An Efficient and Green Synthesis of 3,3'-Benzylidenebis (4-hydroxy-6-methylpyridin-2(1*H*)-one) Derivatives through Multi-component Reaction in Ionic Liquid

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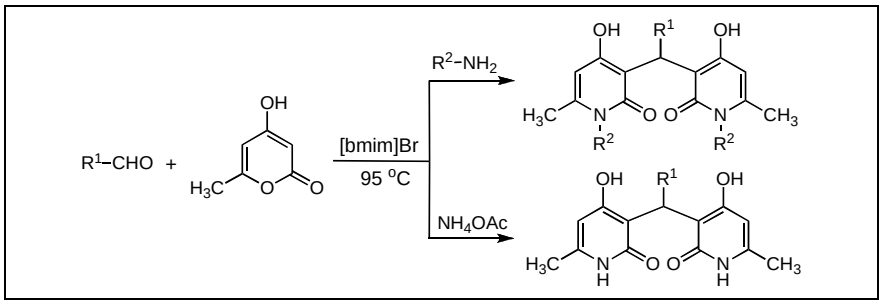
Received July 2, 2007



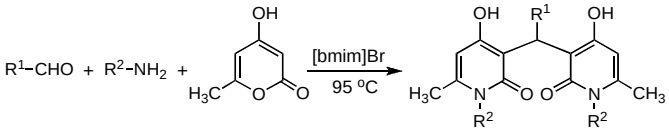
A series of new 3,3'-benzylidenebis(4-hydroxy-6-methylpyridin-2(1*H*)-one) derivatives were synthesized *via* a three-component reaction of an aldehyde, an aniline or ammonium acetate and 6-methyl-4-hydroxypyran-2-one in ionic liquid. These heterocyclic compounds produced could be conveniently separated from the reaction mixture without any volatile organic solvents, and the ionic liquid could be readily reused without efficiency loss after simple treatment.

J. Heterocyclic Chem., **45**, 1275 (2008).

INTRODUCTION

Multi-component reactions (MCRs), in which multiple reactions are combined into one synthetic operation have been used extensively to form carbon-carbon bonds in synthetic chemistry [1]. Such reactions offer a wide range of possibilities for the efficient construction of highly complex molecules in a single procedural step, thus avoiding the complicated purification operations and allowing savings of both solvents and reagents. In the past decade there have been tremendous development in three- and four-component reactions and great efforts continue to be made to develop new MCRs [2]. On the other hand, the replacement of current chemical process with more environmentally benign alternatives is an increasingly attractive goal in organic synthesis. In this field, room temperature ionic liquids have been the subject of considerable current interest as environmentally benign reaction media in organic synthesis because of their unique properties of nonvolatility, nonflammability and recyclables, among others [3]. Numerous chemical reaction, such as polymerization [4], hydrogenation [5], regioselective alkylation [6], Friedel-Crafts reactions [7], dimerization of alkenes [8], Diels-Alder reactions [9], Michael reactions [10], Cross-coupling reactions [11] and some enzymic reactions [12] can be carried out in ionic liquid. The ammonolysis is one of the most important methods for the formation of carbon-nitrogen bond. However, the ammonolysis in ionic liquid has not been reported in the literature. As part of our current studies on the development of new routs to heterocyclic systems [13], we now report an efficient and green synthetic route to 3,3'-benzylidenebis(4-hydroxy-6-methylpyridin-2(1*H*)-ones) *via* the three-component reaction (which including condensation, addition and ammonolysis) of an aldehyde **1**, aniline **2** and 6-methyl-4-hydroxypyran-2-one **3** in ionic liquid (Scheme 1).

Scheme 1



1 **2** **3** **4**

RESULTS AND DISCUSSION

4-Methoxyaniline **2a** has been used as the starting material to synthesize bispyridinones. We therefore first chose **3a** and searched for the optimized conditions for its reaction with 4-methylbenzaldehyde **1a** and 6-methyl-4-hydroxypyran-2-one **3** affording bispyridinones (Scheme 2).

Different solvents including ionic liquids such as [bmim]Br, [bmim]BF_4 and [bmim]PF_6 were examined. The results of these comparative experiments are summarized in Table 1. From the results it is obvious that the ionic liquid [bmim]Br is the best solvent among those examined. So [bmim]Br was chosen as the solvent for this reaction.

Scheme 2

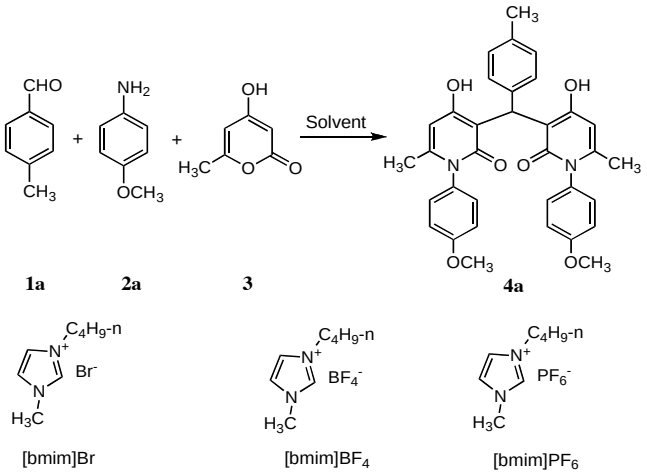


Table 1

Solvent optimization for the synthesis of **4a**

Entry	Solvent	Reaction Temperature (°C)	Time (h)	Yield (%)
1	[bmim]Br	95	3	88
2	[bmim]BF_4	95	4	76
3	[bmim]PF_6	95	5	69
4	EtOH	Reflux	5	30
5	CH_3CN	Reflux	5	Trace
6	H_2O	Reflux	5	N. R.
7	CH_3COCH_3	Reflux	5	N. R.
8	$CHCl_3$	Reflux	5	N. R.
9	HOAc	Reflux	5	N. R.

To examine the efficiency and the applicability of this new three-component reaction, a series of different aldehydes and anilines were tested in [bmim]Br. As shown in Table 2, this protocol could be applied not only to the aromatic aldehydes with either electron-withdrawing groups (such as halide groups) or electron-donating groups (such as alkyl, hydroxyl groups), but also to aliphatic aldehydes. Furthermore, it was particularly noteworthy that the protocol could be applied to aromatic amine with either electron-donating groups (such as alkyl, alkoxyl groups) or electron-withdrawing groups (such as halide groups), which highlighted the wide scope of this three-component reaction. However, when the aliphatic amine (*i. g.* benzylamine) was used in this reaction, the desired product was not obtained. It is due to the higher activity of benzyl amine, which leads to complex products.

Table 2

Synthesis of **4** in [bmim]Br

Entry	R^1	R^2	Time (h)	Yield (%)
4a	4-$CH_3C_6H_4$	4-$CH_3OC_6H_4$	3	88
4b	4-$CH_3C_6H_4$	4-$CH_3C_6H_4$	3	70
4c	4-$CH_3C_6H_4$	C_6H_5	4	81
4d	4-$CH_3C_6H_4$	4-ClC_6H_4	3	85
4e	4-$CH_3C_6H_4$	4-BrC_6H_4	2.5	73
4f	4-ClC_6H_4	4-FC_6H_4	4	94
4g	$C_6H_5CH_2$	4-$CH_3C_6H_4$	6	69
4h	2-HOC_6H_4	4-$CH_3C_6H_4$	5	90
4i	4-BrC_6H_4	4-$CH_3OC_6H_4$	3	81
4j	2,4-$Cl_2C_6H_3$	4-$CH_3OC_6H_4$	4	80

As expected, when the aniline **2** was replaced by ammonium acetate **5**, another series of 3,3'-benzylidene-bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) **6** were obtained under the same reaction conditions (Scheme 3). The results are summarized in Table 3.

Scheme 3

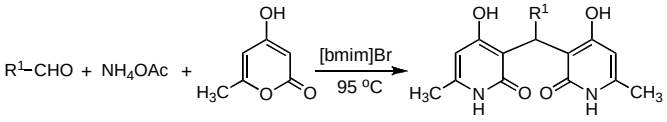


Table 3

Synthesis of **6** in [bmim]Br

Entry	R^1	Time (h)	Yield (%)	Mp (°C)
6a	4-$CH_3C_6H_4$	2	98	>300
6b	4-BrC_6H_4	2	96	>300
6c	2-thienyl	2	89	>300
6d	$C_6H_5CH_2$	2	88	>300
6e	2,4-$Cl_2C_6H_3$	1.5	94	>300
6f	3,4-$Cl_2C_6H_3$	1.5	95	>300
6g	4-ClC_6H_4	1.5	89	>300
6h	2-$CH_3OC_6H_4$	2	84	>300

In this study, all the products **4** and **6** were characterized by mp, IR and ^{1}H NMR spectral data as well as elemental analysis. Furthermore, the structure of **4a** was confirmed by X-ray crystallographic analysis. Figure **1** shows the molecular structure of **4a**. The crystallographic data of this compound is summarized in Table 4.

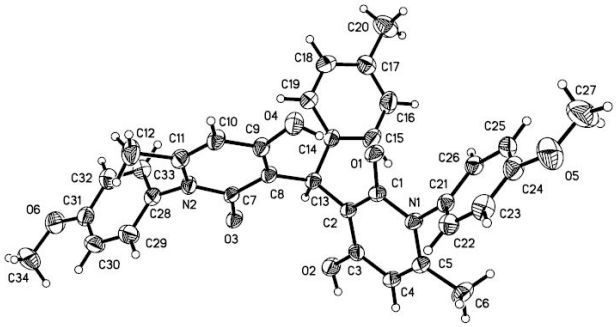


Figure 1. X-ray structure of **4a.**

Although the detailed mechanism of the above reaction remains to be fully clarified, the formation of 3,3'-benzylidenebispyridinone derivatives could be explained by a possible reaction sequence presented in Scheme 4. Product **4** may be synthesized *via* sequential condensation addition, ammonolysis, cyclization and dehydration. First, the condensation of aldehyde **1** and aniline **2** gave Schiff base **7**. The addition of Schiff base **7** to 6-methyl-4-hydroxypyran-2-one **3** then furnished the intermediate

Table 4

Crystallographic Data for **4a**

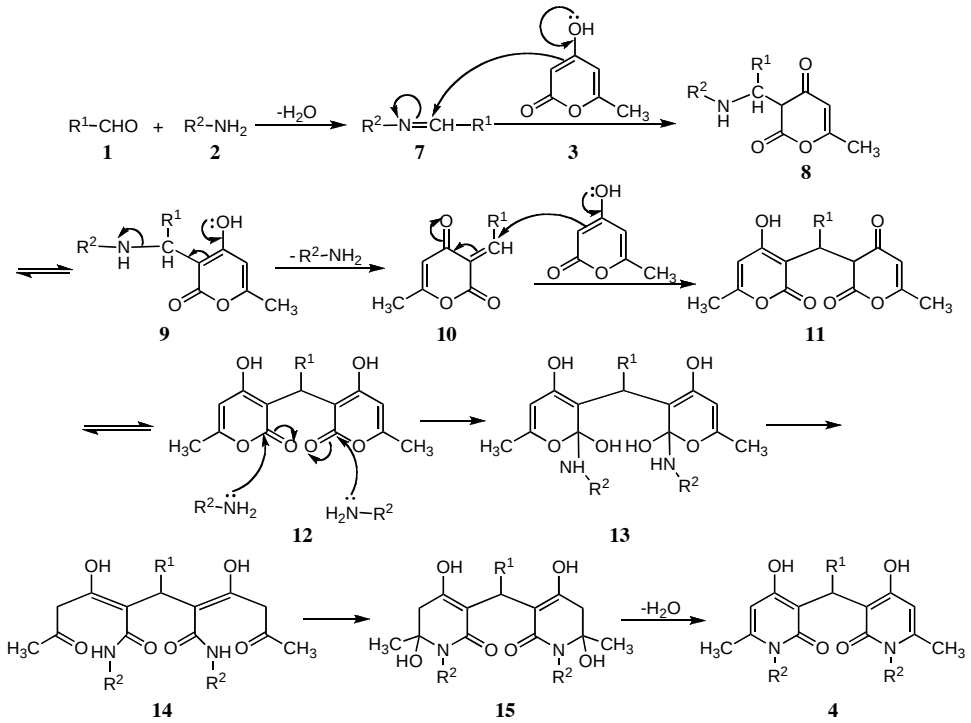
Empirical formula	$C_{34}H_{32}N_2O_6$
Formula weight	564.62
Wave length (Å)	0.71073
Crystal system	Monoclinic
Space group	$P2_1/n$
a (Å)	13.647(3)
b (Å)	13.759(3)
c (Å)	16.189(3)
α (°)	90
β (°)	110.355(4)
γ (°)	90
V (Å^3)	2850.0(10)
Z	4
Dcalc. (Mg/m^3)	1.316
Absorption coefficient(mm^{-1})	0.091
F(000)	1192
Crystal size (mm)	0.36 × 0.28 × 0.22
θ Range (°)	2.00 to 25.01
Limiting indices	-10 ≤ h ≤ 16
	-16 ≤ k ≤ 16
	-19 ≤ l ≤ 15
Reflections collected	14775
Independent reflections	5028
Data/restraints/parameters	5028/0/380
Goodness-of-fit on F^2	1.000
Final R indices [$I>2\sigma(I)$]	$R_1 = 0.0552$
	w$R = 0.1342$
R indices (all data)	$R_1 = 0.1445$
	w$R = 0.1807$
Largest diff. Peak and hole (e Å^{-3})	0.229 and -0.230

product **12**, which upon addition, intermolecular cyclization and dehydration gave rise to **4**.

The recovery and reuse of solvent and/or catalyst are highly preferable in terms of green synthetic process. Therefore, with the success of the above reactions, we continued our research by studying the reuse of [bmim]Br. It turned out that the recovery and reuse of [bmim]Br is very convenient and highly efficient. Thus, at completion of the reaction process, precipitated products were collected by suction and recrystallization from ethanol, and [bmim]Br could be recovered easily by concentrating the filtrate under reduced pressure and then drying at 100 °C for several hours. Studies by using **1a**, **2a** and **3** as model substrates showed that the recovered [bmim]Br could be successively recycled in subsequent reactions without almost any decrease in its efficiency. It should be noted that even in the sixth round, reuse of [bmim]Br recovered from the fifth round still produced the corresponding product with fairly good yield (95%).

In conclusion, we have developed a novel three-component reaction of an aldehyde, 6-methyl- 4-hydroxypyran-2-one and either aniline or ammonium acetate for the synthesis of 3,3'-benzylidenbis(4-hydroxy-6-methylpyridin-2(1*H*)-one) derivatives using ionic liquid as reaction medium. Particularly valuable features of this method include good yields of the products, shorter reaction time, environmental friendliness and straight forward procedure.

Scheme 4



EXPERIMENTAL

Melting points were determined in open capillaries and are uncorrected. IR spectra were recorded on a Tensor 27 spectrometer. ^{1}H NMR spectra were determined on a Bruker DPX 400 MHz spectrometer using TMS as internal standard, dimethyl sulfoxide-d_6 as solvent. Microanalyses were carried out on a Perkin-Elmer 2400 II instruments. X-ray diffraction was recorded on a Bruker Smart-1000 CCD diffractometer.

General procedure for the synthesis of 3,3-benzylidene-bis(6-methyl-4-hydroxy-1-arylpyridin-2(1*H*)-one) 4. A mixture of aldehyde **1** (1 mmol), aniline **2** (2 mmol) and 6-methyl-4-hydroxypyran-2-one **3** (2 mmol) was suspended in [bmim]Br (2 mL) and stirred at 95 °C for several hours. The reaction was monitored by TLC. After completion of the reaction, the reaction mixture was allowed to cool to room temperature and was added with 5 mL water. The precipitate was collected by suction and recrystallized from ethanol to give products **4** with high purity. The filtrate was concentrated under reduced pressure and dried at 100 °C to recover ionic liquid for subsequent use.

3,3'-(4-Methylbenzylidene)bis(4-hydroxy-6-methyl-1-(4-methoxyphenyl)pyridin-2(1*H*)-one) (4a). This compound was obtained as pale yellow needles with mp 288-289 ˚C; ir (potassium bromide): 1647, 1508, 1247 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.93 (s, 6H, 2 × CH_3), 2.25 (s, 3H, CH_3), 3.81 (s, 6H, 2 × CH_3O), 5.92 (s, 1H, CH), 6.16 (s, 2H, C^5-H, $C^{5'}$-H), 6.99-7.06 (m, 8H, ArH), 7.17-7.21 (m, 4H, ArH), 11.93 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{34}H_{32}N_2O_6$: C, 72.32; H, 5.71; N, 4.96. Found: C, 72.58; H, 5.63; N, 5.06.

3,3'-(4-Methylbenzylidene)bis(4-hydroxy-6-methyl-1-(4-methylphenyl)pyridin-2(1*H*)-one) (4b). This compound was obtained as colorless needles with mp >300 ˚C; ir (potassium bromide): 1646, 1508, 1267 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.92 (s, 6H, 2 × CH_3), 2.25 (s, 3H, CH_3), 2.37 (s, 6H, 2 × CH_3), 5.93 (s, 1H, CH), 6.17 (s, 2H, C^5-H, $C^{5'}$-H), 7.00 (d, J = 8.0 Hz, 2H, ArH), 7.05 (d, J = 8.0 Hz, 2H, ArH), 7.13-7.20 (m, 4H, ArH), 7.30-7.35 (m, 4H, ArH), 11.90 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{34}H_{32}N_2O_4$: C, 76.67; H, 6.06; N, 5.26. Found: C, 76.83; H, 5.98; N, 5.34.

3,3'-(4-Methylbenzylidene)bis(4-hydroxy-6-methyl-1-phenylpyridin-2(1*H*)-one) (4c). This compound was obtained as colorless needles with mp >300 ˚C; ir (potassium bromide): 1643, 1489, 1268 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.91 (s, 6H, 2 × CH_3), 2.25 (s, 3H, CH_3), 5.96 (s, 1H, CH), 6.18 (s, 2H, C^5-H, $C^{5'}$-H), 7.01 (d, J = 8.4 Hz, 2H, ArH), 7.05 (d, J = 8.4 Hz, 2H, ArH), 7.27-7.33 (m, 4H, ArH), 7.45-7.56 (m, 6H, ArH), 11.86 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{32}H_{28}N_2O_4$: C, 76.17; H, 5.59; N, 5.55. Found: C, 76.12; H, 5.50; N, 5.68.

3,3'-(4-Methylbenzylidene)bis(4-hydroxy-6-methyl-1-(4-chlorophenyl)pyridin-2(1*H*)-one) (4d). This compound was obtained as pale yellow needles with mp 275-277 ˚C; ir (potassium bromide): 1648, 1485, 1267 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.93 (s, 6H, 2 × CH_3), 2.25 (s, 3H, CH_3), 5.98 (s, 1H, CH), 6.18 (s, 2H, C^5-H, $C^{5'}$-H), 7.00 (d, J = 8.0 Hz, 2H, ArH), 7.04 (d, J = 8.0 Hz, 2H, ArH), 7.32-7.39 (m, 4H, ArH), 7.56-7.62 (m, 4H, ArH), 11.78 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{32}H_{26}Cl_2N_2O_4$: C, 67.02; H, 4.57; N, 4.88. Found: C, 67.24; H, 4.65; N, 4.73.

3,3'-(4-Methylbenzylidene)bis(4-hydroxy-6-methyl-1-(4-bromophenyl)pyridin-2(1*H*)-one) (4e). This compound was obtained as dark yellow needles with mp 265-267 ˚C; ir (potassium bromide): 1648, 1488, 1267 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.93 (s, 6H, 2 × CH_3), 2.25 (s, 3H, CH_3), 5.97 (s, 1H, CH), 6.18 (s, 2H, C^5-H, $C^{5'}$-H), 6.99 (d, J = 8.0 Hz, 2H, ArH), 7.04 (d, J = 8.0 Hz, 2H, ArH), 7.26-7.33 (m, 4H, ArH), 7.69-7.75 (m, 4H, ArH), 11.80 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{32}H_{26}Br_2N_2O_4$: C, 58.03; H, 3.96; N, 4.23. Found: C, 58.18; H, 4.05; N, 3.92.

3,3'-(4-Chlorobenzylidene)bis(4-hydroxy-6-methyl-1-(4-fluorophenyl)pyridin-2(1*H*)-one) (4f). This compound was obtained as colorless needles with mp > 300 ˚C; ir (potassium bromide): 1648, 1505, 1269 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.92 (s, 6H, 2 × CH_3), 6.04 (s, 1H, CH), 6.18 (s, 2H, C^5-H, $C^{5'}$-H), 7.13 (d, *J* = 8.4 Hz, 2H, ArH), 7.29 (d, *J* = 8.4 Hz, 2H, ArH), 7.32-7.40 (m, 8H, ArH), 11.84 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{31}H_{23}ClF_2N_2O_4$: C, 66.37; H, 4.13; N, 4.99. Found: C, 66.45; H, 4.09; N, 5.06.

3,3'-(Benzylmethylidene)bis(4-hydroxy-6-methyl-1-(4-methylphenyl)pyridin-2(1*H*)-one) (4g). This compound was obtained as pale yellow needles with mp 260-262 ˚C; ir (potassium bromide): 1646, 1500, 1265 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.84 (s, 6H, 2 × CH_3), 2.37-2.41 (m, 8H, CH_2, 2 × CH_3), 4.72 (t, J = 8.0 Hz, 1H, CH), 6.07 (s, 2H, C^5-H, $C^{5'}$-H), 7.06-7.16 (m, 5H, ArH), 7.20-7.26 (m, 4H, ArH), 7.32-7.37 (m, 4H, ArH), 11.40 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{34}H_{32}N_2O_4$: C, 76.67; H, 6.06; N, 5.26. Found: C, 76.55; H, 5.84; N, 5.51.

3,3'-(2-Hydroxybenzylidene)bis(4-hydroxy-6-methyl-1-(4-methylphenyl)pyridin-2(1*H*)-one) (4h). This compound was obtained as dark yellow needles with mp 206-209 ˚C; ir (potassium bromide): 1669, 1507, 1262 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.88 (s, 6H, 2 × CH_3), 2.37 (s, 6H, 2 × CH_3), 6.02 (s, 1H, CH), 6.09 (s, 2H, C^5-H, $C^{5'}$-H), 6.62-6.67 (m, 2H, ArH), 6.93-6.97 (m, 1H, ArH), 7.05-7.11 (m, 5H, ArH), 7.29-7.33 (m, 4H, ArH), 9.06 (s, 1H, OH), 11.67 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{33}H_{30}N_2O_5$: C, 74.14; H, 5.66; N, 5.24. Found: C, 74.19; H, 5.74; N, 5.27.

3,3'-(4-Bromobenzylidene)bis(4-hydroxy-6-methyl-1-(4-methoyphenyl)pyridin-2(1*H*)-one) (4i). This compound was obtained as yellow needles with mp 275-277 ˚C; ir (potassium bromide): 1646, 1507, 1248 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.93 (s, 6H, 2 × CH_3), 3.81 (s, 6H, 2 × CH_3O), 5.97 (s, 1H, CH), 6.17 (s, 2H, C^5-H, $C^{5'}$-H), 7.02-7.08 (m, 6H, ArH), 7.18-7.23 (m, 4H, ArH), 7.42 (d, J = 8.8 Hz, 2H, ArH), 11.91 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{33}H_{29}BrN_2O_6$: C, 62.96; H, 4.64; N, 4.45. Found: C, 63.13; H, 4.59; N, 4.56.

3,3'-(2,4-Dichlorobenzylidene)bis(4-hydroxy-6-methyl-1-(4-methoxyphenyl)pyridin-2(1*H*)-one) (4j). This compound was obtained as colorless needles with mp 287-289 ˚C; ir (potassium bromide): 1643, 1508, 1251 cm^{-1}; ^{1}H nmr (dimethyl sulfoxide-d_6): δ 1.89 (s, 6H, 2 × CH_3), 3.80 (s, 6H, 2 × CH_3O), 6.06 (s, 2H, C^5-H, $C^{5'}$-H), 6.24 (s, 1H, CH), 7.03 (d, J = 8.0 Hz, 4H, ArH), 7.11 (d, J = 8.0 Hz, 4H, ArH), 7.24 (d, J = 8.8 Hz, 1H, ArH), 7.30 (dd, J_1 = 2.0 Hz, J_2 = 8.8 Hz, 1H, ArH), 7.43 (d, J = 2.0 Hz, 1H, ArH), 11.58 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{33}H_{28}Cl_2N_2O_6$: C, 63.98; H, 4.56; N, 4.52. Found: C, 64.08; H, 4.52; N, 4.61.

General procedure for the synthesis of 3,3'-benzylidene-bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) 6. A mixture of aldehyde **1** (1 mmol), ammonium acetate **5** (2 mmol) and 6-methyl-4-hydroxypyran-2-one **3** (2 mmol) was suspended in [bmim]Br (2 mL) and stirred at 95 °C for several hours. Upon completion, monitored by TLC, the reaction mixture was

allowed to cool to room temperature and was added with 5 mL water. The precipitate was collected by suction and recrystallized from ethanol to give products **6** with high purity. The filtrate was concentrated under reduced pressure and dried at 100 °C to recover ionic liquid for subsequent use.

3,3'-(4-Methylbenzylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6a). This compound was obtained as pale yellow needles with mp >300 ˚C; ir (potassium bromide): 1634, 1512, 1253 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.17 (s, 6H, 2 × CH_3), 2.25 (s, 3H, CH_3), 5.83 (s, 1H, CH), 5.91 (s, 2H, C^5-H, $C^{5'}$-H), 6.90 (d, *J* = 8.0 Hz, 2H, ArH), 7.03 (d, *J* = 8.0 Hz, 2H, ArH), 11.67 (br., s, 2H, 2 × NH), 11.91 (br., s, 1H, OH), 12.51 (br., s, 1H, OH). *Anal*. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.39; H, 5.64; N, 7.81.

3,3'-(4-Bromobenzylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6b). This compound was obtained as pale yellow needles with mp > 300 ˚C; ir (potassium bromide): 1631, 1485, 1253 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.17 (s, 6H, 2 × CH_3), 5.86 (s, 1H, CH), 5.92 (s, 2H, C^5-H, $C^{5'}$-H), 6.95 (d, *J* = 8.4 Hz, 2H, ArH), 7.42 (d, *J* = 8.4 Hz, 2H, ArH), 11.73 (br., s, 2H, 2 × NH), 12.32 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{19}H_{17}BrN_2O_4$: C, 54.69; H, 4.11; N, 6.71. Found: C, 54.81; H, 4.06; N, 6.89.

3,3'-(2-Thioenylmethylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6c). This compound was obtained as pale yellow needles with mp > 300 ˚C; ir (potassium bromide): 1633, 1504, 1253 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.16 (s, 6H, 2 × CH_3), 5.90 (s, 2H, C^5-H, $C^{5'}$-H), 6.09 (s, 1H, CH), 6.57 (s, 1H, ArH), 6.87-6.84 (m, 1H, ArH), 7.24 (d, J = 5.2 Hz, 1H, ArH), 11.66 (br., s, 3H, OH, 2 × NH), 12.90 (br., s, 1H, OH). *Anal*. Calcd. for $C_{17}H_{16}N_2O_4S$: C, 59.29; H, 4.68; N, 8.13. Found: C, 59.43; H, 4.55; N, 8.37.

3,3'-(Benzylmethylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6d). This compound was obtained as pale yellow needles with mp > 300 ˚C; ir (potassium bromide): 1629, 1494, 1262 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.10 (s, 6H, 2 × CH_3), 3.40-3.52 (m, 2H, CH_2), 4.64 (t, *J* = 8.0 Hz, 1H, CH), 5.82 (s, 2H, C^5-H, $C^{5'}$-H), 7.21-7.09 (m, 5H, ArH), 11.66 (br., s, 2H, 2 × NH), 11.92 (br., s, 1H, OH), 13.15 (br., s, 1H, OH). *Anal*. Calcd. for $C_{20}H_{20}N_2O_4$: C, 68.17; H, 5.72; N, 7.95. Found: C, 68.26; H, 5.79; N, 7.78.

3,3'-(2,4-Dichlorobenzylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6e). This compound was obtained as pale yellow needles with mp > 300 ˚C; ir (potassium bromide): 1625, 1462, 1258 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.12 (s, 6H, 2 × CH_3), 5.83 (s, 2H, C^5-H, $C^{5'}$-H), 6.18 (s, 1H, CH), 7.20 (d, *J* = 8.4 Hz, 1H, ArH), 7.31 (d, *J* = 8.4 Hz, 1H, ArH), 7.40 (s, 1H, ArH), 11.44 (br., s, 2H, 2 × NH), 11.81 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{19}H_{16}Cl_2N_2O_4$: C, 56.04; H, 3.96; N, 6.88. Found: C, 56.13; H, 3.91; N, 6.97.

3,3'-(3,4-Dichlorobenzylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6f). This compound was obtained as brown needles with mp > 300 ˚C; ir (potassium bromide): 1633, 1461, 1255 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.17 (s, 6H, 2 × CH_3), 5.93 (s, 2H, C^5-H, $C^{5'}$-H), 5.95 (s, 1H, CH), 6.98 (d, *J* = 8.4 Hz, 1H, ArH), 7.12 (s, 1H, ArH), 7.50 (d, *J* = 8.4 Hz, 1H, ArH), 11.76 (br., s, 2H, 2 × NH), 12.21 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{19}H_{16}Cl_2N_2O_4$: C, 56.04; H, 3.96; N, 6.88. Found: C, 55.88; H, 4.05; N, 6.76.

3,3'-(4-Chlorobenzylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6g). This compound was obtained as yellow needles with mp > 300 ˚C; ir (potassium bromide): 1636, 1491, 1255 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.17 (s, 6H, 2 × CH_3), 5.90-5.93 (m, 3H, CH, C^5-H, $C^{5'}$-H), 7.01 (d, *J* = 8.0 Hz, 2H, ArH), 7.28 (d, *J* = 8.0 Hz, 2H, ArH), 11.74 (br., s, 2H, 2 × NH), 12.32 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{19}H_{17}ClN_2O_4$: C, 61.21; H, 4.60; N, 7.51. Found: C, 61.37; H, 4.56; N, 7.38.

3,3'-(2-Methoxybenzylidene)bis(4-hydroxy-6-methylpyridin-2(1*H*)-one) (6h). This compound was obtained as colorless needles with mp > 300 ˚C; ir (potassium bromide): 1632, 1490, 1262 cm^{-1}; ^1H nmr (dimethyl sulfoxide-d_6): δ 2.13 (s, 6H, 2 × CH_3), 3.52 (s, 3H, CH_3O), 5.84 (s, 3H, CH, C^5-H, $C^{5'}$-H), 6.02 (s, 1H, CH), 6.86-6.80 (m, 2H, ArH), 7.08-7.15 (m, 2H, ArH), 11.47 (br., s, 2H, 2 × NH), 12.62 (br., s, 2H, 2 × OH). *Anal*. Calcd. for $C_{20}H_{20}N_2O_5$: C, 65.21; H, 5.47; N, 7.60. Found: C, 65.19; H, 5.53; N, 7.54.

Acknowledgement. We are grateful to the National Nature Science Foundation of China (20472062 and 20672079), the Natural Science Foundation of Jiangsu Province (BK2006048) and the Natural Science Foundation of Jiangsu Education Department (06KJA15007) for financial support.

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