyclic alcohols. Similar results were achieved with non-substituted rhodium-carbonyl catalysts (run 1, 2 in Table 3) or with catalytic systems of low P/Rh ratio (run 3). An increase in this ratio changed the product distribution significantly (run 4), preventing reduction of

TABLE 1

HYDROFORMYLATION OF NORTROPIDINES [a]

Substrate	Catalyst	Conversion (%)	R_s [b] (%)	Product distribution			
				2-subst. aldehyde (%)	3-subst. aldehyde (%)	Tropane deriv. (%)	Alcohols (%)
Tropidine	$HRh(CO)(PPh_3)_3$	92	90	10	86	2	2
	$[Rh(NBD)Cl]_2 + PPh_3$	94	89 [c]	11	87	1	1
	$[Rh(NBD)Cl]_2 + PBu_3$	93	95 [d]	5	92	2	1
	$[Rh(NBD)Cl]_2 + PPh_3 + Et_3N$	90	89	11	88	<1	<1
	$[Rh(NBD)Cl]_2 + PBu_3 + Et_3N$	90	95	5	93	1	1
N-i-Pr-nor-tropidine	$[Rh(NBD)Cl]_2 + PPh_3$	86	96	4	92	2	2
	$[Rh(NBD)Cl]_2 + PBu_3$	80	95	5	93	1	1
N-CH_2Ph-nor-tropidine	$[Rh(NBD)Cl]_2 + PPh_3$	88	> 99	<1	95	3	<1
	$[Rh(NBD)Cl]_2 + PBu_3$	79	> 99	<1	90	8	<1

[a] 100°C, 80 bar ($CO/H_2 = 1/1$), 6 h; $Rh/P/Et_3N/olefin = 1/3/5/20$; 1 mmol substrate in 5 ml benzene. [b] $R_s = \frac{\text{3-substituted (symmetrical) aldehyde}}{\text{total aldehyde}} \times 100$. [c] 84% 3-equat., 5% 3-ax., 3% 2-equat., 8% 2-ax. aldehyde (determined by ^1H NMR). [d] 94% 3-equat., 1% 3-ax., 1% 2-equat., 4% 2-ax. aldehyde (determined by ^1H NMR).

TABLE 2

HYDROFORMYLATION OF TROPIDINE WITH CATALYSTS PREPARED "in situ" CONTAINING VARIOUS PHOSPHINES [a]

Run	Phosphine	Phosphine parameters		Conversion (%)	R_s (%)	Product distribution			
		Electronic parameter (χ)	Cone angle (θ)			2-subst. aldehyde (%)	3-subst. aldehyde (%)	Tropane (%)	Alcohols (%)
1	$P(n\text{-}Bu)_3$	5.25	132	93	95	5	92	2	1
2	$P(i\text{-}Bu)_3$	5.7	139	91	92	8	89	2	1
3	PPh_3	13.2	145	94	89	11	87	1	1
4	$P(i\text{-}Pr)_3$	3.45	160	62	89	10	82	3	5
5	$P(c\text{-}Hex)_3$	1.4	170	9	86	11	67	22	0
6	P(neo-menthyl)Ph_2	9.7	170	91	93	2	31	7	60
7	$P(o\text{-Tolyl})_3$	10.6	194	100	90	0.4	3.6	0	96

[a] For reaction conditions see Table 1, footnote *a*.

TABLE 3

HYDROFORMYLATION OF TROPIDINE WITH VARIOUS CATALYSTS [a]

Run	Catalyst	Rh/P	Conversion (%)	Product distribution		
				Aldehydes (%)	Tropane (%)	Alcohols (%)
1	$Rh_4(CO)_{12}$	1/0	100	0	3	97
2	$[Rh(NBD)Cl]_2$	1/0	93	13	1	86
3	$[Rh(NBD)Cl]_2 + PBu_3$	1/1	99	4	0	96
4	$[Rh(NBD)Cl]_2 + PBu_3$	1/2	100	99 [b]	0	1

[a] For reaction conditions see Table 1, footnote *a*. [b] $R_s = 96\%$.

aldehydes. In contrast to the selectivities, the reaction rates are greatly influenced by the nature of the phosphine. This is evident also in hydroformylation of tropidine (Fig. 1) with catalytic systems from 20 different phosphine ligands. It is evident that catalysts containing non-bulky trialkyl- or triaryl-phosphines are the most active.

Hydroformylation of *N*-methyl-1,2,3-6-tetrahydropyridine was slower and gave moderate regioselectivities (Table 4). There are significant differences between the PPh_3- and PBu_3-containing catalytic systems in this reaction; for example, only the

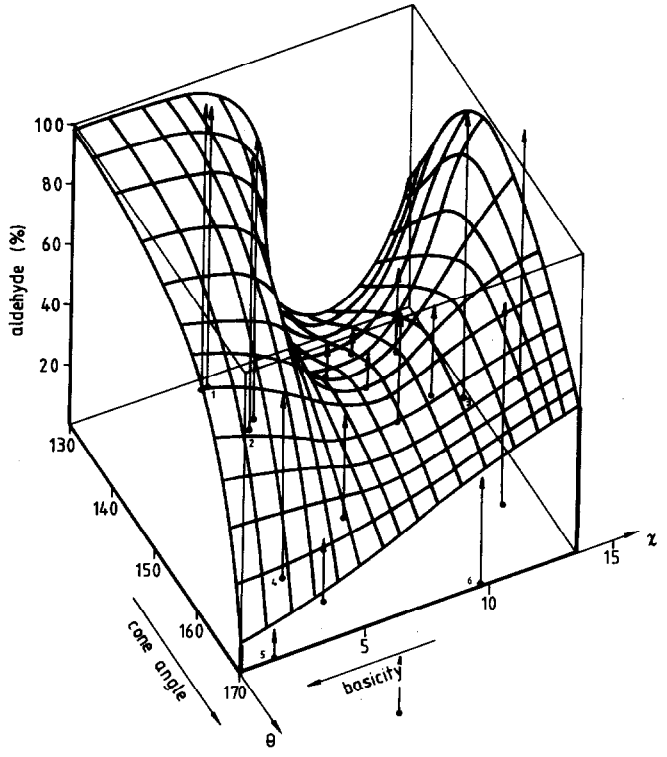

Fig. 1. Hydroformylation of tropidine with catalysts prepared "in situ" and containing various phosphines. The reaction conditions are specified in footnote *a* of Table 1, and the numbering of the phosphines (1–7) is as in Table 2.

TABLE 4

HYDROFORMYLATION OF *N*-METHYL-1,2,3,6-TETRAHYDROPYRIDINE [a]

Run	Catalyst	Conversion (%)	R'_s [b] (%)	Product distribution		
				3-subst. aldehyde (%)	4-subst. aldehyde (%)	*N*-methyl-piperidine (%)
1	$HRh(CO)(PPh_3)_3$	64	60	39	59	2
2	$[Rh(NBD)Cl]_2 + PPh_3$	60	58	41	56	3
3	$[Rh(NBD)Cl]_2 + PPh_3 + Et_3N$	59	57	40	52	8
4	$[Rh(NBD)Cl]_2 + PBu_3$	50	79	20	72	8
5	$[Rh(NBD)Cl]_2 + PBu_3 + Et_3N$	59	60	38	58	4
6	$[Rh(NBD)Cl]_2 + P(c\text{-}Hex)_3$	8	71	17	42	41
7	$[Rh(NBD)Cl]_2 + P(neo\text{-}menthyl)Ph_2$	60	61	11	18	71
8	$[Rh(NBD)Cl]_2 + P(o\text{-}Tolyl)_3$	59	59	1	2	97
9	$[Rh(NBD)Cl]_2$	64	–	0	0	100

[a] For reaction conditions see Table 1, footnote *a*. [b] $R'_s = \frac{\text{4-substituted (symmetrical) aldehyde}}{\text{total aldehyde}} \times 100$.

latter system is influenced by addition of Et_3N, which changes both the rate and the regioselectivity. This can be accounted for on the assumption that in the presence of the less basic substrate ($pK_a = 9.3$) HCl abstraction takes place in PPh_3-containing systems whereas in the case of PBu_3 there is an equilibrium between the monohydrido-rhodium-carbonyl species and the rhodium-carbonyl-chloro derivatives. Abstraction of HCl from latter is favoured by addition of the more basic Et_3N, the selectivity and activity thus being changed to those for mono-hydrido-rhodium-carbonyl-phosphine catalysts.

In systems containing bulky phosphines (run 7, 8), as for the non-substituted rhodium-carbonyl catalysts (run 9), hydrogenation of the substrate occurs rather than hydroformylation.

Mechanistic aspects of the reactions will be considered in a later paper.

Experimental

Materials

Benzene was dried and distilled under argon. The catalytic precursors $[Rh(NBD)Cl]_2$, $HRh(CO)(PPh_3)_3$, $Rh_4(CO)_{12}$ and phosphines were purchased from Strem Chemicals Inc., and *N*-methyl-1,2,3,6-tetrahydropyridine (THP) from Aldrich. Tropane derivatives were prepared by the Robinson–Schöpf synthesis followed by hydrogenation with $NaBH_4$ and dehydration by sulphuric acid.

Hydroformylation reaction (General procedure)

The catalytic system was prepared "in situ" under argon in a Schlenk tube from 0.025 mmol $[Rh(NBD)Cl]_2$ and 0.15 mmol phosphine in 5 ml benzene and injected together with 1 mmol substrate into a 20 ml shaking stainless steel autoclave flushed with argon.

A 1 : 1 mixture of carbon monoxide hydrogen (both supplied as pure) was introduced up to the desired pressure and raised to the chosen temperature. After 6 h reaction the autoclave was rapidly cooled, the gases discharged and the mixture

analysed by GLC. The aldehydes formed were studied by ^1H NMR spectroscopy after fractional distillation. GLC analyses were performed on a Hewlett-Packard 5830 chromatograph equipped with a 20 m × 0.25 mm i.d. glass capillary column coated with SP-2100 stationary phase (film-thickness 0.25 m) and a flame-ionization detector. Argon was used as carrier gas and the column temperature was programmed from 50 to 250°C at 10°C/min. ^1H NMR spectra were recorded in $CDCl_3$ on a Varian CFT-20 (80 MHz) spectrometer.

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