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Phosphabarrelene–rhodium complexes as highly active catalysts for isomerization free hydroformylation of internal alkenes†

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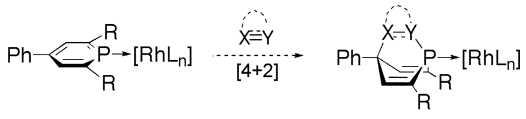
A new class of phosphabarrelene–rhodium catalysts is described which allows for the first time hydroformylation of internal alkenes with very high activity and which proceeds essentially free of alkene isomerization.

Hydroformylation of alkenes is an industrially important process relying on homogeneous catalysis and a synthetically attractive carbon–carbon bond forming reaction meeting the criteria of atom economy.[1,2] However, a number of selectivity issues remain to be solved among which the challenge of chemoselective low pressure hydroformylation of internal alkenes is an industrially and synthetically important one.[2] Previous research by van Leeuwen *et al.* has identified bulky monodentate phosphite–rhodium catalysts as highly active catalysts for hydroformylation of di- and trisubstituted alkenes.[3] Recently, phosphonite systems have been reported to show similar behavior.[4] Unfortunately, the lability of phosphites towards hydrolysis and a tendency to undergo degradation reaction have hampered their technical use. In order to circumvent catalyst stability problems we developed monodentate phosphabenzene–rhodium catalysts **1** for the efficient low pressure hydroformylation of terminal and internal alkenes.[5]

All of the catalysts designed for hydroformylation of internal alkenes show simultaneously a rather high activity towards alkene isomerization. This behavior may be desirable if an isomerizing hydroformylation is the goal.[4,6] However, if a position selective hydroformylation of an internal alkene is the desired synthetic transformation, hydroformylation accompanied by alkene isomerization represents a significant synthetic problem. To the best of our knowledge an efficient catalyst to circumvent this problem is so far unknown.

We herein report on a new class of phosphabarrelene–rhodium catalysts **2** which display very high activity towards hydroformylation of internal alkenes with an unusually low tendency towards alkene isomerization.



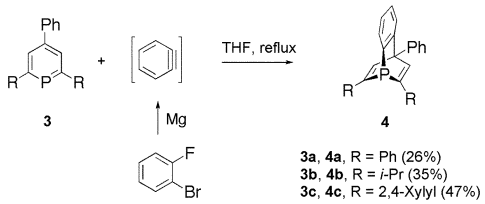
1 **2**

In previous studies on phosphabenzene–rhodium catalysts **1** we observed that hydroformylation activity is controlled significantly by the steric demand of the donor ligand.[5] Hence, it was of interest to probe the effect of expanding a planar phosphabenzene skeleton into a "third dimension". Thus, Diels–Alder addition of a reactive dienophile to the phosphabenzene nucleus would generate a phosphabarrelene cage. A few systems of this structure are known from the work of G. Märkl,[7] but have never been explored as ligands in homogeneous catalysis.

Addition of benzyne, generated *in situ* from *ortho*-bromofluorobenzene, to phosphabenzenes **3** furnished the phosphabarrelenes **4a–c** in moderate to fair yield as air stable colorless crystalline compounds (Scheme 1).

X-ray crystal structure analysis of **4a** (Fig. 1) revealed a strong pyramidalization at the phosphorus atom (**4a**: Σ (CPC) = 283° compared to PPh_3: Σ (CPC) = 308°).[8] This should result in a higher s-character of the P-lone pair of **4** which should render the phosphabarrelene a weaker σ-donor ligand and a better π-acceptor ligand compared to a corresponding strain free phosphane.[9]

Catalyst performance was tested upon hydroformylation of internal cyclic olefins first, because it allows monitoring of hydroformylation activity undisturbed by alkene isomerization (Table 1). In both cases (n = 1, 2) the phosphabarrelene–rhodium catalyst (Rh/**4c**) performed with the highest activity. Turnover frequencies up to 12000 h^{-1} were observed. In the case of



Scheme 1 Preparation of phosphabarrelenes **4**.

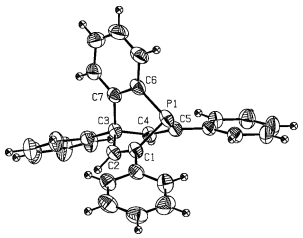
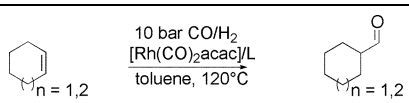


Fig. 1 X-ray plot of the structure of **4a** in the solid state.

Table 1 Results of the hydroformylation of cyclohexene and cycloheptene with $[Rh(CO)_2acac]$/L at 120 °C, 10 bar (CO/H_2, 1 : 1) in toluene (c_0 = 3.56 M) after 10 min (cycloalkene/L/Rh, 4160 : 20 : 1)



Entry[a]	L	Substrate	Conversion (%)[b]	TOF/h^{-1}
1	PPh_3	n = 1	0.04	11
2	**3c**	n = 1	8	1906
3	**4a**	n = 1	2.8	707
4	**4b**	n = 1	3.5	875
5	**4c**	***n* = 1**	**46**	**11429**
6	PPh_3	n = 2	5	1228
7	**3c**	n = 2	4	918
8	**4c**	***n* = 2**	**49**	**12231**

[a] All catalysts were preformed at 5 bar CO/H_2 (1 : 1) for 30 min at reaction temperature. The reaction was started by injection of the alkenic substrate. [b] Conversion was determined after 10 min reaction time in every case by GC analysis; TOF = turnover frequency of aldehyde formation.

† Electronic supplementary information (ESI) available: an experimental procedure for the preparation of phosphabarrelene **4c** as well as for the performance of hydroformylation reactions. See http://www.rsc.org/suppdata/cc/b3/b315709a/

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cyclohexene Rh/**4c** is even six times faster than Rh/phosphabenzene **3c** and 1000 times faster than Rh/PPh_3 – one of the industrially employed hydroformylation catalysts.

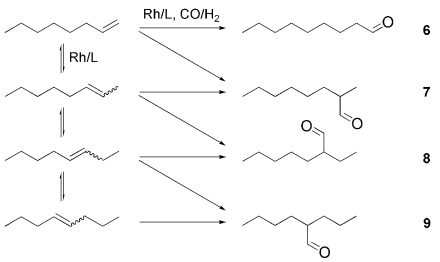
To evaluate the catalysts' tendency to undergo isomerization upon hydroformylation of internal alkenes 2-octene was selected for study. Formation of nonanal (**6**) and/or 2-propylhexanal (**9**) would indicate alkene isomerization prior to hydroformylation (Scheme 2).

Thus, hydroformylation of 2-octene was performed at 70 °C and a syngas pressure of 10 bar with rhodium catalysts prepared from phosphabarrelenes **4a–c** and the results are compared to those obtained from rhodium catalysts derived from triphenylphosphane, triaryl phosphite P[O(2,4-di-*t*BuC_6H_3)$_3$] (**5**) and phosphabenzene **3c** (Table 2).

As expected the standard industrial catalyst Rh/PPh_3 performed with low activity (see Table 2, entry 1). Employing catalysts designed for hydroformylation of internal alkenes, the Rh/phosphite (**5**) and the Rh/phosphabenzene (**3c**) systems, showed a remarkable activity with complete consumption of starting material. However, in both cases a significant amount of 2-propylhexanal and *n*-nonanal was formed, which indicates severe alkene isomerization prior to hydroformylation (Table 2, entries 2, 3). Conversely, the Rh/phosphabarrelene (**4c**) showed a high activity towards hydroformylation of the internal C/C double bond of 2-octene, but in this case hydroformylation occurs essentially free of alkene isomerization (Table 2, entry 4).

To see whether this unusual but synthetically useful behavior of the Rh/phosphabarrelene **4c** catalyst is more general, we looked also at heterocyclic alkenes which are known to isomerize easily.[10] Thus, hydroformylation of heteroatom-substituted cyclopentenes such as 2,5-dihydrofuran and *N*-Boc-pyrroline was examined and the results were compared with those obtained from the Rh/phosphite (**5**) catalyst (Table 3).

Both catalysts showed a remarkable activity upon hydroformylation of 2,5-dihydrofuran (Table 3, entries 1, 2). However, whereas the phosphite system produced 27% of the 2-aldehyde as a result of severe alkene isomerization, in the case of the xylylbarrelene the tendency towards isomerization is very low. Even better results were obtained in the case of the *N*-Boc-pyrroline. Here, the Rh/phosphite (**5**) catalyst furnished almost 20% of the 2-aldehyde arising from prior alkene isomerization. Conversely, the Rh/xylylbarrelene (**4c**) operated isomerization free to give the 3-aldehyde under very mild reaction conditions as the exclusive product (Table 3, entries 3, 4).



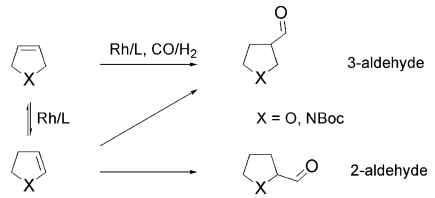
Scheme 2 Possible aldehydes from hydroformylation of 2-octene.

Table 2 Results of the hydroformylation of oct-2-ene (*E*/*Z* = 77 : 23) with [Rh(CO)$_2$acac]/L at 70 °C, 10 bar (CO/H_2, 1 : 1) in toluene (c_0 = 7.68 M) after 4 h (oct-2-ene/L/Rh, 7187 : 20 : 1)

Entry[a]	L	Oct-2-ene (%)[b]	Oct-3/4-ene (%)[b]	**6** (%)[b]	**7** (%)[b]	**8** (%)[b]	**9** (%)[b]
1	PPh_3	73.7	1.2	0.0	16.9	8.2	0.0
2	**5**	0.0	0.2	2.9	51.1	33.5	12.2
3	**3c**	0.5	3.9	6.4	54.1	22.4	12.7
4	**4c**	**4.5**	**2.0**	**0.0**	**57.6**	**35.7**	**0.2**

[a] See footnote *a* in Table 1. [b] Reaction mixture composition was analyzed by GC.

Table 3 Results of the hydroformylation of 2,5-dihydrofuran and *N*-Boc-pyrroline



Entry[a]	Substrate X =	L	3-aldehyde[b] (%)	2-aldehyde[b] (%)
1	O	**5**	67	27
2	**O**	**4c**	**79**	**6**
3	NBoc	**5**	82	18
4	**NBoc**	**4c**	**72**	**—**

[a] Conditions: with [Rh(CO)$_2$acac]/L at 50 °C, 10 bar (CO/H_2, 1 : 1) in toluene (c_0 = 1.537 M) after 4 h (substrate/L/Rh, 2011 : 20 : 1). [b] Determined by ^{1}H NMR, aldehyde selectivity 100% in all cases.

In summary, phosphabarrelene–rhodium complexes have been developed as extremely active hydroformylation catalysts. Most notably, and in contrast to known catalysts designed for hydroformylation of internal alkenes, the phosphabarrelene catalysts enable a position selective hydroformylation of an internal C/C double bond essentially free of alkene isomerization.

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