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Diastereoselective Synthesis

Diastereoselective Synthesis of Dialkylated Bis(phosphino)ferrocenes: Their Use in Promoting Silver-Mediated Nucleophilic Fluorination of Chloroquinolines

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Dedicated to our friend I. R. Butler for his inspiring and innovative work on ferrocene functionalization

Abstract: The diastereoselective synthesis of dialkylated ferrocenyl bis(phosphane)s bearing aryl, alkyl, and hetero- or polycyclic substituents on the phosphino groups is reported, together with their characterization in the solid state by X-ray structure analysis and in solution by multinuclear NMR spectroscopy. Introduction of various alkyl groups on the ferrocene backbone, namely, *tert*-butyl, isopropyl, and trimethylsilyl, has a significant influence on the stereoselectivity of the ensuing lithiation/phosphination reactions. Only the introduction of the *tert*-butyl groups ensures both a high yield and perfect diastereoselectivity, which leads to the exclusive formation of the *rac* planar chiral *tert*-butylated diphosphanes. The introduction of electron-rich and -poor phosphorus-based functional groups, namely, furyl-, isopropyl-, cyclohexyl-, phenyl-, mesityl-phosphino, and benzophosphindole, is achieved and gives new alkylated ferrocenyl diphosphanes in moderate to high yields. Investigations are conducted to apply these robust alkylated diphosphanes as auxiliaries in the very challenging palladium-catalyzed nucleophilic fluorination of chloroquinolines at the C–Cl bond. Unexpectedly, a significant favorable effect from the ferrocenyl phosphanes is evidenced by using the commercial AgF reagent for this fluorination that renders any palladium addition useless. This innovative nucleophilic fluorination thus avoids harsh conditions (strictly anhydrous) and highly specialized reagents.

Introduction

Functionalized ferrocene derivatives have a wide range of applications related to homogeneous catalysis, electrochemistry, material sciences, and biomedical researches.[1] The unique combination of the axial rigidity and rotational flexibility of the ferrocene platform attracted the interest of synthetic chemists early on for the design of phosphane-based compounds mainly used as ligands for transition metals.[2–4] Our group developed highly substituted ferrocenyl phosphanes incorporating multiple phosphino groups arranged in a well-controlled geometry (see compound **1** and **2** in Scheme 1).[5–7] These species were used with success as ligands in palladium-catalyzed organic synthesis reactions directed towards selective C–C and C–heteroatom (i.e., C–N, C–O, and C–S) bond formation.[8–11] For such a class of polyphosphanes, efficient conformational control of the ferrocene backbone was introduced by using the steric effects of bulky *tert*-butyl groups placed on each of the cyclopentadienyl (Cp) rings. The synthesis of the ferrocenyl diphosphane congeners (see compound **3** in Scheme 1) by assembling substituted (phosphino)cyclopentadienyl salts systematically led to mixtures of diastereoisomers.[7] This synthetic complication impeded the development and investigation of substituted ferrocenyl diphosphanes as ligands for transition-metal catalysis. Substituted ferrocenyl diphosphanes thus remain underdeveloped, whereas related, but structurally simpler, dppf analogues [dppf = 1,1′-bis(diphenylphosphino)ferrocene] and its analogues have found many applications.[1a,1b,12,13]

Because of the interest of ferrocenyl phosphanes in palladium-catalyzed C–heteroatom (i.e., C–N, C–O, and C–S) bond formation, we envisioned that simple and robust chelator candidates may help in C–F bond formation from "F⁻" nucleophile sources. Palladium–ligand systems that were able to achieve very challenging *trans*-halogenation from triflate, bromide, and iodide derivatives to fluorinated analogues were only recently reported.[14] However, only highly sophisticated monophosphane ligands were used to date, and the employment of chloride substrates was not reported. Additionally, metal-catalyzed selective nucleophilic fluorination of heteroarenes, which is complementary to electrophilic fluorination,[15] is very topical, as such fluorinated compounds are present in pharmaceuticals,

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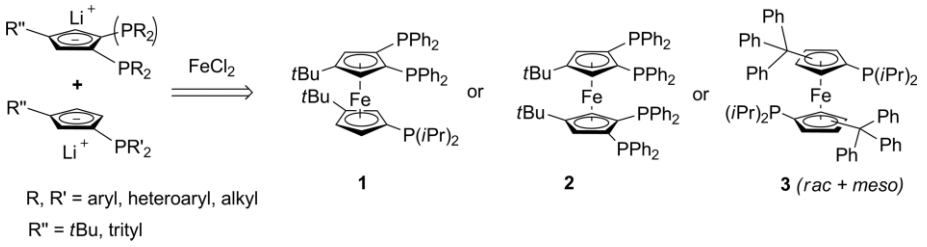


Scheme 1. Substituted ferrocenyl di- and triphosphanes synthesized by cyclopentadienyl salt assembly.

agrochemicals, molecular materials, and medical imaging radiotracers.[16] Consequently, relevant approaches from copper chemistry[17] or by using direct SN_{Ar},[18,19] albeit under strictly anhydrous conditions, have been reported. Thus, examination of performances from air-stable robust system under less sensitive conditions remains pertinent.

We focused the present work on the synthesis of novel disubstituted ferrocenyl diphosphanes alkylated at the metallocene backbone by different groups, including *tert*-butyl and related alkyl groups. We investigated synthetic routes to obtain diastereomerically pure ferrocenyl diphosphanes. For substituted diphosphanes, the influence of backbone steric control on the stereoselectivity of the successive lithiation/phosphination reactions was clearly evidenced. To assess this steric control, the X-ray structures in the solid state of each diphosphane class were determined. The selenation of tertiary phosphanes to give $^1J_{P,Se}$ coupling constant values is reported as a means to estimate the electron-donating properties of the synthesized substituted diphosphanes. Consequently, a new class of alkylated planar chiral diphosphanes with a constrained conformation was readily accessible by diastereoselective synthesis. These species were tested in the very challenging palladium-catalyzed C–Cl nucleophilic fluorination of chloroquinolines. Unexpectedly, a significant favorable effect from the ferrocenyl phosphane without additional palladium was evidenced by using the commercial AgF reagent for fluorination. This work evidences thus that in combination with AgF, phosphanes in substoichiometric amounts can be used as powerful systems for the fluorination of chloroarenes.

Results and Discussion

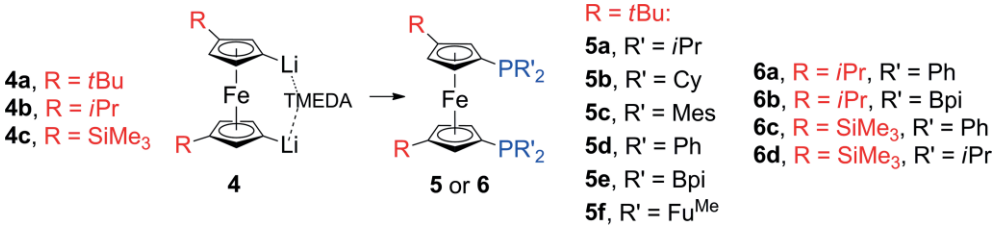
Synthesis and Characterization of Polysubstituted Ferrocenyl Diphosphanes

The modular synthesis of ferrocenyl diphosphanes from the assembly of cyclopentadienyl salts forms mixtures of planar chiral *rac* and achiral *meso* diastereomers, as no stereochemical control is exerted during the synthesis.[7,20] Workup and purification procedures are thus unavoidable, which limits the global efficiency of the process. To circumvent this issue, we anticipated that ferrocenyl dilithium salts **4** (Scheme 2) may be key components of the synthesis of polysubstituted ferrocenylphosphanes. Indeed, we recently observed that functionalization of **4a** led to planar chiral *rac* derivatives with high diastereoselectivity.[21] We were eager to determine whether this could be extended to related compounds **4b** and **4c**. We first targeted the diastereoselective synthesis of novel *tert*-butylated symmetric diphosphanes **5** bearing aryl, alkyl, and hetero- or polycyclic substituents (Cy = cyclohexyl, Bpi = benzophosphindole, Mes = 2,4,6-trimethylphenyl, Fu^{Me} = 2-methyl-5-furyl).

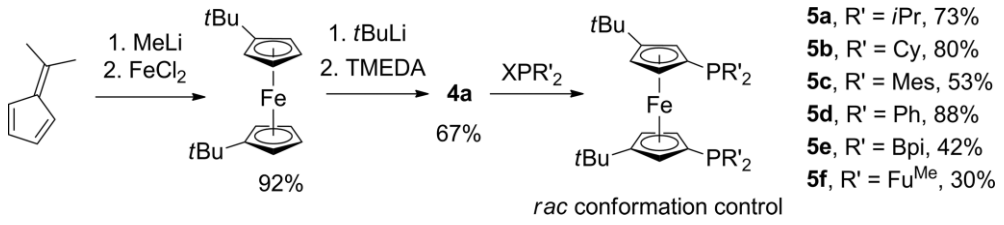
Diphosphanes **6** bear substituents that were believed to help with conformational control of the ferrocene platform, especially the isopropyl and trimethylsilyl groups, which are structurally related to *tert*-butyl but are, respectively, less and more congested.

1,1′-Di(*tert*-butyl)ferrocene was easily synthesized in high yield starting from 6,6-dimethylfulvene in two steps (Scheme 3). Selective dilithiation was then achieved by using *tert*-butyllithium in the presence of tetramethylethylenediamine (TMEDA) in THF at 0 °C to form **4a** in fairly good yield (67 %). Diastereomerically pure ferrocenyl diphosphanes **5a**–**f** were obtained from treatment of **4a** with the corresponding electrophiles in THF at –80 °C. Good to excellent yields of **5a**–**c** were obtained (73, 80, and 88 %, respectively). The yields were lower with the use of chlorobenzophosphindole, bis(2,4,6-trimethylphenyl)phosphorus chloride, and bromobis(methylfuryl)phosphane as electrophiles (**5d**–**f**; yields of 42, 53, and 30 %, respectively), mostly because of their lower stability under the reaction conditions.

Compound **5f** also underwent partial decomposition during purification, even if activated silica gel and dry solvents were used. The ^{31}P NMR spectroscopy data of **5a**–**f** are reported in Table 1. We estimated the electron-donating character of novel phosphanes **5a**–**f** by measuring the $^1J_{P,Se}$ coupling constants of their diselenide derivatives [Se(**5a**–**f**) in Table 1].



Scheme 2. Synthesis of alkylated ferrocenyl diphosphanes (major diastereoisomer is planar chiral *rac*).



Scheme 3. Diastereoselective synthesis of ferrocenyl diphosphanes **5a**–**e**.

Table 1. ^{31}P NMR ($CDCl_3$, 182 MHz) spectroscopy data of *tert*-butylated ferrocenyl diphosphanes **5a**–**f** and Se(**5a**–**f**).[a]

Complex	PR_2	$\delta(^{31}P)$ [ppm]	$\delta(^{31}P{=}Se)$ [ppm]	$^1J_{P,Se}$ [Hz]
5a	$P(iPr)_2$	1.3	58.9	710
5b	PCy_2	–8.6	50.7	705
5c	$PMes_2$	–37.1	16.5	700
5d	PPh_2	–20.1	31.5	736
5e	P(Bpi)	–22.9	23.0	735
5f	$P(Fu^{Me})_2$	–65.3	–6.5	759

[a] Benchmark $^1J_{P,Se}$ values for $Se{=}PPh_3$ and Se(dppf) are 730 and 737 Hz, respectively.

An increase in these coupling constants indicates an increase in the s character of the phosphorus lone-pair orbital, that is, an electron-withdrawing effect of the phosphane on the selenium.[22] As a benchmark, the $^1J_{P,Se}$ value for triphenylphosphane selenide, $Se{=}PPh_3$, and for 1,1′-bis(diphenylphosphino)ferrocene selenide, Se(dppf), were reported to be 730 and 737 Hz, respectively.[22a,22c] The $^1J_{P,Se}$ values determined for **5d** and **5e** (736 and 735 Hz, respectively) indicate a basic character of the phosphino groups, very similar to dppf. Unsurprisingly, compounds **5a**, **5b**, and **5c** with $^1J_{P,Se}$ values of 710, 705, and 700 Hz are highly electron-donating, whereas the $^1J_{P,Se}$ value of **5f** found at 759 Hz is indicative of the electron-poor character of this diphosphane. The highest "donation character" of the mesityl groups compared to the cyclohexyl and isopropyl alkyl groups is, however, noticeable.

Solid-state characterization from the growth of single crystals was also achieved. The X-ray structure determined for original heterocyclic ferrocene **5e** discloses two independent enantiomers in the asymmetric units (Figure 1). Both molecules have almost identical geometrical parameters. For the sake of clarity in the following discussion, the labeling is given only for one molecule, and the corresponding parameters for the enantiomer are given in brackets. The molecules belong to the

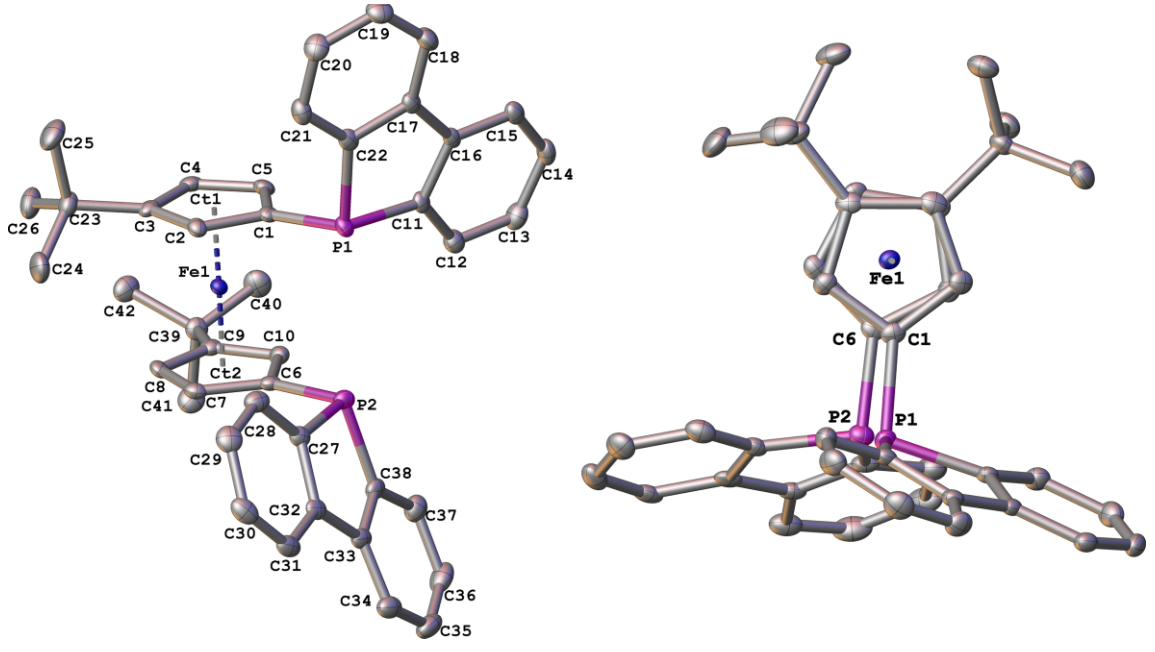


Figure 1. Molecular structures of diphosphane **5e**. Only one enantiomer is represented and hydrogen atoms are omitted for clarity. Selected bond lengths [Å], distances [Å], angles [°], and corresponding parameters for the second enantiomer are given in brackets: Fe1–Ct1 1.6564(11) [1.6616(11)], Fe1–Ct2 1.6586(11) [1.6629(11)], C1–P1 1.812(2) [1.815(2)], C6–P2 1.819(2) [1.816(2)], P1···P2 3.3932(9) [3.3377(9)], Ct1–Fe1–Ct2 179.28(6) [179.55(6)], P1–Ct1–Ct2–P2 5.74(3) [–9.54(3)].

C_2 point group. Superposition of the two molecules, after inversion, leads to a root mean square deviation (RMSD) equal to 0.20 Å and a maximal distance difference equal to 0.49 Å for atoms belonging to the *tert*-butyl groups. The Cp rings are in an almost perfect eclipsed conformation, and the two phosphino group are arranged one above the other with short distances P1···P2 3.3932(9) Å [3.3377(9) Å] and tight torsion angles P1–Ct1–Ct2–P2 5.74(3)° [–9.54(3)°]. The conformation of the ferrocene backbone of this diphosphane is consistent with those of related tetraphosphanes[5] and, as such, might be attributed to efficient steric conformational control of the *tert*-butyl groups. In compound **5e**, the benzophosphindole groups adopt an *exo* position relative to the ferrocene.

In the X-ray structure determined for phosphino ferrocene **5c**, the Cp rings adopt a staggered conformation, different from **5e** but still with a *cisoid* conformation of the phosphino groups. Consequently, the spatial separation between the two phosphorus atoms is longer than that for **5e** [P1···P2 4.3792(7) Å], together with a larger torsion angle [P1–Ct1–Ct2–P2 47.10(3)°] (Figure 2).

Compounds **6a** and **6b**, analogues of **5d** and **5e**, respectively, were then synthesized from **4b** (Scheme 4). The synthesis of the 1,1′-diisopropylferrocene precursor was achieved in a high yield of 89 % from a mixture of (isopropyl)cyclopentadiene isomers. Under conditions that were identical to those used to synthesize **4a**, diastereoselective dilithiation was achieved,

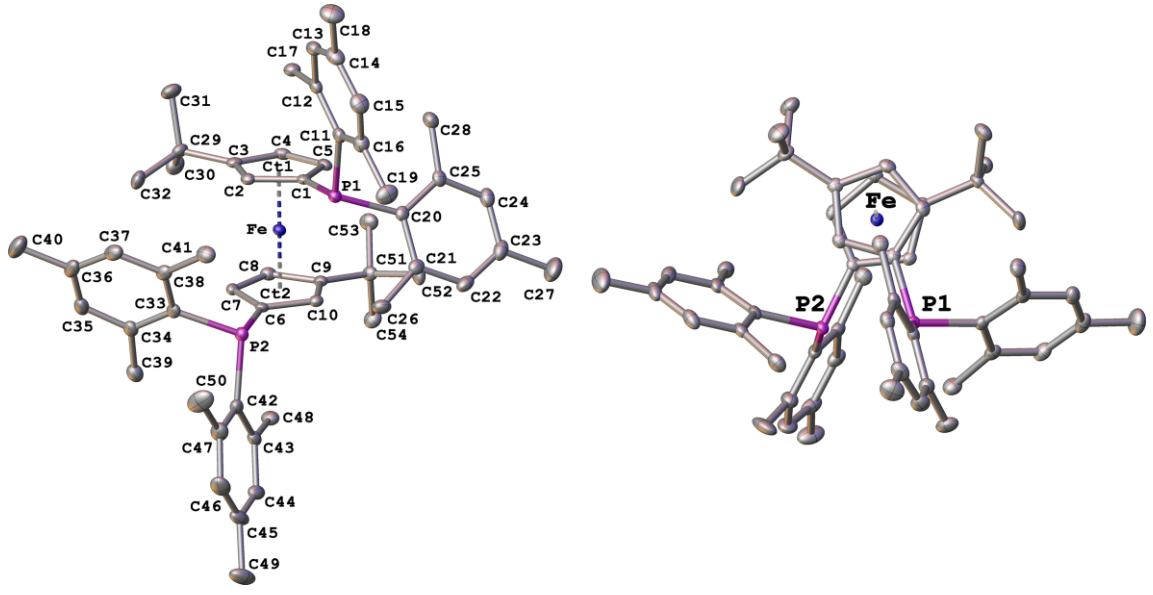
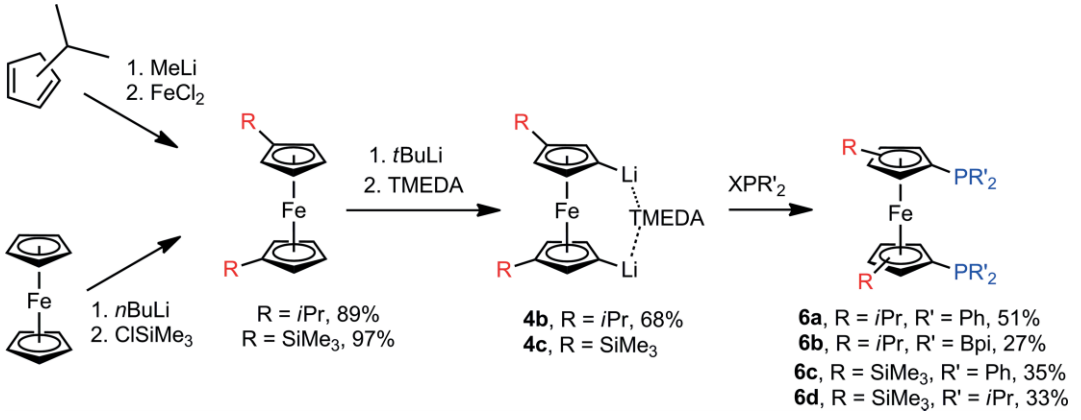


Figure 2. Molecular structures of diphosphane **5c**. Only one half of a dichloromethane solvent molecule and hydrogen atoms are omitted for clarity. Selected bond lengths [Å], distances [Å], and angles [°]: Fe–Ct1 1.6589(8), Fe–Ct2 1.6597(8), C1–P1 1.815(2), C6–P2 1.816(2), P1···P2 4.3792(7), Ct1–Fe–Ct2 175.81(5), P1–Ct1–Ct2–P2 47.10(3).



Scheme 4. Synthetic roads to alkylated ferrocenyl diphosphanes **6a**–**d**: there is a decrease in diastereoselectivity relative to that observed for *tert*-butylated compounds **5a**–**f**.

which gave pure **4b** in 68 % yield. Then, the introduction of benzophosphindole groups from the reaction of **4b** with chlorobenzophosphindole was difficult and gave **6b** in only a moderate yield of 27 % (compared to 42 % for **5d**). We recovered about 50 % of diisopropylferrocene and 20 % of a monophosphination product after purification.

However, more importantly, compound **6b** was isolated as a 85:15 mixture of *rac* and *meso* isomers. This indicated a significant loss of diastereoselectivity in the reaction relative to that observed for the conversion of **4a** into **5d**. This suggested that the lower steric hindrance of the *i*Pr groups relative to that of the *t*Bu groups was detrimental to diastereoselectivity control. Compound **6a** was isolated in a higher, but still moderate, 51 % yield, even if a one-pot reaction was performed starting from diisopropylferrocene. Diastereoselectivity in favor of the *rac* isomers, albeit not total, was found better than for the synthesis of **6b** with a ratio of 90:10.

The synthesis of **4c** was better achieved from ferrocene directly by following a reported procedure (Scheme 4).[23] The one-pot synthesis of **6c** was indeed reported to provide a yield of 45 % without isolation of the dilithium ferrocene intermediate salt and would have led to the chiral planar isomer only. Compound **4c** was found to be fairly air sensitive and much less stable than analogues **4a** and **4b**. Thus, pure **6c** and **6d** were obtained in moderate yields of 35 and 33 %, respectively, from one-pot protocols without isolation of **4c**. In our hands, unsatisfactory diastereoselectivity was again observed, and in each case, an isomeric mixture was obtained with ratios of 90:10 and 93:7 for the *rac* and *meso* diastereoisomers, respectively. Only *tert*-butylated compounds were thus involved in fully diastereoselective processes. The ^{31}P NMR spectroscopy data gathered for the cyclopentadienyl-substituted bis(diphenylphosphino)ferrocenes and their selenide derivatives are collected in Table 2. The effects of the R substituents, *tert*-butyl, isopropyl, trimethylsilyl, and trityl, on the electron-donating features of the diphenylphosphino groups are minor, as confirmed by the ^{31}P chemical shifts and $^{1}J_{P,Se}$ values ranging from 735 to 741 Hz, which were close to the Se(dppf) $^{1}J_{P,Se}$ value. The values of $^{1}J_{P,Se}$ for Se(**6b**) and Se(**6d**) were found to be 736 and 712 Hz, respectively, which confirmed the overwhelming effects of the functional groups of the phosphanes on their basicity.

Table 2. ^{31}P NMR ($CDCl_3$, 182 MHz) spectroscopy data of *tert*-butylated ferrocenyl diphosphanes **5a**–**f** and Se(**5a**–**f**).

Complex	R(Cp)	$\delta(^{31}P)$ [ppm]	$\delta(^{31}P{=}Se)$ [ppm]	$^{1}J_{P,Se}$ [Hz]
dppf	H	–19.8	28.2	737
5d	*t*Bu	–20.1	31.5	736
6a	*i*Pr	–17.2	31.7	735
6c	Me_3Si	–21.1	30.7	738
trityl-dppf[a]	Ph_3C	–24.0	31.4	741

[a] From ref.[7a,b]

The X-ray diffraction structures were resolved for **6a** and **6c** from single crystals. Figure 3 illustrates the molecular structure of **6a**. The phosphino groups adopt a *transoid* conformation with a wide torsion angle of P1–Ct1–Ct2–P2 127.29(3)°. The P···P spatial distance of 6.1935(9) Å is, therefore, much longer than that in **5c** or **5e** {4.3792(7) or 3.3932(9) Å [3.3377(9) Å], respectively} and is clearly a consequence of a lower degree of steric control from the smaller *i*Pr groups than from the *tert*-butyl groups, as shown by their mutual arrangement.

The molecular structure of **6c** is illustrated in Figure 4. The asymmetric unit contains two independent enantiomers belonging to the C_2 point group. Both molecules have almost identical geometrical parameters. Superposition of the two molecules, after inversion, leads to a RMSD equal to 0.58 Å and a maximal distance difference equal to 1.42 Å for atoms belonging to the phenyl groups. The Cp rings are in a staggered conformation with a *cisoid* conformation of the phosphino groups {P1···P2 4.2333(5) Å [4.1405(6) Å], torsion angle P1–Ct1–Ct2–P2 37.19(2)° [–34.02(3)°]}, which is reminiscent of those obtained for **5e**.

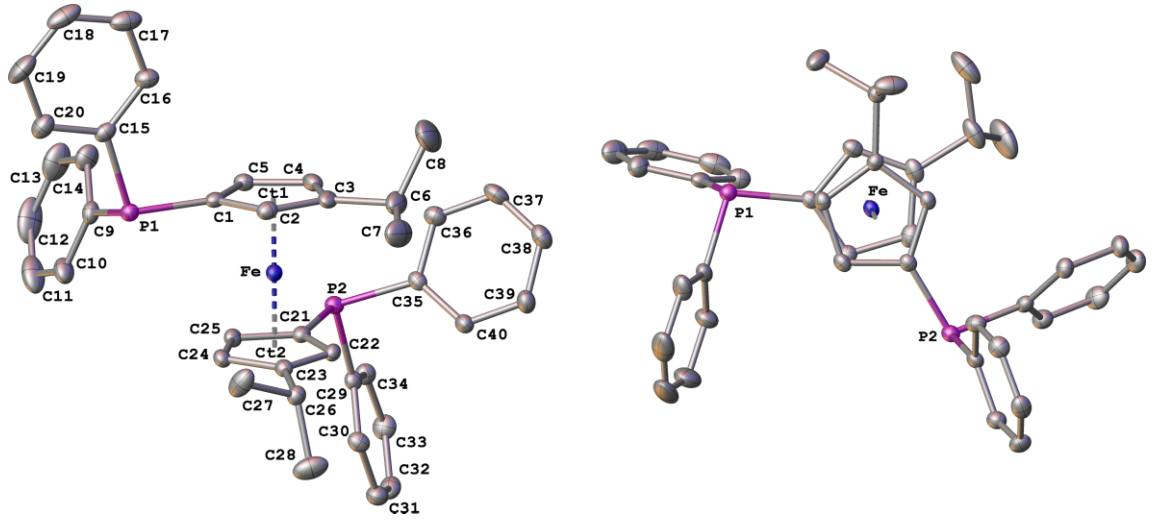


Figure 3. Molecular structures of compound **6a**. Hydrogen atoms are omitted for clarity. Selected bond lengths [Å], distances [Å], and angles [°]: Fe–Ct1 1.6531(13), Fe–Ct2 1.6532(11), C1–P1 1.811(3), C21–P2 1.823(2), P1···P2 6.1935(9), Ct1–Fe–Ct2 178.71(6), P1–Ct1–Ct2–P2 127.29(3).

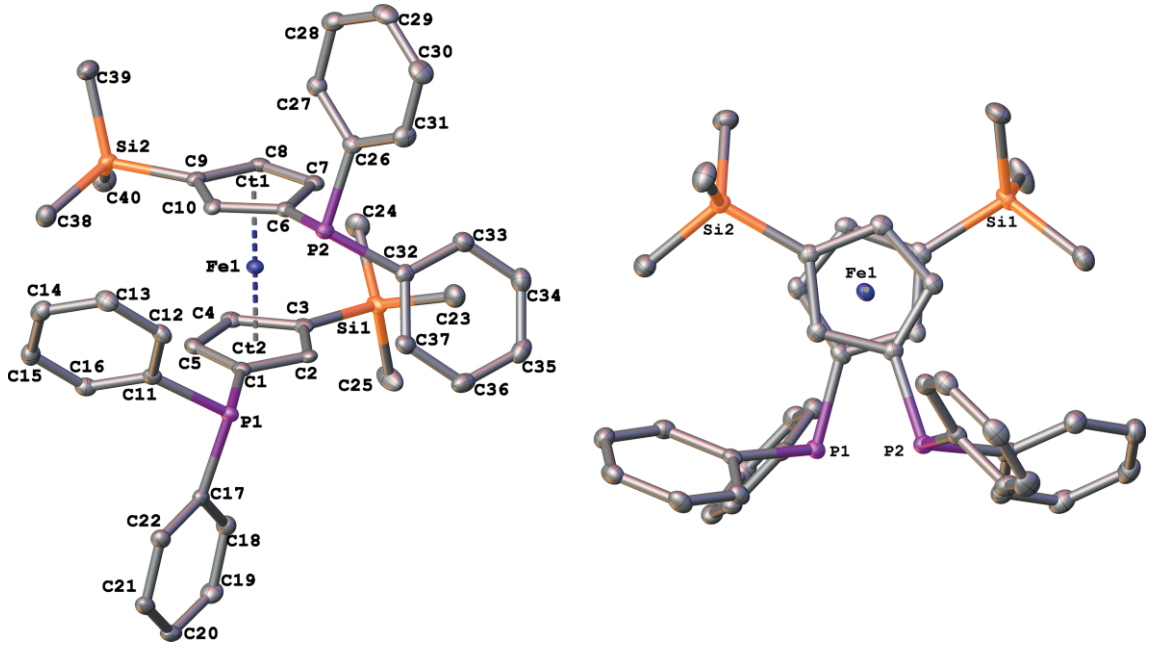


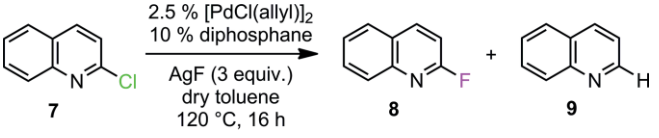
Figure 4. Molecular structures of compounds **6c**. Only one enantiomer is represented and hydrogen atoms are omitted for clarity. Selected bond lengths [Å], distances [Å], angles [°], and corresponding parameters for the second enantiomer are given in brackets: Fe1–Ct1 1.6558(8) [1.6594(8)], Fe1–Ct2 1.6576(8) [1.6599(8)], C1–P1 1.8141(16) [1.8138(16)], C6–P2 1.8168(16) [1.8150(16)], C3–Si1 1.8674(16) [1.8727(17)], C9–Si2 1.8678(16) [1.8703(17)], P1···P2 4.2333(5) [4.1405(6)], Ct1–Fe1–Ct2 177.35(4) [176.46(4)], P1–Ct1–Ct2–P2 37.19(2) [–34.02(3)], Si1–Ct1–Ct2–Si2 117.03(2) [–116.21(2)].

Effects of Ferrocenyl Diphosphanes in the Nucleophilic Fluorination of 2-Chloroquinolines

The nucleophilic fluorination of 2-chloroquinoline was first examined under conditions similar to those reported by Buchwald for related transhalogenation.[14a,14c] In the presence of $[PdCl(\eta^3\text{-}C_3H_5)]_2$ (2.5 mol-%) and AgF (3.0 equiv.) in dry toluene with the new ferrocenyl diphosphanes (10 mol-%) under an atmosphere of argon, we were glad to achieve promising conversions in the presence of the alkylated diphosphanes (Table 3, entries 3–8). This was not achieved in the absence of the phosphane (Table 3, entry 1) or by using the dppf ligand (Table 3, entry 2).

Even if *tert*-butylated bis(diphenylphosphino)ferrocene **5d** was by far found to be the most efficient (Table 3, entry 6), under these conditions the reaction was extremely sensitive to moisture and possible trace amounts of O_2 and side reactions with palladium were highly favored (e.g., dehalogenation, homocoupling). The action of palladium was also responsible for partial fluorination of the diphosphanes, as attested by the NMR spectroscopy data: $\delta(^{31}P)$ = 45.12 ppm and $\delta(^{19}F)$ = –73.29 ppm with $^1J_{P,F}$ = 1020 Hz.[24] Further investigations focused on optimizing the reactions by using diphosphane **5d** also indicated severe troubles with reproducibility, possibly linked to the quality of Pd^{II}. However, during the course of conducting blank experiments by removing each component from the catalytic system, we were surprised to observe that removal of palladium overcame the limitations above described. Therefore, further optimization was achieved with the palladium-free system by using **5d** and various sources of nucleophilic "F^-" or additives, without drastic drying of the toluene solvent, as reported in Table 4.

Table 3. Palladium fluorination of 2-chloroquinoline (**7**).[a]

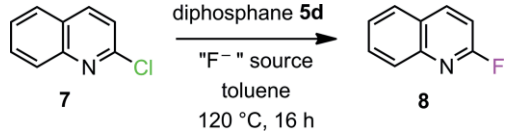


Entry	Diphosphane	Yield[b] of **8** [%]	Yield[b] of **9** [%]
1	–	3	0
2	dppf	18	2
3	**5a**	55	1
4	**5b**	62	0
5	**5c**	3	0
6	**5d**	97	3
7	**5e**	25	0[c]
8	**6a**	90	4[c]
9	**6b**	2	0
10	**6c**	19	22[d]
11	**6d**	39	0

[a] Besides the formation of fluorinated **8**, dehalogenation to **9** may occur. [b] Yields determined by GC and NMR spectroscopy. [c] Homocoupling of **7**. [d] The formation of unidentified side products was observed.

By using 3.0 equivalents of AgF in the absence of diphosphane **5d**, the transhalogenation of 2-chloroquinoline (**7**) to 2-fluoroquinoline (**8**) was achieved in only a very low yield (Table 4, entry 1). The absence of palladium, however, left **7** unchanged. In the presence of various substoichiometric amounts of **5d**, ranging from 10 to 100 mol-% (Table 4, entries 2–5), the selective conversion of **7** into **8** reach up to 95 % by using 50 mol-% of **5d** (Table 4, entry 4).[25] Curiously, the addition of a larger amount of **5d** was deleterious to the conversion (Table 4, entry 5). Monitoring of the reaction mixture

Table 4. Palladium-free fluorination of 2-chloroquinoline (**7**).[a]



Entry	**5d** [mol-%]	Source of F^- [equiv.]	Additive [mol-%]	Yield[b] of **8** [%]
1	–	AgF (3.0)	–	2
2	10	AgF (3.0)	–	30
3	25	AgF (3.0)	–	53
4	50	AgF (3.0)	–	92[c]
5	100	AgF (3.0)	–	58
6	50	AgF (1.0)	–	32
7	50	AgF (2.0)	–	50
8	50	AgF_2 (3.0)	–	<1
9	50	CsF (3.0)	$AgNO_3$ (20)	16
10	50	CsF (3.0)	$AgNO_3$ (100)	29
11	50	CsF (3.0)	$AgNO_3$ (300)	<1
12	50	KF (3.0)	$AgNO_3$ (300)	0

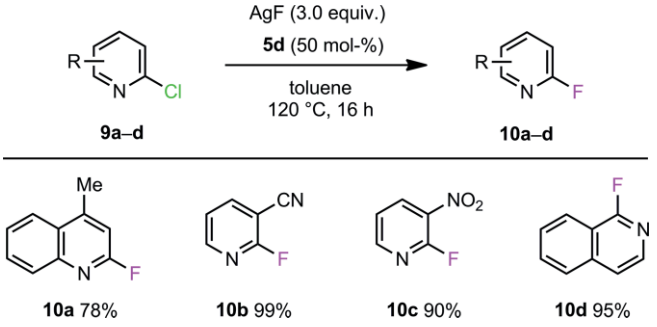
[a] Dehalogenation to **9** was no longer observed, incomplete conversion left **7** unchanged. [b] Yields determined by GC and NMR spectroscopy. [c] Average of three consistent runs ranging from 87 to 95 %.

by ^{31}P NMR spectroscopy under operating conditions indicated the absence of signals in the range of –250 to 150 ppm that could be correlated with coordination of phosphane to silver in some paramagnetic edifice. Changes in the amount of AgF added indicated that a quantity lower than 3.0 equivalents was less efficient for fluorination (Table 4, entries 6 and 7). Concerning the nucleophilic source, AgF_2, a rather marginally used reagent, was recently identified by Fier and Hartwig as a highly efficient fluorination reagent for direct nucleophilic S_NAr of pyridine derivatives.[18] Under our conditions, AgF_2 was inefficient as a transhalogenation agent (Table 4, entry 8).

We checked if other sources of silver could be catalytically used in combination with sources of nucleophilic "F^-". The commonly used CsF reagent was tested in combination with 20 to 100 mol-% $AgNO_3$, but only modest conversion of **7** was achieved (Table 4, entries 9 and 10). An excess amount of $AgNO_3$ was even more deleterious to the transhalogenation reaction. Finally, the cheaper KF reagent was also useless (Table 4, entry 11).

The most favorable conditions that we found for this clean transhalogenation (Table 4, entry 4) were applied to other quinoline substrates with some success (Scheme 5). Functional groups such as methyl, cyano, and nitro were tolerated on the quinoline (substrates **9a**–**c**, respectively), and the reaction was also selectively applied to α-chlorinated quinoline isomer **9d**; fluorinated analogues **10a**–**d** were delivered in good yields above 75 %.

This work shows that phosphanes in substoichiometric amounts in combination with AgF can provide a powerful system for the fluorination of chloroarenes. Further work is ongoing to understand the precise role of the diphosphane, which is expected to interact either with the silver salt or the C2 chloride, or possibly both. It may be anticipated that further optimization of the phosphane auxiliary may help to extend the scope of this system.



Scheme 5. Fluorination of quinoline and isoquinoline derivatives.

Conclusions

The diastereoselective synthesis of novel disubstituted ferrocenyl diphosphanes bearing aryl, alkyl, and hetero- and polycyclic substituents on the phosphorus atom was achieved. Steric control of the ferrocene backbone was the result of the introduction of *tert*-butyl, isopropyl, and trimethylsilyl groups on the backbone before lithiation in the presence of TMEDA. Subsequent phosphination and lithiation sequences favored the *rac* stereochemistry in the final substituted diphosphane ferrocenes. Symmetric diphosphanes were synthesized in good to excellent yields, especially if the ferrocene bearing *tert*-butyl substituents was used. Only *tert*-butyl groups ensured perfect diastereoselectivity in the formation of the diphosphanes. Characterization of typical products by X-ray structure analysis and multinuclear NMR spectroscopy was reported. The air-stable, moisture-insensitive diphosphanes demonstrated their utility in the nucleophilic fluorination of 2-chloroquinoline derivatives by using AgF under conditions for which dry toluene was not required and the addition of palladium was deleterious to selectivity.

Experimental Section

General Conditions: All reagents were purchased from commercial suppliers and were used without purification. All reactions were performed under an atmosphere of dry argon in oven-dried glassware by using Schlenk and vacuum-line techniques. Solvents were dried and deoxygenated before distillation from sodium benzophenone ketyl. The identities and purities of the products were established at the "Chemical Analysis Platform and Molecular Synthesis University of Burgundy" by using high-resolution mass spectrometry, elemental analysis, and multinuclear NMR spectroscopy. ^1H NMR (300 MHz) and ^{13}C NMR (75 or 125 MHz) spectra were recorded with a Bruker AVANCE III instrument in $CDCl_3$ solutions. Chemical shifts are reported in ppm relative to $CHCl_3$ (^1H: 7.26 ppm and ^{13}C: 77.16 ppm) and coupling constants *J* are given in Hz. High-resolution mass spectra were obtained with a Thermo LTQ-Orbitrap XL with ESI source. Flash chromatography was performed on silica gel (230–400 mesh). Elemental analysis experiments were performed with a Thermo Electron Flash EA 1112 Series.

CCDC 1477185 (for **5c**), 1405169 (for **5e**), 1405627 (for **6a**), and 1405168 (for **6c**) contain the supplementary crystallographic data for this paper. These data can be obtained free of charge from The Cambridge Crystallographic Data Centre.

1,1′-Bis(Diisopropylphosphino)-3,3′-di(*tert*-butyl)ferrocene (5a): To a solution of dilithium 1,1′-di(*tert*-butyl)ferrocene TMEDA salt (2.08 g, 4.88 mmol) in THF (50 mL) at –80 °C was added dropwise a solution of $ClPiPr_2$ (1.56 mL, 9.76 mmol) in THF (25 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/heptane, 3:97). Compound **5a** was isolated in a pure form as a red crystalline solid (1.89 g, 73 % yield). The analyses are similar to reported data from non-diastereoselective synthesis.[7a]

1,1′-Bis(dicyclohexylphosphino)-3,3′-di(*tert*-butyl)ferrocene (5b): To a solution of dilithium 1,1′-di(*tert*-butyl)ferrocene TMEDA salt (2.45 g, 5.75 mmol) in THF (50 mL) at –80 °C was added dropwise a solution of $ClPCy_2$ (2.53 mL, 11.5 mmol) in THF (25 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/heptane, 5:95). Compound **5b** was isolated in a pure form as a red crystalline solid (3.18 g, 80 % yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.85–1.85 (m, 44 H, *H*Cy), 1.24 [s, 18 H, *H*(*t*Bu)], 3.89 (m, 2 H, *H*Cp), 3.95 (m, 2 H, *H*Cp), 4.07 (m, 2 H, *H*Cp) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 22.9 (d, $J_{C,P}$ = 15.4 Hz, *C*Cy), 26.4 (d, $J_{C,P}$ = 7.7 Hz, *C*Cy), 26.6 (d, $J_{C,P}$ = 5.1 Hz, *C*Cy), 27.2–27.7 (m, *C*Cy), 28.7 (d, $J_{C,P}$ = 3.9 Hz, *C*Cy), 29.6 (d, $J_{C,P}$ = 6.4 Hz, *C*Cy), 30.7 [s, *C*(*t*Bu)], 31.5 (d, $J_{C,P}$ = 19.6 Hz, *C*Cy), 31.9 [s, *Me*(*t*Bu)], 31.9 [s, *Me*(*t*Bu)], 32.7–33.1 (m, *C*Cy), 34.2 (d, $J_{C,P}$ = 14.9 Hz, *C*Cy), 67.2 (s, *C*Cp), 68.5 (m, *C*Cp), 72.8 (s, *C*Cp), 73.1 (s, *C*Cp), 103.8 (d, $J_{C,P}$ = 5.6 Hz, *C*Cp) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = –8.57 ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{42}H_{69}FeP_2^+$ $[M + H]^+$ 691.42239; found 691.42109. $C_{42}H_{69}FeP_2$ (691.80): calcd. C 73.03, H 9.92; found C 72.51, H 9.37.

1,1′-Bis[di(2,4,6-methylphosphino)]-3,3′-di(*tert*-butyl)ferrocene (5c): To a solution of dilithium 1,1′-di(*tert*-butyl)ferrocene TMEDA salt (0.7 g, 1.64 mmol) in THF (30 mL) at –40 °C was added dropwise a solution of $ClPMes_2$ (1.00 g, 3.28 mmol) in THF (40 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/heptane, 3:97). Compound **5c** was isolated in a pure form as an orange crystalline solid after recrystallization from MeOH (1.13 g, 30 % yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 0.81 [s, 18 H, *H*(*t*Bu)], 2.19 (br. s, 18 H, Me_{Mes}), 2.22 (br. s, 18 H, Me_{Mes}), 3.99 (m, 2 H, *H*Cp), 4.067 (m, 2 H, *H*Cp), 4.26 (m, 2 H, *H*Cp), 6.66 (br. s, 4 H, *H*Mes), 6.83 (br. s, 4 H, *H*Mes) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 20.7 [s, *Me*(Mes)], 20.9 [s, *Me*(Mes)], 30.5 [s, *C*(*t*Bu)], 30.6 [s, *Me*(*t*Bu)], 66.7 (s, *C*Cp), 72.2 (s, *C*Cp), 75.1 (s, *C*Cp), 75.6 (s, *C*Cp), 77.7 (t, $J_{C,P}$ = 14.8 Hz, *C*Cp), 104.6 (t, $J_{C,P}$ = 3.5 Hz, *C*Cp), 109.9 (br. s, *C*Mes), 131.3 (d, $J_{C,P}$ = 13.8 Hz, *C*Mes), 134.2 (d, $J_{C,P}$ = 32.5 Hz, *C*Mes), 135.8 (s, *C*Mes), 138.5 (s, *C*Mes) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = –37.08 ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{54}H_{68}FeP_2^+$ $[M + H]^+$ 835.42239; found 835.42021. $C_{54}H_{68}FeP_2$ (834.93): calcd. C 77.68, H 8.21; found C 77.51, H 8.34.

1,1′-Bis(diphenylphosphino)-3,3′-di(*tert*-butyl)ferrocene (5d): To a solution of dilithium 1,1′-di(*tert*-butyl)ferrocene TMEDA salt (2 g, 4.96 mmol) in THF (20 mL) at –80 °C was added dropwise a solution of $ClPPh_2$ (1.74 mL, 9.39 mmol) in THF (20 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/heptane, 3:97). Compound **5d** was isolated in a pure form as an orange crystalline solid (2.74 g, 88 % yield). The analyses were similar to reported data from non-diastereoselective synthesis.[20]

1,1′-Bis(benzophosphindole)-3,3′-di(*tert*-butyl)ferrocene (5e): To a solution of dilithium 1,1′-di(*tert*-butyl)ferrocene TMEDA salt (1.38 g, 3.23 mmol) in THF (20 mL) at –80 °C was added dropwise a solution of [ClP(Bpi)][26] (1.41 g, 6.47 mmol) in THF (20 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (toluene/heptane, 2:3). Compound **5e** was isolated in a pure form as an orange crystalline solid (0.9 g, 42 % yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.20 [s, 18 H, *H*(*t*Bu)], 3.68 (m, 2 H, *H*Cp), 4.07 (m, 2 H, *H*Cp), 4.04 (m, 2 H, *H*Cp), 4.54 (m, 2 H, *H*Cp), 7.29 (dt, *J* = 7.44 and 1.21 Hz, 2 H, *H*Bpi), 7.40 (m, 4 H, *H*Bpi), 7.52 (dt, *J* = 7.44 and 1.21 Hz, 2 H, *H*Bpi), 7.79 (m, 2 H, *H*Bpi), 7.88 (d, *J* = 7.63 Hz, 2 H, *H*Bpi), 7.96 (d, *J* = 7.63 Hz, 2 H, *H*Bpi), 7.40 (m, 2 H, *H*Bpi) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 30.8 [s, *C*(*t*Bu)], 31.9 [s, *Me*(*t*Bu)], 67.5 (s, *C*Cp), 68.6 (s, *C*Cp), 70.8 (q, $J_{C,P}$ = 11.9 Hz, *C*Cp), 77.2 (m, *C*Cp), 105.4 (t, $J_{C,P}$ = 2.5 Hz, *C*Cp), 121.1 (s, *C*Bpi), 121.5 (s, *C*Bpi), 126.9 (t, $J_{C,P}$ = 3.6 Hz, *C*Bpi), 127.4 (t, $J_{C,P}$ = 3.6 Hz, *C*Bpi), 128.1 (s, *C*Bpi), 128.7 (s, *C*Bpi), 129.8 (t, $J_{C,P}$ = 12.4 Hz, *C*Bpi), 131.4 (t, $J_{C,P}$ = 12.4 Hz, *C*Bpi), 141.1 (m, *C*Bpi), 142.4 (m, *C*Bpi), 144.3 (m, *C*Bpi), 145.0 (t, $J_{C,P}$ = 2.2 Hz, *C*Bpi) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = –22.97 ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{42}H_{40}FeP_2^+$ $[M]^+$ 662.195465; found 662.19626. $C_{42}H_{40}FeP_2$ (662.57): calcd. C 76.14, H 6.09; found C 75.61, H 6.18.

1,1′-Bis[di(5-methyl-2-furyl)phosphino]-3,3′-di(*tert*-butyl)-ferrocene (5f): To a solution of dilithium 1,1′-di(*tert*-butyl)ferrocene TMEDA salt (4.15 g, 9.74 mmol) in THF (50 mL) at –80 °C was added dropwise a solution of $BrP(Fu^{Me})_2$ (5.32 g, 19.48 mmol) in THF (20 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (EtOAc/heptane, 3:97). Compound **5f** was isolated in a pure form as an orange crystalline solid after recrystallization from MeOH (1.13 g, 30 % yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.10 [s, 18 H, *H*(*t*Bu)], 2.26 (s, 6 H, *Me*Fu), 2.36 (s, 6 H, *Me*Fu), 3.97 (m, 2 H, *H*Cp), 4.07 (m, 2 H, *H*Cp), 4.29 (m, 2 H, *H*Cp), 5.88 (m, 2 H, *H*Fu), 6.02 (m, 2 H, *H*Fu), 6.28 (m, 2 H, *H*Fu), 6.81 (m, 2 H, *H*Fu) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 14.1 (s, *Me*Fu), 14.2 (s, *Me*Fu), 30.6 [s, *C*(*t*Bu)], 31.7 [s, *Me*(*t*Bu)], 69.4 (s, *C*Cp), 72.2 (s, *C*Cp), 72.7 (m, *C*Cp), 72.9 (t, $J_{C,P}$ = 18.2 Hz, *C*Cp), 105.3 (t, $J_{C,P}$ = 4.0 Hz, *C*Fu), 106.8 (m, *C*Fu), 107.0 (t, $J_{C,P}$ = 4.0 Hz, *C*Fu), 107.2 (d, $J_{C,P}$ = 5.7 Hz, *C*Cp), 119.3 (t, $J_{C,P}$ = 15.3 Hz, *C*Fu), 122.2 (d, $J_{C,P}$ = 2.5 Hz, *C*Fu), 122.7 (t, $J_{C,P}$ = 8.3 Hz, *C*Fu), 150.2 (d, $J_{C,P}$ = 6.9 Hz, *C*Fu), 150.3 (d, $J_{C,P}$ = 6.9 Hz, *C*Fu), 152.2 (m, *C*Fu), 156.2 (t, $J_{C,P}$ = 1.5 Hz, *C*Fu), 156.8 (m, *C*Fu) ppm. ^{31}P{^{1}H} NMR (121.5 MHz, $CDCl_3$): δ = –65.25 ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{38}H_{44}FeO_4P_2^+$ $[M]^+$ 682.55780; found 682.20697. $C_{38}H_{44}FeO_4P_2$ (682.56): calcd. C 66.87, H 6.50; found C 66.09, H 6.67.

1,1′-Bis(diphenylphosphino)-3,3′-diisopropylferrocene (6a): To a solution of dilithium 1,1′-diisopropylferrocene TMEDA salt (0.23 g, 0.34 mmol) in diethyl ether (20 mL) at –80 °C was added dropwise a solution of $ClPiPr_2$ (0.11 mL, 0.68 mmol) in diethyl ether (10 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (toluene/heptane, 2:3). Compound **6a** was isolated in a pure form after recrystallization from acetonitrile as a yellow crystalline solid (0.110 g, 51 % yield). ^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.02 [d, *J* = 6.5 Hz, 6 H, *Me*(*i*Pr)], 1.09 [d, *J* = 6.5 Hz, 6 H, *Me*(*i*Pr)], 2.34 (m, *J* = 6.5 Hz, 2 H, *CH*Me_2), 3.51 (s, 2 H, *H*Cp), 3.96 (s, 2 H, *H*Cp), 4.20 (s, 2 H, *H*Cp), 7.26 (m, 16 H, *H*Ph), 7.33–7.28 (m, 4 H, *H*Ph) ppm. ^{13}C{^{1}H} NMR (75 MHz, $CDCl_3$): δ = 23.0 [s, *Me*(*i*Pr)], 24.7 [s, *Me*(*i*Pr)], 27.5 [s, *C*(*i*Pr)], 70.5 (t, J_{CP} = 2.2 Hz, *C*Cp), 71.6 (s, J_{CP} = 2.5 Hz, *C*Cp),

74.8 (t, J_{CP} = 24.7 Hz, *C*Cp), 75.4 (dd, J_{CP} = 4.9 and 2.1 Hz, *C*Cp), 100.9 (t, J_{CP} = 2.6 Hz, *C*Cp), 128.1 (s, *C*Ph), 128.1 (s, *C*Ph), 128.2 (s, *C*Ph), 128.2 (s, *C*Ph), 128.8 (s, *C*Ph), 133.1 (d, J_{CP} = 21.2 Hz, *C*Ph), 134.5 (d, J_{CP} = 21.2 Hz, *C*Ph), 138.8 (d, J_{CP} = 9.9 Hz, *C*Ph), 140.5 (d, J_{CP} = 9.9 Hz, *C*Ph) ppm. $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ = –17.22 ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{40}H_{41}FeP_2^+$ $[M + H]^+$ 639.20129; found 639.20129. $C_{40}H_{41}FeP_2$ (639.56): calcd. C 75.24, H 6.31; found C 74.63, H 7.43.

1,1′-Bis(benzophosphindole)-3,3′-diisopropylferrocene (6b): To a solution of dilithium 1,1′-diisopropylferrocene TMEDA salt (1.22 g, 3.07 mmol) in THF (30 mL) at –80 °C was added dropwise a solution of [ClP(Bpi)][26] (1.33 g, 6.47 mmol) in THF (30 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (toluene/heptane, 2:3). Compound **6b** was isolated as a mixture of *rac* and *meso* forms (ratio 85:15) as an orange crystalline solid (0.51 g, 27 % yield). Even after several recrystallizations under different conditions, some impurities were still present. Data for **6b**-*rac*: ^1H NMR (300 MHz, $CDCl_3$): δ = 1.09 [d, *J* = 6.5 Hz, 6 H, *Me*(*i*Pr)], 1.13 [d, *J* = 6.5 Hz, 6 H, *Me*(*i*Pr)], 2.62 (m, *J* = 6.5 Hz, 2 H, *CH*Me_2), 3.52 (s, 2 H, *H*Cp), 3.98 (s, 2 H, *H*Cp), 4.11 (s, 2 H, *H*Cp), 7.30–7.52 (m, 8 H, *H*Bpi), 7.74–7.96 (m, 8 H, *H*Bpi) ppm. $^{13}C\{^1H\}$ NMR (75.0 MHz, $CDCl_3$): δ = 23.0 [s, *Me*(*i*Pr)], 24.5 [s, *Me*(*i*Pr)], 27.6 (s, *C*HMe_2), 68.3 (m, J_{CP} = 2.3 Hz, *C*Cp), 69.5 (m, J_{CP} = 2.1 Hz, *C*Cp), 72.5 (d, J_{CP} = 22.7 Hz, *C*Cp), 77.2 (s, *C*Bpi), 100.2 (t, J_{CP} = 2.4 Hz, *C*Cp), 121.1 (s, *C*Bpi), 121.4 (s, *C*Bpi), 127.0 (m, *C*Bpi), 127.2 (m, *C*Bpi), 128.6 (d, J_{CP} = 20.8 Hz, *C*Bpi), 130.2 (d, J_{CP} = 23.0 Hz, *C*Bpi), 131.0 (d, J_{CP} = 21.9 Hz, *C*Bpi), 141.4 (m, *C*Bpi), 142.8 (m, *C*Bpi), 143.4 (d, J_{CP} = 4.3 Hz, *C*Bpi), 144.0 (m, *C*Bpi) ppm. $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ = –20.19 (*rac*) and –20.71 (*meso*) ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{40}H_{36}FeP_2^+$ $[M]^+$ 634.16416; found 634.16580. $C_{40}H_{36}FeP_2$ (634.52): calcd. C 75.72, H 5.72; found C 76.21, H 6.44.

1,1′-Bis(diphenylphosphino)-3,3′-bis(trimethylsilane)ferrocene (6c):[23b] To a solution of dilithium 1,1′-bis(trimethylsilane)ferrocene TMEDA salt (1.88 g, 4.1 mmol) in THF (50 mL) at –80 °C was added dropwise a solution of $ClPPh_2$ (1.51 mL, 8.2 mmol) in THF (30 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (toluene/heptane, 2:3 + 1 % Et_3N). Compound **6c** was isolated in a pure form as an orange crystalline solid (1.00 g, 35 % yield). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.0 (s, 18 H, Me_3Si), 3.90 (m, 2 H, *H*Cp), 4.07 (m, 2 H, *H*Cp), 4.19 (m, 2 H, *H*Cp), 7.19–7.32 (m, 16 H, *H*Ph), 7.60 (m, 4 H, *H*Ph) ppm. $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ = –21.12 ppm.

1,1′-Bis(diisopropylphosphino)-3,3′-bis(trimethylsilane)-ferrocene (6d): To a solution of dilithium 1,1′-bis(trimethylsilane)ferrocene TMEDA salt (2.61 g, 5.7 mmol) in THF (50 mL) at –80 °C was added dropwise a solution of $ClPiPr_2$ (1.9 mL, 11.97 mmol) in THF (20 mL). After the addition, the mixture was warmed to room temperature and stirred overnight. Then, the solvent was removed in vacuo. The crude product was purified by column chromatography on silica gel (heptane 100 %). Compound **6d** was isolated in a pure form after recrystallization from MeOH as a red crystalline solid (1.13 g, 33 % yield). ^1H NMR (300 MHz, $CDCl_3$): δ = 0.26 (s, 18 H, Me_3Si), 0.74 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 0.77 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.02 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.07 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.15 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.19 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.32 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.39 [d, *J* = 7.0 Hz, 3 H, *Me*(*i*Pr)], 1.83 (m, 2 H, *CH*Me_2), 2.06 (m, 2 H, *CH*Me_2), 4.05 (m, 2 H, *H*Cp), 4.07 (m, 2 H, *H*Cp), 4.25 (m, 2 H, *H*Cp) ppm. $^{13}C\{^1H\}$ NMR (75 MHz, $CDCl_3$): δ = 0.6 (s, SiCH_3), 18.8 (m, $J_{C,P}$ = 3.4 Hz, *Ci*Pr), 20.1 (d, $J_{C,P}$ = 12.9 Hz, *Ci*Pr), 20.8 (d, $J_{C,P}$ = 16.5 Hz, *Ci*Pr), 22.3 (d, $J_{C,P}$ = 20.6 Hz, *Ci*Pr), 23.3 (m, *Ci*Pr), 24.5 (m, *Ci*Pr), 72.8 (s, *C*Cp), 75.0 (s, *C*Cp), 77.1 (s, *C*Cp), 78.7 (d, $J_{C,P}$ = 20.3 Hz, *C*Cp), 80.2 (d, $J_{C,P}$ = 21.3 Hz, *C*Cp) ppm. $^{31}P\{^1H\}$ NMR (121.5 MHz, $CDCl_3$): δ = –1.43 ppm. HRMS (ESI+, CH_2Cl_2/MeOH): calcd. for $C_{28}H_{52}FeP_2Si_2^+$ $[M + H]^+$ 563.25104; found 563.24977. $C_{28}H_{52}FeP_2Si_2$ (562.69): calcd. C 59.77, H 9.31; found C 58.75, H 8.58.

Silver-Mediated Fluorination Reactions: A Schlenk tube equipped with a stirring bar was charged with the pyridine derivative (1 mmol), ligand (0.5 mmol) and AgF (3 mmol) under an inert atmosphere before toluene (3 mL) was added. The mixture was stirred at 120 °C for 17 h in an oil bath. At room temperature, the mixture was then diluted with ethyl acetate, filtered on silica gel, and concentrated in vacuo for analysis by GC and NMR spectroscopy. The crude product was purified by column chromatography on silica gel (EtOAc/heptane).

2-Fluoroquinoline (8): Analyses were similar to reported data.[19a] ^1H NMR (300 MHz, $CDCl_3$): δ = 7.09 (dd, *J* = 8.7 and 2.8 Hz, 1 H), 7.54 (m, 1 H), 7.74 (m, 1 H), 7.83 (m, 1 H), 7.94 (d, *J* = 8.4 Hz, 1 H), 8.25 (t, *J* = 8.4 Hz, 1 H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –61.7 ppm.

4-Methyl-2-fluoroquinoline (10a): Analyses were similar to reported data.[27] ^1H NMR (300 MHz, $CDCl_3$): δ = 2.71 (d, *J* = 8.4 Hz, 3 H), 6.91 (m, 1 H), 7.53 (td, *J* = 8.2 and 1.0 Hz, 1 H), 7.71 (td, *J* = 8.2 and 1.0 Hz, 1 H), 7.94 (m, *2* H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –63.0 ppm.

2-Fluoro-3-cyanopyridine (10b): Analyses were similar to reported data.[28] ^1H NMR (300 MHz, $CDCl_3$): δ = 7.62 (td, *J* = 8.0 and 2.0 Hz, 1 H), 8.08 (td, *J* = 8.0 and 2.0 Hz, 1 H), 8.47 (m, 1 H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –63.0 ppm.

2-Fluoro-3-nitropyridine (10c): Analyses were similar to reported data.[29] ^1H NMR (300 MHz, $CDCl_3$): δ = 7.47 (dd, *J* = 8.0 and 4.75 Hz, 1 H), 8.22 (dd, *J* = 8.0 and 1.75 Hz, 1 H), 8.22 (dd, *J* = 4.75 and 1.75 Hz, 1 H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –67.6 ppm.

1-Fluoro-isoquinoline (10d): Analyses were similar to reported data.[30] ^1H NMR (300 MHz, $CDCl_3$): δ = 7.50 (m, 1 H), 7.63 (td, *J* = 8.2 and 1.2 Hz, 1 H), 7.75 (td, *J* = 6.9 and 1.3 Hz, 1 H), 7.84 (m, 1 H), 8.03 (dd, *J* = 5.8 and 1.2 Hz, 1 H), 8.15 (m, 1 H) ppm. ^{19}F NMR (282 MHz, $CDCl_3$): δ = –71.2 ppm.

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Keywords: Sandwich complexes · Diastereoselectivity · Phosphanes · Fluorination · Halex reaction

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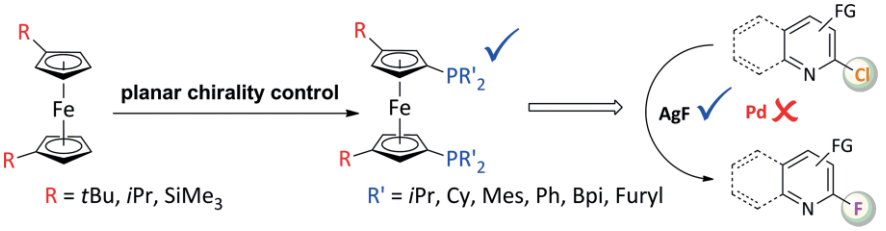
Diastereoselective Synthesis



The diastereoselective synthesis of dialkylated ferrocenyl bis(phosphane)s bearing aryl, alkyl, and hetero/polycyclic groups on the phosphorus atom is reported together with their characterization by X-ray analysis and NMR spectroscopy. In combination with AgF, these ferrocenyl diphosphanes allow the selective fluorination of 2-chloroquinoline derivatives, whereas palladium is highly deleterious.

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