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Design of Unusual Captodative Methylene Substrates: 1-Alkyl-4(3)-(azolylmethyl)pyridinium Salts[1]

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Abstract: The unprecedented spontaneous oxidation of a carbon atom linked to captor (acceptor) and donor non-classical functional groups of several examples of 1-alkyl-4(3)-(1*H*-azolylmethyl)pyridinium salts **1** and **2** exemplifies a concomitant application of the areno-analogy principle and the captodative effect in organic synthesis. A remarkably driving force by the nature of non-classical acceptor and donor heteroaromatic rings is observed upon the chemical behavior of the title compounds **1** and **2**, modulating the susceptibility with which the methylene spacers oxidize to their oxomethyl counterparts **5** and **6**. Access to dipolar 1-alkyl-3-pyridiniomethyl-3(5)-1,2,4-triazolate inner salts **4** was achieved.

Kauffmann's areno-analogy principle permits heteroaromatic fragments[2] to be related with classical functional groups.[3-5] Accordingly, a vast array of possibilities emerge starting from diphenylmethane.[6] Among these, we have focused our attention on the title monocationic diheteroarylmethanes **1**, **2** and dipolar counterparts **3**, **4** containing both a π-deficient and a π-excessive moiety linked with a captodative methylene center[7,8] (*C-CH$_2$-C' bond type*). Thus, the azolylmethylpyridinium salts **1** and **2** constitute a family of new heterocyclic compounds whose unprecedented spontaneous oxidation to their oxomethyl analogues **5** and **6**[9] exemplifies an application of the areno-analogy principle[2] and the captodative effect for free radicals postulated by Viehe[7,8] (Figure 1). Several examples of the quaternary heteroaromatic salts **1** and **2** are known and have been structurally characterized, although they are mostly unstable even in air.[9] However, by modulation of the non-classical acceptor and donor groups it is possible to design more stable compounds of type **2**, and therefore to obtain the novel heterocyclic betaines **4**.

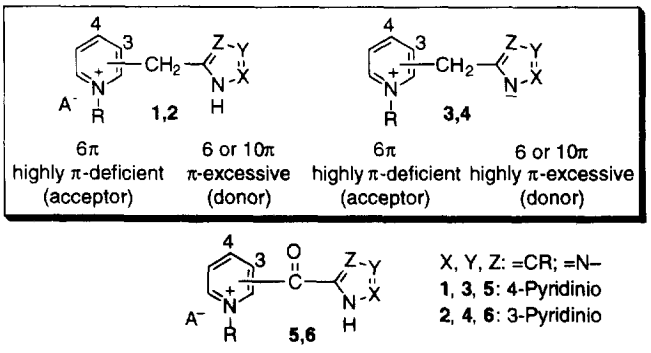


Figure 1

Among the variety of molecules emerging from the general type structures **1**, **2** and **3**, **4** we report the results that show the propensity of several selected examples[10,11] of 2-substituted benzimidazoles **1a,b,f** and **2b,c** as well as 3(5)-substituted-1,2,4-triazoles **1d** and **1e** to undergo spontaneous oxidation, leading to their oxomethyl counterparts **5a,b,f** and **6b,c** together with **5d,e** respectively (Figure 2). The pyridylmethylazoles **7a,b,d,e** and **8b-e** were the key precursors (*vide infra*).

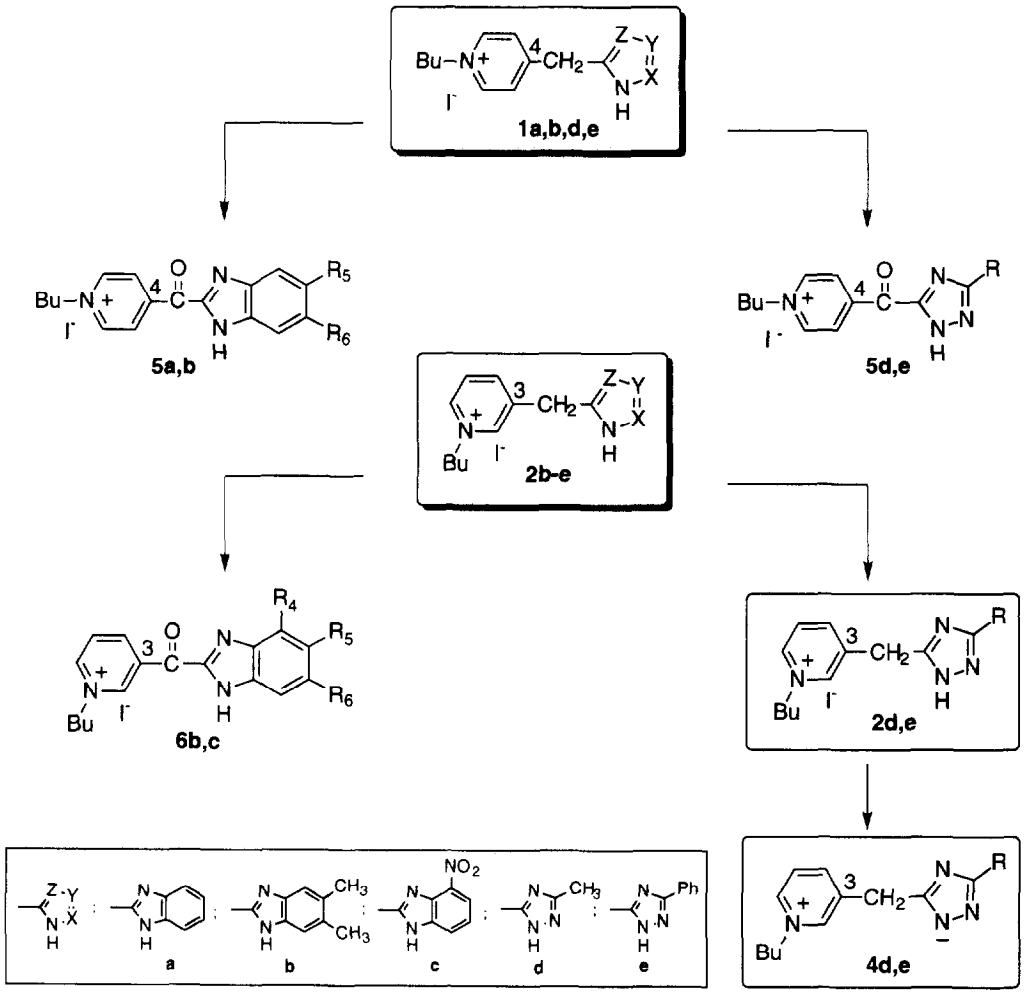
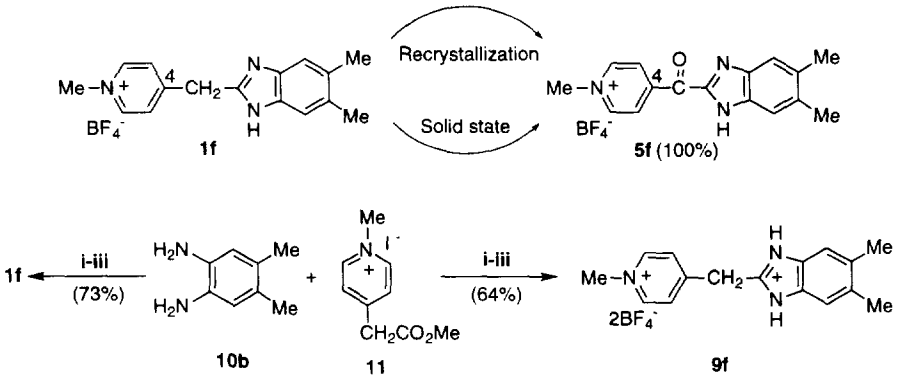


Figure 2

In contrast, the influence of decreasing the π-excessive character of the azole nucleus[4,11a] in certain compounds of type **2** together with the presence of a 3-pyridinio moiety,[4a] led to 1-butyl-3-[1*H*-1,2,4-triazol-3(5)ylmethyl]pyridinium salts **2d** and **2e**, which turned out to be very stable in air. An intriguing question arises concerning the susceptibility to oxidation of the novel compounds within the 1,2,4-triazole series, not only the immediate precursors of type **2**, *e.g.* **2d** and **2e**, but also the hitherto unknown dipolar structures of type **4** , *e.g.* **4d** and **4e** (Figure 2).

Results and Discussion

The 4-(5,6-dimethyl-1*H*-benzimidazol-2-ylmethyl)-1-methylpyridinium tetrafluoroborate **1f** was unstable in solution[12] and, we first examined its chemical stability and found that it was rapidly oxidized by air both in solution and in the solid state. Thus, compound **1f** was quantitatively converted into its oxomethyl analogue **5f**, whereas its positively charged benzimidazolium counterpart 2-(1-methyl-4-pyridiniomethyl)-benzimidazolium bis(tetrafluoroborate) **9f**[13] was found to be stable (Scheme 1).

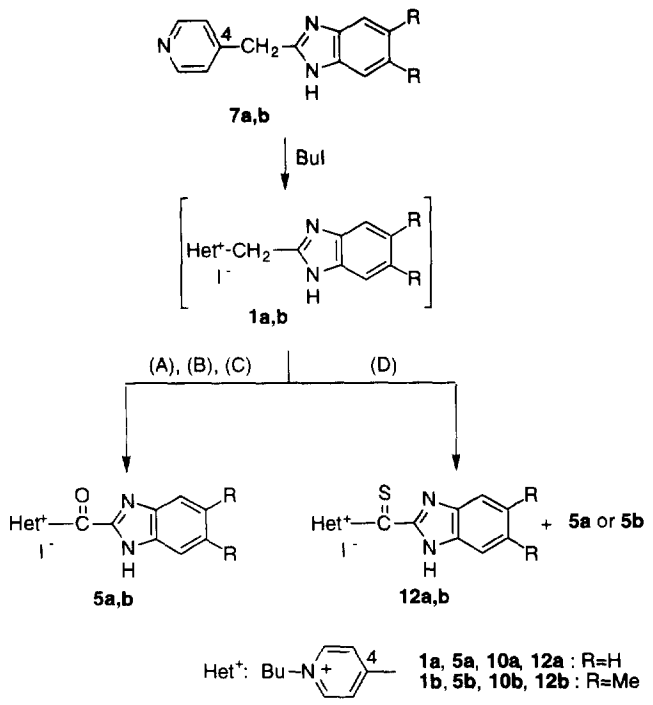


Scheme 1. (**i**): PPA, 160 °C, 10h; (**ii**) Na_2CO_3 to pH 8; (**iii**)50% HBF_4-H_2O, to pH 6 for **1f** and to pH 4 for **9f**

As outlined in Scheme 2 (Method A), the model benzimidazolylmethylpyridinium salts **1a** and **1b** were synthesised by a different approach suitably applied to other homologues[14a] and vinylogues.[14b,c] Thus, quaternization of the previously reported[12] key intermediates **7a** and **7b** was performed using 1-iodobutane[15a] as alkylating agent under neutral conditions (Menschutkin type reaction).[15b] Once compounds **1a** and **1b** had been obtained, they underwent spontaneous oxidation affording their corresponding oxomethylene derivatives **5a** and **5b**.

Next, in order to shed light on this result, we examined the course of the quaternization reaction of the 2-(4-pyridylmethyl)-1*H*-benzimidazoles **7a,b** with rigorous exclusion of air,[16] and also the degree of oxidation of the title salts **1a,b** in the presence of classical free-radical inhibitors (*e.g.* galvinoxyl) or elementary sulfur. Some experiments were carried out as shown in Scheme 2 (Methods B-D), and the distributions of compound pairs **1a,b** and **5a,b** or **12a,b** are listed in Table 1. Useful information can be gained from these experiments and the results indicate that oxidation of compounds **1a** and **1b** leading to **5a** and **5b** occurs through a captodative effect for free radicals, especially since the oxidative process is inhibited by the addition of galvinoxyl. A further indication of the presence of this captodative methylene center is the fact that sulfuration by reaction of elementary sulfur with model compounds **1a,b** produced their thiomethylene analogues **12a,b** as shown in Scheme 2 (Method D), along with **5a** or **5b**.

With this results in mind, we designed the key pyridylmethylazoles **7d,e**, and **8b-e**[17] by simple molecular modifications in both heteroaromatic moieties (Figure2).[4,11] Subsequently, the chemical behavior toward oxidation of the abovementioned model azolylmethylpyridinium salts containing either a benzimidazole nucleus **2b,c** or a 1,2,4-triazole one **1d,e** and **2d,e** was examined (see Figure 2 and later).



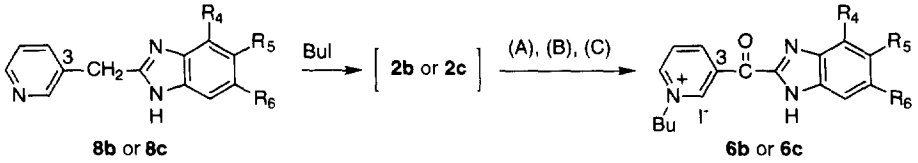
Scheme 2. Reagents and conditions: (A) Method A; BuI (5 equiv.), anhydr. MeCN, reflux under a nitrogen atmosphere. (B) Method B; BuI (5 equiv.), degassed anhydr. MeCN; reflux under an argon atmosphere. (C) Method C; As Method B, with Galvinoxyl (catalytic amount). (D) Method D; As Method B, with elementary sulfur (two-fold). See Table 1.

Table 1. Quaternization Reactions of compounds **7a** and **7b** with BuI

substrate	method[a]	reaction time (h)	product distribution[b] (%)					
			1a	**5a**	**12a**	**1b**	**5b**	**12b**
7a	A	38	55	45(85)	—			
7b	A	36				41	59(58)	—
7a	B	85	92(88)	8	—			
7b	B	96				86(64)	14	—
7a	C	32	100(94)	—	—			
7b	C	24				100(83)	—	—
7a	D	70	52(45)	2	46			
7b	D	72				28	4	68(54)

[a] See Scheme 2. [b] Ratio determined by ^{1}H NMR of reaction mixture. Numbers in parentheses are the unoptimized isolated yields of analytical samples. The extremely air-sensitive compounds **1a** and **1b** should be handled with care and stored at -15 °C under an argon atmosphere.

Quaternization of the benzimidazolylpyridylmethanes **8b**[12] and **8c**[17a] with 1-iodobutane was then studied using standard conditions (Method A, Scheme 2). The structural components[4] within the resulting 1-butyl-3-(1*H*-benzimidazol-2-ylmethyl)pyridinium salts **2b,c** favoured the oxidation through the captodative effect, and they were easily transformed into their oxomethyl analogues **6b** and **6c** (Scheme 3 and Table 2). In fact, both preparation and isolation of betaines of type **4** with 2-benzimidazolate nuclei (*e.g.* **4b** and **4c**) are likely to be difficult and, even if synthesis is achieved, their structural features may favour oxidation to the oxomethyl analogues (*vide infra*).



Scheme 3. Reagents and conditions: (A) Method A; As method A in Scheme 2, acetone or ethyl acetate recrystallization, >61% . (B) Method B; As method B in Scheme 2. (C) Method C; As method C in Scheme 2. Product ratio determined by ^{1}H NMR for the reaction mixture in (A), (B) and (C), see Table 2.

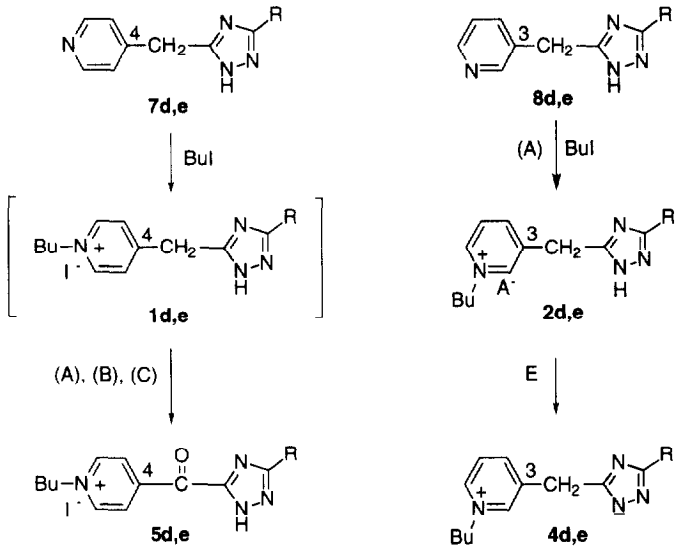
Table 2. Quaternization reactions of compounds **8b-e** and **7d,e** with BuI

substrate	method[a]	reaction time (h)	product distribution[b] (%)	
			2b	**6b**
8b	A	24	25	75(68)
8b	B	24	45	55
8b	C	24	66	33
			2c	**6c**
8c	A	32	53	47(61)
			1d	**5d**
7d	A	22	30	70(73)
7d	B	22	90	10
7d	C	22	99	1
			1e	**5e**
7e	A	26	45	55(65)
7e	B	26	92	8
7e	C	26	99	1
			2d	
8d	A	30	(85)	
			2e	
8e	A	30	(87)	

[a] See Schemes 3 and 4. [b] Ratio determined by ^{1}H NMR of reaction mixture. Numbers in parentheses are the unoptimized isolated yields of analytical samples.

Different behavior was observed in the quaternary heteroaromatic compounds **1d,e** (1-butyl-4-pyridinio) and **2d,e** (1-butyl-3-pyridinio) containing a 3(5)-substituted-1*H*-1,2,4-triazol-5(3)yl group as outlined in Scheme 4. When quaternizing the (4-pyridylmethyl)-1,2,4-triazoles **7d** and **7e** using standard conditions, the corresponding oxomethylpyridinium salts **5d** and **5e** were obtained *via* the air-sensitive 1,2,4-triazolylpyridinium salts **1d** and **1e**[18a] (Table 2).

On the contrary, the (3-pyridylmethyl)-1,2,4-triazoles **8d** and **8e** led to 1-butyl-3-(3(5)-substituted-1*H*-1,2,4-triazol-5(3)-ylmethyl)pyridinium salts **2d** and **2e**, which turned out to be stable to air oxidation. Moreover, this chemical stability persisted in the corresponding betaines **4d,e**. Thus, from the 3-pyridinium salts **2d** and **2e**, the first synthesis and characterization of the hitherto unknown 3(5)-(1-butyl-4-pyridiniomethyl)-1,2,4-triazolate inner salts **4d** and **4e** was achieved.[18b]



Scheme 4. Reagents and conditions: (A). Method A; As method A in Scheme 2, acetone or ethyl acetate recrystallization, >65% . (B) Method B; As method B in Scheme 2 . (C) Method C; As method C in Scheme 2. Product ratio determined by ^{1}H NMR from the reaction mixture , see Table 2. (E) Method E; Anion-exchange resin IRA-401 (OH^- form),[1] >84%.

Physical data of all new compounds described in this work are listed in Table 3 (see Experimental Section). The compounds were unambiguously characterized on the basis of their spectroscopic data (IR, ^{1}H NMR and ^{13}C NMR) and all the products isolated were analytically pure. The IR spectra (KBr) of the oxomethyl derivatives **5** and **6** showed a band in the range 1680-1650 cm^{-1}($\nu_{C=O}$) and the ^{13}C NMR $(CD_3)_2SO$ spectra showed a signal δ *ca.* 180 ppm. The thiocarbonyl derivative **12b** showed a band at 1630 cm^{-1}($\nu_{C=S}$) and the ^{13}C NMR $(CD_3)_2SO$ spectra showed a signal δ *ca.* 213 ppm.

^1H and ^{13}C NMR chemical shifts of betaines **4d,e** proved to be crucial for proof of their dipolar structure. Selected ^1H and ^{13}C NMR chemical shifts of betaines **4d**[19] and **4e** and their precursors **2d,e**, together with the other new salts described in this work are shown in Tables 4 and 5; individual assignments were made using the appropriate NMR experiments.[20]

Table 4. Selected ^1H NMR Data[20] of (Pyridiniomethyl)triazolate **4d,e**, and the Salts (Pyridiniomethyl)benzimidazolium **9f**, (Benzimidazolylmethyl)pyridinium **1a,b**, (Benzimidazolylcarbonyl)pyridinium **5a,b,f**, **6b,c**, (Benzimidazolylthiocarbonyl)pyridinium **12b**, (Triazolylcarbonyl)pyridinium **5d,e** and (Triazolylmethyl)pyridinium **2d,e**[a]

compd	pyr	A⁻	X	R	H2'	H3'	H4'	H5'	H6'	CH_2	H4	H5	H6	H7
9f	4				9.09	8.23	—	8.23	9.09	4.95	7.70	—	—	7.70
5f	4				9.20	8.84	—	8.84	9.20	—	7.63[b]	—	—	7.42[b]
1a	4	I^-	CH_2		9.11	8.19	—	8.19	9.11	4.86	7.76	7.52	7.52	7.76
1b	4	I^-	CH_2		9.11	8.16	—	8.16	9.11	4.84	7.56	—	—	7.56
5a	4	I^-	CO		9.34	8.90	—	8.90	9.34	—	7.77[b]	7.45[b]	7.45[b]	7.77[b]
5b	4	I^-	CO		9.33	8.88	—	8.88	9.33	—	7.60[b]	—	—	7.40[b]
6b	3	I^-	CO		9.90	—	9.30	8.70	9.53		7.63[b]	—	—	7.42[b]
6c	3	I^-	CO		9.99	—	9.34	8.40	9.48		—	8.31	7.64	8.22
12b	4	I^-	CS		9.08	8.10	—	8.10	9.08	—	7.46	—	—	7.46
											H_2", 6	"H_3", 5"		H_4"
5d	4	I^-	CO	H	9.29	8.66	—	8.66	9.29	—	—	—		—
5e	4	I^-	CO	H	9.34	8.79	—	8.79	9.34	—	8.10	7.60		7.60
4d[d]	3	—	CH_2	-	9.07	—	8.48	8.01	8.89	4.01	—	—		—
2d	3	I^-	CH_2	H	9.15	—	8.50	8.11	9.02	4.23	—	—		—
$\Delta\delta$[c]					-0.08	—	-0.02	-0.10	-0.13	-0.22				
4e	3	—	CH_2	-	9.085	—	8.49	8.03	8.885	4.13	7.90	7.29		7.17
2e	3	BF_4^-	CH_2	H	9.18	—	8.60	8.14	9.02	4.39	7.94	7.46		7.46
$\Delta\delta$[c]					-0.09	—	-0.11	-0.11	-0.135	-0.26	-0.04	-0.17		-0.23

[a] In $(CD_3)_2SO$. [b] Broad or anisochronous signals of benzimidazole H-4 /7 or H-5 / 6 protons were observed owing to slow proton exchange between N-1 and N-3. NH proton signal *ca.* 12.0 ppm. [c] $\Delta\delta$: observed chemical shifts difference between betaines and their corresponding salts. [d] Compound unstable in $(CD_3)_2SO$.

Comparison of the ^1H NMR chemical shifts observed of betaines **4d**, and **4e** with those of their corresponding triazolylmethylpyridinium salts **2d,e** (see $\Delta\delta$ in Table 4) reveals that the methylene interannular spacer was the most affected and showed a shift to highfield ($\Delta\delta$ CH_2 *ca.* -0.24 ppm) in a lesser extend than the H-5 in the pyridinium ring ($\Delta\delta$ = -0.10 ppm). Moreover, the δC values of carbon atoms (see Table 5, Experimental Section) 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.[14] As for the ^{1}H NMR data of the labile (azolylmethyl)pyridinium salts **1d,e** and **2b,c** are listed in Table 6 (Experimental Section).

Summing up, for examples of the 4(3)-(azolylmethyl)pyridinium salts **1** and **2** the nature of the non-classical acceptor and donor heteroaromatic moieties modulates the susceptibility of the methylene spacer to oxidation. For compounds **1a,b**, **1d-f** and **2b,c** air was sufficient for oxidation and they were spontaneously transformed to their oxomethyl analogues **5a,b**, **5d-f** and **6b,c**, whereas the 1-butyl-3-[1*H*-1,2,4-triazol-3(5)ylmethyl]pyridinium salts **2d** and **2e** turned out to be very stable in the air, leading to the first synthesis and characterization of 1-butyl-3-pyridiniomethyl-3(5)-1,2,4-triazolate **4d** and **4e**, for which no atmospheric oxidation was observed. This unprecedented spontaneous oxidation of a methylene carbon atom linked to captor and donor non-classical functional groups of compounds **1** and **2** illustrates a confluent utility of the areno-analogy principle[2] and the captodative effect[7] for synthetic applications.

Experimental Section

General Methods. Melting point: CTP–MP 300 hot-plate apparatus with ASTM 2C thermometer (given in Table 3). IR (KBr disks or thin film): Nicolet 205 FT spectrophotometer. ^{1}H NMR: Varian Gemini 200 (200 MHz) spectrometer. ^{13}C NMR: Varian Gemini 200 and Varian Unity 300 spectrometers (50.3 MHz and 75.5 MHz). HMQC and HMBC:[20c] Varian VXR-500 spectrometer (500 MHz). NMR spectra were determined in dimethyl-d_6 sulfoxide,[20d] 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 F_{254} plates; solvent systems, A, methanol-diethyl ether (8:2); B, chloroform-methanol (8:2); C, methanol-chloroform (8:2); 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)[14c] 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. 1,2-Diamino-3-nitrobenzene,[21] 4-pyridylacetic acid hydrazide,[22] 3-pyridylacetic acid hydrazide,[22] 4-(5,6-dimethyl-1*H*-benzimidazol-2-ylmethyl)-1-methylpyridinium tetrafluoroborate (**1f**),[12] 4-(methoxycarbonylmethyl)-1-methylpyridinium iodide (**11**),[23] 2-(4-pyridylmethyl)-1*H*-benzimidazole (**7a**),[12] 5,6-dimethyl-2-(4-pyridylmethyl)-1*H*-benzimidazole (**7b**),[12] and 5,6-dimethyl-2-(3-pyridylmethyl)-1*H*-benzimidazole (**8b**)[12] were prepared as described in the literature. Ethyl 4-pyridyl acetate, ethyl 3-pyridyl acetate, ethyl acetimidate hydrochloride, ethyl benzimidate hydrochloride, 3-pyridylacetic acid hydrochloride, and 1,2-diamino-4,5-dimethylbenzene (**10b**) are commercially available.

Formation of 4-(5,6-dimethyl-1*H*-benzimidazol-2-ylcarbonyl)-1-methylpyridinium tetrafluoroborate 5f and 5,6-dimethyl-2-(1-methyl-4-pyridiniomethyl)benzimidazolium bis(tetrafluoroborate) 9f. A stirred suspension of 1,2-arylenediamine **10b** (0.68 g, 5.0 mM) and 1-methyl-4-(methoxycarbonylmethyl)pyridinium iodide (**11**; 1.47 g, 5.0 mM) in PPA (20 g) under an atmosphere of nitrogen was heated at 160 °C (bath temperature) for 10 h. The cooled mixture was poured into ice-water (30 mL) and the resulting solution was treated with solid sodium carbonate to pH 8. This solution was then

acidified with 50% HBF_4-H_2O to pH 4, concentrated to a volume *ca.* 10 mL, and the solid was filtered, washed with water (2 x 5 mL), dried and recrystallized, to give 1.13 g (64%) of **9f** (Table 3).

Following the same procedure, but acidifying with 50% HBF_4-H_2O to pH 6, 4-(5,6-dimethyl-1*H*-benzimidazol-2-ylmethyl)-1-methylpyridinium tetrafluoroborate (**1f**) was obtained.[12] Compound **1f** was highly air-sensitive, and both in solution and in the solid state was quantitatively transformed at room temperature into its oxomethyl analogue **5f** (Table 3).

Preparation of 4(7)-nitro-2-(3-pyridylmethyl)-1*H*-benzimidazole (8c). A stirred suspension of 1,2-diamino-3-nitrobenzene[21] (1.0 g, 6.5 mM) and 3-pyridylacetic acid hydrochloride (1.1 g, 6.5 mM) in PPA (20 g) under an atmosphere of nitrogen was heated at 165 °C (bath temperature) for 3 h. The cooled mixture was poured into ice-water (200 mL) and the resulting solution was treated with solid sodium carbonate to pH 8. The precipitated solid was filtered, washed with water (2 x 10 mL), dried and recrystallized, to afford 0.78 g (48%) of **8c** (Table 3).

Preparation of 3(5)-(4(3)-pyridylmethyl)-1,2,4-triazoles 7d,e and 8d,e. A stirred solution of NaOH (0.3 g, 7.4 mM) was cooled at 0 °C with an ice bath and ethyl acetimidate hydrochloride or ethyl benzimidate hydrochloride (7.4 mM) was added portionwise. After the addition had finished, the suspension was filtered, and a solution of 4- or 3-pyridylacetic acid hydrazide[22] (6.65 mM) in dry ethanol (30 mL) was added dropwise to the filtrate. The mixture was heated at 60 °C (bath temperature) for the time specified in Table 3. For the acylamidrazones **13d, 13e** and **14e** the reaction mixture was cooled with an ice bath for 1 h and the solid that precipitated was filtered, washed with ethanol (3 x 2 mL), dried and recrystallized, to give the compounds **13d** (55%), **13e** (41%) and **14e** (51%) (Table 3). For 4-pyridylacetylbenzamidrazone **14d** the solution was evaporated to dryness, and the resulting residue was triturated with acetone (10 mL) to give a white solid, which was filtered, washed in acetone (2 x 2 mL), dried and recrystallized to afford 0.09 g (47%) of **14d** (Table 3).

Acylamidrazones **13d,e** and **14e,d** (**13d** or **13e**: 2.6 mM; **14e** or **14d**: 2.0 mM) were heated in a bath at 5-10 °C above their melting points (see Table 3), until the evolution of water vapor bubbles from the reaction ceased. The cooled mixture was triturated with diethyl ether (5 mL) for compounds **7d**, **8d**, and with acetonitrile (5 mL) for compounds **7e**, **8e**, to give a solid which was filtered, washed in diethyl ether (1 x 2 mL) or acetonitrile (1 x 2 mL), dried and recrystallized to afford the 3(5)-(4(3)-pyridylmethyl)-1,2,4-triazoles **7d,e** and **8e,d** (Table 3).

***N*-Quaternization of 4(3)-pyridylmethylazoles 7a,b, 7d,e, and 8d-e. Preparation of 1-butyl-4(3)-(azolylmethyl)pyridinium salts 1a,b, 1d,e, and 2b-e, and/or 1-butyl-4(3)-(azolylcarbonyl)pyridinium salts 5a,b, 5d,e, and 6b,c, and/or 1-butyl-4(3)-(azolylthiocarbonyl)pyridinium salts 12a,b. Method A.** Freshly distilled *n*-butyl iodide (5 or 6 eq) was added to a stirred solution of 4(3)-pyridylmethylazoles **7a,b**, **7d,e**, or **8b-d** (**7a** or **7b**: 4.78 mM; **8b**: 0.8 mM; **8c**: 0.4 mM; **7d** or **8d**: 0.6 mM; **7e** or **8e**: 0.43 mM) in dry acetonitrile (**7a**: 200 mL; **7b**: 180 mL; **8b**: 90 mL; **7d,e**, **8c-e**: 40 mL) under an atmosphere of nitrogen, and the solution was then maintained in a bath at *ca.* 85 °C for the time specified in Tables 1 and 2. The product distribution ratio in the reaction mixture was determined by ^1H NMR (Tables 1 and 2). The reaction mixture was cooled, the solvent was removed in a rotary evaporator and the solid residue was recrystallized to afford the 1-butyl-4(3)-(azolylcarbonyl)pyridinium salts **5a** (85%), **5b** (58%), **6b** (68%), **6c** (61%), **5d** (73%),

5e (65%) and the 1-butyl-3-(triazolylmethyl)pyridinium salt **2d** (85%) (Table 3; see also Tables 1 and 2). For compound **2e** the reaction mixture was evaporated to drynesss to give an oil, which was then passed through an anion-exchange resin IRA-401 (OH^- form). The neutral eluates were acidified with 50% HBF_4-H_2O and the solvent was removed *in vacuo*. The residue was triturated with acetone (5 mL) to afford a solid which was filtered, washed in acetone (1 x 2 mL), dried and recrystallized to give the tetrafluoroborate **2e** (87%) (Table 3; see also Table 2).

Analysis by ^1H NMR of the mother liquor from recrystallization of compounds **5a,b**, **5d,e**, and **6b,c** indicated that those were solely formed.

Method B. Freshly distilled and degassed *n*-butyl iodide (5 or 6 eq) was added to a stirred solution of 4(3)-pyridylmethylazoles **7a,b**, **7d,e** or **8b** (**7a**: 0.48 mM; **7b**: 0.42 mM; **7d**, **7e**, or **8b**: 0.6 mM) in dry degassed acetonitrile (**7a**, **7b**: 20 mL; **7d,e** or **8b**: 40 mL) under an atmosphere of argon, and the solution was then maintained in a bath at *ca.* 85 °C for the time specified in Tables 1 and 2. The product distribution ratio in the reaction mixture was determined by ^1H NMR (Tables 1 and 2). For compound **1a** the reaction mixture was cooled and the solution was evaporated to a volume of *ca.* 4 mL. The solid precipitated was filtered, washed in acetonitrile (2 x 2 mL) under an atmosphere of argon, and dried to give **1a** (0.17 g, 88%) (Table 3; see also Table 1). By attempting recrystallization in several solvents, compound **1a** was quantitatively transformed into its oxoanalogue **5a**. For compound **1b** the reaction mixture was cooled and the solid precipitated was filtered, washed with acetonitrile (2 x 1 mL) under an atmosphere of argon, and dried. The solid was resuspended in acetonitrile (10 mL), filtered, washed in acetonitrile (1 mL) under an atmosphere of argon and dried to afford **1b** (0.11 g, 64%) (Table 3; see also Table 1). By attempting recrystallization in several solvents, compound **1b** was quantitatively transformed into its oxoanalogue **5b**.

Method C. Freshly distilled and degassed *n*-butyl iodide (5 or 6 eq) was added to a stirred solution of 4(3)-pyridylmethylazoles **7a,b**, **7d,e** or **8b** (**7a**: 0.48 mM; **7b**: 0.42 mM; **7d,e**, or **8b**: 0.6 mM) and galvinoxyl (20% in weight) in dry degassed acetonitrile (40 mL) under an atmosphere of argon, and the solution was then maintained in a bath at *ca.* 85 °C for the time specified in Tables 1 and 2. The product distribution ratio in the reaction mixture was determined by ^1H NMR (Tables 1 and 2). For compounds **1a** and **1b** the reaction mixture was cooled and the solution was evaporated to a volume of *ca.* 5 mL. The precipitated solid was filtered, washed in acetonitrile (5 x 2 mL) under an atmosphere of argon, and dried to afford **1b** (0.35 g, 83%) (Table 3; see also Table 1). Compound **1a** was also washed in dichloromethane (5 x 2 mL) under an atmosphere of argon, and dried to give (0.18 g, 83%) of **1a** (Table 3; see also Table 1).

Method D. Freshly distilled and degassed *n*-butyl iodide (5 or 6 eq) was added to a stirred solution of 2-(4-pyridylmethyl)benzimidazoles **7a** or **7b** (0.48 mM and 0.42 mM, respectively) and elementary sulfur (0.96 mM and 0.84 mM, respectively) in dry degassed acetonitrile (25 mL) under an atmosphere of argon, and the solution was then maintained in a bath at *ca.* 85 °C for the time specified in Tables 1 and 2. The product distribution ratio in the reaction mixture was determined by ^1H NMR (Tables 1). The reaction mixture was cooled and the solution was evaporated to a volume of *ca.* 5 mL. The precipitated solid was filtered, washed in acetonitrile (2 x 1 mL) under an atmosphere of argon, and dried to afford the benzimidazolylmethylpyridinium salt **1a** (85 mg, 45%) (Table 3; see also Table 1) or the benzimidazolylthiocarbonylpyridinium salt **12b** which was then recrystallized (0.24 g, 54%) (Table 3; see also Table 1).

Preparation of 3(5)-(1-butyl-4-pyridiniomethyl)-1,2,4-triazolate 4e and 4d. Method E. A column packed with an anion-exchange Amberlite resin IRA-401 was used and the chloride form was converted to the hydroxy form.[14c] A solution of 1-butyl-3-(triazolylmethyl)pyridinium salts **2d,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 **4e,f** (Table 3).

Table 3. Physical data of compounds **1a,b**, **2d,e**, **4d,e**, **5a,b**, **5d-f**, **6b,c**, **7d,e**, **8c-e**, **9f**, **12b**, **13d,e** and **14d,e**

compd	method[a] (yield, %)	mp (°C)[solvent][b]	reaction time (h)	TLC[c]	molecular formula[d]
9f	*c, e* (64)	201-2 [i]	10	A	$C_{16}H_{19}N_3B_2F_8$
5f	*c, e* (100)	> 300	*c, e*	A	$C_{16}H_{16}N_3OBF_4$
8c	*c* (48)	223-4 [ii]	3	B	$C_{13}H_{10}N_4O_2$
13d	*c, f* (55)	187-8 [iii]	3	B	$C_9H_{12}N_4O$
14d	*c, f* (47)	135-8 [iii]	8	B	$C_9H_{12}N_4O$
13e	*c, f* (41)	163-4 [iv]	3	B	$C_{14}H_{14}N_4O$
14e	*c, f* (51)	155-6 [iv]	2	B	$C_{14}H_{14}N_4O$
7d	*c, f* (95)	132-3 [v]	*c*	B	$C_9H_{10}N_4$
7e	*c, f* (91)	156-7 [v]	*c*	B	$C_{14}H_{12}N_4$
8d	*c, f* (90)	89 [v]	*c*	B	$C_9H_{10}N_4$
8e	*c, f* (86)	187 [vi]	*c*	B	$C_{14}H_{12}N_4$
5a	A (85)*g, h*	240-1 [iv]	38	A	$C_{17}H_{18}N_3OI$
5b	A (58)*g, h*	249-50 [vii]	36	A	$C_{19}H_{22}N_3OI$
6b	A (68)*g, i*	263 [viii]	24	C*j*	$C_{19}H_{22}N_3OI$
6c	A (61)*g, i*	244-7 [vii]	32	C*j*	*k*
5d	A(73)*g, l*	184-5 [ix]	22	C*j*	$C_{13}H_{17}N_4OI$
5e	A(65)*g, l*	197-8 [v]	26	C*j*	$C_{18}H_{19}N_4OI$
2d	A(85)	*m*	30	C*j*	*k*
2e	A(87)	168-9 [vii]	30	C*j*	$C_{18}H_{21}N_4BF_4$
1a	B(88) / C(94)*g, h*	241	85 / 32	A	*k*
1b	B(64) / C(83)*g, h*	284	96 / 24	B	$C_{19}H_{24}N_3I$
12b	D(54)	> 310 [vi]	72	B	$C_{19}H_{22}N_3SI.H_2O$
4d	E(85)	*m*	*c*	C*j*	*n*
4e	E(84)	166-70 [iv]	*c*	C*j*	$C_{18}H_{20}N_4.2H_2O$

[a] Yields were not optimized. [b] Recrystallization solvent: (i) diethyl ether-acetone (3:1); (ii) methanol; (iii) acetonitrile-methanol (7:3); (iv) acetonitrile; (v) acetone; (vi) ethanol; (vii) ethyl acetate; (viii) ethanol-diethyl ether (7:3); (ix) ethyl acetate-methanol (8:2). [c] See Experimental Section. [d] Satisfactory analytical data (±0.4% for C, H, N) were obtained for new compounds. [e] See Scheme 1. [f] See Scheme 5 in Experimental Section. [g] Only the most suitable method for isolation is quoted. [h] See Scheme 2 and Table 1. [i] See Scheme 3 and Table 2. [j] The R_f values were always below 0.1 for all the used solvent systems. [k] Satisfactory elemental analysis was not obtained. [l] See Scheme 4 and Table 2. [m] Oily compound. [n] The instability of compound **4d** precluded attempting its elemental analysis.

Table 5. Selected ^{13}C NMR Data[20] of (Pyridiniomethyl)triazolate **4d,e**, and the Salts (Pyridiniomethyl)benzimidazolium **9f**, (Benzimidazolylmethyl)pyridinium **1a,b**, (Benzimidazolylcarbonyl)pyridinium **5a,b,f**, **6b,c**, (Benzimidazolylthiocarbonyl)pyridinium **12b** (Triazolylcarbonyl)pyridinium **5d,e** and (Triazolylmethyl)pyridinium **2d,e**[a, b]

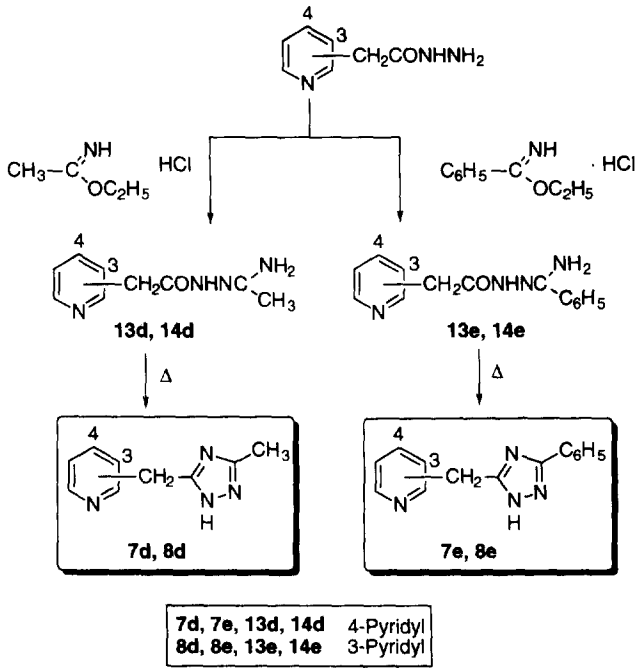
compd	$C_{2'}$	$C_{3'}$	$C_{4'}$	$C_{5'}$	$C_{6'}$	CH_2	CO	C_2	C_{3a}	C_4	C_5	C_6	C_7	C_{7a}
9f	146.2	128.7	148.6	128.7	146.2	31.9	—	153.0	135.9	114.1	130.2	130.2	114.1	135.9
5f	146.7	128.2	146.6	128.2	146.7	—	180.6	149.3	142.7[c]	121.3[c]	133.8[c]	137.5[c]	112.9[c]	133.9
1a	144.9	129.0	149.8	129.0	144.9	32.5	—	154.0	*d*	114.5	125.5	125.5	114.5	*d*
1b	145.3	129.1	149.6	129.1	145.3	32.1	—	153.6	135.7	114.1	130.5	130.5	114.1	135.7
5a	146.0	128.7	147.3	128.7	146.0	—	180.8	149.2	143.8[c]	122.0[c]	124.3[c]	127.3[c]	113.5[c]	135.0
5b	145.9	128.6	146.6	128.6	145.9	—	180.3	149.4	142.7[c]	121.3[c]	128.6[c]	133.8[c]	112.9[c]	137.5
6b	146.9	135.3	147.3	128.0	146.7	—	178.5	146.3	142.3[c]	121.1[c]	137.0[c]	133.5[c]	112.7[c]	137.0
6c	147.3	135.0	147.8	128.1	146.6	—	179.0	150.0	141.1	137.6	121.8	124.8	124.8	132.7
12b	144.5	129.9	145.1	129.9	144.5	—	213	155.2	133.1	115.4	130.5	130.5	115.4	133.1
								C_3	C_5	$C_{1''}$	$C_{2'',6''}$	$C_{3'',5''}$		$C_{4''}$
5d	145.8	127.9	149.7	127.9	145.8	—	181.3	155.8	155.8	—	—	—		—
5e	145.8	128.1	149.3	128.1	145.8	—	180.9[f]	157.6[f]	157.6[f]	*d*	126.7	131.1		129.4
2d	148.2	141.2	145.2	130.4	146.4	32.6	—	159.1[f]	160.8[f]	—	—	—		
4e	144.6	141.9	145.7	127.6	142.4	31.9		159.0	161.1	134.8	125.3	128.3		126.5
2e	144.9	138.5	146.0	127.9	143.3	30.1		157.5	158.0	128.65	126.2	129.2		130.1
$\Delta\delta$[e]	-0.3	+3.4	-0.3	-0.3	-0.9	+1.8		+1.5	+3.1	+6.15	-0.9	-0.9		-3.6

[a] In $(CD_3)_2SO$. [b] ^{13}C NMR for compound **4d** was not recorded due to its unstability in $(CD_3)_2SO$. [c] Anisochronous signals of benzimidazole C-4/C-7 and C-5/C-6 carbon atoms were observed owing to slow proton exchange between N-1 and N-3. [d] No signal observed. [e] $\Delta\delta$: Observed chemical shifts difference between betaines and their corresponding salts. [f] Weak and broad signal.

Table 6. ^1H NMR Data of the labile (Benzimidazolylmethyl)pyridinium **2b,c** and (Triazolylmethyl)pyridinium **1d, e**[a,b]

compd	$H_{2'}$	$H_{3'}$	$H_{4'}$	$H_{5'}$	$H_{6'}$	CH_2	H_4	H_5	H_6	H_7	CH_3	CH_2N^+[c]
2b	9.20	—	8.61	8.20	9.10	4.64	7.41	—	—	7.41	2.31	4.64
2c	9.18	—	8.60	8.14	9.03	4.61	—	8.02	7.37	8.12	—	4.61
							$H_{2'',6}$	"$H_{3''}$, 5"		$H_{4''}$		
1d	8.98	8.03	—	8.03	8.98	4.30	—	—		—	2.29	4.55
1e	9.00	8.10	—	8.10	9.00	4.49[d]	7.96	7.48[d]		7.48[d]	—	4.55

[a] In $(CD_3)_2SO$. [b] Values shown refer to data taken from ^1H NMR of aliquots of the reaction mixture. [c] Only δ for the α-protons to nitrogen are listed. [d] Broad signals.



Scheme 5. Preparation of 3(5)-(4(3)-pyridylmethyl)triazoles **7d,e**, and **8d,e**

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18. (a) By recrystallization in a variety of solvents or by transformation in the solid state at room temperature. (b) The oily betaine **4d** had to be handled with care, since it was thermally-sensitive and formation of decomposition by-products was observed (see Table 3). Solid **4e** could be stored without problems.
19. The instability of compound **4d** in $(CD_3)_2SO$ precluded recording its ^{13}C NMR spectrum.
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