TMSCH$_2$Li–LiDMAE: a new nonnucleophilic reagent for C-2 lithiation of halopyridines

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Abstract—A new superbasic reagent has been discovered by combining TMSCH$_2$Li and LiDMAE in hexane. This reagent was found highly efficient for the C-2 lithiation of sensitive chloro- and fluoropyridines. The metallation occurred chemo- and regioselectively at 0 °C avoiding the nucleophilic addition or substrate degradation commonly obtained with other alkylolithiums even at lower temperatures.

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1. Introduction

The C-2 lithiation of the pyridine ring has proved to be a synthetically important process to introduce opportune functionalities subsequently giving access to numerous pharmacophores, polydentate ligands (e.g., bipyridines) and chiral catalysts. Several methodologies have been developed to lithiate selectively the C-2 position. The bromine–lithium exchange was probably the most useful since adequately placed bromine ensured the selectivity. However, the reactions were performed at low temperatures to avoid substrate degradation and the availability of C-2 brominated pyridines often restricted the reaction to derivatives with a low degree of functionality. Another way was to increase the alpha proton’s acidity by reacting the substrate with a Lewis acid. The intermediate pyridinium salt was then efficiently lithiated with LiTMP but mixtures of mono- and bifunctional derivatives are always obtained. The hydrogen–lithium exchange appeared as the more elegant process since brominated precursors and a tedious activation step were avoided. However, this was probably the more complicated approach since the base used had to be sufficiently basic to abstract the alpha protons while not nucleophilic to prevent side addition since the base used had to be sufficiently basic to abstract the alpha protons while not nucleophilic to prevent side addition at the electrophilic C-2 position. The success was met by associating n-BuLi with Me$_2$N(CH$_2$)$_2$OLi in nonpolar solvents such as hexane or toluene. The obtained reagent named BuLi–LiDMAE effected clean alpha metallations of numerous pyridine derivatives with tolerance of sensitive functionalities such as chlorine, acidic methyles, and anisyles and pyrolyl groups. BuLi–LiDMAE is now a well-recognized reagent included in the portfolio of metallating agents. However, it still suffers from drawbacks, which need to be overcome. All lithiations require an excess of base (typically 3−4 equiv) implying the use of the corresponding excess of electrophilic reagent to avoid its consumption by the base before trapping the lithiopyridine. This was problematic when an expensive electrophile was used or could complicate the purification step, the side addition product being present in the medium. Furthermore the newly introduced substituent could be attacked by the excess of basic reagent if sensitive such as an aldehyde. Since BuLi–LiDMAE is an n-BuLi-containing reagent, nucleophilicity towards the most electrophilic heterocycles remains problematic and low temperatures (typically −80 to −100 °C) are required to metallate substrates such as halopyridines.

Since we are continuously looking for the most efficient and easily handled reagent we have launched a research program aiming at replacing n-BuLi by other alkylolithiums. It is well known that the degrees of aggregation and solvation have a significant impact on the reactivity and selectivity of organolithium complexes. Generally the smaller the aggregate size the more reactive they are. In contrast to n-BuLi, branched t-PrLi, s-BuLi and t-BuLi are not hexameric, but rather tetrameric, in hexanes. So the association of such bases with LiDMAE should provide more reactive lithiating agents usable in lower amounts than n-BuLi–LiDMAE. The steric effects are also expected to induce lower nucleophilicity towards sensitive heterocycles potentially allowing the metallation to be performed at more practical higher temperatures (0 °C or rt). Unfortunately, our first attempts to associate LiDMAE with classical branched alkylolithiums (s-BuLi or t-BuLi) only led to insoluble mixtures unreactive...
or slightly nucleophilic towards pyridines, and we decided to examine other lithiating agents.

A literature survey reported the beneficial effects of silicon-containing reagents and substrates on several transformations. Accelerating effects and enantiomeric excess enhancement have been observed in asymmetric additions in the presence of silylated catalysts. Moreover, silyl moieties are also known to bring some thermal and air stability to lithiating agents such as lithium hexamethyldisilazide (LiHMDS). Unfortunately, the consequence is also a decrease of the basicity ($pK_a$ 29.5 vs 35.7 for LDA in THF) impeding, for example, abstraction of acidic pyrimidinone protons. Recently, the bulky Me$_3$SiCH$_2$Li (TMSCH$_2$Li) has been reported to be a promising base for ortholithiation of some pyridine derivatives when reacted in the presence of small amounts of disopropylamine (DIA) in THF. Thus, we felt that such an apparently nonnucleophilic reagent could be an excellent candidate for promoting alpha lithiation of pyridine derivatives when associated with LiDMAE in nonpolar solvents. Therefore, we investigated the reactivity of various TMSCH$_2$Li–LiDMAE combinations towards electrophilic chloro- and fluoropyridines.

### 2. Results and discussion

#### 2.1. Lithiation of chloropyridines

The study was initiated with the metallation of 2-chloropyridine for which the behaviour towards $n$-BuLi–LiDMAE is well known (Scheme 1). As shown 3 equiv of this reagent at $-78^\circ$C in hexane were needed to metallate selectively 1 in 92% yield. Higher temperatures (e.g., 0 $^\circ$C) gave nucleophilic addition and substrate degradation. 1 was then treated with TMSCH$_2$Li–LiDMAE combinations in hexane under various temperatures and stoichiometries (Table 1). TMSCH$_2$Li–LiDMAE mixtures were prepared according to procedures previously reported for BuLi–LiDMAE. The experiments in Table 1 clearly underline the differences between $n$-BuLi and TMSCH$_2$Li. At first, the latter did not react with 1 even at 0 $^\circ$C (entries 1–3) while $n$-BuLi gave addition even at $-78^\circ$C leading to a dihydropyridone. Another interesting feature was the effect of the TMSCH$_2$Li–LiDMAE ratio on the selectivity. Indeed while BuLi and LiDMAE had to be used in a 1/1 ratio to ensure selective C-6 lithiation, such a stoichiometry gave mixtures of 1a and 1b with the new reagent (entries 4–6). In contrast the 2/1 ratio gave the best selectivities leading exclusively to

<table>
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<th>Entry</th>
<th>TMSCH$_2$Li (equiv)</th>
<th>LiDMAE (equiv)</th>
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<th>S.M. (%)</th>
<th>1a (%)</th>
<th>1b (%)</th>
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Table 1. Conditions screening for lithiation of 1 with TMSCH$_2$Li–LiDMAE.

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1a whatever the temperature (entries 7–10). The best result was obtained when the metallation was performed at 0 $^\circ$C yielding 1b cleanly in an excellent yield (96%, entry 10) without any nucleophilic addition product. Entries 11 and 13 demonstrated that the 2/1 ratio must be adopted since a decrease of the amount of TMSCH$_2$Li or the use of a 2/2 ratio induced a loss of the regioselectivity. Attempts to metallate at rt did not give any reaction, maybe due to the reagent degradation at such a temperature (entry 12). Finally LiDMAE used in substoichiometric amount also affected a clean metallization despite a slight decrease in the conversion (entry 14). Lower amounts led to much less efficient processes. The low nucleophilicity of TMSCH$_2$Li is remarkable since all experiments were realized using only 1–1.1 equiv of electrophile. This means that TMSCH$_2$Li was less nucleophilic than the formed pyridyllithium allowing efficient introduction of the functionality on the ring. Such a reagent stoichiometry was prohibited with BuLi–LiDMAE and excess of electrophile was necessary (Scheme 1) except on rare occasions when base compatible electrophiles such as TMSCI or Cl$_2$SnBu$_3$ were used.

To gain additional information about the reactivity of the new superbase, we examined various conditions for the quenching step in order to examine the pyridyllithium versus TMSCH$_2$Li nucleophilicity. The temperature was first maintained at 0 $^\circ$C (conditions: entry 10, Table 1) after the metallation step, the electrophile was then introduced at the same temperature. Under these conditions, 1a was obtained in very good yield (85%). Moreover, when THF usually added to release the pyridyllithium from aggregates to enhance its reactivity was omitted, 1a was still obtained in excellent yield (89%). These experiments additionally stress the low nucleophilicity of TMSCH$_2$Li allowing one to perform the metallation in more practical conditions.

The scope of the reaction was then investigated by reaction with a range of electrophiles such as halides, aldehydes or amides, which were introduced in stoichiometric amounts (Table 2). For reasons of solubility and to minimize degradation of these sensitive reagents, it was preferred to perform the trapping step at $-78^\circ$C using THF as a co-solvent.
As shown, all the expected products were synthesized in good yields using only 1.1 equiv of electrophile. Impressive was the stability of aldehyde 1d that is usually highly electrophilic towards n-BuLi. A notable improvement was obtained using piperidine carboxaldehyde instead of DMF. Expectedly, PhCHO was found to be more sensitive to nucleophilic attack by the excess of TMSCH₂Li nevertheless providing the corresponding alcohol 1f in 60% yield, the remaining product being only unreacted 1. The yield could be raised to 80% by employing an additional equivalent of benzaldehyde. Finally, the reaction of the diethylcarbamide (entries 8–10) was handicapped by fast subsequent reaction of the lithiopyridine with the target amide leading to the corresponding bis-(6-chloro-pyridin-2-yl)-methaneone 1h was the main product. The yield could be raised to 80% by employing an additional equivalent of carbamide and a reversed addition order. Interestingly, the amide 1g was not attacked by the excess of TMSCH₂Li but only by the pyridyllithium. This contrasted with the reactivity of BuLi–LiDMAE which always led to the corresponding pyridylbutylketone.¹⁶

A range of sensitive electrophiles was then reacted with lithiated 2 and 3. All reactions were clean and gave the expected products in good to high yields (Scheme 3).

From these excellent results obtained under mild conditions and using low amounts of reagents we decided to examine further the scope of the reaction by investigating the metalation in the fluoropyridine series.

### 2.2. Lithiation of fluoropyridines

Fluoropyridines are important substrates for many reasons. At first fluorine is far more electronegative than chlorine inducing dramatic changes in the reactivity of the pyridine ring. The consequences are a strong increase of the electrophilicity and proton acidities especially for those ortho to fluorine, so major changes could be expected on chemo- and regioselectivity.

These electronic properties have also made the introduction of fluorine in heterocyclic structures of high interest for the pharmaceutical purpose. Indeed, fluorine and hydrogen are isosteric atoms; consequently, steric or chelating effects under −78 °C were needed with other lithiating agents. Thanks to its low nucleophilicity, the reagent also generally allowed the use of electrophiles in stoichiometric amounts.

Then we turned to the extension of this promising selective reagent to the metallation of 3- and 4-chloropyridines 2 and 3, the latter being the most electrophilic in this series. First conditions screening showed that TMSCH₂Li behaved in the same way with these isomers. No reaction occurred in the absence of LiDMAE and the conditions used for 2-chloropyridine could be applied successfully for the C-2 lithiation of 2 and 3 except that the metallation time had to be extended to 2 h for the complete conversion of 3. The reaction performed at 0 °C did not give any nucleophilic addition product even with 3 nor did it result in isomerisation leading to C-4 lithiation with 2. The reactivity was different from those of n-BuLi–LiDMAE which had to be used in excess (3–4 equiv) at −60 and −78 °C for the metallation of 2 and 3, respectively, to avoid nucleophilic addition and C-4 lithiation of 2.⁴b

A range of sensitive electrophiles was then reacted with lithiated 2 or 3. Preparation of C-2 substituted chloropyridines under mild conditions.

From these excellent results obtained under mild conditions and using low amounts of reagents we decided to examine further the scope of the reaction by investigating the metalation in the fluoropyridine series.

### Scheme 3. Preparation of C-2 substituted chloropyridines under mild conditions.

Thus the new TMSCH₂Li–LiDMAE reagent effected the first clean alpha lithiation of 1 at 0 °C while temperatures...
able to interfere with the substrate–biological site interactions never accompany the electronic effect.

Recently, 2-fluoropyridine (4) has been lithiated successfully at C-6 using 3 equiv of BuLi–LiDMAE. The temperature had to be maintained at -100 °C to avoid substrate degradation.\(^\text{18}\) 3-Fluoropyridine (5) has been lithiated with various basic systems and low temperatures were always employed (-40 to -78 °C). The C-2 lithiation of this substrate was less easily directed since protons at C-4 were also highly activated by the fluorine group. This implied a thorough control of temperature and the appropriate lithiating agent.\(^\text{Sc.d,19}\) A few examples of 4-fluoropyridine lithiation have been reported also at low temperatures. The formed C-3 lithio intermediate was often instable leading to pyridine formation lowering the synthetic interest of this substrate.\(^\text{19}\) Moreover, 4-fluoropyridine is not easily available from standard commercial sources and its preparation is quite tedious.

So we rather focused on the lithiation of 2-fluoropyridine 4 and 3-fluoropyridine 5. Our first observation was surprising since 4 did not react at all with TMSCH\(_2\)Li (1–2 equiv) at 0 °C in hexane indicating the low nucleophilecity of the reagent towards the substrate. This first positive outcome encouraged us to attempt the lithiation with TMSCH\(_2\)Li–LiDMAE. We were pleased to obtain a quantitative C-6 lithiation at 0 °C! The reaction medium did neither reveal nucleophilic addition product nor material loss due to degradation. The 2/1 TMSCH\(_2\)Li–LiDMAE ratio was found to be the best to ensure efficient reaction. Sulfenyl, alcohol and ketone functionalities were introduced in good yields. It must be pointed out here that the isolated yields were lower than the GC yields due to the volatility of the products (Scheme 4).

**Table 3.** Effect of the TMSCH\(_2\)Li–LiDMAE ratio on the lithiation selectivity of 5

<table>
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<tr>
<th>Entry</th>
<th>TMSCH(_2)Li (equiv)</th>
<th>LiDMAE (equiv)</th>
<th>S.M. (%)</th>
<th>5a (%)</th>
<th>6 (%)</th>
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<td>2</td>
<td>-</td>
<td>90</td>
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\(^a\) All reactions performed on 1.84 mmol of 1. \(^b\) GC yields, S.M. = starting material.

The lithiation of 3-fluoropyridine 5 was then investigated (Table 3). A first blank test was realized with TMSCH\(_2\)Li at 0 °C (entry 1). The absence of nucleophilicity was clearly established since the metallation was complete and gave a mixture of C-2 and C-4 functionalized derivatives 5a and 6. At this stage a decrease of the metallation temperature could have been envisioned but we first decided to maintain the temperature at 0 °C and to attempt to control the selectivity only by adding LiDMAE to the basic system. Under these conditions, the incorporation of LiDMAE in the 2/1 ratio significantly favoured the C-2 versus C-4 lithiation (entry 2). A stoichiometric amount of LiDMAE led to a far more selective metallation giving mainly 5a in 87% besides 6 in 12% yield. An increase of the global base amount to 2 equiv gave the best selectivity affording 5a in 90% yield with the formation of the bismetillation product 7.

As shown in Table 3, the 5a-6 ratio was strongly dependent on the amount of LiDMAE. This underlined the severe competition between the acidities of H-4 and H-2. The TMSCH\(_2\)Li–LiDMAE (1/1) reagent probably ensured the formation of an aggregate with the pyridine nitrogen which was sufficiently robust to maintain the basic reagent near the H-2 proton and promote the selective lithiation (Scheme 5). This was different with the 2/1 ratio where TMSCH\(_2\)Li could be released from the aggregates to deprotonate the other position.

The reaction was finally examined with a range of electrophiles leading selectively to the corresponding derivatives in excellent yields, which were found better than with 2-fluoropyridine (Scheme 6). The bismetillation product was never obtained after reaction with aldehydes of amides supporting a subsequent lithiation of 5a during the quenching step with MeSSMe.\(^2\)

**Scheme 4.** Clean lithiation of 4 with TMSCH\(_2\)Li–LiDMAE and preparation of derivatives.

**Scheme 5.** Proposed aggregate for selective C-2 lithiation.

**Scheme 6.** C-2 lithiation of 3-fluoropyridine.
3. Conclusion

A new superbasic reagent has been discovered by combining TMSCH₂Li and LiDMAE in hexane. This reagent, when used in a 2/1 ratio was found highly efficient for the C-2 lithiation of sensitive chloro- and fluoropyridines. The metallation occurred chemoselectively at 0 °C without any trace of the nucleophilic addition commonly observed with other alkyl-lithiums even at lower temperatures. The usually tedious regioselective control of 3-fluoropyridine lithiation was achieved by simply adjusting the TMSCH₂Li–LiDMAE ratio to 1/1. Moreover, the low nucleophilicity of the base allowed using only stoichiometric amounts of electrophilic reagents. Although using the more expensive TMSCH₂Li, the newly reported C-2 lithiating reagent is a profound improvement of the known BuLi–LiDMAE superbase for lithiation of halopyridines. Work is now progressing to further investigate the scope of the TMSCH₂Li–LiDMAE superbase especially with more electrophilic heterocycles.

4. Experimental

4.1. General

All solvents were distilled and stored over sodium wire before use. 2-Dimethylaminoethanol was distilled under nitrogen and stored on molecular sieves. TMSCH₂Li (FMC Lithium) was used as a 0.92 M solution in hexanes. All reagents were commercially available and used as such except for 4-chloropyridine, which was released from its hydrochloride salt by basic treatment (aq K₂CO₃). ¹H and ¹³C NMR spectra were obtained in CDCl₃ (unless otherwise stated) on a Bruker AC400 instrument at 200 and 50 MHz, respectively. GC experiments were performed on a Shimadzu chromatograph (FID detection) through a 15 m capillary HP1 column. Products 1a, 1c–e, 4a, 18, 2a–c, 4b, 3a–c, and 4b were found spectroscopically identical to the previously reported compounds.

4.2. General procedure for C-2 lithiation of chloro-pyridines 1–3 and 2-fluoropyridine 4

TMSCH₂Li (6 mL, 5.52 mmol) was added dropwise to a solution of 2-dimethylaminoethanol (164 mg, 1.84 mmol) in hexane (6 mL) at 0 °C. After 30 min of stirring, a solution of the appropriate halopyridine (1.84 mmol) in hexane (6 mL) was then added dropwise. The solution was then stirred for 1 h (2 h for 3) at the same temperature and then treated at −78 °C with a solution of the appropriate electrophile (2.02 mmol), except for benzaldehyde (3.68 mmol), in THF (18 mL). The temperature was maintained at −78 °C for 1 h and at 0 °C for 30 min. Hydrolysis was then performed at this temperature with water (10 mL). The reaction medium was then extracted twice with ether (25 mL), the organic layer dried over MgSO₄ and evaporated under vacuum. The crude product was first subjected to GC analysis and purified if needed by chromatography on silica gel eluting with hexane–AcOEt mixtures using a gradient from 95/5 to 90/10.

4.2.1. 6-Chloro-pyridine-2-carboxylic acid diethylamide (1g).²⁰ Yield, 32%. ¹H NMR (CDCl₃): δ=1.35 (t, J=7.3 Hz, 6H), 3.49 (q, J=7.3 Hz, 4H), 7.38 (d, J=7.6 Hz, 1H), 7.54 (d, J=7.6 Hz, 1H), 7.75 (t, J=7.6 Hz, 1H). ¹³C NMR (CDCl₃): δ=15.4, 43.5, 121.9, 125.1, 139.7, 150.1, 155.3, 203.1.

4.2.2. Bis-(6-chloro-pyridin-2-yl)-methanone (1h). Yield, 80%. ¹H NMR (CDCl₃): δ=7.55 (d, J=8.0 Hz, 2H), 7.87 (t, J=7.5 Hz, 2H), 8.04 (d, J=7.5 Hz, 2H). ¹³C NMR (CDCl₃): δ=124.1, 127.8, 139.5, 151.1, 153.7, 189.6. Anal. Calcd for C₁₁H₈Cl₂N₂O: C, 52.20; H, 2.39; N, 11.07%. Found: C, 51.97; H, 2.23; N, 11.16%.

4.2.3. (3-Chloro-pyridin-2-yl)-phenyl-methanol (2d).²¹ Yield, 70%. ¹H NMR (CDCl₃): δ=5.31 (br s, 1H), 6.03 (s, 1H), 7.24–7.39 (m, 6H), 6.69 (dd, J=7.9 and 1.3 Hz, 1H), 8.57 (dd, J=4.8 and 1.3 Hz, 1H). ¹³C NMR (CDCl₃): δ=72.1, 123.8, 126.9, 128.1, 128.4, 128.5, 130.1, 137.9, 141.7, 146.2, 157.5.

4.2.4. (4-Chloro-pyridin-2-yl)-phenyl-methanol (3d).²² Yield, 80%. ¹H NMR (CDCl₃): δ=4.93 (br s, 1H), 5.72 (s, 1H), 7.17–7.41 (m, 7H), 8.44 (dd, J=5.8 Hz, 1H). ¹³C NMR (CDCl₃): δ=75.2, 121.9, 124.2, 127.1, 128.7, 128.8, 142.5, 149.1, 163.2.

4.2.5. 2-Fluoro-6-methylsulfanyl-pyridine (4a).²³ Yield, 69%. ¹H NMR (CDCl₃): δ=2.55 (s, 3H), 6.59 (dd, J=6.9 and 0.9 Hz, 1H), 7.07 (dd, J=7.9 and 1.9 Hz, 1H), 7.59 (d, J=7.9 Hz, 1H). ¹³C NMR (CDCl₃): δ=12.5, 104.1, 118.5, 140.65, 157.5, 163.4.

4.2.6. (6-Fluoro-pyridin-2-yl)-phenyl-methanone (4c). Yield, 62%. ¹H NMR (CDCl₃): δ=7.15 (dd, J=8.1 and 1.2 Hz, 1H), 7.46–7.60 (m, 2H), 7.62 (q, J=6.9 Hz, 1H), 7.94–8.10 (m, 4H). ¹³C NMR (CDCl₃): δ=112.8, 113.4, 122.3, 128.1, 131.2, 133.5, 142.2, 142.4, 160.2, 164.1, 192.1 ppm. Anal. Calcd for C₁₄H₁₁FNO: C, 71.64; H, 4.01; N, 6.96%. Found: C, 71.35; H, 4.23; N, 6.69%.

4.3. General procedure for C-2 lithiation of 3-fluoro-pyridine 5

TMSCH₂Li (8 mL, 7.36 mmol) was added dropwise to a solution of 2-dimethylaminoethanol (328 mg, 3.68 mmol) in hexane (8 mL) at 0 °C. After 30 min of stirring, a solution of 5 (178 mg, 1.84 mmol) in hexane (8 mL) was then added dropwise. The solution was then stirred for 1 h at the same temperature and then treated at −78 °C with a solution of the appropriate electrophile (1.1 or 1.5 mmol for benzaldehyde) in THF (24 mL). The temperature was maintained at −78 °C for 1 h and at 0 °C for 30 min. Hydrolysis was then performed at this temperature with water (3 mL). The reaction medium was then extracted with ether (10 mL), the organic layer dried over MgSO₄ and evaporated under vacuum. The crude product was first subjected to GC analysis and purified if needed by eluting with hexane–AcOEt mixtures using a gradient from 95/5 to 90/10.

4.3.1. 3-Fluoro-2-methylsulfanyl-pyridine (5a). Yield, 87%. ¹H NMR (CDCl₃): δ=2.58 (s, 3H), 6.99 (m, 1H), 7.26 (dt, J=8.5 and 0.9 Hz, 1H), 8.28 (dd, J=5.9 and 1.5 Hz, 1H). ¹³C NMR (CDCl₃): δ=12.1, 119.7, 120.6, 120.9, 145.1, 148.3, 158.6 ppm. Anal. Calcd for C₉H₈FNS: C, 50.33; H, 4.22; N, 9.78%. Found: C, 50.47; H, 4.18; N, 9.52%.
4.3.2. (3-Fluoro-pyridin-2-yl)-phenyl-methanol (5b). Yield, 91%. 1H NMR (CDCl$_3$): $\delta = 5.35$ (s, 1H), 5.98 (s, 1H), 7.14–7.41 (m, 7H), 8.36 (dd, $J = 4.6$ and 1.5 Hz, 1H). 13C NMR (CDCl$_3$): $\delta = 70.3$, 123.5, 123.8, 124.2, 126.9, 127.9, 128.6, 142.3, 144.0, 149.1, 154.3, 158.4 ppm. Anal. Calcd for C$_{12}$H$_{10}$FNO: C, 70.93; H, 4.96; N, 6.89%. Found: C, 70.68; H, 4.83; N, 6.93%.

4.3.3. (3-Fluoro-pyridin-2-yl)-phenyl-methanone (5c). Yield, 87%. 1H NMR (CDCl$_3$): $\delta = 7.44–7.63$ (m, 5H), 7.92 (d, $J = 4.9$ Hz, 6H), 8.52 (dd, $J = 5.7$ and 1.4 Hz, 1H). 13C NMR (CDCl$_3$): $\delta = 124.7$, 125.1, 127.0, 128.5, 130.5, 133.9, 135.9, 144.9, 156.1, 160.2, 191.1 ppm. Anal. Calcd for C$_{12}$H$_{8}$FNO: C, 71.64; H, 4.01; N, 6.96%. Found: C, 71.57; H, 4.10; N, 7.04%.

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References and notes

17. 2-Fluoropyridine underwent nucleophilic addition by n-BuLi–TMEDA even at $-40^\circ$C, see Marsais, F.; Granger, P.; Quéguiner, G. J. Org. Chem. 1981, 46, 4494–4497.