Ligand Design

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Imidazolin-2-ylidenaminophosphines as Highly Electron-Rich Ligands for Transition-Metal Catalysts

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Dedicated to Professor Manfred Scheer on the occasion of his 60th birthday

Abstract: *A variety of chemical transformations benefit from the use of strong electron-donating ancillary ligands, such as alkylphosphines or N-heterocyclic carbenes when electron-rich metal centers are required. Herein, we describe a facile and highly modular access to monodentate and bidentate imidazolin-2-ylidenamino-substituted phosphines. Evaluation of the phosphine's electronic properties substantiate that the formal replacement of alkyl or aryl groups by imidazolin-2-ylidenamino groups dramatically enhance their donor ability beyond that of alkylphosphines and even N-heterocyclic carbenes. The new phosphines have been coordinated onto palladium(II) centers, and the beneficial effect of the novel substitution patterns has been explored by using the corresponding complexes in the palladium-catalyzed Suzuki–Miyaura cross-coupling reaction of non-activated aryl chloride substrates.*

The success of homogeneous catalysis is linked largely to the development of a diverse range of ancillary ligands with tunable steric and electronic properties. Such tailoring of the ligand architecture is crucial to ensure optimum steric protection and stereoelectronic control of the catalytic species and very often allows a remarkable degree of control over the outcome of transition-metal-promoted reactions. In this context, phosphine ligands (PR_3) are arguably the most versatile ancillary ligands because their donor ability and steric requirements can be easily adjusted in a predictable manner by variation of the R substituents.[1] Specifically, when electron-rich metal centers are required strong electron-releasing alkylphosphines are the ligands of choice over arylphosphines.[2] Their application in catalysis has led to major breakthroughs in many fields of academic and industrial research, as exemplified by olefin metathesis,[3] hydroformylation,[4] catalytic C–H bond activation,[5] and palladium-catalyzed cross-coupling reactions.[6]

The synthesis of new strong-donor ligands has therefore become an important challenge of chemical research. During the past two decades, another class of ligands, namely N-heterocyclic carbenes (NHCs), have gained considerable significance as ancillary ligands in transition-metal catalysis, in particular because of their stronger σ-donor character compared to tertiary phosphines.[7] Consequently, the recent isolation of the very basic cyclic (alkyl)(amino)carbenes (CAACs)[8] and imidazolin-5-ylidenes (also termed abnormal NHCs)[9] were major breakthroughs. In contrast, concerning the donor properties of phosphines, tri-*tert*-butylphosphine is still regarded as the benchmark electron-rich ligand.[10] A successful approach to electron-rich phosphines was reported by Moloy and Petersen, who showed that despite the electron-withdrawing effect of the amino substituents, tris(*N*-pyrrolidinyl)phosphines has equal donor properties to tris(*n*-butyl)phosphine.[11] They attributed this effect to the potent N-to-P lone pair donation. Further investigation by Woollins revealed that for the third dialkylamino substituent this effect is offset by the electron-withdrawing character of the nitrogen atoms, and they showed that phosphines comprising two pyrrolidinyl groups and one alkyl substituent can be equally strong donors as tri-*tert*-butylphosphine.[12]

We reasoned that a promising strategy to increase the electron-donating ability of phosphines would be to decorate them with strong π-donating substituents such as the imidazolin-2-ylidenamino groups. The ability of the anionic imidazolin-2-iminato ligands to efficiently act as imido-type 2σ,4π-electron donors towards metal atoms has been extensively explored by Tamm and co-workers.[13] Recent success in stabilizing electron-deficient species, such as a phosphinonitrene[14] and iminophosphenium salts[15] by using two phosphorus-bound imidazolidin-2-ylidenamino groups inspired us to exploit their strong π-donating character for the design of extremely electron-rich phosphines with potential applications in catalysis.

Herein, we describe a general procedure for the synthesis of imidazolin-2-ylidenaminophosphines (IAPs) (Figure 1). The successive replacement of the R substituents in phosphines PR_3 by strong π-donating imidazolin-2-ylidenamino

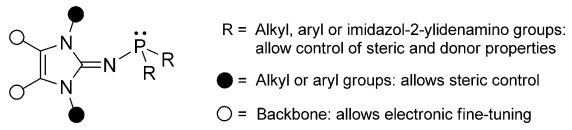

Figure 1. Structural features of IAPs and their influence on the donor properties of IAPs.

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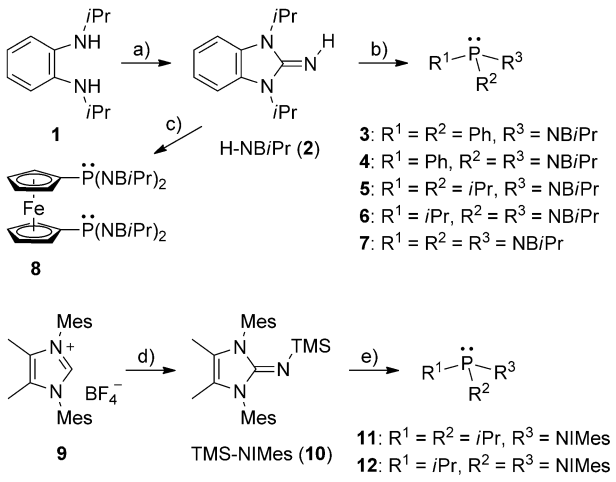
groups makes IAPs more electron rich than alkylphosphines and even abnormal N-heterocyclic carbenes. Moreover, owing to the NHC-nature of the backbone, steric and electronic fine-tuning of IAPs is easily achieved by drawing on the versatile class of NHCs as exemplified by using 1,3-diisopropylbenzimidazolin-2-ylidenamino (NB*i*Pr) and 1,3-dimesityl-4,5-dimethylimidazolin-2-ylidenamino (NIMes) substituents in our studies. We also demonstrate the beneficial effect of the imidazolin-2-ylidenamino substitution in a series of IAPs in Suzuki–Miyaura reactions using non-activated aryl chlorides as challenging substrates.

For the synthesis of IAPs two straightforward procedures were developed (see Scheme 1 and the Supporting Information). NB*i*Pr-substituted phosphines **3**–**8** were prepared in excellent yields through a two-step sequence. The reaction of diamine **1**[16] with cyanogen bromide and subsequent basic workup afforded imine **2** in 90% yield. Deprotonation of **2** and treatment with the respective chlorophosphine afforded the IAPs **3**–**8** as white (**3**–**7**) or orange (**8**) solids in very good yields. An alternative route to IAPs is based on readily available imidazolium salts (Scheme 1). Following a synthetic approach reported by Tamm,[17] deprotonation of the imidazolium salt **9** at −78 °C gives the free NHC, which reacts with trimethylsilyl azide to afford imine **10** upon N_2 elimination in fair yield. Treatment of **10** with chlorodiisopropylphosphine afforded IAP **11** upon elimination of trimethylsilyl chloride in a clean reaction as an off-white solid. The sterically demanding phosphine **12** was prepared by reacting imine **10** with PCl_3 and subsequent treatment of the phosphenium chloride salt with isopropylmagnesium chloride to afford IAP **12** as a white solid in very good yield.

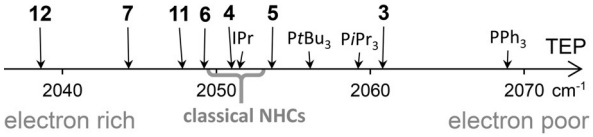
To evaluate the donor endowment of the new phosphines, we determined the Tolman electronic parameter (TEP) by analysis of the A_1 CO stretching frequency of $[Ni(CO)_3\mathbf{L}]$ complexes.[1] The observed TEP values indicate that the donor power of the IAPs is higher than that of the electron-rich alkylphosphines (Table 1) with the exception of **3** having a TEP value with the same order of magnitude as P*n*Bu$_3$ (2060.3 cm^{-1}). Remarkably, IAPs **6**, **7**, **11**, and **12** are even better donor ligands than classical NHCs. By analyzing the X-ray molecular structures of free triaminophosphines and those of their transition-metal complexes, Woollins et al. concluded that only two nitrogen lone pairs donate electron density towards phosphorus, while the third nitrogen lone pair is oriented such that the nitrogen atom simply acts as an electron-withdrawing substituent.[12] In contrast to this observation, the TEP value of NB*i*Pr-substituted phosphines **3**–**7** increases almost unvaryingly with a higher degree of substitution (Ph substitution: av. 8.2 cm^{-1}, *i*Pr substitution: av. 5.0 cm^{-1}). Phosphines **11** and **12**, decorated with the NIMes backbone, show an even more prominent gain in donor power. Monosubstitution shifts the TEP value (P*i*Pr$_3$: 2059.2 cm^{-1}) by 11.4 cm^{-1} (**11**: 2047.8 cm^{-1}) below that of classical NHCs, and the second substitution by another 9.2 cm^{-1} (**12**: 2038.6 cm^{-1}) below that of abnormal NHCs. These values support the notion that the NIMes substituent is a much better π donor than the NB*i*Pr group, and also indicates that if appropriately substituted, IAPs can surpass the donor abilities of CAACs or abnormal NHCs.

To demonstrate the reliability of the TEP analysis for the IAPs, we decided to examine their donor ability by means of a second method, which is not based on the CO stretching frequency. Huynh et al. recently reported a parameter that utilizes the ^{13}C NMR chemical shift of the carbene carbon atom in *trans*-$[PdBr_2(B\mathit{i}Pr)\mathbf{L}]$ complexes as a probe for the measurement of the donor strength of the ligand **L**.[18] The



Scheme 1. Synthesis of IAPs. Reagents and conditions (yields): a) BrCN, toluene, 110 °C, and then KOH (90%); b) *n*BuLi, THF, −78 °C, and then chlorophosphine, room temperature; **3** (94%), **4** (89%), **5** (84%), **6** (86%), **7** (94%); c) *n*BuLi, THF, −78 °C, and then $[Fe(C_5H_4PCl_2)_2]$ (81%); d) KO*t*Bu, toluene, −78 °C, and then $TMSN_3$, 110 °C (49%); e) **11**: P*i*Pr$_2$Cl, THF, (99%); **12**: PCl_3, THF, −78 °C, and then *i*PrMgCl, THF, −78 °C, (87%).

Table 1: TEP values and Huynh's parameter of IAPs **3**–**7**, **11**, and **12**. The values of commonly used phosphines and NHCs are included for comparison.

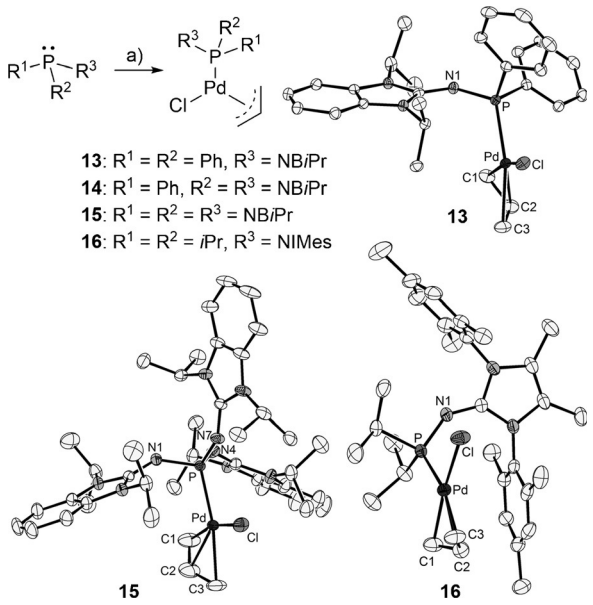


Entry	Ligand **L**	TEP[a] $[Ni(CO)_3L]$	$\delta C_{carbene}$[b] $[PdBr_2(BiPr)L]$
1	P(NB*i*Pr)Ph$_2$ (**3**)	2060.8	178.0
2	P(NB*i*Pr)$_2$Ph (**4**)	2051.0	183.0
3	P(NB*i*Pr)*i*Pr$_2$ (**5**)	2053.6	181.5
4	P(NB*i*Pr)$_2$*i*Pr (**6**)	2049.2	184.5
5	P(NB*i*Pr)$_3$ (**7**)	2044.3	186.1
6	P(NIMes)*i*Pr$_2$ (**11**)	2047.8	183.7
7	P(NIMes)$_2$*i*Pr (**12**)	2038.6	–[d]
8	PPh$_3$	(2068.9)	(173.1)
9	P*i*Pr$_3$	(2059.2)	175.9
10	P*t*Bu$_3$	(2056.1)	–
11	IPr[c]	(2051.5)	(177.5)

[a] Values in cm^{-1}; measured in CH_2Cl_2, (literature values[1,19]). [b] Values in ppm; measured in $CDCl_3$ and internally referenced to the solvent residual signal at δ = 77.7 ppm relative to TMS, (literature values[18]). [c] 1,3-bis(2,6-diisopropylphenyl)imidazolin-2-ylidene. [d] *trans*-$[PdBr_2(BiPr)(\mathbf{12})]$ not formed.

analysis of the ^{13}C carbene signal of these complexes containing IAPs revealed the same qualitative trend as the TEP analysis (Table 1). However, Huynh's method rates the donor strength of the IAPs as higher. Accordingly, IAP **3** exhibits a donor ability comparable to NHCs and is already more electron-rich than alkylphosphines, while phosphines **4**, **6**, **7**, and **11** exceed the donor ability of abnormal NHCs.[18]

Numerous catalytic processes that require electron-rich ligands at the metal center should benefit from the electronic and steric properties of IAPs. As an example of such a process, we decided to test the viability of IAPs in palladium-catalyzed Suzuki–Miyaura cross-coupling reactions of non-activated aryl chlorides. Previously, high reactions rates were observed with sterically hindered electron-rich alkyl phosphine and NHC ligands,[6,7a–c] in some cases even at room temperature,[20] while triphenylphosphine does not promote the coupling reaction.[21] Thus, we were curious to see what influence the NB*i*Pr-substitution pattern for IAPs **3**, **4**, and **7** has on the catalytic performance. We adopted the reaction conditions from a previous study by Nolan et al. who showed that the catalytic system involving [PdCl(allyl)(NHC)] as the catalyst and NaO*t*Bu as the base is highly active for the Suzuki–Miyaura cross-coupling of aryl chlorides.[22] The [PdCl(allyl)**L**] complexes **13**–**16** (Scheme 2) were readily

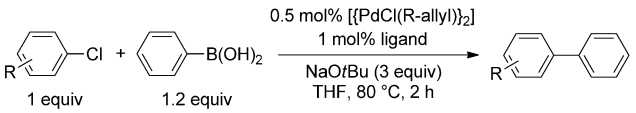


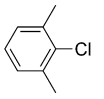
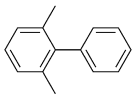
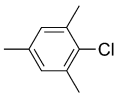
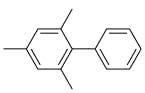
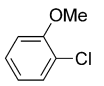
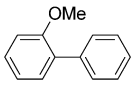
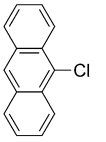
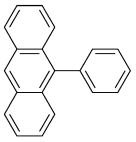
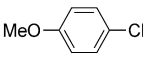
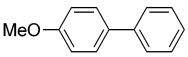
Scheme 2. Synthesis of the [PdCl(allyl)(IAP)] complexes **13**–**16** a) [{PdCl(allyl)}$_2$]. Molecular structures of **13**, **15**, and **16**. Hydrogen atoms are omitted for clarity; thermal ellipsoids are set at 50% probability. Selected bond lengths [Å]: **13**: Pd–Cl 2.3651(4), Pd–P 2.2872(4), P–N1 1.6395(12). **15**: Pd–Cl 2.3568(8), Pd–P 2.2829(7), P–N1 1.646(3), P–N4 1.653(3), P–N7 1.637(3). **16**: Pd–Cl 2.3792(6), Pd–P 2.2967(6), P–N1 1.624(2).

prepared in quantitative yields by addition of IAPs **3**, **4**, **7**, and **11** to [{PdCl(allyl)}$_2$], and isolated as air stable off-white solids.[23] X-ray diffraction studies confirmed the expected connectivity. The steric influence of the phosphine units on the palladium atom was analyzed by determination of their buried volume from the X-ray data of the [PdCl(allyl)**L**] complexes. A higher degree of NB*i*Pr-substitution increases the buried volume[24] for PPh_3 (29.6%), **3** (39.7%), and **7** (43.4%). The steric demand of IAP **11** (45.9%) resembles that of Buchwald-type phosphines,[6c] and nicely illustrates how effectively the steric bulk of IAPs can be modulated.

Our model system reveals a clear correlation between the catalytic performance of the [PdCl(allyl)(IAP)] catalyst with the degree of NB*i*Pr-substitution of the corresponding IAP ligands (Table 2). While PPh_3 does not promote the catalytic

Table 2: Suzuki–Miyaura cross-coupling of aryl chlorides with phenylboronic acid.



entry	aryl chloride	product	ligand	yield [%][a]	
1			PPh_3	0	
2			**3**	9	10
3			**4**	62	83
4			**7**	94	99
5			**3**	8	7
6			**4**	56	70
7			**7**	99	99
8			**3**	7	8
9			**4**	26	61
10			**7**	42	77
11			**3**	69	84
12			**4**	97	98
13			**7**	97	99
14			**3**	4	4
15			**4**	13	18
16			**7**	19	23

[a] Yields as determined by NMR spectroscopy (average of two runs) using the palladium dimers [{PdCl(allyl)}$_2$] | [{PdCl(cinnamyl)}$_2$].

process (entry 1),[21] the use of the mono-substituted IAP **3** provides low catalytic activity. The increasing donor strength and steric demand of IAPs **4** and **7** gives superior catalytic performances for all the aryl chloride substrates tested. The same trend was observed for **3**, **4**, and **7** when [{PdCl(cinnamyl)}$_2$] was used as palladium source (Table 2). The higher yields compared to the allyl-system are in agreement with the reported more facile activation of [PdCl(cinnamyl)(NHC)] complexes.[20a] This example beautifully demonstrates the ability of IAPs to increase the electron density at Pd centers and reveals the vast potential of IAPs in the development and improvement of transition-metal-catalyzed reactions.

In summary, our studies provide a conceptually new approach to the design of extremely electron-rich phosphines

based on the use of imidazolin-2-ylidenamino groups directly attached to the phosphorus atom. The IAPs are readily obtained through a short and highly modular synthesis, which also allows for the design of multi-dentate variants as exemplified by the preparation of IAP **8**. When used as a ligand, IAPs show excellent donor abilities, which can even exceed those of CAACs or abnormal NHCs. The beneficial effect of this property in the field of homogeneous catalysis has been explored in Pd-catalyzed Suzuki reactions using non-activated aryl chlorides as challenging substrates. Considering the convenient access to IAPs with diverse ligand architectures, in addition to the variety of chemical transformations that benefit from the use of strong electron-donating ligands, we anticipate that IAPs are likely to find widespread use as ancillary ligands in transition-metal-catalyzed reactions.

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