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Unconventional Acceptor and Donor Functional Groups Linked by a Captodative Spacer¹

Ermitas Alcalde,* Maria Gisbert, Josep M. Pons and Lluïsa Pérez-García

Laboratorio de Química Orgánica, Facultad de Farmacia, Universidad de Barcelona, E-08028 Barcelona, Spain

Abstract: The chemical stability to oxidation of a set of compounds built up from acceptor and donor subunits linked by a methylene or a hydroxymethylene group was studied. Whereas 1-butyl-3-[1,2,4-triazol-5(3)-ylmethyl]pyridinium salts **2d,e** showed high stability to oxidation, 1-butyl-4-[imidazol-4(5)-ylhidroxymethyl]pyridinium salt **14f** was oxidised spontaneously to the corresponding carbonyl compound, indicating the capability of the oxidation phenomenon to be controlled by the nature of the building blocks. Copyright © 1996 Elsevier Science Ltd

Both the areno-analogy principle^{2,3} and the captodative effect for free radicals^{4,5} have interacted within several examples of 1-alkyl-4(3)-azolylmethylpyridinium salts 1 and 2.⁶ Hence, a remarkable directing effect modulated by the nature of non-classical acceptor and donor heteroaromatic groups^{3,7} is observed in the chemical behaviour of compounds 1 and 2; there is a change in the susceptibility with which the methylene spacers oxidise to their oxomethyl analogues 3 and 4, leading to the designed 1-butyl-3-[1*H*-1,2,4-triazolyl-3(5)-methyl]pyridinium salts 2d,e which turn out to be stable to air oxidation (Figure 1). Furthermore, this chemical stability persisted in the corresponding 1-butyl-3-pyridinio-3(5)-1,2,4-triazolate betaines 5d,e.⁶



Figure 1. Compounds 1-5 arising from the modulation of the susceptibility of the methylene spacer to oxidation.⁶

We focused our attention on the synthetic utility of the aforementioned spontaneous oxidation, since it appears to be an attractive way of access to the hitherto unknown oxomethylpyridinium triazolate inner salts 6 and 7 with a functionalized spacer (Figure 2). In this connection, heterocyclic betaines^{8,9} with a methylene spacer —e.g. 5— have recently been incorporated as building blocks for the construction of novel quadrupolar [1₄]heterophanes.^{8b,10} In either the dipolar or the quadrupolar chemical entities, an *oxomethyl spacer* may allow an entrance to the *hydroxymethyl* counterpart that imply systems containing stereogenic center(s), and the hydrophilic/lipophilic balance can thus be modulated.¹¹

With these aims in mind, we describe the preparation of new series within betaines 6 and 7 incorporating a carbonyl moiety as the interannular spacer. The 4(3)-pyridylmethylazoles 8 and 9 previously reported⁶ were the key precursors. Conversion of the 4-pyridylmethylbenzimidazole 8b into the corresponding hydroxymethyl analogue 10b — via the oxidized carbonyl intermediate 11b— were also studied (Figure 2), as well as the oxomethylpyridinium imidazole salt 3f (vide infra, Schemes 3-5).





RESULTS AND DISCUSSION

Quaternization of (4-pyridylmethyl)-s-triazoles 8 d,e as well as (3-pyridylmethyl)-2-benzimidazoles 9a-c, under standard conditions, afforded the corresponding oxomethylpyridinium salts 3d,e and 4a-c — via the air-sensitive s-triazolylmethylpyridinium salts — upon recrystallisation in a variety of solvents, or by transformation in the solid state at ambient temperature. In contrast, the 1-butyl-3-[3(5)-substituted-1H-1,2,4-triazol-5(3)-ylmethyl]pyridinium salts 2d,e proved to be stable, and they were transformed into the corresponding inner salts 5d,e, for which stability persisted.⁶ In this study, it was possible to isolate pure

oxomethylbetaines **6d**,e when their precursors **3d**,e were deprotonated (Scheme 1), using a standard protocol.^{6,8} In constrast, within the 2-substituted benzimidazoles isolation of the corresponding inner salts **7a-c** from the oxomethyl derivatives **4a-c** was precluded due to their intrinsic instability.



Scheme 1. Heterocyclic betaines with a methylene 5d,e or oxomethylene 6d,e spacer.

The susceptibility of the methylene spacer in betaines **5d**,e and precursors **2d**,e to oxidation (Scheme 2) was examined and the results are gathered in Table 1. In accordance with their apparent stability, no aerial oxidation was observed. Indeed, compounds **2d**,e were completely stable solids, and the transformation of **2e** into **4e** required the passage of pure oxygen through a solution of the compound, while **2d** did not oxidise at



Scheme 2. Induced oxidation of quaternary salts 2d,e and betaines 4d,e by oxygen bubbling.

all (Scheme 2). The structural features within the dipolar molecules 5d, e favour their oxidation — under more forcing conditions than atmospheric ones — to the oxomethyl betaines 7d, e, which were then quenched as the corresponding tetrafluoroborates 4d, e (Table 1).¹²

Table 1. Reactions of compound pairs 2d, e and 5d, e with oxygen										
substrate ^a	temp (°C)	reaction time (h)	product distribution ^b							
			2d <i>c</i>	4d <i>C</i>	$2e^{C}$	4e ^C				
2d	60	6, 24, 30	100	0						
2e	60	6, 24			100	0				
2e	60	30			85	15				
			2 d ^d	4d ^d	2e ^d	4e ^d				
5d	60	1	е	е						
5d	rt	2	80	20						
5d	rt	8, 16	50	50						
5d	rt	> 16	е	е						
5e	60	2			75	25				
5e	60	8, 16			43	57				
5e	60	> 16			40	60				

Se60> 164060a See Scheme 2. b Ratio determined by ${}^{1}H$ NMR of reaction mixture. c As the I-
salt. d As the BF4- salt. e Only alteration and decomposition products were

observed.12

The introduction of a 4(5)-substituted imidazole ring as the π -electron rich moiety in these compounds, and examination of the quaternisation reaction of the pyridylhydroxymethylimidazole **10f** (Scheme 3), were also performed. Treatment of 1-trityl-4-iodoimidazole **12f** — prepared using a literature procedure¹³ — with ethyl magnesium bromide according to a protocol described by Ley and coworkers¹⁴, followed by reaction with 4-pyridinecarbaldehyde, afforded the carbinol **13f**, which was deprotected using HCl (aq, 1M) in ethanol solution. The (4-pyridyl)hydroxymethylimidazole **10f** was found to be very stable.^{14,15} Finally, the quaternization of **10f** with 1-iodobutane under standard conditions produced the imidazolylhydroxymethylpyridinium iodide **14f**, which oxidised spontaneously to the oxomethyl counterpart **3f** (Scheme 3).



Scheme 3

A synthetic application for the spontaneous oxidation reported was considered and we studied the reduction of the pyridylcarbonylbenzimidazole **11b** (Scheme 4) prepared from the methylene analogue **8b**.¹⁶ Reduction was achieved by treatment of carbonylbenzimidazole **11b** with sodium borohydride, affording the hydroxy derivative **10b** in 78% yield (Scheme 4). In contrast with the hydroxyimidazole **10f** (*vide supra*, Scheme 3), the 4–pyridylhydroxymethylbenzimidazole **10b** turned out to be unstable, and was spontaneously reconverted into the starting ketone **11b** (Scheme 4).



Finally, the susceptibility of carbinol **10b** to oxidation necessitates an alkylative reduction procedure, in order to prepare the alkoxy-derivative **15b**, either in one step, or through the ketal intermediate **16b** (Scheme 5.). Several attempts at this reduction were made, using a variety of reagents and conditions (Scheme 5. See also Experimental Section). First, treatment of compound **11b** with triethylsilane in ethanol in the presence of concentrated sulfuric acid (Method A)¹⁷ or by catalytic hydrogenation using PtO₂ at room temperature and pressure (Method B)¹⁸ gave no reaction (Scheme 5). Transformation of **11b** into the acyclic ketal was also attempted by using trialkylorthoformates in the presence of an acid catalyst (sulfuric acid¹⁹ (Method C), Nafion-H resin²⁰ (Method D and E) or methanesulfonic acid²¹ (Method F)) but without success. Finally, the use of similar conditions to those described by Newkome and coworkers¹⁹ for the formation of ketals of bis(2-pyridyl)ketones (Method G) resulted in the formation of the desired ketal **17b** in very low yield, and therefore the synthesis of compound **15b** was not studied any further.



Scheme 5

Physical data of all new compounds described in this work are listed in Table 2 (see Experimental Section). The compounds were unambiguously characterized on the basis of their spectroscopic data (IR, ¹H NMR and ¹³C NMR) and all the products isolated were analytically pure. The IR spectra (KBr) of the oxomethyl derivatives **6d**,e showed a band in the range 1680-1650 cm⁻¹($v_{c=0}$) and the ¹³C NMR (CD₃)₂SO spectra showed a signal δ *ca.* 180 ppm.

Both ¹H and ¹³C NMR data of betaines **6d**, e provide evidence of their dipolar structure. Selected ¹H and ¹³C NMR chemical shifts of betaines **6d** and **6e** and their precursors **3d**, e, ⁶ together with the several new compounds described in this work are shown in Tables 3 and 4; individual assignments were made using the appropriate NMR experiments.²²

Table 3.Selected ¹H NMR Data²² of 3(5)-(1-Butyl-4-pyridiniocarbonyl)-1,2,4-triazolate**6d**, e, 4-[1-Hydroxy-1-(4-pyridyl)methyl]-1-tritylimidazole**13f**, 4(5)-[1-Hydroxy-1-(4-pyridyl)methyl]-1H-imidazole**10f**, 1-Butyl-4-(imidazol-4(5)ylcarbonyl)pyridiniumiodide**3f**, 5,6-Dimethyl-2-(4-pyridylcarbonyl)-1H-benzimidazole**11b**, and 5,6-Dimethyl-2-[1-hydroxy-1-(4-pyridyl)methyl)-1H-benzimidazole**10b**^a

compd	pyr	A-	X	R	H2',6'	H3',5'	H _{2",6"}		'H3",5"	H4"
6d	4		co	_	9.17	8.68				
3d <i>b</i>	4	I-	CO	Н	9.29	8.66	_			—
$\Delta \delta^{C}$					-0.12	+0.02				
6e	4	—	CO	—	9.21	8.77	8	8.09	7.39	7.30
3e ^b	4	I-	CO	Н	9.34	8.79	8.10		7.60	7.60
$\Delta \delta^{C}$					-0.13	-0.02	-4	0.01	-0.21	-0.30
							CH	H ₂		H4(5)
13 f	4		CH(OH)	CPh_3	8.45	7.29	5.57	7.35		6.76
10 f	4		CH(OH)	Н	8.47	7.37	5.64	7.53		6.84 <i>d</i>
3 f	4	I-	CO	Н	9.28	8.61	—	8.28		8.24
							CH	H4		H7
11 b	4		CO	Н	8.86	8.29	_	7.64d		7.38d
10 b	4		CH(OH)	Н	8.52	7.46	5.90	7.24		7.24

^a In (CD₃)₂SO. ^b ¹H-NMR data for compounds **3d**,e are reported elsewhere.² ^c $\Delta \delta$: observed chemical shifts difference between betaines and their corresponding salts. ^d Broad or anisochronous signals of either imidazole H-4/5 or benzimidazole H-4 /7 protons were observed owing to slow proton exchange between N-1 and N-3. NH proton signal *ca*. 12.0 ppm.

Comparison of the ¹H NMR chemical shifts observed for betaines **6d**, and **6e** with those of their corresponding triazolylmethylpyridinium salts **3d**,**e** (see $\Delta\delta$ in Table 3) revealed that the H-2,6 pyridinium protons were the most affected and showed a shift to highfield ($\Delta\delta$ ca. -0.12 ppm), and also that the higher electrondensity of the triazolate nucleus is reflected in the chemical shifts of its substituent, *i.e.* conjugation shifts H-4 of the phenyl substituent to higher field ($\Delta\delta = -0.30$ ppm). Moreover, the δ C values of carbon atoms (see Table 4) were in agreement with data reported for a variety of 3(5)-1,2,4-triazolate, 1*H*-1,2,4-triazol-3(5)-yl and 1*H*-benzimidazo-2-yl species.²³

Table 4.Selected ¹³C NMR Data²² of 3(5)-(1-Butyl-4-pyridiniocarbonyl)-1,2,4-triazolate 6d,e,4(5)-[1-hydroxy-1-(4-pyridyl)methyl]-1H-imidazole10 f,1-Butyl-4-(imidazol-4(5)ylcarbonyl)pyridiniumiodide 3f,5,6-Dimethyl-2-(4-pyridylcarbonyl)-1H-benzimidazole11 b,11 b,and5,6-Dimethyl-2-[1-hydroxy-1-(4-pyridyl)methyl)-1H-benzimidazole10 f/l

compd	C2',6'	C3',5'	C4'	СН	со	C3	C5	C1"	C2",6"	C3",5	" C4"
6d	145.05	128.0	153.5	_	179.8	161.3	161.7	_		_	_
$3d^b$	145.8	127.9	149.7		181.3	155.8	155.8			_	
$\Delta \delta^{C}$	-0.75	+0.1	+3.8		-1.5	+5.5	+5.9				
6e	145.1	128.1	153.1		180.2	162.2	163.8	134.2	125.9	128.4	127.4
3e ^b	145.8	128.1	149.3		180.9 <i>d</i>	157.6 <i>d</i>	157.6 ^d	е	126.7	131.	129.4
$\Delta \delta^{C}$	-0.7	0	+3.8		-0.7	+4.6	+6.2		-0.8	-2.7	-2.0
						C	2	(.4		C5
10 f	149.4	121.8	153.7	68.2	-	13	5.5	114	4.5 ^f		114.5 <i>f</i>
3f	145.8	127.5	150.8		182.2	13	8.8	136	5.7 <i>f</i>		129.0 <i>f</i>
						C ₂	C _{3a}	C4	C5	C6	C7 C7a
11 b	150.7	124.1	142.6		183.4	142.7	147.1 <i>f</i>	121.4 ^f	133.1 <i>f</i>	136.6 ^f	112.8 ^f 133.6 ^f
10 b	150.0	121.8	155.2	69.0	_	151.4	138.5 ^f	115.5 ^f	130.4 ^f	130.4^{f}	115.5 ^f 138.5 ^f

^{*a*} In (CD₃)₂SO. ^{*b*} ¹H-NMR data for compounds **3d**, *e* are reported elsewhere.². ^{*c*} $\Delta\delta$: Observed chemical shifts difference between betaines and their corresponding salts. ^{*d*}Weak and broad signal. ^{*e*} No signal observed. ^{*f*} Broad or anisochronous signals of imidazole C-4/5 or benzimidazole C-3a/C-7a or C-4/C-7 or C-5/C-6 carbon atoms were observed owing to slow proton exchange between N-1 and N-3.

In accordance with the areno-analogy principle, for several examples of azolylmethylpyridinium salts 1 and 2 the spontaneous oxidation of the methylene linker depends on the nature of their heterocyclic components. For the π -electrodeficient nucleus the relative order was 4->3-pyridinium substitution, whereas for the π -electroexcessive ring the interelation was 2-benzimidazole>3(5)-triazolate >>3(5)-triazole. The chemical behaviour of the uncharged (4-pyridyl)hydroxymethylazoles 10b and 10f can be rationalized in a similar way by taking into account the nature and substitution position of the π -excessive moiety in the relative order 2-benzimidazolyl>>4(5)-imidazolyl. By modulation the spontaneous oxidation, the first examples of 1-alkyl-4-pyridiniocarbonyl-3(5)-1,2,4-triazolates are reported and the method may be adapted for synthesis of heterocyclic betaines with utility in non-linear optical materials as well as building blocks for the construction of more elaborate architectures within quadrupolar heterophanes.

EXPERIMENTAL SECTION

General Methods. Melting point: CTP-MP 300 hot-plate apparatus with ASTM 2C thermometer (given in Table 2). IR (KBr disks or thin film): Nicolet 205 FT spectrophotometer. ¹H NMR: Varian Gemini 200 (200

MHz) spectrometer. ¹³C NMR: Varian Gemini 200 and Varian Unity 300 spectrometers (50.3 MHz and 75.5 MHz). HMQC and HMBC: Varian VXR-500 spectrometer (500 MHz). NMR spectra were determined in dimethyl- d_6 sulfoxide, ^{22b} and chemical shifs are expressed in parts per million (δ) relative to the central peak of dimethyl- d_6 sulfoxide. TLC: Merck precoated silica gel 60 F254 plates; solvent systems, A, methanol-chloroform (8:2); B, dichloromethane-methanol (9:1); C, chloroform-methanol (9:1); D, dichloromethane-ethanol (8.5:1.5); after being developed, the plates were air dried and analyzed under an UV lamp. Anion-exchange: a column (0.5-in. diameter) was packed with anion-exchange resin IRA-401 (OH⁻ form)^{8a} up to a height of 5 in. When a rotary evaporator was used, the bath temperature was 25 °C. In general, the compounds were dried overnight at 25 °C in a vacuum oven. Microanalyses were performed on a Carlo Erba 1106 analyzer.

Materials. 1-Butyl-4(3)-(azolylcarbonyl)pyridinium salts **3d**,e, ² and **4b**,c,² 1-butyl-4(3)-(azolylmethyl)pyridinium salts **2d**,e,² 3(5)-(1-butyl-4-pyridiniomethyl)-1,2,4-triazolate **5d**,e,² 4-iodo-1-tritylimidazole (**12f**)¹⁵ and 5,6-dimethyl-2-(4-pyridylmethyl)-1*H*-benzimidazole (**8b**)¹⁶ were prepared as described in the literature. 4-Pyridinecarboxaldehyde is commercially available.

Preparation of 3(5)-(1-butyl-4-pyridiniocarbonyl)-1,2,4-triazolate 6d,e, and attempted preparation of 2-(1-butyl-3-pyridiniocarbonyl)benzimidazolate 7b,c. A column packed with an anionexchange Amberlite resin IRA-401 was used and the chloride form was converted to the hydroxy form.² A solution of 1-butyl-4-(triazolylcarbonyl)pyridinium salts **3d,e** (0.3 mM) in 85% EtOH (50 mL) was passed through the column. The neutral eluates were concentrated on a rotary evaporator to give the corresponding inner salts **6d,e,** (Table 2).

By following a similar procedure starting from 1-butyl-3-(2-benzimidazolylcarbonyl)pyridinium salts **4b.c**, only formation of decomposition or alteration products could be detected.

Preparation of 1-butyl-3-(1,2,4-triazol-3(5)-ylcarbonyl)pyridinium tetrafluoroborates 4d.BF4, 4e.BF4⁻. Dry oxygen was bubbled through a solution of 3(5)-(1-butyl-3-pyridiniomethyl)-1,2,4-triazolate inner salts **5d,e** (0.3 mM) in dry acetonitrile (60 mL) for the time and at the temperature specified in Table 1. The reaction mixture was acidified with 50% HBF4-H₂O and the solution was evaporated to dryness. Analysis by ¹H NMR of the reaction mixture showed the products distribution ratio listed in Table 1.

Preparation of 1-butyl-3-(1,2,4-triazol-3(5)-ylcarbonyl)pyridinium iodides 4d.I⁻,4e.I⁻. Dry oxygen was bubbled through a solution of 1-butyl-3-(triazolylmethyl)pyridinium salts **2d,e** (0.2 mM) in dry acetonitrile (45 mL) and the solution was maintained at 60 °C for the time specified in Table 1. The reaction mixture was evaporated to dryness. Analysis by ¹H NMR of the reaction mixture showed the product distribution ratio listed in Table 1.

Preparation of 4-[1-hydroxy-1-(4-pyridyl)methyl]-1-tritylimidazole (13f). A 3M solution of ethylmagnesium bromide in diethyl ether (0.84 mL, 2.5 mM) was added to a stirred solution of 1-trityl-4-iodoimidazole **12f**¹⁵ (1.0 g, 2.3 mM) in dry dichloromethane (9 mL) under an atmosphere of argon, and the solution was maintained at room temperature for 30 min. 4-Pyridinecarboxaldehyde (0.23 mL, 2.5 mM) was then added dropwise, and stirring was maintained for 12 h. A saturated aqueous solution of ammonium chloride (25 mL) was added to the reaction mixture, which was extracted with dichloromethane (3 x 25 mL).

The combined organic layers were dried (Na_2SO_4) and the solvent was removed *in vacuo* to afford 0.9 g (94%) of **13f** (Table 2).

Preparation of 4(5)-[1-hydroxy-1-(4-pyridy])methyl]-1H-imidazole (10f). A solution of 4-[1-hydroxy-1-(4-pyridyl)methyl]-1-tritylimidazole **13f** (1.18 g, 2.8 mM) in ethanol (20 mL) and a solution of 1N hydrochloric acid (5.6 mL, 5.6 mM) were refluxed for 1 h. The reaction mixture was concentrated *in vacuo* and water was added (5 mL). After filtering the suspension, the filtrate was neutralized with K_2CO_3 and washed with dichloromethane (3 x 15 mL). The aqueous layer was evaporated to dryness and the solid residue was suspended in dry ethanol (15 mL) to remove some inorganic material and filtered and the solvent was removed *in vacuo*. The residue obtained was washed in diethyl ether (3 x 4 mL) and recrystallized to give 0.33 g (68%) of **10f** (Table 2).

N-Quaternization of 4(5)-pyridylmethylimidazole 10f. Preparation of 1-butyl-4-(imidazol-4(5)ylcarbonyl)pyridinium iodide (3f). *n*-Butyl iodide (0.31 g, 1.71 mL) was added to a stirred suspension of 4(5)-pyridylmethylimidazole 10f (0.2 g, 1.14 mM) in dry acetonitrile (20 mL) under an atmosphere of nitrogen, and the solution was then maintained in a bath at *ca*. 85 °C for the time specified in Table 2. The reaction mixture was cooled, the solvent was removed in a rotary evaporator and the solid residue was washed with acetone (3 x 10 mL) to afford the 1-butyl-4-(imidazolylcarbonyl)pyridinium salt **3f** (0.13 g, 32%) (Table 2).

Preparation of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b). Selenium oxide (1.76 g, 15.8 mM) was added to a solution of 5,6-dimethyl-2-(4-pyridylmethyl)-1*H*-benzimidazole (**8b**)¹⁶ (3.3 g, 13.9 mM) in dry ethanol (75 mL), and the solution was then maintained in a bath at *ca*. 70 °C for the time specified in Table 2. The reaction mixture was filtered hot and the solvent from the filtrate was removed*in vacuo* affording a solid residue. Purification by column chromatography (SiO₂, CH₂Cl₂ / EtOH (85:15) gave **11b** (1.32 g, 38%) (Table 2).

Preparation of 5,6-dimethyl-2-[1-hydroxy-1-(4-pyridyl)methyl)-1*H***-benzimidazole (10b)**. Sodium borohydride (19 mg, 0.5 mM) was added portionwise to a solution of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.5 g, 2.0 mM) in dry methanol (500 mL) at -5 °C. The reaction mixture was allowed to warm up to room temperature and water (20 mL) was added. The solvent was removed *in vacuo*, the residue was dissolved in water (25 mL) and neutralized with a 15% solution of hydrochloric acid. The precipitate formed was collected by filtration and dried to provide 10b (0.39 g, 78%) (Table 2).

Attempt of preparation of 15b. Method A. A concentrated solution of sulphuric acid (0.5 mL) was added dropwise to a suspension of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.25 g, 1.0 mM) and triethylsilane (0.13 g, 1.1 mM) in dry ethanol (2 mL) at 0 °C under an atmosphere of nitrogen. The reaction mixture was allowed to warm up to room temperature and stirring was maintained for 1 week.

The reaction mixture was neutralized with a 2M solution of sodium carbonate, the precipitate collected by filtration and dried. **Method B**. Platinum oxide (5 mg) was added to a solution of 2-(4-pyridylcarbonyl)benzimidazole **11b** (0.1 g, 0.4 mM) in 2.5 M solution of hydrochloric acid in ethanol (100 mL) and the mixture was hydrogenated at room temperature and atmospheric pressure for 15 h. The reaction mixture was filtered and the solvent was removed *in vacuo*.

Following either Method A or B only the starting material 11b was recovered.

E. ALCALDE et al.

Attempted preparation of 16b. Various attempts were made in order to prepare ketal 16b by reaction of 2-(4-pyridylcarbonyl)benzimidazole 11b and orthoformates. Method C. A concentrated solution of sulphuric acid (4 drops) was added to a suspension of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.25 g, 1.0 mM) and trimethyl orthoformate (2 mL, 18.6 mM) in dry toluene (50 mL). The reaction mixture was refluxed under a Dean-Stark trap for 24 h. Method D. An acid resin Nafion-H (100 mg) was added to a solution of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.1 g, 0.4 mM) and triethyl orthoformate (0.07 mL, 0.4 mM) in dichloromethane (50 mL) under an atmosphere of nitrogen, and the suspension was maintained at room temperature for 1 week. Method E. An acid resin Nafion-H (100 mg) was added to a solution of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.1 g, 0.4 mM) and triethyl orthoformate (0.24 mL, 1.5 mM) in dichloromethane (50 mL) under an atmosphere of nitrogen, and the suspension was maintained at 50 °C for 1 week. Method F. Trifluoromethanosulfonic acid (12 mg, 0.08 mM) was added to a solution of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.1 g, 0.4 mM) and triethyl orthoformate (0.43 mL, 4.0 mM) and methanol (0.16 mL, 4.0 mM) in nitromethane (5 mL) under an atmosphere of nitrogen at 5 °C. The reaction mixture was refluxed for 24 h.

The course of the reaction was monitored by TLC and 1 H-NMR (DMSO-d₆) of aliquots. Following Methods C and F only decomposition products were formed, whereas for Methods D and E only the starting material **11b** was recovered.

Preparation of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole ethylene acetal 17b. Method G. A concentrated solution of sulphuric acid (4 drops) was added to a suspension of 5,6-dimethyl-2-(4-pyridylcarbonyl)-1*H*-benzimidazole (11b) (0.10 g, 0.4 mM) and ethylene glycol (2 mL, 36.0 mM) in dry toluene (50 mL). The reaction mixture was refluxed under a Dean-Stark trap for 5 days. After cooling down to room temperature the reaction mixture was poured over a 10% aqueous solution of sodium carbonate (50 mL) and extracted with toluene (3 x 25 mL). The organic extracts were washed in brine (5 x 50 mL), dried (Na₂SO₄) and evaporated. Analysis of the residue by ¹H-NMR showed that it was formed by a mixture of the ethylene acetal 17b (ca. 5%) and the starting material 11b as the main product.

¹H-NMR (DMSO-d₆) δ : 2.25 (s, 6H), 3.90-4.20 (m, 4H), 7.24 (s, 2H), 7,49 (d, 2H, J = 8 Hz), 8,60 (d, 2H, J = 8 Hz).

compd	yield, % ^a	mp (°C)[solvent] ^b	reaction time (h)	TLC(Rf) ^C	molecular formula ^d
6d	78	148-51	с	Ae	C13H16N4O.H2O
6e	90	183-4 [i]	С	Ae	C18H18N4O.H2O
13f	94	f	12	B (0.4)	C28H23N3O
10f	68	149-50 [ii]	1	B (0.1)	C9H9N3O
3f	32	176-8	17	B (0.1)	C13H16N3OL2H2O
11b	38	257-8	22	C (0.8)	C15H13N3O.1/2H2O
10b	78	260-1	С	D (0.4)	g

Table 2. Physical Data of Compounds 3f, 6d,e, 10b, 11b, 10f and 13f

^{*a*} Yields were not optimized. ^{*b*} Recrystallization solvent: (i) acetonitrile; (ii) acetone. ^{*c*} See Experimental Section. ^{*d*} Satisfactory analytical data ($\pm 0.4\%$ for C, H, N) were obtained for new compounds. ^{*e*} The R_f values were always below 0.1 for all the used solvent systems. ^{*f*} Hygroscopic compound. ^{*g*} Satisfactory elemental analysis was not obtained, due to the susceptibility of 10b to oxidation; all attempts at recrystallizing the hydroxymethylbenzimidazole 10b in various solvents (*i.e.* acetone or isopropyl alcohol) afforded the carbonylbenzimidazole 11b.

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