Chelating phosphines by nucleophilic substitution of fluorine in 3,4,5-trifluorobenzonitrile and tetrafluorophthalonitrile

Vladimir I. Sorokin,*[a] Mark Nieuwenhuyzen[b] and Graham C. Saunders[b]

[a] *Department of Organic Chemistry, Rostov State University, 344090 Rostov-on-Don, Russian Federation. Fax: +7 863 297 4156; e-mail: vsorokin@aaanet.ru*
[b] *School of Chemistry and Chemical Engineering, Queen's University Belfast, Belfast BT9 5AG, UK. Fax: +44 28 9097 6524; e-mail: g.saunders@qub.ac.uk*

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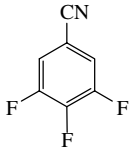
Directed nucleophilic substitution of two fluorine atoms in title compounds 1, 2 by diphenylphosphine groups was used to prepare new chelating electron-deficient diphosphine ligands 3 and 4; the structure of 4 was confirmed by XRD analysis.

Chelating diphosphines are important, versatile ligands for transitional metals, enabling the catalysis of a vast array of reactions.[1] Although phosphines are typically electron-donating, those bearing electron-withdrawing substituents are poor donors and, therefore, useful ligands for enhancing the Lewis acidity of cationic transitional metal sites, which are the catalytic centres for reactions such as Baeyer–Villiger oxidation, alkene polymerization and similar transformations.[2–4]

The main synthetic approach to preparation of aromatic phosphine ligands is arene or haloarene metallation followed by reaction with halogenated phosphines or their equivalents.[1,5] Direct nucleophilic substitution of the fluorine in fluoroarenes by phosphide or equivalent is used rarely, but it is of particular utility for the preparation of phosphines with electron-withdrawing fluoroaryl substituents.[6] Although a number of arene-1,4-diphosphines have been prepared using this route,[7] to our knowledge it has been used for only one potentially chelating arene-1,2-diphosphine, $(Et_2P)_2C_6F_2(CN)_2$, which was synthesised from tetrafluorophthalonitrile and diethylphosphine.[8] However, the characterizing data for this compound could not establish unequivocally the 1,2-disubstitution pattern, which was based solely on the chemical shift of a singlet resonance observed in the ^{19}F NMR spectrum.

We wished to develop the potentially powerful methodology of nucleophilic attack on fluoroarenes to prepare chelating diphosphine ligands with electron-withdrawing arene backbones. Through the judicious placement of electron-withdrawing substituents, such as nitrile and nitro, which are firstly *para*-directing, then *ortho*-directing,[9] and substituents, which cannot be substituted by nucleophiles, such as hydrogen and trifluoromethyl, attack by phosphides can be directed to give the desired 1,2-diphosphinoarene products. For example, nucleophilic attack by one phosphide on 3,4,5-trifluorobenzonitrile **1** is expected to occur *para* to the nitrile group, and since substitution *ortho* to the nitrile group is prevented a second phosphide will substitute at the *meta* position to give an 1,2-diphosphinoarene. A similar product is expected from nucleophilic attack by two phosphides on tetrafluorophthalonitrile **2**, which is predicted to occur *para* to each nitrile group. To confirm the validity of our approach, we investigated the disubstitution of fluorine by phosphide in **1** and **2**.



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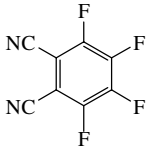
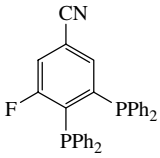


2

Treatment of benzonitrile **1** with two equivalents of diphenylphosphide in THF gave desired disubstituted derivative **3** in 47% yield.[†,‡] Further substitution in the presence of another equivalent of diphenylphosphide was not observed. The substitution pattern was confirmed by the $^{31}P\{^1H\}$ and $^{19}F\{^1H\}$ NMR spectra of diphosphine **3**, which comprise two doublet of doublet resonances and a doublet of doublet resonance, respectively. Furthermore, the magnitude of the 3-bond phosphorus-phosphorus coupling of 169 Hz is similar to the value of 145.2 Hz reported for the analogous diphosphine $1,2\text{-}C_6H_4(PPh_2)_2$.[10]



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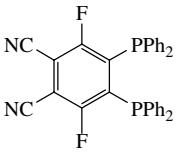


4

The reaction between **2** and diphenylphosphide was much more vigorous and even at low temperature intractable tars were produced. Treatment of **2** with two equivalents of the milder nucleophile diphenylphosphine[8] gave desired product **4** in 60% yield.[§] The substitution pattern was confirmed by a single-crystal X-ray diffraction study of diphosphine **4**.[¶] The $^{31}P\{^1H\}$

† ^1H, ^{19}F and ^{31}P NMR spectra were recorded using a Bruker DPX300 spectrometer. ^1H (300.01 MHz) spectra were referenced internally using the residual protio solvent resonance relative to $SiMe_4$ (δ 0 ppm) and ^{19}F (282.26 MHz) and ^{31}P (121.45 MHz) spectra externally to $CFCl_3$ (δ 0 ppm) and 85% H_3PO_4 (δ 0 ppm), respectively. All chemical shifts are quoted in δ (ppm), using the high frequency positive convention, and coupling constants in Hz. IR spectra were recorded on a Perkin–Elmer RX.1 FTIR spectrophotometer. Mass spectra were recorded on a VG Autospec X series mass spectrometer.

‡ *5-Fluoro-3,4-bis(diphenylphosphino)benzonitrile* **3**. A 0.5 M solution of potassium diphenylphosphide in THF (4.2 ml, 2.1 mmol) was added slowly to a stirred solution of 3,4,5-trifluorobenzonitrile (0.15 g, 1 mmol) in THF at 0 °C. The resulting brown mixture was stirred for additional 30 min at 0 °C, then 30 min at ambient temperature, and poured onto ice. The reaction products were extracted into diethyl ether (3×10 cm^3). The ethereal extract was dried over anhydrous $MgSO_4$ and solvent was removed under reduced pressure. The yellow residue was passed through a short column with silica gel, using dichloromethane as an eluent. The solvent was evaporated to obtain 0.21 g (47% yield) of 5-fluoro-3,4-bis(diphenylphosphino)benzonitrile. Yellow crystals from ethanol, mp 178–180 °C. ^1H NMR ($CDCl_3$) δ: 7.13–7.34 (m). ^{19}F NMR ($CDCl_3$) δ: –92.37 (dd, $^3J_{PF}$ 17.1 Hz, $^4J_{PF}$ 5.4 Hz). ^{31}P NMR ($CDCl_3$) δ: –7.5 (dd, 1P, P-3, $^3J_{PP}$ 169 Hz, $^4J_{PF}$ 5.4 Hz), –17.7 (dd, 1P, P-4, $^3J_{PF}$ 17.1 Hz). IR (KBr, ν/cm^{-1}): 2233 (C≡N). MS (EI, 70 eV) *m/z* (%): 489 (M^+, 100), 428 (37), 412 (99), 226 (36), 185 (16), 183 (51). HRMS (EI): $C_{31}H_{22}NFP_2$ requires *m/z* 489.1211, found 489.1203.

§ *3,6-Difluoro-4,5-bis(diphenylphosphino)phthalonitrile* **4**. Diphenylphosphine (0.22 g, 1.2 mmol) was added to a solution of tetrafluorophthalonitrile (0.10 g, 0.5 mmol) in 2 ml of anhydrous acetonitrile, the resulting pale yellow solution was stirred under reflux during 12 h. Acetonitrile was evaporated in a vacuum, and the orange residue was crystallised from ethanol to obtain 0.16 g (60% yield) of 3,6-difluoro-4,5-bis(diphenylphosphino)phthalonitrile. Orange crystals, mp 213–215 °C. ^1H NMR ($CDCl_3$) δ: 7.32 (m). ^{19}F NMR ($CDCl_3$) δ: –91.94 (m, A part of an AA′XX′ spin system). ^{31}P NMR ($CDCl_3$) δ: –10.0 (m, X part of an AA′XX′ spin system). IR (KBr, ν/cm^{-1}): 2242 (C≡N). MS (EI, 70 eV) *m/z* (%): 532 (M^+, 80), 489 (21), 455 (100), 428 (50), 412 (24), 185 (30), 183 (50). HRMS (EI): $C_{32}H_{20}N_2F_2P_2$ requires *m/z* 532.1069, found 532.1060.

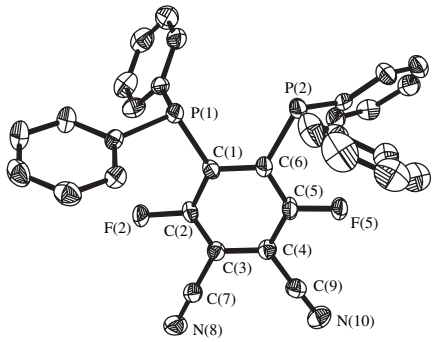


Figure 1 Structure of **4**. Thermal ellipsoids are at the 30% level. Hydrogen atoms are omitted for clarity. Bond lengths (Å): P(1)–C(1) 1.865(5), P(2)–C(6) 1.857(5), C(2)–F(2) 1.348(5), C(3)–C(7) 1.423(7), C(4)–C(9) 1.441(8), C(5)–F(5) 1.337(5), C(7)–N(8) 1.131(6), C(9)–N(10) 1.142(7); bond angles (°): P(1)–C(1)–C(6) 117.1(3), C(1)–C(6)–P(2) 121.1(3).

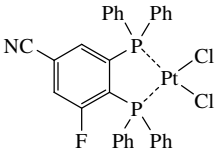
and $^{19}F\{^1H\}$ NMR spectra of **4** were not informative, comprising multiplet resonances consistent with an AA′XX′ spin system with outer lines of insufficient intensity to be observed.

The chelating ability of **3** and **4** was confirmed by trial reactions with $(MeCN)_2PtCl_2$ in dichloromethane. The $^{31}P\{^1H\}$ NMR spectrum of the product obtained from **3** showed two multiplet resonances at δ 44.2 and 43.2 with platinum satellites ($^1J_{PtP}$ = 3617 and 3630 Hz) and that from **4** showed a multiplet resonance at δ 47.3 with platinum satellites ($^1J_{PtP}$ = 3649 Hz).

¶ *Crystal data for 3,6-difluoro-4,5-bis(diphenylphosphino)phthalonitrile* **4**: $C_{32}H_{20}F_2N_2P_2$, M = 532.11, orthorhombic, space group $P2_12_12_1$, a = 13.126(7), b = 12.523(6) and c = 16.099(10) Å, V = 2646(2) Å^3, T = 298(2) K, Z = 4, d_{calc} = 1.336 g cm^{-3}, μ(MoKα) = 0.203 mm^{-1}, reflections collected 9936, unique reflections 5582 (R_{int} = 0.0374), R_1, wR_2 [$I > 2\sigma(I)$] = 0.0681, 0.1663, R_1, wR_2 (all data) = 0.1169, 0.1985. Flack parameter –0.06 (17).

Atomic coordinates, bond lengths, bond angles and thermal parameters have been deposited at the Cambridge Crystallographic Data Centre (CCDC). These data can be obtained free of charge *via* www.ccdc.cam.uk/conts/retrieving.html (or from the CCDC, 12 Union Road, Cambridge CB2 1EZ, UK; fax: +44 1223 336 033; or deposit@ccdc.cam.ac.uk). Any request to the CCDC for data should quote the full literature citation and CCDC reference number 297136. For details, see 'Notice to Authors', *Mendeleev Commun.*, Issue 1, 2006.

These data are similar to the values of δ_P 40.1 and $^1J_{PtP}$ 3606 Hz reported for $[\{1,2\text{-}C_6H_4(PPh_2)_2\}PtCl_2]$[10] and are entirely consistent with expected complexes **5** and **6**.



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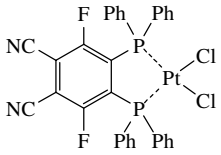

6

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References

1 L. Brandsma, S. F. Vasilevsky and H. D. Derkruijsse, *Application of Transition Metal Catalysts in Organic Synthesis*, Springer, Berlin, Heidelberg, 1999, p. 335.
2 R. Wursche, T. Debaerdemaeker, M. Klinga and B. Rieger, *Eur. J. Inorg. Chem*., 2000, 2063.
3 O. Lot, I. Suisse, A. Mortreux and F. Agbossou, *J. Mol. Catal. A*, 2000, **164**, 125.
4 D. Konya, F. Robert, Y. Gimbert and A. E. Greene, *Tetrahedron Lett*., 2004, **45**, 6975.
5 L. A. Wall, R. E. Donadio and W. J. Pummer, *J. Am. Chem. Soc*., 1960, **82**, 4846.
6 (*a*) L. S. Kobrina, *Fluorine Chem. Rev*., 1974, **7**, 1; (*b*) Y. A. Viets, N. B. Karlstedt, A. V. Chuchryukin and I. P. Beletskaya, *Zh. Org. Khim.*, 2000, **36**, 778 (*Russ. J. Org. Chem*., 2000, **36**, 750); (*c*) R. M. Bellabarba, M. Nieuwenhuyzen and G. C. Saunders, *Organometallics*, 2003, **22**, 1802.
7 (*a*) S. Sasaki, Y. Tanabe and M. Yoshiful, *Bull. Chem. Soc. Jpn.*, 1999, **72**, 563; (*b*) L. I. Goryunov, J. Grobe, V. D. Shteingarts, B. Krebs, A. Lindemann, E.-U. Würthwein and C. Mück-Lichtenfeld, *Chem. Eur. J*., 2000, **6**, 4612; (*c*) T. Norman and G. Hogarth, *J. Chem. Soc., Dalton Trans*., 1996, 1077.
8 J. M. Birchall, R. N. Haszeldine and J. O. Morley, *J. Chem. Soc. C*, 1970, 456.
9 (*a*) V. M. Vlasov, *J. Fluorine Chem*., 1993, **61**, 193; (*b*) G. M. Brooke, *J. Fluorine Chem*., 1997, **86**, 1.
10 H. C. E. McFarlane and W. McFarlane, *Polyhedron*, 1999, **18**, 2117.

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