

ORTHO-DIRECTED LITHIATION STUDIES OF 4-CHLORO-PICOLINANILIDE : INTRODUCTION OF FUNCTIONAL GROUPS AT C-3 AND THEIR ELABORATION TO CHAIN EXTENDED DERIVATIVES VIA CARBON-CARBON BOND FORMATION

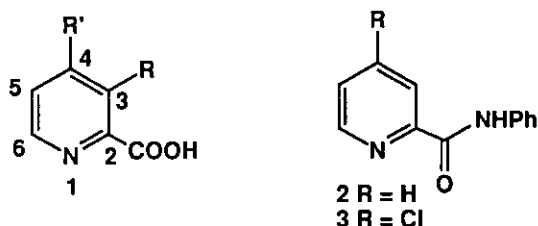
Marcus V. Nora de Souza and Robert H. Dodd*

Institut de Chimie des Substances Naturelles, Centre National de la Recherche Scientifique, 91198 Gif-sur-Yvette Cedex, France

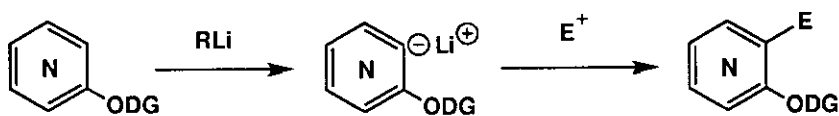
Abstract - An improved synthesis of 4-chloropicolinanilide (**3**) is presented. Treatment of **3** with lithium diisopropylamide (LDA) in THF, followed by addition of an electrophile (methyl iodide, iodine, carbon dioxide, trimethylstannyl chloride), gave exclusively the products of C-3 substitution (respectively, the 3-methyl-, 3-iodo, 3-carboxylic acid and 3-trimethylstannyl derivatives of **3**). Further treatment of the 3-methyl derivative (**7**) with carbon dioxide or ethyl bromoacetate produced the one- and two-carbon homologues of 4-chloroquinolinanilide (**8** and **9**, respectively). The palladium acetate-catalyzed reaction of 4-chloro-3-iodopicolinanilide (**10**) with various unsaturated derivatives (trimethylsilylacetylene, tri-n-butyl(vinyl)tin, styrene, acrylonitrile, methyl acrylate) afforded the corresponding C-3 cross-coupled products in 70-80% yield. Reaction of **10** with allyl alkoxide, followed by treatment of the product (**17**) with tri-n-butyltin hydride, provided the 2-methylfuro[3,2-c]pyridine derivative (**18**) in 85% yield.

As part of a research program aimed at developing new agents acting on the central nervous system, we have been interested in synthesizing trifunctionalized derivatives of pyridine, in particular, those

belonging to the family of 3,4-disubstituted derivatives of picolinic acid (**1**). Over the past two decades, ortho-directed metalation/electrophilic substitution of aromatic nuclei has so developed that application of this type of technology to π -deficient substrates, of which pyridine is a prime example, is now well documented (Scheme 1).¹ In this regard, Epszajn and coworkers have described many of the reaction



conditions necessary for efficient ortho-metalation of picolinamide substrates.^{2,3} In particular, they have shown that, among the amide derivatives of picolinic acid, the anilide (**2**) represents one of the most efficient ortho-directing groups in this series. Thus, in addition to ortho-lithiation studies on picolinanilide (**2**) itself,^{3,4} successful utilization of the 4-chloro derivative of **2**, i.e. **3** for this type of



ODG = ortho-directing group

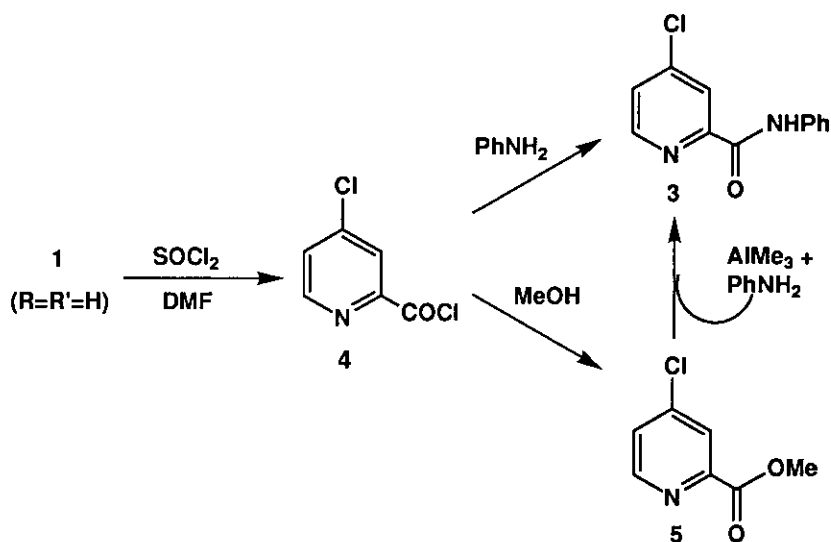
Scheme 1

reaction has allowed introduction at C-3 of methyl, formyl, trimethylsilyl and hydroxyethyl groups.⁵ Compound (**3**) thus appeared to us to be a good starting point for the synthesis of trifunctionalized pyridine derivatives, our stated objective. In this paper, then, we extend the work of Epszajn and coworkers by preparing, *via* ortho-directed metalation, derivatives of **3** having functional groups at C-3 which are in turn used to introduce more complex substituents at this position. In addition, an improved procedure for the preparation of the starting substrate (**3**) is presented.

RESULTS AND DISCUSSION

The starting material for our studies, 4-chloropicolinanilide (**3**) has been previously synthesized in six steps *via* the 4-nitro-*N*-oxide derivative of picolinic acid.⁵ We thus sought a more efficient preparation of

compound (3). Recently, two separate reports have described improved, high yielding procedures for preparation of methyl 4-chloropicolinate (5) by simply refluxing picolinic acid (1, R = R' = H) in thionyl chloride in the presence of either DMF⁶ or water⁷ followed by treatment with methanol (Scheme 2). Since these reactions presumably proceed *via* the acid chloride (4), application of this procedure to the

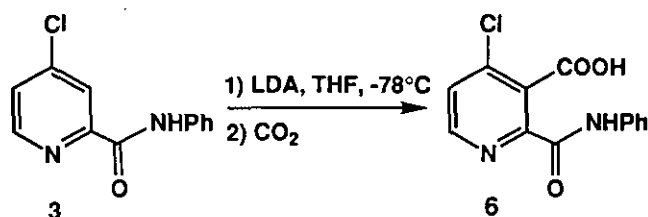


Scheme 2

preparation of anilide (3) appeared to be a viable alternative to the *N*-oxide route. Thus, reaction of acid chloride (4), prepared from picolinic acid using the thionyl chloride/DMF methodology, with aniline provided the desired anilide (3) in 75% yield. Some discrepancies in the melting points and ¹H-NMR data of 3 prepared by this method and that prepared by the *N*-oxide route⁵ encouraged us to confirm the identity of 3 by preparing this compound from the known methyl ester (5). Thus, reaction of trimethylaluminum, aniline with ester (5) also afforded anilide (3), identical in all respects with the compound prepared directly from the acid chloride (4).

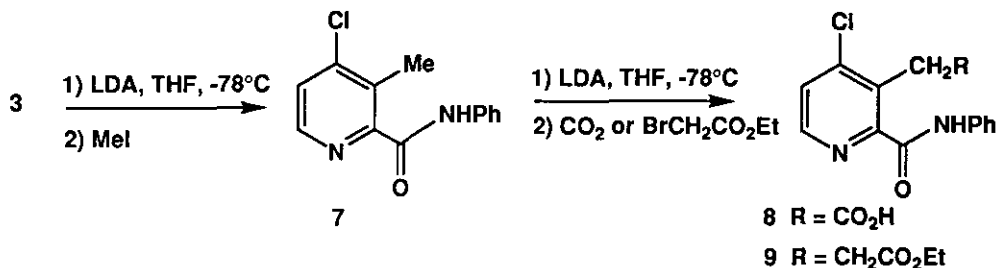
We next studied the introduction of functional groups regiospecifically at C-3 of compound (3) using ortho-metalation techniques. Such functional groups would ideally permit further derivatization to more complex picolinanilides. Although an obvious candidate for such functionalization would be the formyl group, Epszajn and coworkers have shown that while ortho-lithiation of compound (3) using *n*-butyllithium followed by reaction with DMF effectively leads to selective formylation at C-3, this formyl group undergoes spontaneous intramolecular attack by the adjacent amide NH rendering it unavailable for

further transformation.⁵ An alternative to the formyl group is the carboxylic acid, which can also be advantageously used to attach additional substituents. Thus, ortho-lithiation of **3** using LDA in THF at -78°C followed by addition of carbon dioxide gave an excellent yield of the 3-carboxylic acid (**6**) (Scheme 3). The latter, formally a derivative of 4-chloroquinolinic acid, has previously only been accessible by way of permanganate oxidation of 4-chloroquinoline.⁸



Scheme 3

The methyl group is not, *a priori*, generally considered to be a functional group. In the form of ortho-toluamides, though, the methyl group can be efficiently deprotonated with lithiated bases and the resulting anions reacted with electrophiles to achieve chain extensions or ring annelations (e.g., by reaction with imines).⁹ Heteroaromatic examples of these types of reactions are somewhat rarer.¹⁰ We thus attempted to obtain the one-carbon and two-carbon homologues of the quinolinic acid derivative (**6**) *via* this route. Thus, sequential reaction of **3** with LDA and then with excess methyl iodide afforded the known 4-chloro-3-methylpicolinanilide (**7**)⁵ (Scheme 4). In contrast to the reported preparation of **7** from **3** using *n*-butyllithium as the base, in which significant quantities of the 3,*N*-dimethylated derivative were also formed, we observed exclusively formation of the monomethylated compound (**7**) using LDA as

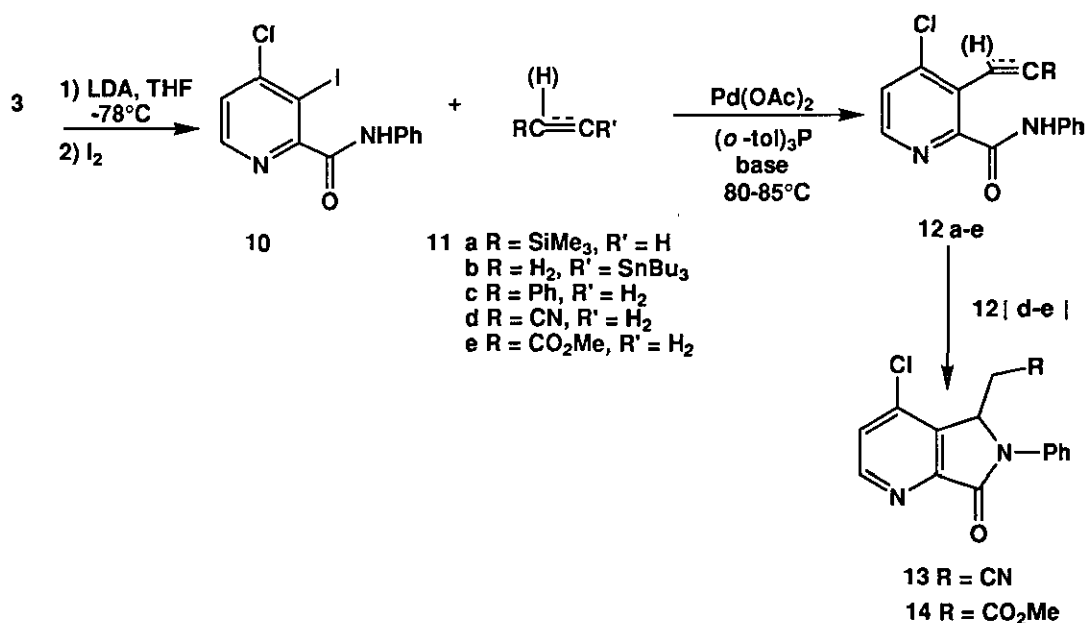


Scheme 4

base. Further treatment of the 3-methyl derivative (**7**) with LDA, followed by reaction with carbon dioxide or with ethyl bromoacetate, gave the carboxylic acid derivatives (**8** and **9**), respectively. This

technique thus represents a very convenient method of preparing the upper homologues of quinolinic acid.

The ability to introduce an iodide atom on an aromatic nucleus makes available the rich synthetic possibilities offered by palladium catalyzed C-C coupling reactions with unsaturated compounds. While preparation of 3-iodopicolinanilide *via* ortho-metalation/iodination of picolinanilide has recently been reported,¹¹ that of the 4-chloro-3-iodo analogue (**10**) (Scheme 5) has not. This compound was thus efficiently synthesized by reaction of the LDA-promoted anion of **3** with iodine. Coupling of **10** with

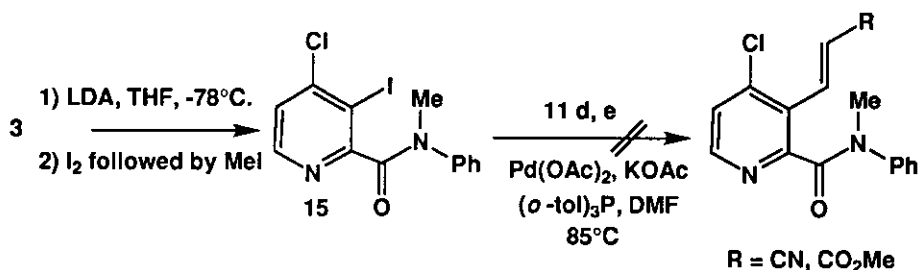


Scheme 5

various unsaturated derivatives in the presence of catalytic palladium acetate and tri-*o*-tolylphosphine was then studied. Thus, iodo compound (**10**) reacted with (trimethylsilyl)acetylene (**11a**) in triethylamine at 85 °C to give the 3-acetylenepicolinanilide derivative (**12a**) in 56% yield. Similarly, palladium-catalyzed coupling of **10** with tributyl(vinyl)tin (**11b**) or with styrene (**11c**) (using in both cases acetonitrile as solvent) gave the 3-ethylene derivatives (**12b** and **12c**), respectively, in approximately 80% yield. Attempts to couple **10** with acrylonitrile (**11d**) or with methyl acrylate (**11e**) using these reaction conditions failed. However, when the reactions were run using DMF as solvent and potassium acetate as base (instead of triethylamine), good yields (~ 75%) of the corresponding coupled products were obtained. The absence of vinylic protons and of the amide NH in the ¹H-NMR spectra of the isolated

reaction products indicated that cyclization of the initially formed cyano- and carboxyethylene derivatives (**12d** and **12e**) to the pyrrolopyridine compounds (**13** and **14**), respectively, had occurred.

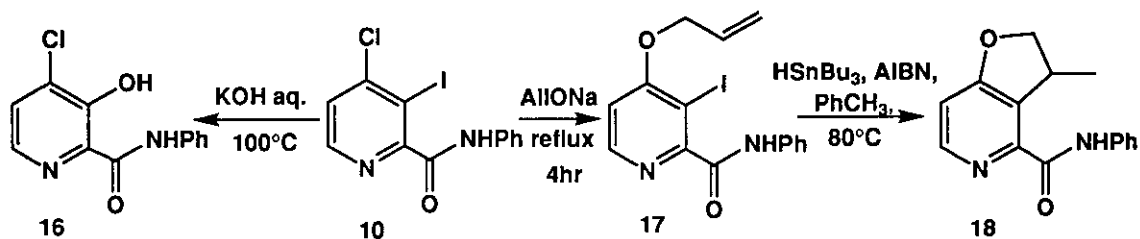
In an effort to circumvent this cyclization reaction, the *N*-methyl derivative of the 3-iodo substrate (**15**) was prepared (Scheme 6). This was conveniently achieved by iodinating compound (**3**) using LDA and iodine as before, followed by quenching of the reaction mixture with excess methyl iodide.



Scheme 6

Unfortunately, the reaction conditions which allowed coupling of compound (**10**) with acrylonitrile and methyl acrylate (Pd(OAc)₂, P(*o*-tol)₃, DMF, KOAc, 85 °C) failed in the case of the *N*-methyl analogue (**15**), possibly due to the increased steric bulk presented by the supplementary methyl group.

Two more useful transformations of the 3-iodopicolinanilide derivative (**10**) are shown in Scheme 7. Firstly, refluxing **10** in 50% aqueous potassium hydroxide for 4 h led to exclusive formation of the 4-chloro-3-hydroxy analogue (**16**). This represents a further example of selective functional group introduction at C-3. Secondly, the iodide atom of **10** can also serve as a source of free radicals for

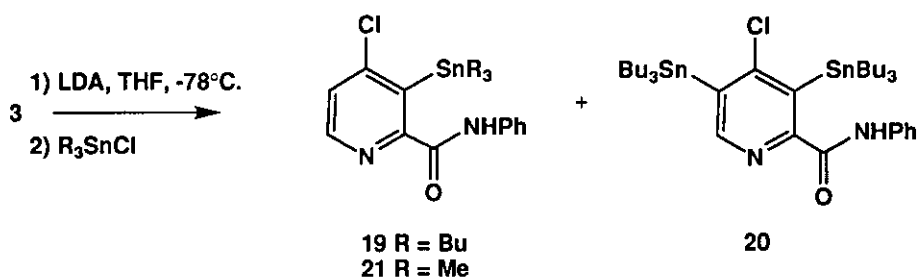


Scheme 7

cyclization reactions. Thus, refluxing **10** in THF in the presence of sodium allyl alkoxide led to displacement of the 4-chloro substituent, giving allyl ether (**17**). Then, treatment of **17** with tributyltin hydride and AIBN in toluene at 80 °C resulted in formation of the 3-methylfuro[2,3-*b*]pyridine derivative (**18**) in

85% yield. This free radical pathway to furopyridines represents an interesting alternative to a recently published methodology for the synthesis of this class of compounds which relied on palladium-catalyzed formation of the furan ring from substrates analogous to **17**.¹²

Finally, in order to further increase the span of synthetically useful functional groups at C-3 of 4-chloropicolinanilide (**3**), we studied the introduction of trialkylstannyl groups at this position *via* ortho-metalation. Such groups would, in particular, give access to the highly versatile Stille-type transition-metal cross coupling reactions.¹³ Treatment of **3** with LDA and then with tri-*n*-butylstannyl chloride gave, as the major product, the 3-stannyl derivative (**19**) (Scheme 8). A small quantity (5%) of the 3,5-distannyl compound (**20**) was also isolated from the reaction mixture. The formation of this distannylated by-product can be rationalized by the fact that the chloride atom at C-4 of **3** is also a good ortho-



Scheme 8

director^{1b} and that the C-5 position is much less sterically hindered than the C-3 position. This is supported by the finding that when the sterically less demanding trimethylstannyl chloride was used as the electrophile in the ortho-metalation reaction, only the monostannyl derivative (**21**) was formed. Our attempts to use monostannylated derivatives (**19** and **21**) for palladium-catalyzed coupling reactions with halogenated aromatics using standard conditions have so far been unsuccessful. Again, as in the case of compound (**19**), steric factors would appear to be the primary reason for this failure.

In conclusion, we have shown in this paper that 4-chloropicolinanilide (**3**), for which an improved preparative route is also presented, is a useful substrate for the introduction, *via* ortho-directed metalation, of functional groups at C-3 (carboxylic acid, methyl, iodo) which can, in turn, serve for further synthetic modifications at this position. The methyl group (i.e. **7**), in particular, permits, *via* LDA-promoted proton abstraction, preparation of one-carbon and two-carbon homologues (**8** and **9**, respectively), of quinolinic acid derivatives. The iodo function of **10**, on the other hand, allows access to

both palladium-catalyzed C-C coupling reactions with unsaturated substrates as well as free-radical type cyclization reactions. The failure of the *N*-methylpicolinanilide (**15**) as well as the 3-stannyl derivatives (**19** and **21**) to undergo palladium-catalyzed coupling reactions points to certain steric restrictions to the synthetic exploitation of these substrates. The study of this problem is currently being pursued.

EXPERIMENTAL

General - Melting points were determined on a Büchi apparatus and are uncorrected. IR spectra of samples were obtained either as films or as KBr pellets with a Nicolet 205 FT-IR spectrophotometer. ¹H-NMR and ¹³C-NMR spectra were determined on Bruker 250 MHz or 300 MHz instruments. Chemical shifts are given as δ values with reference to Me₄Si as internal standard. Electron impact and chemical ionization MS were recorded on an AEI MS-50 and AEI MS-9 spectrometer, respectively. High resolution MS were obtained using a Kratos MS-80 spectrometer. Thin-layer chromatography was performed on Merck silica gel 60 plates with fluorescent indicator. The plates were visualized with UV light (254 nm). All column chromatography was conducted on Merck 60 silica gel (230-400 mesh) at medium pressure (200 mbar). Methyl iodide and tri-*n*-butylstannyl chloride were distilled before use. Elemental analyses were performed at the ICSN, CNRS, Gif-sur-Yvette, France.

4-Chloropicolinanilide (3) - To thionyl chloride (150 mL) held at 45 °C under argon was added dropwise DMF (5 mL, 0.06 mol) and then, in small portions, picolinic acid (50 g, 0.41 mol). The mixture was stirred at 45 °C for 15 min after completion of the additions (SO₂ is evolved) and afterwards for 24 h at 80 °C. The reaction mixture was cooled and concentrated to dryness under reduced pressure, residual traces of thionyl chloride being removed by codistillation with toluene *in vacuo*. The residue was dissolved in dichloromethane (50 mL) and this solution was added dropwise over 30 min to a solution of aniline (133 mL) in dichloromethane (100 mL) held at 0 °C. After completion of the addition, the reaction mixture was allowed to warm to rt and stirring was continued for a further 3 h. The solution was washed with water (100 mL) and the aqueous layer was extracted with dichloromethane (50 mL). The organic phases were combined, dried over sodium sulfate and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate-heptane 2:8) affording compound (**3**) as a tan solid (70 g, 75%). Crystallization of this material from heptane gave colorless plates, mp 86 °C (lit.,⁵ mp 92-94 °C). IR (film) 3337, 1680 cm⁻¹. ¹H-NMR (250 MHz, CDCl₃) δ : 7.16 (t,

1H, J = 8.0 Hz, H-4'), 7.38 (t, 2H, J = 8.0 Hz, H-3'), 7.45 (dd, 1H, J = 2.1 and 5.2 Hz, H-5), 7.75 (d, 2H, J = 8.0 Hz, H-2'), 8.26 (d, 1H, J = 2.1 Hz, H-3), 8.48 (d, 1H, J = 5.2 Hz, H-6), 9.90 (s, 1H, exchangeable with D₂O, NH) ; ¹³C-NMR (62.5 MHz, CDCl₃) δ : 120.4, 123.7, 125.3, 127.3, 129.8, 138.1, 146.9, 149.5, 151.9, 161.4. HRCIMS calcd for C₁₂H₁₀N₂O ³⁵Cl m/z 233.0481, found 233.0485 ; calcd for C₁₂H₁₀N₂O ³⁷Cl m/z 235.0452, found 235.0452. Anal. Calcd for C₁₂H₉N₂OCl : C, 62.06 ; H, 3.91 ; N, 12.07 ; Cl, 15.07. Found : C, 61.93 ; H, 4.18 ; N, 11.81 ; Cl, 15.29.

4-Chloropicolinanilide (3) from 5 - To anhydrous dichloromethane (40 mL) held at -10 °C under argon was added dropwise a solution of trimethylaluminium in heptane (2.63 mL of a 2.0 M solution ; 5.26 mmol). After 10 min, aniline (0.16 mL, 1.72 mmol) was added dropwise and the reaction mixture was allowed to stir at -10 °C for 20 min and then at rt for 15 min. A solution of compound (5) (0.3 g, 1.72 mmol) in dichloromethane (5 mL) was added and the reaction mixture was refluxed for 24 h. After cooling to rt, the mixture was extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, washed with water (30 mL) and dried over sodium sulfate. Removal of the solvents under reduced pressure left a crude product which was purified by column chromatography on silica gel (ethyl acetate-heptane 1:9) affording pure 3 in 77% yield (310 mg). The physical and spectral data for compound (3) prepared in this manner were identical to the compound prepared directly from 1 (see above).

4-Chloropicolinanilide 3-carboxylic acid (6) - A solution of compound (3) (1.05 g, 4.52 mmol) in anhydrous THF (100 mL) was treated dropwise at -78 °C under argon with a solution of LDA in THF (4.72 mL of a 2.0 M solution ; 9.44 mmol). After completion of the addition (10 min), the reaction mixture was stirred for 90 min at -78 °C, excess dry ice was added and stirring was continued for 20 min. The solution was warmed to 0 °C, saturated aqueous ammonium chloride (50 mL) was added and the mixture was extracted with ethyl acetate (3 x 50 mL). The organic extracts were combined, washed with water (30 mL) and dried over sodium sulfate. Removal of the solvents under reduced pressure left compound (6) as a solid which was suspended in ethyl acetate and collected by filtration (500 mg, 42%), mp 165-167 °C (ethyl acetate). IR (film) 3317, 1716, 1683 cm⁻¹. EIMS m/z 276 (M⁺, ³⁵Cl isotope), 278 (M⁺, ³⁷Cl isotope). ¹H-NMR (250 MHz, MeOH-d₄) δ : 7.12 (t, 1H, J = 7.4 Hz, H-4'), 7.34 (t, 2H, J = 7.4 Hz, H-3'), 7.70 (m, 3H, H-5, H-2'), 8.05 (d, 1H, J = 5.2 Hz, H-6). ¹³C-NMR (75 MHz, MeOH-d₄) δ :

121.6, 125.8, 128.3, 129.3, 132.5, 138.8, 143.6, 150.4, 162.4, 168.6, 177.5. Anal. Calcd for $C_{13}H_9N_2O_3Cl$: C, 56.43; H, 3.28; N, 10.14. Found: C, 56.45; H, 3.55; N, 9.86.

4-Chloro-3-methylpicolinanilide (7) - A solution of compound (**3**) (1.05 g, 4.52 mmol) in anhydrous THF (75 mL) was treated dropwise at $-78\text{ }^\circ\text{C}$ under argon with a solution of LDA in THF (4.72 mL of a 2.0 M solution; 9.44 mmol). After completion of the addition (10 min), the reaction mixture was stirred for 90 min at $-78\text{ }^\circ\text{C}$, methyl iodide (1.73 mL, 27.1 mmol) was added dropwise and stirring was continued for 90 min. The solution was warmed to $0\text{ }^\circ\text{C}$, aqueous sodium hydrogen sulfite (20 mL of a 37.5% solution) was added, and the mixture was extracted with ethyl acetate (3 x 100 mL). The organic extracts were combined, washed with water (40 mL) and dried over sodium sulfate. Removal of the solvents under reduced pressure left a residue which was purified by column chromatography on silica gel (ethyl acetate-heptane 1:1) affording compound (**7**) as a white solid (0.74 g, 67%), mp $80\text{ }^\circ\text{C}$ (heptane) (lit.,⁵ mp $84\text{--}86\text{ }^\circ\text{C}$). IR (film) 3333, 1686 cm^{-1} . EIMS m/z 247 (MH^+ , ^{35}Cl isotope), 249 (MH^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ : 2.89 (s, 3H, CH_3), 7.16 (t, 1H, $J = 8.2\text{ Hz}$, H-4'), 7.33-7.43 (m, 3H, H-5, H-3'), 7.71 (d, 2H, $J = 8.2\text{ Hz}$, H-2'), 8.26 (d, 1H, $J = 4.9\text{ Hz}$, H-6), 10.07 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3) δ : 15.6, 119.5, 122.7, 124.1, 126.6, 128.8, 134.2, 137.7, 145.0, 148.7, 162.7. Anal. Calcd for $C_{13}H_{11}N_2\text{OCl}$: C, 63.29; H, 4.46; N, 11.36. Found: C, 63.55; H, 4.84; N, 11.03.

3-Carboxymethyl-4-chloropicolinanilide (8) - Following the same procedure as for the preparation of **6**, compound (**7**) (0.4 g, 1.62 mmol) in THF (20 mL) was treated with LDA (1.8 mL of a 2.0 M solution in THF; 3.6 mmol) and, after 15 min, with excess dry ice. At the end of the reaction period (15 min), the solution was worked up as before, affording compound (**8**) as a white solid (0.38 g, 81%), mp $157\text{--}160\text{ }^\circ\text{C}$ (ethyl acetate). IR (film) 3338, 1698, 1675 cm^{-1} . EIMS m/z 290 (M^+ , ^{35}Cl isotope), 292 (M^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (300 MHz, DMSO-d_6) δ : 4.51 (s, 2H, CH_2), 7.12 (t, 1H, $J = 7.1\text{ Hz}$, H-4'), 7.36 (dd, 2H, $J = 7.7$ and 7.1 Hz , H-3'), 7.75 (d, 1H, $J = 4.9\text{ Hz}$, H-5), 7.85 (d, 2H, $J = 7.7\text{ Hz}$, H-2'), 8.55 (d, 1H, $J = 4.9\text{ Hz}$, H-6), 10.37 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (75 MHz, DMSO-d_6) δ : 35.7, 121.4, 121.5, 125.7, 128.6, 130.4, 132.3, 140.0, 148.9, 152.0, 164.7, 171.7. Anal. Calcd for $C_{14}H_{11}N_2\text{O}_3\text{Cl} \cdot 0.25\text{ CH}_3\text{CO}_2\text{C}_2\text{H}_5$: C, 57.61; H, 4.19; N, 8.96. Found: C, 57.41; H, 4.35; N, 8.76.

4-Chloro-3-ethoxycarbonylethylpicolinanilide (9) - Following the same procedure as for the preparation of **6**, compound (**7**) (100 mg, 0.41 mmol) in THF (10 mL) was treated with LDA (0.45 mL of a 2.0 M solution in THF ; 0.9 mmol) and, after 15 min, with ethyl bromoacetate (0.32 mL, 2.0 mmol). After 15 min at -78 °C, the reaction mixture was worked up as before. The crude product was purified by chromatography on silica gel (ethyl acetate-heptane 8:2) affording compound (**9**) as an oil in 80% yield (110 mg). IR (film) 3330, 1732, 1684 cm^{-1} . CIMS m/z 333 (MH^+ , ^{35}Cl isotope), 335 (MH^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ : 1.26 (t, 3H, $J = 7.7$ Hz, CH_2CH_3), 2.74 (t, 2H, $J = 8.5$ Hz, ArCH_2), 3.71 (t, 2H, $J = 8.5$ Hz, CH_2CO), 4.15 (q, 1H, $J = 7.7$ Hz, CH_2CH_3), 7.15 (t, 1H, $J = 6.4$ Hz, H-4'), 7.38 (dd, 2H, $J = 6.4$ and 8.0 Hz, H-3'), 7.51 (d, 1H, $J = 5.1$ Hz, H-5), 7.70 (d, 2H, $J = 8.0$ Hz, H-2'), 8.38 (d, 1H, $J = 5.1$ Hz, H-6), 10.08 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3) δ : 14.3, 24.7, 33.5, 53.5, 120.0, 124.6, 127.3, 129.2, 136.8, 137.8, 146.1, 147.7, 149.2, 162.5, 172.7. Anal. Calcd for $\text{C}_{17}\text{H}_{17}\text{N}_2\text{O}_3\text{Cl}$: C, 61.36 ; H, 5.15 ; N, 8.12. Found : C, 60.98 ; H, 5.21 ; N, 8.24.

4-Chloro-3-iodopicolinanilide (10) - Following the same procedure as for the preparation of compound (**7**), compound (**3**) (2.0 g, 8.6 mmol) in THF (100 mL) was treated at -78 °C with LDA (9.44 mL of a 2.0 M solution ; 18.9 mmol) and, after 90 min, with a solution of iodine (6.57 g, 25.9 mmol) in THF (10 mL). After 90 min, the reaction mixture was worked up as before and the crude product was purified by chromatography on silica gel (ethyl acetate-heptane, 3:7) affording, in addition to a small quantity of starting material (**3**) (80 mg, 8%), the title compound (**10**) (2.84 g, 88%) as a white solid, mp 152-154 °C (ethanol). IR (film) 3365, 1687 cm^{-1} . CIMS m/z 359 (MH^+ , ^{35}Cl isotope), 361 (MH^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ : 7.16 (t, 1H, $J = 7.0$ Hz, H-4'), 7.34 (dd, 2H, $J = 7.0$ and 5.0 Hz, H-3'), 7.54 (d, 1H, $J = 5.0$ Hz, H-5), 7.72 (dd, 2H, $J = 5.0$ and 0.6 Hz, H-2'), 8.38 (d, 1H, $J = 5.0$ Hz, H-6), 9.81 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3) δ : 95.7, 120.0, 124.7, 126.2, 129.1, 137.7, 147.4, 152.1, 152.9, 161.3. Anal. Calcd for $\text{C}_{12}\text{H}_8\text{N}_2\text{OClI}$: C, 40.23 ; H, 2.25 ; N, 7.82. Found : C, 40.29 ; H, 2.21 ; N, 7.68.

General procedure for the palladium-catalyzed coupling of iodopyridine derivative (3) with olefins - To a solution of compound (**3**) (0.2 g, 0.55 mmol) and the olefin (1.67-2.8 mmol) in acetonitrile (20 mL), DMF (5 mL) or triethylamine (20 mL) was added tri-*o*-tolylphosphine (0.33 mmol), the base (1.6 mmol of triethylamine or potassium acetate) and palladium acetate (0.16 mmol). The solution was

degassed by bubbling argon for 15 min and then heated at 85 °C under argon for 12 h. The reaction mixture was cooled to rt, diluted with ethyl acetate (50 mL) and washed with saturated aqueous NaCl solution (20 mL) and with water (20 mL). The organic phase was dried over sodium sulfate, the solvents were removed under reduced pressure and the residue was purified by column chromatography on silica gel. Base choice, reaction times, chromatography eluents and product yields are given below for each example.

4-Chloro-3-trimethylsilylacetylenepicolinanilide (12a) - Following the general procedure described above, the title compound was prepared from **3** and (trimethylsilyl)acetylene (**11a**) (0.38 mL, 2.8 mmol) using triethylamine (20 mL) as both solvent and base. Purification of the crude product by chromatography (ethyl acetate-heptane 3:7) afforded **12a** as a white solid in 56% yield (100 mg), mp 68-70 °C (ethyl ether). IR (film) 3347, 2300, 1694 cm^{-1} . CIMS m/z 329 (MH^+ , ^{35}Cl isotope), 331 (MH^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ : -0.32 (s, 9H, $\text{Si}(\text{CH}_3)_3$), 7.13 (t, 1H, $J = 7.4$ Hz, H-4'), 7.35 (dd, 2H, $J = 8.3$ and 7.4 Hz, H-3'), 7.56 (d, 1H, $J = 5.0$ Hz, H-5), 7.75 (dd, 2H, $J = 8.3$ and 0.8 Hz, H-2'), 8.38 (d, 1H, $J = 5.0$ Hz, H-6), 9.83 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3) δ : -1.5, 29.8, 53.2, 97.1, 119.9, 124.4, 126.3, 129.1, 133.4, 145.9, 150.0, 151.8, 160.4. HRCIMS calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}^{35}\text{ClSi}$ m/z 329.0877 found 329.0876; calcd for $\text{C}_{17}\text{H}_{18}\text{N}_2\text{O}^{37}\text{ClSi}$ m/z 331.0847 found 331.0861.

4-Chloro-3-vinylpicolinanilide (12b) - Following the general procedure described above, the title compound was prepared from **3** and tributyl(vinyl)tin (**11b**) (0.49 mL, 1.67 mmol) using acetonitrile (20 mL) as the solvent and triethylamine (0.2 mL, 1.67 mmol) as the base. Purification of the crude product by chromatography (ethyl acetate-heptane 2:8) afforded compound (**12b**) as an oil in 81% yield (113 mg). IR (film) 3328, 1677, 1600 cm^{-1} . CIMS m/z 259 (MH^+ , ^{35}Cl isotope), 261 (MH^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (200 MHz, CDCl_3) δ : 5.64 (dd, 1H, $J = 1.1$ and 17.9 Hz, $\text{CH} = \text{CH}_a$), 5.88 (dd, 1H, $J = 1.1$ and 12.0 Hz, $\text{CH} = \text{CH}_b$), 7.24-7.43 (m, 2H, $\text{HC} = \text{CH}_2$, H-4'), 7.49 (t, 2H, $J = 8.0$ Hz, H-3'), 7.68 (d, 1H, $J = 5.0$ Hz, H-5), 7.85 (d, 2H, $J = 8.0$ Hz, H-2'), 8.38 (d, 1H, $J = 5.0$ Hz, H-6), 10.00 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (50 MHz, CDCl_3) δ : 119.9, 121.3, 124.5, 127.7, 130.6, 131.6, 134.8, 137.8, 145.5, 146.3, 149.0, 162.2. Anal. Calcd for $\text{C}_{14}\text{H}_{11}\text{N}_2\text{OCl}$.0.12 C_7H_{16} : C, 65.84; H, 4.77; N, 10.35. Found: C, 65.47; H, 4.75; N, 9.96.

E-4-Chloro-3-(2-styryl)picolinanilide (12c) - Following the general procedure described above, the title compound was prepared from **3** and styrene (**11c**) (0.32 mL, 2.8 mmol) using acetonitrile (20 mL) as the solvent and triethylamine (0.2 mL, 1.67 mmol) as the base. Purification of the crude product by chromatography (ethyl acetate-heptane 2:8) afforded compound (**12c**) as a white powder in 78% yield (145 mg), mp 126-128 °C (ethanol). IR (film) 3328, 1683, 1600 cm^{-1} . CIMS m/z 335 (MH^+ , ^{35}Cl isotope), 337 (MH^+ , ^{37}Cl isotope). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 6.91 (d, 1H, $J = 16.0$ Hz, $\text{CH} = \text{CHPh}$), 7.15 (t, 1H, $J = 7.2$ Hz, H-4'), 7.27-7.42 (m, 5H, ArH), 7.60 (m, 3H, ArH, H-5), 7.75 (m, 3H, ArH, $\text{HC} = \text{CHPh}$), 8.39 (d, 1H, $J = 5.0$ Hz, H-6), 10.03 (s, 1H, NH). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 120.5, 122.7, 125.0, 127.6, 128.3, 128.7, 129.3, 129.6, 134.9, 136.5, 137.5, 138.4, 146.5, 148.6, 162.8. Anal. Calcd for $\text{C}_{20}\text{H}_{15}\text{N}_2\text{OCl}$. $0.35\text{C}_2\text{H}_5\text{OH}$: C, 70.85 ; H, 4.88 ; N, 7.98. Found : C, 70.86 ; H, 5.21 ; N, 7.82.

(R,S)-7-Chloro-1-cyanomethyl-2-phenylpyrrolo[3,4-b]pyridine-3(1H)-one (13) - Following the general procedure described above, the title compound was prepared from **3** and acrylonitrile (**11d**) (0.19 mL, 2.8 mmol) using DMF (5 mL) as the solvent and potassium acetate (160 mg, 1.67 mmol) as the base. The crude product was purified by chromatography (ethyl acetate), affording compound (**13**) as an oil in 72% yield (114 mg). IR (film) 2250, 1718 cm^{-1} . $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ : 3.08 (dd, 1H, $J = 3.0$ and 17.3 Hz, CH_aCN), 3.45 (dd, 1H, $J = 3.0$ and 17.3 Hz, CH_bCN), 5.46 (t, 1H, $J = 3.0$ Hz, CHCH_2), 7.38-7.60 (m, 6H, ArH, H-6), 8.83 (d, 1H, $J = 5.2$ Hz, H-5). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 19.6, 54.8, 113.8, 124.6, 126.8, 127.8, 130.1, 134.0, 134.6, 140.2, 153.7, 164.0. HRCIMS calcd for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}^{35}\text{Cl}$ m/z 284.0591 found 284.0603 ; calcd for $\text{C}_{15}\text{H}_{11}\text{N}_3\text{O}^{37}\text{Cl}$ m/z 286.0561 found 286.0558.

(R,S)-7-Chloro-1-methoxycarbonylmethyl-2-phenylpyrrolo[3,4-b]pyridin-3(1H)-one (14) - Following the general procedure described above, the title compound was prepared from **3** and methyl acrylate (**11e**) (0.25 mL, 2.8 mmol) using DMF (5 mL) as the solvent and potassium acetate (160 mg, 1.67 mmol) as the base. The crude product was purified by chromatography (ethyl acetate-heptane 9:1) affording compound (**14**) as an oil in 75% yield (132 mg). IR (film) 1736, 1717 cm^{-1} . $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 3.00 (d, 2H, $J = 4.0$ Hz, CH_2CO_2), 3.38 (s, 3H, CH_3), 5.59 (t, 1H, $J = 4.0$ Hz, CHCH_2), 7.26 (t, 1H, $J = 7.2$ Hz, H-4'), 7.40-7.53 (m, 5H, ArH, H-6), 8.69 (d, 1H, $J = 5.0$ Hz, H-5). $^{13}\text{C-NMR}$ (75 MHz, CDCl_3) δ : 34.2, 52.0, 55.7, 124.6, 126.4, 127.0, 135.5, 135.7, 139.9, 152.0, 152.5, 164.0, 169.2. HREIMS calcd for

$C_{16}H_{14}N_2O_3^{35}Cl$ m/z 317.0693 found 317.0692 ; calcd for $C_{16}H_{14}N_2O_3^{37}Cl$ m/z 319.0663 found 319.0684.

4-Chloro-3-iodo-N-methylpicolinanilide (15) - Following the same procedure as for the preparation of **7**, compound (**3**) (2 g, 8.62 mmol) was treated successively, at $-78\text{ }^\circ\text{C}$, with LDA (9.44 mL of a 2 M solution in THF ; 18.9 mmol) and, after 90 min, with a solution of iodine (6.57 g, 25.9 mmol) in THF (10 mL). After 90 min of additional stirring, the reaction mixture was warmed to $0\text{ }^\circ\text{C}$, methyl iodide (20 mL) was added dropwise and stirring was continued for 12 h at rt. Aqueous sodium hydrogen sulfite (20 mL of a 37.5% solution) was then added and, after the usual work-up, the crude reaction product was purified by column chromatography on silica gel, providing compound (**15**) (2.23 g, 74%) as a white powder, mp $143\text{-}145\text{ }^\circ\text{C}$ (ethyl acetate) . IR (film) 1650 cm^{-1} . CIMS m/z 373 (MH^+ , ^{35}Cl isotope), 375 (MH^+ , ^{37}Cl isotope). 1H -NMR (250 MHz, $CDCl_3$) δ : 3.69 (s, 3H, NCH_3), 7.25-7.65 (m, 6H, PhH, H-5), 8.38 (d, 1H, $J = 5.2\text{ Hz}$, H-6). ^{13}C -NMR (62.5 MHz, $CDCl_3$) δ : 37.0, 95.8, 123.6, 126.9, 127.5, 128.9, 142.1, 148.5, 149.1, 161.1, 167.7. Anal. Calcd for $C_{13}H_{10}N_2OCl$. 0.5 H_2O : C, 40.88 ; H, 2.88 ; N, 7.34. Found : C, 40.92 ; H, 2.71 ; N, 7.28.

4-Chloro-3-hydroxypicolinanilide (16) - A solution of compound (**10**) (1 g, 2.8 mmol) in ethanol (1 mL) was treated with aqueous potassium hydroxide (5 mL of a 50% solution) and refluxed for 4 h. The precipitate formed during the course of the reaction was then collected by filtration, washed successively with water and cold ethanol and dried, affording compound (**16**) as a white powder (0.53 g, 76%) mp $> 300\text{ }^\circ\text{C}$ (ethanol). IR (film) 3306, 1687 cm^{-1} . 1H -NMR (250 MHz, $DMSO-d_6$) δ : 7.10 (t, 1H, $J = 7.8\text{ Hz}$, H-4'), 7.29 (d, 1H, $J = 4.5\text{ Hz}$, H-5), 7.41 (t, 2H, $J = 7.8\text{ Hz}$, H-3'), 7.49 (d, 1H, $J = 4.5\text{ Hz}$, H-6), 7.81 (d, 2H, $J = 7.8\text{ Hz}$, H-2'), 9.22 (s, 1H, exchangeable with D_2O , NH). ^{13}C -NMR (50 MHz, $DMSO-d_6$) δ : 119.3, 122.1, 125.8, 128.7, 133.6, 137.0, 140.4, 140.7, 163.7, 164.7. HRCIMS calcd for $C_{12}H_{10}N_2O_2^{35}Cl$ m/z 249.0431 found 249.0437 ; calcd for $C_{12}H_{10}N_2O_2^{37}Cl$ m/z 251.0401 found 251.0425.

4-Allyloxy-3-iodopicolinanilide (17) - Allyl alcohol (1.16 mL, 20 mmol) was added to a suspension of sodium (0.23 g, 10 mmol) in THF (20 mL) and the mixture was stirred at rt until complete disappearance of the sodium. The resulting solution was brought to reflux and a solution of compound (**10**) (2 g, 5.6

mmol) in THF (5 mL) was added dropwise over 10 min. Reflux was maintained for 4 h and, after cooling to rt, water (5 mL) was added. The solution was extracted with ethyl acetate (3 x 50 mL), the combined organic extracts were washed with water (20 mL), dried over sodium sulfate and evaporated under reduced pressure. The residue was purified by column chromatography on silica gel (ethyl acetate-heptane 2:8), providing compound (**17**) as a white powder (1.72 g, 81%), mp 118-120 °C (heptane). IR (film) 3314, 1681, 1600 cm^{-1} . CIMS m/z 381 (MH^+). $^1\text{H-NMR}$ (300 MHz, CDCl_3) δ : 4.75 (d, 2H, $J = 1.2$ Hz, OCH_2), 5.39 (dd, 1H, $J = 1.2$ and 10.7 Hz, $\text{CH} = \text{CH}_a$), 5.60 (dd, 1H, $J = 1.2$ and 16.5 Hz, $\text{CH} = \text{CH}_b$), 6.00-6.20 (m, 1H, $\text{CH} = \text{CH}_2$), 6.81 (d, 1H, $J = 5.5$ Hz, H-5), 7.14 (t, 1H, $J = 7.0$ Hz, H-4'), 7.38 (dd, 2H, $J = 7.8$ and 7.0 Hz, H-3'), 7.76 (d, 2H, $J = 7.8$ Hz, H-2'), 8.35 (d, 1H, $J = 5.5$ Hz, H-6), 10.02 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3) δ : 78.2, 84.5, 108.7, 118.9, 119.9, 124.4, 129.0, 131.0, 138.0, 148.6, 150.6, 161.9, 165.3. Anal. Calcd for $\text{C}_{15}\text{H}_{13}\text{N}_2\text{O}_2 \cdot \text{H}_2\text{O}$: C, 45.25 ; H, 3.77 ; N, 7.03. Found : C, 45.08 ; H, 3.66 ; N, 6.91.

2,3-Dihydro-3-methyl-4-N-phenylfuro[3,2-c]pyridine-4-carboxamide (18) - A solution of compound (**17**) (0.2 g, 0.77 mmol) in toluene (15 mL) was heated at 80 °C under argon and a solution of tri-*n*-butyltin hydride (0.27 mL, 0.9 mmol) and AIBN (20 mg, 0.12 mmol) in toluene (10 mL) was slowly added dropwise. After completion of the addition (1.5 h), the reaction mixture was stirred for a further 3 h at 80 °C. The solution was then cooled, the solvent was removed under reduced pressure and the residue was purified by column chromatography on silica gel (ethyl acetate-heptane 1:9) affording compound (**18**) as an oil (114 mg, 85%). IR (film) 3326, 1687 cm^{-1} . $^1\text{H-NMR}$ (250 MHz, CDCl_3) δ : 1.43 (d, 3H, $J = 7.0$ Hz, CH_3), 4.11-4.24 (m, 1H, CHCH_3), 4.42 (dd, 1H, $J = 2.7$ and 8.7 Hz, OCH_a), 4.67 (pseudo t, 1H, $J = 8.5$ Hz, OCH_b), 6.89 (d, 1H, $J = 5.0$ Hz, H-5), 7.18 (t, 1H, $J = 7.0$ Hz, H-4'), 7.39 (dd, 2H, $J = 7.0$ and 6.9 Hz, H-3'), 7.75 (d, 2H, $J = 6.9$ Hz, H-2'), 8.31 (d, 1H, $J = 5.0$ Hz, H-6), 10.17 (s, 1H, exchangeable with D_2O , NH). $^{13}\text{C-NMR}$ (62.5 MHz, CDCl_3) δ : 31.1, 36.0, 80.4, 108.2, 119.8, 124.4, 129.2, 131.5, 138.0, 145.0, 148.4, 162.2, 168.7. HRCIMS calcd for $\text{C}_{15}\text{H}_{15}\text{N}_2\text{O}_2$ m/z 255.1132 found 255.1134.

4-Chloro-3-(tri-*n*-butyl)stannylpicolinanilide (19) and Di-(tri-*n*-butyl)stannyl-4-chloropicolinanilide (20) - Following the procedure described for the preparation of **6**, compound (**3**) (1.0 g, 4.3 mmol) in THF (75 mL) was treated at -78 °C with a solution of LDA in THF (4.72 mL of a

2.0 M solution ; 9.44 mmol) and, after 90 min, with tri-*n*-butylstannyl chloride (3.5 mL, 12.9 mmol). The reaction mixture was stirred for 90 min at -78 °C and then worked up as before. Column chromatography of the crude product on silica gel using heptane as eluent afforded compound (**20**) as an oil (0.17 g, 5%). IR (film) 3334, 2871, 1681 cm⁻¹. ¹H-NMR (250 MHz, CDCl₃) δ : 0.84-1.62 (m, 54H, Bu), 7.14 (t, 1H, J = 7.6 Hz, H-4'), 7.39 (t, 2H, J = 7.6 Hz, H-3'), 7.74 (d, 2H, J = 7.6 Hz, H-2'), 8.37 (s, 1H, H-6), 10.12 (s, 1H, exchangeable with D₂O, NH). ¹³C-NMR (62.5 MHz, CDCl₃) δ : 8.21-32.0, 119.7, 124.7, 129.1, 138.0, 139.3, 142.0, 153.9, 156.1, 163.8, 164.5. HREIMS calcd for C₃₆H₆₁N₂O ³⁵ClSn₂ m/z 810.2512 found 810.2510.

Continued elution of the chromatography column with ethyl acetate-heptane (1:9) provided the major product (**19**) as an oil (1.88 g, 84%). IR (film) 3339, 2920, 1686 cm⁻¹. CIMS m/z 523 (MH⁺, ³⁵Cl isotope), 525 (MH⁺, ³⁷Cl isotope). ¹H-NMR (250 MHz, CDCl₃) δ : 0.84-1.60 (m, 27H, Bu), 7.15 (t, 1H, J = 7.7 Hz, H-4'), 7.36-7.42 (m, 3H, H-3', H-5), 7.74 (d, 2H, J = 7.7 Hz, H-2'), 8.39 (d, 1H, J = 5.0 Hz, H-6), 10.12 (s, 1H, exchangeable with D₂O, NH). ¹³C-NMR (75 MHz, CDCl₃) δ : 13.8, 16.2, 28.0, 29.8, 120.3, 124.9, 127.3, 129.7, 138.4, 141.0, 148.4, 156.4, 157.0, 163.8. Anal. Calcd for C₂₄H₃₅N₂OClSn. 0.1C₇H₁₆ : C, 55.74 ; H, 6.88 ; N, 5.27. Found : C, 55.79 ; H, 7.12 ; N, 5.08.

4-Chloro-3-trimethylstannylpicolinanilide (21) - Following the procedure described for the preparation of **6**, compound (**3**) (1.0 g, 4.3 mmol) in THF (75 mL) was treated at -78 °C with a solution of LDA in THF (4.72 mL of a 2.0 M solution, 9.42 mmol) and, after 90 min, with a solution of trimethylstannyl chloride in THF (10.7 mL of a 1.0 M solution ; 10.7 mmol). The reaction mixture was stirred for 90 min at -78 °C and then worked-up as before. Column chromatography of the crude product on silica gel (ethyl acetate-heptane 2:8) provided compound (**21**) as white crystals (1.54 g, 87%), mp 87-90 °C (ethanol). IR (film) 3318, 2910, 1684 cm⁻¹ ; CIMS m/z 397 (MH⁺, ³⁵Cl isotope), 399 (MH⁺, ³⁷Cl isotope). ¹H-NMR (300 MHz, CDCl₃) δ : 4.86 (s, 9H, CH₃), 7.17 (t, 1H, J = 7.0 Hz, H-4'), 7.38-7.42 (m, 3H, H-3', H-5), 7.74 (d, 2H, J = 7.9 Hz, H-2'), 8.39 (d, 1H, J = 5.0 Hz, H-6), 10.17 (s, 1H, exchangeable with D₂O, NH). ¹³C-NMR (62.5 MHz, CDCl₃) δ : 1.1, 119.8, 124.5, 126.8, 129.1, 137.6, 139.3, 148.1, 155.4, 155.7, 163.0. Anal. Calcd for C₁₅H₁₇N₂OClSn. 0.6 H₂O : C, 44.30 ; H, 4.48 ; N, 6.89. Found : C, 44.49 ; H, 4.42 ; N, 6.57.

ACKNOWLEDGEMENT

We thank the Brazilian Ministry of Education (CAPES) for a fellowship (M.V.N.S.).

REFERENCES

1. For reviews, see : a) V. Snieckus, *Chem. Rev.*, 1990, **90**, 879. b) G. Queguiner, F. Marsais, V. Snieckus, and J. Epszajn, *Adv. Heterocycl. Chem.*, 1991, **52**, 187.
2. J. Epszajn, Z. Berski, J. Z. Brzezinski, and A. Jozwiak, *Tetrahedron Lett.*, 1980, **21**, 4739.
3. J. Epszajn, A. Bieniek, J. Z. Brzezinski, and A. Jozwiak, *Tetrahedron Lett.*, 1983, **24**, 4735.
4. J. Epszajn, A. Bieniek, and M. W. Plotka, *J. Chem. Res. (S)*, 1986, 20.
5. J. Epszajn, A. Bieniek, and J. A. Kowalska, *Tetrahedron*, 1991, **47**, 1697.
6. O. Lohse, *Synth. Commun.*, 1996, **26**, 2017.
7. K. S. Gudmundsson, J. M. Hinkley, M. S. Brieger, J. C. Drach, and L. B. Townsend, *Synth. Commun.*, 1997, **27**, 861.
8. E. Späth and G. Koller, *Ber.*, 1923, **56B**, 2454.
9. For examples, see : a) N. S. Narasimhan and R. S. Mali, *Synthesis*, 1983, 957. b) D. B. Reitz and S. M. Massey, *J. Org. Chem.*, 1990, **55**, 1375. c) S. O. da Silva, I. Ahmad, and V. Snieckus, *Can. J. Chem.*, 1979, **57**, 1598. d) M. Watanabe, M. Sahara, M. Kubo, S. Furukawa, R. J. Billedeau, and V. Snieckus, *J. Org. Chem.*, 1984, **49**, 742. e) M. Watanabe, M. Date, K. Kawanishi, M. Tsukazaki, and S. Furukawa, *Chem. Pharm. Bull.*, 1989, **36**, 2564.
10. R. D. Clark and J. Jahangir, *J. Org. Chem.*, 1987, **52**, 5378.
11. J. Epszajn, M. W. Plotka, and A. Grabowska, *Synth. Commun.*, 1997, **27**, 1075.
12. S. Y. Cho, S. S. Kim, K.-H. Park, S. K. Kang, J.-K. Choi, K.-J. Hwang, and E. K. Yum, *Heterocycles*, 1996, **43**, 1641.
13. J. K. Stille, *Angew. Chem., Int. Ed. Engl.*, 1986, **25**, 508.

Received, 12th June, 1997