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Heterocyclic Betaines. Methylenepyridinium and Methyleneimidazolium Azolate Inner Salts. Synthesis and Structure

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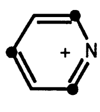
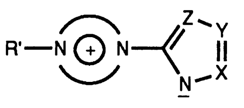
A convenient synthesis of the hitherto unknown methylenepyridinium and methyleneimidazolium azolate inner salts is reported. Their structural characterization on the basis of the spectroscopic ^{1}H and ^{13}C NMR data and experimental dipole moments in the range of 12.34 to 15.34 Debye is discussed.

Heterocyclic betaines attract considerable interest mainly because their dipolar character has a dominant influence upon their chemistry.1) Among the variety of structures which they can adopt, there are isolated examples of the inner salts of azinium azolate **1** and azolium azolate **2**. Only a few examples have hitherto been reported and most of them in connection with our research work on the chemistry of heterocyclic betaines.2-5)

We herein describe the results concerning a new type of heterocyclic betaines related to the N-ylides **1** and **2**: the methylenepyridinium and methyleneimidazolium azolate inner salts **3** and **4**. The incorporation of a methylene group as the interannular linkage augmented their experimental dipole moments in the range of 12.34 to 15.34 Debye, an unusual value for organic molecules excluding polymers (natural or synthetic). These betaines are of interest as they can be incorporated as subunit(s) in host molecules, and could confer unusual properties to the cavities -either cavitates or clathrates-.



1



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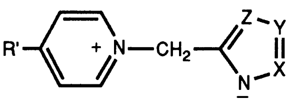

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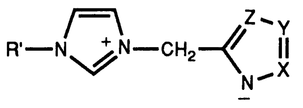
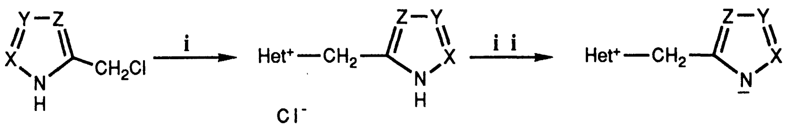


4

X, Y, Z : = CR - ; = N -
● : = CR -

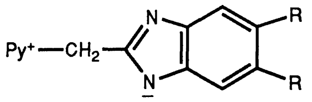
The first synthesis of simple inner salts of methylenepyridinium benzimidazolate **5**-**8**, triazolate **9**,**10** and methyleneimidazolium benzimidazolate **11**-**14**, triazolate **15**,**16** has been achieved according to a two-step procedure (Scheme 1). Thus, reaction of chloromethylazoles **29**-**31** with a pyridine or a 1-alkylimidazole gave azolylmethylpyridinium and imidazolium chlorohydrates **17**-**28**, which were deprotonated using an anionic (OH$^-$ form) ion-exchange resin. The new betaines **5**-**16** were obtained in 27%-83% overall yields, and their preparation was uncovered following trial of a variety of methods.6)



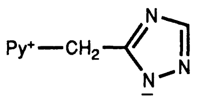
29-31 **17-28** **5-16**

Scheme 1. Reagents and conditions : i, pyridine or N-alkylimidazole as reagent and solvent, or 4-dimethylaminopyridine in dimethylformamide, at 130 °C under an atmosphere of nitrogen; ii, anion-exchange resin IRA-401 (OH^- form)[2]. Overall yields: **5-8** and **11-14** > 63%; **9, 10, 15, 16** > 27%.

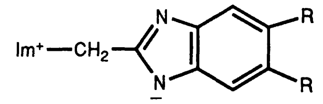
The structures of the new betaines **5-16** and their precursors **17-28** have been unambiguously characterized on the basis of their spectroscopic data and all of them gave satisfactory elemental analysis.



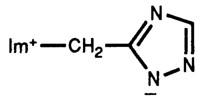
5-8



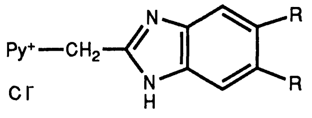
9,10



11-14

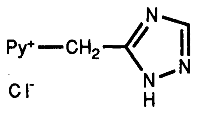


15,16



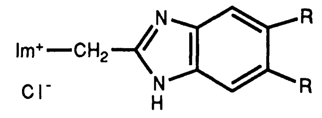
17-20

	R	R'
5 , 17	H	H
6 , 18	Me	H
7 , 19	H	NMe_2
8 , 20	Me	NMe_2



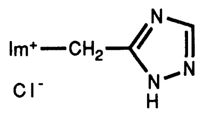
21,22

	R'
9 , 21	H
10 , 22	NMe_2



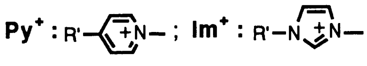
23-26

	R	R'
11 , 23	H	Me
12 , 24	Me	Me
13 , 25	H	n-Bu
14 , 26	Me	n-Bu



27,28

	R'
15 , 27	Me
16 , 28	n-Bu



The IR spectra of the compounds **17-28** showed absorptions in the range of 3.400-3.200 cm^{-1} (ν_{NH}) and 2.775-2.500 cm^{-1} (hydrochlorides) while these bands were absent for the methylenepyridinium and methyleneimidazolium azolate inner salts **5-10** and **11-16**.

^1H and ^{13}C NMR data for betaines **5-16** have been very important for structural proof of their highly dipolar structure, as they were for the previously reported betaines **1** and **2**. The chemical shifts of the CH protons in the azolate moiety move upfield with respect to their precursors **17-28** and the δC values were in excellent agreement with data reported for the carbon atoms of benzimidazolate and 1,2,4-triazolate species;[2-5] as to the ^1H and ^{13}C NMR data for the quaternary pyridinium or imidazolium rings, they accord perfectly with data for betaines of pyridinium azolate **1** and imidazolium azolate **2** respectively.[2-5] If necessary, individual assignments have been made using the appropriate NMR techniques.

Furthermore, the methyleneimidazolium azolate inner salts[7] **11-16** protonated in trifluoroacetic acid to give the corresponding conjugated acid (azolylmethylimidazolium trifluoroacetates), which reversibly regenerated the betaine on treatment with 25% ammonium hydroxide. On the other hand, the lower stability in solution of the methylenepyridinium azolate inner salts **5**, **6**, and **9** prevented execution of the above mentioned assay.

On comparing the proton and carbon atom chemical shift values7) for the new betaines **5-16** and their corresponding azolylmethylpyridinium and imidazolium salts **17-28**, it is particularly noteworthy that the methylene interannular linkage values are the most affected ones. Thus, for betaines **5-16** the methylene proton signals are displaced upfield (*ca.* 0.35 ppm), but those of the carbon atoms downfield (*ca.* 4.5 ppm). Table 1 summarizes the selected spectral data7) of the representative compounds **7**, **13**, **16**, **10**, and **19**, **25**, **28**, **22**.

Table1. Selected ^1H and ^{13}C NMR data of the representative compounds7) **7**, **13**, **16**, **10** and **19**, **25**, **28**,**22**

Comp.	R	R'	H-2',6'	H-3',5'	CH_2	H-4,7	H-5,6	CH_2	C-2
7	H	NMe_2	8.38	6.99	5.41	7.26	6.72	58.2	155.2
19	H	NMe_2	8.45	7.09	5.75	7.53	7.18	53.6	148.8
			H-2'	H-4'					
13	H	Bu	9.31	7.73	5.40	7.27	6.71	50.8	156.6
25	H	Bu	9.48	7.86	5.78	7.55	7.19	46.4	148.0
						H-3(5)		CH_2	C-3(CH)
16	-	Bu	9.23	7.72	5.28	7.58		47.8	151.5
28	-	Bu	9.29	7.79	5.55	8.63		46.2	145.6
			H-2',6'	H-3',5'					
10	-	NMe_2	8.29	6.96	5.28	7.58		55.3	151.5
22	-	NMe_2	8.36	7.06	5.55	8.51		53.4	145.7

The electronic structure of betaines **3** and **4** requires a high degree of charge separation which would be reflected in the dipole moment. Table 2 shows the large experimental dipole moments8) of the anhydrous methylenepyridinium benzimidazolate and methyleneimidazolium benzimidazolate inner salts **7** (12.34 D) and **13** (12.56 D), being even higher for the triazolate analogues **10** (14.82 D) and **16** (15.34 D). These values have been extrapolated to extreme dilution ($\omega < 0.00015$) to avoid self-association with concomitant decrease of the measured dipole moments.

Table 2. Dipole Moments and Polarization data in Dioxane at 298 K for betaines **7**, **10**, **13**, and **16**

Compd	α	ß	R_{MD}	$P_{2\infty}$	μexp (D)
7	75.0	≈ 0	76.12	3191.98	12.34
10	134.0	≈ 0	58.28	4549.40	14.82
13	77.06	≈ 0	76.65	3303.96	12.56
16	142.21	≈ 0	58.75	4878.60	15.34

As can be observed from the experimentally studied betaines **7**, **10**, **13**, and **16**, the introduction of a methylene group into the interannular C-N bond of the previously reported[2-5] mesomeric betaines of pyridinium azolate **1** and imidazolium azolate **2** significantly increases the dipole moment in keeping with the high dipolar structure show by the betaine structure and its large charge separation.

The highly dipolar character of the title inner salts **3** and **4** confers to this new class of heterocyclic compounds an interest worthy of development, both considered as a molecular and inclusion compounds.

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6) For example, a solution of 2-chloromethylbenzimidazole[10)] **29** (1g, 6mM) and DMAP (2.2 g, 18 mM) in anhyd dimethylformamide (5mL) or 1-butylimidazole (2.3 mL, 18 mM), under an atmosphere of nitrogen, was heated on a bath at 130 °C for 1.5 h. After cooling, acetone (25 mL) or anhyd diethyl ether (50 mL) was added to give compound **19** or **25** which was then filtered, washed with acetone (2 x 15 mL) or diethyl ether (2 x 15 mL), and recrystallized from absolute ethanol or acetone to provide 1.38 g (80% yield) of **19** (mp 263-4 °C) or 1.22 g (70% yield) of **25** (mp. 173 °C). A solution of compound **19** or **25** (0.7 mM) in 85% ethanol (200 mL) was passed through a column packed with anion-exchange resin IRA-401 (OH^- form)[2]. The neutral eluates were concentred in a rotary evaporator at 25 °C to give the corresponding betaine **7** (mp 199 °C) and **13** (mp 140 °C) in 95% yield.
7) ^1H and ^{13}C NMR spectra were recorded on a Varian Gemini and they were taken in $(CD_3)_2SO$.
8) Dipole moments measurements: the Halverstadt and Kumler[5,9)] extrapolation method was used for calculation of total polarization.
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