Synthesizing Multidentate Ferrocenylphosphines: A Powerful Route to Dissymmetrically Tri-Substituted Ferrocenes. X-ray Structure and ^{13}C NMR of a Diaryl–Alkyl-phosphino Ferrocene

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(Received June 21, 2004; CL-040708)

As a powerful route to multidentate ferrocenylphosphines, the synthetic strategy which consists in successively reacting $FeCl_2$ with the suitably substituted cyclopentadienyllithium salts was carried out. The new mixed diaryl/alkyl triphosphine 1,2-bis(diphenylphosphino)-1′-(diisopropylphosphino)-4-*tert*-butylferrocene, $Fc(P)_2{}^tBu(P^iPr)$, was obtained in good yield (70%). A very rare *through-space* nuclear spin–spin coupling $J_{CP} = 5.5$ Hz was evidenced from its reported ^{13}C NMR and X-ray molecular structure characterizations.

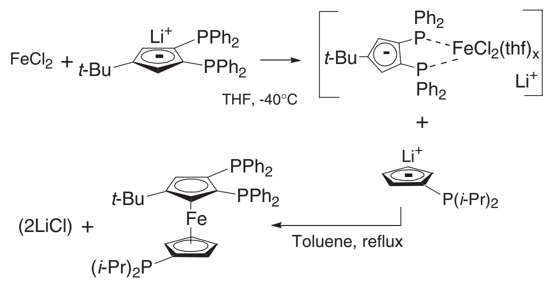
The tertiary aryl- and alkylphosphines play a very important role in modern metal-catalyzed organic reactions. For instance, most of the efficient catalytic procedures reported for the Suzuki–Miyaura (biaryl formation) or the Sonogashira–Hagihara (enyne formation) cross-coupling reactions are conducted in the presence of phosphine auxiliary ligands.[1,2] Besides the classical mono- and bidentate phosphines, we and others recently disclosed the efficiency and the versatility of *multidentate phosphines* (tri-, tetraphosphine, or more) catalytic auxiliaries for fine chemical synthesis.[3,4]

An examination of the literature reveals that only few ferrocenylpolyphosphine ligands (a sub-group of the aforementioned multidentate phosphines) are available for use in organic chemistry and catalysis.[5,6] In especial, proper descriptions of the synthesis and the characterization of ferrocenyltriphosphines are very scarce.[7] This is surprising since the related 1,1′-bis(diphenylphosphino)ferrocene (dppf) is among the most useful ferrocene derivatives, and is widely used in homogeneous catalysis.[8] Additionally, while there have been recently several key developments in the synthetic methodology of 1,2-substituted ferrocene derivatives,[9] to our knowledge only the Butler's group reported significant advances for the access to tri-substituted ferrocenes.[7]

The selectivity problems encountered when the phosphorylation of the ferrocene backbone is operated partly explain the limited development of ferrocenylpolyphosphine ligands. For example, the successive treatment of diphenylphosphino-ferrocene with *n*-BuLi and $ClPPh_2$ typically yields not less than four products: unreacted diphenylphosphinoferrocene (22%), dppf (15%), 1,3,1′-tris(diphenylphosphino)ferrocene (51%), and 1,2,1′-tris(diphenylphosphino)ferrocene (6%).[6]

In Scheme 1 is displayed the selective access to the original ferrocenyl triphosphine named $Fc(P)_2{}^tBu(P^iPr)$, i.e. 1,2-bis(diphenylphosphino)-1′-(diisopropylphosphino)-4-*tert*-butylferrocene. $Fc(P)_2{}^tBu(P^iPr)$ is obtained in good yield, in two successive steps reacting $FeCl_2$ with the appropriately substituted synthons (phosphorylated-Cp lithium salts, ^{s}CpLi).[10]

The key feature of the synthesis is the postulated formation of a $FeCl_2$/thf adduct incorporating the first ^{s}CpLi synthon. To support this hypothesis, previous attempts to form dissymmetrically substituted ferrocenes starting from ^{s}CpLi synthons which are not 1,2-phosphorylated invariably led to important amounts of the undesired *symmetric* ferrocenes derivatives.[11] This hypothesis still awaits confirmation since the deep-violet solution obtained at −40 °C, after the first step, is difficult to characterize. However, related results were reported which correlate this adduct formation.[12] The yield is lowered partly due to the formation in about 20% yield of the already known symmetric tetrakis(arylphosphine)ferrocene compound.[4,13] Nevertheless the product isolation is easy by using classical SiO_2 chromatography (toluene/hexane 1:4) under air.



Scheme 1. Synthesis of the aryl/alkylphosphine $Fc(P)_2$-$^tBu(P^iPr)$.

Single crystals suitable for X-ray diffraction were obtained from recrystallisation in hot ethanol. An ORTEP view of the molecular structure is presented in Figure 1.[14]

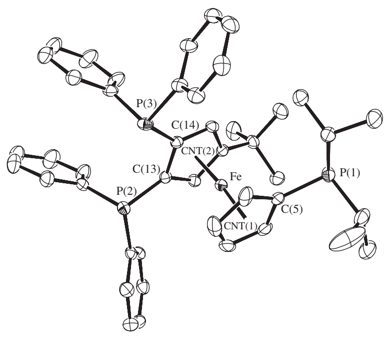


Figure 1. Molecular structure of $Fc(P)_2{}^tBu(P^iPr)$ (ORTEP 50%).

Even if the synthesis of a few ferrocenyl triphosphines of this type has been reported,[7,12] to the best of our knowledge, we report herein the first X-ray structure for this family of compound. Atom distances and bond angles are consistent with data reported for ferrocenylpolyphosphines.[4] The Cp rings are staggered, with a twist angle calculated from the mean value of the dihedral angles Ci–CNT(1)–CNT(2)–Ci* = 30.4(5)°.

The NMR phosphorus signals detected at −0.93 ppm for $P(i\text{-}Pr)_2$ and −22.01 ppm for PPh_2 give evidence of the basicity of the former. The ^{1}H NMR spectrum is consistent with the ^{31}P data.[10] In the ^{13}C NMR spectrum of $Fc(P)_2{}^t Bu(P^i Pr)$, two pairs of isochronous methyl groups are distinguished for the isopropyl moieties ($\delta = 20.55$, 20.69 ppm, the overlap of two doublets yields a pseudo-triplet). The two *C*H of the isopropyl moieties are magnetically equivalents ($\delta = 23.63$ ppm). All the other carbon atoms were attributed,[10] showing for the atoms of the Cp rings six signals at 71.7(3′,4′-*C*), 72.2(3,5-*C*), 74.2(2′,5′-*C*), 81.0(1′-*C*), 81.6(1,2-*C*), 108.1(4-*C*). Signals for the Ph-ring carbons' are observed, as expected, in the range 127–140 ppm.

The most remarkable feature in the ^{13}C NMR data is a net spin–spin nuclear coupling constants ($J_{CP} = 5.5$ Hz) between the three carbon atoms of the ^{t}Bu group and the phosphorus atom holding the isopropyl groups (unambiguously demonstrated by selective decoupling phosphorus). Interestingly, these atoms *are not* linked to the same Cp ring. Thus, the shortest distance between the involved nucleus is a five bound (C–C–C–Fe–C–P) distance that would not lead to a detectable $^5J_{CP}$. Consistently, no other coupling constant $^4J_{CP}$ or $^5J_{CP}$ are observed. The X-ray structure reveals the proximity in space of the atoms (shortest through-space distance d P···C = 3.64 Å), favored by the staggered conformation. The lone-pair of the phosphorus is pointing toward the carbon atoms of the ^{t}Bu group as schematized in Figure 2. This kind of nonbonded interactions which requires steric crowding is very rare, and has been experimentally evidenced mainly for J_{FF} couplings.[15]

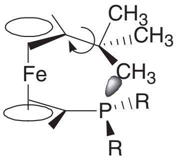


Figure 2. A phosphorus lone-pair at the origin of a through-space $^{ts}J_{CP}$.

We first reported through-space J_{PP} in ferrocenyl phosphine compounds involving a phosphorus lone-pair in the transmittal of the spin information.[13] This study shows that analogous through-space J_{CP} also exist in ferrocenylpolyphosphines.

Finally, the synthetic strategy described herein allowed us to synthesize a number of other dissymmetrical ferrocene-based triphosphines, these works will be reported in due time. Current investigations concern the coordination chemistry and the properties in catalysis of this class of phosphines.

This research was supported by the "Conseil Régional de Bourgogne." Thanks are due to B. Rebière for crystallographic acquisition.

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10 A solution of $(Ph_2P)_2Cp({}^tBu)Li$ (1.85 g, 3.7 mmol) in THF was added at −40 °C to a stirred suspension of anhydrous $FeCl_2$ (0.45 g, 3.55 mmol) in THF. After 2 h the mixture was reacted with a THF solution of $({}^iPr_2P)_2CpLi$ (0.67 g, 3.55 mmol). The mixture was evaporated in vacuo and the residue was refluxed in 40 mL of toluene for 3 h. From the cooled reaction mixture, the crude product was obtained in solution and after filtration was purified by chromatography to provide 1.80 g (70% yield) of $Fc(P)_2{}^tBu(P^iPr)$. Found C 72.8, H 6.7%. Calcd. C 72.7, H 6.8%. In $CDCl_3$, **^{13}C{^{1}H}** NMR (100.62 MHz): $\delta = 20.55$ and 20.69 (2d (pseudo-t), 2C each, $^2J_{CP} = 13.7$ Hz, $^iPrCH_3$), 23.6 (d, 2C, $^1J_{CP} = 12.2$ Hz, ^iPrCH), 31.7 (s, 1C, $^tBuCCH_3$), 32.4 (d, 3C, $^{\text{through-space}}J_{CP} = 5.5$ Hz, $^tBuCCH_3$), 71.7 (d, 2C, $^3J_{CP} <$ 1 Hz, (3′,4′)Cp*C*H), 72.2 (s, 2C, (3,5)Cp*C*H), 74.2 (d, 2C, $^2J_{CP} =$ 9.8 Hz, (2′,5′)Cp*C*H), 81.0 (d, 1C, $^1J_{CP} = 21.8$ Hz, $CpCP\{^iPr_2\}$), 81.6 (dd (pseudo-t), 2C, $2 \times J_{CP} \cong 11$ Hz, $CpCPPh_2$), 108.1 (s, 1C, CpC^tBu), 128.0(s, 2C, *p*-Ph), 128.0 (t, 4C, $J_{CP} \cong 3.5$ Hz, *m*-Ph), 128.7 (t, 4C, $J_{CP} \cong 4.5$ Hz, *m*-Ph), 129.7 (s, 2C, *p*-Ph), 133.1 (t, 4C, $J_{CP} \cong 10$ Hz, *o*-Ph), 136.0 (t, 4C, $J_{CP} \cong 11.5$ Hz, *o*-Ph), 138.2 (t, 2C, $J_{CP} \cong 2.5$ Hz, *ipso*-Ph), 139.5 (t, 2C, $J_{CP} \cong 4.5$ Hz, *ipso*-Ph); **^{1}H** NMR (400.13 MHz): $\delta = 7.73$ (m, 4H, Ph), 7.40 (m, 6H, Ph), 7.12–6.95 (m, 10H, Ph), 4.21 (t, 2H, $J_{HP} = 1.2$ Hz, 3,5*H*Cp), 4.17 (t, 2H, $^3J_{HH} =$ 2.0 Hz, 3′,4′(or 2′,5′)*H*Cp), 3.96 (m, 2H, $J_{HP} < 2.0$ Hz, $^3J_{HH} =$ 2.0 Hz, 2′,5′(or 3′,4′)*H*Cp), 1.53 (hept(d), 1H, $^2J_{HP} =$ 2.6 Hz, $^3J_{HH} = 7.0$ Hz, CH^iPr), 1.38 (s, 9H, ^{t}Bu), 0.93 (dd, 6H, $^3J_{HP} =$ 12.8 Hz, $^3J_{HH} = 6.8$ Hz, $CH_3{}^iPr$), 0.67 (dd, 6H, $^3J_{HP} = 13.0$ Hz, $^3J_{HH} = 7.0$ Hz, $CH_3{}^iPr$); **^{31}P{^{1}H}** NMR (161.98 MHz): $\delta = -0.93$ (s, 1P, $P\{^iPr_2\}$), −22.01 (s, 2P, PPh_2).

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14 **Crystal data**: $Fc(P)_2{}^tBu(P^iPr)$ ($C_{44}H_{49}P_3Fe$, fw 726.59) crystallized in the monoclinic space group $P2_1/c$ with $a = 12.5305(2)$ Å, $b = 28.8020(4)$ Å, $c = 11.5722(1)$ Å, $\beta = 113.153(1)°$, $V =$ 3840.07(9) Å^3, $Z = 4$, $D_{calc} = 1.257$ g·cm^{-3}. 8778 independent reflections were measured and used in refinement, $wR_2 = 0.0913$ ($R_1 = 0.0419$ for 5828 independent reflections with $I > 2\sigma(I)$). Data were collected on a Nonius Kappa CDD at 110 K. The structure was solved by a Patterson search program and refined by full-matrix least-squares methods based on F^2 using SHELX97.

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Published on the web (Advance View) September 11, 2004; DOI 10.1246/cl.2004.1296