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Metal-template *Ortho*-regioselective Synthesis of 2'-Hydroxyphenylpyridinemethanols

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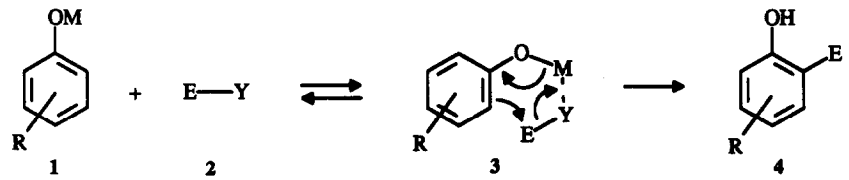
Abstract: 2'-Hydroxyphenylpyridinemethanols **7** were synthesized by metal-template *ortho*-regioselective alkylation of phenols **5** with 2-, 3- and 4-pyridinealdehydes **6**.

Introduction

The metal-template catalysis was extensively studied and utilized as a powerful instrument promoting *ortho*-regioselective functionalization of multireactive aromatic substrates such as phenols with different electrophilic reagents.[1] A fundamental requirement of this synthetic methodology is that the metal-phenolate **1** and the electrophile **2** should produce the self-organized adduct **3** in which the electrophile and the phenol *ortho*-carbon are oriented in such a way that the subsequent intracomplex regioselective reaction can easily occur (Scheme 1).



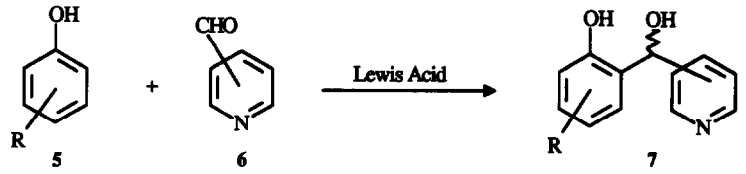
Scheme 1

In practice most of such reactions have utilized oxophilic metal-phenolates and carbonyl electrophiles in non polar solvents to promote the formation of the oriented complex like **3** and to achieve the *ortho*-regioselective control.

Recently we were interested in the preparation of new macrocyclic ligands from phenols and aldehydes.[2] To this end we studied the possibility of constructing hydroxylated di- and triphenylmethanes by *ortho*-regioselective condensation between oxophilic metal-phenolates and aromatic aldehydes.[3]

Results and Discussion

We report herein a simple, efficient and highly selective method for synthesizing 2'-hydroxyphenylpyridinemethanols **7** from phenols **5** and pyridinealdehydes **6** in the presence of a convenient Lewis acid.



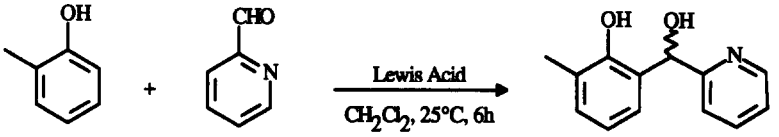
5 6 7

Scheme 2

Compounds of general formula **7** represent fundamental building blocks for the synthesis of phenol-based linear and cyclic ligands and are useful synthons for the preparation of a class of histamine antagonists[4] as well as cardiovascular[5] and bronchodilating[6] agents.

In a first series of experiments we examined the influence of the Lewis acid on the model reaction between 2-methylphenol **5b** and 2-pyridinealdehyde **6x** in dry methylene chloride at 25°C for 6 hours (Table 1).

Table 1. Reaction between 2-methylphenol **5b** and 2-pyridinealdehyde **6x** in the presence of different Lewis acids.



5b **6x** **7bx**

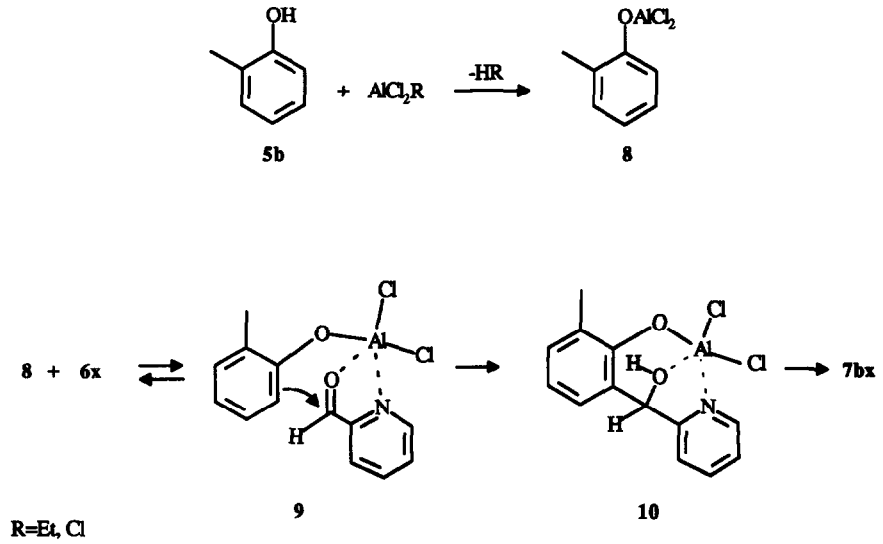
Entry	Lewis acid	Recovered **5b** (%)	**7bx** Yield (%)
1	$EtAlCl_2$	40	56
2	$AlCl_3$	40	54
3	EtMgBr	90	8
4	BCl_3	92	2
5	$SnCl_4$	92	3
6	$TiCl_4$	90	6

These results clearly indicate that $EtAlCl_2$ and $AlCl_3$ are the best promoters of the present reaction being **7bx** obtained in satisfactory yield and excellent selectivity (entries 1 and 2). Moreover there is only a small reaction of **5b** with **6x** when BCl_3, $SnCl_4$ and $TiCl_4$ are utilized.

It is worthy of note that the use of 2-methylphenoxymagnesium bromide results in production of **7bx** with poor yield (8%)[7] if compared with that previously observed in the reaction of various bromomagnesium

phenolates with different carbonyl compounds including aromatic aldehydes.[8] This result seems to be in agreement with the inertia of bromomagnesium phenolates early observed in similar reactions with carbonyl compounds bearing strongly electronwithdrawing groups in the α-position.[9]

Based on our results, the typical pathway for the present reaction is illustrated as follows (Scheme 3). Dichloroaluminium phenolate **8**, obtained by reaction of the phenol **5b** with $EtAlCl_2$ or $AlCl_3$ according to early reports from literature,[10] produces with the aldehyde **6x** the adduct **9**. As can be seen in Scheme 3, chelation around the aluminium through the oriented complex **9**, which involves both the phenolic substrate and the carbonyl compound, results in complete *ortho*-regiocontrol of the aromatic substitution affording **10** as the sole reaction product.



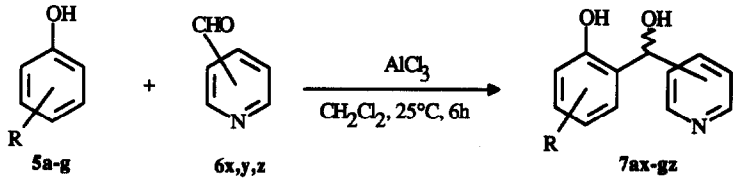
Scheme 3

Much evidence has been accumulated in the past for several reactions that involve such complexes as intermediates.[11]

Furthermore, the use of an aldehyde bearing an α-electronwithdrawing pyridino group allows the exclusive production of the α-(2'-hydroxy-3'-methylphenyl)-2-pyridinemethanol **7bx** without any triphenylmethane type compound,[12] due to the difficult of loosing water from **10** and avoiding the consequent formation of the more reactive *ortho*-methylenequinone intermediate.[13]

We utilized the present method to perform the simple synthesis of 2'-hydroxyphenylpyridinemethanols **7** from variously substituted phenols **5** and 2-, 3- and 4-pyridinealdehydes **6x, 6y** and **6z**. Synthetic results are reported in Table 2.

Table 2. $AlCl_3$-promoted reaction between different phenols (**5a-g**) and 2-pyridinaldehyde (**6x**), 3-pyridinaldehyde (**6y**) and 4-pyridinaldehyde (**6z**).



Entry	Phenol	R	Pyridinealdehyde	Product 7	Yield (%)	Selectivity (%)[a]
1	**5a**	H	**6x**	**7ax**	58	91
2	"	"	**6y**	**7ay**	26	89
3	"	"	**6z**	**7az**	21	87
4	**5b**	2-CH_3	**6x**	**7bx**	54	93
5	"	"	**6y**	**7by**	34	92
6	"	"	**6z**	**7bz**	37	93
7	**5c**	3-CH_3	**6x**	**7cx**	74	91
8	"	"	**6y**	**7cy**	42	89
9	"	"	**6z**	**7cz**	28	89
10	**5d**	4-Bu^t	**6x**	**7dx**	55	95
11	"	"	**6y**	**7dy**	61	97
12	"	"	**6z**	**7dz**	77	96
13	**5e**	4-OCH_3	**6x**	**7ex**	83	82
14	"	"	**6y**	**7ey**	32	84
15	"	"	**6z**	**7ez**	5	83
16	**5f**	4-Cl	**6x**	**7fx**	24	91
17	"	"	**6y**	**7fy**	11	93
18	"	"	**6z**	**7fz**	13	92
19	**5g**	2,3-(CH_2-CH=CH-CH_2)	**6x**	**7gx**	34	80
20	"	"	**6y**	**7gy**	34	81
21	"	"	**6z**	**7gz**	28	78

[a] Selectivity=Yield/Reacted Phenol x100

Results from Table 2 are in agreement with a typical metal-template electrophilic substitution process as depicted in Scheme 3 (see for example entries 10, 11, 12 and 16, 17, 18). The observed higher reactivity of 2-pyridinealdehyde as compared with that of 3- and 4- isomers (entries 1, 4, 7, 13, and 16) is possibly due to the chelation of the metal with both formil group and nitrogen atom through pentacoordinate aluminium which enhances particularly the electrophilicity of the aldehyde and produces homogeneous reaction medium. Contrarily, the reactions with 3- and 4-pyridinealdehydes are heterogeneous, probably due to the intermolecular interactions which produce polymeric aggregates. This effect could be responsible for the lower reactivity.

In order to support the chelation hypothesis we performed studies by ^{27}Al NMR spectroscopy.

We chose 2,4,6-trimethylphenoxyaluminium dichloride as unreactive phenolic model. Its dichloromethane-d_2 solution exibits a broad ^{27}Al resonance centered at δ=89.3 ppm ($\Delta\nu_{1/2}$=2500 Hz) attributable to tetracoordinated aluminium species along with a shoulder at δ=40.2 ppm probably due to pentacoordinated metal species. This is in agreement with the presence in solution of self-association dimers and/or trimers with tetra and pentacoordination.[14a]

The adduct obtained by adding 1 equivalent of 2-pyridinealdehyde to the solution of the dichlorophenoxide shows a completely different spectrum with two signals at δ=58.3 ppm ($\Delta\nu$=1000 Hz) and at δ=100.5 ppm ($\Delta\nu$=250 Hz) in a 3:1 ratio.

These peaks are attributable to mononuclear Al species, as association oligomers should be dissociated by the addition of one equivalent of the bidentate ligand.

The major peak at higher field falls in the typical region of alumunium pentacoordinated complexes[14b] and should be due to the expected pentacoordinated chelation complex involving both oxygen and nitrogen atoms of the ligand.

On the other hand the other signal exhibiting a chemical shift typical of tetracoordinated species is not univocally attributable.

Moreover, the formation of a soluble complex supports the existence of a chelated complex, since in the case of benzaldehyde or *p*-isopropylbenzaldehyde no soluble complexes could be obtained by interaction with the dichloroaluminium phenoxide.

Acknowledgements

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Experimental

Melting points were obtained on an Electrothermal melting point apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer 298 spectrophotometer. ^1H NMR spectra were recorded on a Bruker AC300 spectrometer at 300 MHz. Chemical shifts are expressed in ppm relative to TMS as internal standard.^{27}Al NMR spectra in CD_2Cl_2 were recorded at 52.1 MHz on Bruker CXP200 instrument using $[Al(H_2O)_6]^{3+}$ as external reference. Mass spectra were obtained on a Finnigan SSQ 710 instrument at 70 eV. Microanalyses were carried out at the Istituto di Chimica Farmaceutica dell'Università degli Studi di Parma, Italy. TLC analyses were performed on Stratocrom SIF silica gel plates (Carlo Erba) developed with dichloromethane-MeOH mixtures.

Synthesis of α-(2'-hydroxyphenyl)-pyridinemethanols (7). General Procedure. A solution of the selected phenol (0.01 mol) in dry dichloromethane (50 ml) was added dropwise to a stirred suspension of $AlCl_3$ (1.33 g, 0.01 mol) in dry dichloromethane (50 ml) under nitrogen. After 30 min, a solution of the selected pyridinaldehyde (1.07 g, 0.01 mol) in dry dichloromethane (50 ml) was added. The stirring was continued for 5 h at room temperature. The reaction was quenched with a saturated solution of NH_4Cl (60 ml) and the resulting mixture was extracted with methylene chloride (2 x 50 ml) and ethyl acetate (1 x 50 ml). The organic phase was dried (Na_2SO_4) and distilled off and the residue was chromatographed on silica gel plates with 5-20% dichloromethane-MeOH mixtures to give the products.

α-(2'-Hydroxyphenyl)-2-pyridinemethanol (**7ax**). Pale yellow crystals (Et_2O), m.p. 105-7°C (Found: C, 71.80; N, 6.84; H, 5.66. Calc. for $C_{12}H_{11}NO_2$: C, 71.63; N, 6.96; H, 5.51%); ^1H NMR ($CDCl_3$), δ (ppm) 3.9 (br s, 1H, OH), 5.96 (s, 1H, CH), 6.90 (td, 1H, H-5', J=7.5 and 1.1 Hz), 6.95 (dd, 1H, H-3', J=7.5 and 1.1 Hz), 7.21 (td, 1H, H-4', J=7.5 and 1.5 Hz), 7.25 (m, 1H, H-5), 7.32 (dd, 1H, H-6', J=7.5 and 1.5 Hz), 7.43 (d, 1H, H-3, J=7.7 Hz), 7.73 (td, 1H, H-4, J=7.7 and 1.7 Hz), 8.51 (m, 1H, H-6), 10.2 (br s, 1H, OH); IR (KBr) 3378 cm^{-1} (OH); MS (CI) *m/z* 230 (M+29, 3%), 202 (M+1, 62), 184 (100).

α-(2'-Hydroxyphenyl)-3-pyridinemethanol (**7ay**). Pale yellow crystals (Et_2O), m.p. 48-51°C (Found: C, 71.48; N, 7.07; H, 5.68. Calc. for $C_{12}H_{11}NO_2$: C, 71.63; N, 6.96; H, 5.51%); ^1H NMR ($CDCl_3$), δ (ppm) 6.01 (s, 1H, CH), 6.84 (td, 1H, H-5', J=7.8 and 1.0 Hz), 6.88 (d, 1H, H-3', J=7.8 Hz), 7.00 (dd, 1H, H-6', J=7.8 and 1.6 Hz), 7.18 (td, 1H, H-4', J=7.8 and 1.6 Hz), 7.28 (dd, 1H, H-5, J=7.9 and 4.9 Hz), 7.77 (dt, 1H, H-4, J=7.9 and 1.5 Hz), 8.39 (dd, 1H, H-6, J=4.9 and 1.5 Hz), 8.53 (d, 1H, H-2, J=1.9 Hz); IR (KBr) 3150 cm^{-1} (OH); MS (CI) *m/z* 230 (M+29, 20%), 202 (M+1, 90), 184 (100).

α-(2'-Hydroxyphenyl)-4-pyridinemethanol (**7az**). Pale yellow crystals (Et_2O), m.p. 146-8°C (Found: C, 71.50; N, 6.82; H, 5.65. Calc. for $C_{12}H_{11}NO_2$: C, 71.63; N, 6.96; H, 5.51%); ^1H NMR ($CDCl_3$), δ (ppm) 5.94 (s, 1H, CH), 6.87 (dd, 1H, H-3', J=7.7 and 1.3 Hz), 6.88 (t, 1H, H-5', J=7.7 Hx), 7.04 (dd, 1H, H-6', J=7.7 and 1.6 Hz), 7.21 (td, 1H, H-4', J=7.7 and 1.6 Hz), 7.34 (d, 2H, H-3 and H-5, J=6.2 Hz), 8.45 (d, 2H, H-2 and H-6, J=6.2 Hz); IR (KBr) 3407 cm^{-1} (OH); MS (EI) *m/z* 201 (M^+, 7%), 183 (100), 154 (17).

α-(2'-Hydroxy-3'-methylphenyl)-2-pyridinemethanol (**7bx**). Pale yellow crystals (Et_2O), m.p. 71-4°C (Found: C, 72.40; N, 6.62; H, 5.94. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; N, 6.51; H, 6.09%); ^1H NMR ($CDCl_3$), δ (ppm) 2.25 (s, 3H, CH_3), 4.0 (br s, 1H, OH), 5.93 (s, 1H, CH), 6.81 (t, 1H, H-5', J=7.6 Hz), 7.08 (d, 1H, H-4', J=7.6 Hz), 7.15 (d, 1H, H-6', J=7.6 Hz), 7.24 (m, 1H, H-5), 7.40 (d, 1H, H-3, J=7.8 Hz), 7.71 (td, 1H, H-4, J=7.8 and 1.7 Hz), 8.51 (d, 1H, H-6, J=4.8 Hz), 10.2 (br s, 1H, OH); IR (KBr) 3367 cm^{-1} (OH); MS (CI) *m/z* 216 (M+1, 16%), 215 (M^+, 100).

α-*(2'-Hydroxy-3'-methylphenyl)-3-pyridinemethanol* (**7by**). Pale yellow crystals (Et_2O), m.p. 126-8°C (Found: C, 72.67; N, 6.42; H, 6.20. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; N, 6.51; H, 6.09%); ^1H NMR ($CDCl_3$), δ (ppm) 2.24 (s, 3H, CH_3), 5.97 (s, 1H, CH), 6.7-6.9 (m, 2H, H-4' and H-6'), 7.1 (m, 1H, H-5'), 7.24 (dd, 1H, H-5, J=7.9 and 4.8 Hz), 7.73 (td, 1H, H-4, J=7.9 and 1.7 Hz), 8.32 (dd, 1H, H-6, J=4.8 and 1.7 Hz), 8.43 (d, 1H, H-2, J=1.7 Hz); IR (KBr) 3155 cm^{-1} (OH); MS (CI) *m/z* 244 (M+29, 21%), 216 (M+1, 89), 197 (100).

α-*(2'-Hydroxy-3'-methylphenyl)-4-pyridinemethanol* (**7bz**). Pale yellow crystals (Et_2O), m.p. 154-6°C (Found: C, 72.63; N, 6.66; H, 5.92. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; N, 6.51; H, 6.09%); ^1H NMR ($CDCl_3$), δ (ppm) 2.22 (s, 3H, CH_3), 5.90 (s, 1H, CH), 6.78 (t, 1H, H-5', J=7.4 Hz), 6.85 (d, 1H, H-4', J=7.4 Hz), 7.09 (d, 1H, H-6', J=7.4 Hz), 7.30 (d, 2H, H-3 and H-5, J=5.4 Hz), 8.40 (d, 2H, H-2 and H-6, J=5.4 Hz); IR (KBr) 3361 cm^{-1} (OH); MS (CI) *m/z* 244 (M+29, 23%), 216 (M+1, 100), 198 (80).

α-*(2'-Hydroxy-4'-methylphenyl)-2-pyridinemethanol* (**7cx**). Pale yellow crystals (Et_2O), m.p. 133-5°C (Found: C, 72.68; N, 6.69; H, 5.93. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; N, 6.51; H, 6.09%); ^1H NMR ($CDCl_3$), δ (ppm) 2.28 (s, 3H, CH_3), 4.0 (br s, 1H, OH), 5.89 (s, 1H, CH), 6.70 (d, 1H, H-5', J=7.7 Hz), 6.76 (s, 1H, H-3'), 7.17 (d, 1H, H-6', J=7.7 Hz), 7.23 (dd, 1H, H-5, J=7.6 and 5.7 Hz), 7.40 (d, 1H, H-3, J=7.6 Hz), 7.71 (td, 1H, H-4, J=7.6 and 1.6 Hz), 8.49 (d, 1H, H-6, J=5.7 Hz), 10.1 (br s, 1H, OH); IR (KBr) 3206 cm^{-1} (OH); MS (CI) *m/z* 244 (M+29, 3%), 216 (M+1, 100), 198 (99).

α-*(2'-Hydroxy-4'-methylphenyl)-3-pyridinemethanol* (**7cy**). Pale yellow crystals (Et_2O), m.p. 153-6°C (Found: C, 72.42; N, 6.40; H, 6.17. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; N, 6.51; H, 6.09%); ^1H NMR ($CDCl_3$-MeOD), δ (ppm) 2.26 (s, 3H, CH_3), 6.02 (s, 1H, CH), 6.65 (s, 1H, H-3'), 6.66 (d, 1H, H-5', J=8.1 Hz), 6.99 (d, 1H, H-6', J=8.1 Hz), 7.29 (dd, 1H, H-5, J=7.9 and 4.9 Hz), 7.79 (br d, 1H, H-4, J=7.9 Hz), 8.37 (d, 1H, H-6, J=4.9 Hz), 8.57 (s, 1H, H-2); IR (KBr) 3190 cm^{-1} (OH); MS (CI) *m/z* 244 (M+29, 41%), 216 (M+1, 100), 198 (99).

α-*(2'-Hydroxy-4'-methylphenyl)-4-pyridinemethanol* (**7cz**). Pale yellow crystals (Et_2O), m.p. 172-4°C (Found: C, 72.67; N, 6.36; H, 6.21. Calc. for $C_{13}H_{13}NO_2$: C, 72.54; N, 6.51; H, 6.09%); ^1H NMR ($CDCl_3$-MeOD), δ (ppm) 2.27 (s, 3H, CH_3), 5.95 (s, 1H, CH), 6.65 (s, 1H, H-3'), 6.66 (d, 1H, H-5', J=8.2 Hz), 6.98 (d, 1H, H-6', J=8.2 Hz), 7.40 (d, 2H, H-3 and H-5, J=5.9 Hz), 8.43 (d, 2H, H-2 and H-6, J=5.9 Hz); IR (KBr) 3205 cm^{-1} (OH); MS (EI) *m/z* 215 (M^+, 15%), 196 (100).

α-*(2'-Hydroxy-5'-tertbutylphenyl)-2-pyridinemethanol* (**7dx**). Pale yellow crystals (Et_2O), m.p. 129-31°C (Found: C, 74.80; N, 5.30; H, 7.61. Calc. for $C_{16}H_{19}NO_2$: C, 74.68; N, 5.44; H, 7.44%); ^1H NMR

($CDCl_3$), δ (ppm) 1.29 (s, 9H, $(CH_3)_3C$), 4.0 (br s, 1H, OH), 5.92 (s, 1H, CH), 6.88 (d, 1H, H-3', J=8.4 Hz), 7.22 (dd, 1H, H-4', J=8.4 and 2.5 Hz), 7.1-7.3 (m, 1H, H-5), 7.32 (d, 1H, H-6', J=2.5 Hz), 7.42 (d, 1H, H-3, J=7.8 Hz), 7.73 (td, 1H, H-4, J=7.8 and 1.4 Hz), 8.50 (d, 1H, H-6, J=4.8 Hz), 10.05 (br s, 1H, OH); IR (KBr) 3339 cm^{-1} (OH); MS (CI) *m/z* 286 (M+29, 13%), 258 (M+1, 100), 242 (99).

α-*(2'-Hydroxy-5'-tertbutylphenyl)-3-pyridinemethanol* (**7dy**). Pale yellow crystals (Et_2O), m.p. 157°C (Found: C, 74.52; N, 5.61; H, 7.33. Calc. for $C_{16}H_{19}NO_2$: C, 74.68; N, 5.44; H, 7.44%); ^1H NMR ($CDCl_3$), δ (ppm) 1.24 (s, 9H, $(CH_3)_3C$), 5.97 (s, 1H, CH), 6.81 (d, 1H, H-3', J=8.5 Hz), 7.04 (d, 1H, H-6', J=2.4 Hz), 7.19 (dd, 1H, H-4', J=8.5 and 2.4 Hz), 7.26 (dd, 1H, H-5, J=8.2 and 4.8 Hz), 7.77 (dt, 1H, H-4, J=8.2 and 1.5 Hz), 8.37 (dd, 1H, H-6, J=4.8 and 1.5 Hz), 8.54 (d, 1H, H-2, J=1.5 Hz); IR (KBr) 3205 cm^{-1} (OH); MS (CI) *m/z* 286 (M+29, 20%), 258 (M+1, 71), 239 (100).

α-*(2'-Hydroxy-5'-tertbutylphenyl)-4-pyridinemethanol* (**7dz**). Pale yellow crystals (Et_2O), m.p. 160-2°C (Found: C, 74.77; N, 5.31; H, 7.55. Calc. for $C_{16}H_{19}NO_2$: C, 74.68; N, 5.44; H, 7.44%); ^1H NMR ($CDCl_3$), δ (ppm) 1.27 (s, 9H, $(CH_3)_3C$), 5.95 (s, 1H, CH), 6.79 (d, 1H, H-3', J=8.5 Hz), 7.07 (d, 1H, H-6', J=2.4 Hz), 7.22 (dd, 1H, H-4', J=8.5 and 2.4 Hz), 7.3 (br s, 2H, 2 OH), 7.33 (d, 2H, H-3 and H-5, J=6.1 Hz), 8.46 (d, 2H, H-2 and H-6, J=6.1 Hz); IR (KBr) 3165 cm^{-1} (OH); MS (CI) *m/z* 286 (M+29, 10%), 258 (M+1, 52), 240 (40).

α-*(2'-Hydroxy-5'-methoxyphenyl)-2-pyridinemethanol* (**7ex**). Pale yellow crystals (Et_2O), m.p. 105-7°C (Found: C, 67.40; N, 5.88; H, 5.79. Calc. for $C_{13}H_{13}NO_3$: C, 67.52; N, 6.06; H, 5.67%); ^1H NMR ($CDCl_3$), δ (ppm) 3.73 (s, 3H, OCH_3), 5.95 (s, 1H, CH), 6.72 (dd, 1H, H-4', J=8.7 and 3.0 Hz), 6.87 (d, 1H, H-3', J=8.7 Hz), 6.92 (d, 1H, H-6', J=3.0 Hz), 7.22 (m, 1H, H-5), 7.49 (d, 1H, H-3, J=7.8 Hz), 7.72 (td, 1H, H-4, J=7.8 and 1.5 Hz), 8.45 (d, 1H, H-6, J=4.7 Hz); IR (KBr) 3247 cm^{-1} (OH); MS (EI) *m/z* 231 (M^+, 75%), 213 (36), 198 (100), 182 (34), 170 (62).

α-*(2'-Hydroxy-5'-methoxyphenyl)-3-pyridinemethanol* (**7ey**). Pale yellow crystals (Et_2O), m.p. 47-50°C (Found: C, 67.67; N, 6.22; H, 5.50. Calc. for $C_{13}H_{13}NO_3$: C, 67.52; N, 6.06; H, 5.67%); ^1H NMR ($CDCl_3$), δ (ppm) 3.67 (s, 3H, OCH_3), 5.93 (s, 1H, CH), 6.61 (d, 1H, H-6', J=2.8 Hz), 6.66 (dd, 1H, H-4', J=8.7 and 2.8 Hz), 6.75 (d, 1H, H-3', J=8.7 Hz), 7.21 (dd, 1H, H-5, J=7.9 and 4.9 Hz), 7.76 (br d, 1H, H-4, J=7.9 Hz), 8.25 (d, 1H, H-6, J=4.9 Hz), 8.45 (s, 1H, H-2); IR (KBr) 3270 cm^{-1} (OH); MS (EI) *m/z* 231 (M^+, 10%), 212 (100), 170 (15).

α-*(2'-Hydroxy-5'-methoxyphenyl)-4-pyridinemethanol* (**7ez**). Pale yellow crystals (Et_2O), m.p. 165-8°C (Found: C, 67.61; N, 6.18; H, 5.82. Calc. for $C_{13}H_{13}NO_3$: C, 67.52; N, 6.06; H, 5.67%); ^1H NMR ($CDCl_3$-MeOD), δ (ppm) 3.73 (s, 3H, OCH_3), 5.99 (s, 1H, CH), 6.70 (dd, 1H, H-4', J=8.8 and 2.7 Hz), 6.76

(d, 1H, H-6', J=2.7 Hz), 6.77 (d, 1H, H-3', J=8.8 Hz), 7.43 (d, 2H, H-3 and H-5, J=5.8 Hz), 8.43 (d, 2H, H-2 and H-6, J=5.8 Hz); IR (KBr) 3279 cm^{-1} (OH); MS (CI) *m/z* 260 (M+29, 21%), 232 (M+1, 100), 214 (89).

α-*(2'-Hydroxy-5'-chlorophenyl)-2-pyridinemethanol* (**7fx**). Pale yellow crystals (Et_2O), m.p. 130-2°C (Found: C, 61.30; Cl, 14.88; N, 5.82; H, 4.43. Calc. for $C_{12}H_{10}ClNO_2$: C, 61.16; Cl, 15.04; N, 5.94; H, 4.28%); ^1H NMR ($CDCl_3$), δ (ppm) 5.96 (s, 1H, CH), 6.84 (d, 1H, H-3', J=8.5 Hz), 7.09 (dd, 1H, H-4', J=8.5 and 2.4 Hz), 7.23 (m, 1H, H-5), 7.32 (d, 1H, H-6', J=2.4 Hz), 7.51 (d, 1H, H-3, J=7.6 Hz), 7.75 (t, 1H, H-4, J=7.6 Hz), 8.43 (d, 1H, H-6, J=4.5 Hz); IR (KBr) 3344 cm^{-1} (OH); MS (EI) *m/z* 237 (M+2, 24%), 235 (M^+, 90), 217 (35), 182 (100), 154 (62).

α-*(2'-Hydroxy-5'-chlorophenyl)-3-pyridinemethanol* (**7fy**). Pale yellow crystals (Et_2O), m.p. 130-2°C (Found: C, 61.02; Cl, 15.20; N, 6.07; H, 4.16. Calc. for $C_{12}H_{10}ClNO_2$: C, 61.16; Cl, 15.04; N, 5.94; H, 4.28%); ^1H NMR ($CDCl_3$-MeOD), δ (ppm) 6.03 (s, 1H, CH), 6.75 (d, 1H, H-3', J=8.5 Hz), 7.07 (dd, 1H, H-4', J=8.5 and 2.3 Hz), 7.21 (d, 1H, H-6', J=2.3 Hz), 7.30 (dd, 1H, H-5, J=7.8 and 4.8 Hz), 7.80 (br d, 1H, H-4, J=7.8 Hz), 8.37 (d, 1H, H-6, J=4.8 Hz), 8.57 (s, 1H, H-2); IR (KBr) 3240 cm^{-1} (OH); MS (EI) *m/z* 237 (M+2, 2%), 235 (M^+, 8), 216 (100), 182 (11).

α-*(2'-Hydroxy-5'-chlorophenyl)-4-pyridinemethanol* (**7fz**). Pale yellow crystals (Et_2O), m.p. 169-71°C (Found: C, 61.31; Cl, 15.16; N, 6.09; H, 4.11. Calc. for $C_{12}H_{10}ClNO_2$: C, 61.16; Cl, 15.04; N, 5.94; H, 4.28%); ^1H NMR ($CDCl_3$-MeOD), δ (ppm) 6.00 (s, 1H, CH), 6.76 (d, 1H, H-3', J=8.6 Hz), 7.08 (dd, 1H, H-4', J=8.6 and 2.5 Hz), 7.19 (d, 1H, H-6', J=2.5 Hz), 7.42 (d, 2H, H-3 and H-5, J=5.9 Hz), 8.43 (d, 2H, H-2 and H-6, J=5.9 Hz); IR (KBr) 3160 cm^{-1} (OH); MS (EI) *m/z* 237 (M+2, 5%), 235 (M^+, 15), 217 (100), 154 (22).

α-*(1'-Hydroxy-2'-naphthyl)-2-pyridinemethanol* (**7gx**). Pale yellow crystals (Et_2O), m.p. 76°C (Found: C, 76.60; N, 5.44; H, 5.33. Calc. for $C_{16}H_{13}NO_2$: C, 76.48; N, 5.57; H, 5.22%); ^1H NMR (C_6D_6), δ (ppm) 6.12 (s, 1H, CH), 7.22 (dd, 1H, H-5, J=7.7 and 5.1 Hz), 7.3-7.5 (m, 5H, H-8', H-5', H-4', H-3' and H-3), 7.70 (td, 1H, H-4, J=7.7 and 1.6 Hz), 7.7-7.8 (m, 1H, H-7' or H-6'), 8.3 (m, 1H, H-6' or H-7'), 8.52 (d, 1H, H-6, J=5.1 Hz); IR (KBr) 3245 cm^{-1} (OH); MS (CI) *m/z* 280 (M+29, 28%), 252 (M+1, 100), 234 (16), 144 (18).

α-*(1'-Hydroxy-2'-naphthyl)-3-pyridinemethanol* (**7gy**). Pale yellow crystals, dec. before melting (Et_2O) (Found: C, 76.36; N, 5.70; H, 5.11. Calc. for $C_{16}H_{13}NO_2$: C, 76.48; N, 5.57; H, 5.22%); ^1H NMR ($CDCl_3$), δ (ppm) 6.05 (s, 1H, CH), 6.85 (d, 1H, H-4', J=8.5 Hz), 7.13 (dd, 1H, H-5, J=7.9 and 4.9 Hz), 7.24 (d, 1H, H-3', J=8.5 Hz), 7.4-7.5 (m, 2H, H-8' and H-5'), 7.6-7.8 (m, 2H, H-4 and H-7' or H-6'), 8.2-8.3 (m, 2H, H-6 and H-6' or H-7'), 8.38 (d, 1H, H-2, J=2.1 Hz); IR (KBr) 3170 cm^{-1} (OH); MS (CI) *m/z* 280 (M+29, 13%), 252 (M+1, 77), 234 (100), 108 (11).

α-(1'-Hydroxy-2'-naphthyl)-4-pyridinemethanol (**7gz**). Pale yellow crystals, dec. before melting (Et_2O) (Found: C, 76.33; N, 5.48; H, 5.39. Calc. for $C_{16}H_{13}NO_2$: C, 76.48; N, 5.57; H, 5.22%); ^1H NMR ($CDCl_3$), δ (ppm) 6.04 (s, 1H, CH), 7.01 (d, 1H, H-4', J=8.5 Hz), 7.3 (m, 3H, H-3, H-5 and H-3'), 7.4-7.5 (m, 2H, H-8' and H-5'), 7.7-7.8 (m, 1H, H-7' or H-6'), 8.2 (m, 1H, H-6' or H-7'), 8.31 (d, 2H, H-2 and H-6, J=6.2 Hz); IR (KBr) 3245 cm^{-1} (OH); MS (CI) *m/z* 280 (M+29, 34%), 251 (M^+, 100), 233 (70), 108 (21).

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