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Toolbox for Regioselective Lithiations of Furo[2,3-*c*]pyridine

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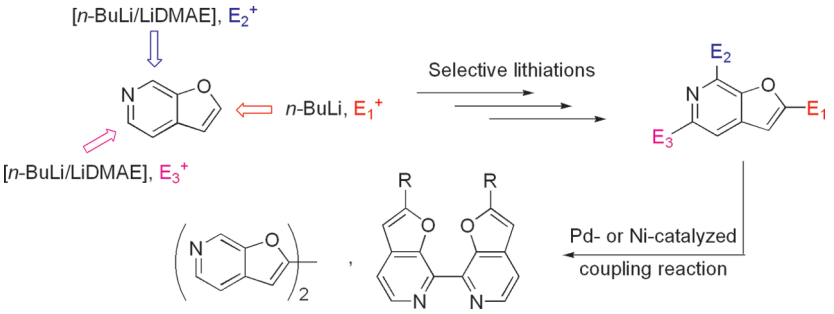

A detailed procedure for successive regioselective lithiations of furo[2,3-*c*]pyridine is described by using *n*-BuLi and the [*n*-BuLi/LiDMAE] superbase. Several polysubstituted furo[2,3-*c*]pyridines have been efficiently synthesized and some of them were engaged in Pd- or Ni-catalyzed coupling reactions leading to 2,2′- or 7,7′-bifuro[2,3-*c*]pyridine ligands.

Introduction

Over the past few decades, many efforts have been made to develop metalation reactions for the functionalization of heterocycles.[1−7] Such reactions are proving to be powerful tools because of the large range of functionalities that can be introduced. In recent years, new reagents have been developed and toolboxes have been designed to modify regioselectivities and/or to tolerate sensitive functional groups during lithiation of substituted azaheterocycles (e.g., pyridines, quinolines, etc.).[8−15] Since these organometallic methods are becoming more efficient, elaborate heterocycles can be studied. Due to their potential biological applications, fused heterocycles containing several complexing heteroatoms appear to be the next interesting targets.

In our ongoing research in heterocyclic chemistry,[16−19] furopyridines have attracted our attention because of their isosterism with (aza)indole, chromane, or dioxinopyridine derivatives which are important moieties largely represented

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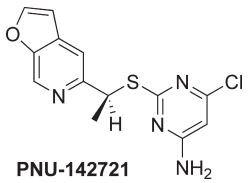
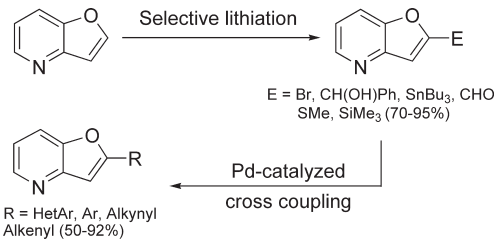


FIGURE 1. PNU-142721: an efficient HIV-1 non-nucleoside reverse transcriptase inhibitor.

SCHEME 1. Selective Functionalization of Furo[3,2-*b*]pyridine



in many bioactive molecules.[20−28] An outstanding example is the furo[2,3-*c*]pyridine contained in PNU-142721, a derivative reported by Morris and co-workers as an efficient HIV-1 non-nucleoside reverse transcriptase inhibitor (Figure 1).[29,30]

In the literature, substituted furopyridines are usually synthesized by furan ring formation involving Pd-catalyzed reactions.[31−36] Functionalities are then inserted during the cyclization process that limits the nature of introduced groups. Despite the fact that metalation of furopyridines presents great potential because of its 5 possible reactive sites, only few papers report hydrogen−metal exchange reactions with these substrates. The presence of two heteroatoms is an additional interesting parameter for the complexation of lithiated species and thus for the regioselectivity of the metalation process. To our knowledge, only Shiotani and co-workers have studied the effect of several alkyllithiums on furopyridines.[37−40] Even if most of them were substituted derivatives, the formation of the simple 2-lithiofuropyridine intermediate was described, followed by electrophile quenching with dimethylformamide (DMF) and diphenyl disulfide (Ph_2S_2). We recently improved and extended this lithiation sequence for the synthesis of various 2-substituted furo[3,2-*b*]pyridines (Scheme 1).[17]

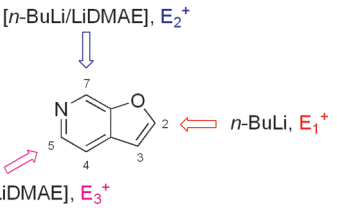
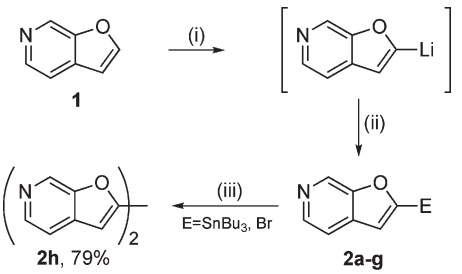


FIGURE 2. Successive regioselective metalation procedure.

SCHEME 2. Preparation of 2-Substituted Furo[2,3-*c*]pyridines 2a−h[a,b]



2a E=$SiMe_3$	77%	**2e** E=SMe	78%
2b E=D	76%[c]	**2f** E=Br	75%[d]
2c E=Cl	71%[d]	**2g** E=$SnBu_3$	80%[e]
2d E=CH(OH)Ph	81%	**2h**	79%

[a]Reagents and conditions: (i) *n*-BuLi (1.5 equiv), −78 °C, 1 h, THF. (ii) E^+ = Me_3SiCl, DCl/D_2O, C_2Cl_6, PhCHO, Me_2S_2, CBr_4 or Bu_3SnCl (2 equiv), −95 or −78 °C, 15 min or 1 h, THF then H_2O. (iii) **2f** (1 equiv), **2g** (1.1 equiv), $PdCl_2(PPh_3)_2$ (5 mol %), DMF, 110 °C, 5 h. [b]Isolated yields after centrifugal thin-layer chromatography purification. [c]DCl/D_2O (DCl 35 wt % in D_2O, 20 equiv) was used as electrophile, **2b** was 95% deuterated. [d]Trapping step was performed at −95 °C. [e]Trapping step was performed for 15 min at −95 °C.

Among the six isomeric series of the furopyridine framework ([*b*]-, [*c*]-, or [*f*]-fused heterocycles) we will presently turn our attention to furo[2,3-*c*]pyridine **1**, with the aim to regioselectively functionalize several positions of this scaffold, specifically via selective metalation on the α-position of heteroatoms by using *n*-butyllithium (*n*-BuLi) or the [*n*-BuLi/LiDMAE] superbase (Figure 2).

Results and Discussion

In a preliminary study, the lithiation of furo[2,3-*c*]pyridine **1** by *n*-BuLi was examined. Taking advantage of the methodology described for furo[3,2-*b*]pyridine,[17] **1** was prepared starting from 3-hydroxypyridine in a 4-step procedure including Sonogashira cross-coupling as the key step (see the Supporting Information). Lithiation of **1** was next carried out by using 2 equiv of *n*-BuLi at −78 °C for 1 h in

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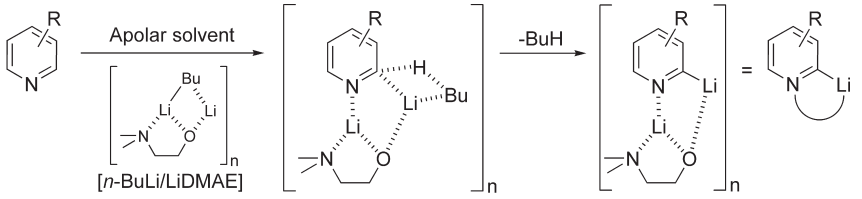
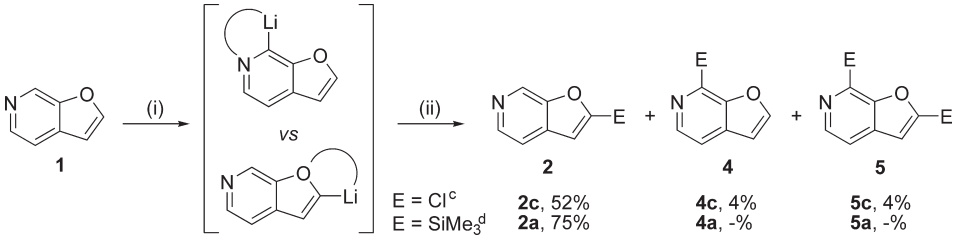
SCHEME 3. Specific Aggregation of the [*n*-BuLi/LiDMAE] Superbase on Pyridine Nitrogen



R=Cl, SMe, OMe...

Note : This is a representation of one of the possible aggregate between [*n*-BuLi/LiDMAE] and pyridine substrate.

SCHEME 4. Competitive Lithiation on the C-2 and C-7 Positions with the [*n*-BuLi/LiDMAE] Superbase[a,b]



[a]Reagents and conditions: (i) [*n*-BuLi/LiDMAE] (3 equiv), −78 °C, 1 h, toluene. (ii) $E^+ = C_2Cl_6$ or Me_3SiCl (3 equiv), −78 °C, 1 h, THF then H_2O. [b]Isolated yields after centrifugal thin-layer chromatography purification. [c]10% of **1** was recovered. [d]**4a** and **5a** are unstable and lead to degradation compounds.

tetrahydrofurane (THF) allowing deprotonation on the C-2 position. Upon treatment with chlorotrimethylsilane (Me_3SiCl) as electrophile, compound **2a** was obtained in a good yield (70%). Under these conditions, nucleophilic addition of *n*-BuLi on the C-7 position was also detected and 7-butyl-2-trimethylsilylfuro[2,3-*c*]pyridine **3** was isolated as a byproduct (12%). To limit this side reaction, we decided to reduce the amount of base to 1.5 equiv of *n*-BuLi. Despite a small decrease of conversion rate (90% instead of >95%), **2a** was obtained in a better yield (77%) without nucleophilic addition of *n*-BuLi. For synthesis purposes this sequence was extended by using various representative electrophiles allowing subsequent functionalization (Scheme 2). Derivatives **2a**−**g** were formed in 71−81% yields. It is to be noted that derivatives **2c**, **2f**, and **2g** were more efficiently obtained when the trapping step was performed at −95 °C, while **2a**, **2b**, **2d**, and **2e** were prepared at −78 °C. The potential usefulness of synthesized compounds was exemplified by the efficient preparation of **2h** from **2g** and **2f** in a 79% yield under usual Stille conditions.

To create a toolbox for the functionalization of furo[2,3-*c*]pyridine **1**, we next turned our attention to other possible sites of lithiation, and especially to the C-5 and C-7 positions (α to the pyridine nitrogen atom). For several years, our group has had a great interest in the development of the [*n*-BuLi/LiDMAE] superbase.[8−11,18,19] Combining *n*-BuLi and lithium dimethylaminoethoxide (LiDMAE), this monometallic non-nucleophile superbase exhibits specific aggregation on the pyridine nitrogen atom[41] to reach regioselective and unprecedented lithiation on the α-position of pyridine nitrogen, even if an ortho-directing group (Cl, SMe, OMe, etc.)[18,19,42] is present (Scheme 3).

We then carried out deprotonation of furo[2,3-*c*]pyridine **1** using [*n*-BuLi/LiDMAE] superbase at −78 °C for 1 h in toluene and after chlorination with hexachloroethane (C_2Cl_6) as the electrophile, a mixture of three products was detected. Deprotonation on the C-2 position was favored since 2-chlorofuro[2,3-*c*]pyridine **2c** was isolated as the major product with 52% yield. Nevertheless, deprotonation on the C-7 position was also observed and derivatives **4c** and **5c** were obtained with low yields (4% each) underlining a lithium chelating competition between the oxygen and the nitrogen atoms to the advantage of the oxygen atom (Scheme 4). Such an effect was previously observed by our group during the metalation of azaphtalan derivatives with the [*n*-BuLi/LiDMAE] superbase.[43] We noticed that **2c** was quite unstable and partially led to degradation compounds at −78 °C. However, if trapping temperature was decreased to −95 °C as described in Scheme 2, **2c** was more efficiently obtained, and only traces of **4c** and **5c** were detected.

DFT calculation of Mulliken charges was performed to estimate relative acidities of the various hydrogen atoms of furo[2,3-*c*]pyridine **1** and then to understand regioselectivity of the deprotonation. The result showed that the hydrogen atom in the C-2 position is actually more acidic than the hydrogen atom in the C-7 position (see the Supporting Information for more details about DFT calculation).

On the basis of our experience of [*n*-BuLi/LiDMAE] induced metalation on the α-position of pyridine nitrogen, we then decided to conduct complementary experiments on two deuterated furo[2,3-*c*]pyridines **2b** and **4b** to study the isotopic effect (see Scheme 6 for the preparation of **4b**). Metalation

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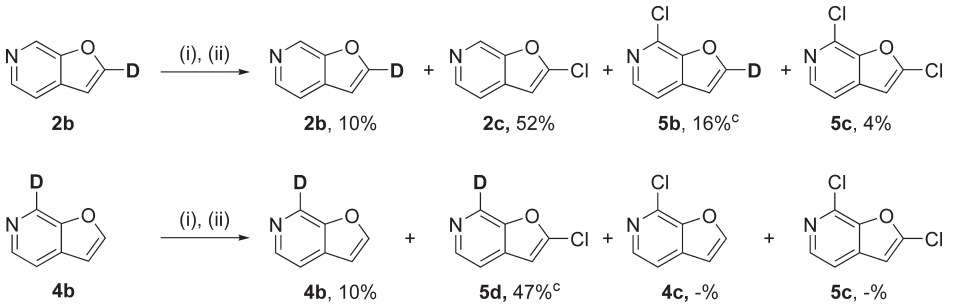
SCHEME 5. Study of Chelating Competition between Oxygen and Nitrogen Atoms[a,b]



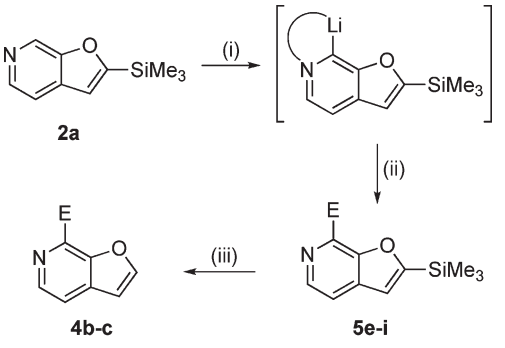
[a]Reagents and conditions: (i) [*n*-BuLi/LiDMAE] (3 equiv), −78 °C, 1 h, toluene. (ii) C_2Cl_6 (3 equiv), −78 °C, 1 h, THF then H_2O. [b]Isolated yield after centrifugal thin-layer chromatography purification. [c]**5b** and **5d** were 98% deuterated.

was carried out with [*n*-BuLi/LiDMAE] under the same conditions as precedently described for lithiation of furo[2,3-*c*]pyridine **1**. When **2b** reacted, metalation was slowed down in the C-2 position because of the isotopic effect, and then 7-chloro-2-deuteriofuro[2,3-*c*]pyridine **5b** resulting from lithiation on the C-7 position was isolated in a 16% yield. However, **2c** was again obtained as the major product in a 52% yield evidencing that aggregation is still preferred on the oxygen atom nearest the most acidic hydrogen atom despite the isotopic effect on the C-2 position, which is unusual for the [*n*-BuLi/LiDMAE] superbase. On the other hand, metalation of **4b** furnished exclusive lithiation on the C-2 position, because of the isotopic effect on the C-7 position, and then 98% deuterated **5d** was obtained while **4c** or **5c** was not detected. This showed that C-7Li/C-2Li exchange was mostly improbable; otherwise formation of **2c**, **4c**, or **5c** would have been observed (Scheme 5).

To achieve lithiation on the C-7 position, an easily removable protective group on the C-2 position was used.[44] A trimethylsilyl group is an excellent unit to perform lithiation on the C-7 position. Classically used in Hiyama couplings,[45] the trimethylsilyl moiety tolerates non-nucleophile lithiated agents and can be removed by a fluoride treatment. In Table 1 we report the most significant results for lithiation of **2a**.

When *n*-BuLi was used as the base followed by chlorination with C_2Cl_6, an intractable mixture of products was detected. We then decided to use H_2O as the electrophile to simplify this mixture and to elucidate the reaction's behavior. As a consequence, after the metalation step and hydrolysis of the reaction medium, two products resulting from *n*-BuLi nucleophilic addition and desilylation were detected. Only traces of the starting material were recovered, corroborating that no lithiation occurred on the C-7 position (entry 1). In contrast, the [*n*-BuLi/LiDMAE] superbase in hexane allowed clean lithiation on the C-7 position, without addition of a butyl moiety or deprotection of the trimethylsilyl group. This result once more confirmed the non-nucleophile character of the [*n*-BuLi/LiDMAE] superbase. To perform complete conversion of the substrate, a metalation at −45 °C and 3 equiv of base were necessary (entry 4) since a decrease in the amount of base or in metalation temperature led to 70% conversion (entries 2 and 3). Despite the ability of the [*n*-BuLi/LiDMAE] superbase to allow metalation on the C-5 position, no trace of **6** was observed. This high regioselectivity in the C-7 position versus the C-5 position might be explained by the activation effect and the stabilization of lithiated species near the oxygen atom.

SCHEME 6. Preparation of 2,7-Disubstituted and 7-Substituted Furo[2,3-*c*]pyridines 5e−i and 4b−c[a,b]



4b E=D	89%	**5a** E=SiMe$_3$	0%
4c E=D	85% (72%)[e]	**5e** E=Cl	85%
		5f E=D	80%[c]
		5g E=SMe	73%
		5h E=SnBu$_3$	74%[d]
		5i E=CH(OH)Ph	60%

[a]Reagents and conditions: (i) [*n*-BuLi/LiDMAE] (3 equiv), −45 °C, 1 h, hexane. (ii) E^+ = Me_3SiCl, C_2Cl_6, DCl/D_2O, Me_2S_2, Bu_3SnCl or PhCHO (3 equiv), −78 °C, 1 h, THF then H_2O. (iii) TBAF (1.1 equiv), 24 h, rt, THF/H_2O (5/1). [b]Isolated yields after centrifugal thin-layer chromatography purification. [c]**5f** was 100% deuterated. [d]Kugelrohr distillation was used for the purification. [e]*n*-BuLi (1.2 equiv), −45 °C, 1 h, THF then H_2O.

This sequence was extended by using various representative electrophiles, and compounds **5e−i** were obtained in good to excellent yields (60−85%, see Scheme 6). Despite all our efforts, **5a** could not be isolated because of the high instability of this compound. It should also be noted that bifunctional compounds **5e** and **5h** represent very interesting molecules for further selective functionalization on the C-2 and C-7 positions.

Tetrabutyl ammonium fluoride (TBAF) was used to afford desilylation conducted to the expected 7-substituted furo[2,3-*c*]pyridines **4b−c** in very good yields (85−89%, see Scheme 6).

We subsequently confirmed that *n*-BuLi constitutes a good alternative reagent to TBAF for removing the trimethylsilyl group when the C-7 position is substituted. Indeed, by

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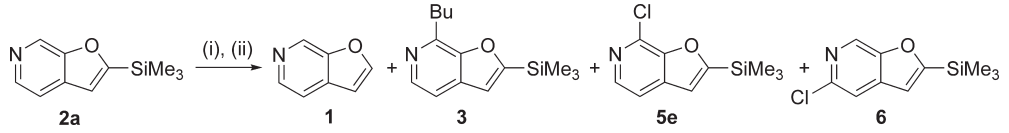
TABLE 1. Regioselective Lithiation of 2a[a]



entry	base	equiv of base	metalation temp *T*, °C	solvent	1	2a	3	5e	6
1	*n*-BuLi[b]	1.2	−78	THF	38	4	47		
2	[*n*-BuLi/LiDMAE][c]	3	−78	hexane		31		65	
3	[*n*-BuLi/LiDMAE][c]	2	−45	hexane		30		60	
4	[*n*-BuLi/LiDMAE][c]	3	−45	hexane		traces		85	

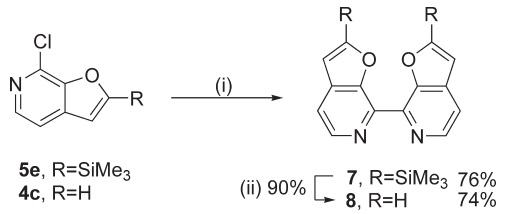
[a]Reagents and conditions: (i) base (*n* equiv), *T* °C, 1 h, solvent. (ii) C_2Cl_6 (3 equiv), −78 °C, 1 h, THF then H_2O. [b]H_2O was added as the electrophile, GC yields. [c]Isolated yields after centrifugal thin-layer chromatography purification.

treatment of **5e** with 1.2 equiv of *n*-BuLi at −45 °C in THF, **4c** was efficiently obtained in a good yield (72%) without byproduct.

As an extension of this work, we tried to use the prepared chlorinated compounds in the synthesis of bipyridinic ligands. 2,2′-Bipyridines are largely represented as versatile ligands due to their ability to form stable complexes with metal ions.[46] Since they combine a π-electron-rich furan ring and a π-electron-deficient pyridine ring, 7,7′-bifuro[2,3-*c*]pyridines might have interesting properties as ligands with applications in the domains of catalysis, photochemistry, or asymmetric transformations. Under the usual Ni-induced homocoupling conditions,[47] **5e** and **4c** afforded compounds **7** and **8** in very good yields (76% and 74%, respectively, see Scheme 7). Furthermore, **8** was efficiently obtained by using TBAF on **7** in an excellent 90% isolated yield. 7,7′-Bifuro[2,3-*c*]pyridine ligands were then prepared in only three or four steps starting from unsubstituted furo[2,3-*c*]pyridine **1**, in 50% and 41% overall yields, respectively.

Our initial goal was to offer a complete toolbox for the functionalization of furopyridines. Since furo[2,3-*c*]pyridines having potential biological properties[29,48,49] are generally substituted on the C-5 position, we next envisioned the further metalation of the **5e** compound. Due to its specific properties, the [*n*-BuLi/LiDMAE] superbase seemed to be the most efficient reagent to afford deprotonation on this position. The most significant results for the lithiation of **5e** followed by electrophilic treatment with DCl/D_2O, C_2Cl_6, or MeSSMe are reported in Table 2.

SCHEME 7. Preparation of 7,7′-Bifuro[2,3-*c*]pyridines 7 and 8[a,b]



[a]Reagents and conditions: (i) $NiCl_2 \cdot 6H_2O$, Zn, PPh_3, DMF, 50 °C, 4 h. (ii) TBAF (2.2 equiv), 24 h, rt, THF/H_2O (5/1). [b]Isolated yields after centrifugal thin-layer chromatography purification.

Metalation of **5e** at −45 °C in hexane allowed lithiation on the C-5 position. After deuterolysis with deuterium chloride solution in deuterium oxide (DCl/D_2O), 58% of the expected 7-chloro-5-deuterio-2-trimethylsilylfuro[2,3-*c*]pyridine **9b** was obtained. However, DCl/D_2O trapping also revealed an unexpected chlorine/lithium exchange and 24% of 7-deuteriofuro[2,3-*c*]pyridine **5f** was isolated. Cl/Li permutation is usually carried out with use of lithium powder with a catalytic amount of 4,4′-di-*tert*-butylbiphenyl (DTBB),[50,51] and such an exchange appears unusual with organolithium bases since chlorine is commonly used as a directing group in metalation processes. Nevertheless, in this specific case, a strong activation of the C−Cl bond induced by the neighboring oxygen atom might explain the successful sequence. Besides, recent work conducted on azaindoles derivatives exhibits similar reactivity by using *t*-BuLi.[52] When C_2Cl_6 was used as the electrophilic source, a mixture of the expected dichloro compound **9a** (71−80%) resulting from lithiation on the C-5 position and **5e** (14−21%) afforded by Cl/Li exchange was isolated (entries 2−4). A better result was obtained by using 4 equiv of base at −45 °C for 1 h in hexane followed by addition of 4 equiv of electrophile from −78 °C to room temperature in THF. It could be noted that an increase in trapping temperature to 20 °C was necessary to yield **9a** more efficiently. To extend this lithiation sequence, we next turned our attention to the reaction with other

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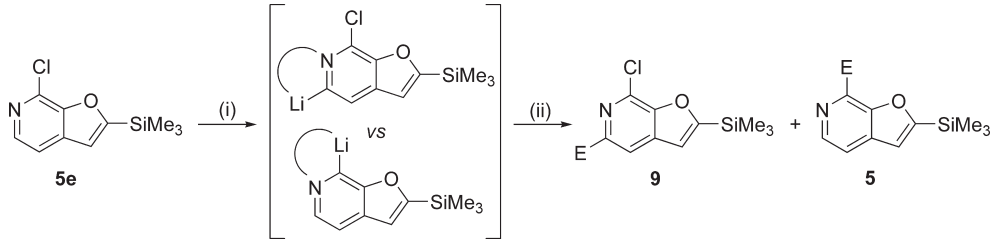
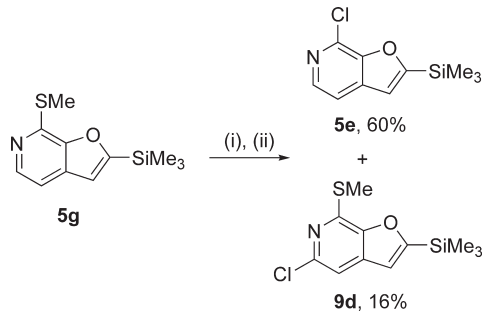
TABLE 2. Preparation of 5,7-Disubstituted-2-trimethylsilylfuro[2,3-*c*]pyridines 9[a]



		trapping step			yields (%)[b]	
entry	equiv of base	*T*, °C	equiv	E	**9**	**5**
1	3	−78 °C to rt	20	D	**9b**, 58[c]	**5f**, 24
2	3	−78 °C to rt[d]	3	Cl	**9a**, 72	**5e**, 21
3	4	−78 °C to rt[d]	4	Cl	**9a**, 80	**5e**, 14
4	5	−78 °C to rt[d]	5	Cl	**9a**, 71	**5e**, 20
5	3	−78 °C[e]	3	SMe	**9c**, 39	**5g**, 10[f]

[a]Reagents and conditions: (i) [*n*-BuLi/LiDMAE] (*n* equiv), −45 °C, 1 h, hexane. (ii) E^+ = DCl/D_2O, C_2Cl_6 or Me_2S_2 (n equiv), *T* °C, 1 h, THF then H_2O. [b]Isolated yields after centrifugal thin-layer chromatography purification. [c]**9b** was 99% deuterated. [d]Trapping step for 1 h at −78 °C then 1 h from −78 °C to room temperature. [e]If temperature was allowed to warm to room temperature, a complex mixture (**9c**, **5g**, **5e**, **2a**, and desilylated products) was detected (GC/MS). [f]8% of **2a** was recovered resulting from low reactivity of lithio intermediate at −78 °C.

SCHEME 8. Preparation of 5-Chloro-7-methylthio-2-trimethylsilylfuro[2,3-*c*]pyridines 9d[a,b]



[a]Reagents and conditions: (i) [*n*-BuLi/LiDMAE] (3 equiv), −45 °C, 1 h, hexane; (ii) C_2Cl_6 (3 equiv), −78 °C, 1 h, THF then H_2O. [b]Isolated yields after centrifugal thin-layer chromatography purification.

electrophiles. Then **9c** was obtained with a moderate 39% isolated yield, resulting from treatment with dimethyl disulfide. In this case, the trapping temperature had to be kept at −78 °C to avoid desilylation by nucleophilic methythiolate, and consequently, a decrease of the conversion rate was observed (84%). It is worth mentioning that condensation on benzaldehyde and acetaldehyde was studied too, demonstrating the formation of a nonseparable mixture of 5- and 7-substituted alcohols and starting materials.

To continue our study of metalation on the C-5 position of furo[2,3-*c*]pyridine derivatives, we finally focused our attention on 7-methylthiofuro[2,3-*c*]pyridine **5g.** Lithiation of **5g** was carried out with 3 equiv of [*n*-BuLi/LiDMAE] at −45 °C for 1 h in hexane followed by addition of C_2Cl_6 as the electrophile in THF, and surprisingly, the methylthio group was also partially replaced during the metalation process, which led to a mixture of **5e**, **9d**, and starting material (60%, 16%, and 16% yields, respectively, see Scheme 8).

A methylthio group is sometimes employed as a directing group during metalation processes; nevertheless, in some specific cases, a sulfur/lithium exchange was observed. Yus and Foubelo in particular described such a permutation in β-functionalized sulfur derivatives.[53,54] In our case, the SMe in the β-position of the oxygen atom exhibits these suitable conditions to allow a SMe/Li exchange. Such a result once more illustrates the highly activated character of the C-7 position neighboring the oxygen atom in furo[2,3-*c*]pyridine.

Conclusion

In summary, we have described the efficient synthesis of polysubstituted furo[2,3-*c*]pyridines via successive regioselective lithiation reactions, using *n*-BuLi or [*n*-BuLi/LiDMAE] as bases. For each step, products were obtained in low to very good yields (16−85%) and some of them were engaged in Pd- or Ni-catalyzed homocoupling for efficient preparation of 2,2′- or 7,7′-bifuro[2,3-*c*]pyridines (63% or 41−50% overall yields, respectively). From a fundamental point of view, regioselectivity depending on the nature of the base was studied, and unusual Cl/Li and SMe/Li permutations were highlighted, proving the highly activated character on the C-7 position of furo[2,3-*c*]pyridine.

Experimental Section

General. ^1H and ^{13}C NMR spectra were recorded at 400 or 250 or 200 and 100 or 63 or 50 MHz respectively with $CDCl_3$ as solvent and TMS as internal standard (for ^1H NMR). HRMS spectra were recorded on a BRUKER micrOTOF-Q spectrometer. MS spectra were recorded on a SHIMADZU GCMS-QP2010 spectrometer. Melting temperatures are uncorrected. Centrifugal thin-layer chromatography purification was performed with Chromatotron.

Reagents. All reagents were commercially available and were purified by distillation when necessary. *n*-BuLi was used as a commercial 1.6 M solution in hexanes. 2-(Dimethylamino)-ethanol (DMAE) was distilled and stored over molecular sieves before use. Toluene, hexane, and THF were distilled and stored

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on sodium wire before use. Centrifugal thin-layer chromatography purifications were performed on silica gel (Merck silica gel 60 PF_{254} containing gypsum).

General Procedure for the Preparation of 2-Substituted Furo[2,3-*c*]pyridines (2a−g). To a solution of furo[2,3-*c*]pyridine **1** (190 mg, 1.6 mmol, 1.0 equiv) in THF (15 mL) was added dropwise *n*-BuLi (1.5 mL, 2.4 mmol, 1.5 equiv) at −78 °C, under argon atmosphere. After 1 h of stirring at −78 °C, the appropriate electrophile (3.2 mmol, 2.0 equiv) was added in THF (5 mL) at −78 or −95 °C. After the mixture was stirred for 15 min or 1 h, the hydrolysis was performed with H_2O (10 mL) at the desired trapping temperature. The aqueous layer was then extracted twice with AcOEt (10 mL). The combined organic layers were washed with an aqueous saturated $NaHCO_3$ solution (20 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography.

a. 2-Trimethylsilylfuro[2,3-*c*]pyridine (2a). The product was prepared according to the general method described herein with chlorotrimethylsilane (347 mg, 3.2 mmol, 2.0 equiv) as electrophile, for 1 h at −78 °C. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 9/1 to 7/3 as eluent and led to the expected derivative **2a** (235 mg, 77%) as a yellow liquid: ^{1}H NMR δ_H 0.37 (s, 9H), 6.94 (s, 1H), 7.49 (d, J = 5.1 Hz, 1H), 8.36 (d, J = 5.1 Hz, 1H), 8.88 (s, 1H); ^{13}C NMR δ_C −1.9, 115.0, 115.9, 133.9, 134.5, 141.8, 155.3, 168.3; IR (NaCl) ν 1255; MS (EI) m/z 191 ([M]$^+$, 54), 176 (100), 133 (21); ESI-HRMS calcd for $C_{10}H_{14}NOSi$ (M + H)$^+$ 192.0839, found 192.0834.

b. 2-Deuteriofuro[2,3-*c*]pyridine (2b). The product was prepared according to the general method described herein with deuterium chloride 35 wt % in deuterium oxide (2.64 mL, 32.0 mmol, 20.0 equiv) as electrophile, at −78 °C and then 1 h from −78 °C to rt. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 7/3 to 5/5 as eluent and led to the expected derivative **2b** (146 mg, 76%) as a yellow liquid: ^{1}H NMR δ_H 6.82 (s, 1H), 7.57 (d, J = 5.2 Hz, 1H), 8.44 (d, J = 5.2 Hz, 1H), 8.92 (s, 1H); ^{13}C NMR δ_C 105.9, 116.2, 134.1, 142.5, 147.8, 148.1, 152.3; MS (EI) m/z 120 ([M]$^+$, 100), 92 (19), 65 (28).

c. 2-Chlorofuro[2,3-*c*]pyridine (2c). The product was prepared according to the general method described herein with hexachloroethane (758 mg, 3.2 mmol, 2.0 equiv) as electrophile, for 1 h at −95 °C. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 10/0 to 7/3 as eluent and led to the expected derivative **2c** (174 mg, 71%) as an orange solid: mp, ^{1}H NMR, IR, and MS are in conformity with literature;[55] ^{13}C NMR δ_C 102.9, 115.2, 133.0, 135.0, 143.3, 146.0, 151.6.

d. Furo[2,3-*c*]pyridin-2-ylphenylmethanol (2d). The product was prepared according to the general method described herein with benzaldehyde (339 mg, 3.2 mmol, 2.0 equiv) as electrophile, for 1 h at −78 °C. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 5/5 to 0/10 as eluent and led to the expected derivative **2d** (292 mg, 81%) as a beige solid: mp 110−113 °C; ^{1}H NMR δ_H 4.50 (br s, 1H), 5.97 (s, 1H), 6.61 (s, 1H), 7.34−7.53 (m, 6H), 8.25 (d, J = 4.8 Hz, 1H), 8.64 (s, 1H); ^{13}C NMR δ_C 70.6, 102.9, 116.1, 127.0, 128.7, 128.9, 133.5, 135.0, 140.3, 142.3, 152.4, 163.3; IR (KBr) ν 3400−2900, 1258; MS (EI) m/z 225 ([M]$^+$, 73), 208 (68), 148 (37), 105 (100), 77 (61); ESI-HRMS calcd for $C_{14}H_{12}NO_2$ (M + H)$^+$ 226.0863, found 226.0868.

e. 2-Methylthiofuro[2,3-*c*]pyridine (2e). The product was prepared according to the general method described herein with dimethyl disulfide (301 mg, 3.2 mmol, 2.0 equiv) as electrophile, for 1 h at −78 °C. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 8/2 to 6/4 as eluent and led to the expected derivative **2e** (206 mg, 78%) as an orange solid: mp 47−50 °C; ^{1}H NMR δ_H 2.60 (s, 3H), 6.55 (s, 1H), 7.38 (d, J = 5.1 Hz, 1H), 8.36 (d, J = 5.1 Hz, 1H), 8.75 (s, 1H); ^{13}C NMR δ_C 15.8, 104.1, 114.6, 132.7, 135.4, 142.9, 153.3, 158.2 ; IR (KBr) ν 1255; MS (EI) m/z 165 ([M]$^+$, 100), 150 (36), 122 (22), 95 (15); ESI-HRMS calcd for C_8H_8NOS (M + H)$^+$ 166.0321, found 166.0313.

f. 2-Bromofuro[2,3-*c*]pyridine (2f). The product was prepared according to the general method described herein with carbone tetrabromide (CBr_4) (1062 mg, 3.2 mmol, 2.0 equiv) as electrophile, for 1 h at −95 °C. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 10/0 to 7/3 as eluent and led to the expected derivative **2f** (238 mg, 75%) as a brown solid; this derivative is particularly unstable and should be used within few minutes after purification. An analytical sample gave the following data: ^{1}H NMR δ_H 6.78 (s, 1H), 7.47 (d, J = 5.2 Hz, 1H), 8.41 (d, J = 5.2 Hz, 1H), 8.82 (s, 1H); ^{13}C NMR δ_C 107.9, 114.9, 132.9, 133.5, 143.0; IR (KBr) ν 1253; MS (EI) m/z 199 ([M+2]$^+$, 95), 197 ([M]$^+$, 100), 118 (12), 90 (78), 63 (83); ESI-HRMS calcd for C_7H_5BrNO (M + H)$^+$ 197.9549, found 197.9556.

g. 2-Tri-*n*-butylstannylfuro[2,3-*c*]pyridine (2g). The product was prepared according to the general method described herein with chlorotri-*n*-butyltin (1042 mg, 3.2 mmol, 2.0 equiv) as electrophile, for 15 min at −95 °C. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 10/0 to 8/2 as eluent and led to the expected derivative **2g** (522 mg, 80%) as a colorless liquid: ^{1}H NMR δ_H 0.91 (t, J = 7.3 Hz, 9H), 1.16−1.24 (m, 6H), 1.30−1.43 (m, 6H), 1.54−1.67 (m, 6H), 6.91 (s, 1H), 7.49 (d, J = 5.2 Hz, 1H), 8.35 (d, J = 5.2 Hz, 1H), 8.87 (s, 1H); ^{13}C NMR δ_C 10.5, 13.8, 27.3, 29.0, 115.2, 117.1, 133.5, 134.6, 141.7, 171.2; IR (NaCl) ν 3000−2800, 1255; MS (EI and CI) m/z 352 ([M − C_4H_9]$^+$, 100), 296 (54), 238 (95), 120 (39); ESI-HRMS calcd for $C_{19}H_{32}NOSn$ (M + H)$^+$ 410.1504, found 410.1508.

h. 2,2′-Bifuro[2,3-*c*]pyridine (2h). To a suspension of $PdCl_2(PPh_3)_2$ (18 mg, 0.025 mmol, 5 mol %) under argon atmosphere in DMF (2 mL) were added the 2-tri-*n*-butylstannylfuro[2,3-*c*]pyridine **2g** (224 mg, 0.55 mmol, 1.1 equiv) and the 2-bromofuro[2,3-*c*]pyridine **2f** (99 mg, 0.50 mmol, 1.0 equiv) in DMF (1 mL). After being stirred at 110 °C for 5 h, the reaction medium was diluted in CH_2Cl_2 (20 mL) and filtrated on Celite. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 7/3 to 0/10 as eluent and led to the expected derivative **2h** (93 mg, 79%) as an orange powder. Derivative **2h** presents a very low solubility in most solvents: mp > 240 °C; ^{1}H NMR δ_H 7.32 (s, 1H), 7.64 (d, J = 5.3 Hz, 1H), 8.51 (d, J = 5.3 Hz, 1H), 8.99 (s, 1H); ^{13}C NMR δ_C 104.8, 116.5, 134.5, 134.7, 143.6, 149.5, 152.6; IR (KBr) ν 1263; MS (EI) m/z 236 ([M]$^+$, 100), 207 (7), 179 (7), 153 (15), 118 (10), 63 (17); ESI-HRMS calcd for $C_{14}H_9N_2O_2$ (M + H)$^+$ 237.0659, found 237.0661.

Preparation of 7-Substituted Furo[2,3-*c*]pyridine (4b,c). a. 7-Deuteriofuro[2,3-*c*]pyridine (4b). To a solution of 7-deuterio-2-trimethylsilylfuro[2,3-*c*]pyridine **5f** (181 mg, 0.94 mmol, 1.0 equiv) in a mixture of THF/H_2O (5 mL/1 mL) was added tetrabutyl ammonium fluoride (1 mL, 1 M in THF, 1.00 mmol, 1.1 equiv) at 0 °C. After 24 h of stirring at room temperature H_2O (5 mL) was added. The aqueous layer was then extracted twice with AcOEt (5 mL). The combined organic layers were washed with an aqueous saturated $NaHCO_3$ solution (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography with hexane/AcOEt 7/3 to 5/5 as eluent and led to the expected derivative **4b** (101 mg, 89%) as an orange liquid: ^{1}H NMR δ_H 6.78 (d, J = 0.8 Hz, 1H), 7.52 (dd, J = 5.2 Hz, J' = 1.1 Hz, 1H), 7.72 (d, J = 0.8 Hz, 1H), 8.39 (dd, J = 5.2 Hz, J' = 1.1 Hz, 1H); ^{13}C NMR δ_C 105.7, 115.8, 133.3, 133.6, 142.0,

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147.8, 151.8; IR (NaCl) ν 1269; MS (EI) m/z 120 ($[M]^+$, 100), 92 (19), 64 (22).

b. 7-Chlorofuro[2,3-*c*]pyridine (4c). To a solution of 7-chloro-2-trimethylsilylfuro[2,3-*c*]pyridine **5e** (212 mg, 0.94 mmol, 1.0 equiv) in a mixture of THF/H_2O (5 mL/1 mL) was added tetrabutyl ammonium fluoride (1 mL, 1 M in THF, 1.00 mmol, 1.1 equiv) at 0 °C. After 24 h of stirring at room temperature H_2O (5 mL) was added. The aqueous layer was then extracted twice with AcOEt (5 mL). The combined organic layers were washed with an aqueous saturated $NaHCO_3$ solution (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography with hexane/AcOEt 9/1 to 8/2 as eluent and led to the expected derivative **4c** (123 mg, 85%) as a white powder: mp and ^{1}H NMR, are in conformity with literature;[55] ^{13}C NMR δ_C 107.1, 115.9, 134.3, 135.8, 142.0, 147.9, 148.6; IR (KBr) ν 1285; MS (EI) m/z 155 ($[M+2]^+$, 33), 153 ($[M]^+$, 100), 118 (64), 90 (19), 63 (39).

General Procedure for the Preparation of [*n*-BuLi/LiDMAE] Superbase. To a solution of DMAE (712 mg, 8.0 mmol, 1.0 equiv) in anhydrous hexane or toluene (14 mL) at −5 °C was added dropwise *n*-BuLi (10 mL, 1.6 M in hexanes, 16.0 mmol, 2.0 equiv) under argon atmosphere. After 15 min at 0 °C, [*n*-BuLi/LiDMAE] superbase is ready to be used.

General Procedure for the Preparation of 2,7-Disubstituted Furo[2,3-*c*]pyridines (5e−i). To a solution of [*n*-BuLi/LiDMAE] (12 mL, 4.00 mmol, 3.0 equiv) prepared as described herein in hexane was added dropwise a solution of 2-trimethylsilylfuro-[2,3-*c*]pyridine **2a** (254 mg, 1.33 mmol, 1.0 equiv) in anhydrous hexane (3 mL) at −45 °C, under argon atmosphere. After the mixture was stirred for 1 h at −45 °C, the appropriate electrophile (4.00 mmol, 3.0 equiv) was added in THF (5 mL) at −78 °C. After 1 h of stirring at −78 °C, the hydrolysis was performed with H_2O (10 mL) at the desired trapping temperature. The aqueous layer was then extracted twice with AcOEt (10 mL). The combined organic layers were washed with an aqueous saturated $NaHCO_3$ solution (20 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography.

a. 7-Chloro-2-trimethylsilylfuro[2,3-*c*]pyridine (5e). The product was prepared according to the general method described herein with hexachloroethane (948 mg, 4.00 mmol, 3.0 equiv) as electrophile. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 10/0 to 8/2 as eluent and led to the expected derivative **5e** (255 mg, 85%) as a yellow liquid: ^{1}H NMR δ_H 0.40 (s, 9H), 7.00 (s, 1H), 7.44 (d, J = 5.2 Hz, 1H), 8.14 (d, J = 5.2 Hz, 1H); ^{13}C NMR δ_C −1.9, 115.5, 115.8, 134.3, 136.4, 141.5, 150.9, 169.4; IR (NaCl) ν 1253; MS (EI) m/z 225 ($[M]^+$, 51), 210 (100), 174 (77), 93 (18), 63 (21); ESI-HRMS calcd for $C_{10}H_{13}ClNOSi$ $(M+H)^+$ 226.0449, found 226.0453.

b. 7-Deuterio-2-trimethylsilylfuro[2,3-*c*]pyridine (5f). The product was prepared according to the general method described herein with deuterium chloride 35 wt % in deuterium oxide (2.19 mL, 26.60 mmol, 20.0 equiv) as electrophile. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 9/1 to 7/3 as eluent and led to the expected derivative **5f** (204 mg, 80%) as an orange liquid: ^{1}H NMR δ_H 0.37 (s, 9H), 6.95 (s, 1H), 7.49 (d, J = 5.2 Hz, 1H), 8.36 (d, J = 5.2 Hz, 1H); ^{13}C NMR δ_C −1.9, 115.0, 115.8, 133.7, 134.4, 141.9, 155.2, 168.1; IR (NaCl) ν 1253; MS (EI) m/z 192 ($[M]^+$, 49), 177 (100), 83 (8).

c. 7-Methylthio-2-trimethylsilylfuro[2,3-*c*]pyridine (5g). The product was prepared according to the general method described herein with dimethyl disulfide (376 mg, 4.00 mmol, 3.0 equiv) as electrophile. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt 10/0 to 9/1 as eluent and led to the expected derivative **5g** (230 mg, 73%) as a yellow oil: ^{1}H NMR δ_H 0.38 (s, 9H), 2.72 (s, 3H), 6.93 (s, 1H), 7.23 (d, J = 5.2 Hz, 1H), 8.23 (d, J = 5.2 Hz, 1H); ^{13}C NMR δ_C −1.7, 12.1, 112.2, 115.4, 132.7, 141.8, 143.4, 152.6, 167.3; IR (NaCl) ν 1253; MS (EI) m/z 237 ($[M]^+$, 100), 204 (21), 192 (33), 176 (17), 103 (11), 73 (16); ESI-HRMS calcd for $C_{11}H_{16}NOSSi$ $(M+H)^+$ 238.0716, found 238.0710.

d. 7-Tri-*n*-butylstannyl-2-trimethylsilylfuro[2,3-*c*]pyridine (5h). The product was prepared according to the general method described herein with chlorotri-*n*-butyltin (1300 mg, 4.00 mmol, 3.0 equiv) as electrophile. Purification was performed with Kugelrohr distillation and led to the expected derivative **5h** (473 mg, 74%) as an orange liquid: ^{1}H NMR δ_H 0.37 (s, 9H), 0.82−0.90 (m, 9H), 1.21−1.47 (m, 12H), 1.52−1.69 (m, 6H), 6.92 (s, 1H), 7.36 (d, J = 5.1 Hz, 1H), 8.53 (d, J = 5.1 Hz, 1H); ^{13}C NMR δ_C −1.9, 10.2, 13.8, 27.4, 29.2, 114.1, 115.0, 130.0, 143.5, 156.6, 162.2, 166.7; IR (NaCl) ν 3000−2800, 1253; MS (EI) m/z 482 ($[M+1]^+$, 8), 424 (36), 364 (11), 310 (100), 192 (25), 73 (22); ESI-HRMS calcd for $C_{22}H_{40}NOSiSn$ $(M+H)^+$ 482.1899, found 482.1887.

e. Phenyl(2-trimethylsilylfuro[2,3-*c*]pyridin-7-yl)methanol (5i). The product was prepared according to the general method described herein with benzaldehyde (424 mg, 4.00 mmol, 3.0 equiv) as electrophile. Purification by centrifugal thin-layer chromatography was performed with hexane/AcOEt: 9/1 to 7/3 as eluent and led to the expected derivative **5i** (237 mg, 60%) as a white solid: mp 69−72 °C; ^{1}H NMR δ_H 0.31 (s, 9H), 6.22 (s, 1H), 6.90 (s, 1H), 7.20−7.60 (m, 6H), 8.30 (d, J = 5.1 Hz, 1H); ^{13}C NMR δ_C −2.0, 71.3, 115.0, 115.6, 127.0, 127.6, 128.2, 135.1, 140.1, 142.7, 145.0, 151.3, 168.1; IR (KBr) ν 3412, 1253; MS (EI) m/z 297 ($[M]^+$, 100), 220 (100), 191 (61), 176 (18), 73 (30); ESI-HRMS calcd for $C_{17}H_{20}NO_2Si$ $(M+H)^+$ 298.1258, found 298.1247.

General Procedure for the Preparation of 7,7′-Bifuro[2,3-*c*]-pyridines (7 and 8). To a blue stirred solution of $NiCl_2 \cdot 6H_2O$ (238 mg, 1.0 mmol, 1.0 equiv) and PPh_3 (1048 mg, 4.0 mmol, 4.0 equiv) in DMF (5 mL) at 50 °C was added activated zinc powder (65 mg, 1.0 mmol, 1.0 equiv). Then the mixture was stirred during 1 h at 50 °C and the color changed to become red-brown before addition of furo[2,3-*c*]pyridine derivatives **5e** or **4c** (1.0 mmol, 1.0 equiv). The mixture was then stirred for 3 h at 50 °C. After cooling at room temperature, mixture was treated with NH_4OH 40% solution (5 mL), then the aqueous layer was then extracted twice with AcOEt (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was quickly filtrated on a pad of silica gel before purification by centrifugal thin-layer chromatography.

a. 2,2′-Bistrimethylsilyl-7,7′-bifuro[2,3-*c*]pyridine (7). The product was prepared according to the general method described herein starting from 7-chloro-2-trimethylsilylfuro[2,3-*c*]-pyridine **5e** (225 mg, 1.0 mmol, 1.0 equiv). Purification by centrifugal thin-layer chromatography was performed with CH_2Cl_2/MeOH 98/2 as eluent and led to the expected bifuro[2,3-*c*]pyridinyl derivative **7** (144 mg, 76%) as a beige powder: mp 121−123 °C; ^{1}H NMR δ_H 0.32 (s, 18H), 7.07 (s, 2H), 7.63 (d, J = 5.2 Hz, 2H), 8.61 (d, J = 5.2 Hz, 2H); ^{13}C NMR δ_C −1.6, 115.3, 116.4, 136.0, 139.5, 142.1, 153.6, 168.4; IR (KBr) ν 1253; MS (EI) m/z 380 ($[M]^+$, 92), 365 (100), 175 (35), 73 (39); ESI-HRMS calcd for $C_{20}H_{25}N_2O_2Si_2$ $(M+H)^+$ 381.1449, found 381.1445.

b. 7,7′-Bifuro[2,3-*c*]pyridine (8). The product was prepared according to the general method described herein starting from 7-chlorofuro[2,3-*c*]pyridine **4c** (154 mg, 1.0 mmol, 1.0 equiv). Purification by centrifugal thin-layer chromatography was performed with CH_2Cl_2/MeOH 99/1 to 98/2 as eluent and led to the expected bifuro[2,3-*c*]pyridinyl derivative **8** (88 mg, 74%) as a white powder: mp, ^{1}H NMR, and IR are in conformity with literature;[56] ^{13}C NMR δ_C 106.1, 117.0, 135.8, 139.8, 142.2, 148.7, 150.4; MS (EI) m/z 236 ($[M]^+$, 100), 210 (25), 63 (23).

Preparation of 2,5,7-Trisubstituted Furo[2,3-*c*]pyridines (9a−d). a. 5,7-Dichloro-2-trimethylsilylfuro[2,3-*c*]pyridine (9a). To a solution of [*n*-BuLi/LiDMAE] (8 mL, 2.66 mmol, 4.0 equiv)

(56) Shiotani, S.; Taniguchi, K. *J. Heterocycl. Chem.* **1997**, *34*, 493–499.

prepared as described herein in hexane was added dropwise a solution of 7-chloro-2-trimethylsilylfuro[2,3-*c*]pyridine **5e** (150 mg, 0.66 mmol, 1.0 equiv) in anhydrous hexane (3 mL) at −45 °C, under argon atmosphere. After the mixture was stirred for 1 h at −45 °C, hexachloroethane (630 mg, 2.66 mmol, 4.0 equiv) was added as the electrophile, in THF (3 mL) at −78 °C. After 1 h of stirring at −78 °C the temperature was allowed to warm to room temperature for 1 h, and the hydrolysis was performed with H_2O (10 mL). The aqueous layer was then extracted twice with AcOEt (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography with hexane/AcOEt 10/0 to 95/5 as eluent and led to the expected derivative **9a** (138 mg, 80%) as a white solid: mp 56−58 °C; ^{1}H NMR δ_H 0.40 (s, 9H), 6.95 (s, 1H), 7.42 (s, 1H); ^{13}C NMR δ_C −2.0, 115.0, 115.3, 132.4, 139.2, 141.5, 150.4, 172.0; IR (KBr) ν 1253; MS (EI) m/z 259 ([M]$^+$, 44), 244 (100), 208 (55), 93 (19); ESI-HRMS calcd for $C_{10}H_{12}Cl_2NOSi$ (M + H)$^+$ 260.0060, found 260.0066.

b. 7-Chloro-5-deuterio-2-trimethylsilylfuro[2,3-*c*]pyridine (9b). To a solution of [*n*-BuLi/LiDMAE] (6 mL, 2.00 mmol, 3.0 equiv) prepared as described herein in hexane was added dropwise a solution of 7-chloro-2-trimethylsilylfuro[2,3-*c*]pyridine **5e** (150 mg, 0.66 mmol, 1.0 equiv) in anhydrous hexane (3 mL) at −45 °C, under argon atmosphere. After 1 h of stirring at −45 °C, deuterium chloride 35 wt % in deuterium oxide (1.1 mL, 13.20 mmol, 20.0 equiv) was added as the electrophile, in THF (5 mL) at −78 °C. After 1 h of stirring from −78 °C to room temperature, the hydrolysis was performed with H_2O (10 mL). The aqueous layer was then saturated with $NaHCO_3$ and extracted twice with AcOEt (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography with hexane/AcOEt 10/0 to 8/2 as eluent and led to the expected derivative **9b** (87 mg, 58%) as a colorless liquid: ^{1}H NMR δ_H 0.38 (s, 9H), 6.99 (s, 1H), 7.42 (s, 1H); ^{13}C NMR δ_C −1.9, 115.4, 115.8, 134.2, 136.3, 141.1, 150.8, 169.3; MS (EI) m/z 226 ([M]$^+$, 66), 211 (100), 175 (54).

c. 7-Chloro-5-methylthio-2-trimethylsilylfuro[2,3-*c*]pyridine (9c). To a solution of [*n*-BuLi/LiDMAE] (6 mL, 2.00 mmol, 3.0 equiv) prepared as described herein in hexane was added dropwise a solution of 7-chloro-2-trimethylsilylfuro[2,3-*c*]pyridine **5e** (150 mg, 0.66 mmol, 1.0 equiv) in anhydrous hexane (3 mL) at −45 °C, under argon atmosphere. After 1 h of stirring at −45 °C, dimethyl disulfide (188 mg, 2.00 mmol, 3.0 equiv.) was added as the electrophile, in THF (3 mL) at −78 °C. After 1 h of stiring at −78 °C the hydrolysis was performed with H_2O (10 mL). The aqueous layer was then extracted twice with AcOEt (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography with cyclohexane/Et_2O 10/0 to 9/1 as eluent and led to the expected derivative **9c** (70 mg, 39%) as a white powder: mp 46−49 °C; ^{1}H NMR δ_H 0.38 (s, 9H), 2.59 (s, 3H), 6.86 (s, 1H), 7.27 (s, 1H); ^{13}C NMR δ_C −1.9, 15.0, 112.1, 115.1, 133.0, 137.7, 149.1, 151.1, 170.3; IR (KBr) ν 1253; MS (EI) m/z 271 ([M]$^+$, 100), 238 (39), 225 (14), 93 (22), 73 (47); ESI-HRMS calcd for $C_{11}H_{14}ClNNaOSSi$ (M + Na)$^+$ 294.0146, found 294.0148.

d. 5-Chloro-7-methylthio-2-trimethylsilylfuro[2,3-*c*]pyridine (9d). To a solution of [*n*-BuLi/LiDMAE] (6 mL, 2.00 mmol, 3.0 equiv) prepared as described herein in hexane was added dropwise a solution of 7-methylthio-2-trimethylsilylfuro[2,3-*c*]pyridine **5g** (158 mg, 0.66 mmol, 1.0 equiv) in anhydrous hexane (3 mL) at −45 °C, under argon atmosphere. After 1 h of stirring at −45 °C, hexachloroethane (474 mg, 2.00 mmol, 3.0 equiv) was added as the electrophile, in THF (3 mL) at −78 °C. After 1 h of stirring at −78 °C the hydrolysis was performed with H_2O (10 mL). The aqueous layer was then extracted twice with AcOEt (10 mL). After drying ($MgSO_4$), filtration, and solvent evaporation, the crude product was purified by centrifugal thin-layer chromatography with cyclohexane/Et_2O 10/0 to 9/1 as eluent and led to the expected derivative **9d** (29 mg, 16%) as a colorless oil: ^{1}H NMR δ_H 0.38 (s, 9H), 2.70 (s, 3H), 6.86 (s, 1H), 7.20 (s, 1H); ^{13}C NMR δ_C −1.8, 12.4, 111.2, 115.0, 135.8, 142.7, 143.3, 151.7, 169.6; IR (NaCl) ν 1253; MS (EI) m/z 271 ([M]$^+$, 100), 256 (12), 238 (21), 226 (30), 120 (12), 73 (37); ESI-HRMS calcd for $C_{11}H_{15}ClNOSSi$ (M + H)$^+$ 272.0327, found 272.0334.

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Supporting Information Available: Procedure for the synthesis of **1**, spectroscopic data for **3**, **5b**, **5c**, and **5d**, and NMR spectra of all new compounds. This material is available free of charge via the Internet at http://pubs.acs.org.