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New Syntheses of Substituted Pyridines via Bromine–Magnesium Exchange

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Abstract—Bromine–magnesium exchange using *i*PrMgCl in THF at room temperature on 2-, 3- and 4-bromopyridines allowed the synthesis of various functionalized pyridines. The methodology was successfully used for the synthesis of 4-azaxanthone. Moreover, single exchange reactions observed on 2,6-, 3,5-, 2,3- and 2,5-dibromopyridines, with complete regioselectivity in the case of 2,3- and 2,5-dibromopyridines, afforded substituted bromopyridines, which were then involved in a second exchange step to provide difunctionalized pyridines.

Introduction

Interest in pyridine natural products and pharmaceuticals, as well as pyridine building blocks for various applications such as material science and supramolecular chemistry, has resulted in extensive efforts on synthesis methodologies. Lithiation reactions allow many functionalizations[1] either by direct reaction with electrophiles or transmetalation to allow cross-coupling reactions.

Nevertheless, lithiation often requires low temperature, which can be difficult to realize on an industrial scale. Moreover, halogen–lithium exchange is very sensitive to reaction temperature, particularly for bromopyridines.[1a,2] In this case, the reaction has to be performed at −100°C in tetrahydrofuran (THF) or around −40°C in diethyl ether, in order to avoid side-reactions such as deprotonation, addition to the substrate, elimination of lithium bromide (to give pyridynes), bromine migration ('halogen dance') or even ring opening reactions.

So, we have been interested in the development of pyridylmagnesium reagents that could be involved in either electrophilic trapping or coupling reactions.

Halogen–magnesium exchange reactions were preferred for generating pyridylmagnesium halides since the direct access to pyridine Grignard reagents by the oxidative addition of magnesium to the halopyridine is difficult to achieve, even with magnesium activation.[3]

A survey of the literature revealed that significant results were reported from iodopyridines,[4] which, however, are expensive and rarely commercially available. In those cases, iodine–magnesium exchange was observed when the iodides were treated with alkyl or phenylmagnesium halides. Paradies[5] described chlorine–magnesium exchange by reaction of chloropyridines with phenylmagnesium halides, but the results could not be repeated. As far as bromopyridines are concerned, bromine exchange was reported by Paradies[5] using phenylmagnesium halides, and Meunier[6] using isopropylmagnesium chloride in THF at −25°C. The resulting Grignard derivatives were trapped with electrophiles, but no yields were mentioned.[5]

We recently reported[7] a convenient access to pyridylmagnesium chlorides, starting from commercially available bromopyridines. Herein, details of our investigations on the elaboration of mono and difunctionalized pyridines from the corresponding bromo and dibromopyridines are recorded.[8]

Results and Discussion

Various alkylmagnesium halides, reaction times, and solvents were tested in order to optimize the exchange conditions on bromopyridines and the trapping of the pyridine Grignard reagents with electrophiles. It was found that *i*PrMgCl was the best exchange reagent; *t*BuMgCl among different bulky reagents did not give satisfying results. The reaction was performed in various solvents such as diethyl ether, dioxanes, tetrahydropyran, hexamethylenephosphoramide, THF, or even mixtures of these solvents. THF proved to be the best solvent for the exchange reaction. It was demonstrated by gas chromatography

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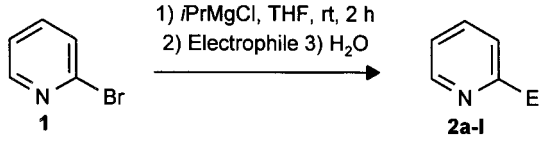
that, under these conditions, the halogen that was attached to the pyridine Grignard reagent was chlorine, as isopropyl bromide was selectively formed.

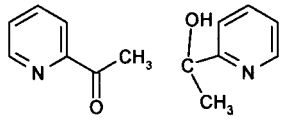
As far as trapping with electrophiles is concerned, several amine complexing agents of magnesium were tested in order to increase the reactivity of the pyridylmagnesium chloride. It was observed that the addition of the complexing agent enhanced not only the nucleophilicity but also the basicity of the Grignard reagent. As a result, the effect largely depends on the nature of the electrophile. Thus, addition of triethylamine (1 equiv.) to the reaction mixture before introduction of the electrophile, improved the yields in some cases.

2-Bromopyridine (**1**) reacts with *i*PrMgCl in THF at room temperature. The 2-pyridylmagnesium chloride thus obtained was treated with various electrophiles at room temperature. Deuteriolysis afforded almost quantitatively completely 2-deuterated pyridine, accompanied by less than 10% of 2-bromopyridine (**1**). Reaction with benzaldehyde (entry 1) provided the corresponding alcohol in high yield (80%), the remaining 20% being essentially pyridine (less than 5% of starting compound **1** is recovered), as shown by GC assays. The 2-bromopropane formed during the exchange seems to have no effect on the reactions. In the case of enolizable carbonyl compounds (entries 2–7), moderate to good yields of alcohols were obtained. Acid chlorides (entries 8 and 9) gave low yields of the corresponding ketones, and mixtures of degradation compounds were formed. Disulfides (entries 10 and 11) produced the expected sulfides in moderate yields. Iodine (entry 12) allowed the synthesis of 2-iodopyridine (**2l**) in an excellent yield (Scheme 1, Table 1).



Scheme 1.

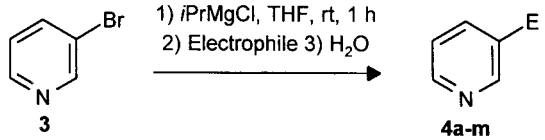
Table 1. 2-Pyridylmagnesium chloride: trapping with various electrophiles

Entry	Electrophile	E	Product	Yield (%)[a]
1	PhCHO	CH(OH)Ph	**2a**	80
2	CH_3CHO	$CH(OH)CH_3$	**2b**	79
3	CH_3CH_2CHO	$CH(OH)CH_2CH_3$	**2c**	54
4	$CH_3(CH_2)_4CHO$	$CH(OH)(CH_2)_4CH_3$	**2d**	42
5	$PhCH_2CHO$	$CH(OH)CH_2Ph$	**2e**	42
6			**2f**	25
7	CH_3COCH_3	$C(OH)(CH_3)_2$	**2g**	30
8	PhCOCl	COPh	**2h**	11[b]
9	CH_3COCl	$COCH_3$	**2i**	15
10	PhSSPh	SPh	**2j**	45[b]
11	CH_3SSCH_3	SCH_3	**2k**	40[b]
12	I_2	I	**2l**	97

[a] Isolated yields based on **1**.
[b] 1 equiv. of triethylamine was added before quenching with the electrophile.

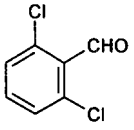
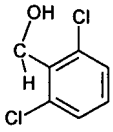
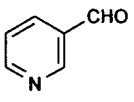
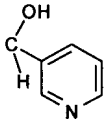
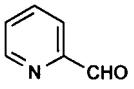
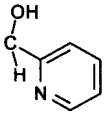
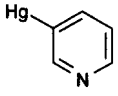
Under the same exchange reaction conditions, 3-bromopyridine (**3**) readily reacts with *i*PrMgCl, and the resulting pyridylmagnesium chloride was trapped with various electrophiles in moderate to high yields. In the case of acetaldehyde (entry 6), an excess of electrophile was successfully used at a lower temperature. It was noted that in the case of benzoyl chloride, the tertiary alcohol resulting from the reaction of 3-pyridylmagnesium chloride with ketone **4i** was never observed and did not explain the low yield. It was shown that 3-pyridylmagnesium chloride is not a suitable reagent for alkylation (entry 11), but that it allows a simple access to bis(3-pyridyl)mercury (**4m**) (entry 14) (Scheme 2, Table 2). In summary, 2- and 3-pyridylmagnesium chlorides could be easily prepared, but the former were less reactive towards electrophiles.

Due to its instability, 4-bromopyridine (**5b**) has to be used in the magnesium-exchange reaction immediately after neutralization of the corresponding commercial hydrochloride (**5a**). Bromine–magnesium exchange was also

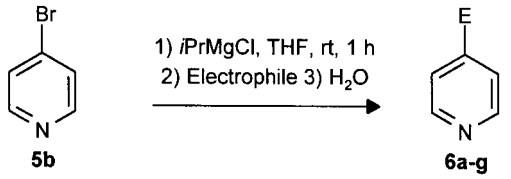


Scheme 2.

Table 2. 3-Pyridylmagnesium chloride: trapping with various electrophiles

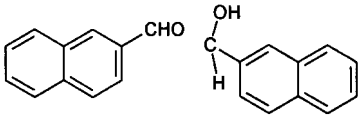
Entry	Electrophile	E	Product	Yield (%)[a]
1	PhCHO	CH(OH)Ph	**4a**	84, 93[b]
2			**4b**	74
3			**4c**	32, 40[b]
4			**4d**	46
5	*t*BuCHO	$CH(OH)tBu$	**4e**	78
6	CH_3CHO	$CH(OH)CH_3$	**4f**	51, 14[b], 74[c]
7	PhCOPh	$C(OH)Ph_2$	**4g**	51
8	EtCOEt	$C(OH)Et_2$	**4h**	58, 16[b]
9	PhCOCl	COPh	**4i**	35[d]
10	*i*PrCOCl	CO*i*Pr	**4j**	12[d]
11	CH_3I or CH_3CH_2I	CH_3 or CH_2CH_3		0
12	CH_3SSCH_3	SCH_3	**4k**	49, 58[b]
13	I_2	I	**4l**	78
14	$HgBr_2$[e]		**4m**	80

[a] Isolated yields based on **3**.
[b] 1 equiv. of triethylamine was added before quenching with the electrophile.
[c] 10 equiv. of CH_3CHO were used at −20°C.
[d] Addition of RCOCl at −70°C and gentle warming to rt.
[e] 0.5 equiv. was used.



Scheme 3.

Table 3. 4-Pyridylmagnesium chloride: trapping with various electrophiles

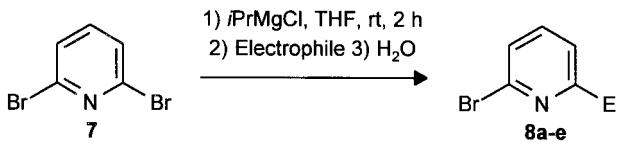
Entry	Electrophile	E	Product	Yield (%)[a]
1	PhCHO	CH(OH)Ph	**6a**	64
2			**6b**	40
3	$CH_3(CH_2)_4CHO$	$CH(OH)(CH_2)_4CH_3$	**6c**	42
4	$(CH_3)_2CHCHO$	$CH(OH)CH(CH_3)_2$	**6d**	39
5	PhCOPh	$C(OH)Ph_2$	**6e**	29
6	PhSSPh	SPh	**6f**	45[b]
7	I_2	I	**6g**	51

[a] Isolated yields based on hydrochloride **5a**.
[b] 1 equiv. of triethylamine was added before quenching with the electrophile.

observed, and trapping reactions could be achieved in moderate to good yields (Scheme 3, Table 3).

This study was then extended to dibromopyridines with the purpose of studying the regioselectivity of the exchange.

2,6-Dibromopyridine (**7**) reacts almost quantitatively with *i*PrMgCl in a single exchange reaction (even with an excess of reagent), as demonstrated by deuteriolysis (entry 1). The yields largely depend on the trapping step with the electrophiles (Scheme 4, Table 4).

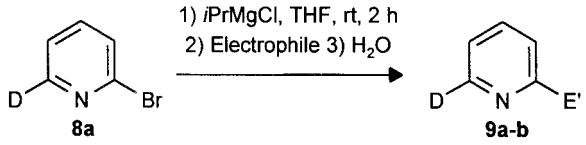


Scheme 4.

Table 4. 6-Bromo-2-pyridylmagnesium chloride: trapping with various electrophiles

Entry	Electrophile	E	Product	Yield (%)[a]
1	D_2O	D	**8a**	95[b,c]
2	PhCHO	CH(OH)Ph	**8b**	42[c]
3	$ClSi(CH_3)_3$	$Si(CH_3)_3$	**8c**	74[c]
4	CH_3SSCH_3	SCH_3	**8d**	45[c]
5	I_2	I	**8e**	90[d]

[a] Isolated yields based on **7**.
[b] 100% of deuterium incorporation was observed from the ^1H NMR spectra integration values.
[c] 2 equiv. of *i*PrMgCl and electrophile were used.
[d] 4 equiv. of *i*PrMgCl and I_2 were used.



Scheme 5.

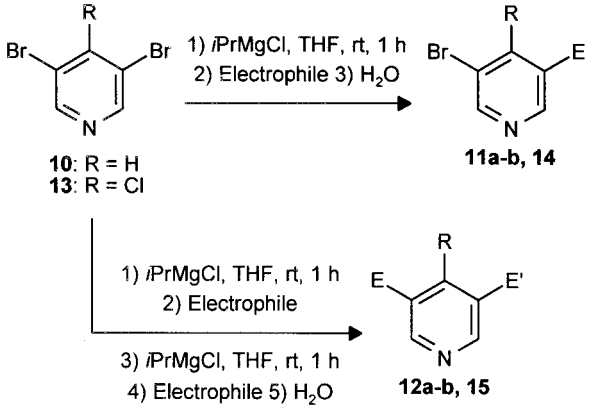
Table 5. 2-(6-d)Pyridylmagnesium chloride: trapping with electrophiles

Product	E′	Yield (%)[a]
9a	CH(OH)Ph	66
9b	I	42

[a] Isolated yields based on **8a**.

The second bromine–magnesium exchange could be performed on the bromo derivative **8a**; subsequent reaction with an electrophile provided the expected 2,6-disubstituted pyridines **9a**–**b** (Scheme 5, Table 5).

A single exchange was also established from 3,5-dibromopyridine (**10**), and afforded 3-bromo-5-substituted pyridines **11a**–**b** in good yields. Consecutive exchange of the second bromine atom in a one-pot procedure could be carried out to give 3,5-disubstituted pyridines **12a**–**b**. So, two different substituents can be introduced at C3 and C5, using this one-pot methodology.

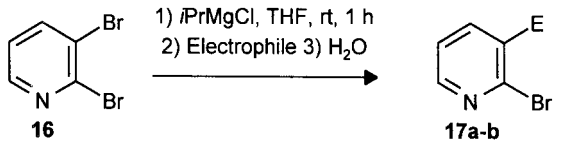


Scheme 6.

Table 6. 5-Bromo-3-pyridylmagnesium chloride and one pot 3- and 5-pyridylmagnesium chlorides: trapping with electrophiles

Product	R	E	E′	Yield%[a]
5-Bromo-3-pyridylmagnesium chloride				
11a	H	D		82[b]
11b	H	CH(OH)Ph		76
14	Cl	H		99
One pot 3- and 5-pyridylmagnesium chlorides				
12a	H	CH(OH)Ph	CH(OH)Ph	49
12b	H	$Si(CH_3)_3$	CH)(OH)Ph	52
15f	Cl	CH(OH)Ph	CH(OH)Ph	74

[a] Isolated yields based on **10** or **13**.
[b] 100% of deuterium incorporation was observed from the ^1H NMR spectra integration values.

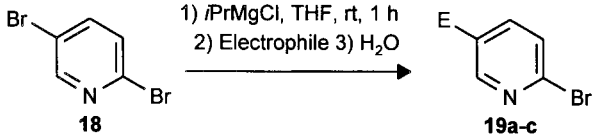


Scheme 7.

Table 7. 2-Bromo-3-pyridylmagnesium chloride: trapping with electrophiles

Product	E	Yield (%)[a]
17a	CH(OH)Ph	92
17b	I	80

[a] Isolated yields based on **16**.



Scheme 8.

Table 8. 2-Bromo-5-pyridylmagnesium chloride: trapping with electrophiles

Product	E	Yield (%)[a]
19a	D	64[b]
19b	CH(OH)Ph	86
19c	I	82

[a] Isolated yields based on **16**.
[b] 100% of deuterium incorporation was observed from the ^{1}H NMR spectra integration values.

In order to study the effect of an additional halogen substituent, 4-chloro-3,5-dibromopyridine (**13**) was treated under the same conditions. A single exchange reaction at C3 gave, quantitatively, 3-bromo-4-chloropyridine (**14**) after hydrolysis of the reaction mixture. The one-pot procedure applied to dibromo compound **13** led to difunctionalized pyridine **15** in 74% yield (the same procedure applied to dibromo derivative **10** only proceeds in 49% yield). The chlorine atom at C4 seems to enhance the rate of the bromine–magnesium exchange and/or the reactivity of the Grignard intermediate (Scheme 6, Table 6).

Reacting 2,3-dibromopyridine[8] (**16**) with *i*PrMgCl at room temperature, followed by quenching with benzaldehyde or iodine, afforded 2-bromo-3-substituted pyridines **17a**–**b** in high yields (Scheme 7, Table 7). The observed selectivity of the exchange could be related to the strength of the carbon–bromine bond; conjugation of the bromine at C2 with C=N bond could justify the regioselective reaction at C3.

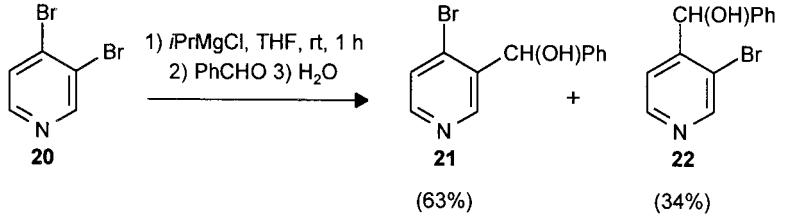
2-Bromo-5-substituted pyridines, (**19a**–**c**), were synthesized from 2,5-dibromopyridine (**18**), following the same procedure as for the 2,3 isomer. The same selectivity was observed (Scheme 8, Table 8). Thus, from dibromopyridines **16** and **18**, bromine–magnesium exchange first occurred at C3 or C5, as previously reported[2d,f] when these compounds were treated with butyllithium in THF at −100°C.

3,4-Dibromopyridine (**20**) reacts under the same conditions to give exchange at C3 and C4 in a respectively 65:35 ratio (Scheme 9).

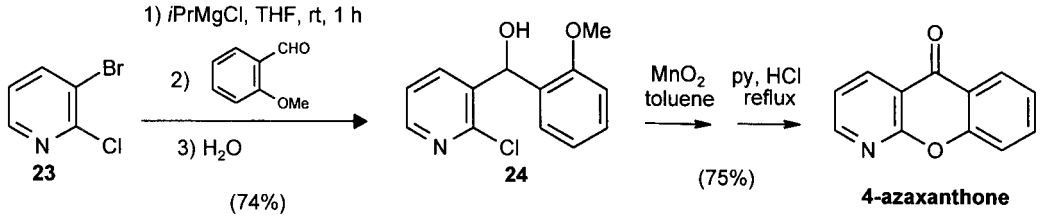
This lack of regioselectivity has already been reported in the case of bromine–lithium exchange.[2f]

Bromine–magnesium exchange has been successfully used for the synthesis in the azaxanthone series.[9] 3-Bromo-2-chloropyridine (**23**) reacted under the conditions previously described to give the desired alcohol **24** in good yield. Compound **24** can easily be converted to 4-azaxanthone via oxidation and cyclization steps.[10] The overall yield of the synthesis is 55% (Scheme 10).

In conclusion, 2-, 3- and 4-substituted pyridines could be



Scheme 9.



Scheme 10.

prepared from the corresponding bromo derivatives by bromine–magnesium exchange reaction. The main advantage of this methodology is the relative stability of these organometallic species: bromine–lithium exchange has to be performed at low temperature to prevent side reactions whereas bromine–magnesium exchange proceeds well at room temperature. Under these conditions, the overall reaction proved to be highly chemoselective and no side products were detected. Regioselectivity of the reaction on dibromopyridines, as well as yields obtained after trapping with electrophiles, are analogous to that observed during bromine–lithium exchange reaction.[2] Subsequent coupling reactions at C2 on bromo substituted pyridines thus obtained could allow the synthesis of more diversified substituted pyridines.

Experimental

Melting points were measured on a Kofler apparatus. The NMR spectra were recorded in $CDCl_3$ or DMSO-d_6 with a Bruker AM 200 spectrometer (^1H at 200 MHz and ^{13}C at 50 MHz). IR spectra were taken on a Perkin Elmer FT IR 205 spectrometer, and main IR absorptions are given in cm^{-1}. Elemental analyses were performed on a Carlo Erba 1106 apparatus.

Starting materials

THF was distilled from benzophenone/Na. Reactions were carried out under dry Ar. Silica gel (Geduran Si 60, 0.063–0.200 mm) was purchased from Merck. *i*PrMgCl (2 M) in THF was purchased from Aldrich. 2- and 3-Bromopyridines were supplied by Acros; 4-bromopyridine hydrochloride, 2,5-, 2,6- and 3,5-dibromopyridines by Lancaster. 3-Bromo-2-chloropyridine,[11a] 4-chloro-3,5-dibromopyridine,[11b] 2,3-dibromopyridine[8] and 3,4-dibromopyridine[11c] were prepared according to literature procedures. Procedures were generally performed on a 10 mmol scale.

2-Substituted pyridines 2a–l: general procedure A

*i*PrMgCl (10 mmol) was added to **1** (0.95 mL, 1.6 g, 10 mmol) in THF (10 mL) at rt. After 2 h, the electrophile (10 mmol) was added. After 18 h at rt, water (50 mL) was added. Extraction with CH_2Cl_2 (3×20 mL), drying over $MgSO_4$ and column chromatography on silica gel (eluent) afforded **2a**–**l**.

α-Phenyl-2-pyridinemethanol (2a). Procedure A, using benzaldehyde as an electrophile gave 80% (CH_2Cl_2/Et_2O, 90:10) of **2a**: mp 72–73°C (lit.[12] mp 72–74°C); ^1H NMR ($CDCl_3$) δ 3.79 (s, 1H, OH), 5.81 (s, 1H, CHOH), 7.3 (m, 8H, $H_{3,4,5}$, Ph), 8.51 (dd, 1H, H_6), $J_{4,6}$=2.0, $J_{5,6}$=4.7 Hz (the ^1H NMR data are in accordance with those of the literature);[12a] ^{13}C NMR ($CDCl_3$) δ 75.4 (CHOH), 121.7 (C_3), 122.4 (C_5), 127.4 ($C_{2',6'}$), 128.2 ($C_{4'}$), 128.9 ($C_{3',5'}$), 137.2 (C_4), 140.1 ($C_{1'}$), 148.2 (C_6), 158.2 (C_2); IR (KBr) ν 3340, 3112, 3094, 1594, 1494, 1435, 1050 cm^{-1}. Anal. Calcd for $C_{12}H_{11}NO$ (185.23): C, 77.81; H, 5.99; N, 7.56. Found: C, 77.98; H, 6.03; N, 7.68%.

α-Methyl-2-pyridinemethanol (2b). Procedure A, using acetaldehyde as an electrophile gave 79% (CH_2Cl_2/Et_2O, 90:10) of **2b**: mp 38–40°C (Lit. 12b mp 39–40°C); ^1H NMR ($CDCl_3$) δ 1.42 (d, 3H, CH_3), 4.80 (q, 1H, CHOH), 5.97 (s, 1H, OH), 7.00 (m, 1H, H_5), 7.29 (d, 1H, H_3), 7.62 (m, 1H, H_4), 8.30 (dd, 1H, H_6), $J_{4,6}$=2.0, $J_{5,6}$=5.0, J_{CH3-CH}=6.6, $J_{3,4}$=8.1 Hz (the ^1H NMR data are in accordance with those of the literature);[12] ^{13}C NMR ($CDCl_3$) δ 22.6 (CH_3), 68.2 (CHOH), 118.4 (C_3), 120.8 (C_5), 135.9 (C_4), 146.2 (C_6), 163.2 (C_2); IR (KBr) ν 3367, 2974, 2929, 1712, 1596, 1435, 1120, 1084, 787 cm^{-1}. Anal. Calcd for C_7H_9NO (123.16): C, 68.27; H, 7.37; N, 11.37. Found: C, 68.51; H, 7.45; N, 11.07%.

α-Ethyl-2-pyridinemethanol (2c). Procedure A, using propanal as an electrophile gave 54% (CH_2Cl_2/Et_2O, 90:10) of **2c**: oil; ^1H NMR ($CDCl_3$) δ 0.99 (t, 3H, CH_3), 1.90 (q, 2H, CH_2), 4.82 (t, 1H, CHOH), 5.30 (s, 1H, OH), 6.97 (m, 1H, H_5), 7.31 (d, 1H, H_3), 7.64 (m, 1H, H_4), 8.50 (d, 1H, H_6), $J_{5,6}$=4.1, $J_{CH3-CH2}$=6.8, $J_{3,4}$=8.0 Hz; ^{13}C NMR ($CDCl_3$) δ 9.9 (CH_3), 31.4 (CH_2), 74.7 (CHOH), 120.8 (C_3), 122.5 (C_5), 137.1 (C_4), 148.3 (C_6), 163.2 (C_2) (the NMR data are in accordance with those of the literature);[12d] IR (neat) ν 3387, 3242, 2967, 2934, 2897, 2243, 2101, 1597, 1436, 1049, 732, 565 cm^{-1}. Anal. Calcd for $C_8H_{11}NO$ (137.18): C, 70.04; H, 8.08; N, 10.21. Found: C, 69.78; H, 8.27; N, 10.14%.

α-Pentyl-2-pyridinemethanol (2d). Procedure A, using hexanal as an electrophile gave 42% (Et_2O) of **2d**: oil; ^1H NMR ($CDCl_3$) δ 0.81 (t, CH_3, 3H), 1.5 (m, 8H, CH_2), 4.20 (s, 1H, OH), 4.60 (t, 1H, CHOH), 7.15 (dd, 1H, H_5), 7.27 (dd, 1H, H_3), 7.63 (m, 1H, H_4), 8.42 (dd, 1H, H_6), $J_{4,6}$=1.9, $J_{5,6}$=5.0, $J_{CH3-CH2}$=6.3, J_{CH-CH2}=6.4, $J_{3,4}$=7.8, $J_{4,5}$=8.0 Hz (the ^1H NMR data are in accordance with those of the literature);[12e] ^{13}C NMR ($CDCl_3$) δ 14.5 (CH_3), 22.9 (CH_2), 25.3 (CH_2), 32.2 (CH_2), 38.9 (CH_2), 73.2 (CHOH), 120.7 (C_3), 122.6 (C_5), 137.0 (C_4), 148.5 (C_6), 162.8 (C_2); IR (neat) ν 3390, 2930, 1731, 1572, 1470, 1434, 1049, 750 cm^{-1}. Anal. Calcd for $C_{11}H_{17}NO$ (179.26): C, 73.70; H, 9.56; N, 7.81. Found: C, 73.76; H, 9.88; N, 7.54%.

α-Benzyl-2-pyridinemethanol (2e). Procedure A, using phenylacetaldehyde as an electrophile gave 42% (CH_2Cl_2/Et_2O, 90:10) of **2e**: mp 116–118°C (Lit. 12f mp 117–119°C); ^1H NMR ($CDCl_3$) δ 3.13 (d, 2H, CH_2), 3.90 (s, 1H, OH), 4.99 (t, 1H, CHOH), 7.3 (m, 8H, $H_{3,4,5}$, Ph), 8.62 (dd, 1H, H_6), $J_{4,6}$=2.0, $J_{5,6}$=5.0, J_{CH2-CH}=6.1 Hz (the ^1H NMR data are in accordance with those of the literature);[12f] ^{13}C NMR ($CDCl_3$) δ 45.6 (CH_2), 74.4 (CHOH), 121.1 (C_3), 122.8 (C_5), 126.8 ($C_{4'}$), 128.7 ($C_{2',6'}$), 130.0 ($C_{3',5'}$), 136.8 (C_4), 138.1 ($C_{1'}$), 148.8 (C_6), 161.6 (C_2); IR (KBr) ν 3085, 3029, 2912, 1596, 1434, 1332, 1100, 1077, 1054, 1006, 774, 699 cm^{-1}. Anal. Calcd for $C_{13}H_{13}NO$ (199.25): C, 78.36; H, 6.58; N, 7.03. Found: C, 78.65; H, 6.77; N, 6.75%.

α-Methylbis(2-pyridine)methanol (2f). Procedure A, using 2-acetylpyridine as an electrophile gave 25% (CH_2Cl_2/Et_2O, 90: 10) of **2f**: mp 46–48°C (Lit. 12g mp 47–49°C); ^1H NMR ($CDCl_3$) δ 1.97 (s, 3H, CH_3), 5.20 (s, 1H, OH), 7.1 (dd, 2H, $2H_5$), 7.7 (m, 4H, $2H_4$, $2H_3$), 8.46 (d, 2H, $2H_6$), $J_{5,6}$=4.8, $J_{3,4}$=4.2, $J_{4,5}$=7.1 Hz (the ^1H NMR data are in accordance with those of the literature);[12h] ^{13}C NMR

($CDCl_3$) δ 29.1 (CH_3), 75.9 (COH), 120.4 ($2C_3$), 121.8 ($2C_5$), 136.6 ($2C_4$), 147.4 ($2C_6$), 164.2 ($2C_2$); IR (KBr) ν 3380, 1595, 1575, 1150 cm^{-1}. Anal. Calcd for $C_{12}H_{12}N_2O$ (200.24): C, 71.98; H, 6.04; N, 13.99. Found: C, 71.70; H, 6.35; N, 13.71%.

α,α-Dimethyl-2-pyridinemethanol (2g). Procedure A, using acetone as an electrophile gave 30% (CH_2Cl_2/Et_2O, 80:20) of **2g**: mp 50°C (Lit. 12i mp 50–52°C); ^1H NMR ($CDCl_3$) δ 1.51 (s, 6H, CH_3), 5.90 (s, 1H, OH), 7.7 (m, 3H, $H_{3,4,5}$), 8.33 (d, 1H, H_6), $J_{5,6}$=5.0 Hz (the ^1H NMR data are in accordance with those of the literature).[12e] Anal. Calcd for $C_8H_{11}NO$ (137.18): C, 70.04; H, 8.08; N, 10.21. Found: C, 70.23; H, 7.85; N, 10.33%.

2-Benzoylpyridine (2h). Procedure A, using benzoyl chloride as an electrophile (in this case, the reaction mixture was cooled to −70°C before addition of the electrophile and slowly warmed to room temperature) gave 11% (CH_2Cl_2) of **2h** when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile: mp 39–40°C (Lit. 12j mp 39.5–41°C); ^1H NMR ($CDCl_3$) δ 7.5 (m, 5H, Ph), 8.1 (m, 3H, $H_{3,4,5}$), 8.65 (dd, 1H, H_6), $J_{4,6}$=2.0, $J_{5,6}$=5.0 Hz (the NMR data are in accordance with those of the literature).[12k] Anal. Calcd for $C_{12}H_9NO$ (183.21): C, 78.67; H, 4.95; N, 7.65. Found: C, 78.38; H, 4.85; N, 7.37%.

2-Acetylpyridine (2i). Procedure A, using acetyl chloride as an electrophile (in this case, the reaction mixture was cooled to −70°C before addition of the electrophile and slowly warmed to room temperature) gave 15% (CH_2Cl_2/AcOEt, 80:20) of **2i**: oil; ^1H NMR ($CDCl_3$) δ 2.67 (s, 3H, CH_3), 7.02 (m, 1H, H_5), 7.33 (d, 1H, H_3), 7.60 (m, 1H, H_4), 8.48 (dd, 1H, H_6), $J_{4,6}$=1.9, $J_{3,4}$=4.7, $J_{5,6}$=5.0 Hz; ^{13}C NMR ($CDCl_3$) δ 25.6 (CH_3), 121.4 (C_3), 127.0 (C_5), 136.7 (C_4), 148.8 (C_6), 153.4 (C_2), 199.8 (CO) (the NMR data are in accordance with those of the literature);[12l] IR (neat) ν 3353, 3183, 1664, 1636, 1610, 1382, 669 cm^{-1}. Anal. Calcd for C_7H_7NO (121.14): C, 69.41; H, 5.82; N, 11.56. Found: C, 69.48; H, 5.87; N, 11.41%.

2-(Phenylthio)pyridine (2j). Procedure A, using diphenyl disulfide as an electrophile gave 45% (CH_2Cl_2/Et_2O, 90:10) of **2j** when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile: oil; ^1H NMR ($CDCl_3$) δ 6.76 (d, 1H, H_3), 7.0 (m, 3H, H_5, Ph), 7.3 (m, 3H, Ph), 8.2 (m, 2H, $H_{4,6}$), $J_{3,4}$=4.9 Hz (the ^1H NMR data are in accordance with those of the literature);[12m] ^{13}C NMR ($CDCl_3$) δ 119.5 (C_5), 120.9 (C_3), 128.7 ($C_{4'}$), 129.3 ($C_{3',5'}$), 130.5 ($C_{1'}$), 134.5 ($C_{2',6'}$), 136.4 (C_4), 149.1 (C_6), 161.0 (C_2); IR (neat) ν 3048, 1953, 1574, 1142, 1024, 751 cm^{-1}. Anal. Calcd for $C_{11}H_9NS$ (187.27): C, 70.55; H, 4.84; N, 7.48; S, 17.12. Found: C, 70.36; H, 4.74; N, 7.60; S, 17.80%.

2-(Methylthio)pyridine (2k). Procedure A, using dimethyl disulfide as an electrophile gave 40% (CH_2Cl_2/Et_2O, 90:10) of **2k** when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile: oil; ^1H NMR ($CDCl_3$) δ 2.35 (s, 3H, CH_3), 6.70 (m, 1H, H_3), 6.95 (m, 1H, H_5), 7.30 (m, 1H, H_4), 8.24 (d, 1H, H_6), $J_{5,6}$=4.0 Hz; ^{13}C NMR ($CDCl_3$) δ 12.2 (CH_3), 118.1 (C_5), 120.5 (C_3), 134.8 (C_4), 148.5 (C_6), 159.0 (C_2) (the NMR data are in accordance with those of the literature);[12n] IR (neat) ν 2925, 1581, 1415, 1126, 757 cm^{-1}. Anal. Calcd for C_6H_7NS (125.20): C, 57.56; H, 5.64; N, 11.19; S, 25.61. Found: C, 57.84; H, 5.49; N, 11.42; S, 25.33%.

2-Iodopyridine (2l). Procedure A, using iodine as an electrophile (in this case, the reaction mixture was treated with 50 mL of a 0.5 N aqueous sodium thiosulfate solution instead of water) gave 97% (CH_2Cl_2/Et_2O, 95: 5) of **2l**: oil; bp 92°C/15 mm Hg; ^1H NMR ($CDCl_3$) δ 7.5 (m, 3H, $H_{3,4,5}$), 8.3 (m, 1H, H_6); ^{13}C NMR ($CDCl_3$) δ 118.1 (C_2), 122.7 (C_5), 134.5 (C_3), 137.3 (C_4), 150.4 (C_6) (the NMR data are in accordance with those of the literature);[12n] IR (neat) ν 1553, 1445, 1411, 755 cm^{-1}. Anal. Calcd for C_5H_4IN (205.00): C, 29.30; H, 1.97; N, 6.83. Found: C, 29.06; H, 1.76; N, 6.85%.

3-Substituted pyridines 4a–m: general procedure B

*i*PrMgCl (10 mmol) was added to **3** (0.96 mL, 1.6 g, 10 mmol) in THF (10 mL) at rt. After 1 h, the electrophile (10 mmol) was added. After 18 h at rt, water (50 mL) was added. Extraction with CH_2Cl_2 (3×20 mL), drying over $MgSO_4$ and column chromatography on silica gel (eluent) afforded **4a**–**m**.

α-Phenyl-3-pyridinemethanol (4a). Procedure B, using benzaldehyde as an electrophile gave 84% (CH_2Cl_2), 93% when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, of **4a**: mp 67–69°C (Lit. 13a mp 62.5–63.5°C); ^1H NMR ($CDCl_3$) δ 5.00 (s, 1H, OH), 5.81 (s, 1H, CHOH), 7.15 (dd, 1H, H_5), 7.2 (m, 5H, Ph), 7.71 (ddd, 1H, H_4), 8.20 (dd, 1H, H_6), 8.37 (d, 1H, H_2), $J_{2,4}$=$J_{4,6}$=1.7, $J_{5,6}$=4.8, $J_{4,5}$=7.9 Hz; ^{13}C NMR ($CDCl_3$) δ 73.4 (CHOH), 123.4 (C_5), 126.4 ($C_{2',6'}$), 127.6 ($C_{4'}$), 128.4 ($C_{3',5'}$), 135.4 (C_4), 140.1 (C_3), 143.3 ($C_{1'}$), 147.6 (C_6), 147.7 (C_2); IR (KBr) ν 3155, 2852, 2668, 1592, 1578, 1495, 1476, 1451, 1424, 1332, 1052, 1038, 1024, 759, 713, 699 cm^{-1}. Anal. Calcd for $C_{12}H_{11}NO$ (185.23): C, 77.81; H, 5.99; N, 7.56. Found: C, 77.54; H, 6.11; N, 7.40%.

α-(2,6-Dichlorophenyl)-3-pyridinemethanol (4b). Procedure B, using 2,6-dichlorobenzaldehyde as an electrophile gave 74% (CH_2Cl_2) of **4b**: mp 96–98°C ([13b] mp 96–98°C); ^1H NMR ($CDCl_3$) δ 6.50 (s, 1H, OH), 6.64 (s, 1H, CHOH), 7.0 (m, 4H, H_5, Ph), 7.71 (d, 1H, H_4), 8.20 (d, 1H, H_6), 8.33 (s, 1H, H_2), $J_{5,6}$=3.7, $J_{4,5}$=7.4 Hz (the ^1H NMR data are in accordance with those of the literature);[13b] ^{13}C NMR ($CDCl_3$) δ 68.9 (CHOH), 123.1 (C_5), 129.2 ($C_{3',5'}$), 129.5 ($C_{4'}$), 134.1 (C_4), 135.2 ($C_{2',6'}$), 137.3 (C_3), 138.2 ($C_{1'}$), 146.2 (C_2), 146.7 (C_6); IR (KBr) ν 3160, 2877, 1595, 1579, 1561, 1344, 1292, 1196, 1182, 1088, 1057, 1029, 868, 843, 775, 762, 733, 709, 643 cm^{-1}. Anal. Calcd for $C_{12}H_9Cl_2NO$ (254.12): C, 56.72; H, 3.57; N, 5.51. Found: C, 56.70; H, 3.65; N, 5.65%.

Bis(3-pyridine)methanol (4c). Procedure B, using 3-formylpyridine as an electrophile gave 32% (CH_2Cl_2/AcOEt, 50:50), 40% when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, of **4c**: viscous oil; ^1H NMR ($CDCl_3$) δ 5.00 (s, 1H, OH), 5.23 (s, 1H, CHOH), 6.95 (dd, 1H, H_5), 7.45 (d, 1H, H_4), 8.05 (d, 1H, H_6), 8.23 (s, 1H, H_2), $J_{5,6}$=4.0, $J_{4,5}$=7.6 Hz (the ^1H NMR

data are in accordance with those of the literature);[13b] ^{13}C NMR ($CDCl_3$) δ 70.7 (CHOH), 123.4 (C_5), 134.4 (C_4), 139.5 (C_3), 147.2 (C_2), 147.8 (C_6); IR (KBr) ν 3243, 1660, 1584, 1581, 1479, 1428, 1059, 1028, 808, 714 cm^{-1}. Anal. Calcd for $C_{11}H_{10}N_2O$ (186.22): C, 70.95; H, 5.41; N, 15.04. Found: C, 71.10; H, 5.35; N, 14.86%.

α-(3-Pyridyl)-2-pyridinemethanol (4d). Procedure B, using 2-formylpyridine as an electrophile gave 46% (CH_2Cl_2/AcOEt, 50:50) of **4d**: viscous oil; ^1H NMR ($CDCl_3$) δ 5.60 (s, 1H, CHOH), 6.10 (s, 1H, OH), 6.8 (m, 2H, $H_{5,5'}$), 7.25 (m, 2H, $H_{3,4}$), 7.53 (d, 1H, $H_{4'}$), 7.95 (d, 1H, $H_{6'}$), 8.05 (d, 1H, H_6), 8.29 (s, 1H, $H_{2'}$), $J_{5,6}$=3.8, $J_{5,6}$=3.9, $J_{4,5}$=7.5, $J_{4,5}$=7.6 Hz; ^{13}C NMR ($CDCl_3$) δ 73.4 (CHOH), 120.4 (C_3), 122.2 (C_5), 123.2 ($C_{5'}$), 134.6 (C_4), 136.9 ($C_{4'}$), 139.2 ($C_{3'}$), 147.5 (C_6), 147.5 ($C_{6'}$), 148.0 ($C_{2'}$), 161.8 (C_2); IR (KBr) ν 3270, 1667, 1594, 1476, 1435, 1062, 768, 713 cm^{-1}. Anal. Calcd for $C_{11}H_{10}N_2O$ (186.22): C, 70.95; H, 5.41; N, 15.04. Found: C, 70.81; H, 5.50; N, 15.17%.

α-(*tert*-Butyl)-3-pyridinemethanol (4e). Procedure B, using 2,2-dimethylpropanal as an electrophile gave 78% (CH_2Cl_2/Et_2O, 80:20) of **4e**: mp 80–83°C (Lit. 13c mp 79–82°C); ^1H NMR ($CDCl_3$) δ 0.63 (s, 9H, 3 CH_3), 4.10 (s, 1H, CHOH), 5.82 (s, 1H, OH), 6.89 (dd, 1H, H_5), 7.43 (d, 1H, H_4), 7.95 (d, 1H, H_6), 8.04 (s, 1H, H_2), $J_{5,6}$=4.9, $J_{4,5}$=7.6 Hz; ^{13}C NMR ($CDCl_3$) δ 25.5 (CH_3), 35.3 ($C(CH_3)_3$), 78.7 (CHOH), 122.4 (C_5), 135.4 (C_4), 138.6 (C_3), 147.0 (C_2), 148.1 (C_6) (the NMR data are in accordance with those of the literature);[13c] IR (KBr) ν 3234, 2965, 2868, 1591, 1578, 1483, 1424, 1363, 1310, 1237, 1212, 1175, 1066, 1042, 1029, 1012, 815, 759, 716, 630 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO$ (165.24): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.70; H, 9.32; N, 8.59%.

α-Methyl-3-pyridinemethanol (4f).[13d] Procedure B, using acetaldehyde as an electrophile gave 51% (CH_2Cl_2), 14% when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, 74% when CH_3CHO (5.6 mL, 4.4 g, 100 mmol) was added at −20°C, of **4f**: oil; ^1H NMR ($CDCl_3$) δ 1.21 (d, 1H, CH_3), 4.60 (s, 1H, CHOH), 6.88 (s, 1H, OH), 6.89 (dd, 1H, H_5), 7.43 (dd, 1H, H_4), 8.00 (dd, 1H, H_6), 8.15 (s, 1H, H_2), $J_{4,6}$=1.9, $J_{5,6}$=4.7, $J_{4,5}$=7.9, J_{CH3-CH}=6.6 Hz; ^{13}C NMR ($CDCl_3$) δ 24.9 (CH_3), 66.6 (CHOH), 123.2 (C_5), 133.4 (C_4), 142.0 (C_3), 146.4 (C_2), 147.1 (C_6); IR (neat) ν 3346, 2971, 2928, 1728, 1667, 1595, 1591, 1427, 1370, 1091, 714 cm^{-1}. Anal. Calcd for C_7H_9NO (123.16): C, 68.27; H, 7.37; N, 11.37. Found: C, 67.99; H, 7.66; N, 11.08%.

α,α-Diphenyl-3-pyridinemethanol (4g). Procedure B, using benzophenone as an electrophile gave 51% (CH_2Cl_2/AcOEt, 80:20) of **4g**: mp 115–116°C (Lit. 13e mp 115–117°C); ^1H NMR ($CDCl_3$) δ 6.60 (s, 1H, OH), 7.12 (dd, 1H, H_5), 7.2 (m, 10H, Ph), 7.71 (d, 1H, H_4), 8.08 (d, 1H, H_6), 8.20 (s, 1H, H_2), $J_{5,6}$=4.8, $J_{4,5}$=8.5 Hz; ^{13}C NMR ($CDCl_3$) δ 80.0 (COH), 122.8 (C_5), 127.2 ($2C_{1'}$), 127.9 ($2C_{2,6}$, 2 $C_{3,5}$), 135.9 (C_4), 143.3 (C_3), 146.4 ($2C_4$), 146.9 (C_2), 148.6 (C_6); IR (KBr) ν 3152, 2800, 1588, 1489, 1428, 1223, 1163, 1039, 1022, 897, 775, 758, 704 cm^{-1}. Anal. Calcd for $C_{18}H_{15}NO$ (261.33): C, 82.73; H, 5.79; N, 5.36. Found: C, 82.44; H, 5.95; N, 5.20%.

α,α-Diethyl-3-pyridinemethanol (4h). Procedure B, using pentan-3-one as an electrophile gave 58% (CH_2Cl_2/Et_2O, 80:20), 16% when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, of **4h**: oil; ^1H NMR ($CDCl_3$) δ 0.63 (t, 6H, 2CH_3), 1.59 (q, 4H, 2CH_2), 6.95 (s, 1H, OH), 7.12 (dd, 1H, H_5), 7.58 (d, 1H, H_4), 8.18 (d, 1H, H_6), 8.40 (s, 1H, H_2), $J_{5,6}$=4.8, $J_{4,5}$=7.9 Hz (the ^1H NMR data are in accordance with those of the literature);[13f] ^{13}C NMR ($CDCl_3$) δ 7.5 (CH_3), 34.4 (CH_2), 63.4 (COH), 122.9 (C_5), 134.3 (C_4), 142.0 (C_3), 146.0 (C_2), 146.4 (C_6); IR (neat) ν 3204, 2968, 2937, 2880, 1580, 1460, 1419, 1376, 1098, 969, 898, 811, 715 cm^{-1}. Anal. Calcd for $C_{10}H_{15}NO$ (165.24): C, 72.69; H, 9.15; N, 8.48. Found: C, 72.41; H, 9.43; N, 8.32%.

3-Benzoylpyridine (4i). Procedure B, using benzoyl chloride as an electrophile gave 35% (CH_2Cl_2 and then CH_2Cl_2/AcOEt, 50:50) when added at −70°C and the mixture gently warmed to room temperature, of **4i**: mp 36–37°C ([13g] mp 36–38°C); ^1H NMR ($CDCl_3$) δ 7.5 (m, 6H, H_5, Ph), 8.10 (ddd, 1H, H_4), 8.79 (dd, 1H, H_6), 8.98 (d, 1H, H_2), $J_{2,4}$=$J_{4,6}$=1.9, $J_{5,6}$=5.0, $J_{4,5}$=7.9 Hz (the ^1H NMR data are in accordance with those of the literature).[13h] Anal. Calcd for $C_{12}H_9NO$ (183.21): C, 78.67; H, 4.95; N, 7.65. Found: C, 78.45; H, 5.11; N, 7.37%.

3-(Isobutyryl)pyridine (4j). Procedure B, using isobutyryl chloride as an electrophile gave 12% (CH_2Cl_2 and then CH_2Cl_2/AcOEt, 50:50) when added at −70°C and the mixture gently warmed to room temperature, of **4j**: oil; ^1H NMR ($CDCl_3$) δ 1.15 (d, 6H, 2CH_3), 3.45 (sept, 1H, $CH(CH_3)_2$), 7.35 (dd, 1H, H_5), 8.16 (dd, 1H, H_4), 8.70 (dd, 1H, H_6), 9.12 (s, 1H, H_2), $J_{4,6}$=1.8, $J_{5,6}$=5.1, J_{CH-CH3}=6.6, $J_{4,5}$=7.9 Hz (the ^1H NMR data are in accordance with those of the literature);[13b] ^{13}C NMR ($CDCl_3$) δ 19.2 (CH_3), 36.3 ($CH(CH_3)_2$), 124.1 (C_5), 131.7 (C_3), 136.1 (C_4), 150.1 (C_2), 153.6 (C_6), 203.5 (CO); IR (neat) ν 3363, 2972, 2933, 2874, 1699, 1585, 1467, 1418, 1385, 1237, 981, 703 cm^{-1}. Anal. Calcd for $C_9H_{11}NO$ (149.19): C, 72.46; H, 7.43; N, 9.39. Found: C, 72.19; H, 7.40; N, 9.15%.

3-(Methylthio)pyridine (4k). Procedure B, using dimethyl disulfide as an electrophile gave 49% (CH_2Cl_2/Et_2O, 95:5), 58% when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, of **4k**: oil; ^1H NMR ($CDCl_3$) δ 2.98 (s, 3H, CH_3), 6.70 (dd, 1H, H_5), 7.05 (ddd, 1H, H_4), 7.91 (dd, 1H, H_6), 8.00 (d, 1H, H_2), $J_{4,6}$= 1.5, $J_{2,4}$=2.0, $J_{5,6}$=4.8, $J_{4,5}$=8.0 Hz; ^{13}C NMR ($CDCl_3$) δ 14.9 (CH_3), 122.9 (C_5), 133.3 (C_4), 135.0 (C_3), 145.5 (C_6), 147.2 (C_2) (the NMR data are in accordance with those of the literature);[13i] IR (neat) ν 3396, 3036, 2921, 1559, 1469, 1435, 1404, 1109, 1018, 793, 705 cm^{-1}. Anal. Calcd for C_6H_7NS (125.19): C, 57.56; H, 5.64; N, 11.19. Found: C, 57.37; H, 5.91; N, 11.37%.

3-Iodopyridine (4l). Procedure B, using iodine as an electrophile gave 78% (CH_2Cl_2) of **4l**: mp 52–53°C (Lit. 13j mp 52.3–53°C); ^1H NMR ($CDCl_3$) δ=7.16 (dd, 1H, H_5), 8.09 (ddd, 1H, H_4), 8.63 (dd, 1H, H_6), 8.92 (d, 1H, H_2), $J_{4,6}$=1.4, $J_{2,4}$=1.9, $J_{5,6}$=1.7, $J_{4,5}$=8.2 Hz (the ^1H NMR data are in accordance with those of the literature);[13k] ^{13}C NMR ($CDCl_3$): δ 93.5 (C_3), 125.1 (C_5), 144.1 (C_4), 148.0 (C_6), 155.7 (C_2). Anal. Calcd for C_5H_4IN (205.00):

C, 29.30; H, 1.97; N, 6.83. Found: C, 29.60; H, 1.87; N, 6.98%.

Bis(3-pyridyl)mercury (4m). Procedure B, using mercury(II) bromide as an electrophile gave 80% of **4m**, after filtration of the reaction mixture, washing with water (100 mL) and drying: mp 238°C ([13l] mp 239°C); ^{1}H NMR (DMSO-d_6) δ 7.32 (dd, 1H, H_5), 7.94 (m, 1H, H_4), 8.33 (dd, 1H, H_6), 8.59 (dd, 1H, H_2), $J_{2,4}$=1.5, $J_{4,6}$=1.7, $J_{5,6}$=4.8, $J_{4,5}$=7.3, $J_{2,Hg}$=60, $J_{4,Hg}$=109 Hz; ^{13}C NMR (DMSO-d_6) δ 124.4 (C_5), 146.1 (C_4), 148.3 (C_6), 157.8 (C_2), 164.7 (C_3); IR (KBr) ν 3448, 3020, 1654, 1560, 1464, 1393, 1294, 1022, 797, 714, 623, 380 cm^{-1}. Anal. Calcd for $C_{10}H_8HgN_2$ (356.78): C, 33.67; H, 2.26; N, 7.85. Found: C, 33.90; H, 2.16; N, 7.59%.

2-Chloro-α-(2-methoxyphenyl)-3-pyridinemethanol (24). Procedure B was used, starting from **23** (1.9 g, 10 mmol). Using *o*-anisaldehyde as an electrophile gave 74% (CH_2Cl_2) of **24**: mp 123–124°C (Lit. 10 mp 124°C); ^{1}H NMR ($CDCl_3$) δ 3.85 (s, 3H, OCH_3), 4.48 (d, 1H, OH), 6.35 (d, 1H, CHOH), 7.1 (m, 5H, H_5, Ph), 7.90 (dd, 1H, H_4), 8.25 (dd, 1H, H_6), $J_{4,6}$=1.9, J_{CH-OH}=4.0, $J_{5,6}$=5.0, $J_{4,5}$=7.5 Hz; ^{13}C NMR ($CDCl_3$) δ 54.3 (OCH_3), 66.3 (CHOH), 109.7 ($C_{3'}$), 119.6 ($C_{5'}$), 121.6 (C_5), 126.7 ($C_{6'}$), 128.2 ($C_{4'}$), 128.9 ($C_{1'}$), 136.7 (C_4), 136.9 (C_3), 146.9 (C_6), 148.9 (C_2), 155.8 ($C_{2'}$); IR (KBr) ν 3340, 1600, 1590, 1580, 1570 cm^{-1}. Anal. Calcd for $C_{13}H_{12}ClNO_2$ (249.70): C, 62.53; H, 4.84; N, 5.61. Found: C, 62.29; H, 4.90; N, 5.63%.

4-Substituted pyridines 6a–g: general procedure C

Compound **5a** (1.9 g, 10 mmol) was treated with 5% aqueous Na_2CO_3 (50 mL). Extraction with Et_2O (3×20 mL), drying over $MgSO_4$ and removal of the solvent afforded **5b**, which was immediately dissolved in THF (10 mL). *i*PrMgCl (10 mmol) and after 1 h 30, the electrophile were added at rt. After 18 h, water (50 mL) was added. Extraction with CH_2Cl_2 (3×20 mL), drying over $MgSO_4$ and column chromatography on silica gel (eluent) afforded **6a–g**.

α-Phenyl-4-pyridinemethanol (6a). Procedure C, using benzaldehyde as an electrophile gave 64% (CH_2Cl_2/Et_2O, 80:20) of **6a**: mp 125°C ([14a] mp 125–126.5°C); ^{1}H NMR ($CDCl_3$) δ 5.71 (s, 1H, CHOH), 6.10 (s, 1H, OH), 7.2 (m, 7H, $H_{3,5}$, Ph), 8.20 (d, 2H, $H_{2,6}$), $J_{2,3}$=5.3 Hz (the ^{1}H NMR data are in accordance with those of the literature);[14b] ^{13}C NMR ($CDCl_3$) δ 74.3 (CHOH), 121.4 ($C_{3,5}$), 126.7 ($C_{2',6'}$), 127.8 ($C_{4'}$), 128.5 ($C_{3',5'}$), 143.1 ($C_{1'}$), 146.7 ($C_{2,6}$), 153.9 (C_4); IR (KBr) ν 3132, 2825, 1599, 1453, 1260, 1094, 1046, 1002, 787, 762, 702, 658, 604 cm^{-1}. Anal. Calcd for $C_{12}H_{11}NO$ (185.23): C, 77.81; H, 5.99; N, 7.56. Found: C, 77.55; H, 5.79; N, 7.28%.

α-(2-Naphthyl)-4-pyridinemethanol (6b). Procedure C, using 2-naphthaldehyde as an electrophile gave 40% (CH_2Cl_2/AcOEt, 80:20) of **6b**: mp 149–150°C; ^{1}H NMR ($CDCl_3$) δ 4.70 (s, 1H, OH), 5.90 (s, 1H, CHOH), 7.6 (m, 9H, $H_{3,5}$, naphthyl), 8.37 (d, 2H, $H_{2,6}$), $J_{2,3}$=5.9 Hz; ^{13}C NMR ($CDCl_3$) δ 74.7 (CHOH), 121.3 ($C_{3,5}$), 124.4, 125.5, 126.1, 126.3, 127.6, 127.8, 128.6, 132.9 and 133.0 ($C_{a,b}$), 140.1 (C_2), 149.2 ($C_{2,6}$), 152.9 (C_4); IR (KBr) ν 3152, 2845, 1605, 1411, 1334, 1273, 1053, 1003, 828, 743 cm^{-1}. Anal. Calcd for $C_{16}H_{13}NO$ (235.29): C, 81.68; H, 5.57; N, 5.95. Found: C, 81.63; H, 5.62; N, 6.25%.

α-Pentyl-4-pyridinemethanol (6c).[14c] Procedure C, using hexanal as an electrophile gave 42% (Et_2O) of **6c**: oil; ^{1}H NMR ($CDCl_3$) δ 0.78 (t, CH_3, 3H), 1.5 (m, 8H, CH_2), 4.57 (t, 1H, CHOH), 5.05 (s, 1H, OH), 7.18 (d, 2H, $H_{3,5}$), 8.27 (d, 2H, $H_{2,6}$), $J_{2,3}$=5.1, $J_{CH3-CH2}$=6.3, J_{CH-CH2}=6.4 Hz; ^{13}C NMR ($CDCl_3$) δ 14.4 (CH_3), 22.9 (CH_2), 25.6 (CH_2), 32.0 (CH_2), 39.3 (CH_2), 72.8 (CHOH), 121.5 ($C_{3,5}$), 149.3 ($C_{2,6}$), 155.7 (C_4); IR (neat) ν 3400, 2956, 2931, 2859, 1605, 1416, 1065, 1004, 825 cm^{-1}. Anal. Calcd for $C_{11}H_{17}NO$ (179.26): C, 73.70; H, 9.56; N, 7.81. Found: C, 73.57; H, 9.29; N, 8.08%.

α-Isopropyl-4-pyridinemethanol (6d).[14d] Procedure C, using isobutyraldehyde as an electrophile gave 39% (CH_2Cl_2/AcOEt, 80:20) of **6d**: oil; ^{1}H NMR ($CDCl_3$) δ 0.81 (2d, $2CH_3$, 6H), 1.86 (m, 1H, CH), 4.34 (d, 1H, CHOH), 4.80 (s, 1H, OH), 7.16 (d, 2H, $H_{3,5}$), 8.28 (d, 2H, $H_{2,6}$), $J_{2,3}$=4.7, J_{CH-CH2}=5.7, J_{CH3-CH}=6.8 Hz; ^{13}C NMR ($CDCl_3$) δ 17.7 (CH_3), 19.3 (CH_3), 35.4 (CH), 77.9 (CHOH), 122.3 ($C_{3,5}$), 149.2 ($C_{2,6}$), 154.1 (C_4); IR (neat) ν 3234, 2962, 2932, 2873, 1605, 1416, 1048, 1019, 1004, 783 cm^{-1}. Anal. Calcd for $C_9H_{13}NO$ (151.21): C, 71.49; H, 8.67; N, 9.26. Found: C, 71.38; H, 8.44; N, 8.96%.

α,α-Diphenyl-4-pyridinemethanol (6e). Procedure C, using benzophenone as an electrophile gave 29% (AcOEt) of **6e**: mp 237–239°C ([14e] mp 238–239°C); ^{1}H NMR (DMSO-d_6) δ 6.75 (s, 1H, OH), 7.20 (d, 2H, $H_{3,5}$), 7.5 (m, 10H, Ph), 8.53 (d, 2H, $H_{2,6}$), $J_{2,3}$=5.6 Hz (the ^{1}H NMR data are in accordance with those of the literature);[14f] IR (KBr) ν 3085, 2789, 1659, 1596, 1445, 1427, 1278, 1050, 1002, 698 cm^{-1}. Anal. Calcd for $C_{18}H_{15}NO$ (261.33): C, 82.73; H, 5.79; N, 5.36. Found: C, 82.91; H, 5.87; N, 5.08%.

4-(Phenylthio)pyridine (6f). Procedure C, using diphenyl disulfide as an electrophile gave 45% (CH_2Cl_2/Et_2O, 90:10) when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, of **6f**: oil; ^{1}H NMR ($CDCl_3$) δ 6.85 (AA′XX′, 2H, $H_{3,5}$), 7.4 (m, 3H, Ph), 7.5 (m, 2H, Ph), 8.26 (AA′XX′, 2H, $H_{2,6}$), $J_{2,3}$=5.3 Hz (the ^{1}H NMR data are in accordance with those of the literature);[14g] ^{13}C NMR ($CDCl_3$) δ 121.2 ($C_{3,5}$), 129.8 (C_1), 130.1 (C_4), 130.3 ($C_{3,5}$), 135.6 ($C_{2,6}$), 149.9 ($C_{2,6}$), 150.7 (C_4); IR (neat) ν 3400, 3050, 3032, 1573, 1541, 1477, 1440, 1407, 1066, 804, 751, 706, 691 cm^{-1}. Anal. Calcd for $C_{11}H_9NS$ (187.27): C, 70.55; H, 4.84; N, 7.48; S, 17.12. Found: C, 70.26; H, 4.86; N, 7.42; S, 16.82%.

4-Iodopyridine (6g). Procedure C, using iodine as an electrophile gave 51% (CH_2Cl_2) of **6g**: mp 98–100°C, dec. (Lit. 14h mp 100°C, dec.); ^{1}H NMR ($CDCl_3$) δ 7.72 (d, 1H, $H_{3,5}$), 8.29 (d, 1H, $H_{2,6}$), $J_{2,3}$=5.5 Hz; ^{13}C NMR ($CDCl_3$) δ 105.1 (C_4), 132.8 ($C_{3,5}$), 150.0 ($C_{2,6}$) (the NMR data are in accordance with those of the literature).[14i] Anal. Calcd for C_5H_4IN (205.00): C, 29.30; H, 1.97; N, 6.83. Found: C, 29.40; H, 1.85; N, 6.98%.

2-Bromo-6-substituted pyridines 8a–e

Procedure A was used, starting from **7** (2.4 g, 10 mmol).

2-Bromo(6-d)pyridine (8a). Using D_2O as an electrophile gave 95%, 100% *d* (CH_2Cl_2) of **8a**: oil; ^1H NMR ($CDCl_3$) δ 7.27 (d, 1H, H_5), 7.50 (d, 1H, H_3), 7.56 (t, 1H, H_4), $J_{4,5}$=7.0, $J_{3,4}$=7.9 Hz (the ^1H NMR data are in accordance with those of the literature);[15a] ^{13}C NMR ($CDCl_3$) δ 122.8 (C_5), 128.5 (C_3), 138.8 (C_4), 142.4 (C_2), 150.0 (C_6); IR (neat) ν 3051, 1571, 1561, 1447, 1414, 1106, 1076, 987, 759, 700 cm^{-1}. Anal. Calcd for C_5H_3BrDN (159.01): C, 37.77; "H",[15b] 2.61; N, 8.81. Found: C, 37.52; "H", 2.83; N, 8.90%.

6-Bromo-α-phenyl-2-pyridinemethanol (8b). Using benzaldehyde as an electrophile gave 42% (CH_2Cl_2) of **8b**: oil; ^1H NMR ($CDCl_3$) δ 4.59 (s, 1H, CHOH), 4.90 (s, 1H, OH), 7.3 (m, 8H, $H_{3,4,5}$, Ph); ^{13}C NMR ($CDCl_3$) δ 75.5 (CHOH), 120.4 (C_5), 127.2 (C_3), 127.4 ($C_{2,6}$), 128.5 (C_4), 129.1 ($C_{3,5}$), 139.7 (C_4), 141.2 ($C_{1'}$), 142.6 (C_2), 164.8 (C_6); IR (neat) ν 3380, 2874, 1582, 1557, 1495, 1434, 1123, 1046, 986, 784, 737, 700 cm^{-1}. Anal. Calcd for $C_{12}H_{10}BrNO$ (264.12): C, 54.57; H, 3.82; N, 5.30. Found: C, 54.39; H, 3.98; N, 5.04%.

6-Bromo-2-pyridyltrimethylsilane (8c). Using chlorotrimethylsilane as an electrophile gave 74% (CH_2Cl_2/Et_2O, 90:10) of **8c**: oil; ^1H NMR ($CDCl_3$) δ 0.24 (s, 9H, $Si(CH_3)_3$), 7.33 (m, 3H, $H_{3,4,5}$) (the ^1H NMR data are in accordance with those of the literature);[15d] ^{13}C NMR ($CDCl_3$) δ 0.0 ($Si(CH_3)_3$), 129.2 (C_3), 129.2 (C_5), 138.3 (C_4), 145.3 (C_6), 170.0 (C_2); IR (neat) ν 2958, 2926, 1542, 1419, 1370, 1249, 1107, 842, 757, 748 cm^{-1}. Anal. Calcd for $C_8H_{12}BrNSi$ (230.18): C, 41.74; H, 5.25; N, 6.09. Found: C, 41.52; H, 5.32; N, 5.89%.

6-Bromo-2-(methylthio)pyridine (8d). Using dimethyl disulfide as an electrophile gave 45% (CH_2Cl_2/Et_2O, 95:5) when triethylamine (1.4 mL, 1.0 g, 10 mmol) was added before the electrophile, of **8d**: oil; ^1H NMR ($CDCl_3$) δ 2.48 (s, 3H, SCH_3), 7.04 (2 d, 2H, $H_{3,5}$), 7.23 (t, 1H, H_4) (the ^1H NMR data are in accordance with those of the literature);[15d] ^{13}C NMR ($CDCl_3$) δ 13.9 (SCH_3), 120.5 (C_3), 123.3 (C_5), 138.2 (C_4), 142.0 (C_6), 161.5 (C_2); IR (neat) ν 2925, 1568, 1537, 1411, 1384, 1158, 1116, 770, 648 cm^{-1}. Anal. Calcd for C_6H_6BrNS (204.09): C, 35.31; H, 2.96; N, 6.86; S, 15.71. Found: C, 35.44; H, 3.18; N, 6.96; S, 15.52%.

2-Bromo-6-iodopyridine (8e). Using iodine as an electrophile gave 90% (CH_2Cl_2/Et_2O, 90:10) of **8e**: mp 134°C; ^1H NMR (DMSO-d_6) δ 7.34 (dd, 1H, H_4), 7.57 (d, 1H, H_5), 7.78 (d, 1H, H_3), $J_{4,5}$=7.7, $J_{3,4}$=8.0 Hz; ^{13}C NMR (DMSO-d_6) δ 117.6 (C_6), 128.0 (C_5), 134.6 (C_3), 140.6 (C_2), 141.4 (C_4); IR (KBr) ν 1654, 1537, 1434, 1409, 1128, 1026 cm^{-1}. Anal. Calcd for C_5H_3BrIN (283.89): C, 21.15; H, 1.07; N, 4.93. Found: C, 20.98; H, 1.19; N, 4.99%.

2-Substituted (6-d)pyridines 9a–b

Procedure A was used, starting from **8a** (0.95 mL, 1.6 g, 10 mmol).

α-Phenyl-2-(6-d)pyridinemethanol (9a). Using benzaldehyde as an electrophile gave 66%, 100% *d* (CH_2Cl_2/Et_2O, 90:10) of **9a**: mp 72–73°C; ^1H NMR ($CDCl_3$) δ 5.87 (s, 1H, CHOH), 6.10 (s, 1H, OH), 7.3 (m, 8H, $H_{3,4,5}$, Ph); ^{13}C NMR ($CDCl_3$) δ 76.6 (CHOH), 122.3 (C_3), 123.4 (C_5), 128.1 ($C_{2,6}$), 128.7 (C_4), 129.6 ($C_{3,5}$), 138.2 (C_4), 144.6 (C_1), 150.0 (C_6), 163.2 (C_2); IR (KBr) ν 3340, 3112, 3094, 1594, 1494, 1435, 1050 cm^{-1}. Anal. Calcd for $C_{12}H_{10}DNO$ (186.23): C, 77.39; "H",[15b] 6.01; N, 7.52. Found: C, 77.66; "H", 6.12; N, 7.47%.

2-Iodo(6-d)pyridine (9b). Using iodine as an electrophile (in this case, the reaction mixture was treated with 50 mL of a 0.5 N aqueous sodium thiosulfate solution instead of water) gave 42%, 100% *d* (CH_2Cl_2/Et_2O, 95:5) of **9b**: oil; bp 92°C/15 mm Hg; ^1H NMR ($CDCl_3$) δ 7.5 (m, 3H, $H_{3,4,5}$); ^{13}C NMR ($CDCl_3$) δ 118.1 (C_2), 122.7 (C_5), 134.5 (C_3), 137.3 (C_4), 150.4 (C_6); IR (neat) ν 1553, 1445, 1411, 755 cm^{-1}. Anal. Calcd for C_5H_3DIN (206.00): C, 29.15; 'H',[15b] 2.01; N, 6.80. Found: C, 28.92; "H", 2.14; N, 6.95%.

3-Bromo-5-substituted pyridines 11a–b

Procedure B was used, starting from **10** (2.4 g, 10 mmol).

3-Bromo(5-d)pyridine (11a). Using D_2O as an electrophile gave 82%, 100% *d* (CH_2Cl_2/Et_2O, 90:10) of **11a**: oil; ^1H NMR ($CDCl_3$) δ 7.76 (s, 1H, H_4), 8.51 (s, 1H, H_6), 8.68 (s, 1H, H_2); ^{13}C NMR ($CDCl_3$) δ 121.3 (C_3), 125.0 (C_5), 139.0 (C_4), 148.1 (C_6), 151.4 (C_2); IR (KBr) ν 3043, 1571, 1463, 1413, 1095, 1086, 1007, 792, 700, 612 cm^{-1}. Anal. Calcd for C_5H_3BrDN (159.01): C, 37.77; 'H',[15b] 2.61; N, 8.81. Found: C, 37.60; "H", 2.80; N, 8.95%.

5-Bromo-α-phenyl-3-pyridinemethanol (11b). Using benzaldehyde as an electrophile gave 76% (CH_2Cl_2) of **11b**: viscous oil; ^1H NMR ($CDCl_3$) δ 5.66 (s, 1H, CHOH), 5.94 (s, 1H, OH), 7.2 (m, 5H, Ph), 7.90 (s, 1H, H_4), 8.20 (s, 1H, H_2), 8.21 (s, 1H, H_6); ^{13}C NMR ($CDCl_3$) δ 72.1 (CHOH), 120.0 (C_5), 125.8 ($C_{2,6}$), 127.3 (C_4), 128.0 ($C_{3,5}$), 136.2 (C_4), 141.2 (C_3), 142.0 (C_1), 144.9 (C_2), 148.0 (C_6); IR (neat) ν 3365, 2872, 1454, 1422, 1045, 1023, 700 cm^{-1}. Anal. Calcd for $C_{12}H_{10}BrNO$ (264.12): C, 54.57; H, 3.82; N, 5.30. Found: C, 54.85; H, 3.78; N, 5.15%.

3-Bromo-4-chloropyridine (14).[16a] The foregoing procedure, applied to **13** instead of **10**, using H_2O as an electrophile gave 99% (CH_2Cl_2/cyclohexane, 25:75) of **14**: mp 18°C; bp 94°C/20 mm Hg; ^1H NMR ($CDCl_3$) δ 7.33 (d, 1H, H_5), 8.30 (d, 1H, H_6), 8.59 (s, 1H, H_2), J_{5-6}=5.2 Hz; ^{13}C NMR ($CDCl_3$) δ 121.0 (C_3), 125.0 (C_5), 143.5 (C_4), 148.5 (C_2), 152.5 (C_6) (the NMR data are in accordance with those of the literature);[16b] IR (neat) ν 2926, 2855, 2367, 1598, 1568, 1450, 1267, 828 cm^{-1}. Anal. Calcd for C_5H_3BrClN (192.44): C, 31.21; H, 1.57; N, 7.28. Found: C, 30.95; H, 1.39; N, 7.31%.

3,5-Disubstituted pyridines 12a–b: general procedure D

*i*PrMgCl (10 mmol) was added to **10** (2.4 g, 10 mmol) in THF (10 mL) at rt. After 1 h, the first electrophile (10 mmol) was added. After 18 h at rt, *i*PrMgCl (10 mmol) was added to the reaction mixture. The second

electrophile (10 mmol) was added 1 h later. After 18 h at rt, water (50 mL) was added. Extraction with CH_2Cl_2 (3×20 mL), drying over $MgSO_4$ and column chromatography on silica gel (eluent) afforded **12a–b**.

α,α′-Diphenyl-3,5-pyridinedimethanol (12a). Procedure D, using benzaldehyde as an electrophile gave 49% (CH_2Cl_2/AcOEt, 80:20) of **12a**: viscous oil; ^{1}H NMR (DMSO-d_6) δ 5.85 (s, 2H, CHOH), 6.25 (s, 2H, OH), 7.3 (m, 10H, Ph), 7.89 (s, 1H, H_4), 8.53 (s, 2H, $H_{2,6}$), J_{CH-OH}=3.1 Hz; ^{13}C NMR (DMSO-d_6) δ 72.7 (2CHOH), 126.6 (2$C_{2,6}$), 127.4 (2C_4), 128.7 (2$C_{3,5}$), 134.3 (C_4), 140.9 (2 C_1), 141.3 ($C_{3,5}$), 145.2 ($C_{2,6}$); IR (KBr) ν 3400, 2830, 1648, 1590, 1493, 1453, 1433, 1043, 1025, 757, 700 cm^{-1}. Anal. Calcd for $C_{19}H_{17}NO_2$ (291.35): C, 78.33; H, 5.88; N, 4.81. Found: C, 78.06; H, 5.59; N, 4.75%.

α-Phenyl-5-(trimethylsilyl)-3-pyridinemethanol (12b). Procedure D, using chlorotrimethylsilane and benzaldehyde as electrophiles gave 52% (CH_2Cl_2/Et_2O, 80:20) of **12b**: mp 111–113°C; ^{1}H NMR ($CDCl_3$) δ 0.01 ($Si(CH_3)_3$), 5.02 (s, 1H, OH), 5.50 (s, 1H, CHOH), 7.1 (m, 5H, Ph), 7.66 (s, 1H, H_4), 8.08 (2 s, 2H, $H_{2,6}$); ^{13}C NMR ($CDCl_3$) δ 0.0 ($Si(CH_3)_3$), 75.2 (CHOH), 127.9 ($C_{2,6}$), 129.0 (C_4), 129.9 ($C_{3,5}$), 136.3 (C_5), 140.5 (C_3), 140.7 (C_4), 145.0 (C_1), 149.3 (C_2), 153.2 (C_6); IR (KBr) ν 3136, 2953, 2894, 1570, 1456, 1440, 1395, 1252, 1226, 1039, 1028, 841, 754, 697 cm^{-1}. Anal. Calcd for $C_{15}H_{19}NOSi$ (257.41): C, 69.99; H, 7.44; N, 5.44. Found: C, 70.08; H, 7.23; N, 5.53%.

4-Chloro-α,α′-diphenyl-3,5-pyridinedimethanol (15). Procedure D, applied to **13** instead of **10**, using benzaldehyde as an electrophile gave 74% (CH_2Cl_2/AcOEt, 90:10) of **15**: mp 152–156°C; ^{1}H NMR (DMSO-d_6) δ 6.10 (s, 2H, OH), 6.27 (s, 2H, CHOH), 7.3 (m, 10H, Ph), 8.83 (s, 2H, $H_{2,6}$); ^{13}C NMR (DMSO-d_6) δ 70.4/70.6 (2CHOH), 127.2 (2$C_{2,6}$), 127.7 (2C_4), 128.6 (2$C_{3,5}$), 137.9 (C_4), 139.7/139.2 (2C_1), 143.2 ($C_{3,5}$), 148.5/148.3 ($C_{2,6}$), signals are doubled, due to the presence of stereoisomers; IR (KBr) ν 3401, 3030, 2816, 2683, 1577, 1454, 1419, 1241, 1159, 1076, 1048, 1028, 914, 833, 813, 763, 699 cm^{-1}. Anal. Calcd for $C_{19}H_{16}ClNO_2$ (325.80): C, 70.05; H, 4.95; N, 4.30. Found: C, 69.88; H, 5.02; N, 4.15%.

2-Bromo-3-substituted pyridines 17a–b

Procedure B was used, starting from **16** (2.4 g, 10 mmol).

2-Bromo-α-phenyl-3-pyridinemethanol (17a). Using benzaldehyde as an electrophile gave 92% (CH_2Cl_2) of **17a**: mp 124–125°C (Lit. 2g mp 125°C); ^{1}H NMR ($CDCl_3$) δ 3.50 (s, 1H, OH), 6.12 (s, 1H, CHOH), 7.3 (m, 6H, H_5, Ph), 7.90 (d, 1H, H_4), 8.19 (d, 1H, H_6), $J_{4,6}$=1.8, $J_{5,6}$=4.6, $J_{4,5}$=7.7 Hz; ^{13}C NMR ($CDCl_3$) δ 73.6 (CHOH), 123.0 (C_5), 127.0 ($C_{2,6}$), 127.9 (C_4), 128.4 ($C_{3,5}$), 136.9 (C_4), 140.1 (C_1), 141.3 (C_2), 141.9 (C_3), 148.7 (C_6); IR (KBr) ν 3183, 3036, 2909, 1566, 1493, 1449, 1414, 1400, 1330, 1257, 1213, 1194, 1086, 1032, 840, 796, 758, 742, 693 cm^{-1}. Anal. Calcd for $C_{12}H_{10}BrNO$ (264.12): C, 54.57; H, 3.82; N, 5.30. Found: C, 54.51; H, 3.68; N, 5.15%.

2-Bromo-3-iodopyridine (17b). Using iodine as an electrophile gave 80% (CH_2Cl_2/cyclohexane, 25:75) of **17b**: mp 95–97°C; ^{1}H NMR ($CDCl_3$) δ 7.02 (dd, 1H, H_5), 8.08 (dd, 1H, H_4), 8.30 (dd, 1H, H_6), $J_{4,6}$=1.7, $J_{5,6}$=4.6, $J_{3,4}$=7.8 Hz; ^{13}C NMR ($CDCl_3$) δ 99.4 (C_3), 123.3 (C_5), 148.0 (C_2), 148.3 (C_4), 148.6 (C_6); IR (KBr) ν 1724, 1550, 1380, 1247, 1124, 1052, 1006, 794 cm^{-1}. Anal. Calcd for C_5H_3BrIN (283.89): C, 21.15; H, 1.07; N, 4.93. Found: C, 20.94; H, 1.26; N, 5.05%.

2-Bromo-5-substituted pyridines 19a–c

Procedure B was used, starting from **18** (2.4 g, 10 mmol).

2-Bromo(5-d)pyridine (19a). Using D_2O as an electrophile gave 64%, 100% *d* (CH_2Cl_2/Et_2O, 80:20) of **19a**: oil; ^{1}H NMR ($CDCl_3$) δ 7.51 (d, 1H, H_3), 7.57 (d, 1H, H_4), 8.39 (s, 1H, H_6), $J_{3,4}$=8.0 Hz; ^{13}C NMR ($CDCl_3$) δ 122.0 (C_5), 128.6 (C_3), 138.9 (C_4), 142.6 (C_2), 150.5 (C_6); IR (KBr) ν 3052, 1571, 1561, 1448, 1414, 1106, 1077, 1042, 987, 759, 700 cm^{-1}. Anal. Calcd for C_5H_3BrDN (159.01): C, 37.77; "H",[15b] 2.61; N, 8.81. Found: C, 37.82; "H", 2.89; N, 8.71%.

2-Bromo-α-phenyl-5-pyridinemethanol (19b).[17a] Using benzaldehyde as an electrophile gave 86% (CH_2Cl_2) of **19b**: mp 88–90°C; ^{1}H NMR ($CDCl_3$) δ 5.00 (s, 1H, OH), 5.74 (s, 1H, CHOH), 7.2 (m, 5H, Ph), 7.33 (d, 1H, H_3), 7.49 (d, 1H, H_4), 8.11 (s, 1H, H_6), $J_{3,4}$=8.2 Hz; ^{13}C NMR ($CDCl_3$) δ 72.9 (CHOH), 126.4 ($C_{2,6}$), 127.8 (C_4), 127.9 (C_3), 128.6 ($C_{3,5}$), 137.2 (C_4), 139.2 (C_5), 140.2 (C_2), 142.6 (C_1), 148.1 (C_6); IR (KBr) ν 3400, 3044, 2887, 1578, 1563, 1451, 1406, 1384, 1303, 1189, 1091, 1040, 1015, 812, 761, 737, 701 cm^{-1}. Anal. Calcd for $C_{12}H_{10}BrNO$ (264.12): C, 54.57; H, 3.82; N, 5.30. Found: C, 54.25; H, 3.69; N, 4.99%.

2-Bromo-5-iodopyridine (19c). Using iodine as an electrophile gave 82% (CH_2Cl_2/cyclohexane, 25:75) of **19c**: mp 124–126°C ([17b] mp 125–126°C); ^{1}H NMR ($CDCl_3$) δ 7.19 (d, 1H, H_3), 7.83 (dd, 1H, H_4), 8.50 (d, 1H, H_6), $J_{4,6}$=2.3, $J_{3,4}$=8.3 Hz; ^{13}C NMR ($CDCl_3$) δ 91.7 (C_5), 129.8 (C_3), 141.2 (C_2), 146.4 (C_4), 155.9 (C_6); IR (KBr) ν 3018, 1544, 1439, 1354, 1085, 995, 828, 624, 477 cm^{-1}. Anal. Calcd for C_5H_3BrIN (283.89): C, 21.15; H, 1.07; N, 4.93. Found: C, 20.96; H, 1.13; N, 4.85%.

4-Bromo-α-phenyl-3-pyridinemethanol (21) and 3-bromo-α-phenyl-4-pyridinemethanol (22). Procedure B, starting from **20** (2.4 g, 10 mmol), using benzaldehyde as an electrophile, was used to give (CH_2Cl_2) **21** and **22** in 63 and 34% yield, respectively. Compound **(21)**: mp 150°C, dec; ^{1}H NMR (DMSO-d_6) δ 5.99 (s, 1H, CHOH), 6.30 (s, 1H, OH), 7.3 (m, 5H, Ph), 7.63 (d, 1H, H_5), 8.29 (d, 1H, H_6), 8.81 (s, 1H, H_2), $J_{5,6}$=5.3 Hz; ^{13}C NMR (DMSO-d_6) δ 72.3 (CHOH), 127.2 ($C_{2,6}$), 127.7 (C_4), 127.8 (C_5), 128.6 ($C_{3,5}$), 132.3 (C_4), 139.9 (C_1), 143.1 (C_3), 149.4 (C_6), 150.0 (C_2); IR (KBr) ν 3096, 2855, 1576, 1466, 1406, 1226, 1062, 1047, 750, 701 cm^{-1}. Anal. Calcd for $C_{12}H_{10}BrNO$ (264.12): C, 54.57; H, 3.82; N, 5.30. Found: C, 54.80; H, 3.89; N, 5.08%. Compound **(22)**:[18] mp 130–132°C; ^{1}H NMR ($CDCl_3$) δ 3.70 (s, 1H, OH), 6.11 (s, 1H, CHOH), 7.3 (m, 5H, Ph), 7.73 (d, 1H, H_5), 8.38 (d, 1H, H_6), 8.50 (s, 1H, H_2), $J_{5,6}$=5.3 Hz; ^{13}C

NMR ($CDCl_3$) δ 73.8 (CHOH), 120.6 (C_3), 122.6 (C_5), 127.2 ($C_{2,6}$), 128.2 (C_4), 128.6 ($C_{3,5}$), 140.6 (C_1), 148.2 (C_6), 151.4 (C_4), 151.5 (C_2); IR (KBr) ν 3139, 3083, 2838, 1587, 1456, 1402, 1311, 1057, 1024, 765, 733, 700, 659 cm^{-1}. Anal. Calcd for $C_{12}H_{10}BrNO$ (264.12): C, 54.57; H, 3.82; N, 5.30. Found: C, 54.35; H, 3.79; N, 5.09%.

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