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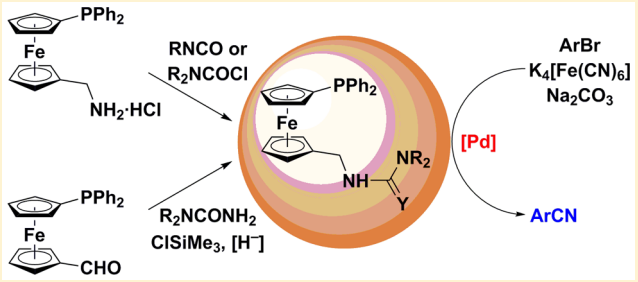
# Phosphinoferrocene Ureas: Synthesis, Structural Characterization, and Catalytic Use in Palladium-Catalyzed Cyanation of Aryl Bromides

Karel Škoch, Ivana Císařová, and Petr Štěpnička*

Department of Inorganic Chemistry, Faculty of Science, Charles University in Prague, Hlavova 2030, 128 40 Prague 2, Czech Republic

Supporting Information

**ABSTRACT:** Phosphinoferrocene ureas $Ph_2PfcCH_2NHCONR_2$, where $NR_2$ = $NH_2$ (**1a**), NHMe (**1b**), $NMe_2$ (**1c**), NHCy (**1d**), and NHPh (**1e**); the analogous thiourea $Ph_2PfcCH_2NHCSNHPh$ (**1f**); and the acetamido derivative $Ph_2PfcCH_2NHCOMe$ (**1g**) (Cy = cyclohexyl, fc = ferrocene-1,1′-diyl) were prepared via three different approaches starting from $Ph_2PfcCH_2NH_2$·HCl (**3**·HCl) or $Ph_2PfcCHO$ (**4**). The reactions of the representative ligand **1e** with $[PdCl_2(cod)]$ (cod = cycloocta-1,5-diene) afforded $[PdCl(\mu\text{-Cl})(\mathbf{1e}\text{-}\kappa P)_2]_2$ or $[PdCl_2(\mathbf{1e}\text{-}\kappa P)_2]_2$ depending on the metal-to-ligand stoichiometry, whereas those with $[PdCl(\eta^3\text{-}C_3H_5)]_2$ and $[PdCl(L^{NC})]_2$ produced the respective bridge cleavage products, $[PdCl(\eta^3\text{-}C_3H_5)(\mathbf{1e}\text{-}\kappa P)]$ and $[PdCl(L^{NC})(\mathbf{1e}\text{-}\kappa P)]$ ($L^{NC}$ = [(2-dimethylamino-$\kappa N$)methyl]phenyl-$\kappa C^1$). Attempts to involve the polar pendant in coordination to the Pd(II) center were unsuccessful, indicating that the phosphinoferrocene ureas **1** bind Pd(II) preferentially as modified phosphines rather than bifunctional donors. When combined with palladium(II) acetate, the ligands give rise to active catalysts for Pd-catalyzed cyanation of aryl bromides with potassium hexacyanoferrate(II). Optimization experiments revealed that the best results are obtained in 50% aqueous dioxane with a catalyst generated from 1 mol % of palladium(II) acetate and 2 mol % of **1e** in the presence of 1 equiv of $Na_2CO_3$ as the base and half molar equivalent of $K_4[Fe(CN)_6]\cdot 3H_2O$. Under such optimized conditions, bromobenzenes bearing electron-donating substituents are cyanated cleanly and rapidly, affording the nitriles in very good to excellent yields. In the case of substrates bearing electron-withdrawing groups, however, the cyanation is complicated by the hydrolysis of the formed nitriles to the respective amides, which reduces the yield of the desired primary product. Amine- and nitro-substituted substrates are cyanated only to a negligible extent, the former due to their metal-scavenging ability.




## INTRODUCTION

Modification of phosphines via introduced functional groups has been recognized as an efficient route toward new tailored ligands for coordination chemistry and catalysis. The latter field, in particular, advantageously capitalizes on the modification of pristine phosphine donors. For instance, phosphines modified with highly polar moieties such as sulfonato, carboxyl, or hydroxy groups have been successfully incorporated into catalysts for organic reactions performed in less environmentally demanding aqueous reaction media including pure water, homogeneous aqueous mixtures, and biphase mixtures.[1] The range of polar phosphine derivatives has been recently extended by those bearing urea substituents (**A** and **B** in Scheme 1).[2] The presence of urea pendants in these donors has been shown to be responsible for the formation of supramolecular assemblies via hydrogen bond interactions, which in turn affect their catalytic properties.

In the chemistry of phosphinoferrocene ligands,[3] the urea moiety has been used relatively scarcely, most often as a stable and structurally defined linking group in the preparation of immobilized or water-soluble donors[4] and conjugates of ferrocene with biologically relevant molecules.[5] Genuine applications of urea-functionalized phosphinoferrocene donors appear to be represented only by the preparation of urea- and thiourea-modified BPPFA-type donors (**C** in Scheme 1; BPPFA = 1,1′-bis(diphenylphosphino)-2-(1-dimethylaminoethyl)-ferrocene[6]) and their applications in asymmetric catalytic hydrogenations.[7,8] In addition, our laboratory recently reported the synthesis of phosphinoferrocene carboxamides[9] bearing extended urea-based pendants (**D** in Scheme 1) and their use in Pd-catalyzed cross-coupling of arylboronic acids with acyl chlorides to yield benzophenones.[10] This situation markedly contrasts with the numerous studies devoted to the electrochemical sensing properties of ferrocenyl- and ferrocenylmethyl-substituted ureas.[11]

In this contribution, we report on the preparation, coordination properties, and catalytic performance in the Pd-catalyzed cyanation of aryl bromides of a new type of phosphinoferrocene ureas (**1** in Scheme 1). The urea moiety in these functional hybrid ligands[12] is attached to the ferrocene scaffold via a methylene spacer, which increases conformational

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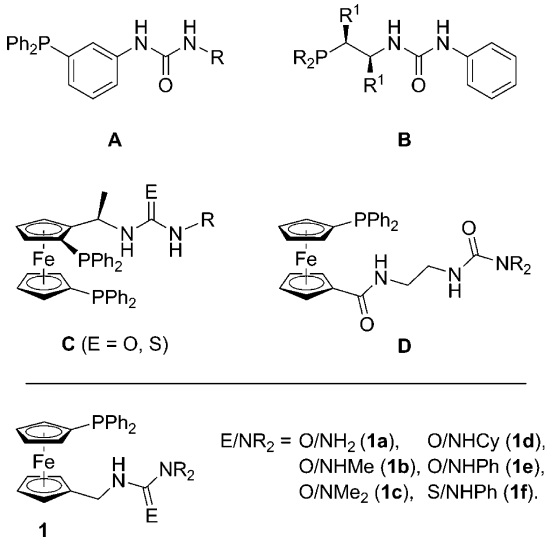
**Scheme 1**

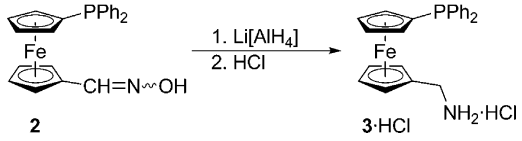



flexibility[13] and enhances the ditopic nature of these polar donors.

## RESULTS AND DISCUSSION

**Synthesis of Phosphinoferrocene Ureas.** Three different methods were employed for the synthesis of phosphinoureas **1**, partly due to their exclusivity with respect to the substituents at the terminal nitrogen atoms as well as for comparison of different preparative routes leading to this type of functionally modified, polar phosphinoferrocene donors. The first, perhaps inevitable approach, method A, was based on the conventional and widely applicable addition of amines across isocyanates. The amine **3** required for this reaction was prepared by hydride reduction of the known oxime **2** (Scheme 2),[14] which is in turn

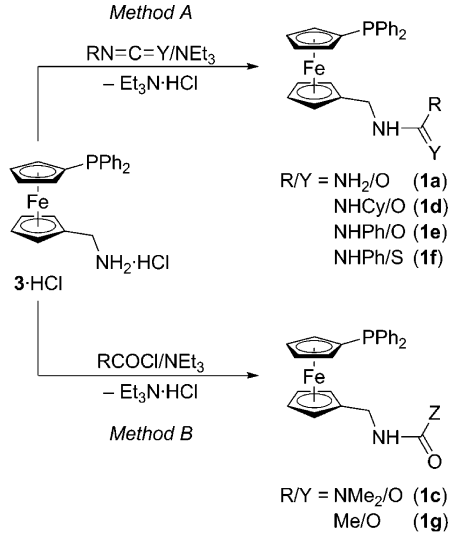
**Scheme 2. Preparation of 3·HCl**




accessible from 1′-(diphenylphosphino)ferrocene-1-carbaldehyde (**4**).[15] The amine was advantageously isolated in the form of stable and easy-to-handle hydrochloride (**3**·HCl), which separates in reasonable yield from the solution of the crude product upon addition of methanolic HCl. Contamination of **3**·HCl with the corresponding phosphine oxide, which is otherwise difficult to separate (e.g., by chromatography), does not exceed 5% in this case.

Gratifyingly, the reaction of amine **3** generated *in situ* from the hydrochloride and triethylamine proceeded in the anticipated manner, leading to 1,3-disubstituted ureas **1d** and **1e** in very good isolated yields (Scheme 3). Not surprisingly, this method could be successfully adopted for the synthesis of thiourea **1f** (yield: 94%). However, when applied to the preparation of *N*-ferrocenylmethyl urea **1a** by the action of sodium cyanate on the amine, method A furnished a relatively lower yield (37%) of the desired urea derivative, presumably because of a low equilibrium concentration of HNCO as the active reagent[16] in the presence of excess triethylamine.

**Scheme 3. Synthesis of Phosphinoferrocene Ureas from *in Situ* Generated Amine 3**

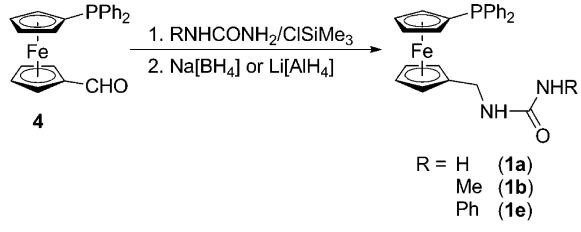



Nevertheless, because most of the starting amine hydrochloride remained unreacted and could be isolated (57% of the starting amine was recovered), the yield of **1a** with respect to unconsumed **3**·HCl was very satisfactory (86%). It should be noted that compound **1a** is typically contaminated by traces of the respective phosphine oxide (**1aO**), which cannot be efficiently removed by chromatography or crystallization.

The second approach, method B, employed for the preparation of trisubstituted urea **1c** and the acetamido (i.e., non-urea) derivative **1g**, which was included in the series of prospective ligands for comparison, was also rather straightforward, making use of the reactions of amine **3** with the corresponding acyl or carbamoyl chlorides (Scheme 3). As in the previous case, free amine **3** was liberated *in situ* from its hydrochloride by the action of triethylamine, which was used in excess to also serve as a scavenger of the formed HCl. Even these reactions proceeded satisfactorily and afforded the aforementioned products in isolated yields exceeding 90%.

The last alternative (method C, Scheme 4) relied on the direct reaction of aldehyde **4** with the respective urea by

**Scheme 4. Preparation of Phosphinoferrocene Ureas by Reductive Alkylation**




condensation and reduction of the presumed imine intermediates (reductive alkylation).[17] This method was tested mainly because it could possibly eliminate the two steps required to convert **4** to **3**. Thus, the reaction of **4** with *N*-phenylurea performed in the presence of chlorotrimethylsilane as the condensation agent and subsequent reduction with Li[$AlH_4$] led to **1e** in a good 82% yield. The choice of the reducing agent proved to be crucial since a similar reaction with Na[$BH_4$] and simultaneous addition of acetic acid afforded a



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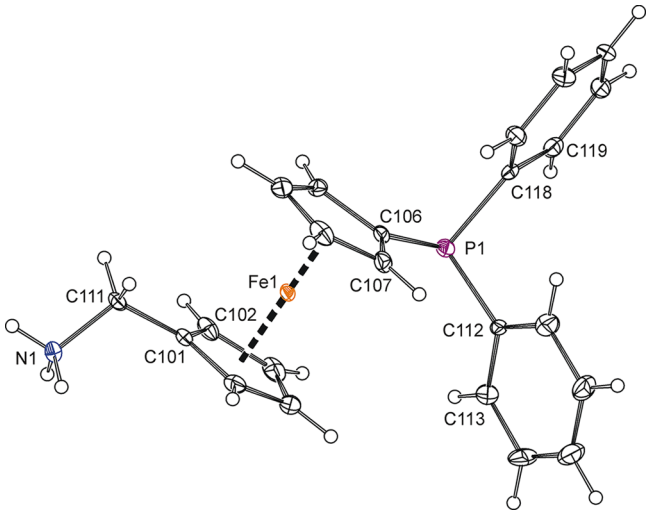


**Figure 1.** PLATON plot of cation 1 in the structure of **3**·HCl showing atom labeling and displacement ellipsoids at the 30% probability level. Note: Atom numbering in molecule 2 is strictly analogous.

product containing considerable amounts (approximately 30%) of the respective borane adduct, **1e**·$BH_3$ ($\delta_P$ 16.5). On the other hand, method C proved unsuitable for the preparation of **1a** because it mainly led to [1′-(diphenylphosphino)-ferrocenyl]methanol[15] (68% of this alcohol and only ca. 9% of **1a** were isolated with Li[$AlH_4$]) or yielded the desired product **1a** contaminated with the respective phosphine oxide and borane adduct, only the latter of which could be efficiently removed by crystallization (reaction with Na[$BH_4$]; chromatography proved to be inefficient in separating **1a**, **1aO**, and **1a**·$BH_3$).

On the other hand, method C becomes particularly important when no isocyanate or carbamoyl chloride required for the conventional additions or condensations is available or at least reasonably accessible. In the present case, method C was employed for the synthesis of *N*-methylurea **1b**. Thus, "reductive alkylation" of **4** with *N*-methylurea in the presence of $ClSiMe_3$ in THF−$CH_3CO_2H$ followed by reduction by Na[$BH_4$] provided **1b** in a 73% yield with less than 5% contaminants (phosphine oxide and borane adduct; further purification could be achieved through recrystallization). Similar reaction in the presence of Li[$AlH_4$] as a more energetic reducing agent afforded a cleaner product but in a lower yield because a considerable part of the starting aldehyde was reduced directly to the corresponding alcohol (isolated yields of **1b** and the alcohol were 30% and 49%, respectively).

All newly prepared compounds were characterized by multinuclear NMR and IR spectroscopy, electrospray ionization (ESI) mass spectrometry, and elemental analysis. In their $^1$H NMR spectra, the compounds showed signals typical of the phosphinoferrocenyl moiety, namely, a set of virtual multiplets (three triplets and one quartet) attributable to the unsymmetrically 1,1′-disubstituted ferrocene moiety bearing one phosphine substituent and a multiplet due to protons at the $PPh_2$ group. Corresponding signals were found in the $^{13}$C NMR spectra. Signals of the methylene linkers in **1a**−**e** and **1g** were observed at $\delta_H$ around 4.0 and $\delta_C$ 38−39, whereas those of **1f** appeared shifted to lower fields ($\delta_H$ 4.34, $\delta_C$ 44.25). $^{13}$C NMR resonances of the C═O units, another characteristic feature in the NMR spectra, were observed at $\delta_C$ ca. 155−159 for ureas **1a**−**e**, at $\delta_C$ 180.16 for thiourea **1f**, and at $\delta_C$ 169.73 for the *N*-acetyl derivative **1g**. Finally, the $^{31}$P NMR signals of **3**·HCl and **1a**−**g** were found within the narrow range of $\delta_P$ −16 to −18 ppm.

The ESI mass spectra of ureas **1** displayed pseudomolecular ions of the type $[M + X]^+$, where X = H, Na, and K. In contrast, the mass spectrum of **3**·HCl showed a strong signal attributable to the [1′-(diphenylphosphino)ferrocenyl]methylium cation, $Ph_2PfcCH_2^+$, analogous to the stabilized $[FcCH_2]^+$ fragment (Fc = ferrocenyl) typically appearing in the mass spectra of ferrocenylmethyl derivatives.[18]

In addition to characterization by various solution techniques, the crystal structures of **3**·HCl, **1a**, **1e**, and **1f** were determined by single-crystal X-ray diffraction analysis. Compound **3**·HCl (Figure 1 and Table 1) crystallizes with the symmetry of the monoclinic space group $P2_1/n$ and two molecules per asymmetric unit. The two independent molecules differ only marginally, mainly in the mutual orientation of the cyclopentadienyl rings (see $\tau$ angles in Table 1 and the overlap in the Supporting Information, Figure S1), and their geometric parameters are unexceptional. Hence, the reason for their "multiplication" most likely lies in the complexity of the hydrogen-bonded array in the crystal state.

Individual ions constituting the crystal structure of **3**·HCl assemble via charge-assisted N−H···Cl hydrogen bonds (N···Cl = 3.054(4)−3.143(4) Å), forming infinite columnar assemblies oriented parallel to the crystallographic *b*-axis. The bulky nonpolar phosphinoferrocenyl moieties are directed away from the "central" polar domains and thus decorate the hydrogen-bonded stacks on their exterior (Figure 2).

**Table 1. Selected Geometric Data for the Two Independent Cations in the Crystal Structure of 3·HCl (in Å and deg)[a]**

| parameter | molecule 1 | parameter | molecule 2 |
|---|---|---|---|
| Fe−Cg1 | 1.654(2) | Fe−Cg1 | 1.655(2) |
| Fe−Cg2 | 1.651(2) | Fe−Cg2 | 1.650(2) |
| ∠Cp1,Cp2 | 1.0(3) | ∠Cp1,Cp2 | 1.5(3) |
| $\tau$ | −156.8(4) | $\tau$ | −171.3(4) |
| P1−C106 | 1.825(5) | P2−C206 | 1.821(5) |
| P1−C112 | 1.846(5) | P2−C212 | 1.836(5) |
| P1−C118 | 1.840(5) | P2−C218 | 1.844(5) |
| N1−C111 | 1.482(6) | N2−C211 | 1.497(6) |
| C101−C111−N1 | 112.5(4) | C201−C211−N2 | 111.4(4) |

[a]Definitions: Cp1 and Cp2 are the azoniamethyl- [C(101−105) and C(201−205) in molecules 1 and 2] and phosphine-substituted [C(106−110) and C(206−210) in molecules 1 and 2] cyclopentadienyl rings, respectively. Cg1 and Cg2 are their respective centroids. $\tau$ represents the torsion angle C*n*01−Cg1−Cg2−C*n*06, where *n* = 1 and 2 for molecules 1 and 2, respectively.



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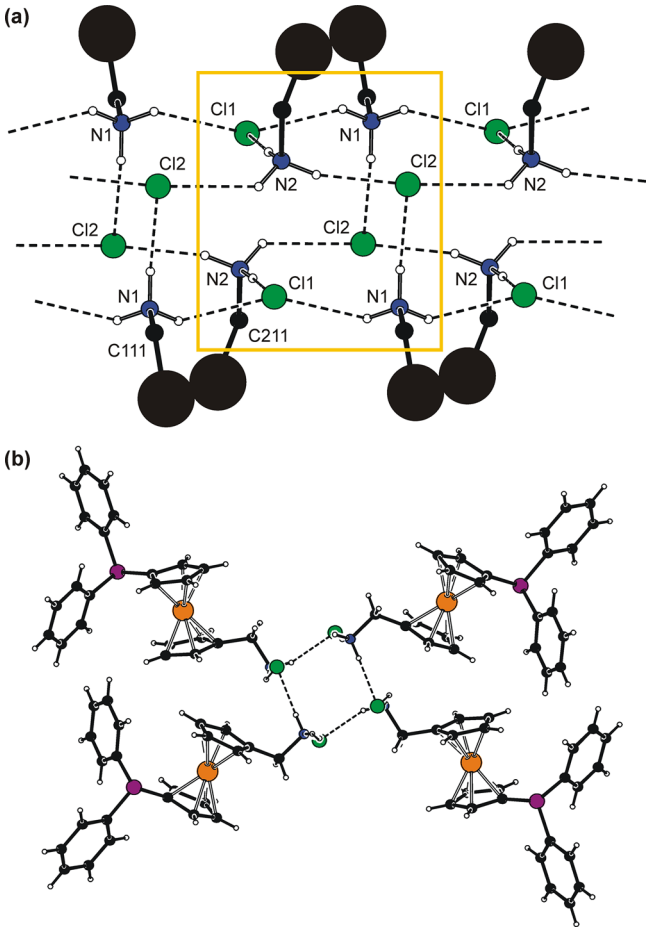


**Figure 2.** (a) Section of the hydrogen-bonded array in the structure of **3**·HCl. For convenience, the repeating unit is enclosed within a yellow box. Only the NH hydrogens are shown, and the bulky phosphinoferrocenyl moieties have been replaced with black circles to avoid complicating the figure. (b) Projection of a single columnar stack along the *b*-axis.

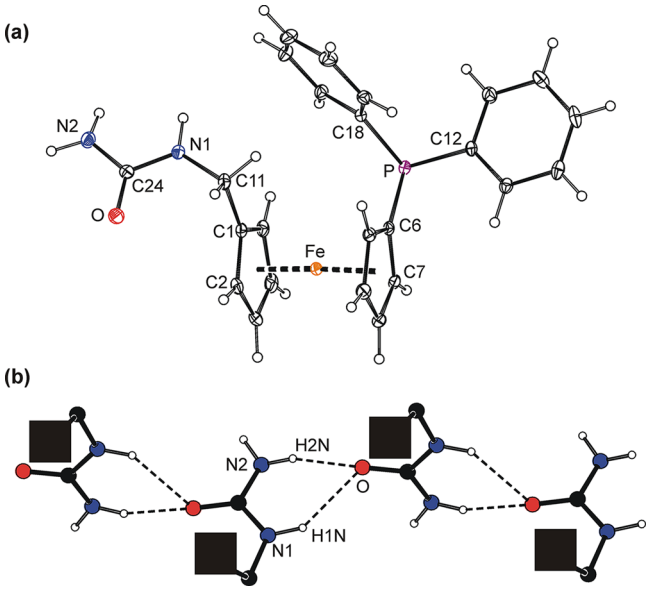


**Figure 3.** (a) PLATON plot of the molecular structure of **1a**. Displacement ellipsoids enclose the 30% probability level. (b) Section of the hydrogen-bonded chains in the structure of **1a**. For clarity, only the NH hydrogens are shown, and the phosphinoferrocenyl moieties have been replaced with black squares.

**Table 2. Selected Geometric Parameters for 1a, 1e, and 1f (in Å and deg)**

| parameter[a] | **1a** (Y = O) | **1e** (Y = O) | **1f** (Y = S) |
|---|---|---|---|
| Fe−Cg1 | 1.646(1) | 1.6458(9) | 1.662(2) |
| Fe−Cg2 | 1.639(1) | 1.6402(9) | 1.656(2) |
| ∠Cp1,Cp2 | 4.5(2) | 2.6(1) | 1.8(2) |
| $\tau$ | −68.1(2) | −90.0(1) | 157.7(3) |
| P−C6 | 1.805(2) | 1.815(2) | 1.823(3) |
| P−C12 | 1.836(2) | 1.840(2) | 1.838(4) |
| P−C18 | 1.829(2) | 1.838(2) | 1.838(4) |
| C1−C11 | 1.503(3) | 1.504(3) | 1.505(5) |
| C11−N1 | 1.454(3) | 1.452(3) | 1.452(5) |
| C1−C11−N1 | 113.8(2) | 112.0(2) | 110.3(3) |
| N1−C24 | 1.354(3) | 1.346(2) | 1.344(5) |
| N2−C24 | 1.353(3) | 1.376(2) | 1.343(5) |
| N2−C25 | n.a. | 1.408(3) | 1.434(5) |
| C24−Y | 1.241(2) | 1.238(2) | 1.699(4) |
| N1−C24−N2 | 115.4(2) | 113.2(2) | 117.0(3) |

[a]Definitions: Cp1 and Cp2 are the $CH_2$- [C(1−5)] and phosphine-substituted [C(6−10)] cyclopentadienyl rings, respectively. Cg1 and Cg2 stand for the respective centroids. $\tau$ is the torsion angle C1−Cg1−Cg2−C6. n.a. = not applicable.

The molecular structure of **1a** is depicted in Figure 3, and the selected geometric parameters for all structurally characterized phosphinoureas (i.e., **1a**, **1e**, and **1f**) are compiled in Table 2. Generally, the structural parameters determined for **1a** fall into the typical ranges.[19,20] The individual Fe−C distances vary slightly (2.020(3)−2.068(2) Å), which in turn results in tilting of the cyclopentadienyl ring planes by ca. 5°. The cyclopentadienyl rings assume an approximately synclinal eclipsed (ideal value:[21] 72°) conformation, and the urea pendant is directed below the ferrocene unit and takes part in intermolecular interactions.

The individual molecules of **1a** associate in a manner typical for *N*,*N*′-disubtituted ureas by forming infinite chains through pairs of N−H···O hydrogen bonds between proximal[22] NHCONH moieties, whose oxygen atoms behave as bifurcate hydrogen bond acceptors.[23] These hydrogen bonds thus involve only hydrogen atoms in an *anti* position with respect to the urea oxygen and are significantly asymmetric (N1···O = 3.212(3) Å; N2···O = 2.870(2) Å). The third NH proton available in **1a** (H3N) does not take part in hydrogen bonding with any conventional acceptor. Nonetheless, it is positioned appropriately for an interaction[24] with the "residual" electron density attributable to the lone pair of phosphorus, which manifests itself as the most intense peak in the final difference electron density map (see the Supporting Information, Figure S2).

Although the molecules of **1e** and **1f** (Figure 4 and Table 2) differ "only" by the chalcogen atom in the urea pendant, their structures are considerably dissimilar. The individual distances and angles are quite unexceptional and, for **1e**, compare well with those determined for a calix[4]arene modified by two $FcCH_2NHCONH-$ redox-active pendants (Fc = ferrocenyl).[25] The main difference lies in the molecular conformation and solid-state assemblies the compounds constitute in their crystals.

The cyclopentadienyl rings in the molecules of **1e** and **1f** are tilted by only 2.6(1)° and 1.8(2)°, respectively. They adopt


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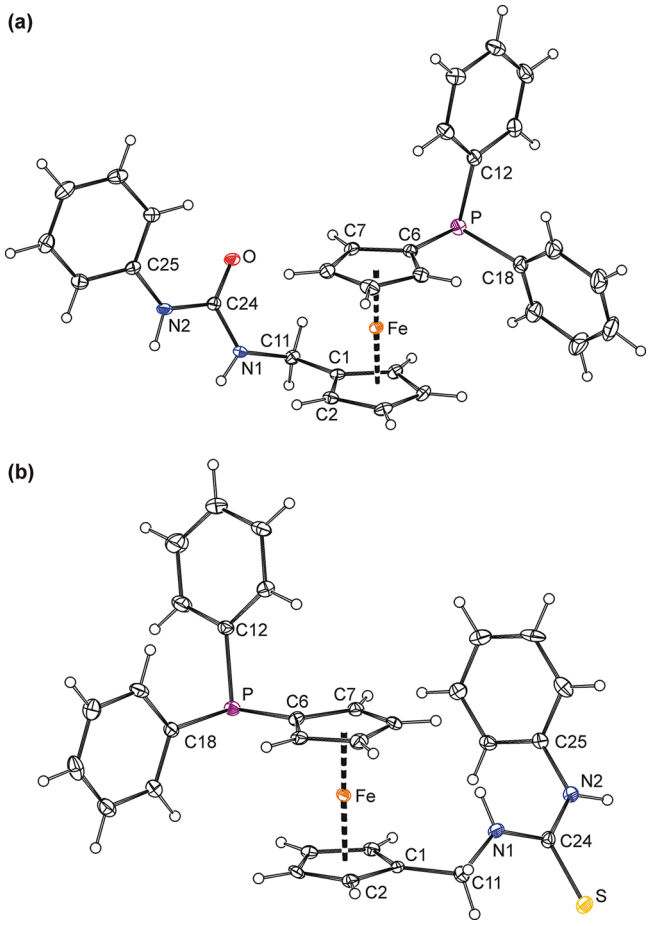


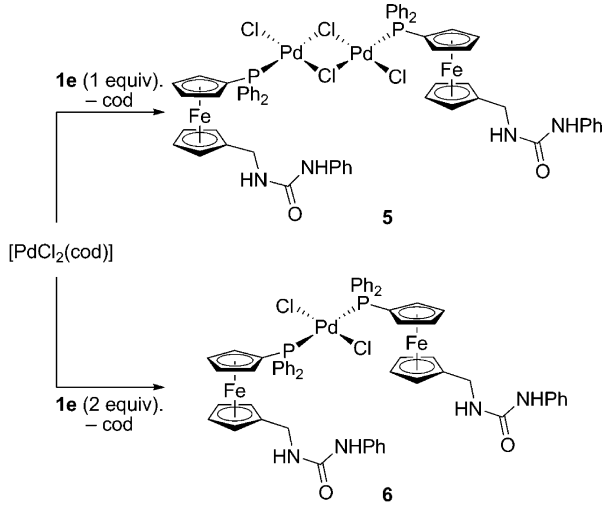

**Figure 4.** PLATON plots of the molecular structures of (a) **1e** and (b) **1f**. Displacement ellipsoids are scaled to the 30% probability level.

different mutual orientations, namely, an intermediate conformation between synclinal eclipsed and anticlinal staggered in **1e** and a conformation close to ideal anticlinal eclipsed in **1f**. Another substantial difference can be observed in the arrangement of the urea pendants. Whereas the urea moiety in **1e** has both hydrocarbyl groups in *syn* positions with respect to the oxygen of the central C═O bond, the substituents at the NHC(S)NH assume *syn* ($CH_2$) and *anti* (Ph) positions. Together with reorientation of the entire urea pendant with respect to the ferrocene units (cf. the C2/5−C1−C11−N1 angles 64.9(3)/−112.1(3)° for **1a**, 17.6(3)/−165.1(2)° for **1e**, and −149.7(4)/34.8(5)° for **1f**), this positioning directs the phenyl ring closer to the ferrocene unit and results in twisting of the terminal phenyl group with respect to the urea moiety, as evidenced by the dihedral angles subtended by the phenyl and the NC(E)N (E = O or S) planes being 24.8(1)° and 63.3(2)° for **1e** and **1f**, respectively. (Note: The values of the C11−N1−C24−N2 angles are higher than 175° in all three structures, thereby ruling out any signification torsion at the connecting urea motifs.)

The different geometries of the urea pendants are clearly associated with differences in the solid-state architecture. Compound **1e** forms the typical one-dimensional chain described by the C(4)[$R^1_2$(6)] descriptors[23a] in graph set notation[26] and observed as the main motif in the crystal structure of **1a** (see the Supporting Information, Figure S3; N1···O = 3.053(2) Å, N2···O = 2.884(2) Å). In contrast, the molecules of **1f** associate into simple centrosymmetric dimers via the relatively softer (weaker) N−H···S interactions (N2···S = 3.335(3) Å) and make use of only one of the available NH protons (N2−H2N, which is *syn* with respect to the sulfur atom; see Figure S4 in the Supporting Information).

**Preparation of Palladium(II) Complexes.** The coordination properties of the phosphinoferrocene ureas were examined in palladium(II) complexes using **1e** as a representative ligand. The experiments confirmed that the compounds behave as modified phosphines rather than as true bifunctional donors. For instance, the reaction of **1e** with [$PdCl_2$(cod)] (cod = cycloocta-1,5-diene) at 1:1 molar ratio provided the dipalladium(II) chloride-bridged complex **5** ($\delta_P$ 33.6;[27] Scheme 5). A similar reaction with two molar equivalents of **1e** with

**Scheme 5. Synthesis of Palladium(II) Complexes 5 and 6**[a]

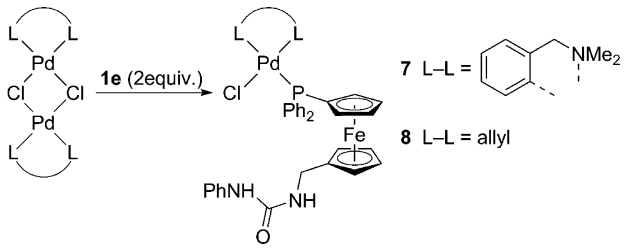



[a]cod = cycloocta-1,5-diene.

respect to Pd proved to be complicated due to unexpected side reactions and required careful optimization to produce the bisphosphine complex **6** ($\delta_P$ 16.5[28]).

The reactions of **1e** with dipalladium precursors [$Pd(L^{NC})(\mu$-$Cl)]_2$ and [$Pd(\eta^3$-$C_3H_5)(\mu$-$Cl)]_2$ also gave rise to the expected "simple" phosphine complexes **7** and **8**, both resulting via cleavage of the chloride bridges in the starting Pd complexes (Scheme 6). Repeated attempts to induce a chelate

**Scheme 6. Synthesis of Palladium(II) Complexes 7 and 8**




coordination of **1e** by removal of the Pd-bound chloride in **7** by either a soluble Ag(I) or Tl(I) salt (Ag[$SbF_6$] and Tl[$PF_6$]) or via an intramolecular replacement following deprotonation of the NH group(s) with *t*-BuOK were unsuccessful, affording only complicated and easily decomposing reaction mixtures.

Although partly disordered, the molecular structures of **7**·$2CHCl_3$ and **8** could be determined by X-ray diffraction



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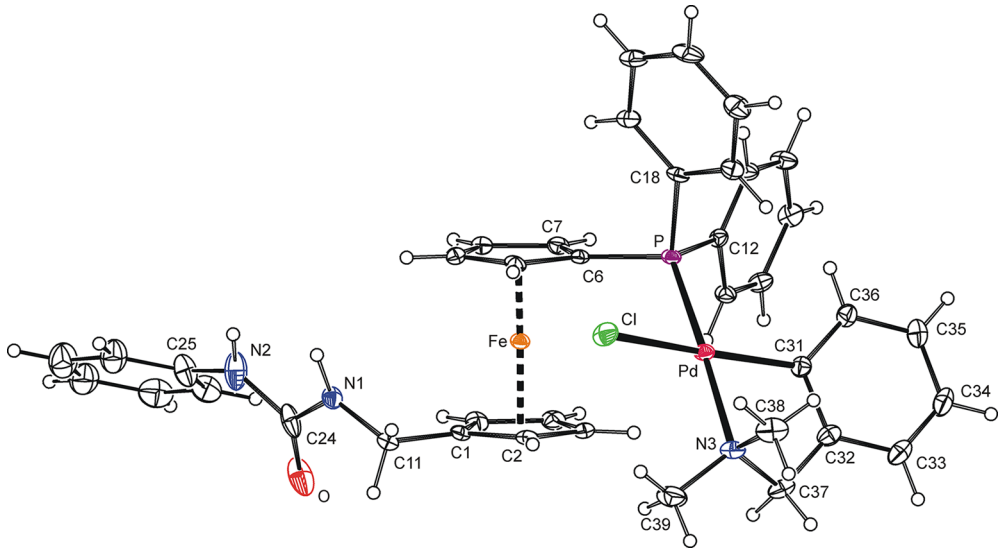


**Figure 5.** PLATON plot of the molecular structure of **7**. The displacement ellipsoids are scaled to the 30% probability level. For clarity, only one orientation of the disordered phenyl group is shown (for a complete drawing, see the Supporting Information). Selected geometric data (in Å and deg): Pd−Cl 2.4160(9), Pd−P 2.2576(8), Pd−N(3) 2.153(3), Pd−C(31) 2.005(4), P−Pd−Cl 91.87(3), Cl−P−N3 90.28(8), N2−Pd−C31 81.9(1), C31−Pd−P 97.1(1).

analysis. The structures are presented in Figures 5 and 6, respectively, along with relevant geometric parameters.

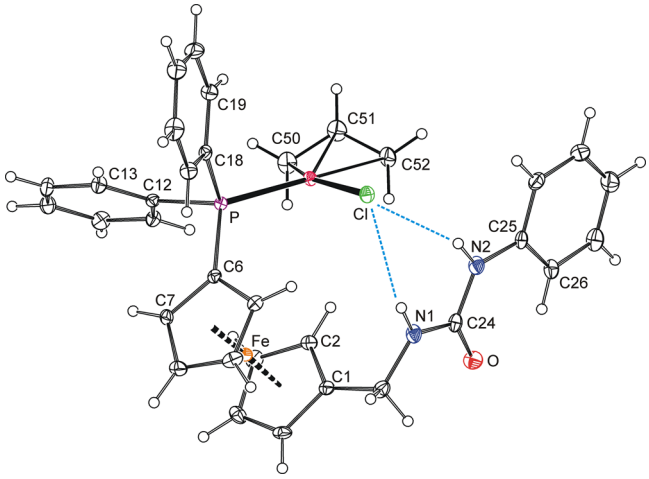


**Figure 6.** PLATON plot of the molecular structure of **8** (30% probability displacement ellipsoids) showing only the dominant orientation of the $\pi$-allyl moiety and the N−H···Cl hydrogen bonds as dashed lines (for a complete structural drawing, see the Supporting Information, Figure S6). Coordination geometry parameters (in Å and deg): Pd−Cl 2.3826(6), Pd−P 2.3013(6), Pd−C50 2.124(5), Pd−C51 2.138(5), Pd−C52 2.221(7), Cl−Pd−P 95.35(2), P−Pd−C50 102.8(1), Cl−Pd−C52 94.6(2).

The structure of solvated **7** corroborates the *trans*-P−N relationship already deduced from the NMR parameters of the $CH_2NMe_2$ moiety, namely, the $^3J_{PC}$ and $^4J_{PH}$ coupling constants.[29] The compound has the expected square-planar coordination environment around the palladium center, which is distorted due to the presence of a small metallacycle (the Pd−C and Pd−N bonds are the shortest among the Pd-donor distances, and the C−Pd−N angle is the most acute interligand angle).[29a,c,e,g] The five-membered palladium ring has an envelope conformation with the nitrogen N3 at the tip position.

Ferrocene cyclopentadienyls in the structure of **7** are tilted by as little as 0.5(2)° (Fe−Cg1 and Fe−Cg2 are 1.646(2) and 1.647(2) Å, respectively) and assume a conformation near anticlinal eclipsed ($\tau$ = 136.3(2)°, cf. ideal value: 144°). The urea moiety is rotated by 68.5(2)° with respect to the plane of the cyclopentadienyl ring C(1−5), forming a pair of N−H···Cl hydrogen bridges toward chloride in a proximal, inversion-related molecule of the complex (see the Supporting Information, Figure S7; N1···Cl = 3.335(3) Å, N2···Cl = 3.351(2) Å).

The $\eta^3$-allyl moiety in the structure of **8** is disordered over two positions that are approximately related by reflection through the plane constituted by the remaining ligands (i.e., the {Pd, Cl, P} plane). The allyl unit intersects the latter plane at an angle of 65.7(6)° (60.5(8)° for the less abundant orientation), and the Pd−C distances gradually increase on going from C50 to C52, following the trend dictated by *trans* influence (P > Cl).[30] Similar structural features have been observed in the structures of analogous ($\eta^3$-allyl)Pd(II) complexes with phosphinoferrocene ligands.[10,31]

Similarly to **7**, the urea protons in **8** form hydrogen bridges to the Pd-bound chloride, although within the same molecule (N1···Cl = 3.408(2) Å, N2···Cl = 3.380(2) Å). However, because the N−H···Cl interactions are intramolecular, the urea moiety is oriented nearly perpendicularly to the plane of its parent cyclopentadienyl ring C(1−5) (dihedral angle: 89.8(1)°; see Figure 6), and the ferrocene unit has a less open conformation ($\tau$ = 99.5(2)°, N.B. the tilting is slightly higher: 3.4(1)°; Fe−Cg1/Cg2 = 1.657(1)/1.649(1) Å).

**Pd-Catalyzed Cyanation of Aryl Bromides.** In view of the presence of the highly polar urea tags in the newly prepared phosphinoferrocene donors, we decided to evaluate their catalytic potential in aqueous, Pd-catalyzed cyanation of aryl bromides leading to synthetically valued benzonitriles,[32] using potassium hexacyanoferrate(II) as an environmentally benign, hydrolytically stable, and water-soluble cyanide source.[33] For the initial screening of the reaction conditions, we chose the cyanation of 4-bromoanisole (**9g**), providing the corresponding nitrile **10g** and amide **11g** as its hydrolytic side-product


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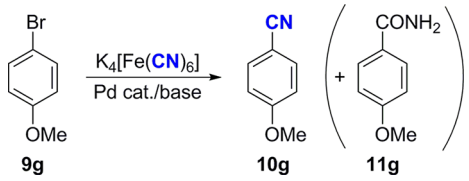
(Scheme 7). This reaction can be easily followed by $^1$H NMR spectroscopy using the signals of the methoxy groups as

**Scheme 7. Model Cyanation Reaction**




characteristic markers. A catalyst generated *in situ* by mixing palladium(II) acetate with two equivalents of ligand **1e** was used in most of the screening experiments.

Aiming at understanding the effect of aqueous reaction media on the reaction course,[1,34] the possible influence of the solvent was evaluated first. The results presented graphically in Figure 7

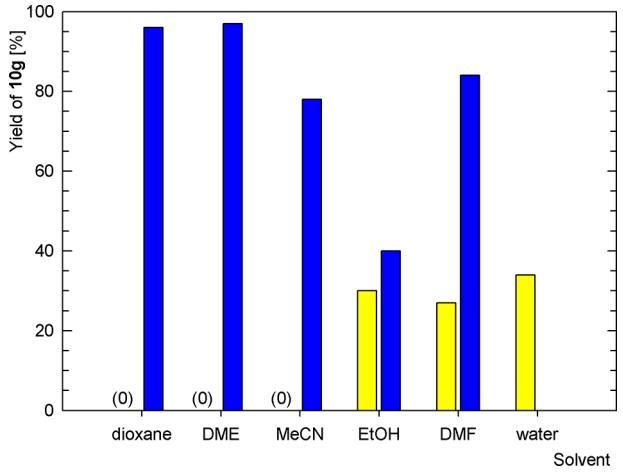



**Figure 7.** Effect of the solvent on the yield of the coupling product **10g**. Pure solvents (yellow bars) are compared with their 1:1 (by volume) aqueous mixtures (blue bars). Conditions: substrate **9g** (1.0 mmol), $K_2CO_3$ (1.0 mmol), and $K_4[Fe(CN)_6]\cdot 3H_2O$ (0.5 mmol) were reacted in the presence of *in situ* generated catalyst (1 mol % Pd, 2 mol % **1e**; see Experimental Section) in the respective solvent (4 mL) at 100 °C for 3 h. NMR yields are given.

demonstrate that the yields of **10g** achieved in an aqueous mixture (solvent–water 1:1 by volume) were better than those obtained in any tested *pure* organic solvent. This observation likely reflects the solubility of the inorganic components in the reaction mixture because the difference in the reaction outcome was most pronounced for ethereal solvents such as (1,4-) dioxane and 1,2-dimethoxyethane (DME) and for acetonitrile, in which the polar reagents would be practically insoluble.

It is also noteworthy that the yield of the coupling product obtained in pure water was lower than that in all other water–organic solvent mixtures tested. Again, this result can be accounted for by the solubility of the reaction components and phase mixing phenomena. We observed that the addition of the mixed solvent typically gave rise to a heterogeneous reaction mixture (two liquid phases). However, this mixture was partly or even fully homogenized upon heating to the reaction temperature (100 °C), which in turn allowed for efficient interaction between the organic substrate, the catalyst, and the highly polar inorganic reagents (i.e., the base and $CN^-$ source).

On the basis of the results of the solvent screening experiments, dioxane was chosen for further reaction tests as an inexpensive aprotic solvent possessing favorable properties, including a reasonably high boiling point and unlimited miscibility with water. More detailed tests showed that changing the water/dioxane ratio also significantly affects the reaction course. For instance, whereas no coupling product was obtained from reactions performed in pure and 80% dioxane (Figure 8), the yield of **10g** suddenly grew to 92% upon

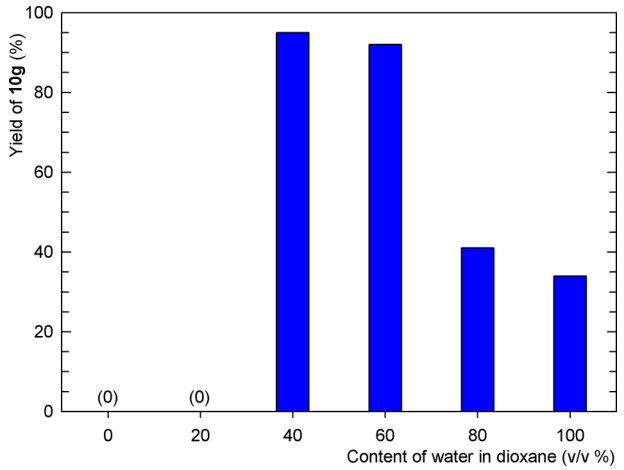



**Figure 8.** Effect of the composition of the water–dioxane mixture on the yield of the coupling product **10g**. For detailed conditions, see caption of Figure 7

increasing the water content to 40 vol %. In accord with our previous results,[35] the best results were obtained in 40:60–60:40 solvent mixtures (cf. 96% yield of **10g** in 50% dioxane). A further increase in the water content to 80% and 100% markedly decreased the yield of the coupling product. Consequently, a 1:1 dioxane–water mixture was employed as the solvent for this particular reaction in all subsequent experiments.

Experiments were also focused on the possible effects of the palladium source and the base. The evaluation of various common palladium precursors at 1 mol % Pd loading (Table 3) has indeed shown that the type of palladium precursor plays an important role. The most satisfactory yields of the coupling

**Table 3. Survey of Various Pd Precursors in the Model Coupling Reaction[a]**

| Pd source | yield of **10g** [%] | Pd source | yield of **10g** [%] |
|---|---|---|---|
| $Pd(OAc)_2$ | 88 | $[PdCl_2(cod)]$ | 89 |
| $Pd(OAc)_2$ | 56[b] | $K_2[PdCl_4]$ | <5[f] |
| $Pd(OAc)_2$ | 29[c] | $[PdCl_2(MeCN)_2]$ | 91 |
| $Pd(OAc)_2$ | 24[d] | $[PdCl(L^{NC})]_2$ | 52[b] |
| $Pd(OAc)_2$ | <5[e] | $[PdCl(\eta^3\text{-}C_3H_5)]_2$ | 18[b] |
| $Pd(O_2CCF_3)_2$ | 92 | $[Pd_2(dba)_3]$ | 30 |

[a]Conditions: substrate **9g** (1.0 mmol), $K_2CO_3$ (1.0 mmol), and $K_4[Fe(CN)_6]\cdot 3H_2O$ (0.5 mmol) were reacted in the presence of *in situ* generated catalyst (1 mol % Pd, 2 mol % **1e**; see Experimental Section) in dioxane–water (1:1, 4 mL) at 100 °C for 3 h. The yield was determined by integration of $^1$H NMR spectra using mesitylene as an internal standard. [b]Pd:**1e** = 1:1. [c]Reaction with 0.5 mol % Pd. [d]Reaction at 80 °C. [e]Reaction at 60 °C. [f]The catalyst was prepared in methanol due to the insolubility of the starting Pd complex in dichloromethane.



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product (around 90%) were obtained with catalysts resulting from simple palladium(II) carboxylates, viz., $Pd(OAc)_2$ and $Pd(O_2CCF_3)_2$, at a Pd:**1e** ratio of 1:2. For practical reasons, the former Pd(II) salt appears particularly attractive because it not only gives rise to a highly active catalyst but is also relatively inexpensive and readily available. Notably, catalysts generated from other Pd(II) precursors as well as from $[Pd_2(dba)_3]$ as an immediate source of Pd(0) performed significantly worse. Similarly, lowering the amount of the ligand to 1 equiv with respect to palladium or decreasing the reaction temperature (100 °C → 80 and 60 °C) considerably reduced the yield of **10g** with the $Pd(OAc)_2$/**1e** catalyst.

The catalytic results achieved with different bases are presented in Table 4. Sodium and potassium carbonate

**Table 4. Survey of Various Bases**[a]

| base | yield of **10g** [%] | base | yield of **10g** [%] |
|---|---|---|---|
| $Li_2CO_3$ | 50 | $NaHCO_3$ | 8 |
| $Na_2CO_3$ | 92 | $Na_3PO_4$ | 49[c] |
| $Na_2CO_3$ | 45[b] | $Na_2HPO_4$ | 8[b] |
| $K_2CO_3$ | 88 | $NaH_2PO_4$ | 0[d] |
| $K_2CO_3$ | 80[b] | NaOAc | <5 |
| $Cs_2CO_3$ | 28 | NaOH | 12[e] |

[a]Conditions: substrate **9g** (1.0 mmol), base (1.0 mmol unless specified otherwise), and $K_4[Fe(CN)_6]\cdot 3H_2O$ (0.5 mmol) were reacted in the presence of *in situ* generated catalyst (1 mol % $Pd(OAc)_2$, 2 mol % **1e**; see Experimental Section) in dioxane−water (1:1, 4 mL) at 100 °C for 3 h. The yield was determined by integration of $^1$H NMR spectra using mesitylene as an internal standard. [b]0.5 mmol of base. [c]0.33 mmol of $Na_3PO_4$. Amide **11g** (<5%) was also detected. [d]***Caution!*** *(Partial) hydrolysis to HCN likely occurs.* [e]Amide **11g** (42%) also formed.

afforded comparable, very good yields (around 90%) when employed in a 1:1 molar ratio with respect to the substrate **9g**. When the amount of these bases was reduced by half (i.e., to one molar equivalent of alkali metal cation per **9g**), the yields of the coupling product decreased, although to different extents, to approximately half in the case of $Na_2CO_3$ and by only 8% with $K_2CO_3$. Both the lighter ($Li_2CO_3$) and the heavier ($Cs_2CO_3$) congeners of these carbonates produced **10g** in lower yields, the former most likely due its relatively poor solubility in the reaction system. Likewise, sodium hydrogen carbonate as well as other bases tested (sodium phosphates, sodium acetate, and sodium hydroxide) did not match the results obtained for either simple carbonate from which the common $Na_2CO_3$ was selected as the most suitable for further reactions because of its good performance and lower molar weight (less material was needed).

To further minimize the amount of inorganic reagents required for the cyanation reaction to proceed with good yields and to limit the amount of waste produced, we have studied the effect of the amount of the cyanide source on the yield of the coupling product. Unfortunately, the results presented in Table 5 indicate that the amount of $K_4[Fe(CN)_6]\cdot 3H_2O$ cannot be reduced further below approximately 0.5 molar equivalents (i.e., 3 equiv of $CN^-$) with respect to **9g** without reducing the yields of the corresponding nitrile in the present case.

Having established the optimal reaction conditions in terms of the reaction solvent, base, and palladium source, we turned to studying the properties of individual phosphinoferrocene ligands (Table 6). The best catalytic results showed catalysts resulting from ligands equipped with urea moieties bearing

**Table 5. Effect of the Amount of $CN^-$ Equivalents on the Yield of Nitrile 10g**[a]

| amount of $K_4[Fe(CN)_6]\cdot 3H_2O$ [mmol] | CN equiv | yield of **10g** [%] |
|---|---|---|
| 1.00 | 6 | 96 |
| 0.50 | 3 | 92 |
| 0.33 | 2 | 65 |
| 0.17 | 1 | 46 |

[a]Conditions: substrate **9g** (1.0 mmol), $Na_2CO_3$ (1.0 mmol), and varying amounts of $K_4[Fe(CN)_6]\cdot 3H_2O$ were reacted in the presence of *in situ* generated catalyst (1 mol % $Pd(OAc)_2$, 2 mol % **1e**; see Experimental Section) in dioxane−water (1:1, 4 mL) at 100 °C for 3 h. The yield was determined by integration of $^1$H NMR spectra using mesitylene as an internal standard.

**Table 6. Catalytic Results Achieved with Different Ligands**[a]

| ligand | yield of **10g** [%] | ligand | yield of **10g** [%] |
|---|---|---|---|
| **1a** | 52 | **1e** | 92 |
| **1b** | 53 | **1f** | 0 |
| **1c** | 55 | **1g** | 40 |
| **1d** | 86 | $FcPPh_2$ | 30 |

[a]Conditions: substrate **9g** (1.0 mmol), $Na_2CO_3$ (1.0 mmol), and $K_4[Fe(CN)_6]\cdot 3H_2O$ (0.5 mmol) were reacted in the presence of *in situ* generated catalyst (1 mol % $Pd(OAc)_2$, 2 mol % ligand; see Experimental Section) in dioxane−water (1:1, 4 mL) at 100 °C for 3 h. The yields were determined by integration of $^1$H NMR spectra using mesitylene as an internal standard.

more bulky and lipophilic substituents (phenyl and cyclohexyl), with phenyl urea **1e** being the most efficient (92% of **10g**). Donors possessing urea substituents with relatively smaller terminal substituents (NHMe and $NMe_2$) as well as the monosubstituted urea **3a** furnished only ca. 50% yields of **10g**, whereas a further reduction of the polar pendants, such in the acetylamino derivative **1g**, caused the yield to decrease even further.

The reaction performed in the absence of any supporting ligand (i.e., employing only $Pd(OAc)_2$ as the catalyst) did not proceed in any appreciable extent under otherwise identical conditions (results not tabulated), suggesting that the supporting phosphine ligand represents a vital component of the catalytic system (unlike many other cross-coupling reactions). In addition, from the dependence of the reaction yield on the structure of the phosphine ligands, it appears likely that the urea moiety is also involved in the catalytic reaction, e.g., by (temporary) coordination of the metal center or through its solubility-tuning properties. The most indicative signs are the dramatically different performance of catalysts based on the analogous phenyl-substituted urea and thiourea ligands (**1e** vs **1f**) and the fact that the catalyst based on $FcPPh_2$ as a P-monodentate donor produced a rather low yield of the coupling product.

As the last step, we studied the scope of the cyanation reaction by altering the structure of the aryl bromide substrate (Scheme 8). The results collected in Table 7 demonstrate that the reaction proceeds satisfactorily with electron-rich, alkylated substrates, despite moderate steric hindrance (see entries 1−5

**Scheme 8. General Scheme of the Cyanation Reaction**

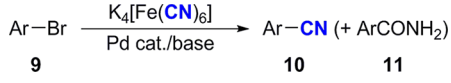




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Table 7. Cyanation of Different Aryl Bromides[a]

| entry | Ar in ArBr (9) | conversion to (yield of)[b] 10 after 3 h [%] | conversion (yield)[b] after 24 h [%] 10 | 11 |
|---|---|---|---|---|
| 1 | 2-$MeC_6H_4$ (**9a**) | 92 (89) | | |
| 2 | 3-$MeC_6H_4$ (**9b**) | 96 (90) | | |
| 3 | 4-$MeC_6H_4$ (**9c**) | 100 (94) | | |
| 4 | 4-*t*-$BuC_6H_4$ (**9d**) | 88 (84) | 91 (84) | n.d. (9) |
| 5 | 2,4,6-$Me_3C_6H_2$ (**9e**) | 48 (n.d.) | 100 (97) | |
| 6 | 4-$PhC_6H_4$ (**9f**) | 100 (96) | | |
| 7 | 4-$MeOC_6H_4$ (**9g**) | 100 (92) | | |
| 8 | 3,4-$(MeO)_2C_6H_3$ (**9h**) | 98 (94) | | |
| 9 | 3,4-$(OCH_2O)C_6H_3$ (**9i**) | 62 (60) | | |
| 10 | 4-$AcC_6H_4$ (**9j**) | 9 (n.d.) | 16 (15) | 84 (82) |
| 11 | 4-$F_3CC_6H_4$ (**9k**) | 18 (n.d.) | 16 (n.d.) | 84 (80) |
| 12 | 4-$ClC_6H_4$ (**9l**) | 25 (n.d.) | 17 (14) | 83 (80) |
| 13 | 4-$O_2NC_6H_4$ (**9m**) | 0 | <5 | |
| 14 | 4-$H_2NC_6H_4$ (**9n**) | 10 (n.d.) | 10 (n.d.) | |
| 15 | 4-$Me_2NC_6H_4$ (**9o**) | 10 (n.d.) | 9 (n.d.) | |
| 16 | 4-$AcNHC_6H_4$ (**9p**) | 60 (55) | 50 (48) | 32 (25)[d] |
| 17 | 4-$HO_2CC_6H_4$ (**9q**) | 93 (84)[c] | | |
| 18 | 1-naphthyl (**9r**) | 18 (n.d.) | 100 (94) | |
| 19 | 2-naphthyl (**9s**) | 99 (94) | | |
| 20 | 1-pyrenyl (**9t**) | | n.d. (79) | |
| 21 | Fc (**9u**) | | 21 (18) | |

[a]Conditions: substrate **9** (1.0 mmol), $Na_2CO_3$ (1.0 mmol), and $K_4[Fe(CN)_6]\cdot 3H_2O$ (0.5 mmol) were reacted in the presence of *in situ* generated catalyst (1 mol % $Pd(OAc)_2$, 2 mol % **1e**; see Experimental Section) in dioxane−water (1:1, 4 mL) at 100 °C for 3 or 24 h. [b]$^1$H NMR conversion (isolated yield in parentheses). These values are averages of two independent runs. n.d. = not determined. [c]2 mmol of $Na_2CO_3$ were used. [d]Nitrile **10n** was also formed (conversion: 18%, isolated yield: 16%).

in Table 7). The introduction of a methoxy group(s) or similar substituents, whose +*M* effect prevails over an −*I* effect, does not hamper the cyanation reaction (entries 7−9). On the other hand, substrates bearing groups with a pronounced electron-withdrawing character react less willingly, and the respective nitriles as the primary products are activated toward hydrolysis to the corresponding amides (see entries 10−12).[36] The crystal structures determined for two such amides, **11j** and **11k**, are discussed in the Supporting Information.

The presence of the nitro group in the *para* position of the benzene ring, exerting strong −*M* and −*I* effects, practically stopped the cyanation reaction, and substrate **9m** thus remained unchanged (entry 13). Aryl bromides bearing amine substituents **9n** and **9o** (entries 14 and 15) also reacted only sluggishly, albeit presumably due to the metal-scavenging effect of their donor substituents. This was corroborated by cyanation of 4-bromoacetanilide (**9p**, entry 16), which furnished nitrile **10p** with 60% conversion (55% isolated yield; entry 16) after 3 h. Extending the reaction time to 24 h did not improve the yield of **10p** (isolated yield: 48%) because of partial hydrolysis to the corresponding amide **11p** (isolated yield: 25%) and removal of the acetyl group resulting in the formation of 4-aminobenzonitrile (**10n**; isolated yield: 16%). The cyanation of 4-bromobenzoic acid (**9q**, entry 16) also represents a notable example because the deprotonation of the carboxyl group under the applied reaction conditions (2 equiv of $Na_2CO_3$ are used) activated the substrate, which was then efficiently converted to the corresponding nitrile without any notable hydrolysis (COOH: −*I* and −*M*; $COO^-$: +*I* and +*M*).

In addition to substituted bromobenzenes, we tested a few other brominated arenes. Thus, 1-bromonaphthalene was fully converted to the respective nitrile **10r** over a period of 24 h, whereas the isomeric 2-bromonaphthalene reacted to a similar extent already within 3 h. The described procedure could also be used to prepare 1-cyanopyrene (**10t**) and cyanoferrocene (**10u**), in which case, however, extended reaction times were required, and the latter product was isolated in only a modest 18% yield. In this case, however, 75% of the starting bromoferrocene was recovered unchanged.

In an attempt to further expand the scope of the reaction, we also varied the halide substituent. Quite expectedly, 4-iodoanisole reacted smoothly under the standard conditions (1 mol % Pd, 3 h), affording **10g** in a 95% isolated yield, but no reaction was observed with the less reactive chloride (i.e., 4-chloroanisole). 4-Bromobenzyl bromide (**9v**) was not cyanated either, being cleanly hydrolyzed under the reaction conditions to 4-bromobenzyl alcohol (**12**; 100% conversion, 90% isolated yield after 24 h).

In is also noteworthy that analysis of the crude reaction mixtures (i.e., prior to workup) typically revealed a characteristic low-field signal in the $^1$H NMR spectrum attributable to a ligand decomposition product ($\delta_H$ ca. 8.7). To identify this reaction product and, consequently, the fate of the phosphine ligand, we prepared phosphine oxide **1eO** by standard hydrogen peroxide oxidation of the model ligand **1e**. Indeed, the NMR signals of authentic **1eO** were identical to those observed in the reaction mixtures, thereby confirming that the ligand undergoes oxidation during the reaction.

## CONCLUSION

This contribution describes the synthesis and catalytic applications of a series of phosphinoferrocene donors modified by various urea moieties, appended via a methylene linker. These compounds were synthesized through three different methods, starting from either the newly prepared phosphinoamine **3** (or rather its stable hydrochloride) or aldehyde **4**. The applicability of these methods was demonstrated to depend on the urea pendant to be incorporated into the newly formed molecule, namely, on the number and type of the substituents at the nitrogen atoms.

As exemplified for the model ligand **1e**, phosphinoferrocene ureas **1** coordinate the Pd(II) ion as typical soft donors (functionally modified phosphines) via their phosphine groups, while the polar urea moieties remain available for the formation of hydrogen-bonded assemblies in the solid state. When combined with a suitable palladium source, these ligands give rise to active catalysts for Pd-catalyzed cyanation of aryl bromides with nontoxic $K_4[Fe(CN)_6]\cdot 3H_2O$ in aqueous reaction media. Under the optimized conditions, the cyanation reaction proceeds with very good to excellent yields for bromoarenes devoid of other substituents and substrates modified by electron-donating groups. In the case of



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electron-poor substrates, the yield of cyanation product (the nitrile) is typically reduced by subsequent hydrolysis upon the action of the base present in the reaction mixture. Substrates with amine substituents also pose some problems, presumably because of their metal-scavenging effect.

## EXPERIMENTAL SECTION

**Materials and Methods.** The syntheses were performed under an argon atmosphere using standard Schlenk techniques. Compounds **2**,[14] **4**,[15] $[PdCl_2(cod)]$,[37] and $[(L^{NC})Pd(\mu\text{-}Cl)]_2$[38] were synthesized according to procedures reported in the literature. Commercial *N,N*-dimethylcarbamoyl chloride was distilled before use. Methanol, dichloromethane, and tetrahydrofuran (HPLC grade) were dried with a PureSolv MD5 solvent purification system (Innovative Technology). Other chemicals and solvents used for crystallizations and during chromatography were used as received without any additional purification.

NMR spectra were recorded at 25 °C on a Varian UNITY Inova 400 spectrometer operating at 399.95, 100.58, and 161.90 MHz for $^1$H, $^{13}$C, and $^{31}$P, respectively. Chemical shifts ($\delta$/ppm) are reported relative to internal tetramethylsilane ($^1$H and $^{13}$C) or to external 85% $H_3PO_4$ ($^{31}$P). In addition to the standard notation of signal multiplicity, vt and vq are used to denote virtual multiplets arising from the protons constituting the AA′BB′ and AA′BB′X spin systems in the methylene- and $PPh_2$-substituted cyclopentadienyl rings, respectively (fc = ferrocene-1,1′-diyl). IR spectra were recorded with a Thermo Nicolet Magna 6700 FTIR spectrometer over the range 400−4000 cm$^{-1}$. Low-resolution ESI mass spectra were obtained with an Esquire 3000 (Bruker) spectrometer. Elemental analyses were determined with a PerkinElmer PE 2400 CHN analyzer. The amount of residual solvents, typically present in amorphous products, was verified by NMR analysis and taken into account during all subsequent experiments.

*Synthesis of 1′-(Diphenylphosphino)-1-(aminomethyl)ferrocene Hydrochloride (**3**·HCl).* Aldoxime **2** (250 mg, 0.61 mmol; mixture of *E*- and *Z*-isomers) was dissolved in dry THF (15 mL), and the solution was added dropwise to solid $Li[AlH_4]$ (115 mg, 3.0 mmol) while stirring and cooling in an ice bath. The reaction mixture was stirred at room temperature for 6 h and then recooled on ice and quenched by sequential addition of water (0.55 mL) and 15% aqueous NaOH (0.15 mL). After stirring for another 30 min, the resulting heterogeneous mixture was filtered through a pad of diatomaceous earth (Celite). The filtrate was diluted with diethyl ether (15 mL), washed with brine (5 mL), dried over magnesium sulfate, and, after removal of the drying agent, treated with methanolic HCl (0.81 mL of a 0.75 M solution, 0.61 mmol). The separated product was filtered off and dried under vacuum to afford hydrochloride **3**·HCl as a yellow solid (168 mg, 64%). Crystals for X-ray diffraction measurements were grown from hot methanol−chloroform.

$^1$H NMR (DMSO-$d_6$): $\delta$ 3.55 (s, 2 H, $CH_2$), 4.06 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.11 (vq, $J'$ = 1.9 Hz, 2 H, fc), 4.30 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.50 (vt, $J'$ = 1.8 Hz, 2 H, fc), 7.29−7.41 (m, 10 H, Ph), 8.15 (br s, 3 H, $NH_3^+$). $^{13}$C{$^1$H} NMR (DMSO-$d_6$): $\delta$ 37.73 ($CH_2$), 69.48 (CH of fc), 70.52 (CH of fc), 71.70 (d, $J_{PC}$ = 4 Hz, CH of fc), 73.11 (d, $J_{PC}$ = 15 Hz, CH of fc), 75.99 (d, $^1J_{PC}$ = 7 Hz, *C*-$PPh_2$ of fc), 79.84 (*C*-$CH_2$ of fc), 128.22 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of $PPh_2$), 128.58 ($CH^{para}$ of $PPh_2$), 132.94 (d, $^3J_{PC}$ = 20 Hz, $CH^{meta}$ of $PPh_2$), 138.44 (d, $^1J_{PC}$ = 10 Hz, $C^{ipso}$ of $PPh_2$). $^{31}$P{$^1$H} NMR (DMSO-$d_6$): $\delta$ −17.7 (s). IR (Nujol, cm$^{-1}$): $\nu_{max}$ 3068 m, 2635 w, 2559 w, 1594 w, 1562 w, 1309 w, 1241 w 1162 m, 1104 m, 1026 m, 963 w, 911 w, 884 w, 827 s, 817 s, 746 s, 698 s, 633 w, 522 w, 503 s, 483 s, 452 m, 424 w, 412 w. ESI+ MS: *m*/*z* 383 ($[Ph_2PfcCH_2]^+$). Anal. Calcd for $C_{23}H_{23}ClFeNP$·0.1$CHCl_3$ (447.6): C 61.98, H 5.20, N 3.13. Found: C 61.78, H 5.07, N 3.02 (crystallized sample).

*Synthesis of N-[1′-(Diphenylphosphino)ferrocenyl]urea (**1a**). Method A.* Anhydrous triethylamine (1.0 mL, 7.2 mmol, 16 equiv) was added to a suspension of **3**·HCl (200 mg, 0.46 mol) in dry methanol (15 mL), causing the solid hydrochloride to dissolve the compound. Sodium cyanate (47 mg, 0.6 mmol, 1.5 equiv) dissolved in methanol and water (4 + 4 mL) was added, and the resultant solution was stirred at room temperature overnight. Next, the mixture was diluted with water (10 mL) and extracted with dichloromethane (2 × 10 mL). The organic extracts were combined, washed with brine, dried over anhydrous magnesium sulfate, and evaporated. Subsequent chromatography over silica gel with dichloromethane−methanol (10:1 v/v) led to the development of two orange bands. The first one contained the desired product **1a**, which was isolated by evaporation as an orange, readily crystallizing oil (75 mg, 37%). Evaporation of the second band afforded unreacted free amine (105 mg, 57%). Note: Isolated **1a** is typically contaminated by traces of the corresponding phosphine oxide, which cannot be removed by crystallization. Increasing the amount of NaOCN to 5 equiv did not improve the yield of **1a**.

*Attempted Preparation of **1a** by Method C.* Aldehyde **4** (398 mg, 1.00 mmol) and urea (900 mg, 15 mmol) were mixed with THF (50 mL) and freshly distilled acetic acid (50 mL), and the resultant mixture was cooled in an ice bath. Neat chlorotrimethylsilane (0.16 mL, 1.2 mmol) was added with stirring, and the stirring was continued at room temperature for 3 h, during which time the color of the reaction mixture changed from red to orange. The mixture was recooled in ice, and $Na[BH_4]$ (189 mg, 5.0 mmol) was added in one portion. After the addition, the reaction mixture was stirred at 0 °C for 30 min and then at room temperature for another 2 h, whereupon it turned yellow. The mixture was diluted with saturated aqueous $NaHCO_3$ (60 mL; ***Caution**: gas evolution!*) and extracted with dichloromethane (40 mL). The organic layer was washed with saturated aqueous $NaHCO_3$, water, and brine, dried over magnesium sulfate, and evaporated with chromatography-grade silica gel. Subsequent column chromatography of the crude preadsorbed product over silica gel with dichloromethane−methanol (10:1) and evaporation furnished an orange foam (353 mg), which was analyzed as a mixture of **1a** (approximately 80%), **1aO** (approximately 10%), and **1a**·$BH_3$ (10%). Crystallization from hot ethyl acetate−hexane efficiently removes the borane adduct but not the phosphine oxide. A similar reaction with $Li[AlH_4]$ (5.0 mmol) in THF (no acid added) afforded **1a** in only 9% yield, the majority of the aldehyde being converted to 1′-[(diphenylphoshino)ferrocenyl]methanol (isolated yield: 68%). Crystals used for X-ray diffraction analysis were grown from ethyl acetate−hexane.

$^1$H NMR ($CDCl_3$): $\delta$ 3.97 (d, $^3J_{HH}$ = 4.8 Hz, 2 H, $CH_2$), 3.98 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.08 (vq, $J'$ = 1.8 Hz, 2 H, fc), 4.13 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.41 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.54 (br s, 2 H, $NH_2$), 5.32 (br s, 1 H, NH), 7.31−7.39 (m, 10 H, $PPh_2$). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 39.21 ($CH_2$), 68.86 (CH of fc), 69.01 (CH of fc), 71.46 (d, $J_{PC}$ = 3 Hz, CH of fc), 73.27 (d, $J_{PC}$ = 15 Hz, CH of fc), 75.58 (C-P of fc), 86.86 (*C*-$CH_2$ of fc), 128.28 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of Ph), 128.81 ($CH^{para}$ of Ph), 133.40 (d, $^3J_{PC}$ = 19 Hz, $CH^{meta}$ of Ph), 138.04 (br s, $C^{ipso}$ of Ph), 158.47 (C═O). $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ −16.1 (s). IR (Nujol, cm$^{-1}$): 3355 br w, 3389 br w, 3322 br w, 3191 br m, 1738 w, 1644 br s, 1601 s, 1431 s, 1329 s, 1311 m, 1269 w, 1232 w, 1202 w, 1162 m, 1123 m, 1096 m, 1069 w, 1029 s, 998 w, 929 w, 888 w, 823 m, 781 w, 742 s, 696 s, 655 w, 571 m, 532 s, 488 s, 460 s, 436 m. ESI+ MS: *m*/*z* 443 ($[M + H]^+$), 465 ($[M + Na]^+$), 481 ($[M + K]^+$). Anal. Calcd for $C_{24}H_{23}FeN_2OP$·0.2AcOEt (459.9): C 64.77, H 5.39, N 6.09. Found: C 64.62, H 5.25, N 5.94 (sample crystallized from ethyl acetate−hexane).

*Synthesis of N-[1′-(Diphenylphosphino)ferrocenyl]-N′-methylurea (**1b**). Method C.* Aldehyde **4** (398 mg, 1.00 mmol) and *N*-methylurea were dissolved in a mixture of dry THF (30 mL) and acetic acid (60 mL). Chlorotrimethylsilane (0.15 mL, 1.2 mmol) was added, causing an immediate change in color from the initial red to deep orange. After stirring at room temperature for 3 h, the mixture was cooled in an ice bath, and $Na[BH_4]$ (189 mg, 5.00 mmol) was added in one portion (the color of the reaction changed gradually to yellow). The stirring was continued at 0 °C for 30 min and then at room temperature overnight before quenching with water (100 mL, effervescence). The resultant mixture was extracted with dichloromethane (50 and 20 mL), and the combined organic layers were washed twice with saturated aqueous $NaHCO_3$ (***Caution**: gas evolution!*), water, and brine, dried over magnesium sulfate, and


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evaporated. The crude product was purified by column chromatography (silica gel, dichloromethane−methanol, 20:1 v/v). The major band containing the product and some phosphine oxide was evaporated, and the residue was purified again by chromatography over silica gel using ethyl acetate as the eluent to afford **1b** as an orange solid (335 mg, 73%).

A similar reaction with $Li[AlH_4]$ in THF (without added acetic acid) yielded analytically pure **1b** (30%) together with [1′-(diphenylphoshino)ferrocenyl]methanol (49%). The second chromatography was not needed in this case.

$^1$H NMR ($CDCl_3$): $\delta$ 2.80 (s, 3 H, $CH_3$), 3.95 (br s, 2 H, $CH_2$), 3.98 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.07 (vq, $J'$ = 1.8 Hz, 2 H, fc), 4.12 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.39 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.62 (br s, 1 H, NH), 5.01 (br s, 1 H, NH), 7.30−7.38 (m, 10 H, $PPh_2$). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 27.26 ($CH_3$), 39.19 ($CH_2$), 69.22 (CH of fc), 68.99 (CH of fc), 71.42 (d, $J$ = 4 Hz, CH of fc), 73.25 ($J$ = 15 Hz, CH of fc), 75.60 (br s, *C*-$CH_2$ of fc), 87.22 (C-P of fc), 128.26 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of Ph), 128.76 ($CH^{para}$ of Ph), 133.40 ($^3J_{PC}$ = 19 Hz, $CH^{meta}$ of Ph), 138.20 (br s, $C^{ipso}$ of Ph), 158.71 (C═O). $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ −16.1 (s). IR (Nujol, $cm^{-1}$): $\nu_{max}$ 3326 s, 3294 s, 3137 br m, 3100 m, 3078 m, 3043 m, 1625 s, 1582 s, 1259 m, 1194 w, 1161 m, 1089 w, 1059 w, 1038 m, 1025 m, 998 w, 923 w, 889 w, 831m, 807 s, 776 w, 794 s, 696 s, 667 m, 635 m, 570 w, 529 m, 496 s, 485 s, 453 m, 422 w, 410 w $cm^{-1}$. ESI+ MS: $m/z$ 457 ($[M + H]^+$), 479 ($[M + Na]^+$), 495 ($[M + K]^+$). Anal. Calcd for $C_{25}H_{25}FeN_2OP{\cdot}0.25AcOEt$ (478.3): C 65.28, H 5.69, N 5.86. Found: C 65.19, H 5.44, N 5.91.

*Synthesis of N-[1′-(Diphenylphosphino)ferrocenyl]-N′,N′-dimethylurea (**1c**). Method B.* Anhydrous triethylamine (1.0 mmol, 7.2 mmol) was added to a suspension of **3**·HCl (437 mg, 1.0 mmol) in dry dichloromethane (20 mL). To the resulting clear orange solution was introduced neat *N,N*-dimethylcarbamoyl chloride (0.10 mL, 1.1 mmol), and the resulting mixture was stirred at room temperature overnight. The reaction was terminated by the addition of saturated aqueous $NaHCO_3$ solution (10 min). The organic phase was separated, washed with water and brine, and dried. The product was isolated by flash column chromatography over silica gel with dichloromethane−methanol (20:1 v/v) as the eluent and evaporation under vacuum. Yield of **1c**: 433 mg (92%), yellow solid foam.

$^1$H NMR ($CDCl_3$): $\delta$ 2.91 (s, 6 H, $NMe_2$), 3.99 (br d, $^3J_{HH}$ = 3.8 Hz, 2 H, $CH_2$), 4.01 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.08 (vq, $J'$ = 1.8 Hz, 2 H, fc), 4.13 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.36 (vt, $J'$ = 1.8 Hz, 2H, fc), 4.67 (br s, 1 H, NH), 7.29−7.38 (m, 10 H, Ph). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 36.37 ($NMe_2$), 37.77 ($CH_2$), 69.06 (CH of fc), 69.15 (CH of fc), 71.33 (d, $J_{PC}$ = 4 Hz, CH of fc), 73.22 (d, $J_{PC}$ = 15 Hz, C-P of fc), 87.14 (*C*-$CH_2$ of fc), 128.18 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of Ph), 128.63 ($CH^{para}$ of Ph), 133.41 (d, $^3J_{PC}$ = 20 Hz, $CH^{meta}$ of Ph), 138.58 (d, $^1J_{PC}$ = 8 Hz, $C^{ipso}$ of Ph). 158.11 (C═O). One signal due to ferrocene CH probably overlaps with the solvent resonance. $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ −16.5 (s). IR (Nujol, $cm^{-1}$): 3356 m, 3047 w, 1721 w, 1630 s, 1585 w, 1533 s, 1339 m, 1239 m, 1220 w, 1162 w, 1088 w, 1038 w, 1027 w, 831w, 812 w, 747 m, 699 m, 569 w, 500 m, 486 w, 449 w. ESI+ MS: $m/z$ 471 ($[M + H]^+$), 493 ($[M + Na]^+$), 509 ($[M + K]^+$). Anal. Calcd for $C_{26}H_{27}FeN_2OP{\cdot}0.1CH_2Cl_2$ (478.8): C 65.47, H 5.73, N 3.55. Found: C 65.48, H 5.77, N 5.62.

*Synthesis of N-[1′-(Diphenylphosphino)ferrocenyl]-N′-cyclohexylurea (**1d**). Method A.* Hydrochloride **3**·HCl (219 mg, 0.50 mmol) and triethylamine (1.0 mmol, 7.2 mmol) were mixed in dry dichloromethane (10 mL), producing a clear orange solution, which was cooled on ice. Neat cyclohexyl isocyanate (10 μL, 0.55 mmol) was introduced, and the reaction mixture was stirred at 0 °C for 15 min and then at room temperature overnight. After the reaction was quenched by addition of water (10 mL), the organic layer was separated, and the aqueous residue was extracted with dichloromethane (3 × 10 mL). The combined organic phases were washed with brine, dried over magnesium sulfate, and evaporated under vacuum to afford a crude product, which was purified by chromatography (silica gel, dichloromethane−methanol, 10:1) and then crystallized from hot ethyl acetate−hexane (approximately 1:3) to afford urea **1d** as orange crystals (217 mg, 83%). Crystals suitable for X-ray diffraction analysis were obtained from ethyl acetate−hexane.

$^1$H NMR ($CDCl_3$): $\delta$ 1.06−1.20 (m, 3 H, $CH_2$ of Cy), 1.29−1.41 (m, 2 H, $CH_2$ of Cy), 1.54−1.61 (m, 1 H, $CH_2$ of Cy), 1.64−1.72 (m, 2 H, $CH_2$ of Cy), 1.90−1.98 (m, 2 H, $CH_2$ of Cy), 3.59 (m, 1 H, CH of Cy), 3.95 (d, $^3J_{HH}$ = 4.8 Hz, 2 H, C$H_2$NH), 3.97 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.06 (vq, $J'$ = 1.7 Hz, 2 H, fc), 4.12 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.39 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.64 (br d, $^3J_{HH}$ = 7.7 Hz, 1 H, N*H*Cy), 5.01 (br m, 1 H, $CH_2$N*H*), 7.30−7.39 (m, 10 H, Ph). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 24.87 ($CH_2$ of Cy), 25.63 ($CH_2$ of Cy), 33.94 ($CH_2$ of Cy), 38.99 (*C*$H_2$NH), 48.94 (CH of Cy), 68.76 (CH of fc), 69.01 (CH of fc), 71.40 (d, $J_{PC}$ = 4 Hz, CH of fc), 73.19 (d, $J_{PC}$ = 15 Hz, CH of fc), 75.55 (br s, C-P of fc), 87.53 (*C*-$CH_2$ of fc), 128.25 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of Ph), 128.75 ($CH^{para}$ of Ph), 133.39 (d, $^3J_{HH}$ = 19 Hz, $CH^{meta}$ of Ph), 138.09 (br d, $^1J_{HH}$ = 6 Hz, $C^{ipso}$ of Ph), 157.37 (C═O). $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ −16.4 (s). IR (Nujol, $cm^{-1}$): 3392 m, 3264 br m, 3049 m, 1740 w, 1620 s, 1598 s, 1497 s, 1310 w, 1272 m, 1254 m, 1233 m, 1160 m, 1084 m, 1049 w, 1033 m, 1025 m, 921 w, 871 w, 842 w, 813 m, 750 s, 745 s, 700 s, 634 m, 528 w, 499 s, 484 s, 461 w, 413 w. ESI+ MS: $m/z$ 525 ($[M + H]^+$), 547 ($[M + Na]^+$), 563 ($[M + K]^+$). Anal. Calcd for $C_{30}H_{33}FeN_2OP$ (524.4): C 68.71, H 6.34, N 5.34. Found: C 68.51, H 6.29, N 5.22.

*Synthesis of N-[1′-(Diphenylphosphino)ferrocenyl]-N′-phenylurea (**1e**). Method A.* Anhydrous triethylamine (2.5 mL, 18 mmol) was added to a suspension of **3**·HCl (437 mg, 1.0 mmol) in dichloromethane (35 mL), whereupon the hydrochloride dissolved to yield a clear orange solution. After cooling in an ice bath, neat phenyl isocyanate (86 μL, 1.1 mmol) was added, and the resulting mixture was stirred at 0 °C for 15 min and then at room temperature overnight. Next, the reaction mixture was diluted with water (20 mL), and the organic layer was separated. The aqueous residue was extracted with dichloromethane (10 mL), and the organic phases were combined, washed with brine, dried over anhydrous magnesium sulfate, and, finally, evaporated under vacuum. The crude product was purified by flash chromatography (silica gel, dichloromethane−methanol, 20:1 v/v). The first intense band was collected and evaporated to afford **1e**, which was further crystallized from hot ethyl acetate−hexane (approximately 1:1). Yield: 458 mg (88%), orange microcrystalline solid.

*Method C.* Aldehyde **4** (199 mg, 0.50 mmol) and *N*-phenylurea (136 mg, 1.0 mmol) were dissolved in anhydrous THF (20 mL), and the solution was cooled on ice. Chlorotrimethylsilane (76 μL, 0.60 mmol) was added with stirring at 0 °C, and the reaction was continued at room temperature for 30 min. The color of the reaction mixture changed from deep red to orange, and a fine precipitate formed. Then, the reaction mixture was cooled again to 0 °C, and $Li[AlH_4]$ (57 mg, 1.5 mmol) was added at once. Instant effervescence and a change in color to yellow were observed upon the addition. After the gas evolution ceased (ca. 5 min), the reaction was terminated by a careful addition of degassed water (0.3 mL) and 3 M NaOH (0.1 mL). The cooling bath was removed, and the resultant mixture was stirred for 20 min at room temperature (to complete hydrolysis) and then filtered through a pad of Celite, eluting with diethyl ether. The yellow filtrate was washed with water (3×) and brine, dried over magnesium sulfate, mixed with chromatography-grade silica gel, and, finally, evaporated under reduced pressure. The preadsorbed crude product was transferred to the top of a chromatographic column packed with silica gel in ethyl acetate−hexane (1:3). Elution with the same solvent mixture removed minor impurities. Changing the solvent to pure ethyl acetate eluted the main yellow band due to **1e**, which was collected and evaporate to furnish pure **1e** as an orange solid (212 mg, 82%).

A similar reaction of **4** (199 mg, 0.50 mmol), *N*-phenylurea (136 mg, 1.0 mmol), and chlorotrimethylsilane (76 μL, 0.6 mmol) in THF (10 mL) and acetic acid (10 mL) with $Na[BH_4]$ (95 mg, 2.5 mmol) as the reducing agent followed by aqueous workup provided 250 mg of a solid product, which contained the desired product **1e** strongly contaminated by the respective borane adduct (**1e**·$BH_3$: approximately 30%) according to NMR analysis.

$^1$H NMR ($CDCl_3$): $\delta$ 3.98 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.01 (d, $^3J_{HH}$ = 4.9 Hz, 2 H, $CH_2$), 4.04 (vq, $J'$ = 1.8 Hz, 2 H, fc), 4.13 (vt, $J'$ = 1.8 Hz, 2 H, fc), 4.35 (vt, $J'$ = 1.8 Hz, 2 H, fc), 5.53 (br s, 1 H, NH), 6.99 (br s, 1 H, NH), 7.02−7.06 (m, 1 H, Ph), 7.26−7.39 (m, 14 H, NH*Ph* and



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$PPh_2$). $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta$ 38.80 ($CH_2$), 68.87 (CH of fc), 69.00 (CH of fc), 71.44 (d, $J_{PC}$ = 3 Hz, CH of fc), 73.17 (d, $J_{PC}$ = 14 Hz, CH of fc), 87.11 (C-$CH_2$ of fc), 120.42 ($CH^{ortho}$ of NHPh), 123.41 ($CH^{para}$ of NHPh), 128.35 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of $PPh_2$), 128.91 ($CH^{meta}$ of NHPh), 129.19 ($CH^{para}$ of $PPh_2$), 133.37 (d, $^3J_{PC}$ = 19 Hz, $CH^{meta}$ of $PPh_2$), 137.79 (br, $C^{ipso}$ of $PPh_2$), 138.87 ($C^{ipso}$ of NPh), 155.40 (C═O). Signal due to *C*-P of fc was not observed. $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta$ − 16.3 (s). IR (Nujol, $cm^{-1}$): $\nu_{max}$ 3370 br w, 3318 w, 3183 w, 3092 m, 1645 s, 1598 s, 1544 s, 1324 m, 1310 s, 1250 s, 1189 w, 1159 m, 1089 w, 1051 w, 1025 w, 997 w, 912 w, 862 w, 839 s, 815 m, 756 s, 748 s, 698 s, 514 m, 493 s, 482 s, 451 m, 430 w. ESI+ MS: *m*/*z* 519 ($[M + H]^+$), 542 ($[M + Na]^+$), 557 ($[M + K]^+$). Anal. Calcd for $C_{30}H_{27}FeN_2OP$ (518.4): C 69.51, H 5.25, N 5.41. Found: C 69.30, H 5.08, N 5.29.

*Preparation of N-[1′-(Diphenylphosphino)ferrocenyl]-N′-phenylthiourea (**1f**). Method A.* Hydrochloride **3**·HCl (437 mg, 1.0 mmol) and dry triethylamine (2.5 mL, 18 mmol) were mixed in dry dichloromethane (30 mL), and the resulting clear solution was cooled on ice. Phenyl isothiocyanate (0.13 mL, 1.1 mmol) was added, and the mixture was stirred at 0 °C for 15 min and then at room temperature overnight. The reaction was terminated by addition of water (20 mL), the organic phase was separated, and the aqueous residue was extracted with dichloromethane (approximately10 mL). The combined dichloromethane layer was washed with brine, dried with magnesium sulfate, and evaporated under vacuum. The crude product was purified by flash chromatography (silica gel, dichloromethane−methanol 50:1 v/v) and further crystallized from hot ethyl acetate−hexane (1:1) to yield stoichiometric solvate **1f**·AcOEt as yellow-orange crystals (483 mg, 77%). Crystals of unsolvated **1f** used for X-ray diffraction analysis were grown from ethyl acetate−hexane.

$^1H$ NMR ($CDCl_3$): $\delta$ 3.88 (vq, $\acute{J}$ = 1.8 Hz, 2 H, fc), 4.01 (vt, $\acute{J}$ = 1.9 Hz, 2 H, fc), 4.04 (vt, $\acute{J}$ = 1.8 Hz, 2 H, fc), 4.07 (vt, $\acute{J}$ = 1.8, 2 H, fc), 4.34 (d, $^3J_{HH}$ = 4.9 Hz, 2 H, $CH_2$), 6.27 (br s, 1 H, $CH_2NH$), (101 MHz): $\delta$ 44.25 ($CH_2$), 68.53 (CH of fc), 69.45 (CH of fc), 71.02 (d, *J* = 4 Hz, CH of fc), 73.08 (d, *J* = 14 Hz, CH of fc), 85.09 (*C*-$CH_2$ of fc), 125.77 ($CH^{ortho}$ of NHPh), 127.62 ($CH^{para}$ of NHPh), 128.19 (d, $^2J_{PC}$ = 7 Hz, $CH^{ortho}$ of $PPh_2$), 128.67 ($CH^{meta}$ of NHPh), 130.25 ($CH^{para}$ of $PPh_2$), 133.40 (d, $^3J_{PC}$ = 20 Hz, $CH^{meta}$ of $PPh_2$), 136.06 ($C^{ipso}$ of NHPh), 138.54 (d, $^1J_{PC}$ = 9 Hz, $C^{ipso}$ of $PPh_2$), 180.16 (C═S). The signal due to *C*-P of fc was not observed. $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta$ − 16.7 (s). IR (Nujol, $cm^{-1}$): 3371 w, 3356 m, 3154 br m, 1734 w 1588 w, 1515 s, 1316 m, 1300 m, 1261 m, 1240 m, 1192 w, 1163 m, 1092 w, 1050 w, 1026 m, 970 w, 960 w, 844 w, 833 m, 754 s, 746 s, 699 w, 532 w, 493 m, 480 m, 458 w. ESI+ MS: *m*/*z* 535 ($[M + H]^+$), 557 ($[M + Na]^+$), 573 ($[M + K]^+$). Anal. Calcd for $C_{30}H_{27}FeN_2PS$·AcOEt (622.5) C 65.59, H 5.67, N 4.50. Found: C 66.00, H 5.42, N 4.50.

*Preparation of 1′-(Diphenylphosphino)-1-[(acetylamino)methyl]ferrocene (**1g**). Method B.* Freshly distilled acetyl chloride (45 μL, 0.63 mmol) was added to a solution of amine **3** generated *in situ* by mixing **3**·HCl (250 mg, 0.57 mmol) and triethylamine (0.7 mL, 5 mmol) in dry dichloromethane (10 mL). The reaction mixture was stirred at room temperature overnight before quenching with 3 M HCl (5 mL). The organic phase was separated and washed successively with 3 M HCl, 0.1 M NaOH, water, and brine (5 mL each), dried over magnesium sulfate, and evaporated. The crude product was purified by column chromatography over silica gel using dichloromethane−methanol (5:1, v/v) as the eluent. Following evaporation under vacuum, the product was isolated as a viscous, orange-brown oil (231 mg, 91%).

$^1H$ NMR ($CDCl_3$): $\delta$ 2.03 (s, 3 H, $CH_3$), 4.00−4.03 (m, 4 H, 2× fc + $CH_2$), 4.07 (vq, *J*′ = 1.8 Hz, 2 H, fc), 4.11 (vt, *J*′ = 1.8 Hz, 2 H, fc), 4.38 (vt, *J*′ = 1.8 Hz, 2 H, fc), 6.02 (br s, 1 H, NH), 7.30−7.39 (m, 10 H, Ph). $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta$ 22.23 ($CH_3$), 38.51 ($CH_2$), 69.14 (CH of fc), 69.24 (CH of fc), 71.50 (d, $J_{PC}$ = 4 Hz, 75.35 (br s, C-$PPh_2$ of fc), 71.53 (CH of fc), 73.34 (d, $J_{PC}$ = 14 Hz, CH of fc), 85.79 (*C*-$CH_2$ of fc), 128.29 (d, $^3J_{PC}$ = 7 Hz, $CH^{meta}$ of $PPh_2$), 128.91 ($CH^{para}$ of $PPh_2$), 133.40 (d, $^2J_{PC}$ = 19 Hz, $CH^{ortho}$ of $PPh_2$), 137.82 (br s, $C^{ipso}$ of $PPh_2$), 169.73 (C═O). $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta$ −16.3 (s). IR (Nujol, $cm^{-1}$): 3279 br m, 1721 w, 1645 s, 1585 m, 1552 s, 1288 s, 1265 m, 1230 w, 1202 m, 1161 m, 1122 w, 1077 m, 1053 w, 1033 s, 1024 s, 929 w, 887 w, 864 w, 831 s, 738 s, 694 s, 634 w, 592 m, 569 w, 513 s, 484 s, 474 s, 453 m, 434 m, 413 w. ESI+ MS: *m*/*z* 462 ($[M + H]^+$), 464 ($[M + Na]^+$), 480 ($[M + K]^+$). Anal. Calcd for $C_{25}H_{24}FeNOP$ (441.3): C 68.04, H 5.48, N 3.17. Found: C 67.76, H 5.36, N 2.90.

*Synthesis of Phosphine Oxide **1eO**.* Compound **1e** (40 mg, 77 μmol) was dissolved in acetone (6 mL), and the solution was cooled on ice. Concentrated hydrogen peroxide (0.1 mL 30%) was added, and the resulting mixture was stirred at 0 °C for 20 min. Then, the reaction mixture was diluted with water (ca. 6 mL), and its volume was reduced to half by evaporation under vacuum, whereupon the product separated as a yellow solid. The latter was extracted into dichloromethane, and the extract was dried briefly over anhydrous magnesium sulfate and passed through a short silica gel column using dichloromethane−methanol (10:1) as the eluent. Subsequent evaporation afforded phosphine oxide **1eO** as a yellow-orange, glassy solid. Yield: 40 mg, 97%.

$^1H$ NMR ($CDCl_3$): $\delta$ 3.93 (vt, *J*′ = 1.9 Hz, 2 H, fc), 4.08 (d, $^3J_{HH}$ = 3.7 Hz, 2 H, $CH_2$), 4.32 (vq, *J*′ = 1.8 Hz, 2 H, fc), 4.38 (vt, *J*′ = 1.9 Hz, 2 H, fc), 4.57 (vq, *J*′ = 1.8 Hz, 2 H, fc), 6.93 (tt, *J*′ = 7.4, 1.2 Hz, 1 H, NPh), 7.22−7.28 (m, 2 H, NPh), 7.45−7.72 (m, 13 H, Ph and NH), 8.73 (br s, 1 H, NH). $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta$ 37.96 ($CH_2$), 68.33 (CH of fc), 68.78 (CH of fc), 72.20 (d, $J_{PC}$ = 10 Hz, CH of fc), 72.30 (d, $^1J_{PC}$ = 117 Hz, $C^{ipso}$-P of fc), 72.69 (d, $J_{PC}$ = 13 Hz, CH of fc), 89.21 (*C*-$CH_2$ of fc), 118.10 ($CH^{ortho}$ of NHPh), 121.17 ($CH^{para}$ of NHPh), 128.52 (d, $^2J_{PC}$ = 12 Hz, $CH^{ortho}$ of $PPh_2$), 128.69 ($CH^{meta}$ of NPh), 131.24 (d, $^3J_{PC}$ = 10 Hz, $CH^{meta}$ of $PPh_2$), 132.08 (d, $^4J_{PC}$ = 3 Hz, $CH^{para}$ of $PPh_2$), 132.94 (d, $^1J_{PC}$ = 108 Hz, $C^{ipso}$ of $PPh_2$), 140.72 ($C^{ipso}$ of NHPh), 156.47 (C═O). $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta$ 32.8 (s). ESI+ MS: *m*/*z* 535 ($[M + H]^+$), 557 ($[M + Na]^+$), 573 ($[M + K]^+$). IR (Nujol, $cm^{-1}$): $\nu_{max}$ 3329 br m, 3228 w, 3082 w, 1707 s, 1600 m, 1541 s, 1500 s, 1325 m, 1279 w, 1227 m, 1216 m, 1197 s, 1186 m, 1176 m, 1161 s, 1101 m, 1038 m, 997 w, 896 w, 871 w, 843 w, 754 s, 705 s, 696 s, 633 w, 571 s, 532 m, 507 m, 496 s, 483 m, 443 m. Anal. Calcd for $C_{30}H_{27}FeN_2O_2P$·0.05$CHCl_3$ (540.5): C 66.80, H 5.05, N 5.18. Found: C 66.59, H 5.03, N 4.99.

*Preparation of [PdCl(**1e**-κP)(μ-Cl)]$_2$ (**5**).* A solution of phosphine **1e** (50 mg, 96 μmol) in dichloromethane (5 mL) was added to a solution of $[PdCl_2(cod)]$ (27.5 mg, 96 μmol) in the same solvent (1 mL). The dark reaction mixture was stirred for 1 h and then filtered through a syringe filter (0.45 μm) into pentane (40 mL). The mixture was stored at −18 °C overnight before the precipitated product was filtered off, washed with pentane, and dried under vacuum. Yield of **5**: 66 mg (quant.), grayish solid.

$^1H$ NMR ($CDCl_3$): $\delta$ 4.23, 4.53, 4.54, 4.64, and 4.93 (5× br s, 2 H, fc and $CH_2$); 6.26 (br s, 1 H, $NHCH_2$), 6.95−7.00 (m, 1 H, Ph), 7.17−7.28 (m, 6 H, Ph), 7.35−7.41 (m, 3 H, Ph), 7.44−7.7.51 (m, 5 H, Ph), 7.94 (br s, 1 H, N*H*Ph). $^{13}C\{^1H\}$ NMR ($CDCl_3$): $\delta$ 38.83 ($CH_2$), 67.80 (d, $^1J_{PC}$ = 68 Hz, C-P of fc), 70.00 (CH of fc), 70.99 (CH of fc), 73.32 (d, $J_{PC}$ = 9 Hz, CH of fc), 75.82 (d, $J_{PC}$ = 11 Hz, CH of fc), 89.30 (*C*-$CH_2$ of fc), 118.72 (CH of NHPh), 122.00 ($CH^{para}$ of NHPh), 128.58 (d, $^1J_{PC}$ = 63 Hz, C-P of $PPh_2$), 128.15 (d, $J_{PC}$ = 13 Hz, CH of $PPh_2$), 128.85 ($CH^{para}$ of $PPh_2$), 131.78 (CH of NHPh), 133.45 (d, $J_{PC}$ = 11 Hz, CH of $PPh_2$), 139.76 ($C^{ipso}$ of NHPh), 155.99 (C═O). $^{31}P\{^1H\}$ NMR ($CDCl_3$): $\delta$ 33.6 (s). ESI+ MS: *m*/*z* 623 ($[Pd(\mathbf{1e} - H)]^+$), 659 ($[Pd(\mathbf{1e})Cl]^+$). IR (Nujol, $cm^{-1}$): $\nu_{max}$ 3350 br m, 3055 w, 1655 s, 1597 s, 1548 s, 1498 s, 1311 m, 1236 m, 1166 m, 1099 m, 1059 w, 1030 m, 999 w, 921 w, 896 w, 835 m, 748 s, 712 m, 692 s, 620 w, 548 m, 542 s, 478 s, 447 m. Anal. Calcd for $C_{60}H_{54}Cl_4Fe_2N_4O_2P_2Pd_2$ (1391.4): C 51.79, H 3.91, N 4.03. Found: C 51.66, H 3.86, N 3.85.

*Preparation of [PdCl$_2$(**1e**-κP)$_2$] (**6**).* A dichloromethane solution of $[PdCl_2(cod)]$ (28.3 mg, 29 μmol in 2 mL) was added to a solution of phosphine **1e** (30 mg, 58 μmol) in the same solvent (3 mL). The resulting red solution was stirred for 15 min, concentrated to approximately one-half its original volume by evaporation under vacuum, and precipitated by addition of pentane (20 mL). The separated solid was filtered off, washed with pentane, and dried under vacuum. Yield of **6**: 34 mg (96%), red solid. Note: The crude products


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contained traces of an unidentified impurity (different from **5**, **1e**, and **1eO**), which could be removed by precipitation of the concentrated reaction mixture with pentane.

$^1$H NMR ($CDCl_3$): $\delta$ 4.04 (d, $^3J_{HH}$ = 4.3 Hz, 2 H, $CH_2$), 4.37 (br s, 2 H, fc), 4.40 (br s, 2 H, fc), 4.47 (br s, 2 H, fc), 4.54 (br s, 2 H, fc), 5.63 (br s, 1 H, $CH_2NH$), 6.94–6.98 (m, 1 H, Ph), 7.15–7.23 (m, 5 H, Ph), 7.30–7.38 (m, 5 H, Ph), 7.55–7.62 (m, 4 H, 3× CH of Ph + NHPh). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 38.81 ($CH_2$), 69.34 (CH of fc), 70.41 (CH of fc), 71.70 (apparent t, $J'$ = 27 Hz, C-P of fc), 72.29 (apparent t, $J'$ = 4 Hz, CH of fc), 75.86 (apparent t, $J'$ = 5 Hz, CH of fc), 88.41 (C-$CH_2$ of fc), 119.94 (CH of NHPh), 122.86 ($CH^{para}$ of NHPh), 127.87 (apparent t, $J_{PC}$ = 5 Hz, CH of $PPh_2$), 128.90 (CH of NHPh), 130.56 ($CH^{para}$ of $PPh_2$), 130.77 (apparent t, $^1J_{PC}$ = 25 Hz, $C^{ipso}$-P of $PPh_2$), 134.04 (apparent t, $J_{PC}$ = 6 Hz, CH of $PPh_2$), 139.02 ($C^{ipso}$ of NHPh) 155.62 (C═O). $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ 16.4 (s). ESI+ MS: $m/z$ 519 ([**1e** + H]$^+$), 623 ([Pd(**1e** − H)]$^+$). ESI− MS: $m/z$ 659 ([PdCl(**1e** − 2H)]$^-$), 740 ([Pd(**1e**)$Cl_3$]$^-$), 1247 ([Pd(**1e**)$_2Cl_2$ + Cl]$^-$). IR (Nujol, cm$^{-1}$): $\nu_{max}$ 3343 br m, 3053 w, 1652 s, 1598 s, 1552 s, 1498 s, 1311 m, 1236 m, 1164 m, 1099 m, 1058 w, 1029 m, 999 w, 920 w, 895 w, 833 m, 746 s, 692 s, 539 w, 509 m, 446 w. Anal. Calcd for $C_{60}H_{54}Cl_2Fe_2N_4O_2P_2Pd$ (1214.0): C 59.36, H 4.48, N 4.62. Found: C 59.09, H 4.65, N 4.44.

*Preparation of [PdCl($C_6H_4CH_2NMe_2$-$\kappa^2C^1$,N)(**1e**-$\kappa$P)] (**7**).* A solution of ligand **1e** (50 mg, 96 $\mu$mol) dissolved in dichloromethane (6 mL) was added to [PdCl($L^{NC}$)]$_2$ dissolved in the same solvent (2 mL). The reaction mixture was stirred for 60 min and then evaporated under vacuum to afford **7** as a yellow solid. Yield: 76 mg (quant.). Crystals suitable for X-ray diffraction analysis were obtained upon layering a chloroform solution of the complex with hexane and slow crystallization by liquid-phase diffusion.

$^1$H NMR ($CDCl_3$): $\delta$ 2.81 (d, $^4J_{PH}$ = 2.8 Hz, 6 H, $NMe_2$), 4.12 (d, $^3J_{HH}$ = 2.2 Hz, 2 H, $C_5H_4CH_2$), 4.18 (d, $^4J_{PH}$ = 4.8 Hz, 2 H, $Me_2NCH_2$), 4.29 (vt, $J'$ = 1.9 Hz, 2 H, fc), 4.41 (td, $J'$ = 1.9, 1.0 Hz, 2 H, fc), 4.49 (vq, $J'$ = 1.9 Hz, 2 H, fc), 4.58 (vt, $J'$ = 1.8 Hz, 2 H, fc), 6.24 (ddd, $J$ = 7.7 Hz, 6.5 Hz, 1.0 Hz, 1 H, $C_6H_4$), 6.38 (m, 2 H, 1H of $C_6H_4$ and $CH_2NH$), 6.83 (td, $J$ = 7.4, 1.1 Hz, 1 H, $C_6H_4$), 6.94 (tt, $J$ = 7.4, 1.1 Hz, 1 H, NHPh), 7.01 (dd, $J$ = 7.4, 1.5 Hz, 1 H, $C_6H_4$), 7.21–7.25 (m, 2 H, Ph), 7.29–7.35 (m, 4 H, Ph), 7.39–7.44 (m, 2 H, Ph), 7.49–7.55 (m, 6 H, Ph), 8.23 (s, 1 H, NHPh). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 38.79 ($C_5H_4CH_2$), 50.14 (d, $^3J_{PC}$ = 3 Hz, $N(CH_3)_2$), 68.87 (CH of fc), 69.91 (CH of fc), 72.32 (d, $J_{PC}$ = 7 Hz, CH of fc), 73.38 (d, $^1J_{PC}$ = 3 Hz, C-$PPh_2$ of fc), 73.73 (d, $^3J_{PC}$ = 60 Hz, $Me_2NCH_2$), 75.89 (d, $J_{PC}$ = 9 Hz, CH of fc), 89.05 (C-$CH_2$ of fc), 118.49 (CH of NHPh), 121.83 ($CH^{para}$ of NHPh), 122.58 (CH of $C_6H_4$), 123.94 (CH of $C_6H_4$), 125.04 (d, $J_{PC}$ = 6 Hz, CH of $C_6H_4$), 128.01 (d, $^4J_{PC}$ = 11 Hz, $CH^{para}$ of $PPh_2$), 128.77 (CH of NHPh), 130.68 (d, $J_{PC}$ = 2 Hz, CH of $C_6H_4$), 131.35 (d, $^2J_{PC}$ = 50 Hz, CH of $PPh_2$), 134.33 (d, $^3J_{PC}$ = 12 Hz, CH of $PPh_2$), 138.71 (d, $^1J_{PC}$ = 11 Hz, $C^{ipso}$ of $PPh_2$), 139.95 ($C^{ipso}$ of NHPh), 147.85 (d, $^2J_{PC}$ = 2 Hz, C-Pd of $C_6H_4$), 151.91 (C-$CH_2$ of $C_6H_4$), 155.85 (C═O). $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ 33.9 (s). IR (Nujol, cm$^{-1}$): $\nu_{max}$ 3379 w, 3344 w, 3314 w, 3280 m, 1698 s, 1601 m, 1579 w, 1548 s, 1499 s, 1318 m, 1233 m, 1210 m, 1162 w, 1097 w, 1032 w, 991 w, 839 w, 814 w, 738 m, 693 m, 654 w, 542 m, 522 w, 496 w, 462 w, 443 w. ESI+ MS: $m/z$ 758 ([M − Cl]$^+$). Anal. Calcd for $C_{39}H_{39}ClFeN_3OPPd$ (794.4): C 58.96, H 4.95, N 5.29. Found: C 58.81, H 4.90, N 5.05.

*[PdCl($\eta^3$-$C_3H_5$)(**1e**-$\kappa$P)] (**8**).* A solution of ligand **1e** (50 mg, 96 $\mu$mol) in dichloromethane (6 mL) was added to a solution of [PdCl($\eta^3$-$C_3H_5$)]$_2$ (17.5 mg, 48 $\mu$mol) in the same solvent (2 mL). The resulting solution was stirred for 60 min and then evaporated under vacuum to afford **8** as a glassy solid, which slowly crystallized. Yield of **8**·0.2$CH_2Cl_2$: 69 mg (quant.). Crystals suitable for X-ray diffraction measurements were grown from ethyl acetate–hexane.

$^1$H NMR ($CDCl_3$): $\delta$ 2.83 (d, $J$ = 12.2 Hz, 1 H, $CH_2$-allyl *trans*-Cl), 3.12 (d, $J$ = 6.4 Hz, 1 H, $CH_2$-allyl *trans*-Cl), 3.74 (dd, $J$ = 13.8, 9.8 Hz, 1 H, $CH_2$-allyl *trans*-P), 3.84 (m, 1 H, fc), 3.86 (m, 1 H, fc), 4.11 (dd, $J_{HH}$ = 15.4, 5.1 Hz, 1 H, $CH_2NH$), 4.21 (dd, $J_{HH}$ = 15.4, 5.8 Hz, 1 H, $CH_2NH$), 4.27 (br s, 1 H, fc), 4.38 (br s, 1 H, fc), 4.46–4.52 (m, 3 H, fc), 4.63 (br s, 1 H, fc), 4.71 (td, $J$ = 7.2, 1.7 Hz, 1 H, $CH_2$-allyl *trans*-P), 5.57 (ddd, $J$ = 18.9, 13.9, and 7.6 Hz, 1H, CH-allyl), 6.34 (t, $^3J_{HH}$ = 5.4 Hz, 1 H, $CH_2NH$), 6.96 (m, 1 H, NPh), 7.24–7.29 (m, 2 H, NHPh), 7.35–7.55 (m, 10 H, $PPh_2$), 7.57–7.61 (m, 2 H, NPh), 8.45 (s, 1 H, NHPh). $^{13}$C{$^1$H} NMR ($CDCl_3$): $\delta$ 38.33 ($CH_2NH$), 61.12 (d, $^2J_{PC}$ = 2 Hz,$CH_2$-allyl *trans*-Cl), 67.80 (CH of fc), 67.91 (CH of fc), 69.08 (CH of fc), 69.22 (CH of fc), 71.92 (d, $J_{PC}$ = 7 Hz, CH of fc), 72.18 (d, $J_{PC}$ = 7 Hz, CH of fc), 73.45 (d, $^1J_{PC}$ = 48 Hz, C-P of fc), 74.38 (d, $J_{PC}$ = 11 Hz, CH of fc), 74.78 (d, $J_{PC}$ = 13 Hz, CH of fc), 81.16 (d, $^2J_{PC}$ = 31 Hz, $CH_2$-allyl *trans*-*P*), 89.49 (*C*-$CH_2$ of fc), 118.34 (CH-allyl *meso*; partly overlapped), 118.38 (CH of NHPh), 121.68 ($CH^{para}$ of NHPh), 128.36 (d, $J_{PC}$ = 10 Hz, CH of $PPh_2$), 128.80 (CH of NHPh), 130.32 (d, $^4J_{PC}$ = 2 Hz, $CH^{para}$ of $PPh_2$), 132.94 (d, $J_{PC}$ = 11 Hz, CH of $PPh_2$), 134.54 (dd, $J$ = 45 Hz, 3 Hz, $C^{ipso}$ of $PPh_2$), 140.23 ($C^{ipso}$ of NHPh), 155.95 (C═O). $^{31}$P{$^1$H} NMR ($CDCl_3$): $\delta$ 16.4 (s). IR (Nujol, cm$^{-1}$): $\nu_{max}$ 3359 w, 3317 w, 3269 w, 3088 w, 3071 w, 1688 s, 1595 m, 1544 s, 1310 m, 1269 w, 1233 m, 1167 w, 1097 w, 1054 w, 1024 w, 846 w, 824 w, 758 m, 744 m, 696 m, 626 w, 614 w, 517 m, 503 w, 495 m, 462 w, 444 m. ESI+ MS: $m/z$ 665 ([M − Cl]$^+$). Anal. Calcd for $C_{33}H_{32}ClFeN_2OPPd$·0.1$CH_2Cl_2$ (709.8): C 56.01, H 4.57, N 3.95. Found: C 55.99, H 4.41, N 3.88.

*Pd-Catalyzed Cyanation of Aryl Bromides. General Procedure.* A dry Schlenk tube was charged with the respective ligand (0.02 mmol) and palladium complex (0.01 mmol). These solid educts were dissolved in dichloromethane (2 mL), and the resulting solution was stirred for 5 min before being evaporated under vacuum. Aryl bromide (**8**, 1.0 mmol), $K_4[Fe(CN)_6]\cdot 3H_2O$ (212 mg, 0.50 mmol), and anhydrous sodium carbonate (106 mg, 1.0 mmol) were introduced successively, and the reaction vessel was flushed with argon and sealed with a rubber septum. Dioxane and degassed water (2 mL each) were added, and the Schlenk tube was transferred to an oil bath preheated to 100 °C, in which the reaction mixture was stirred for 3 or 24 h.

Next, the reaction mixture was cooled to room temperature and diluted with ethyl acetate and water (5 mL each). The organic layer was separated, and the aqueous residue was extracted with ethyl acetate (3× 5 mL). The organic layers were combined, washed with brine, dried over anhydrous magnesium sulfate, and evaporated to afford crude products, which were analyzed by NMR spectroscopy. Pure products were isolated by column chromatography over silica gel using ethyl acetate–hexane mixtures as the eluents (see the Supporting Information). Details regarding the screening experiments are presented in the text and tables above. Mesitylene (1.0 mmol) was added to the reaction mixture as an internal standard for $^1$H NMR analysis after the aqueous workup.

**X-ray Crystallography.** Diffraction data ($\pm h$ $\pm k$ $\pm l$, $\theta_{max}$ = 26.0–27.5°, completeness ≥99.5%) were collected at 150(2) K with a Nonius Kappa CCD diffractometer equipped with an Apex II image plate detector and Cryostream Cooler (Oxford Cryosystems) using graphite-monochromatized Mo K$\alpha$ radiation ($\lambda$ = 0.710 73 Å). The data were processed and corrected for absorption by methods included in the diffractometer software. Parameters of the data collection, structure solution, and refinement are available in the Supporting Information (Table S1).

The structures were solved by direct methods (SHELXS97[39]) and refined by full-matrix least-squares routines based on $F^2$ (SHELXL97[39]). Unless specified otherwise, the non-hydrogen atoms were refined with anisotropic displacement parameters. The urea and amide hydrogen atoms (NH) were typically located on the difference electron density maps and refined as riding atoms with $U_{iso}$(H) = 1.2$U_{eq}$(N). Hydrogens residing on the carbon atoms as well as the $NH_3$ protons in the structure of **3**·HCl were included in their calculated positions and refined similarly with $U_{iso}$(H) set to 1.5$U_{eq}$(C) for the methyl groups and to 1.2$U_{eq}$(C) for all other $CH_n$ moieties and the $NH_3$ hydrogens. Further details regarding the structure refinement are as follows.

The terminal phenyl group in the structure of **7**·2$CHCl_3$ is disordered and was modeled over two positions. Carbon atoms in the less abundant component (20%) were refined isotropically, and the hydrogen residing at the nitrogen N2 was placed into its calculated position. Furthermore, the solvent molecules in the structure of **7**·2$CHCl_3$ were heavily disordered in structure voids and were thus modeled by PLATON/SQUEEZE.[40] Finally, the $\eta^3$-allyl moiety in the



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crystal structure of **8** was disordered over two positions related approximately by rotation along the axis connecting the center of gravity of the allyl moiety and the Pd center, similarly to other [PdCl($\eta^3$-$C_3H_5$)(L)]) complexes with **D**-type ligands (see Scheme 1).[10] The refined occupancies of the contributing orientations were ca. 60:40.

All geometric calculations were carried out, and the diagrams were obtained with the recent version of the PLATON program.[41] The numerical values were rounded with respect to their estimated deviations (ESDs) given to one decimal place. Parameters pertaining to atoms in constrained positions (mostly hydrogens) are presented without ESDs.

## ■ ASSOCIATED CONTENT

### Supporting Information

Supporting Information for this article comprises additional structural drawings and description of the crystal structure of **11j** and **11k**, a tabular summary of relevant crystallographic data (Table S1), characterization data for the catalytic products (**10**, **11**, and **12**), and copies of the NMR spectra for the newly prepared compounds. The Supporting Information is available free of charge on the ACS Publications website at DOI: 10.1021/acs.organomet.5b00197.

## ■ AUTHOR INFORMATION


### Corresponding Author

*E-mail: stepnic@natur.cuni.cz.


### Notes

The authors declare no competing financial interest.

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## ■ REFERENCES


(1) (a) Herrmann, W. A.; Kohlpaintner, C. W. *Angew. Chem., Int. Ed. Engl.* **1993**, *32*, 1524−1544. (b) Joó, F. *Aqueous Organometallic Catalysis*; Kluwer: Dordrecht, 2001. (c) Pinault, N.; Bruce, D. W. *Coord. Chem. Rev.* **2003**, *241*, 1−25. (d) *Aqueous-Phase Organometallic Catalysis*, 2nd ed.; Herrmann, W. A., Cornils, B., Eds.; Wiley-VCH: Weinheim, 2004. (e) Shaughnessy, K. H. *Chem. Rev.* **2009**, *109*, 643−710.

(2) (a) Duckmanton, P. A.; Blake, A. J.; Love, J. B. *Inorg. Chem.* **2005**, *44*, 7708−7710. (b) Knight, L. K.; Freixa, Z.; van Leeuwen, P. W. N. M.; Reek, J. N. H. *Organometallics* **2006**, *25*, 954−960. (c) Meeuwissen, J.; Detz, R. J.; Sandee, A. J.; de Bruin, B.; Reek, J. N. H. *Dalton Trans.* **2010**, *39*, 1929−1931. (d) Meeuwissen, J.; Detz, R.; Sandee, A. J.; de Bruin, B.; Siegler, M. A.; Spek, A. L.; Reek, J. N. H. *Eur. J. Inorg. Chem.* **2010**, 2992−2997.

(3) (a) *Ferrocenes: Ligands, Materials and Biomolecules*, Štěpnička, P., Ed.; Wiley & Sons: Chichester, 2008, Part I − Ligands, pp 1−277. (b) Štěpnička, P. In *The Chemistry of Organoiron Compounds*; Marek, I., Rappoport, Z., Eds.; Wiley & Sons: Chichester, 2013; Chapter 4, pp 103−154. (c) Atkinson, R. C. J.; Gibson, V. C.; Long, N. J. *Chem. Soc. Rev.* **2004**, *33*, 313−328. (d) Gómez Arrayás, R.; Adrio, J.; Carretero, J. C. *Angew. Chem., Int. Ed.* **2006**, *45*, 7674−7715.

(4) Representative examples: (a) Pugin, B.; Landert, H.; Spindler, F.; Blaser, H.-U. *Adv. Synth. Catal.* **2002**, *344*, 974−979. (b) Cvengroš, J.; Toma, Š.; Žemberyová, M.; Macquarrie, D. J. *Molecules* **2005**, *10*, 679−692. (c) Pugin, B.; Landert, H. (Novartis AG, Switzerland). Functionalized ferrocenyldiphosphines, a process for their preparation and their use. International Patent WO 9801457, 1998. (d) Pugin, B. (Solvias AG, Switzerland). Diphosphine ligands for metal complexes. International Patent WO 2001004131, 2001.

(5) Selected recent examples: (a) Simenel, A. A.; Morozova, E. A.; Snegur, L. V.; Zykova, S. I.; Kachala, V. V.; Ostrovskaya, L. A.; Bluchterova, N. V.; Fomina, M. M. *Appl. Organomet. Chem.* **2009**, *23*, 219−224. (b) Lapić, J.; Pavlović, G.; Siebler, D.; Heinze, K.; Rapić, V. *Organometallics* **2008**, *27*, 726−735. (c) Károlyi, B. I.; Bősze, S.; Orbán, E.; Sohár, P.; Drahos, L.; Gál, E.; Csámpai, A. *Molecules* **2012**, *17*, 2316−2329.

(6) Hayashi, T.; Mise, T.; Fukushima, M.; Kagotani, M.; Nagashima, N.; Hamada, Y.; Matsumoto, A.; Kawakami, S.; Konishi, M.; Yamamoto, K.; Kumada, M. *Bull. Chem. Soc. Jpn.* **1980**, *53*, 1138−1151.

(7) (a) Zhao, Q.; Li, S.; Huang, K.; Wang, R.; Zhang, X. *Org. Lett.* **2013**, *15*, 4014−4017. (b) Zhao, Q.; Wen, J.; Tan, R.; Huang, T.; Metola, P.; Wang, R.; Anslyn, E. V.; Zhang, X. *Angew. Chem., Int. Ed.* **2014**, *53*, 8467−8470.

(8) For structurally related, planar-chiral tertiary urea derivatives, see: Metallinos, C.; John, J.; Zaifman, J.; Emberson, K. *Adv. Synth. Catal.* **2012**, *354*, 602−606.

(9) Štěpnička, P. *Chem. Soc. Rev.* **2012**, *41*, 4273−4305.

(10) Solařová, H.; Císařová, I.; Štěpnička, P. *Organometallics* **2014**, *33*, 4131−4147.

(11) Selected reviews: (a) Beer, P. D.; Bayly, S. *Top. Curr. Chem.* **2005**, *255*, 125−162. (b) Bayly, S.; Beer, P. D.; Chen, G. Z. In *Ferrocenes: Ligands, Materials and Biomolecules*; Štěpnička, P., Ed.; Wiley & Sons: Chichester, 2008; Part II − Materials, Molecular Devices and Biomolecules, Chapter 8, pp 281−318. (c) Evans, N. H.; Beer, P. D. *Angew. Chem., Int. Ed.* **2014**, *53*, 11716−11754. Further recent examples: (d) Willener, Y.; Joly, K. M.; Moody, C. J.; Tucker, J. H. R. *J. Org. Chem.* **2008**, *73*, 1225−1233. (e) Cormode, D. P.; Evans, A. J.; Davis, J. J.; Beer, P. D. *Dalton Trans.* **2010**, 6532−6541. (f) Evans, N. H.; Serpell, C. J.; Christensen, K. E.; Beer, P. D. *Eur. J. Inorg. Chem.* **2012**, 939−944 and references therein. (g) Huang, X.; Wu, B.; Jia, C.; Hay, B. P.; Li, M.; Yang, X.-J. *Chem.—Eur. J.* **2013**, *19*, 9034−9041 and references therein.

(12) (a) Braunstein, P.; Naud, F. *Angew. Chem., Int. Ed.* **2001**, *40*, 680−399. (b) Slone, C. S.; Weinberger, D. A.; Mirkin, C. A. *Prog. Inorg. Chem.* **1999**, *48*, 233−350. (c) Bader, A.; Lindner, E. *Coord. Chem. Rev.* **1991**, *108*, 27−110.

(13) For examples of ferrocene phosphines bearing an additional $CH_2FG$ moiety (FG = donor functional group) in the position 1′, see: (a) Widhalm, M.; Nettekoven, U.; Mereiter, K. *Tetrahedron: Asymmetry* **1999**, *10*, 4369−4391. (b) Labande, A.; Daran, J.-C.; Manoury, E.; Poli, R. *Eur. J. Inorg. Chem.* **2007**, 1205−1209. (c) Gülcemal, S.; Labande, A.; Daran, J.-C.; Çetinkaya, B.; Poli, R. *Eur. J. Inorg. Chem.* **2009**, 1806−1815. (d) Štěpnička, P.; Schulz, J.; Klemann, T.; Siemeling, U.; Císařová, I. *Organometallics* **2010**, *29*, 3187. (e) Siemeling, U.; Klemann, T.; Bruhn, C.; Schulz, J.; Štěpnička, P. *Dalton Trans.* **2011**, *40*, 4722−4740. (f) Štěpnička, P.; Zábranský, M.; Císařová, I. *ChemistryOpen* **2012**, *1*, 71−79. (g) Štěpnička, P.; Císařová, I. *J. Organomet. Chem.* **2012**, *716*, 110−119. (h) Štěpnička, P.; Císařová, I. *Dalton Trans.* **2013**, *42*, 3373−3389. (i) Debono, N.; Daran, J.-C.; Poli, R.; Labande, A. *Polyhedron* **2015**, *86*, 57−63.

(14) Škoch, K.; Císařová, I.; Štěpnička, P. *Inorg. Chem.* **2014**, *53*, 568−577.

(15) Štěpnička, P.; Baše, T. *Inorg. Chem. Commun.* **2001**, *4*, 682−687.

(16) Transformation of primary amines to monosubstituted ureas are typically achieved through the action of alkali metal cyanate/acid mixtures.

(17) Xu, D.; Ciszewski, L.; Li, T.; Repič, O.; Blacklock, T. J. *Tetrahedron Lett.* **1998**, *39*, 1107−1110.

(18) (a) Henderson, W.; Oliver, A. G. *Polyhedron* **1996**, *15*, 1165−1173. (b) Nekrasov, Yu. S.; Skazov, R. S.; Simenel, A. A.; Snegur, L. V.; Kachala, I. V. *Russ. Chem. Bull.* **2006**, *55*, 1368−1371.

(19) See, for instance, the structure of (diphenylphosphino) ferrocene: Adeleke, J. B.; Liu, L.-K. *Acta Crystallogr., Sect. C: Cryst. Struct. Commun.* **1993**, *49*, 680−682.




DOI: 10.1021/acs.organomet.5b00197
*Organometallics* XXXX, XXX, XXX−XXX

(20) Allen, F. H.; Kennard, O.; Watson, D. G.; Brammer, L.; Orpen, A. G.; Taylor, R. *J. Chem. Soc., Perkin Trans. 2* **1987**, S1−S19.
(21) Gan, K.-S.; Hor, T. S. A. In *Ferrocenes: Homogeneous Catalysis, Organic Synthesis, Materials Science*; Togni, A., Hayashi, T., Eds.; VCH: Weinheim, 1995; Chapter 1, Section 1.3, pp 18−35.
(22) The formed chains are built up from molecules related by the crystallographic *a* glide planes and, therefore, propagate in a direction parallel to the *a*-axis.
(23) (a) Etter, M. C. *Acc. Chem. Res.* **1990**, *23*, 120−126. (b) Custelcean, R. *Chem. Commun.* **2008**, 295−307.
(24) Štěpnička, P.; Císařová, I. *New J. Chem.* **2002**, *26*, 1389−1396.
(25) Evans, A. J.; Matthews, S. E.; Cowley, A. R.; Beer, P. D. *Dalton Trans.* **2003**, 4644−4650. Geometric parameters were calculated from the data deposited in the Cambridge Structural Database (refcode: EQOHIB).
(26) Etter, M. C.; MacDonald, J. C.; Bernstein, J. *Acta Crystallogr., Sect. B: Struct. Sci.* **1990**, *46*, 256−262.
(27) Štěpnička, P.; Císařová, I.; Gyepes, R. *Eur. J. Inorg. Chem.* **2006**, 926−938. See also ref 13h.
(28) (a) Teo, S.; Weng, Z.; Hor, T. S. A. *Organometallics* **2006**, *25*, 1199−1205. (b) Štěpnička, P.; Podlaha, J.; Gyepes, R.; Polášek, M. *J. Organomet. Chem.* **1998**, *552*, 293−301. See also ref 13h.
(29) For selected examples of complexes of the type $[PdCl(C_6H_4CH_2NMe_2\text{-}\kappa^2C^1,P)(Ph_2PfcX\text{-}\kappa P)]$ and related compounds, see: (a) Ma, J.-F.; Yamamoto, Y. *Inorg. Chim. Acta* **2000**, *299*, 164−171. (b) Štěpnička, P.; Císařová, I. *Organometallics* **2003**, *22*, 1728−1740. (c) Štěpnička, P.; Císařová, I. *Collect. Czech. Chem. Commun.* **2006**, *71*, 215−236. (d) Štěpnička, P.; Císařová, I. *Inorg. Chem.* **2006**, *45*, 8785−8789. (e) Tauchman, J.; Císařová, I.; Štepnička, P. *Organometallics* **2009**, *28*, 3288−3302. (f) Štěpnička, P.; Solařová, H.; Lamač, M.; Císařová, I. *J. Organomet. Chem.* **2010**, *695*, 2423−2431. (g) Štěpnička, P.; Solařová, H.; Císařová, I. *J. Organomet. Chem.* **2011**, *696*, 3727−3740. See also refs 10 and 13d.
(30) (a) Appleton, T. G.; Clark, H. C.; Manzer, L. E. *Coord. Chem. Rev.* **1973**, *10*, 335−422. (b) Hartley, F. R. *The Chemistry of Platinum and Palladium*; Applied Science: London, 1973; Chapter 11, p 299.
(31) (a) Štěpnička, P.; Císařová, I. *Collect. Czech. Chem. Commun.* **2006**, *71*, 279−293. (b) Tauchman, J.; Císařová, I.; Štěpnička, P. *Dalton Trans.* **2011**, *40*, 11748−11757.
(32) (a) Sundermeier, M.; Zapf, A.; Beller, M. *Eur. J. Inorg. Chem.* **2003**, 3513−3526. (b) Anbarasan, P.; Schareina, T.; Beller, M. *Chem. Soc. Rev.* **2011**, *40*, 5049−5067.
(33) (a) Schareina, T.; Zapf, A.; Beller, M. *Chem. Commun.* **2004**, 1388−1389. (b) Schareina, T.; Zapf, A.; Beller, M. *J. Organomet. Chem.* **2004**, *689*, 4576−4583.
(34) Butler, R. N.; Coyne, A. G. *Chem. Rev.* **2010**, *110*, 6302−6337.
(35) Schulz, J.; Císařová, I.; Štěpnička, P. *Organometallics* **2012**, *31*, 729−738.
(36) Electron-withdrawing substituents aid the base-induced hydrolysis of the nitriles via decreasing the electron density at the cyano group, thereby facilitating the attack of $OH^-$ on the cyanide carbon. In a model experiment, equimolar amounts of nitrile **9g** and $Na_2CO_3$ (1 mmol each) were allowed to react in dioxane−water (4 mL of 1:1 mixture) at 100 °C overnight, affording amide **10g** in virtually quantitative yield.
(37) Drew, D.; Doyle, J. R. *Inorg. Synth.* **1972**, *13*, 47−55.
(38) Cope, A. C.; Friedrich, E. C. *J. Am. Chem. Soc.* **1968**, *90*, 909−913.
(39) Sheldrick, G. M. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **2008**, *64*, 112−122.
(40) van der Sluis, P.; Spek, A. L. *Acta Crystallogr., Sect. A: Found. Crystallogr.* **1990**, *46*, 194−201.
(41) Spek, A. L. *J. Appl. Crystallogr.* **2003**, *36*, 7−13.



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*Organometallics* XXXX, XXX, XXX−XXX