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# Synthesis of C<sub>2</sub>-Symmetric Diphosphoromonoamidites and Their Use as Ligands in Rh-Catalyzed Hydroformylation: Relationships between Activity and Hydrolysis Stability

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A series of diphosphoramidites has been synthesized with a piperazine, homopiperazine, and an acyclic 1,2-diamine unit in the backbone. New compounds were tested alongside related *N*-acyl phosphoramidites as ligands in the Rh-catalyzed hydro-

formylation of *n*-octenes to investigate their influence on the activity and regioselectivity. A subsequent study of their hydrolysis stability revealed that the most stable ligands induced the highest activity in the catalytic reaction.

## 1. Introduction

The hydroformylation of olefins to afford aldehydes is one of the most important reactions in industry. In particular, linear aldehydes are desired products due to their high potential in consecutive reactions.<sup>[1]</sup> Because internal olefins or mixtures of internal and terminal olefins are cheaper and more readily available than pure terminal olefins, the development of highly *n*-regioselective catalysts is of great importance from academic and economic points of view.<sup>[2]</sup> It has been proven that rhodium, particularly in combination with trivalent phosphorus ligands, enhances the activity and selectivity compared with unmodified catalysts.<sup>[3]</sup> Therefore, the development of new li-

gands is one of the key issues in technical hydroformylation research currently. In recent decades, literally hundreds of P ligands have been developed for this purpose. In particular, triesters of phosphorus acid (phosphites) have seen broad application.<sup>[4]</sup>

In contrast, phosphoramidites have been less frequently used for this purpose, although occasionally they represent synthetic precursors of phosphites. In this regard, the use of phosphoramidites may save a synthetic step. In general, phosphoramidites are readily accessible and their modular structure enables the formation of broad ligand libraries.<sup>[5]</sup> Bidentate and monodentate phosphordiamidites and -triamidites are known. Also, some chiral versions have been designed as ligands for asymmetric transformations. In this regard, monodentate binol-based phosphoromonoamidites have attracted broad attention.<sup>[6,7]</sup> Initial trials to use these compounds as monodentate ligands in hydroformylation were published only a few years ago.<sup>[8]</sup>

Several studies in the literature address the electronic and steric properties of phosphoramidites. In particular, Trzeciak and Ziółkowski advocated the use of tris(*N*-pyrrolyl)phosphine due its high  $\pi$ -acceptor properties, which may force the dissociation of CO from the hydroformylation catalyst.<sup>[9]</sup> The research groups of van Leeuwen and Zhang prepared pyrrolyl-based phosphordiamides and with their assistance achieved high *n*-regioselectivities in the Rh-catalyzed isomerizing hydroformylation of internal olefins.<sup>[10,11]</sup> To the best of our knowledge, no reports exist in which potentially bidentate phosphoromonoamidites have been applied as ligands for hydroformylation.

The disregard of phosphoramidites in hydroformylation can be attributed to the assumed high sensitivity of these compounds towards hydrolysis.<sup>[12]</sup> High hydrolysis stability is a crucial issue for ligands used in hydroformylation, in which water may be formed continuously due to the aldol condensation of

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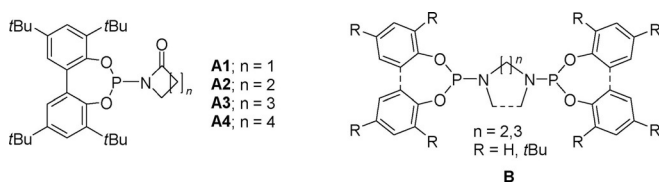
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product aldehydes. Therefore, studies to identify stabilizing structural elements in the ligands are of crucial importance, particularly for technical applications.<sup>[5]</sup>

Recently, we synthesized a set of monodentate phosphoramidites based on lactams of general type **A** and tested them in the Rh-catalyzed hydroformylation of methyl oleate.<sup>[13]</sup> We found to our surprise that the hydrolysis stability of these compounds was strongly dependent on the size of the lactam ring. The derivative based on the four-membered lactam (**A1**) was orders of magnitude more stable than phosphoramidites with a five-, six-, or seven-membered ring in the backbone (**A2–A4**). Moreover, this very stable ligand also formed the most active and selective rhodium catalyst in the hydroformylation of the unsaturated fatty acid ester.



To get more insight into the relationships between reactivity, selectivity, and stability, herein we report the synthesis of some new  $C_2$ -symmetric diphosphoramidites of type **B**. In contrast to amidites of type **A**, these compounds are characterized by electron-rich alkylamino groups linked to the phosphorus. Cyclic diamines and open-chain diamines have been employed for construction of the backbone. In some cases, the aryl rings were decorated with bulky *tert*-butyl groups. Due to the incorporation of two potentially ligating P atoms, the formation of bidentate chelate complexes with a metal seems to be possible. These phosphoramidites were screened in the Rh-catalyzed hydroformylation of *n*-octenes. The results were compared with those obtained with ligands of type **A**. Subsequently, investigations into the stability of the ligands towards oxygen and water were performed.

## 2. Results and Discussion

### 2.1. Synthesis of Phosphoramidites of Type B

Our general strategy for the synthesis of phosphoramidites of type **B** is illustrated in Scheme 1. Diphosphoramidites **4–11** were synthesized from the cyclic six- and seven-membered amines piperazine or homopiperazine and open-chain 1,2-diamines by reaction of two equivalents of relevant phosphorylating reagent **1**, **2**, or **3**.<sup>[6]</sup> During the synthesis of ligands **12** and **13**, starting from the phenyl phosphorochloridite, we faced some difficulties with respect to poor yields. Therefore, we used an alternative route starting from the relevant dichloroaminophosphine.<sup>[14]</sup>

Remarkably, phosphoramidites based on a piperazine or homopiperazine ring were quite stable during our purification procedure and could be isolated in good yields as white solids. Due to the simple and convenient synthesis, we were able to

prepare them on a gram scale. No degradation was observed during manipulation in air; the compounds could be stored under dry conditions at room temperature even for several months. In addition, they also proved to be fairly stable in common organic solvents. In contrast to these observations, the workup of diamidites with an open-chain backbone (**8** and **11**) had to be performed in dry solvents due to an enhanced sensitivity towards moisture.

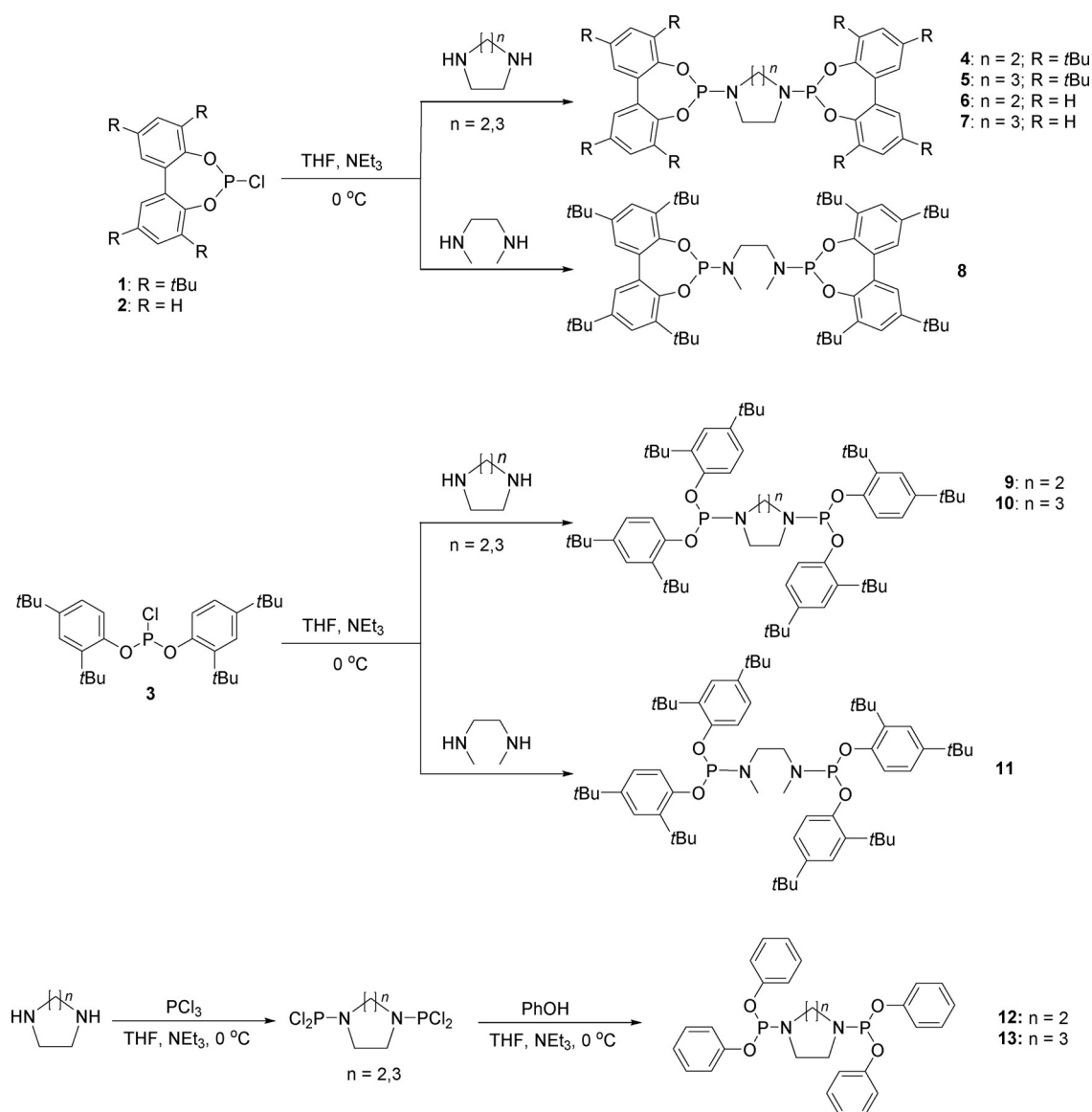
The spectroscopic data for the derivatives of the cyclic diamines, which have the same phosphorus substituents, are very similar, which suggests that the additional  $CH_2$  group in the homopiperazine derivative only has a small influence on the electronic properties of the ligands and the resulting complexes. A molecular structure of phosphoramidite **9** gave proof of the favored chair conformation of the piperazine ring (Figure 1).

The appearance of two broad signals in the  $^{31}P$  NMR spectrum (121.5 MHz) of compound **5**, recorded in  $CD_2Cl_2$  at ambient temperature, pointed to a dynamic process in the molecule. This process may occur in or between the molecules: interconversion between conformers, rotations around bonds with partial double-bond character, or interconversion of atropisomers.<sup>[15]</sup> In particular, the incorporation of the *tert*-butyl substituents in **5** resulted in a higher isomerization barrier. Therefore, the differentiation of diastereomers in the  $^{31}P$  NMR spectra at room temperature was possible.<sup>[16]</sup>

A comparison of the chemical  $^{31}P$  shifts of phosphoramidites of types **A** and **B** shows some interesting features (Table 1). In general, lactam derivatives of type **A** were characterized by resonances in the range of  $\delta = 129$  to 137 ppm. Electron-donating amine substituents, as found in phosphoramidites of type **B**, shifted the resonances to lower field. In general, they were in the range of  $\delta = 133$  to 150 ppm. A still more pronounced effect on the chemical shift was observed on replacement of the bisphenol part by two monophenol groups. Thus, between cyclic compounds **4–8** and acyclic structures **9–11**, differences of up to  $\delta = 15$  ppm have been noted.

### 2.2. Synthesis of Rh Complexes

To investigate the preferred coordination mode of the new ligands, they were treated in toluene with  $Rh(acac)(CO)_2$  in different ratios. Due to our expectations that these potentially bidentate phosphoramidites might act also in a chelating manner, we commenced with a Rh/L ratio of 1:1. Interestingly, these preliminary trials with diphosphoramidites with a piperazine or homopiperazine backbone resulted in a mixture of three compounds: In addition to the unreacted diphosphoramidite, two Rh complexes were found with Rh/ligand ratios of 1:1 or 2:1. Obviously, the preferred chair conformation of the heterocyclic backbones prevented the selective formation of chelate complexes. In addition to bidentate coordination, monodentate binuclear complexes have also been found. To overcome this ambiguous situation in subsequent trials, phosphoramidites **4**, **5**, **9**, and **10** were treated with two equivalents of  $Rh(acac)(CO)_2$  (see Scheme 2).



Scheme 1. Synthesis of phosphoramidites 4–13.

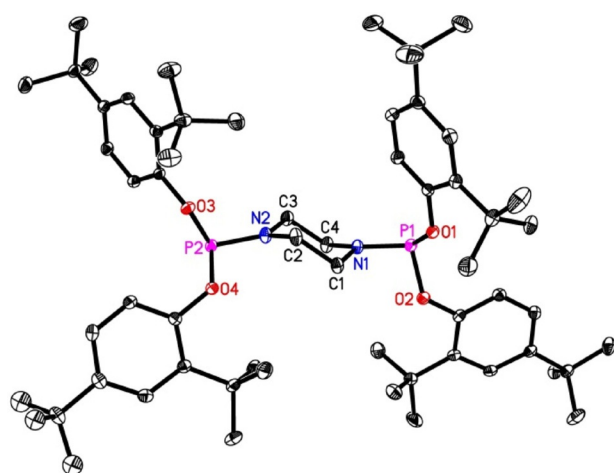
The NMR spectroscopy data of products 14–17 suggested the formation of symmetric binuclear Rh complexes with a bridging diphosphoramidite, in which both phosphorus atoms are situated in the equatorial positions (Table 2). In the  $^1\text{H}$  NMR spectra, the  $\text{CH}_3$  groups of acetylacetonate appear as two singlets and in the IR spectra the  $\text{C}=\text{O}$  signals were detected in the narrow range between 1998 and 2001  $\text{cm}^{-1}$ .

X-ray structural analysis of 17 (Figure 2) confirmed our NMR spectroscopy interpretation: Both P-ligating atoms coordinate to another rhodium center. Obviously, the stable chair-related conformation of the seven-membered ring of the homopiperazine bridge does not allow the formation of a chelate, for which a switch to a modified boat conformation would be the precondition.

### 2.3. Hydroformylations

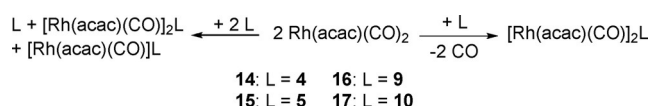
Phosphoramidites of types A and B were tested as ligands in the Rh-catalyzed hydroformylation of *n*-octenes, which represents a technically relevant mixture of isomeric linear octenes (Table 3). With lactam-based ligands of type A, the same dependency on the activity was found as already reported with methyl oleate as the substrate.<sup>[13]</sup> Thus, ligands based on the small lactam ring (A1 and A2) induced the highest activity. Ligands with six- or seven-membered lactams (A3 and A4) gave poor yields. As a consequence, the corresponding *k* values could not be determined. In general, the regioselectivities in favor of the formation of *n*-nonanal were low for all ligands, and thus in the range of typical monodentate ligands.<sup>[1]</sup>

Rh complexes based on ligands of type B, such as 6, 7, 12, and 13, which contain unsubstituted biphenyl and phenyl



**Figure 1.** ORTEP drawing of **9**. Hydrogen atoms have been omitted for clarity. Displacement ellipsoids correspond to 30% probability. Selected bond lengths [Å] and angles [°]: N1–P1 1.6543(17), N2–P2 1.6499(17), O1–P1 1.6502(14), O2–P1 1.6484(14), O3–P2 1.6661(14), O4–P2 1.6445(14); C1–N1–P1 124.48(13), C2–N2–P2 126.22(14).

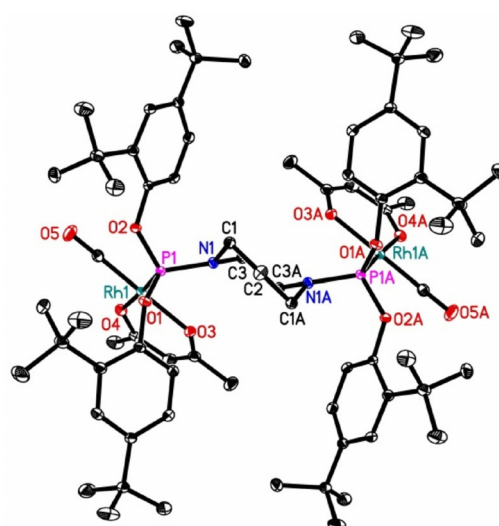
Phosphoramidite	$\delta_{\text{p}}$ [ppm]	Phosphoramidite	$\delta_{\text{p}}$ [ppm]
<b>A1</b>	128.9	<b>7</b>	149.6
<b>A2</b>	136.9	<b>8</b>	149.2
<b>A3</b>	133.0	<b>9</b>	133.3
<b>A4</b>	133.9	<b>10</b>	137.3
<b>4</b>	143.5	<b>11</b>	136.7
<b>5</b>	147.8	<b>12</b>	136.9
<b>6</b>	146.0	<b>13</b>	140.5



**Scheme 2.** Synthesis of Rh complexes **14–17**.

Rh complex	$^{31}\text{P}$ NMR $\delta_{\text{p}}$ [ppm]	$^1J_{\text{PRh}}$ [Hz]	FTIR $\nu[\text{CO}]$ [ $\text{cm}^{-1}$ ]
<b>14</b>	141.8	277	2000.3
<b>15</b>	146.8	280	2001.3
<b>16</b>	128.7	259	1992.2
<b>17</b>	133.3	257	1997.9

units, were characterized by poor conversion. Improved reactivity could be realized after the introduction of bulky substituents on the aryl rings. Thus, Rh complexes **4**, **5**, **8**, **9**, and **10** with *tert*-butyl groups gave much better results. Surprisingly, phosphoramidite **11**, which should be able to chelate at the metal center due its high conformational flexibility, showed



**Figure 2.** ORTEP drawing of **17**. Hydrogen atoms have been omitted for clarity. Displacement ellipsoids correspond to 30% probability. Operator for generating equivalent atoms:  $-x+2, y, -z+1/2$ . Selected bond lengths [Å] and angles [°]: O3–Rh1 2.0454(13), O4–Rh1 2.0633(13), P1–Rh1 2.1940(5), C37–Rh1 1.815(2), N1–P1 1.6571(15), O1–P1 1.6223(13), O2–P1 1.6358(12); C37–Rh1–O4 89.61(7), O3–Rh1–O4 88.65(5), C37–Rh1–P1 87.78(6), O3–Rh1–P1 94.00(4).

Entry	Ligand	P/Rh	Yield <sup>[c]</sup> [%]	<i>n</i> -Selectivity <sup>[c]</sup> [%]	<i>k</i> [min <sup>-1</sup> ]
1	<b>A1</b>	5	96	21.2	0.172
2	<b>A2</b>	5	98	18.6	0.106
3	<b>A3</b>	5	32	24.0	n.d. <sup>[e]</sup>
4	<b>A4</b>	5	20	24.9	n.d. <sup>[e]</sup>
5	<b>4</b>	4	99	18.7	0.183
6	<b>5</b>	4	99	19.5	0.162
7	<b>6</b>	4	38	18.4	n.d. <sup>[e]</sup>
8	<b>7</b>	4	37	14.4	n.d. <sup>[e]</sup>
9	<b>8</b>	4	93	34.3	0.023
10	<b>9</b>	4	92	16.9	0.233
11	<b>10</b>	4	95	18.2	0.151
12	<b>11</b>	4	48	22.9	n.d. <sup>[e]</sup>
13	<b>12</b>	4	0.5	25.0	n.d. <sup>[e]</sup>
14	<b>13</b>	4	4.5	31.9	n.d. <sup>[e]</sup>
15	Alkanox 240 <sup>[d]</sup>	4	95	20	0.194

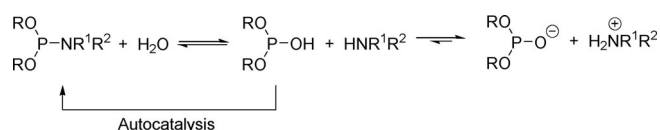
[a] Composition: 3.3% 1-octene, 48.4% *Z/E*-2-octene, 29.2% *Z/E*-3-octene, 16.4% *Z/E*-4-octene, 2.1% skeletal C8-olefinic isomers, 0.6% *n*-octane. [b] Conditions: syngas (50 bar, CO/H<sub>2</sub> 1:1), 120 °C, 4 h. [c] Conversion and regioselectivity were determined by using GC analysis. [d] Tris[2,4-di(*tert*-butyl)phenyl]phosphite. [e] n.d.: not determined.

both poor conversion and low regioselectivity. Therefore, we can also assume monodentate coordination for this ligand (as for the others) during the catalytic reaction. For comparison, tris[2,4-di(*tert*-butyl)phenyl]phosphite, one of the most outstanding monophosphites used in Rh-catalyzed hydroformylation, was included in the hydroformylation study.<sup>[4]</sup> We were pleased to see that some of our best phosphoramidites could rival the catalytic performance of this ligand.

## 2.4. Stability Test

The stability of phosphoramidites **4**, **5**, **9**, and **10** towards water and oxygen was tested by considering established standard conditions previously developed in our group for ligands of type **A**.<sup>[13]</sup> For the hydrolysis experiments, a solution of the phosphoramidite (0.025 mol L<sup>-1</sup>) in THF/[D<sub>8</sub>]THF was treated with 100 equivalents of water at 70 °C in a sealed NMR tube. The progress of hydrolysis was quantitatively monitored by using in situ <sup>31</sup>P NMR spectroscopy. Tri(*n*-octyl)phosphine oxide was employed as the internal standard.

Our studies revealed that even after treatment with water for three months, phosphoramidites **4** and **5** with a rigid bi-phenyl unit did not exhibit any change in the <sup>31</sup>P NMR spectra. This demonstrates the enormous hydrolysis stability of these compounds under these conditions and recalls the known extreme stability of the phosphite Alkanox 240. In contrast, the acyclic and, therefore, conformationally more flexible phenyl ester derivatives **9** and **10** exhibited inferior stability. After approximately six weeks, complete decomposition of both ligands took place (1008 and 1176 h for **9** and **10**, respectively). This is in line with the superior stability found for cyclic phosphites compared with acyclic analogues.<sup>[17]</sup> However, all phosphoramidites with electron-rich N substituents, summarized in the introduction as type **B**, were much more stable than the cyclic *N*-acylamido phosphoramidites of type **A** described in our recent paper.<sup>[13]</sup> We attribute this difference to the beneficial effect of the liberated amine, which prevents further hydrolysis of the formed phosphorous acid by neutralization (Scheme 3). In this manner, the accelerating autocatalytic effect



**Scheme 3.** Reaction of phosphoramidites with water and inhibition of the auto-catalyzed hydrolysis by the effect of free amine.

of strongly acidic degradation products<sup>[18]</sup> on the hydrolysis of the phosphoramidite can be largely suspended. Because alkylamines are more basic than amides, the higher hydrolysis stability of phosphoramidites of type **B** compared with compounds of type **A** can be explained.

Long-term oxidation experiments gave evidence for the extreme high stability of all new compounds towards oxygen.<sup>[19]</sup>

## 3. Conclusions

A set of bisphosphoramidites were synthesized. Complexation studies with rhodium gave evidence that the chelating behavior is not dependent on the architecture of the diamine backbone. Heterocyclic diamines gave rise exclusively to monodentate coordination. Chelation was not observed for open-chain, and thus conformationally more flexible, diamine backbones. In the hydroformylation of *n*-octenes with ligands with hetero-

cyclic diamine backbones, the results equaled or even surpassed those reported for the most prominent monodentate phosphite. As found in a recent study,<sup>[13]</sup> the most stable ligands also afforded the highest activity in the catalytic reaction. It can be concluded that such appropriately designed phosphoramidite ligands can successfully compete with the most prominent phosphites recommended for this purpose to date. Moreover, the generation of basic amines in the hydrolysis reaction blocks the formation of phosphoric acid derivatives, which would initiate the autocatalytic progress of ligand decomposition. In this way, the addition of external amines, frequently suggested for the stabilization of more frequently employed phosphites, is not required.<sup>[20]</sup> However, the large differences observed between a heterocyclic and an acyclic amine backbone is astonishing and requires further research.

## Experimental Section

### General Experimental Methods

All reactions were carried out under an inert atmosphere (argon 5.0) by using standard Schlenk techniques. The solvents were dried by using conventional procedures and distilled under an argon atmosphere. Where possible, the reactions were monitored by using NMR spectroscopy. The yields detailed in the Supporting Information refer to isolated yields, melting points are uncorrected. NMR spectra were recorded by using Bruker AV 250, AV 300, AV 400, and AV 500 MHz spectrometers. Chemical shifts are reported in ppm relative to TMS. The solvent signals (CD<sub>2</sub>Cl<sub>2</sub>, δ<sub>H</sub> = 5.32 ppm, δ<sub>C</sub> = 54.0 ppm; [D<sub>8</sub>]THF, δ<sub>H</sub> = 3.57, 1.72 ppm, δ<sub>C</sub> = 67.4, 25.3 ppm) were used for calibration of the <sup>1</sup>H and <sup>13</sup>C NMR spectra. <sup>31</sup>P NMR spectra are referenced to external H<sub>3</sub>PO<sub>4</sub>. IR spectra were recorded by using a Nicolet 380 FT-IR spectrometer. High-resolution mass spectrometry (HRMS) was recorded by using an Agilent 6210 E1969A TOF spectrometer. Only measurements with an average deviation from the theoretical mass of ± 2 mDa were accounted as being correct. X-ray diffraction data of single crystals of compound **9** and **17** were measured by using a Bruker Kappa APEX II Duo diffractometer. The structures were solved by using direct methods with the SHELXS-97 program<sup>[21]</sup> and refined by using full-matrix least-squares procedures on *F*<sup>2</sup> by using the SHELXL-2014 program.<sup>[22]</sup> XP (Bruker AXS) was used for graphical representations. CCDC 1495179 (**9**), and 1495180 (**17**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre. GC was performed by using an HP 5890 Series II instrument equipped with a PONA column (0.5 mm; 0.2 mm diameter; length 50 m). All reactions were monitored by using TLC (Silica Gel 60, F<sub>254</sub>, E. Merck); the following solvent systems (v/v) were used: 1:1, 5:1, and 10:1 hexane/CH<sub>2</sub>Cl<sub>2</sub> for **A1**, **A2**, and **A3**, respectively, and 99:1 hexane/EtOAc for **B1**. The detection was effected by using UV fluorescence (λ = 254 nm, λ = 365 nm). Preparative flash chromatography was performed by using a packed column (silica gel, RediSep) with a Combi-Flash R<sub>f</sub> system (Teledyne ISCO).

All samples for the in situ <sup>31</sup>P NMR experiments were filled in an Ar atmosphere by using standard Schlenk techniques. The experiments were carried out in a sealed 9 inch, 5 mm NMR tube (Deuterio) equipped with a sealed 12.5 cm capillary (Sigma Aldrich), which was filled with a solution of tri-*n*-octylphosphine oxide (0.259 mol L<sup>-1</sup>) in [D<sub>10</sub>]p-xylene as an external reference and locking solvent. The samples (0.0256 mol L<sup>-1</sup>) were dissolved in a previously

dried THF/[D<sub>8</sub>]THF (1:1) mixture. Water was distilled under an Ar atmosphere and added before measurement.

### General Procedure for the Synthesis of Phosphoramidites 4–11

The corresponding phosphorochloridite<sup>[13,23,24]</sup> (2.0 mmol) in THF (20 mL) was added dropwise over a period of 30 min to a stirred cooled (0 °C) solution of amine (1.0 mmol) and triethylamine (4.0 mmol) in THF (30 mL). After 15 min, the solution was slowly brought to RT and the stirring was continued overnight while triethylammonium hydrochloride separated from the colorless solution. Filtration followed by removal of the solvent under vacuum afforded the crude product, which was purified by using flash chromatography to give the pure amidite as a white solid.

### General Procedure for the Synthesis of Phosphoramidites 12 and 13

A solution of amine (1.0 mmol) and triethylamine (5.0 mmol) in THF (5 mL) was added dropwise to a stirred cooled (0 °C) solution of PCl<sub>3</sub> (10.0 mmol). The reaction mixture was allowed to warm to RT and stirred for 3 h. The resulting HCl gas was released from the reaction vessel by using a bubble counter (slight argon stream). The remaining clear solution was cooled to RT, concentrated, and dried azeotropically with toluene (three times). The resulting residue was used directly in the next step without purification. The oily product was redissolved in THF (20 mL) and cooled to 0 °C. A solution of phenol (4.0 mmol) and triethylamine (5.0 mmol) in THF (5 mL) was then added dropwise to the stirred cooled solution. The reaction mixture was slowly brought up to RT and stirred overnight. The Et<sub>3</sub>N·HCl precipitate was removed by filtration and the mixture was concentrated to give the crude product, which was purified by using flash chromatography to give the pure amidite as a white solid. It should be noted that for compounds **8** and **11**, the use of dried solvents and 1% triethylamine for the workup is indispensable.

### Synthesis of Rh<sup>I</sup> Complexes 14–17

The diphosphoramidite ligand (0.1 mmol) was added dropwise over 10 min to a stirred solution of Rh(acac)(CO)<sub>2</sub> (0.2 mmol) in toluene (5 mL) and the reaction mixture was stirred for 2 h. Then the solvent was evaporated and the obtained solid was dried under vacuum. The residue was washed with hexane (6 mL), and removal of solvent under vacuum afforded the spectroscopically pure products.

### Hydroformylation Procedure

Hydroformylation experiments were carried out in a 200 mL autoclave equipped with a thermocouple, a Bronkhorst hitec mass-flow meter, and a Bronkhorst pressure controller at 120 °C and 50 bar syngas (99.997%; CO/H<sub>2</sub> 1:1) for 4 h at constant pressure. Synthesis gas was introduced through a gas entrainment impeller at 1500 rpm. The autoclave, with the storage vessel for olefin addition under pressure, was purged and filled with argon before the catalyst solution was introduced into the reactor and the olefin to the storage vessel (argon countercurrent). In a typical experiment, the *n*-olefin mixture (3.3% 1-octene, 48.4% *Z/E*-2-octene, 29.2% *Z/E*-3-octene, 16.4% *Z/E*-4-octene, 2.1% skeletal C8-olefinic isomers, 0.6% *n*-octane; 15 mL) and the catalyst solution of Rh(acac)(CO)<sub>2</sub>

and the corresponding phosphoramidite (Table 3) in toluene (41 mL) were used with an olefin/rhodium ratio of 2000:1. The catalyst solution was heated under synthesis gas to the desired reaction temperature for 30 min. After olefin addition, the pressure was kept at 50 bar and the gas consumption was measured by using a mass-flow meter. After a reaction time of 4 h, of the autoclave was cooled to RT and then the pressure was released. Product analysis was performed by using GC. For this purpose, the reaction solution (1 mL) was diluted with *n*-pentane (10 mL) and toluene was used as the internal standard.

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### Conflict of Interest

The authors declare no conflict of interest.

**Keywords:** diphosphoramidites · hydroformylation · regioselectivity · rhodium · structure–activity relationships

- [1] a) A. Börner, R. Franke, *Hydroformylation: Fundamentals, Processes, and Applications in Organic Synthesis*, Wiley-VCH, Weinheim, **2016**; b) R. Franke, D. Selent, A. Börner, *Chem. Rev.* **2012**, *112*, 5675–5732; c) *Rhodium-Catalyzed Hydroformylation* (Eds.: P. W. N. M. van Leeuwen, C. Claver), Kluwer Academic Publishers, Dordrecht, **2002**.
- [2] a) D. Selent, D. Röttger, K.-D. Wiese, A. Börner, *Angew. Chem. Int. Ed.* **2000**, *39*, 1639–1641; *Angew. Chem.* **2000**, *112*, 1694–1696; b) H. Klein, R. Jackstell, K.-D. Wiese, C. Borgmann, M. Beller, *Angew. Chem. Int. Ed.* **2001**, *40*, 3408–3411; *Angew. Chem.* **2001**, *113*, 3505–3508; c) L. A. van der Veen, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Angew. Chem. Int. Ed.* **1999**, *38*, 336–338; *Angew. Chem.* **1999**, *111*, 349–351; d) L. A. van der Veen, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Organometallics* **1999**, *18*, 4765–4777.
- [3] a) D. E. C. Corbridge, *Phosphorus. An Outline of Its Chemistry, Biochemistry and Technology*, 4th ed., Elsevier, New York, NY, **1990**, p. 560; b) E. Fluck in *Topics in Phosphorus Chemistry, Vol. 4* (Eds.: M. Grayson, E. J. Griffith), Wiley-Interscience, New York, NY, **1966**, pp. 291; c) L. A. Hamilton, P. S. Landis in *Organic Phosphorus Compounds, Vol. 4* (Eds.: G. M. Kosolapoff, L. Maier), Wiley-Interscience, New York, NY, **1972**, pp. 504; d) P. C. J. Kamer, P. W. N. M. van Leeuwen, *Phosphorus(III) Ligands in Homogeneous Catalysis: Design and Synthesis*, Wiley & Sons Ltd., Chichester, **2012**.
- [4] a) A. Vidal-Ferran, I. Mon, A. Bauzá, A. Frontera, L. Rovira, *Chem. Eur. J.* **2015**, *21*, 11417–11426; b) H. Fernández-Pérez, J. Benet-Buchholz, A. Vidal-Ferran, *Chem. Eur. J.* **2014**, *20*, 15375–15384; c) J. Klosin, C. R. Landin, *Acc. Chem. Res.* **2007**, *40*, 1251–1259; d) P. W. N. M. van Leeuwen, C. F. J. Roobeek, *Organomet. Chem.* **1983**, *258*, 343–350; e) A. van Rooy, E. N. Orij, P. C. J. Kamer, F. van den Ardweg, P. W. N. M. van Leeuwen, *J. Chem. Soc. Chem. Commun.* **1991**, 1096–1097; f) T. Jongsma, G. Challa, A. G. Abatjoglou, D. R. Bryant, J. M. Maher (Union Carbide Chemicals & Plastics Technology Corporation), EP 0697391, **1996** [*Chem. Abstr.* **1996**, *124*, 316213].
- [5] A. Börner, R. Franke, *Hydroformylation: Fundamentals, Processes, and Applications in Organic Synthesis Vol. 2*, Wiley-VCH, Weinheim, **2016**, pp. 189–210.
- [6] a) J. F. Teichert, B. L. Feringa, *Angew. Chem. Int. Ed.* **2010**, *49*, 2486–2528; *Angew. Chem.* **2010**, *122*, 2538–2582; b) E. Balaraman, K. C. Kumara Swamy, *Tetrahedron: Asymmetry* **2007**, *18*, 2037–2048; c) M. Rodri-

- guez i Zubiri, A. M. Z. Slawin, M. Wainwright, J. D. Woollins, *Polyhedron* **2002**, *21*, 1729–1736.
- [7] a) K. N. Gavrilov, A. A. Shiryaev, I. V. Chuchelkin, A. Börner, *Tetrahedron: Asymmetry* **2012**, *23*, 1052–1057, and references cited therein; b) M. T. Reetz, J.-A. Ma, R. Goddard, *Angew. Chem. Int. Ed.* **2005**, *44*, 412–415; *Angew. Chem.* **2005**, *117*, 416–419; c) L. Lefort, J. A. F. Boogers, A. H. M. de Vries, J. G. de Vries, *Org. Lett.* **2004**, *6*, 1733–1735.
- [8] a) S. E. Lyubimov, E. A. Rastorguev, D. V. Ozolin, V. A. Davankov, *Russian Chem. Bull.* **2013**, *62*, 1210–1213; b) J. Wassenaar, B. de Bruin, J. N. H. Reek, *Organometallics* **2010**, *29*, 2767–2776; c) A. van Rooy, D. Burgers, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Rec. Trav. Chim. Pays-Bas* **1996**, *115*, 492–498; d) J. Mazuela, O. Pàmies, M. Diéguez, L. Palais, S. Rosset, A. Alexakis, *Tetrahedron: Asymmetry* **2010**, *21*, 2153–2157.
- [9] A. M. Trzeciak, T. Glowiak, R. Grzybek, J. J. Ziółkowski, *J. Chem. Soc. Dalton Trans.* **1997**, 1831–1837.
- [10] a) O. Diebolt, H. Tricas, Z. Freixa, P. W. N. M. van Leeuwen, *ACS Catal.* **2013**, *3*, 128–137, and references therein; b) S. C. van der Slot, J. Duran, J. Luten, P. C. J. Kamer, P. W. N. M. van Leeuwen, *Organometallics* **2002**, *21*, 3873–3883.
- [11] a) Y. Yan, X. Zhang, X. Zhang, *J. Am. Chem. Soc.* **2006**, *128*, 16058–16061; b) S. Yu, Y. Chie, Z. Guan, X. Zhang, *Org. Lett.* **2008**, *10*, 3469–3472; c) S. Yu, Y. Chie, Z. Guan, Y. Zou, W. Li, X. Zhang, *Org. Lett.* **2009**, *11*, 241–244.
- [12] a) E. Nurminen, H. J. Lönnberg, *J. Phys. Org. Chem.* **2004**, *17*, 1–17; b) K. Dong, Z. Wang, K. Ding, *J. Am. Chem. Soc.* **2012**, *134*, 12474–12477; c) K. G. Moloy, J. L. Petersen, *J. Am. Chem. Soc.* **1995**, *117*, 7696–7710; d) W. Ahlers, R. Paciello, D. Vogt, P. Hofmann (BASF Aktiengesellschaft), WO 2002083695, **2002** [*Chem. Abstr.* **2002**, *137*, 311033].
- [13] E. Benetskiy, S. Lühr, M. Vilches-Herrera, D. Selent, H. Jiao, L. Domke, K. Dyballa, R. Franke, A. Börner, *ACS Catal.* **2014**, *4*, 2130–2136.
- [14] a) Y. H. Choi, J. Y. Choi, H. Y. Yang, Y. H. Kim, *Tetrahedron: Asymmetry* **2002**, *13*, 801–804; b) M. Vuagnoux-d'Augustin, A. Alexakis, *Chem. Eur. J.* **2007**, *13*, 9647–9662; c) S. Lühr, J. Holz, A. Börner, *ChemCatChem* **2011**, *3*, 1708–1730.
- [15] a) R. Franke, C. Borgmann, D. Hess, K. D. Wiese, *Z. Anorg. Allg. Chem.* **2003**, *629*, 2535–2538; b) J. R. Briggs, G. T. Whiteker, *Chem. Commun.* **2001**, 2174–2175; c) G. T. Whiteker, A. M. Harrison, A. G. Abatjoglou, *J. Chem. Soc. Chem. Commun.* **1995**, 1805–1806; d) C. P. Casey, G. T. Whiteker, *Isr. J. Chem.* **1990**, *30*, 299–304.
- [16] M. Oki, *Recent Advances in Atropisomerism in Topics in Stereochemistry, Vol. 14*, Wiley; Hoboken, NJ, **1983**, pp. 1–82.
- [17] a) A. E. Arbuzov, M. M. Azanovskaya, *Izv. Akad. Nauk SSSR Ser. Khim.* **1951**, 544–550; b) A. E. Arbuzov, V. M. Zoroastrova, *Izv. Akad. Nauk SSSR Ser. Khim.* **1950**, 357–369; c) J. Toháček, J. Sedlár, *Polym. Degrad. Stab.* **1995**, *50*, 345–352; d) M. Papanastasiou, A. W. McMahon, N. S. Allen, A. M. Doyle, B. J. Johnson, K. Keck-Antoine, *Polym. Degrad. Stab.* **2006**, *91*, 2675–2682.
- [18] E. J. Coulson, W. Gerard, H. R. Dudson, *J. Chem. Soc.* **1965**, 2364–2369.
- [19] For the oxidation experiments, the ligand (50 mg) was dissolved in [D<sub>3</sub>]toluene (0.6 mL) and fresh oxygen was bubbled through the solution. After three months, no change was noted in the structure of all phosphoramidites.
- [20] a) Y. Matsui, *Bull. Japan Petrol. Inst.* **1977**, *19*, 62–67; b) A. J. Dennis, G. E. Harrison, J. P. Wyber (to Davy McKee (London) Ltd.), EP 149894, **1984** [*Chem. Abstr.* **1984**, *104*, 226670]; c) M. H. Fisch, G. A. Seubert, Jr., B. A. Hegranes (to Argus Chemical Corp.), EP 167969, **1986** [*Chem. Abstr.* **1986**, *104*, 169576]; d) D. Hess, D. Ortmann, O. Möller, K.-D. Wiese, D. Fridag, W. Büschken (to Oxeno Olefinchemie GmbH), DE 102005042464, **2007** [*Chem. Abstr.* **2007**, *146*, 317783].
- [21] G. M. Sheldrick, *Acta Crystallogr. Sect. A* **2008**, *64*, 112–122.
- [22] G. M. Sheldrick, *Acta Crystallogr. Sect. C* **2015**, *71*, 3–8.
- [23] a) V. N. Tsarev, A. A. Kabro, S. K. Moiseev, V. N. Kalinin, O. G. Bondarev, V. A. Davankov, K. N. Gavrilov, *Russ. Chem. Bull.* **2004**, *53*, 814–818; b) D. J. Frank, A. Franzke, A. Pfaltz, *Chem. Eur. J.* **2013**, *19*, 2405–2415; c) O. Lot, I. Suisse, A. Mortreux, F. Agbossou, *J. Mol. Catal. A: Chem.* **2000**, *164*, 125–130.
- [24] L. P. J. Burton (Ethyl Corporation), US4739000, **1988** [*Chem. Abstr.* **1988**, *109*, 130244].

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