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Novel Oxyfunctionalized Phosphonite Ligands for the Hydroformylation of Isomeric *n*-Olefins

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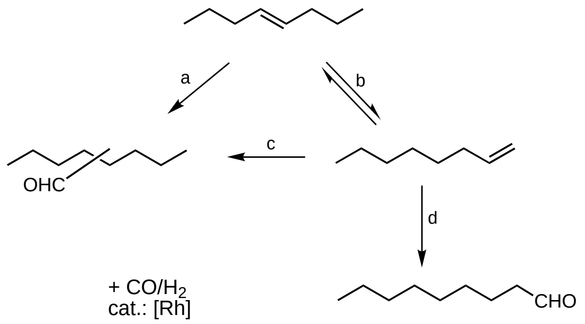
Hydroformylation (oxo synthesis) is one of the most important industrial procedures carried out under homogeneous catalysis. The high economic significance of this C–C coupling reaction results from the successful production of over six million tonnes per year of aldehydes and subsequent products for the plasticizer industry, with propylene as the most important reagent.[1] Knowledge gained from experience demonstrates the advantages of ester plasticizers with a low degree of branching and C-numbers from nine upwards for the alcohol components. An olefin raw material for this application is a technical octene mixture, for which complete conversion of all isomers present and control of regioselectivity to the benefit of terminal aldehyde products are of equal importance (Scheme 1). Hitherto, these two parameters could only be fulfilled by cobalt catalysis under severe reaction conditions. Characteristic productivities are 0.1–0.4 $t\,m^{-3}h^{-1}$ and selectivities for the terminal aldehyde of 50–85 %, which are achieved with 0.1–1 % Co at pressures of 80–350 bar and temperatures of 160–190 °C, as well as an undesirable and extensive hydrogenation activity.[1]



Scheme 1. Isomerizing hydroformylation of internal olefins with the example of 4-octene. a) hydroformylation, b) isomerization, c), d) hydroformylation.

The elimination of these disadvantages by, for example, the use of novel metal complexes, ligands, and technologies is one of the current demands placed upon this area. Highly selective rhodium catalysts based upon bidentate aryl phosphites and diphosphanes with a large coordination angle already exist for the conversion of terminal, long-chain olefins.[2] However, where internal olefins are concerned, technically useful activity is exhibited only with short-chain homologues such as 2-butene.[1,3] Thermally more stable diphosphanes with rigid, bidentate structure and a bias towards *trans* coordination give *n*-selectivities of up to 86 % *n*-nonanal from *trans*-octene-4 at very low turnover frequencies of 15 h^{-1}.[4] In the case of terminal olefins the regioselectivity targeted through the use of diphosphanes of selected structure under the assumption of irreversible olefin insertion may also be reasoned on theoretical grounds.[5] On the other hand, structure prediction for ligands which induce *n*-selectivity and, within the context of target position, necessarily also olefin isomerization is still nonexistent.

Esters of phosphonous acids have hitherto found little application as ligands in homogeneous catalysis.[6] There are examples of oxo reactions with the highly reactive propylene as reagent.[6c] Here we demonstrate that compounds of this class are highly suitable for the hydroformylation of long-chain olefins.

For our investigations we chose the readily available and conformationally flexible phosphonites **4a–d** and **5**, which in each case contain a second donor function in the 2′-position.

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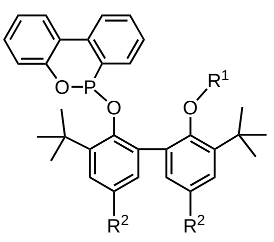
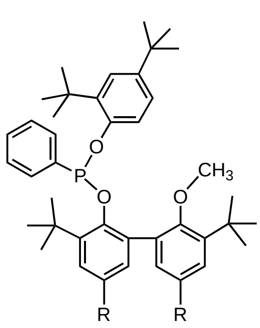
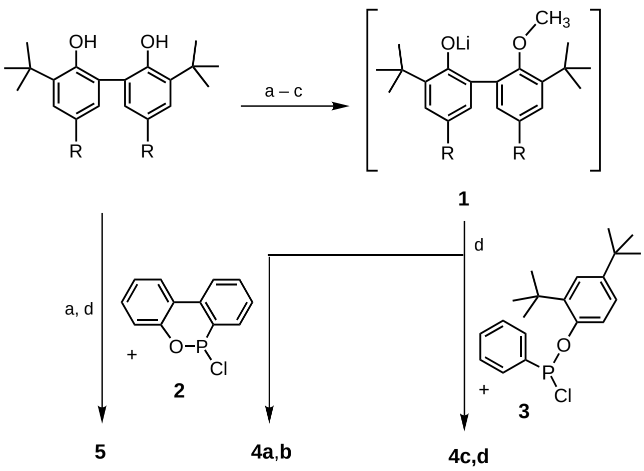


4a: $R^1=CH_3$, $R^2=OCH_3$
4b: $R^1=CH_3$, $R^2=$*tert*-C_4H_9
5 : $R^1=H$, $R^2=OCH_3$



4c: $R=OCH_3$
4d: $R=$*tert*-C_4H_9

The phosphonite ethers **4a–d** are obtainable from the corresponding bisphenols by partial deprotonation with benzyl potassium, subsequent etherification with methyl iodide, in situ formation of the lithium phenolate **1** with *n*-butyllithium, and finally reaction with 6-chloro-6*H*-dibenz[*c,e*]-1,2-oxaphosphorine (**2**)[7] or (2,4-di-*tert*-butylphenyl)phenylphosphonityl chloride (**3**; Scheme 2). Phenol **5** was prepared by reaction of the monopotassium salt of the corresponding bisphenol with **2**. The formation of diastereoisomers was confirmed spectroscopically for **4a–d** and **5**.[8]



Scheme 2. Synthesis of **4a–d** and **5**: a) C_7H_7K (1 equiv), THF, 30 min at 0 °C; b) CH_3I, THF, 8 h at 55 °C; c) *n*BuLi, THF/hexane, 30 min at −20 °C; d) reaction with **2** or **3**: 4 h at 25 °C; 55–85 %. Compound **2** was prepared as described in ref. [7], **3** by reaction of $PhPCl_2$ with 2,4-di-*tert*-butylphenol in the presence of pyridine in THF/Et_2O (85/15).

The catalytic properties of the new ligands was first tested for the hydroformylation of 1-octene (Table 1). Even at low rhodium concentrations of about 14 ppm, reactions with exceptionally high initial activities and almost quantitative conversions were obtained without detectable olefin hydrogenation and alcohol formation. With respect to the ligand effect, the most active catalysts proved to be the derivatives **4a**,**b**, and **5**, derived from the rigid oxaphosphorine **2**. Particularly notable is the catalyst with the phosphonite phenol **5**, a further prototype of a ligand class that has not yet been established in hydroformylation. On the basis of GC analysis and within the effective range of the recorded gas uptake an average turnover frequency of over 83 000 h^{-1} at up to 71 % conversion was measured. Additional information on the activity of the catalyst formed with **5** was provided by the investigation of temperature dependency (Table 2). Even at 60 °C a quantitative conversion with negligible double-bond isomerization of the substrate is realizable. The maximum *n*-selectivity at 80 °C can be explained by the different effects of *T* on the rate of isomerization of the substrate and the ratio of the rates of hydrogenolysis of the intermediate acylrhodium complexes (r_n/r_{iso}), should this be the rate-determining step of the catalysis.[9]

Table 1. Hydroformylation of 1-octene:[a] effect of the ligand.

Ligand	*t* [h]	Yield [%][b]	*n*/*iso*[b]	TOF [h^{-1}][c]
4a	1.5	97	1.22	> 46 000[d]
4b	1.5	93	0.90	> 46 000[d]
4c	3	89	0.66	17 570
4d	3	98	0.61	> 46 000[d]
5	1	94	1.03	> 83 600[d,e]

[a] The reactions were carried out in a 200-mL autoclave with $[\text{1-octene}]_0 = 1.692$ M at 120 °C in toluene under a constant pressure of 50 bar CO/H_2 (1/1) with [(acac)Rh(1,5-cyclooctadiene)] (acac = acetylacetonate anion) as catalyst precursor. [Rh] = 0.1078 mM, Rh:P:(1-octene) = 1:5:15 700. [b] Determined by gas chromatography, by *iso* all branched aldehydes are meant. [c] Turnover frequency in mol aldehyde per mol catalyst per hour at 20 % turnover, calculated on the basis of gas consumption measured with a Hitec gas flow meter from the company Bronkhorst (NL). [d] Limit of measurement range. [e] 71 % turnover in 8 min.

Table 2. Hydroformylation of 1-octene with **5**: temperature dependency.[a]

T [°C]	*t* [h]	Yield [%]	*n*/*iso*	Int. aldeh.[b]	TOF [h^{-1}][c]
120	1	94	1.03	+	83 600[d,e]
100	1	96	1.30	+	> 46 000[d]
80	1	92	1.57	(+)[f]	45 370
70	2	93	1.43	(+)[f]	24 020
60	4	98	1.39	–[g]	7070

[a] For the reaction conditions, except temperature, see Table 1. [b] 3-,4-Aldehydes after double-bond isomerization (determined by gas chromatography). [c]–[e] See footnotes [c]–[e] in Table 1. [f] 1.6 % (at 80 °C) or 0.5 % (at 70 °C) 2-ethylheptanal, no 2-propylhexanal. [g] 2-Octene chemoselectivity: 1.2 %.

Investigations on isomerizing hydroformylation were carried out with an *n*-octene mixture containing 3.3 % 1-octene, obtained by butene dimerization. At 140 °C and 20 bar—favorable conditions for olefin isomerization—about 35 % *n*-pelargonaldehyde was obtained with the catalyst formed with **4a**, with activity increasing in parallel with the P:Rh ratio used (Table 3).

A surprising result came from exchange of methyl ether **4a** with phenol **5** (Table 4). The *n*-selectivity increased above P:Rh ratios of 10:1 to more than 45 %.[10] The conversion rate measured at threefold olefin concentration corresponds to aldehyde yields of 287 $kg\,m^{-3}\,h^{-1}$.

The properties of the catalyst formed from **5** are currently being investigated in more detail. Of interest in this context are literature references on the inhibition of hydroformylation as well as on the increase in olefin isomerization activity

Table 3. Hydroformylation[a] of isomeric *n*-octenes[b] with **4a**: effect of the ligand:metal ratio.

P:Rh	Yield [%]	TOF [h^{-1}][c]	*n*-Nonanal [%][d]	ROH [%][e]
1:1	66	2270	35.1	2.2
2:1	82	3550	35.2	2.2
5:1	88	5350	35.1	2.2
10:1	93	7390	35.4	1.6

[a] For the procedure see footnote [a] in Table 1. Conditions: $T = 140\,^{\circ}C$; $p = 20$ bar CO/H_2 (1/1); $t = 6$ h. [b] 3.3% 1-octene, 48.4% (*Z*)- and (*E*)-2-octene, 29.2% (*Z*)- and (*E*)-3-octene, 16.4% (*Z*)- and (*E*)-4-octene, 2.1% skeletal octene isomers, 0.6% octane. [c] Turnover frequency at 20% conversion. [d] Fraction of the total amount of aldehydes (four isomers). [e] Total alcohol yield relative to the amount of olefin used. *n*-Octane selectivity: < 1.4%.

Table 4. Hydroformylation[a] of isomeric *n*-octenes[b] with **5**: effect of the ligand:metal ratio.

P:Rh	Yield [%]	TOF [h^{-1}][c]	*n*-Nonanal [%][d]	ROH [%][e]
1:1	21	540	31.7	0.6
5:1	38	1000	41.0	1.4
10:1	52	1320	47.8	1.4
20:1	77	3120	45.9	2.0
50:1	86	2840	47.9	0.8
50:1[f]	73	18710	41.8	0.8

[a]–[e] See footnotes [a]–[e] in Table 3. [f] $[\text{Octene isomers}]_0 = 5.08\,\text{M}$.

upon use of rhodium catalysts with phosphane ligands that were functionalized with Brønstedt acids.[11, 12] Variation of the active proton group in **5** with respect to donor capability and acidity (SH, COOH, etc.) and the ring size of a potentially hemilabile chelate complex offers potential for further ligand modification.[13]

The results presented here show for the first time that the productivities and selectivities of the technically established high-pressure processes with rhodium catalysts can be achieved with greatly reduced metal concentration and mild reaction conditions (ca. 20–50° lower in temperature and ca. 60–330 bar lower in pressure) and even exceeded with respect to suppression of hydrogenation activity. The introduction of additional oxy groups into monodentate phosphorus ligands ensures at the same time the necessary high isomerization activity of the catalyst and the tendency towards hydroformylation at the chain end. This generally exceeds the optimistic estimates of the potential development of rhodium catalyst for the isomerizing hydroformylation of internal olefins.[4, 10]

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First Noncovalently Bound Calix[4]arene–Gd^{III}–Albumin Complex

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Gadolinium(III) in its chelated form has long-been recognized as being useful as a contrast enhancement agent in magnetic resonance imaging (MRI) because of its f^7 electronic configuration and long relaxation time. Noncovalent attachment of low molecular weight Gd^{III} complexes to serum

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