ortho-Hydroxyalkylation of Aminopyridines: A Novel Approach to Heterocycles

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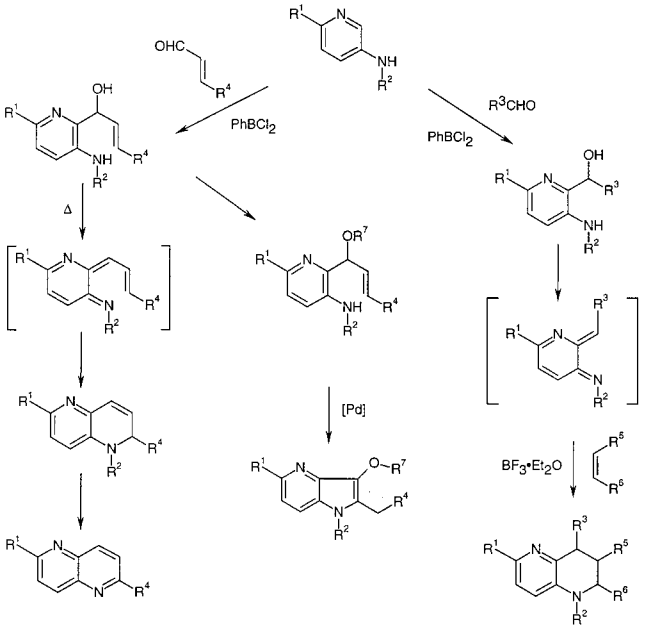
Abstract: Reaction of 6-substituted *N*-alkyl-3-aminopyridines with aldehydes in the presence of dichlorophenylborane gives selectively 2-hydroxyalkyl-3-aminopyridines. Dehydration of the latter under pyrolytic or Lewis acid conditions generates a quinone methide imine intermediate which can undergo electrocyclic or [4+2] cycloaddition reactions to give naphthyridines, dihydronaphthyridines or tetrahydronaphthyridines. Palladium-catalyzed cyclization of the 2-(1-hydroxyallyl)-3-aminopyridines gives the corresponding 4-azaindoles.

Key words: *o*-hydroxyalkylaminopyridines, naphthyridines, dihydronaphthyridines, tetrahydronaphthyridines, 4-azaindoles, heterocycles, boron, Lewis acids

o-Hydroxyalkylaminopyridines are useful synthetic intermediates for preparing nitrogen containing heterocycles. Pyrolysis of these compounds generates a quinone methide imine intermediate that can be trapped by an olefin in a [4+2] cycloaddition to give dihydronaphthyridines.[1] Recently, we reported a facile method to prepare various substituted *o*-*N*-alkylaminobenzyl alcohols as *o*-quinone methide imine precursors.[2] Dehydration of these *o*-*N*-alkylaminobenzyl alcohols under pyrolytic or Lewis acid conditions, followed by trapping the corresponding *o*-quinone methide imine intermediates with an olefin via electrocyclic or [4+2] cycloaddition reactions has led to the synthesis of dihydro- and tetrahydroquinoline derivatives respectively.[2] We also reported that the analogous 2-(1-hydroxyallyl)anilines can be cyclized in the presence of a palladium catalyst to give indoxyls.[3] Herein we report the extension of this methodology to prepare a variety of 2-hydroxyalkyl-3-*N*-alkylaminopyridines and its application to the synthesis of naphthyridines, dihydronaphthyridines, tetrahydronaphthyridines and 4-azaindoles (Scheme 1).



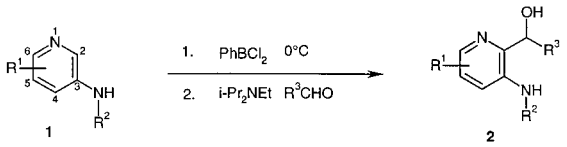
Scheme 1

o-Hydroxyalkylation of *N*-Alkylaminopyridines

Dichlorophenylborane is a versatile reagent that has been used in the ortho-specific alkylation of phenols and anilines.[2,4] We were interested to see if this methodology can be applied to aminopyridines and other heterocycles in spite of the possible coordination of the pyridine nitrogen with the boron reagent and the deactivation of the ring. Also of interest is the regiochemistry of the proposed reaction if it does proceed. 3-Aminopyridine was chosen initially for this study, derivatives of which were available commercially. Using the methodology we developed for *N*-methylaniline,[2] 3-(methylamino)pyridine **(1a)** was treated with dichlorophenylborane at 80 °C for 2 hours. Benzaldehyde and diisopropyethylamine were then added to the aminoborane complex at 0 °C. The mixture was allowed to react at 0 °C for 4 hours and then at room temprature for 20 hours. No alkylation product formation was observed. The lack of reactivity of **1a** may be attributed to the competing complexation of the basic nitrogen on the pyridine ring with the borane reagent. Substitution ortho to the pyridine nitrogen is known to reduce the interaction of that nitrogen with Lewis acids.[5,6] Thus, 2-methoxy-5-(methylamino)pyridine **(1b)** was prepared and the effect of the 2-substitution on the *ortho*-hydroxyalkylation reaction was studied. Treatment of **1b** with dichlorophenylborane followed by the addition of benzaldehyde and diisopropylethylamine gave the corresponding 2-(1-hydroxybenzyl)-3-(methylamino)pyridine **(2a)** in 65% yield (see experimental). In contrast to the *N*-alkylanilines, the formation of the aminoborane complex in this case could be achieved at 0 °C instead of 85 °C. Similarly, 2-chloro-5-(methylamino)pyridine **(1c)** gave a 72% yield of the expected product **2b**. Although the 2-position of 3-aminopyridine is the preferred site of electrophilic substitution,[6] it is still of interest to note that none of the 4-substituted

product was observed. Placing a chloro substituent at the 2-position ortho to the amino group (**1d**) also failed to force alkylation at the 4-position. The results are summarized in Table 1.

Table 1 Synthesis of 3-Amino-2-(1-hydroxybenzyl)pyridines **2a,b**



1 2

	R^1	R^2	R^3	Time (h)	Product	Yield%
1a	H	Me	Ph	20	–	0
1b	6-MeO	Me	Ph	20	2a	65
1c	6-Cl	Me	Ph	20	2b	72
1d	2-Cl	Me	Ph	20	–	0

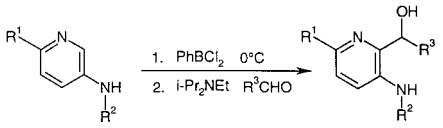
The successful reaction of **1b** and **1c** with benzaldehyde established the feasibility of the *ortho*-hydroxyalkylation reaction of 3-*N*-alkylaminopyridines. The extension of this methodology using other aldehydes was examined next. 2-Methoxy-5-(methylamino)pyridine **(1b)** reacted readily with cinnamaldehyde, an α,β-unsaturated aldehyde, to give the corresponding 2-(1-hydroxy-3-phenylallyl)-3-(methylamino)pyridine **(2c)** in 58% yield. Yields of the reactions of **1b** with acrolein and crotonaldehyde were slightly lower. They gave yields of only 40 and 46% of **2d** and **2e**, respectively. Significant amounts of starting material was recovered in both cases. The reaction did not perform as well with enolizable aldehydes. Compound **1b** gave only 9% of the desired product **2f** (not fully characterized) as a mixture (1:1) of diastereomers when reacted with citronellal and did not react with propionaldehyde at all. 2-Chloro-5-(methylamino)pyridine **(1c)** reacted with cinnamaldehyde to give **2g** in 62% yield but gave only traces of desired product when reacted with acrolein. It appeared that the chloro-substituted pyridine is less reactive. These results are summarized in Table 2.

The 5-allylamino-2-methoxy derivative **1e** behaved similarly. Reaction of **1e** with benzaldehyde and cinnamaldehyde gave **2h** and **2i** in 55 and 40% respectively**.** With crotonaldehyde, **1e** gave only 32% yield of **2j**. In contrast, reaction of the 5-allylamino-2-chloropyridine **(1f)** with benzaldehyde and cinnamaldehyde gave significantly better yields of the corresponding products **2k** (80%) and **2l** (79%), respectively. Even though **1f** gave a better yield of the alkylation product with cinnamaldehyde than **1e**, compound **1f** did not react with acrolein.

Synthesis of Dihydro-1,5-naphthyridines

Thermolysis of 2-(1-hydroxyallyl)-*N*-alkylanilines are known to generate *o*-quinone methide imine intermediates which can undergo electrocyclic reactions to give dihydroquinolines.[2b] Thermolysis of the analogous 2-(1-hydroxyallyl)-3-*N*-(methylamino)pyridines **2** is expected to behave similarly to give the dihydronaphthyridines **3**. Thus, when **2c** was pyrolysed at 180 °C (refluxing dichlorobenzene) for 2.75 hours, the dihydro-1,5-naphthyridine **3a** was isolated in 31% yield. Compound **3a** was very unstable, turning green immediately when in contact with air, and it decomposed rapidly at ambient temperature even under nitrogen. Thermolysis of the crotyl alcohol derivative **2e** gave no isolable product even though there is some evidence that the desired product may have formed. It appeared that the dihydronaphthyridine product that was formed was very unstable and decomposed readily under the reaction conditions. In contrast, the chloropyridine derivative **2g** cyclized readily at lower temperature (150 °C) and shorter time (0.25 h) to give the corresponding dihydronaphthyridine derivative **3b** in 68% yield. Thermolysis of the 5-allylamino-2-methoxy analog **2h** at 180°C for 0.25 hour also gave a better yield of the dihydronaphthyridine product **3c** (65%) than did the *N*-methyl compound **2c**. It is interesting to find that during this reaction the corresponding aromatized naphthyridine **4a** was also isolated in 28% yield. When **2h** was heated to 180 °C for 20 hours, none of the dihydro compound **3c** was obtained, instead, the aromatized naphthyridine **4a** was isolated in 43% yield. Apparently, the intermediate dihydro compound was sensitive to the trace amount of air present in the reaction and aromatized readily with concomitant elimination of the allyl group. Whereas pyrolysis of the crotyl alcohol derivative **2e** gave no isolable product, the 5-allylamino crotyl alcohol derivative **2j** gave 16% yield of the corresponding dihydro product **3d**. The *N*-allyl substituent seems to impart some stability to the dihydro

Table 2 Synthesis of 3-Amino-2-(1-hydroxyalkyl)pyridines **2c-l**



1 2

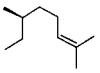
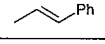
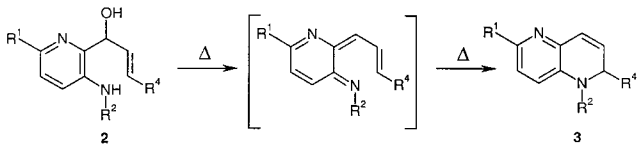
		R^2	R^3	Time (h)	Product	(Yield%)
1b	MeO	Me		2.75	2c	(58)
1b	MeO	Me		4	2d	(40)
1b	MeO	Me		2.75	2e	(46)
1b	MeO	Me		20	--	(0)
1b	MeO	Me		72	2f	(9)
1c	Cl	Me		3.5	2g	(62)
1e	MeO		Ph	3	2h	(55)
1e	MeO			2.75	2i	(40)
1e	MeO			4.5	2j	(32)
1f	Cl		Ph	3	2k	(80)
1f	Cl			4.5	2l	(79)

Table 3 Synthesis of Dihydro-1,5-naphthyridines **3**



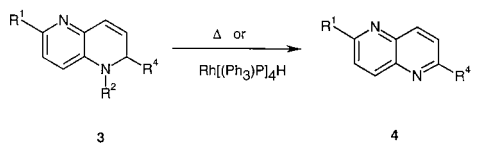
	R^1	R^2	R^4	Temp (°C)	Time (h)	Products	(Yield%)
2c	MeO	Me	Ph	180	2.75	**3a**	(31)
2e	MeO	Me	Me	180	20	--	(0)
2g	Cl	Me	Ph	150	0.25	**3b**	(68)
2h	MeO		Ph	180	0.25	**3c**	(65)
2j	MeO		Me	180	2.5	**3d**	(16)
2l	Cl		Ph	150	0.25	**3e**	(57)

compounds. Thermolysis of the chloro-*N*-allyl derivative **2l** gave a 57% yield of the corresponding dihydronaphthyridine **3e**. The results are summarized in Table 3.

Synthesis of 1,5-Naphthyridines

The ease in removal of the *N*-allyl substituent has led to the preparation of the *N*-allyl-1,2-dihydronaphthyridines described above as precursors to 1,5-naphthyridines. There are few other references in the literature to methods for the synthesis of 1,5-naphthyridines.[7] As mentioned earlier, thermolysis of the 5-allylamino-2-methoxycinnamyl alcohol **(2h)** gave initially the dihydronaphthyridine **3c**, which upon heating for an extended period of time gave the fully aromatized 1,5-naphthyridine **4a** in 43% yield. The dihydronaphthyridine **3c** could also be converted to **4a** in 54% yield when treated with tetrakis(triphenylphosphine)rhodium hydride in the presence of trifluoroacetic acid at 85 °C.[2b] Similarly, **3d** and **3e** were converted to the corresponding 1,5-naphthyridine derivatives **4b** and **4c** in yields of 51 and 52%, respectively. The results are summarized in Table 4.

Table 4 Synthesis of 1,5-Naphthyridines **4**

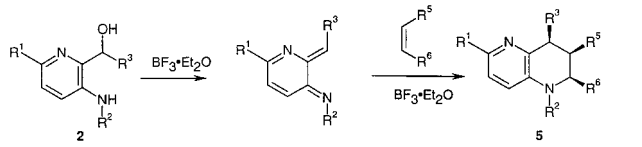


	R^1	R^2	R^4	Condition	Temp (°C)	Time (h)	Products	(Yield%)
3c	MeO		Ph	Δ	180	20	**4a**	(43)
3c	MeO		Ph	$Rh[(Ph_3)P]_4H$	85	4	**4a**	(54)
3d	MeO		Me	$Rh[(Ph_3)P]_4H$	85	1.75	**4b**	(51)
3e	Cl		Ph	$Rh[(Ph_3)P]_4H$	85	20	**4c**	(52)

Lewis Acid-Catalyzed [4+2] Cycloaddition Reactions

ortho-Quinone methide imines generated from treatment of *N*-alkyl-2-(1-hydroxyalkyl)anilines with a Lewis acid have been shown to react with olefins in a [4+2] cycloaddition reaction.[2] Extension of this methodology to 3-alkylaminopyridines **2** was successful. Treatment of **2a** with $BF_3{\cdot}OEt_2$ (2 equiv) and allyltrimethylsilane (2 equiv) at 60°C in dichloroethane gave a 50% yield of the corresponding tetrahydronaphthyridine derivative **5a** (Table 5). The reaction is stereoselective, the two substituents at positions 2 and 4 are *cis* as expected from an *endo* [4+2] cycloaddition reaction. Strong NOE was observed between H-2 and H-4 indicating that the two protons are diaxial. This was further supported by the large *trans* diaxial coupling between H-2 and H-3_{ax}(J = 9.6 Hz) and H-4 and H-3_{ax}(J = 10.1 Hz). Reaction of **2a** with cyclopentene requires THF as cosolvent and gave **5b** in 65% yield with a *cis* ring junction in which all three hydrogens are *cis* to each other. The regio- and relative stereochemistry were determined by 2D-COSY and NOSEY experiments. Strong NOE was observed between the ring junction protons as well as the benzylic proton. Reaction of allyltrimethylsilane with the 2-chloro-*N*-allyl analog **2k** gave the corresponding tetrahydronaphthyridine **5c** in 42% yield. The stereochemistry of **5c** is similar to that of **5a**.

Table 5 Synthesis of Tetrahydronaphthyridines **5**

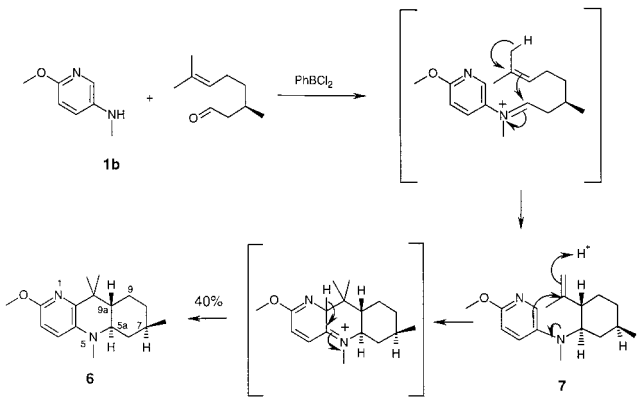


	R^1	R^2	R^3	R^5	R^6	Temp (° C)	Time (h)	Product	(Yield%)
2a	MeO	Me	Ph	H	CH_2SiMe_3	60	4.5	**5a**	(50)
2a	MeO	Me	Ph	-$(CH_2)_3$-		60	1	**5b**	(65)
2k	Cl		Ph	H	CH_2SiMe_3	80	1.2	**5c**	(42)

Synthesis of a Octahydrobenzo[b][1,5]naphthyridine Derivative

As mentioned earlier, *ortho*-hydroxyalkylation of 2-methoxy-5-(methylamino)pyridine **(1b)** with citronellal gave very poor yield of **2f**. This compound was intended as a substrate for an intramolecular [4+2] cycloaddition reaction. However, in a misguided experiment where diisopropylamine was absent, **1b** reacted with citronellal in the presence of dichlorophenylborane to give the octahydrobenzo[*b*][1,5]naphthyridine **6** {$[\alpha]_D$ +23 (c = 0.9, $CHCl_3$)} in 40% yield. The formation of **6** was stereoselective as only one single isomer was obtained. The relative stereochemistry was determined by 2D-COSY and NOSEY, HMQC and HMBC experiments. The vicinal coupling constant of the protons across the ring junction, J(5a, 9a), was measured to be 10.8 Hz which is consistent with a *trans* ring junction. The 7-methyl substituent was determined to be equatorial based on the analysis of the coupling constant of H-7 and H-6_{ax} (δ 0.85). This proton appeared as an apparent quartet, due to approximate equal

geminal and two *trans* diaxial vicinal coupling (11.0 Hz). H-7 and is therefore axial and the methyl substituent is equatorial. The formation of **6** is most likely a cationic process. The proposed mechanism is shown in Scheme 2. A small amount (4%) of the precursor **7** was also isolated.

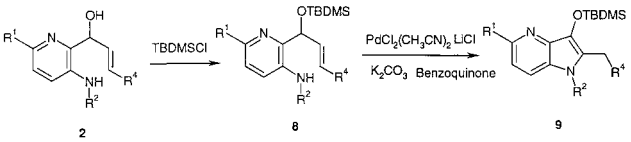


Scheme 2

Synthesis of 4-Azaindoles

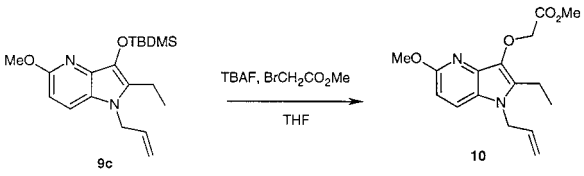
Palladium-catalyzed intramolecular cyclization of 2-allylaniline derivatives to indoles is well documented.[8] Recently, we have reported the palladium-assisted cyclization of 2-(1-hydroxyallyl)anilines to indoxyls.[3] Herein, we have successfully applied this methodology to the synthesis of 4-azaindoxyls **9** in good yields. Protection of the allylic alcohols **2** with a *t*-butyldimethylsilyl substituent followed by the treatment of the resulting siloxyallyl intermediates **8** with 20 mol% of $PdCl_2(MeCN)_2$, 1.5 equivalent of benzoquinone as reoxidant, three equivalents of K_2CO_3, and ten equivalents of LiCl in THF gave the corresponding 4-azaindoxyls **9** in very good yields. The results are summarized in Table 6.

Table 6 Synthesis of 4-Azaindoles



	R^1	R^2	R^4	8 (Yield%)	Temp (° C)	Time (h)	9 (Yield%)
2d	MeO	Me	H	8a (77)	25	1.75	9a (100)
2e	MeO	Me	Me	8b (71)	75	3.5	9b (51)
2j	MeO		Me	8c (49)	75	3.5	9c (63)
2g	Cl	Me	Ph	8d (70)	25	48	9d (54)

Silylation of the 2-methoxy-5-(methylamino)pyridine derivative **2d** gave a 77% yield of **8a**, which was then cyclized to give the azaindole **9a** in essentially quantitative yield. Cyclization of the crotyl alcohol derivative **8b** gave only 51% yield of **9b**. In the case of the *N*-allyl analog **8c**, the cyclization gave 63% of **9c** which was contaminated by an inseparable impurity. Without further characterization, compound **9c** was treated with tetrabutylammonium fluoride in the presence of methyl bromoacetate to give the *O*-alkylated product **10** in 55% yield (Scheme 3). No C-2 alkylated product was observed. The 2-chloro-5-(methylamino)cinnamyl alcohol derivative **8d** behaved similarly, but it required one equiv. of $PdCl_2(MeCN)_2$ for the cyclization and gave the corresponding 4-azaindoxyl derivative **9d** in 54% yield.



Scheme 3

In summary, we have shown that *ortho*-hydroxyalkylation of 3-*N*-alkylaminopyridine can be achieved readily, in a regioselective manner, using dichlorophenylborane as the chelating agent. The resulting 3-*N*-alkylamino-2-(1-hydroxyallyl)pyridines serve as key intermediates in the syntheses of naphthyridines, dihydronaphthyridines, tetrahydronaphthyridines and 4-azaindoles.

^{1}H NMR and ^{13}C NMR spectra were measured with a Bruker AMX300, Bruker ARX400, or Bruker ARX 500 Spectrometer. Melting points were measured on a Büchi 510 melting point apparatus and are uncorrected. Low-resolution mass spectral analyses were performed on a PE/SCIEX LC-MS. Exact masses were obtained by high resolution mass spectroscopy performed by Dr. O. Maimer of McGill University, Montreal, Quebec. Elemental analyses were performed at the University of Montreal, Montreal, Quebec. IR spectra were obtained on a Perkin-Elmer Infrared Spectrophotometer, Model 681. Flash chromatography was performed using Merck silica gel 60, 230–400 mesh and tlc using Merck silica gel 60F 254 sheets.

N-Alkylation of Aminopyridines; General Procedure A

N-Alkylation of aminopyridines was performed by treating the aminopyridine with LDA followed by the addition of an alkyl halide. The LDA was prepared freshly from diisopropylamine (100 mmol) and BuLi (2.5 M) in anhyd THF (100 mL). The LDA was added dropwise to an anhyd THF (100 mL) solution of aminopyridine at –78°C. The mixture was warmed to 0 °C and allowed to react for 1 h before MeI (7.78 mL, 125 mmol) was added dropwise. The reaction was kept at –78 °C for 2 h and then allowed to warm to r.t. overnight. Aq NH_4Cl (200 mL) and EtOAc (400 mL) were added. The organic extracts were washed with brine (200 mL) and dried ($MgSO_4$). The mixture was filtered and concentrated under vacuum. The crude product was purified by flash chromatography on silica gel.

3-Amino-*N*-methylpyridine (1a)

Yield: 17%.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 2.79 (d, 3 H, *J* = 4.6 Hz, CH_3N), 5.20 (br s, 1 H, NH), 6.88 (m, 1 H), 7.05 (m, 1 H), 7.81 (dd, 1 H, *J* = 4.6, 1.3 Hz), 8.00 (d, 1 H, *J* = 3.5 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 121.9, 128.6, 140.5, 142.3, 151.1.

HRMS: *m*/*z* calcd. for $C_6H_9N_2$ (M + 1):109.0765; found:109. 0765.

5-Amino-2-methoxy-*N*-methylpyridine (1b)
Yield: 51%.

IR (film) ν = 3320 (NH), 1570, 1500, 1410, 1360, 1250 cm^{-1}.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 2.77 (d, 3 H, *J* = 5.4 Hz, CH_3N), 3.76 (s, 3 H, CH_3O), 4.59 (br s, 1 H, NH), 6.55 (d, 1 H, *J* = 8.8 Hz, C3-H), 7.04 (dd, 1 H, *J* = 8.8, 2.9 Hz, C4-H), 7.55 (d, 1 H, *J* = 3.0 Hz, C6-H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 35.3, 57.3, 115.3, 129.8, 133.9, 146.2, 161.6.

HRMS: *m*/*z* calcd. for $C_7H_{11}N_2O$ (M + 1):139.0871; found:139.0871.

5-Amino-2-chloro-*N*-methylpyridine (1c)
Yield: 55%.

IR (KBr) ν = 3300 (NH), 1580, 1520, 1465, 1320, 1250 cm^{-1}.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 2.80 (d, 3 H, *J* = 5.2 Hz, CH_3N), 5.37 (s, 1 H, NH), 7.00 (dd, 1 H, *J* = 8.6 Hz, 3.1 Hz, C3-H), 7.11 (d, 1 H, *J* = 8.6 Hz, C4-H), 7.74 (d, 1 H, *J* = 2.9 Hz, C6-H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 126.2, 128.7, 138.7, 142.2, 150.4.

Anal. calcd. for $C_6H_7ClN_2$: C, 50.54; H, 4.95; N, 19.65. Found: C, 50.80; H, 4.97; N, 19.65.

3-Amino-2-chloro-*N*-methylpyridine (1d)
Yield: 88%.

IR (film) ν = 3420, 3330 (NH), 1580, 1490, 1370, 1320, 1005 cm^{-1}.

^{1}H NMR (300 MHz, CD_3COCD_3): δ = 2.88 (d, 3 H, *J* = 5.0 Hz, CH_3N), 5.21 (br s, 1 H, NH), 6.98 (dd, 1 H, *J* = 8.0, 1.6 Hz), 7.17 (dd, 1 H, *J* = 8.0, 4.6 Hz), 7.60 (dd, 1 H, *J* = 4.6, 1.6 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 47.4, 121.6, 128.6, 140.2, 141.4, 147.2.

HRMS: *m*/*z* calcd. for $C_6H_8ClN_2$ (M + 1):143.0376; found:143.0376.

***N*-Allyl-5-amino-2-methoxypyridine (1e)**
Yield: 77%.

IR (KBr) ν = 3350 (NH), 1480, 1370, 1255 cm^{-1}.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 3.74 (t, 2 H, *J* = 5.7 Hz, CH_2N), 3.76 (s, 3 H, CH_3O), 4.77 (br s, 1 H, NH), 5.08 (m, 1 H, CH_2=), 5.26 (m, 1 H, CH_2=), 5.93 (m, 1 H, CH=), 6.55 (d, 1 H, *J* = 8.7 Hz, C3-H), 7.07 (dd, 1 H, *J* = 8.8, 2.9 Hz, C4-H), 7.55 (d, 1 H, *J* = 3 Hz, C6-H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 51.6, 57.4, 115.2, 120.2, 130.3, 135.0, 141.0, 144.9, 161.8.

Anal. calcd.for $C_9H_{12}N_2O$: C, 65.83; H, 7.37; N, 17.06. Found: C, 66.31; H, 7.38; N, 16.94.

HRMS: *m*/*z* calcd. for $C_9H_{12}N_2O$:164.0950; found:164.0949.

***N*-Allyl-5-amino-2-chloropyridine (1f)**
Yield: 81%.

IR (KBr) ν = 3400, 3300 (NH), 1580, 1480, 1450, 1300, 1140 cm^{-1}.

^{1}H NMR (300 MHz, CD_3COCD_3): δ = 3.79 (m, 2 H, CH_2N), 5.12 (ddd, 1 H, *J* = 10.4, 3.3, 1.5 Hz, CH_2=), 5.26 (ddd, 1 H, *J* = 10.4, 3.3, 1.5 Hz, CH_2=), 5.54 (s, 1 H, NH), 5.91 (m, 1 H, CH=), 7.03 (dd, 1 H, *J* = 8.7, 3.0 Hz), 7.10 (dd, 1 H, *J* = 8.7, 0.6 Hz), 7.78 (d, 1 H, *J* = 3.0 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 50.4, 120.3, 126.9, 128.6, 140.0, 140.1, 142.5, 149.2.

HRMS: *m*/*z* calcd. for $C_8H_{10}N_2Cl$ (M+1):169.0533; found:169.0533.

***o*-Hydroxyalkylation of *N*-Alkylaminopyridines; General Procedure B**
Dichlorophenylborane (3.6 mmol) was added to a cold (0 °C) solution of *N*-alkyl-aminopyridine (3 mmol) in dichloroethane (5 mL). The mixture was stirred at 0 °C for 1 h. Diisopropylethylamine (7.2 mmol) was added to the mixture followed by the addition of the corresponding aldehyde (1 to 2 equiv) in dichloroethane (2.5 mL). The temperature was kept constant at 0 °C for the duration of the reaction. The reaction was quenched with aq NH_4OH (3 mL) and mixed vigourosly for 1 min. The mixture was diluted with Et_2O (100 mL), filtered through a Florisil column, and eluted with 25–40% EtOAc/hexane. The eluate was concentrated in vacuo, the crude product was chromatographed on silica gel and eluted with varying ratios of EtOAc/hexane allowing for optimum separation.

[6-(Methoxy)-3-(methylamino)-2-pyridyl]phenylmethanol (2a)
Yield: 65%; mp 124 °C.

IR (KBr) ν = 3370, 3330 (NH, OH), 1500, 1425, 1270 cm^{-1}.

^{1}H NMR (400 MHz, CD_3COCD_3); δ = 2.70 (d, 3 H, *J* = 5.2 Hz, CH_3N), 3.84 (s, 3 H, CH_3O), 4.63 (br s, 1 H, NH), 5.36 (d, 1 H, *J* = 5.7 Hz, OH), 5.77 (d, 1 H, *J* = 5.4 Hz, CHOH), 6.61 (d, 1 H, *J* = 8.7 Hz), 7.07 (d, 1 H, *J* = 8.7 Hz), 7.23 (m, 3 H), 7.42 (d, 2 H, *J* = 8.8 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 35.15, 57.48, 78.72, 114.0, 128.0, 131.6, 132.0, 132.9, 142.8, 147.1, 148.0, 160.0.

HRMS: *m*/*z* calcd. for $C_{14}H_{17}N_2O_2$ (M + 1): 245.1290; found: 245.1289

[6-Chloro-3-(methylamino)-2-pyridyl]phenylmethanol (2b)
Yield: 72%; mp 128 °C.

IR (KBr) ν = 3380 (NH), 3250 (OH), 1575, 1495, 1415 cm^{-1}.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 2.73 (d, 3 H, *J* = 5.2 Hz, CH_3N), 5.52 (br s, 2 H, NH, OH), 5.85 (s, 1 H, CHOH), 6.98 (d, 1 H, *J* = 8.5 Hz), 7.15 (d, 1 H, *J* = 8.5 Hz), 7.23 (m, 1 H), 7.29 (m, 2 H), 7.42 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 80.46, 125.1, 128.1, 131.2, 132.2, 133.0, 140.1, 146.9, 147.8, 151.2.

Anal. calcd. for $C_{13}H_{13}N_2ClO$: C, 62.78; H, 5.27; N, 11.26. Found: C, 63.29; H,5.33; N, 11.01.

HRMS: *m*/*z* calcd for $C_{13}H_{14}N_2ClO$ (M + 1): 249.0795; found: 249.0794.

(*E*)-1-[6-Methoxy-3-(methylamino)-2-pyridyl]-3-phenylprop-2-en-1-ol (2c)
Yield: 58%.

IR (film) ν = 3350 (NH, OH), 1600, 1470, 1260 cm^{-1}.

^{1}H NMR (400 MHz, CD_3COCD_3): δ = 2.80 (d, 3 H, *J* = 5.0 Hz, CH_3N), 3.83 (s, 3 H, CH_3O), 4.77 (br s, 1 H, NH), 4.95 (d, 1 H, *J* = 5.6 Hz, OH), 5.35 (t, 1 H, *J* = 5.4 Hz, C*H*OH), 6.50 (dd, 1 H, *J* = 15.9, 6.6 Hz, CH=C*H*CHOH), 6.62 (d, 1 H, *J* = 8.7 Hz), 6.75 (d, 1 H, *J* = 15.9 Hz, C*H*=CH-CHOH), 7.10 (d, 1 H, *J* = 8.7 Hz), 7.20 (t, 1 H, *J* = 7.4 Hz), 7.30 (t, 2 H, *J* = 7.3 Hz), 7.42 (d, 2 H, *J* = 8.9 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 35.3, 57.5, 77.8, 114.0, 127.8, 131.4, 132.4, 133.5, 134.8, 135.0, 142.2, 143.1, 146.2, 160.2.

HRMS: *m*/*z* calcd for $C_{16}H_{19}N_2O_2$ (M + 1): 271.1446; found: 271.1445.

1-[6-Methoxy-3-(methylamino)-2-pyridyl]prop-2-en-1-ol (2d)
Following the general procedure B, **1b** (415 mg, 3 mmol) was reacted with acrolein (336 mg, 6 mmol) at –20 °C for 0.25 h, then at 0 °C

for 2.5 h to afford, after chromatography, 240 mg (40%) of **2d** and 153 mg (36%) of the starting material.

IR (KBr) ν = 3380 (OH, NH), 1580, 1490, 1420, 1260 cm^{-1}.

^1H NMR (400 MHz, CD_3COCD_3): δ = 2.79 (d, 3 H, *J* = 5.4 Hz, CH_3N), 3.80 (s, 3 H, CH_3O), 4.66 (br s, 1 H, NH), 4.81 (d, 1 H, *J* = 5.8 Hz, OH), 5.08 (dt, 1 H, C*H*$_2$=CH, *J* = 10.3, 1.8 Hz), 5.15 (t, 1 H, *J* = 5.8 Hz, C*H*OH), 5.34 (dt, 1 H, C*H*$_2$=CH, *J* = 17.2, 1.7 Hz), 6.05 (m, 1 H, C*H*=CH_2), 6.60 (d, 1 H, *J* = 8.7 Hz), 7.09 (d, 1 H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 35.1, 57.4, 78.0, 113.9, 118.8, 127.7, 143.0, 143.6, 146.0, 160.1.

HRMS: *m*/*z* calcd for $C_{10}H_{15}N_2O_2$ (M + 1): 195.1134; found: 195.1134.

(*E*)-1-[6-Methoxy-3-(methylamino)-2-pyridyl]but-2-en-1-ol (2e)
Yield: 46%.

IR (KBr) ν = 3360 (NH, OH), 1490, 1470, 1260, 1030 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 1.65 (d, 3H, *J* = 6.3 Hz, CH_3C), 2.78 (d, 3H, *J* = 3.7 Hz, CH_3N), 3.80 (s, 3H, CH_3O), 4.57 (s, 1H, NH), 4.70 (d, 1H, *J* = 5.6 Hz, OH), 5.06 (t, 1H, *J* = 5.5 Hz, CHO), 5.70 (m, 2H, CH_2 =), 6.59 (d, 1H, *J* = 8.6 Hz), 7.06 (d, 1H, *J* = 8.6 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 21.9, 35.2, 57.4, 77.6, 113.6, 127.6, 131.0, 136.8, 142.8, 146.7, 160.1.

HRMS: *m/z* calcd. for $C_{11}H_{17}N_2O_2$ (M+1): 209.1290; found: 209.1290.

(3*R*)-1-[6-Methoxy-3-(methylamino)-2-pyridyl]-3,7-dimethyl-oct-6-en-1-ol (2f)
Following the general procedure B, **1b** (423 mg, 3.06 mmol) was reacted with citronellal (565 mg, 3.67 mmol) at 0 °C for 4.5 h and then at r.t. for 70 h to give, after chromatography, 76 mg (9%) of the material tentatively assigned as the title compound **2f** as a mixture (1:1) of diastereomers and 208 mg (50%) of the starting material.

^1H NMR (400 MHz, CD_3COCD_3): δ = 0.96 (d, 3 H, *J* = 6.5 Hz, C*H*$_3$CHCH$_2$), 1.18 (m, 1 H), 1.40 (m, 1 H, C*H*CH$_3$), 1.55 (m, 1 H), 1.57 (s, 3 H, CH_3C=), 1.60 (m, 1 H), 1.63 (s, 3 H, CH_3C=), 1.75 (m, 1 H), 1.89 (m, 1 H), 1.95 (m, 1 H), 2.77 (d, 3 H, *J* = 4.1 Hz, CH_3N), 3.79 (s, 3 H, CH_3O), 4.45 (m, 1 H, C*H*OH), 4.82 (m, 1 H, OH), 4.92 (br s, 1 H, NH), 5.08 (m, 1 H, C*H*=CMe_2), 6.57 (d, 1 H, *J* = 8.6 Hz), 7.04 (d, 1 H, *J* = 8.6 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 21.8, 21.8, 23.7, 24.7, 30.0, 30.2, 30.3, 35.2, 35.3, 41.7, 42.6, 47.1, 47.2, 57.3, 57.3, 75.3, 76.2, 113.3, 133.3, 127.3, 127.4, 129.9, 129.9, 135.4, 143.1, 143.3, 148.8, 149.1, 160.0, 160.1.

(*E*)-[6-Chloro-3-(methylamino)-2-pyridyl]-3-phenylprop-2-en-1-ol (2g)
Yield: 62%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 2.83 (d, 3 H, *J* = 4.7 Hz, CH_3N), 5.04 (d, 1 H, *J* = 5.0 Hz, OH), 5.39 (m, 1 H, CHO), 5.59 (br s, 1 H, NH), 6.51 (dd, 1 H, *J* = 16, 6.1 Hz, CH=), 6.76 (d, 1 H, *J* = 17 Hz, PhC*H*=), 7.02 (d, 1 H, *J* = 8.5 Hz), 7.15 (d, 1 H, *J* = 8.5 Hz), 7.25 (m, 3 H), 7.42 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 79.4, 124.9, 128.1, 131.5, 132.5, 133.5, 133.9, 135.4, 140.3, 142.0, 148.0, 150.3.

HRMS: *m*/*z* calcd. for $C_{15}H_{16}N_2ClO$ (M + 1): 275.0952; found: 275.0951.

[3-(Allylamino)-6-methoxy-2-pyridyl]phenylmethanol (2h)
Yield: 55%; mp 59–60 °C.

IR (KBr) ν = 3370 (NH), 3150 (OH), 1490, 1275, 1260, 1030 cm^{-1}.

^1H NMR (400 MHz, CD_3COCD_3): δ = 3.67 (t, 2 H, *J* = 5.5 Hz, CH_2C=), 3.84 (s, 3 H, CH_3O), 4.78 (br s, 1 H, NH), 5.00 (dd, 1 H, *J* = 10.3, 1.4 Hz, CH_2=), 5.07 (dd, 1 H, *J* = 17, 1.2 Hz, CH_2=), 5.43 (d, 1 H, *J* = 5.3 Hz, OH), 5.80 (m, 1 H, CH=), 5.82 (d, 1 H, *J* = 5.2 Hz, CHO), 6.58 (d, 1 H, *J* = 8.7 Hz), 7.06 (d, 1 H, *J* = 8.7 Hz), 7.22 (m, 1 H), 7.29 (t, 2 H, *J* = 7.4 Hz), 7.44 (d, 2 H, *J* = 7.5 Hz).

^{13}C NMR (400 MHz, CD_3COCD_3): δ = 51.0, 57.5, 79.3, 113.9, 119.7, 129.3, 131.5, 132.1, 133.0, 140.8, 141.5, 147.4, 147.9, 160.1.

HRMS: *m*/*z* calcd for $C_{16}H_{19}N_2O_2$ (M + 1): 271.1447; found: 271.1446.

(*E*)-1-[3-(Allylamino)-6-methoxy-2-pyridyl]-3-phenylprop-2-en-1-ol (2i)
Yield: 40%.

IR (film) ν = 3380 (NH, OH), 1580, 1490, 1420, 1255 cm^{-1}.

^1H NMR (400 MHz, CD_3COCD_3): δ = 3.79 (m, 2 H, CH_2N), 3.82 (s, 3 H, CH_3O), 5.00 (s, 1 H, NH), 5.06 (d, 1 H, *J* = 1.7 Hz, OH), 5.07 (dd, 1 H, *J* = 10.4, 1.7 Hz, C*H*$_2$=CH), 5.23 (dd, 1 H, *J* = 17.2, 1.8 Hz, C*H*$_2$=CH), 5.38 (m, 1H, C*H*OH), 5.92 (m, 1 H, CH_2=C*H*), 6.49 (dd, 1 H, *J* = 15.9, 6.3 Hz, C*H*=CHPh), 6.55 (d, 1 H, *J* = 7.2 Hz), 6.76 (d, 1 H, *J* = 16.6 Hz, CH=C*H*Ph), 7.10 (d, 1 H, *J* = 8.7 Hz), 7.24 (m, 3 H), 7.40 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 51.1, 57.6, 78.4, 114.0, 120.0, 129.1, 131.4, 132.4, 133.6, 134.9, 135.0, 141.0, 141.8, 142.1, 146.3, 160.4.

HRMS: *m*/*z* calcd for $C_{18}H_{21}N_2O_2$ (M + 1): 297.1603; found: 296.1604.

[3-(Allylamino)-6-methoxy-2-pyridyl]but-2-en-1-ol (2j)
Yield: 32%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 1.66 (m, 3 H, CH_3C=), 3.76 (m, 2 H, CH_2N), 3.80 (s, 3 H, CH_3O), 4.82 (d, 1 H, *J* = 5.1 Hz, OH), 4.82 (br s, 1 H, NH), 5.09 (m, 2 H, CHO, CH_2=), 5.23 (m, 1 H, CH_2=), 5.73 (m, 2 H, CH=CH), 5.93 (m, 1 H, =CHCN), 6.55 (d, 1 H, *J* = 8.7 Hz), 7.07 (d, 1 H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 21.8, 51.1, 57.4, 78.2, 113.6, 119.8, 128.8, 131.1, 136.7, 141.1, 141.5, 146.8, 160.2.

HRMS: *m*/*z* calcd for $C_{13}H_{19}N_2O_2$ (M + 1): 235.1447; found: 235.1446.

[3-(Allylamino)-6-chloro-2-pyridyl]phenylmethanol (2k)
Yield: 80%.

IR (KBr) ν = 3420 (NH), 3250 (OH), 1570, 1490, 1420, 1315, 1165, 1145, 1035 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 3.74 (m, 2 H, CH_2N), 5.03 (m, 2H, CH_2=), 5.57 (d, 1 H, *J* = 4.7 Hz, OH), 5.66 (s, 1 H, NH), 5.79 (m, 1 H, CH=), 5.89 (d, 1 H, *J* = 4.5 Hz, CHO), 6.96 (d, 1 H, *J* = 8.6 Hz), 7.11 (d, 1 H, *J* = 8.5 Hz), 7.25 (m, 3 H), 7.42 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 49.9, 80.9, 119.9, 126.2, 127.9, 131.1, 132.2, 133.0, 139.7, 140.0, 146.5, 146.8, 151.3.

HRMS: *m*/*z* calcd for $C_{15}H_{16}N_2ClO$ (M + 1): 275.0951; found: 275.0952.

[3-(Allylamino)-6-chloro-2-pyridyl]-3-phenylprop-2-en-1-ol (2l)
Yield: 79%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 3.85 (m, 2 H, CH_2N), 5.10 (dq, 1 H, *J* = 10.4, 1.7 Hz, CH_2=), 5.15 (d, 1 H, *J* = 4.8 Hz, OH), 5.24 (dq, 1 H, *J* = 17.3, 1.7 Hz), 5.43 (m, 1 H, CHO), 5.81 (br s, 1 H, NH), 5.90 (m, 1 H, =CHCN), 6.55 (dd, 1 H, *J* = 16.0, 6.0 Hz, C*H*=CPh), 6.75 (dd, 1 H, *J* = 16.0, 1.1 Hz, =C*H*Ph), 7.02 (d, 1 H, *J* = 8.6 Hz), 7.11 (d, 1 H, *J* = 8.6 Hz), 7.27 (m, 3 H), 7.43 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 50.0, 79.9, 120.1, 126.0, 127.9, 131.4, 132.5, 133.5, 133.8, 135.4, 140.0, 140.6, 141.9, 146.8, 150.3.

HRMS: *m/z* calcd. for $C_{17}H_{18}N_2ClO$ (M + 1): 301.1109; found: 301.1108.

Synthesis of 1,2-Dihydro[1,5]naphthyridine; General Procedure C

2-Hydroxyallyl-3-alkylaminopyridine (1 mmol) is dissolved in dichlorobenzene (10 mL) and heated to reflux at 180 °C for 4 h. After the completion of the reaction, the mixture was chromatographed on silica gel column packed with hexane. The sample was eluted first with hexane and then with 10% EtOAc/Hexane.

6-Methoxy-1-methyl-2-phenyl-1,2-dihydro[1,5]naphthyridine (3a)

Yield: 31%.

IR (KBr) ν = 3150, 1560, 1470, 1450, 1410, 1295, 1280, 1135 cm^{-1}.

^1H NMR (400 MHz, CD_3COCD_3): δ = 2.67 (s, 3 H, CH_3N), 3.79 (s, 3 H, CH_3O), 5.18 (d, 1 H, *J* = 5.0 Hz, C*H*Ph), 5.94 (dd, 1 H, *J* = 10.0, 5.2 Hz, CH=C*H*CH), 6.44 (d, 1 H, *J* = 10.1 Hz, C*H*=CHCH), 6.47 (d, 1 H, *J* = 8.7 Hz, C3-H), 6.84 (d, 1 H, *J* = 8.6 Hz, C4-H), 7.30 (m, 5 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 35.5, 52.7, 65.2, 109.8, 121.2, 126.2, 126.9, 128.3, 129.1, 130.4, 137.2, 137.6, 142.1, 156.2.

The product is very unstable. MS showed no parent ion; only the aromatized [1,5]-naphthyridine was observed, *m/z* = 237 (M + 1).

6-Chloro-1-methyl-2-phenyl-1,2-dihydro[1,5]naphthyridine (3b)

Yield: 68%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 2.70 (s, 3 H, CH_3N), 5.32 (d, 1 H, *J* = 5.1 Hz, C*H*Ph), 6.03 (dd, 1 H, *J* = 10, 4.9 Hz, =C*H*CPh), 6.41 (d, 1 H, *J* = 10 Hz, C*H*=CCPh), 6.80 (d, 1 H, *J* = 8.5 Hz), 7.00 (d, 1 H, *J* = 8.5 Hz), 7.32 (m, 5 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 40.0, 69.9, 123.6, 128.2, 129.7, 131.4, 133.1, 133.8, 136.6, 141.6, 145.7, 145.9, 146.6.

HRMS: *m/z* calcd for $C_{15}H_{14}ClN_2$ (M + 1): 257.0846; found: 257.0847.

1-Allyl-6-methoxy-2-phenyl-1,2-dihydro[1,5]naphthyridine (3c) and 2-Methoxy-6-phenyl[1,5]naphthyridine (4a)

Following the general procedure C, **2h** (114 mg, 0.38 mmol) was pyrolysed at 180 °C for 0.25 h to give, after chromatography, 69 mg (65%) of **3c** and 25 mg (28%) of **4a**.

In another experiment, pyrolysis of compound **2h** (192 mg, 0.71 mmol) at 180 °C for 20 h gave only compound **4a** (73 mg, 43%).

3c

^1H NMR (400 MHz, CD_3COCD_3): δ = 3.59 (m, 1 H, CH_2N), 3.78 (s, 3 H, CH_3O), 3.88 (m, 1 H, CH_2N), 5.09 (m, 1 H, CH_2=), 5.18 (m, 1 H, CH_2=), 5.34 (dd, 1 H, *J* = 5.0, 1.5 Hz, C*H*Ph), 5.70 (m, 1 H, C*H*=CH_2), 5.92 (dd, 1 H, *J* = 10.0, 5.0 Hz, =C*H*CPh), 6.39 (m, 1 H, CH=CCPh), 6.44 (d, 1 H, *J* = 8.7 Hz), 6.92 (d, 1 H, *J* = 8.7 Hz), 7.31 (m, 5 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 55.7, 57.3, 68.3, 114.3, 121.2, 126.6, 130.5, 131.7, 132.7, 133.6, 134.5, 138.8, 140.8, 141.7, 148.3, 160.8.

HRMS: *m/z* calcd for $C_{18}H_{19}N_2O$ (M + 1): 279.1497; found: 279.1498.

4a

Mp 114–115 °C.

IR (KBr) ν = 1608, 1470, 1382, 1250 cm^{-1}.

^1H NMR (400 MHz, CD_3COCD_3): δ = 4.06 (s, 3 H, CH_3O), 7.21 (d, 1 H, *J* = 9.0 Hz), 7.50 (m, 3 H), 8.25 (m, 5 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 58.2, 121.7, 126.6, 132.0, 133.7, 134.1, 140.5, 143.9, 145.2, 146.1, 146.6, 159.4, 167.4.

HRMS: *m/z* calcd for $C_{15}H_{13}N_2O$ (M + 1): 237.1028; found: 237.1028.

1-Allyl-6-methoxy-2-methyl-1,2-dihydro[1,5]naphthyridine (3d)

Yield: 16%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 1.10 (d, 3 H, *J* = 6.4 Hz, CH_3C), 3.76 (s, 3 H, CH_3O), 3.84 (m, 2 H, CH_2N), 4.19 (m, 1 H), 5.15 (m, 1 H, CH_2=), 5.29 (m, 1 H, CH_2=), 5.89 (m, 1 H), 5.92 (dd, 1 H, *J* = 9.9, 5.4 Hz), 6.32 (d, 1 H, *J* = 9.9 Hz), 6.41 (d, 1 H, *J* = 8.7 Hz), 6.88 (d, 1 H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 24.0, 56.2, 57.2, 59.2, 113.9, 120.8, 127.6, 130.8, 136.0, 140.1, 140.3, 142.8, 160.7.

MS: *m/z* for $C_{13}H_{17}N_2O$ (M+1):217.

1-Allyl-6-chloro-2-phenyl-1,2-dihydro[1,5]naphthyridine (3e)

Yield: 57%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 3.62 (m, 1 H, CH_2N), 3.90 (m, 1 H, CH_2N), 5.10 (dq, 1 H, *J* = 10.3, 1.6 Hz, CH_2=), 5.18 (dq, 1 H, *J* = 17.3, 1.7 Hz, CH_2=), 5.45 (dd, 1 H, *J* = 4.7, 1.6 Hz), 5.65 (m, 1 H, =CHCN), 5.99 (dd, 1 H, *J* = 10.1, 4.7 Hz), 6.39 (dd, 1 H, *J* = 10.1, 0.8 Hz), 6.85 (d, 1 H, *J* = 8.5 Hz), 6.96 (d, 1 H, *J* = 8.5 Hz), 7.37 (m, 5 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 55.3, 68.7, 121.5, 124.4, 128.0, 129.5, 131.7, 133.1, 133.8, 136.3, 137.5, 141.5, 145.0, 145.4, 147.8.

Synthesis of [1,5]Naphthyridines; General Procedure D

To a solution of **3** (0.25 mmol) in anhyds EtOH was added CF_3CO_2H (0.58 mmol) and $(PPh_3)_4RhH$ (0.10–0.25 mmol). The mixture was refluxed for 2–20 h, then cooled to r.t. Aq 1 N NaOH was added and the mixture was extracted twice with EtOAc. The combined organic layers were washed once with brine and dried ($MgSO_4$). The solvents were removed under vacuum and the product was isolated by column chromatography.

2-Methoxy-6-phenyl[1,5]naphthyridine (4a)

Following the General Procedure D, **3c** (69 mg, 0.25 mmol) was converted to **4a** (32 mg, 54%) after 4 h at 85 °C. Spectral data for **4a** are listed above.

2-Methoxy-6-methyl[1,5]naphthyridine (4b)

Yield: 51%; mp 50–51 °C (Lit. 52 °C).

IR (KBr) ν = 1600, 1590, 1470, 1250 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 2.64 (s, 3 H, CH_3C), 4.01 (s, 3 H, CH_3O), 7.13 (d, 1 H, *J* = 9.0 Hz), 7.51 (d, 1 H, *J* = 8.7 Hz), 8.01 (d, 1 H, *J* = 8.7 Hz), 8.11 (d, 1 H, *J* = 9.0 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 28.8, 57.9, 120.9, 129.9, 139.7, 144.6, 145.3, 146.2, 161.5, 166.9.

HRMS: *m/z* calcd for $C_{10}H_{11}N_2O$ (M + 1): 175.0871; found: 175.0872.

2-Chloro-6-phenyl[1,5]naphthyridine (4c)

Yield: 52%; mp 131–132 °C.

IR (KBr) ν = 1570, 1475, 1100 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 7.56 (m, 3 H), 7.79 (d, 1 H, *J* = 8.8 Hz), 8.32 (m, 2 H), 8.40 (m, 2 H), 8.47 (dd, 1 H, *J* = 8.8, 0.6 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 127.9, 131.1, 132.5, 133.9, 135.0, 141.9, 143.3, 145.5, 147.6, 147.8, 155.3, 162.8.

HRMS: *m/z* calcd for $C_{14}H_{10}ClN_2$ (M + 1): 241.0532; found: 241.0532.

1,2,3,4-Tetrahydro[1,5]naphthyridines; General Procedure E

To a solution of **2** (1.0 mmol) in dichloroethane (5.5 mL) was added an olefin (2–20 mmol) and $BF_3.OEt_2$ (2 mmol). The mixture was

stirred at 60–80°C for 1–4.5 h and cooled to r.t. Aqueous sat. K_2CO_3 solution was added and the mixture was extracted twice with EtOAc. The combined organic layers were washed once with distilled water, once with brine, and dried ($MgSO_4$). The solvents were removed under vacuum and the product was isolated by column chromatography.

6-Methoxy-1-methyl-4-phenyl-2-[(1,1,1-trimethylsilyl)methyl]-1,2,3,4-tetrahydro[1,5]naphthyridine (5a)

Following the General Procedure E, **2a** (253 mg, 1.0 mmol) was reacted with allyltrimethylsilane (237 mg, 2.1 mmol) to give 176 mg (50%) of **5a.**

IR (film) ν = 2920, 1470, 1425, 1382, 1255, 1240 cm^{-1}.

^1H NMR (500 MHz, CD_3COCD_3). δ = 0.01 [s, 9 H, $(CH_3)_3Si$], 0.81 (dd, 1 H, *J* = 14.7, 10.1 Hz, CH_2Si), 1.12 (dd, 1 H, *J* = 14.6, 3.1 Hz, CH_2Si), 2.09 (m, 1 H, C*H*$_2$CPh), 2.35 (ddd, 1 H, *J* = 13.4, 5.9, 3.9 Hz, C*H*$_2$CPh), 2.82 (s, 3 H, CH_3N), 3.39 (m, 1 H, CHN), 3.45 (s, 3 H, CH_3O), 4.16 (dd, 1 H, *J* = 10.1, 5.9 Hz, C*H*Ph), 6.48 (dd, 1 H, *J* = 8.7, 0.9 Hz), 7.15 (m, 4 H), 7.28 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 3.7, 26.4, 41.7, 44.4, 50.6, 56.9, 61.1, 113.1, 130.6, 131.1, 132.7, 133.8, 144.1, 148.0, 150.1, 160.5.

HRMS: *m*/*z* calcd for $C_{20}H_{29}N_2OSi$ (M + 1): 341.2049; found: 341.2048.

2-Methoxy-5-methyl-9-phenyl-5a,6,7,8,8a,9-hexahydro-5*H*-cyclopenta[*b*][1,5]naphthyridine (5b)

Following the General Procedure E, **2a** (245 mg, 1.0 mmol) was reacted with cyclopentene (1.35 g, 20 mmol) in a mixture of dichloroethane (7 mL) and THF (3 mL) at 60 °C for 1 h to give 191 mg (65%) of **5b**.

IR (KBr) ν = 2950, 1470, 1415, 1250, 1015 cm^{-1}.

^1H NMR (500 MHz, CD_3COCD_3): δ = 1.16–1.95 (m, 6 H, $CH_2CH_2CH_2$), 2.78 (m, 1 H, C*H*CPh), 2.81 (s, 3 H, CH_3N), 3.60 (s, 3 H, CH_3O), 3.75 (m, 1 H, CHN), 4.20 (d, 1 H, *J* = 5.2 Hz, C*H*Ph), 6.52 (dd, 1 H, *J* = 8.6, 0.6 Hz), 7.05 (d, 1 H, *J* = 8.6 Hz), 7.24 (m, 3 H), 7.43 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3); δ = 27.8, 33.0, 35.9, 40.4, 52.7, 53.3, 57.2, 69.0, 112.3, 127.9, 130.8, 132.3, 135.4, 142.6, 146.2, 149.3, 160.6.

HRMS: *m*/*z* calcd for $C_{19}H_{23}N_2O$ (M + 1): 295.1810; found: 295.1811.

1-Allyl-6-chloro-4-phenyl-2-[(1,1,1-trimethylsilyl)methyl]-1,2,3,4-tetrahydro[1,5]naphthyridine (5c)

Following the General Procedure E, **2k** (279 mg, 1.0 mmol) was reacted with allyltrimethylsilane (2.3 g, 20 mmol) in a mixture of dichloroethane (7 mL) and THF (3 mL) at 80 °C for 1.25 h to give 159 mg (42%) of **5c**.

IR (film) ν = 2940, 1565, 1435, 1240 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 0.03 [s, 9 H, $(CH_3)_3Si$], 0.77 (dd, 1 H, *J* = 14.6, 11.4 Hz, CH_2Si), 1.11 (dd, 1 H, *J* = 14.6, 2.6 Hz, CH_2Si), 2.17 (m, 1 H, C*H*$_2$CPh), 2.42 (m, 1 H, C*H*$_2$CPh), 3.69 (m, 1 H, CHCSi), 3.85 (m, 1 H, CH_2N), 4.08 (m, 1 H, CH_2N), 4.25 (dd, 1 H, *J* = 9.2, 5.5 Hz, C*H*Ph), 5.22 (m, 2 H, CH_2=), 5.91 (m, 1 H, CH=), 7.01 (s, 2 H), 7.16 (m, 3 H), 7.28 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 3.5, 27.0, 43.6, 50.2, 55.9, 59.5, 120.7, 127.1, 127.4, 131.0, 133.1, 133.7, 139.4, 141.0, 147.0, 149.5, 150.7.

HRMS: m/z calcd. for $C_{21}H_{28}ClN_2Si$ (M + 1): 371.1710; found: 371.1709.

(5a*R*,7*R*,9a*S*)-2-Methoxy-5,7,10,10-tetramethyl-5,5a,6,7,8,9,9a,10-octahydrobenzo[*b*][1,5]naphthyridine (6)

To a solution of **1b** (429 mg, 3.1 mmol) in dichloroethane (8 mL) at 0°C was added dichlorophenylborane (588 mg, 3.7 mmol). The mixture was stirred at 0 °C for 1 h. A solution of (*R*)-(+)-citronellal (574 mg, 3.7 mmol) in dichloroethane (2 mL) was added dropwise and the mixture was stirred at 0 °C for 2.5 h. Aq NH_4OH (3 mL) was added at 0°C and the mixture stirred vigorously for 1 min. It was diluted with Et_2O (ca 100 mL), transferred to a Florisil packed column, and eluted with 60% EtOAc/hexane. The solvents were removed under vacuum. The residue was chromatographed to give 340 mg (40%) of **6** and 38 mg (4%) of **7.**

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$[\alpha]_D$ +23.3 (*c* = 0.9, $CHCl_3$),

IR (film) ν = 2920, 1470, 1410, 1250 cm^{-1}

^1H NMR (500 MHz, CD_3COCD_3): δ = 0.85 (q, 1 H, *J* = 11 Hz, H-6ax), 0.94 (ddd, 1 H, *J* = 12.9, 12.9, 3.7 Hz, H-8ax), 0.96 (d, 3 H, *J* = 6.6 Hz), 1.02 (s, 3 H), 1.23 (ddd, 1 H, *J* = 12.5, 12.5, 3.4 Hz, H-9ax), 1.34 (dd, 1 H, *J* = 10.8, 3.2 Hz, H-9a), 1.37 (s, 3 H), 1.53 (m, 1 H, H-7), 1.77 (br d, 1 H, *J* = 12.9 Hz, H-8eq), 1.95 (ddd, 1 H, *J* = 12.9, 3.2, 3.2 Hz, H-9eq), 2.32 (ddd, 1 H, *J* = 12.5, 1.9, 1.9 Hz, H-6eq), 2.73 (dt, 1 H, *J* = 10.6, 3.7 Hz, H-5a), 2.85 (s, 3 H, NH), 3.79 (s, 3 H, CH_3), 6.43 (d, 1 H, *J* = 8.7 Hz), 7.04 (d, 1 H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 26.9, 28.9, 29.2, 30.5, 36.1, 39.6, 41.7, 42.1, 46.6, 52.7, 57.0, 63.1, 112.7, 130.2, 141.9, 152.2, 159.9.

HRMS: *m*/*z* calcd. for $C_{17}H_{27}N_2O$ (M + 1): 275.2123; found: 275.2124.

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^1H NMR (500 MHz, benzene-d_6): δ = 0.74 (ddd, 1 H, *J* = 12.3, 12.3, 3.4 Hz), 0.80 (d, 3 H, *J* = 6.4 Hz, CH_3C), 0.85 (dd, 1 H, *J* = 12.0, 12.0 Hz), 1.16 (m, 1 H), 1.27 (ddd, 1 H, *J* = 12.5, 12.5, 3.4 Hz), 1.4–1.8 (m, 6 H), 2.05 (dt, 1 H, *J* = 11.4, 3.7 Hz), 2.40 (s, 3 H, CH_3N), 3.32 (dt, 1 H, *J* = 11.4, 3.7 Hz), 3.95 (s, 3 H, CH_3O), 4.75 (s, 2 H), 6.72 (d, 1 H, *J* = 9.0 Hz), 6.88 (dd, 1 H, *J* = 9.0, 3.2 Hz), 7.90 (d, 1 H, *J* = 3.2 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 23.1, 26.7, 30.0, 35.3, 37.0, 39.5, 40.9, 54.3, 57.2, 65.0, 115.0, 115.6, 130.5, 136.0, 146.8, 153.2, 161.3.

MS: *m*/*z* calcd for $C_{17}H_{27}N_2O$ (M + 1): 275; found: 275.

3-Alkylamino-2 -(1-*tert*-butyldimethylsilyloxyallyl)pyridines; General Procedure F

To a solution of **2** (1.5 mmol) in dichloroethane (10 mL) were added dimethylaminopyridine (1.7 mmol), *tert*-butyldimethylsilyl chloride (2.3 mmol), and Et_3N (1.7 mmol). The mixture was stirred at r.t. for 20 h. Sat. aq NH_4Cl solution was added and the mixture extracted twice with EtOAc. The combined organic extracts were washed once with brine and dried ($MgSO_4$). The solvents were removed under vacuum and the residue was purified by column chromatography.

***N*-{2-[(*E*)-1-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}prop-2-enyl]-6-methoxy-3-pyridyl}-*N*-methylamine (8a)**

Yield: 77%.

IR (KBr) ν = 3400 (NH), 2940, 2920, 2840, 1495, 1455, 1410, 1265, 1245 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 0.04 (s, 3 H, CH_3Si), 0.09 (s, 3 H, CH_3Si), 0.89 (s, 9 H, C_4H_9Si), 2.79 (d, 3 H, *J* = 4.3 Hz, CH_3N), 3.77 (s, 3 H, CH_3O), 4.90 (br s, 1 H, NH), 5.11 (dt, 1 H, *J* = 10.4, 1.8 Hz, CHO), 5.33 (m, 2 H, CH_2=), 6.09 (m, 1 H, CH=), 6.58 (d, 1 H, *J* = 8.7 Hz), 7.05 (d, 1 H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = –0.7, 22.9, 30.2, 35.1, 57.3, 84.6, 114.1, 118.4, 127.8, 142.7, 144.2, 145.4, 159.9.

HRMS: *m*/*z* calcd for $C_{16}H_{29}N_2O_2Si$ (M + 1): 309.1998; found: 309.1999.

***N*-[2-((*E*)-1-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}but-2-enyl)-6-methoxy-3-pyridyl]-*N*-methylamine (8b)**
Yield: 71%.

IR (KBr) ν = 3400, 2940, 2920, 2840, 1465, 1250 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 0.05 (s, 3 H, CH_3Si), 0.08 (s, 3 H, CH_3Si), 0.88 (s, 9 H, C_4H_9Si), 1.66 (dd, 3 H, *J* = 4.9, 1.2 Hz, CH_3C=), 2.77 (d, 3 H, *J* = 4.6 Hz, CH_3N), 3.76 (s, 3 H, CH_3O), 4.97 (br s, 1 H, NH), 5.22 (m, 1 H, CHO), 5.77 (m, 2 H, CH=CH), 6.56 (d, 1 H, *J* = 8.7 Hz), 7.04 (d, 1 H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3); δ = –0.09, –0.08, 21.8, 22.8, 30.2, 35.1, 57.2, 84.6, 113.8, 127.7, 130.5, 135.7, 144.0, 146.4, 159.9.

HRMS: *m*/*z* calcd. $C_{17}H_{31}N_2O_2Si$ (M + 1): 323.2155; found: 323.2156.

***N*-{2-[(*E*)-1-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}prop-2-enyl]-6-methoxy-3-pyridyl}-*N*-allylamine (8c)**
Yield: 49%.

^1H NMR (300 MHz, CD_3COCD_3): δ = 0.03 (s, 3 H, CH_3Si), 0.09 (s, 3 H, CH_3Si), 0.88 (s, 9 H, C_4H_9Si). 1.67 (dd, 3 H, *J* = 4.8, 1.2 Hz, CH_3C=), 3.72 (m, 2 H, CH_2N), 3.76 (s, 3 H, CH_3O), 5.11 (m, 2 H, CH_2=, NH), 5.26 (m, 2 H, CH_2=, CHO), 5.76 (m, 2 H, CH=CH), 5.96 (m, 1 H, =CHCN), 6.53 (d, 1 H, *J* = 8.7 Hz), 7.05 (d, 1 H, 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = –0.09, –0.08, 21.8, 22.9, 30.3, 51.2, 57.2, 84.7, 113.8, 119.8, 128.7, 130.5, 135.6, 141.0, 142.6, 146.5, 160.1.

HRMS: *m*/*z* calcd for $C_{19}H_{33}N_2O_2Si$ (M + 1): 349.2311; found: 349.2310.

***N*-{2-[(*E*)-1-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}-3-phenylpro-2-enyl]-6-chloro-3-pyridyl}-*N*-methylamine (8d)**
Yield: 70%.

IR (KBr) ν = 3380 (NH), 2940, 2920, 2840, 1552, 1485, 1425, 1410, 1250 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3); δ = 0.03 (s, 3 H, CH_3Si), 0.15 (s, 3 H, CH_3Si), 0.93 (s, 9 H, C_4H_9), 1.83 (d, 3 H, *J* = 4.3 Hz, CH_3N), 5.49 (dd, 1 H, *J* = 5.7, 2.4 Hz, CHO), 5.62 (br s, 1 H, NH), 6.54 (dd, 1 H, *J* = 16, 5.7 Hz, CH=), 6.77 (d, 1 H, *J* = 16 Hz, PhC*H*=), 7.03 (d, 1 H, *J* = 8.5 Hz), 7.14 (d, 1 H, *J* = 8.5 Hz), 7.27 (m, 3 H), 7.43 (m, 2 H).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = –0.09, –0.08, 22.87, 30.24, 30.31, 84.39, 125.1, 128.2, 131.5, 132.6, 133.1, 133.5, 135.3, 140.4, 141.7, 148.4, 149.6.

HRMS: *m*/*z* calcd for $C_{21}H_{30}ClN_2OSi$ (M + 1): 389.1816; found: 389.1815.

4-Azaindoles 9a–d

3-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}-5-methoxy-1,2-dimethyl-1*H*-pyrrolo[3,2-*b*]pyridine (9a)
To a mixture of LiCl (225 mg, 5.2 mmol), benzoquinone (85 mg, 0.79 mmol), K_2CO_3 (217 mg, 1.6 mmol), and $PdCl_2(MeCN)_2$ (28 mg, 0.11 mmol) in anhyd THF (4 mL) was added a solution of **8a** (162 mg, 0.52 mmol) in THF (2 mL). The mixture was stirred at r.t. for 1.75 h. The mixture was diluted with Et_2O, transferred to a silica gel packed column, and eluted with Et_2O. The solvents were removed under vacuum and the residue was purified by column chromatography to give 163 mg (100%) of **9a**; mp 70 °C.

IR (KBr) ν = 2950, 2920, 1560, 1490, 1455, 1400, 1260, 1175 cm^{-1}.

^1H NMR (400 MHz, CD_3COCD_3): δ = 0.27 [s, 6 H, $(CH_3)_2Si$], 1.05 (s, 9 H, C_4H_9Si), 2.33 (s, 3 H, CH_3C–N), 3.64 (s, 3 H, CH_3N), 3.89 (s, 3 H, CH_3O), 6.43 (d, 1 H, *J* = 8.8 Hz), 7.59 (d, 1H, *J* = 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 0.3, 5.8, 13.1, 23.0, 30.5, 57.5, 108.1, 124.3, 127.9, 131.0, 134.8, 138.6, 163.8.

HRMS: *m*/*z* calcd. for $C_{16}H_{26}N_2O_2Si$ (M + 1): 307.1842; found: 307.1843.

3-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}-2-ethyl-5-methoxy-1-methyl-1*H*-pyrrolo[3,2-*b*]pyridine (9b)
A mixture of **8b** (125 mg, 0.39 mmol), LiCl (166 mg, 3.9 mmol), benzoquinone (63 mg, 0.58 mmol), K_2CO_3 (160 mg, 1.2 mmol), and $PdCl_2(MeCN)_2$ (20 mg, 0.077 mmol) in anhyd THF (5 mL) was heated to reflux for 3.5 h. The resulting mixture was diluted with Et_2O, transferred to a silica gel packed column, and eluted with Et_2O. The solvents were removed under vacuum and the residue was purified by column chromatography to give 63 mg (51%) of **9b.**

IR (KBr) ν = 2940, 2920, 2840, 1550, 1460, 1395, 1255 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 0.31 [s, 6 H, $(CH_3)_2Si$], 1.06 (s, 9 H, C_4H_9Si), 1.21 (t, 3 H, *J* = 7.5 Hz, CH_3C), 2.82 (q, 2 H, *J* = 7.5 Hz, CH_2C=), 3.68 (s, 3 H, CH_3N), 3.90 (s, 3 H, CH_3O), 6.45 (d, 1 H, *J* = 8.7 Hz), 7.60 (d, 1 H, 8.7 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 0.31, 18.4, 21.2, 23.0, 30.4, 33.8, 57.5, 108.2, 124.5, 128.0, 134.2, 136.6, 138.5, 163.9.

HRMS: *m*/*z* calcd. for $C_{17}H_{29}N_2O_2Si$ (M + 1): 321.1998; found: 321.1999.

3-{[1-(*tert*-Butyl)-1,1-dimethylsilyl]oxy}-1-allyl-2-ethyl-5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridine (9c)
A mixture of **8c** (142 mg, 0.41 mmol), LiCl (174 mg, 4.1 mmol), benzoquinone (66 mg, 0.61 mmol), K_2CO_3 (168 mg, 1.2 mmol), and $PdCl_2(MeCN)_2$ (21mg, 0.081 mmol) in anhyd THF (6 mL) was heated to reflux for 4 h. It was diluted with Et_2O, transferred to a silica gel packed column, and eluted with Et_2O. The solvents were removed under vacuum and the residue was purified by column chromatography to afford 89 mg (63%) of **9c**. The compound was contaminated by an unseparable unknown impurity and was not characterized. It was used without further purification in the next step (formation of compound **10**).

2-Benzyl-3-{[1-(*tert*-butyl)-1,1-dimethylsilyl]oxy}-5-chloro-1-methyl-1*H*-pyrrolo[3,2-*b*]pyridine (9d)
A mixture of **8d** (254 mg, 0.65 mmol), LiCl (280 mg, 6.5 mmol), benzoquinone (106 mg, 0.98 mmol), K_2CO_3 (271 mg, 2.0 mmol), and $PdCl_2(MeCN)_2$ (169 mg, 0.65 mmol) in anhyd THF (7 mL) was stirred at r.t. for 48 hours. It was diluted with Et_2O, transferred to a silica gel packed column, and eluted with Et_2O. The solvents were removed under vacuum and the title compound **9d** (136 mg, 54%) was isolated by column chromatography.

IR (film) ν = 2930, 2920, 2840, 1565, 1445, 1190 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 0.30 [s, 6 H, $(CH_3)_2Si$], 1.02 (s, 9 H, C_4H_9Si), 3.57 (s, 3 H, CH_3N), 4.26 (s, 2 H, C*H*$_2$Ph), 7.04 (d, 1 H, *J* = 8.5 Hz), 7.25 (m, 5 H), 7.73 (d, 1 H, *J* = 8.5 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 0.45, 22.9, 30.3, 30.4, 120.2, 124.0, 130.9, 131.3, 133.1, 133.6, 135.8, 135.9, 141.7, 143.6, 147.1.

HRMS: *m*/*z* calcd for $C_{21}H_{28}ClN_2OSi$ (M + 1): 387.1659; found: 387.1658.

Methyl 2-[(1-Allyl-2-ethyl-5-methoxy-1*H*-pyrrolo[3,2-*b*]pyridin-3-yl)oxy]acetate (10)
To a solution of **9c** (89 mg) in THF (4 mL) were added methyl bromoacetate (97 mg, 0.63 mmol) and Bu_4NF (1.0 M in THF, 0.515 mL, 0.515 mmol) successively and the mixture was stirred at r.t. for 3.5 h. Sat. aq NH_4Cl was added and the mixture was extracted twice with EtOAc. The combined organic layers were washed once with distilled water, once with brine, and dried ($MgSO_4$). The title compound **10** (43 mg, 55%) was isolated by column chromatography.

IR (film) ν = 2950, 2920, 1750, 1550, 1400 cm^{-1}.

^1H NMR (300 MHz, CD_3COCD_3): δ = 1.23 (t, 3 H, *J* = 7.6 Hz, CH_3C), 2.84 (q, 2 H, *J* = 15.1, 9.1 Hz, CH_2CN), 3.67 (s, 3 H, CH_3OCO), 3.87 (s, 3 H, CH_3O), 4.74 (m, 2 H, CH_2N), 4.77 (m, 1 H, CH_2=), 5.07 (m, 1 H, CH_2=), 5.15 (s, 2 H, CH_2O), 5.95 (m, 1 H, =CHCN), 6.45 (d, 1 H, *J* = 8.8 Hz), 7.58 (d, 1 H, *J* = 8.8 Hz).

^{13}C NMR (100.6 MHz, CD_3COCD_3): δ = 18.5, 21.3, 50.0, 55.8, 57.2, 73.1, 108.6, 120.2, 125.5, 127.6, 136.8, 136.9, 138.1, 139.5, 163.8, 175.2.

HRMS: *m*/*z* calcd for $C_{16}H_{21}N_2O_4$ (M + 1): 305.1501; found: 305.1500.

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