Full Paper

Applied Organometallic Chemistry

Received: 9 January 2012 Revised: 9 March 2012 Accepted: 9 March 2012 Published online in Wiley Online Library

(wileyonlinelibrary.com) DOI 10.1002/aoc.2856

Stability of some aryllithiums in the presence of cyano group: synthesis of biaromatic cyanoarylboronic acids and silanes

Krzysztof Durka,[a] Krzysztof Gontarczyk,[a] Tomasz Kliś,[a]* Janusz Serwatowski[a] and Krzysztof Woźniak[b]

Lithium diisopropylamine (LDA)-mediated deprotonation reactions of halogenated cyanobenzyloxy-benzenes and cyanobiphenyls were investigated. The resultant organolithium derivatives were converted into the corresponding arylboronic acids or silanes. It was found that the stability of the obtained aryllithiums towards isomerization to the respective benzyllithiums depends strongly on the number of fluorine atoms in the phenyl ring and on the position of the cyano group. Halogenated cyanobiaryls were selectively deprotonated in the position flanked by two halogen atoms; however, the yield depended strongly on the reaction conditions. Addition of LDA to the cyano group was observed on the lithiation of 4-cyano-3',5'-dichlorobiphenyl rather than deprotonation. Copyright © 2012 John Wiley & Sons, Ltd.

Keywords: lithiation; nitriles; boronic acids; silanes

Introduction

Lithiation of benzene derivatives containing electrophilic nitrogen substituents has been investigated for many years. It has been already demonstrated that some aryllithiums can be generated in the presence of the highly reactive -NO_2 group.[1,2] The first studies concerning lithiation of benzonitriles were carried out by Gilman and Melstrom, who obtained 4-lithiobenzonitrile with limited yield using Br–Li interconversion between 4-bromobenzonitrile and *n*-butyllithium in diethyl ether at −70°C.[3] Parham and Jones generated the series of isomeric lithiobenzonitriles from the respective bromobenzonitriles at −100°C in high yield (70–82%).[4] Recent studies have shown that lithiation of bromobenzonitriles is very sensitive towards reaction conditions and may result in many side reactions like addition of organolithiums to the cyano group or subsequent deprotonation of the unreacted starting material.[5] The addition of organolithiums and Grignard reagents to nitriles is a common way to synthesize various carbonyl compounds.[6] The mechanism of this reaction is well known and organolithium compounds are generally more reactive than Grignard reagents.[7] The successful Br–Li interconversion in nitriles can be achieved at −70°C using the reverse addition order (reaction carried out in excess of *n*-BuLi) in THF or THF/Et_2O mixture.[8] Interestingly, the addition of *n*-BuLi to the cyano group was not observed under these reaction conditions. The authors assumed that the carbanionic character of the aromatic ring in the lithiated benzonitriles significantly decreased the electrophilic properties of the cyano group due to the negative charge accumulation at this group. They also suggested that this effect can be explained by assuming polarizing interactions.[9] Lithiation of benzonitriles can be also performed via directed deprotonation; however, lithium amides should be used as a base in order to prevent addition to the cyano group.[10] Indeed, 1-cyanonaphtalene was successfully *ortho*-lithiated with N-lithio 2,2,6,6-tetramethylpiperidine (LTMP) in THF at −78°C and 1,3-dicyanobenzene was lithiated in high yield at the 2-position using lithium diisopropylamine (LDA) at −90°C.[11] To the best of our knowledge, studies on lithiation of benzonitriles have only involved systems containing lithium atom and cyano group bonded to the same benzene ring. As a result, the cyano group in the lithiated benzonitrile is protected from attack by the organolithium reagent. We decided to check the approach towards preparation of aryllithiums containing the cyano group, which is not involved in the mesomeric stabilization of the negative charge. We tested the reactivity of the selected cyanobenzyloxybenzenes. As the lithiation centre and the cyano group in these compounds are in two separate benzene rings, special care should be taken in order to stabilize the obtained aryllithiums towards decomposition. Our approach would allow for the synthesis of new cyanoarylboronic acids[12] or silanes[13] in which the cyano group and boron or silicon atom are bonded to different benzene rings.

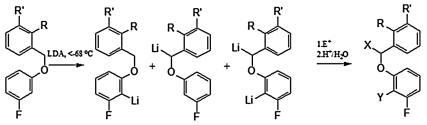
Results and Discussion

Our initial efforts focused on lithiation of **1a** (Scheme 1, entry a). It is known that the position between fluorine and oxygen atoms can be readily deprotonated with LDA owing to their cooperating acidifying effect.[14,15] However, using LDA in THF at −68°C in the presence of Me_3SiCl as the *in situ* electrophile, we obtained a mixture of **1b** (35%), **1c** (53%), **1d** (6%) and unreacted **1a** (6%). Analysis revealed that the benzylic position was deprotonated rather than that between fluorine and oxygen atoms. The reactions occurs with formation of the intermediates **1b-Li** and **1c-Li**. The formation of **1d** shows that **1b-Li** and **1c-Li** undergo a second

* *Correspondence to: Tomasz Kliś, Faculty of Chemistry, Warsaw University of Technology, Noakowskiego 3, 00–664 Warsaw, Poland. E-mail: ktom@ch.pw.edu.pl*

a *Faculty of Chemistry, Warsaw University of Technology, 00-664 Warsaw, Poland*

b *Faculty of Chemistry, Warsaw University, 02-093 Warsaw, Poland*



a) **1a** R = CN, R' = H	**1b-Li**	**1c-Li**	**1d-Li$_2$**	Me_3SiCl in situ	**1b** X=H,Y=-$SiMe_3$ 35% **1c** X =-$SiMe_3$, Y=H 53% **1d** X=Y=-$SiMe_3$, 6%
b) **1a**		**1c-Li**		Me_3SiCl	**1c** X =-$SiMe_3$, Y=H 86%
c) **1a**			**1d-Li$_2$**	2 Me_3SiCl	**1d** X=Y=-$SiMe_3$, 95%
d) **2a** R = Br, R' = H	**2b-Li**			$B(OiPr)_3$	**2b** Y=$B(OH)_2$ 94%
e) **3a** R = H, R' = CN	**3b-Li**	**3c-Li**	**3d-Li$_2$**	Me_3SiCl	**3b** X=H,Y=-$SiMe_3$ 48% **3c** X =-$SiMe_3$, Y=H 40% **3d** X=Y=-$SiMe_3$ 6%

Scheme 1. Influence of the position of the cyano group on the selectivity of lithiation of some cyanobenzyloxy-benzenes

deprotonation to give **1d-Li$_2$**. Interestingly, the sequential lithiation–silylation of **1a** (1 equiv. of LDA and 1 equiv. of Me_3SiCl) afforded exclusively **1c** (Scheme 1, entry b). This can be rationalized by assuming isomerization of the *ortho*-lithiated **1b-Li** to the more stable benzyllithium derivative **1c-Li**. These results showed that the cyano group increases drastically the acidic properties of the benzylic hydrogen atom in **1a**. Replacement of the cyano group with the less electron-withdrawing bromine atom in **2a** resulted in the selective *ortho*-lithiation with formation of **2b-Li** which was trapped *in situ* using $B(OiPr)_3$ with formation of boronic acid **2b** (Scheme 1, entry d).

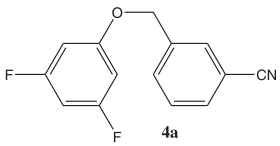
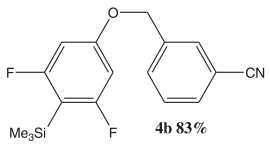
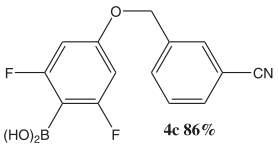
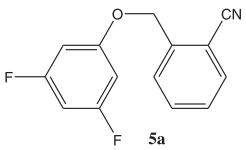
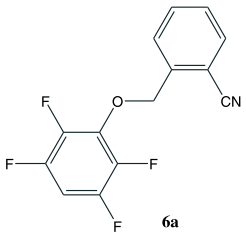
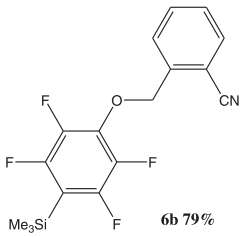
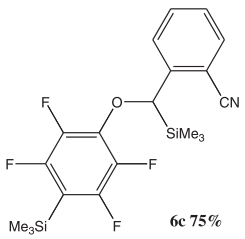
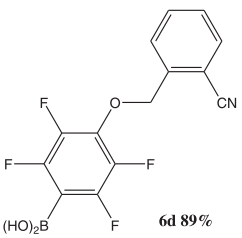
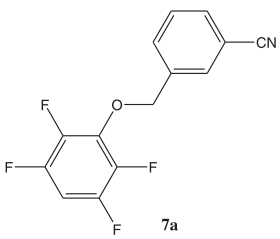
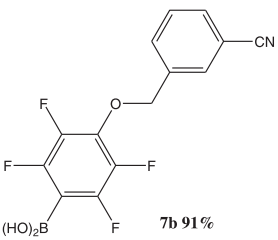
The role of the cyano group here relies not only on the acidification of the benzylic hydrogen by means of the inductive effect, but also on the conjugative stabilization of the formed carbanion.[16,17] It was demonstrated recently that *N,N*-diisopropylamide group favours benzylic deprotonation over aromatic ring deprotonation.[18] The resulting benzylic anion is stabilized conjugatively by withdrawal of electrons from the benzylic group and the lithium atom gains some additional stabilization caused by coordination of the oxygen atom lone pairs to the metal centre. Although the cyano substituent is not capable of forming such a coordinated species, we believe that its electron-withdrawing properties combined with conjugative stabilization ability is sufficient to stabilize the benzylic carbanion. We expected that the change in position of the cyano group from *ortho* in **1a** to *meta* in **3a** will result in an increase of selectivity towards deprotonation in the phenyl ring. Indeed, the reaction proceeds via intermediates **3b-Li**, **3c-Li** and **3d-Li$_2$**, which were next trapped with electrophile to give a mixture of **3b** (48%), **3c** (40%), **3d** (6%) and unreacted **3a** (6%) (Scheme 1, entry e). The formation of a significant amount of **3c** shows that the cyano group enhances the acidity of the benzylic hydrogen even when placed in the *meta* position. We believe that the inductive effect is responsible for reactivity in this case. Interestingly, sequential di-silylation of **1a** using LDA (2 equiv.) and Me_3SiCl (2 equiv.) afforded exclusively **1d** containing one Me_3Si- group in the benzylic position and one between the fluorine and oxygen atoms (Scheme 1, entry c). We believe the reaction occurs with formation of the intermediate **1d-Li$_2$**. On the basis of the obtained results we conclude that lithiation of **1a** occurs at the benzylic position rather than at the phenyl ring. The inability to lithiate **1a** and **3a** selectively in the *ortho* position forced us to move towards the use of **4a** because it contains a very acidic hydrogen atom flanked by two fluorine atoms (Table 1, entry 1). We expected that two fluorine atoms would stabilize the obtained aryllithiums and prevent isomerization. The *in situ* lithiation–silylation of **4a** using LDA (1 equiv.) and Me_3SiCl (1 equiv.) resulted in selective formation of **4b**. We found that this protocol can be successfully applied for selective monosilylation of **6a** to give **6b** (Table 1, entry 4) and disilylation using LDA (2 equiv.) and Me_3SiCl (2 equiv.) with formation of **6c** (Table 1, entry 5). The above results prompted us to synthesize the respective boronic acids from **4a** to **7a**. Thus **4a** was treated with LDA (1 equiv.) at −68°C in the presence of $B(OiPr)_3$ (1 equiv.). However, we recovered the starting material quantitatively. We believe that the reaction did not occur because of the sterical hindrance caused by $B(OiPr)_3$. The quantitative recovery of the starting material in this reaction, however, was a clear sign that the *ortho*-lithiated **4a** is stable at −68°C. Attempted sequential lithiation–boronation of **4a** using LDA (1 equiv.) and $B(OMe)_3$ at −68°C resulted in selective formation of **4c** (Table 1, entry 2). This procedure was next applied to synthesize boronic acids from **5a**, **6a** and **7a**. Whereas boronic acids **6d** and **7b** were obtained almost quantitatively (Table 1, entries 6,7), the attempt to prepare boronic acid from **5a** resulted in a mixture which did not contain any of the desired product. Quite obviously, the *ortho*-lithiated **5a** is not stable on a macroscopic timescale and reacts via benzylic deprotonation. The obtained results suggest that the stability of the *ortho*-lithiated **4a–7a** is the result of the interplay between basicity of the aryllithium, which can be tuned by varying the number and position of fluorine atoms, and the acidity of the benzylic hydrogen, which depends on the position of cyano group.

Crystallization of **6d** from THF gave single crystals suitable for analysis by X-ray diffraction methods. The obtained data revealed that **6d** belongs to the triclinic P-1 space group symmetry with one molecule in the asymmetric part of the unit cell. The -B$(OH)_2$ group adopts *syn-anti* conformation as shown in Fig 1. Contrary to the X-ray structures of benzyloxyarylboronic acids published by our group, the **6d** molecule is essentially planar, except for the -B$(OH)_2$ group, which is distorted out of the plane of the phenyl ring by 26°.[19–21] In the crystal lattice, the adjacent molecules are linked by O-H···O interactions in $R_2^2(8)$ and $R_4^4(8)$ arrangement leading to hydrogen-bonded chain formation, which propagate along the [100] direction (Fig. 2). The geometrical parameters of hydrogen bonds are given in Table 2. Besides the strong O2-H2···O3 interaction, the H2 atom is also involved in intramolecular contact with the F1 fluorine atom. This contact can be regarded as a bifurcated hydrogen bond as the angle sum at the H2 atom is close to 355°.

In the continuation of our studies we tested the reactivity of 4-cyano-3′,5′-difluorobiphenyl **8a** towards deprotonation (Scheme 2).

This compound contains two benzene rings connected directly and we wanted to check whether **8a-Li**, formed after deprotonation between fluorine atoms, would gain some additional stability via polarization effect extended to both the benzene rings and the cyano group. The cyano group in **8a-Li** should be then

Table 1. Preparation of functionalized cyanobenzyloxy-benzenes by deprotonation and subsequent treatment with electrophiles

Entry	Starting material	Conditions	Product
1	 **4a**	LDA, Me_3SiCl *in situ* THF, $<-68°C$	 **4b 83%**
2	**4a**	1. LDA, THF, $<-68°C$ 2. $B(OMe)_3$ 3. HClaq	 **4c 86%**
3	 **5a**	1. LDA, THF, $<-68°C$ 2. $B(OMe)_3$ 3. HClaq	Mixture of products, no desired boronic acid
4	 **6a**	1. LDA, Me_3SiCl, *in situ* THF, $<-68°C$	 **6b 79%**
5	**6a**	2LDA, $2Me_3SiCl$, *in situ* THF, $<-68°C$	 **6c 75%**
6	**6a**	1. LDA, THF, $<-68°C$ 2. $B(OMe)_3$ 3. HClaq	 **6d 89%**
7	 **7a**	1. LDA, THF, $<-68°C$ 2. $B(OMe)_3$ 3. HClaq	 **7b 91%**

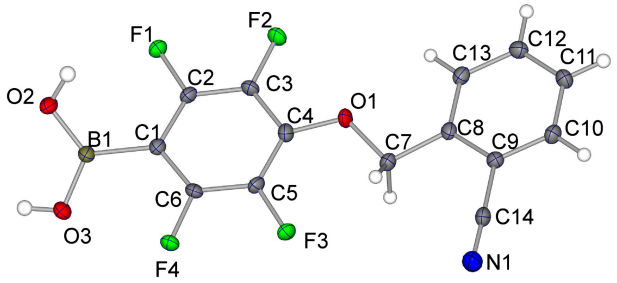


Figure 1. ORTEP drawing of **6d** with displacement ellipsoids plot (50% probability). Selected bond lengths (Å) and angles (°): B1–O3 1.353(2), B1–C1 1.579(3), O2–B1–C1–C2 26.06(3), C4–O1–C7–C8 177.13(2), C4–O1–C7 120.46(2). Crystallographic data for this structure have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication number CCDC 833972

protected towards reaction with LDA. On treatment of **8a** with LDA at −68°C, this compound undergoes clean *ortho*-lithiation between two fluorine atoms to give the respective boronic acid **8b** after boronation using $B(OMe)_3$ as the electrophile (Scheme 2, entry a). Unexpectedly, the similar lithiation–silylation of 4-cyano-3′,5′-dichlorobiphenyl **9a** afforded the respective silane **9c** in very low yield and **9b** was isolated as the main product (Scheme 2, entry c). Formation of **9b** resulted from nucleophilic attack of the LDA molecule on the cyano group. Interestingly, *in situ* silylation of **9a** using LDA and Me_3SiCl afforded exclusively **9c** (Scheme 2, entry d). A possible explanation is that the equilibrium of deprotonation of **9a** is shifted towards LDA, which is consumed via irreversible addition to the cyano group. Interestingly, using 2 equiv. of LDA and Me_3SiCl per 1 equiv. of **8a** or **9a** we obtained **8c** and **9d** respectively (Scheme 2, entries b, e).

Conclusion

Cyanobenzyloxy-benzenes **1a** and **3a–7a** undergo *ortho*-lithiation using LDA; however, benzylic lithiation can compete as the cyano group increases the acidity of the benzylic hydrogen atoms. This is especially important for **1a** and **5a** as the mesomeric and inductive effects caused by the cyano group accelerate deprotonation of the benzylic position. The increase in the number of fluorine atoms in **4a**, **6a** and **7a** stabilizes the *ortho*-lithiated species, preventing isomerization to the corresponding benzyllithiums. Lithiation of halogenated cyanobiphenyls **8a** and **9a** is very sensitive to reaction conditions and proceeds with *ortho*-lithiation between two halogen atoms as well as with addition to the cyano group. The obtained lithiated derivatives react with $B(OMe)_3$ or Me_3SiCl to give the respective arylboronic acids or silanes.

Experimental

^1H and ^{13}C NMR spectra were recorded at room temperature on a Bruker 400 MHz spectrometer. Chemical shifts are given in ppm relative to TMS in ^1H and ^{13}C NMR spectra. All chemicals were received from Aldrich. THF and Et_2O were stored over sodium prior to use. All reactions were carried out under dry argon using standard Schlenk techniques. Melting points were determined in Pyrex capillary tubes with Mel-Temp apparatus.

Typical Procedure for *in situ* Lithiation–Silylation

LDA: THF (20 ml) and diisopropylamine (1.4 ml, 10 mmol) were added to the Schlenk flask and the obtained solution was cooled to ~ −68°C (internal temperature) using an acetone–CO_2 bath. The solution of *n*-BuLi 1.6 M in hexane (6.2 ml, 10 mmol) was next added to the Schlenk flask and the obtained solution was stirred at ~ −68°C for 30 min.

THF (30 ml), 5-(3-cyanobenzyloxy)-1,3-difluorobenzene **4a** (2.5 g, 10 mmol) and Me_3SiCl (1.1 g, 10 mmol) were added to 100 ml three-neck reaction flask equipped with a thermometer and magnetic stirrer. The obtained solution was cooled to ~ −68°C (internal temperature). Freshly prepared LDA (10 mmol) solution was dropped over 10 min via cannula to the cooled solution of reactants. The initially colourless reaction mixture became yellow and next a brownish slurry was formed. The resultant slurry was stirred for 1 h and then the cooling bath was removed and the reaction mixture poured on to water (100 ml). The obtained mixture was acidified with H_2SO_4 (1 M) to attain a slightly acidic pH. Et_2O (50 ml) was next added and the mixture was stirred for 5 min. The organic phase was separated and the aqueous phase was extracted with Et_2O (20 ml). The combined organic solutions were next dried with anhydrous $MgSO_4$ and evaporated to give a solid which was washed and recrystallized from hexane (20 ml) to give **4b** as colourless crystals, m.p. 115–116°C; ^1H NMR (400 MHz, acetone-d_6): δ 7.89 (s, Ar, *H*-C-C-CN, 1H), 7.82 (d, Ar, *H*-C-C_{ipso}, J = 8Hz, 1H), 7.75 (d, Ar, *H*-C-C-CN, J = 8Hz, 1H), 7.64 (t, Ar, C_{ipso}-C-C-*H*, J = 8 Hz, 1H), 6.63 (d, Ar, *H*-C-C-F, J = 9.6 Hz, 2H), 5.26 (s, -CH_2-, 2H), 0.32 (s, CH_3, 9H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 167.71 (d, *C*-F, J = 241 Hz, J = 20 Hz), 161.02 (t, *C*-CF J = 14 Hz),

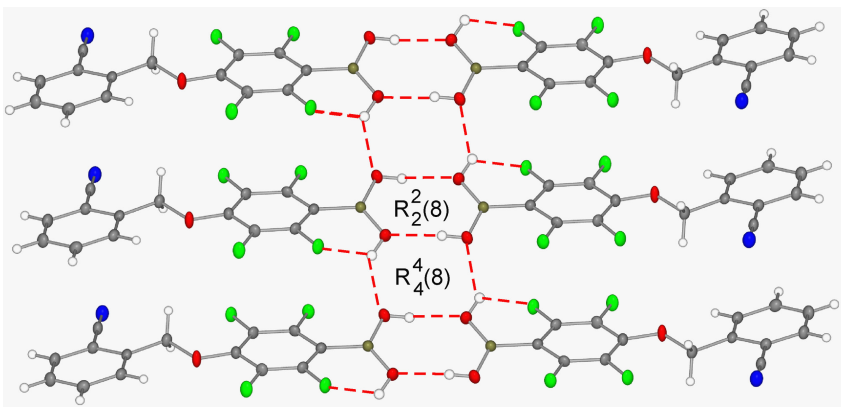


Figure 2. One-dimensional chain arrangement of molecules in the crystal structure of **6d** with intermolecular O-H···O and intramoecular O-H···F hydrogen bonds (red dashed lines)

Table 2. Geometry of hydrogen bond interactions in the structure of **6d**. (*d* and *θ* denote distance and angle, respectively)

Interaction *D*–H···*A*	$d_{D–H}$ (Å)	$d_{H...A}$ (Å)	$d_{D...A}$ (Å)	$\theta_{D–H...A}$ (°)
O2—H2···O3$^{\#1}$	0.84	2.07	2.731 (2)	135 (1)
O3—H3···O2$^{\#2}$	0.84	1.92	2.750 (2)	169 (1)
O2—H2···F1[a]	0.84	2.31	2.823 (2)	120 (1)

[a]Stands for intramolecular contact. Symmetry transformations:
$^{\#1}$ () $x+1, y, z$;
$^{\#2}$ () $-x+2, -y+3, -z$.

137.60, 131.81, 131.38, 130.59, 129.50, 118.46 (*C*N), 112.87, 98.37 (dd, *C*-CF, $J=32$ Hz, $J=2$ Hz), 68.89 (C_{benz}), 0.18 (t, 3CH_3, $J=3$Hz). Anal. Calcd for $C_{17}H_{17}F_2NOSi$: C, 64.33, H, 5.40, N, 4.41. Found: C, 64.00, H, 5.55, N, 4.53.

Compound ***1c***

M.p. 66–67°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.48 (m, Ar, C_{ipso}-C-*H*, $J=8$ Hz, 1H), 7.35 (m, Ar, *H*-C-C-CN, $J=8.0$ Hz, 1H), 7.21 (m, Ar, *H*-C-C_{ipso}, $J=8$ Hz, 1H), 7.11 (m, Ar, *H*-C-C-CN, $J=8.0$ Hz, 1H), 6.95 (m, Ar, *H*-C-C-F $J=8.0$ Hz, 1H), 6.44 (m, Ar, 3H), 5.21 (s, -CH_{benz}-, 1H), 0.19 (s, CH_3, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): 163.48 (d, *C*-F, $J=244$ Hz), 160.38 (d, *C*-CF, $J=11$ Hz), 144.94, 132.96 (d, $J=20$ Hz), 130.17 (d, $J=10$ Hz), 126.54, 126.16, 117.74 (*C*N), 110.70 (d, $J=2$ Hz), 108.81, 107.91, 103.41, 103.16, 73.69 (C_{benz}), −3.93 (3CH_3). Anal. Calcd for $C_{17}H_{18}FNOSi$: C, 68.19, H, 6.06, N, 4.68 Found: C, 68.46, H, 6.43, N, 4.64.

Compound ***1d***

M.p. 81–83°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.65 (dd, Ar, C_{ipso}-C-*H*, $J=8$ Hz, $J=1.6$ Hz, 1H), 7.50 (td, Ar, C_{ipso}-C-C-*H*, $J=8.0$ Hz, $J=0.8$ Hz, 1H), 7.37 (dd, Ar, *H*-C-CN, $J=7.6$ Hz, $J=0.8$ Hz, 1H), 7.26 (td, Ar, C_{ipso}-C-C-C-*H*, $J=8.0$ Hz, $J=1.6$ Hz, 1H), 7.10 (q, Ar, *H*-C-C-C-F, $J=8.0$ Hz, 1H), 6.53 (t, Ar, *H*-C-C-O, $J=7.6$ Hz, 1H), 6.44 (d, *H*-C-C-F, Ar, $J=7.6$ Hz, 1H), 5.46 (s, -CH_{benz}-, 1H), 0.46 (d, CH_{3Ar}, $J=2.4$ Hz, 9H), 0.19 (s, CH_3, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): 167.65 (d, *C*-F, $J=241$ Hz), 164.31 (d, *C*-CF, $J=14$ Hz), 145.05, 133.21, 132.78, 131.57 (d, *C*-CF, $J=10.7$ Hz), 126.60, 126.32, 117.81 (*C*N), 109.32, 108.33, 108.05, 106.95 (d, *C*-CCF, $J=3$ Hz), 73.65 (C_{benz}), 1.21 (d, $J=3.8$ Hz, 3CH_{3Ar}), −3.78 (3CH_3). Anal. Calcd for $C_{20}H_{26}FNOSi_2$: C, 64.64, H, 7.05, N, 3.77 Found: C, 63.45, H, 6.63, N, 3.67.

Compound ***2b***

M.p. 131–133°C; ^{1}H NMR (200 MHz, acetone-d_6): δ 7.67 (td, Ar, $J=8$ Hz, $J=1.2$ Hz, 2H), 7.37 (m, Ar, 4H), 6.85 (d, Ar, *H*-C-C-C-F, $J=8$ Hz, 1H), 6.70 (td, *H*-C-C-O, Ar, $J=8$ Hz, $J=0.4$ Hz, 1H), 5.18 (s, -CH_2- 2H). ^{13}C{^{1}H} NMR (100.6 MHz, acetone-d_6): 166.46 (d, *C*-F, $J=241$ Hz), 163.00 (d, *C*-CF, $J=14$ Hz), 137.00, 133.36, 132.24 (d, *C*-CF, $J=10.6$ Hz), 130.45, 130.07, 128.62, 122.68, 109.00, 108.75, 108.19 (d, *C*-CCF, $J=3$Hz), 70.44 (C_{benz}). Anal. Calcd for $C_{13}H_{11}BBrFO_3$: C, 48.05, H, 3.41. Found: C, 46.91, H, 3.84.

Compound ***4c***

M.p. 162–163°C; ^{1}H NMR (400 MHz, acetone-d_6): δ 7.89 (s, *H*-C-C-CN, Ar, 1H), 7.82 (d, Ar, *H*-C-C_{ipso}, $J=8.0$ Hz, 1H), 7.76 (d, Ar, *H*-C-C-CN, $J=8.0$ Hz, 1H), 7.64 (t, Ar, C_{ipso}-C-C-*H*, $J=8.0$ Hz, 1H), 6.63 (d, Ar, *H*-C-C-F, $J=9.2$ Hz, 2H) 5.25 (s, -CH_2-, 2H); ^{13}C{^{1}H} NMR (100.6 MHz, acetone-d_6): 167.10 (m, *C*-F, $J=240$ Hz), 162.14 (t, *C*-CF, $J=14.6$ Hz), 139.25, 132.84, 132.51, 131.71, 130.57, 119.08 (*C*N), 113.32, 99.16 (d, *C*-CF, $J=32.6$ Hz), 69.74 (C_{benz}). Anal. Calcd for $C_{14}H_{10}BF_2NO_3$: C, 58.17, H, 3.49, N, 4.85 Found: C, 58.84, H, 3.84, N, 4.25.

Compound ***6b***

M.p. 41–43°C; ^{1}H-NMR (400 MHz, $CDCl_3$): δ 7.71 (m, Ar, 2H), 7.66 (td, Ar, C_{ipso}-C-C-C-*H*, $J=7.6$ Hz, $J=1.6$ Hz, 1H), 7.48 (td, Ar, C_{ipso}-C-C-*H*, $J=7.6$ Hz, $J=1.6$ Hz, 1H), 5.44 (s, -CH_2-, 2H), 0.38 (t, CH_3, $J=1.6$ Hz, 9H); ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): 149.11 (m, *C*-F, $J=240$ Hz), 140.54 (m, *C*-F, $J=242$ Hz), 139.20, 133.11, 132.92, 129.08, 129.02, 116.66 (*C*N), 111.62, 110.19 (t, *C*-CF, $J=22.0$ Hz), 110.43 (t, $J=22.8$ Hz), 73.92 (t, $J=3.8$ Hz, C_{benz}), −0.06 (3CH_3). Anal. Calcd for $C_{17}H_{15}F_4NOSi$: C, 57.78, H, 4.28, N, 3.96 Found: C, 58.08, H, 4.94, N, 4.06.

Compound ***6c***

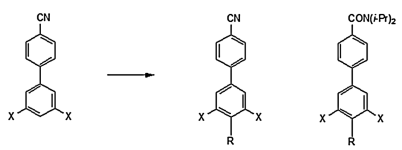
M.p. 70–72°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.61 (m, Ar, 3H), 7.30 (m, Ar, C_{ipso}-C-C-*H*, 1H), 5.69 (s, CH_{benz}, 1H), 0.33 (t, CH_{3Ar}, $J=1.2$ Hz, 9H), 0.18 (s, CH_3, 9H). ^{13}C{^{1}H} NMR (100.6 MHz, $CDCl_3$): 149.11 (m, *C*-F, $J=240$ Hz), 143.97, 140.34 (m, *C*-F, $J=242$ Hz), 132.80, 132.58, 126.94, 126.40, 117.43 (*C*N), 109.22, 80.97 (C_{benz}), −0.03 ($3CH_{3Ar}$), −4.13 (3CH_3). Anal. Calcd for $C_{20}H_{23}F_4NOSi_2$: C, 56.45, H, 5.45, N, 3.29. Found: C, 56.25, H, 5.59, N, 3.38.

Compound ***6d***

M.p. 145–146°C; ^{1}H-NMR (400 MHz, acetone-d_6): δ 8.06 (s, -OH, 2H), 7.86 (d, Ar, C_{ipso}-C-C-C-*H*, $J=7.6$ Hz, 1H), 7.77 (d, Ar, $J=7.6$ Hz, 2H), 7.63 (m, Ar, C_{ipso}-C-C-*H*, 1H), 5.52 (s, -CH_2- 2H); ^{13}C{^{1}H} NMR (100.6 MHz, acetone-d_6): 148.51 (m, *C*-F, $J=242$ Hz), 141.61 (m, *C*-F, $J=249$ Hz), 139.82, 134.13, 133.97, 131.01, 130.59, 117.40 (*C*N), 113.33, 74.66 (C_{benz}). Anal. Calcd for $C_{14}H_8BF_4NO_3$: C, 51.73, H, 2.48, N, 4.31 Found: C, 51.31, H, 2.94, N, 4.82.

Compound ***7b***

M.p. 76–79°C; ^{1}H NMR (400 MHz, acetone-d_6): δ 7.91 (s, Ar, *H*-C-C-CN, 1H), 7.85 (d, Ar, *H*-C-C_{ipso}, $J=8.0$ Hz, 1H), 7.79 (d, Ar, *H*-C-C-CN, $J=8.0$ Hz, 1H), 7.65 (t, Ar, C_{ipso}-C-C-*H*, $J=8.0$ Hz, 1H), 5.42 (s, -CH_2-, 2H); ^{13}C{^{1}H} NMR (100.6 MHz, acetone-d_6): 148.57 (m, *C*-F, $J=246$



a) 8a X = F LDA, $B(OMe)_3$, -68°C 8b R = -$B(OH)_2$, 95%
b) 8a 2LDA, 2 Me_3SiCl, -68°C 8c R = -$SiMe_3$ 95%
c) 9a X = Cl LDA, Me_3SiCl , -68°C 9c R = -$SiMe_3$, 5% 9b R = H 82%
d) 9a LDA, Me_3SiCl, -68°C, in situ 9c R = -$SiMe_3$, 88%
e) 9a 2LDA, 2 Me_3SiCl, -68°C 9d R = -$SiMe_3$ 90%

Scheme 2. Preparation of functionalized cyanobiphenyls by deprotonation and reaction with electrophiles

Hz), 141.57 (m, *C*-F, $J = 245$ Hz), 138.82, 138.24, 133.54, 133.09, 132.43, 130.64, 118.98 (*C*N), 113.35, 75.75 (C_{benz}). Anal. Calcd for $C_{14}H_8BF_4NO_3$: C, 51.73, H, 2.48, N, 4.31 Found: C, 51.32, H, 2.95, N, 4.43.

Compound ***8b***

M.p. 161°C (dec.); ^{1}H NMR (400 MHz, acetone-d_6): δ 7.90 (m, Ar_{CN}, $J = 8.4$ Hz, 4H), 7.32 (m, Ar, $J = 8.8$ Hz, 2H); $^{13}C\{^1H\}$ NMR (100.6 MHz, acetone-d_6): 166.33 (m, *C*-F, $J = 242$ Hz), 143.55 (d, *C*-CF, $J = 5$ Hz), 133.73, 133.65, 128.98, 128.68, 119.07 (*C*N), 112.83, 110.37 (m, $J = 30$ Hz). Anal. Calcd for $C_{13}H_8BF_2NO_2$: C, 60.28, H, 3.11, N, 5.41 Found: C, 60.51, H, 3.94, N, 5.72.

Compound ***8c***

M.p. 77–78°C; ^{1}H NMR (200 MHz, acetone-d_6): δ 7.75 (d, Ar, *H*-C-C-CO, $J = 8$ Hz, 2H), 7.36 (d, Ar, *H*-C-C_{ipso}, $J = 8$ Hz, 2H), 7.27 (d, Ar, *H*-C-C-F, $J_{C\text{-}F} = 8$ Hz, 2H), 3.62 (hp, N-C-*H*, $J = 7$ Hz, 2H), 1.34 (d, CH_{3iPr}, $J = 7$ Hz, 12H), 0.39 (s, $SiCH_3$, 9H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 167.35 (dd, *C*-F, $J = 243$ Hz, $J = 17$ Hz), 166.80 (*C*O), 144.43 (t, C_{ipso}-C_{ipso}, $J = 11$ Hz), 139.85, 138.97, 127.28, 127.07, 126.71, 109.40 (d, $J = 30$ Hz), 48.79 ($2CH_{iPr}$), 20.72 ($4CH_{3iPr}$), 0.22 ($3CH_3$-Si). Anal. Calcd for $C_{22}H_{29}Cl_2NOSi$: C, 67.83, H, 7.50, N, 3.60 Found: C, 67.91, H, 7.62, N, 3.62.

Compound ***9b***

M.p. 124–125°C; ^{1}H NMR (400 MHz, $CDCl_3$): δ 7.52 (d, Ar, *H*-C-C-CO, $J = 8$ Hz, 2H), 7.45 (d, Ar, *H*-C-C_{ipso}, $J = 1.6$ Hz, 2H), 7.34 (d, Ar, *H*-C-C_{ipso}, $J = 8$ Hz, 2H), 7.24 (t, Ar, *H*-C-C-Cl, $J = 1.6$ Hz, 1H), 3.63 (hp, N-C-*H*, $J = 6.8$ Hz, 2H), 1.32 (d, $CH_{3\ iPr}$, $J = 6.8$ Hz, 12H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 167.27 (*C*O), 143.37, 141.20, 138.27, 135.34, 127.39, 127.21, 126.60, 125.56, 48.41 ($2CH_{iPr}$), 20.81 ($4CH_{3iPr}$). Anal. Calcd for $C_{19}H_{21}Cl_2NO$: C, 65.15, H, 6.04, N, 4.00 Found: C, 65.31, H, 5.94, N, 4.06.

Compound ***9c***

M.p. 106–107°C; ^{1}H NMR (400 MHz, dmso-d_6): δ 7.92 (m, Ar, 4H), 7.74 (s, Ar, *H*-C-C-Cl, 2H), 0.48 (s, CH_3, 9H); $^{13}C\{^1H\}$ NMR (100.6 MHz, $CDCl_3$): 142.44, 142.39, 141.59, 136.89, 132.78, 127.53, 127.01, 118.46 (*C*N), 112.14, 2.73 ($3CH_3$). Anal. Calcd for $C_{16}H_{15}Cl_2NSi$: C, 60.00, H, 4.72, N, 4.37 Found: C, 60.31, H, 4.94, N, 4.48.

Compound ***9d***

M.p. 152–153°C; ^{1}H NMR (400 MHz, acetone-d_6): δ 7.73 (d, Ar, *H*-C-C-CO, $J = 8$ Hz, 2H), 7.64 (s, Ar, *H*-C-C-Cl, 2H), 7.35 (d, Ar, *H*-C-C_{ipso}, $J = 8$ Hz, 2H), 3.60 (hp, *i*Pr, $J = 7$ Hz, 2H), 1.33 (d, *i*Pr, $J = 7$ Hz, 12H), 0.53 (s, CH_3, 9H); $^{13}C\{^1H\}$ NMR (100.6 MHz, acetone-d_6): 167.29 (*C*O), 144.30, 142.86, 142.82, 137.79, 135.58, 127.96, 127.69, 127.34, 48.93 ($2CH_{iPr}$), 20.94 ($4CH_{3iPr}$), 2.94 ($3CH_3$-Si). Anal. Calcd for $C_{22}H_{29}Cl_2NOSi$: C, 62.55, H, 6.92, N, 3.32 Found: C, 62.71, H, 6.94, N, 3.38.

Crystal Data for 6d

Single-crystal data were collected on a Bruker AXS Kappa APEX II Ultra diffractometer with TXS rotating anode (Mo KR radiation, $\lambda = 0.71073$ Å) and multilayer optics and equipped with an Oxford Cryosystems nitrogen gas flow attachment. The data collection strategy was optimized and monitored using the appropriate algorithms applied in the APEX2 program package.[22] Data reduction and analysis were carried out with the APEX2 suite of programs (integration was done with SAINT).[23] The data were corrected for Lorentz and polarization effects. The multiscan absorption correction, scaling, and merging of reflection data were done with SORTAV.[24] All structures were solved by direct methods using SHELXS-97 and refined using SHELXL-97.[25] The refinement was based on F^2 for all reflections except those with very negative F^2. Weighted *R* factors (*wR*) and all goodness-of-fit (GooF) values are based on F^2. All non-hydrogen atoms were refined anisotropically. All hydrogen atoms were placed in calculated positions with C-H distance of 0.95 Å (phenyl), 0.99 Å (methylene) and O-H distance of 0.84 Å. They were visible in difference maps and they were included in the refinement in riding-motion approximation with U_{iso}(phenyl H) = 1.2U_{eq}(C), U_{iso}(methylene H) = 1.5U_{eq}(C) and U_{iso}(OH H) =1.5U_{eq}(O). The components of the anisotropic displacement parameters in the direction of the bond of C9 and C14 were restrained to be equal within an effective standard deviation. $C_{14}H_8BF_4NO_3$; MW = 325.02 a.u.; $T = 100(2)$ K; triclinic space group P-1; $a = 4.976(1)$ Å, $b = 5.938(1)$ Å, $c = 21.801(1)$ Å, $\alpha = 95.55(1)°$, $\beta = 92.23(1)°$, $\gamma = 95.31(1)°$, $V = 637.6(1)$ Å^3; $Z = 2$; $d_{calc} = 1.693$ g cm^{-3}; $\mu = 0.155$ mm^{-1}; Of 15 387 reflections collected, 4770 were unique ($R_{int} = 0.0325$). Refinement on F^2 concluded with the values $R1 = 0.0902$ and $wR2 = 0.1365$ for 208 parameters (58 restraints) and 3986 data with $I > 2\sigma(I)$.

Acknowledgements

This work was supported by the Warsaw University of Technology. The X-ray measurements of compound **6d** were undertaken at the Crystallographic Unit of the Physical Chemistry Laboratory, Chemistry Department, University of Warsaw. Support from Aldrich Chemical Company, Milwaukee, WI, USA, through the donation of chemicals and equipment is gratefully acknowledged.

References

[1] a) G. Köbrich, P. Buck, *Chem. Ber.* **1970**, *103*, 1412; b) G. Köbrich, P. Buck, *Chem. Ber.* **1970**, *103*, 1420.
[2] W. C. Black, B. Guay, F. Scheuermayer, *J. Org. Chem.* **1997**, *62*, 758.
[3] H. Gilman, D. S. Melstrom, *J. Am. Chem. Soc.* **1948**, *70*, 4177.
[4] W. E. Parham, L. D. Jones, *J. Org. Chem.* **1976**, *41*, 1187.
[5] K. Menzel, E. L. Fisher, L. DiMichelle, D. E. Frantz, T. D. Nelson, M. H. Kress, *J. Org. Chem.* **2006**, *71*, 2188.
[6] a) J. Clayden, N. Greeves, S. Warren, P. Wothers, *Organic Chemistry*, Oxford University Press, Oxford, **2001**, p. 301; b) J. Clayden, *Organolithiums: Selectivity for Synthesis*, Pergamon, Oxford, **2002**, p. 286.
[7] C. G. Swain, *J. Am. Chem. Soc.* **1947**, *69*, 2306.
[8] S. Luliński, K. Zając, *J. Org. Chem.* **2008**, *73*, 7785.
[9] M. Schlosser, E. Castagnetti, *Chem. Eur. J.* **2002**, *8*, 799.
[10] R. R. Fraser, S. Savard, *Can. J. Chem.* **1986**, *64*, 621.
[11] T. D. Krizan, J. C. Martin, *J. Org. Chem.* **1982**, *47*, 2681.
[12] M. Lysen, P. Vedsø, M. Begtrup, J. L. Kristensen, *J. Org. Chem.* **2006**, *71*, 2518.
[13] V. Diemer, J. S. Garcia, F. R. Leroux, F. Colobert, *J. Fluorine Chem.* **2012**, *134*, 146.
[14] W. Bauer, P. V. R. Schleyer, *J. Am. Chem. Soc.* **1989**, *111*, 7191.
[15] A. I. Meyers, P. D. Pansegran, *Tetrahedron Lett.* **1983**, *24*, 4935.
[16] Y. Ito, K. Kobayashi, T. Saegusa, *J. Am. Chem. Soc.* **1977**, *99*, 3532.
[17] Y. Ito, K. Kobayashi, N. Seko, T. Saegusa, *Bull. Chem. Soc. Jpn.* **1984**, *57*, 73.
[18] A. E. H. Wheatley, J. Clayden, I. H. Hillier, A. C. Smith, M. A. Vincent, L. J. Taylor, J. Haywood, *Beilstein J. Org. Chem.* **2012**, *8*, 50.
[19] T. Klis, J. Serwatowski, *Acta Cryst.* **2009**, *E65*, 2348.
[20] K. Kacprzak, T. Klis, J. Serwatowski, *Acta Cryst.* **2006**, *E62*, 1308.
[21] K. Kacprzak, T. Klis, J. Serwatowski, *Acta Cryst.* **2009**, *E65*, 2250.
[22] APEX2, 2010.3-0; Bruker AXS, Madison, WI, **2010**.
[23] SAINT, 7.68A, Bruker AXS, Madison, WI, **2010**.
[24] a) R. H. Blessing, *J. Appl. Cryst.* **1989**, *22*, 396; b) R. H. Blessing, *Acta Cryst.* **1995**, *A51*, 33.
[25] G. M. Sheldrick, *Acta Cryst.* **2008**, *A64*, 112.