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Novel Imidazolium Benzimidazolate Inner Salts Containing Pentamethylene and Polyether Interannular Spacers. Synthesis and Structural Aspects

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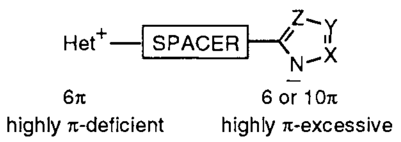
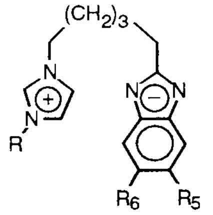
For several analogues of heterocyclic betaines **2** and **3**, the high dipolar character, due to terminal rings with extreme characteristics within heteroaromatic systems, and the nature of the linkers, had a dominant influence upon their physico-chemical properties in solution. Their structural features enhanced non-covalent interactions inducing coiled conformations.

Azinium(azolium) azolate inner salts with different interanular spacers **1** comprise a vast array of highly dipolar chemical entities, and their physical and chemical properties are a result of their dipolar nature. Among them, we have focused our attention on the imidazolium benzimidazolate betaines **2** with a pentamethylene linker, together with the novel podand-type1) dipolar structures **3** related to synthetic ionophores,2) in order to ascertain the ability of the spacer to induce coiled conformations. For betaines from group **2**, related systems such as *N*-ylides **4**3a) and their higher homologues **5**,3b) **6**3c) have previously been studied.



1



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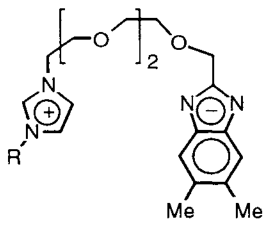
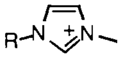


3

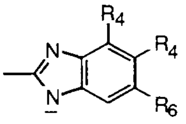
Im$^+$— (CH$_2$)$_n$— Az$^-$

4, n=0
5, n=1
6, n=2

Im$^+$:

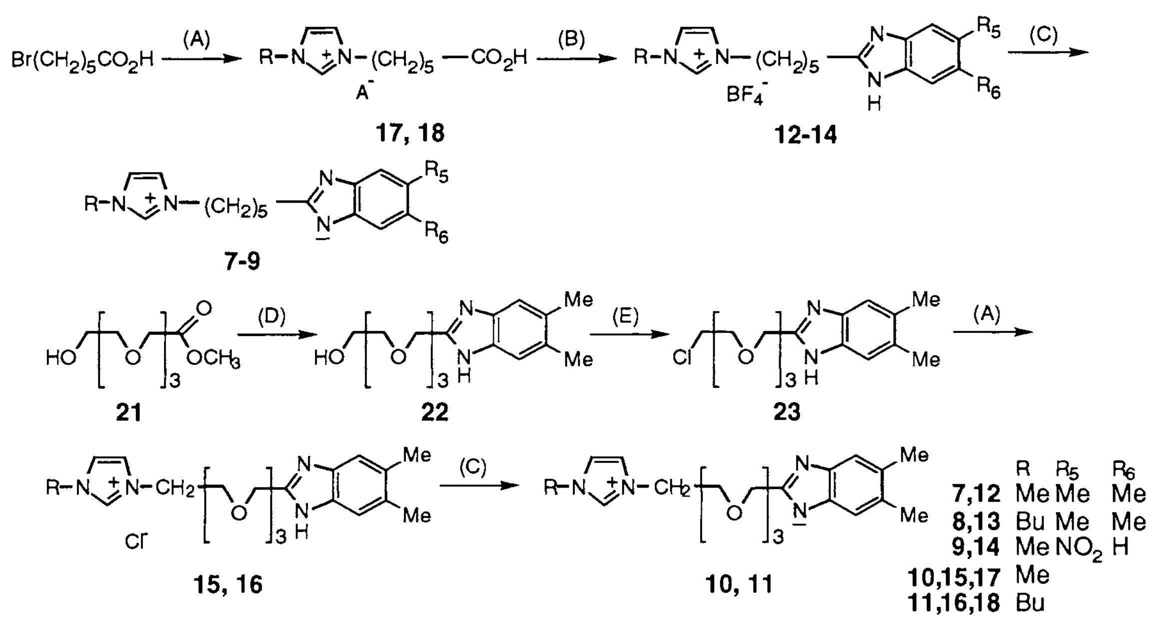


Az$^-$:



In the present communication we report the first synthesis and relevant structural aspects of some simple examples of the betaines **7-11** and their immediate precursors **12-16**, shown in Scheme 1. Compounds with a pentamethylene spacer **7-9** were prepared by a three-step procedure where their immediate precursors **12-14** were obtained following Hein's benzimidazole synthesis.4) Alternatively, the podand-type compounds **10** and **11** were synthesized by a four-step procedure with compound **21**5) as the starting material.

The dipolar structural pattern that characterizes betaines **7-11** implies strong inter and intramolecular forces.7) Another factor to be taken into account arises in connection with the nature of the ionic species detected in solution, since the negative part of dipoles **1** are basic azolate moieties,8a) especially for non-conjugated π-electron systems, as is the case for betaines **7-11** (*vide infra*).8b) Bearing this in mind, the spectroscopic properties[9a)] of the model compounds **7-11**, together with their precursors **12-16**, were shown to be crucial for structural proof and also for providing a deeper insight into the preferred conformations of the novel molecules **7-11** in solution.[9b)]



Scheme 1. Reagents and conditions: (A) method A; *N*-alkylimidazole[6)] in dry acetonitrile for **17**, **18** or as reagent and solvent for **15**, **16**, under an atmosphere of nitrogen; (B) method B; (1) 4,5-dimethyl or 4-nitro-1,2-phenylenediamine **19** or **20** in poly(phosphoric acid), at 160-170 °C for **12**, **13** or 130-140 °C for **14**; (2) ice-water; (3) Na_2CO_3 (2N) to reach pH 8; (4) 50% HBF_4-H_2O to pH 6; (C) method C; anion-exchange resin IRA-401 (OH^- form);[3)] (D) method D; (1) 4,5-dimethyl-1,2-phenylenediamine **19** in 5N HCl, at 135 °C, 35 h; (2) ice-water; (3) Na_2CO_3 (2N) to reach pH 8; (E) method E; thionyl chloride, reflux, 1.5 h. overall yield for **7-9** *ca.* 55% and for **10**, **11** *ca.* 65%.

Table 1 shows the most relevant ^1H and ^{13}C NMR chemical shifts for compounds **7-16**; individual assigments were made using the appropriate NMR experiments. For proton spectra, all the signals were found upfield for betaines **7-11** with respect to their precursors **12-16**. In both series **2** and **3**, the most interesting aspect was the observed shielding effect for the methyl protons, or the butyl α-protons, to the nitrogen atom of the imidazolium moiety together with the δH ring moieties, whereas this shielding effect upon the imidazolium ring have not been observed in betaines from group **5**[3b)] or **6**.[3c)] This indicates the presence of strong intermolecular interactions, which predominated in the less polar solvent (*vide infra*). Indeed, for betaines **7** and **10** in CD_3CN, the CH proton signals of the π-deficient ring were shifted further upfield, whereas those of the π-excessive ring were less affected (see Δδ CD_3CN in Table 1). ROESY experiments in CD_3CN provided additional experimental evidence for the close spatial proximity of the heteroaromatic subunits present in the title betaines.

The long-wavelength UV/vis absorption band for compound pairs **7** and **12**, **9** and **14**, and **10** and **15** were examined[10a)] and the results are listed in Table 2.[11)] The fact that neither pair **7** and **12** nor the podand-type pair **10** and **15** could be distinguished by their electronic absorption spectra is noteworthy. The basicity of the benzimidazolate8) nucleus tends to be solvated in order to gain stability. In contrast, the lower basicity of the 5-nitrobenzimidazolate8) nucleus present in the inner salt **9**, revealed its long-wavelength band, which was shifted from 383 nm in $CHCl_3$ to 409nm in DMSO (a positive solvatochromism of $\Delta\lambda_{max}$ 26 nm).10d) It seems feasible to postulate that solvents of lower polarity may stabilize coiled conformations for betaines of type **2**, e.g. betaine **9**, similar to the *intimate ion pair* in the solvent *cage*.7a)

Table 1. Selected ^1H and ^{13}C NMR data of compound pair **7, 12** and **10-15**

Comp	H-2'	H-4'	H-5'	H-4,7	R	CH_2a)	C-2'	C-2	C-4,7	C-5,6	R
7b)	c	7.60d	7.73d	6.97	3.71	2.63	136.8	162.3	115.3	123.7	35.7
12b)	9.07	7.67d	7.74d	7.20	3.81	2.75	136.7	153.9	114.6	130.1	35.9
Δδe)	--	-0.07	-0.01	-0.23	-0.10	-0.12	+0.1	+8.4	+0.7	-6.4	-0.2
7f)	c	7.11	7.21	7.12	3.49	2.76	--	--	--	--	--
12f)	8.42	7.29	7.33	7.25	3.76	2.81	--	--	--	--	--
Δδe)	--	-0.18	-0.12	-0.13	-0.27	-0.05	--	--	--	--	--
10b)	9.16	7.57	7.68	7.05	3.71	4.48	137.3	158.3	116.1	124.8	35.6
15b)	9.09	7.65	7.71	7.29	3.82	4.66	137.0	150.5	115.3	130.3	35.9
Δδe)	+0.07	-0.08	-0.03	-0.24	-0.11	-0.18	+0.3	+7.8	+0.8	-5.5	-0.3
10f)	8.83g)	7.05	7.27	7.18	3.53	4.61	--	--	--	--	--
15f)	8.94	7.26	7.39	7.32	3.73	4.72	--	--	--	--	--
Δδe)	-0.11	-0.21	-0.12	-0.14	-0.20	-0.11	--	--	--	--	--

a) Only δ for the α-protons of the spacer to the π-excessive nucleus are listed. b) In DMSO-d_6. c) Signal not observed due to H-D exchange. d) NOE $^1H\{^1H\}$ on irradiation at δ R. e) Δδ: observed chemical shift difference between compounds pairs **7**, **10** and **12**, **16**. f) In CD_3CN. g) Broad band.

In summary, dipolar chemical substrates with low molecular weight like **2** and **3** may form reasonable stable host-guest complexes. Efforts are under way to expand this work in to related systems and it will be of interest to study their complexation ability.

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6) Under neutral conditions (Menschutkin reaction conditions).[3b)]

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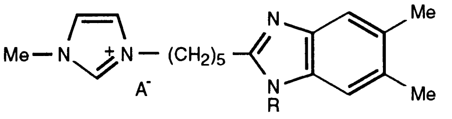
8) a) J.Catalán, J.L.M.Aboud, and J.Elguero, *Adv. Heterocycl. Chem.*, **41**, 187 (1987); b) The role of preferential interactions between water molecules and betaines **1** should also be taken into account for reliable interpretation of physico-chemical data measured in solution.[3)]

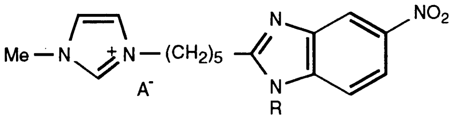
9) (a) Compounds **7-16** gave satisfactory elemental analysis. The IR spectra of compound **12-16** showed absorptions in the ranges of 3500-3400 cm^{-1} ($\surd$NH) and 1100-1000 cm^{-1} ($\surd$BF4$^-$) for **12-14**, and 2800-2500 cm^{-1} (hydrochlorides) for **15**, **16**, while these bands were absent for betaines **7-11**; b) Unfortunately, it was not possible to obtain suitable single crystals of compounds **7-9** for an X-ray structure aalysis, **10-16** being oils.

10) a) The UV/vis spectra were obtained, using a similar protocol previously described for betaines of pyridinium *N*-phenolate[10b)] and pyridinium *N*-benzimidazolate.[10c)] The solute and the solvent were suitably dried; b) M.S.Paley and J.M.Harris, *J. Org. Chem.*, **56**, 568 (1991); c) E.Sturm, U.Krüger, J.Senn-Bilfinger, V.Figala, K.Klemm, T.J.Blake, D.W.Darkin, R.J.Ife, C.A.Leach, R.C.Mitchell, and G.Huttner, *ibid.*, **52**, 4573 (1987); d) In its precursor **14**, this band appeared at 312 nm in $CHCl_3$ and 326 nm in DMSO; $\Delta\lambda_{max}$ (**9-14**) ranged from 71 to 83 nm.

11) Table 2. The long-wavelength UV/vis absorption band of compound pairs **7**, **12** and **9**, **14**[a)]



7 (A$^-$: — ; R: —)
12 (A$^-$: BF$_4^-$; R: H)



9 (A$^-$: — ; R: —)
14 (A$^-$: BF$_4^-$; R: H)

Solvent[b)]	**7**	**12**	**9**	**14**	$\Delta\lambda$ (**9-14**)
$CHCl_3$	290 (3,822)	290 (3,431)	383 (3,634)	312 (3,963)	71
1,4-dioxane	291 (2,799)	290 (3,475)	392 (3,759)	313 (3,347)	79
CH_3CN	290 (3,550)	290 (3,469)	396 (4,001)	318 (2,874)	78
DMSO	291 (3,741)	291 (3,660)	409 (4,037)	326 (3,602)	83
H_2O	—	287 (3,948)	319 (3,904)	316 (3,792)	3
aqueous buffer solution (pH= 9)	—	288 (3,906)	319 (3,793)	319 (3,847)	0

a) λ_{max} in nm, log ε_{max} in parenthesis. b) The solute and solvent were conveniently dry, using a similar protocol previously described (Ref.10), to reduce the presence of water as far as possible.

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