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Heterocyclic Betaines. Novel Ethyleneimidazolium Benzimidazolate Inner Salts. Synthesis, Characterization, and Transformation into 2-Vinyl-1*H*-benzimidazoles

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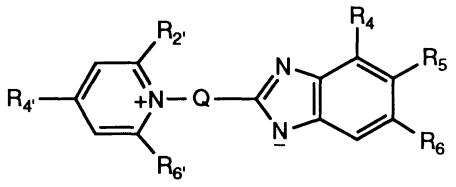
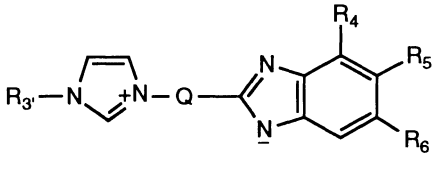
The first synthesis of the hitherto unknown ethyleneimidazolium benzimidazolate inner salts is described. Their dipolar structure is well reflected on the basis of the ^{1}H and ^{13}C NMR parameters. Under neutral and mild conditions the title compounds underwent a type of β-elimination, affording their corresponding 2-vinyl-1*H*-benzimidazoles in high yields.

In previous studies on the chemistry of heterocyclic betaines homologous to the *N*-ylides **1** and **2**,[1] the synthesis and structural properties of methylenepyridinium and methyleneimidazolium benzimidazolate inner salts **3** and **4** were reported.[2] The higher homologues are the inner salts **5** and **6** with an ethylene group as interannular linkage.



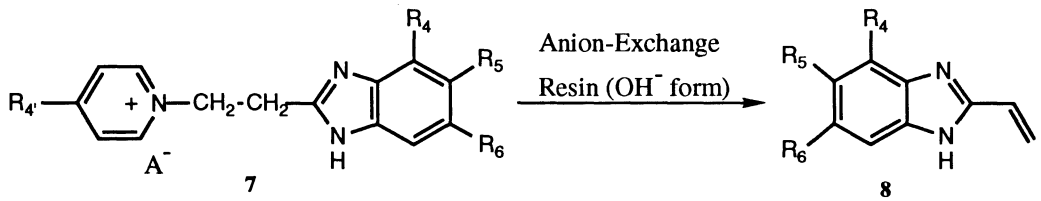
1, 3, 5



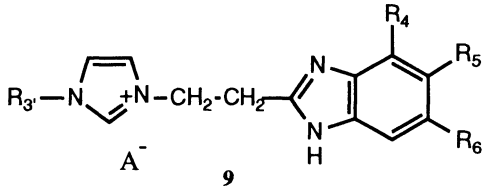
2, 4, 6

	Q
1, 2	–
3, 4	CH_2
5, 6	CH_2CH_2

Due to the early finding that several 1-(2-benzimidazol-2-ylethyl)pyridinium salts **7**, potential precursors of betaines **5**, underwent a type of β-elimination and were transformed at room temperature into their corresponding 2-vinyl-1*H*-benzimidazole monomers **8**[3] using an anion-exchange resin (OH^- form),[4] we were prompted to investigate the chemical behaviour, under alkaline and neutral media, of 1-(2-benzimidazol-2-ylethyl)imidazolium salts **9**,[6] the immediate precursor of betaines **6**.



7 **8**



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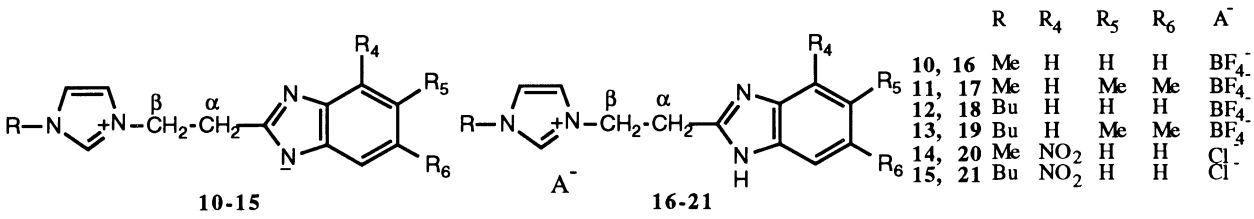
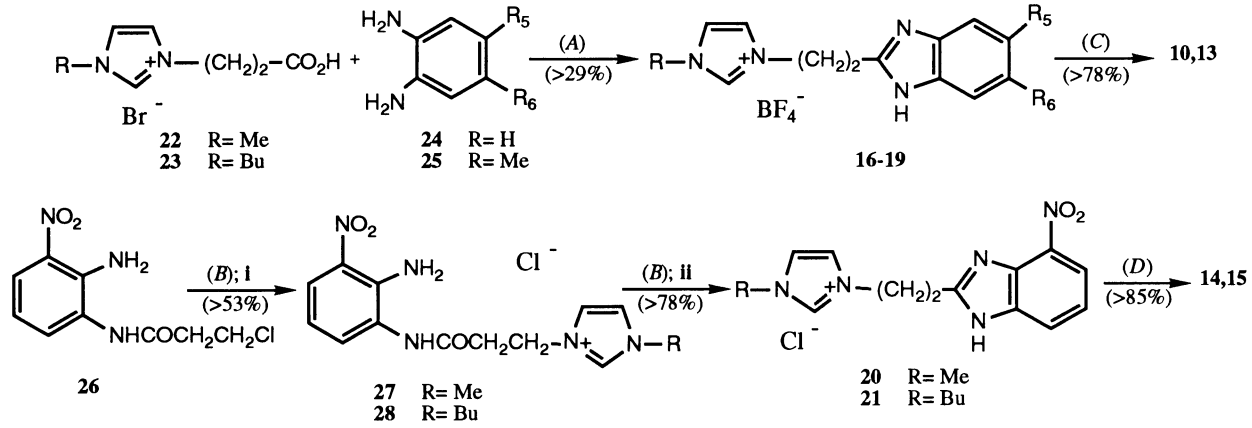
In this communication we report the first synthesis and characterization of several examples of the title inner salts **10-15** and their precursors **16-21**.



The 3-alkyl-1-[2-(1*H*-benzimidazol-2-yl)ethyl]imidazolium salts **16-21** were prepared using two different procedures[7] leading to either compounds **16-19** or compounds **20, 21** (Scheme 1). Then, they were transformed into their corresponding inner salts **10-15** using a strong anion-exchange resin (OH^- form).[8] Notwithstanding, the inner salts **10-15** are fairly unstable especially in solution at temperatures above 20 °C (*vide infra*).

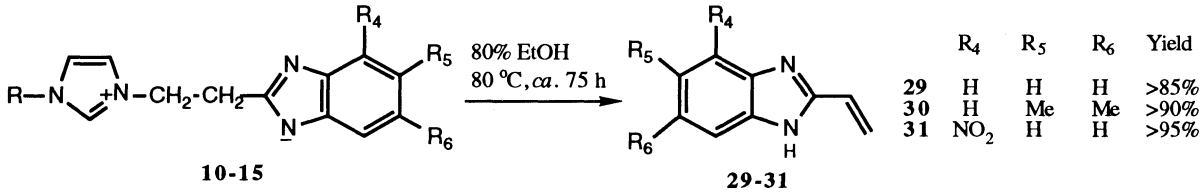


Scheme 1. *Reagents and Conditions*: (*A*), *Method A*. (i) In polyphosphoric acid, at 165 °C, 12 h to 60 h; (ii) the cooled mixture was poured into ice-water; (iii) Na_2CO_3 up to pH 8; (iv) 50% HBF_4-H_2O) to pH 6. (*B*), *Method B*. (i) *N*-alkylimidazole as reagent and solvent, at 100 °C, 5 h; 4 M HCl, at 100 °C, 12 h or 3 h respectively. (*C*), *Method C and D*: Anion-exchange Amberlite resin (OH^- form).[8]

The structures of the new inner salts **10-15** and their immediate precursors **16-21** were unambiguously characterized on the basis of their spectroscopic data and all gave satisfactory elemental analysis. The IR spectra of the compounds **16-21** showed absorption in the range of 3500-3400 cm^{-1} (ν_{NH}) and 2800-2500 cm^{-1} (hydrochlorides) or 1200-1000 cm^{-1} (tetrafluoroborates). These bands were absent for the inner salts **10-15**.

^1H and ^{13}C chemical shifts of **10-15** proved very important for structural proof of their dipolar inner salt structure, as they were for the *N*-ylides **1**, **2**,[1] their homologues **3**, **4**,[2] and other analogous compounds.[5] Both the ^1H and ^{13}C parameters[9] accord perfectly with the nature of the π-excessive and π-deficient heteroaromatic rings and with data for related systems.[1,2,5] With regard to the chemical shift values for the ethylene interannular linkage, the corresponding parameters for the α-CH_2 are much more affected than those for the β-CH_2 counterpart.

As outlined in Scheme 2, the aforementioned ethyleneimidazolium benzimidazolate inner salts **10-15** were transformed into the 2-vinylbenzimidazoles **29-31**. It is noteworthy that the reaction temperature was of crucial importance, and better yields were found at 80 °C. For instance, at *ca.* 15 °C ethanolic solution of the inner salt **11** remained unalterated after four days.



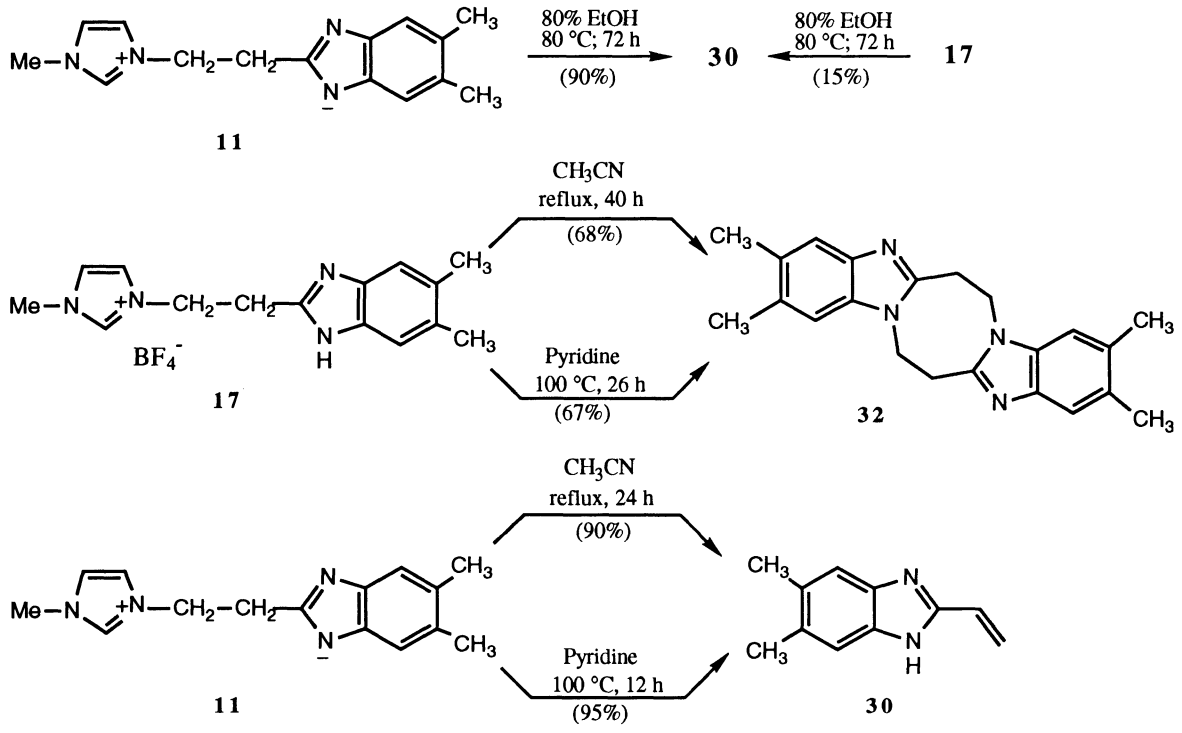
	R_4	R_5	R_6	Yield
29	H	H	H	>85%
30	H	Me	Me	>90%
31	NO_2	H	H	>95%

Scheme 2.

A study of the behaviour of the benzimidazolylethylimidazolium salts **9** and their inner salts counterparts **6** was undertaken, with the hypothesis that the ability of the pairs **6** and **9** to undergo a type of β-elimination[3,10] and formation of the corresponding 2-vinyl-1*H*-benzimidazoles **8** would be favoured by the ethyleneimidazolium benzimidazolate inner salt structure **6**. The model compounds selected were **11** and **17**.

As mentioned above, the inner salts **10-15** were transformed into the corresponding 2-vinyl-benzimidazoles **29-31**, e.g. **11** to **30**. Whereas in a similar way, the benzimidazolylethylimidazolium tetrafluoroborate **17** gave **30** in rather low yield, (Scheme 3).

Heating a solution of 1-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)ethyl]-3-methylimidazolium tetrafluoroborate **17** (in acetonitrile or even in pyridine[11]) resulted in clean conversion to the 1, 5-diazocine **32**[11,12] (Scheme 3). In contrast, the 5,6-dimethyl-2-[2-(3-methyl-1-imidazolio)ethyl]benzimidazolate **11** underwent a type of β-elimination to provide the 5,6-dimethyl-2-vinyl-1*H*-benzimidazole monomer **30**.



Scheme 3.

These results illustrate an example of the chemical behaviour of quaternary heteroaromatic salts as leaving group or nucleofugue (β-elimination *versus* substitution). In this connection, the *N*-pyridinium quaternary salts are by far the most commonly studied.[1,13] To the best of our knowledge, this is the first example in the imidazolium quaternary series. Moreover, both the ethyleneimidazolium benzimidazolate inner salts **6** and their immediate precursors **9** may be used as prototype structures to seek further insight on fundamental topics both in organic and heteroaromatic chemistry.

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1) E.Alcalde and I.Dinarés, *J. Org. Chem.*, **56**, 4233 (1991), and references quoted therein.
2) E.Alcalde, L.Pérez-García, J.-P.Fayet, and M.-C.Vertut, *Chem. Lett.*, **1991**, 845.
3) E.Alcalde, L. Pérez-García, I.Dinarés, and J. Frigola, *J. Org. Chem.*, **56**, 6516 (1991), and references quoted therein.
4) A convenient protocol used for the preparation of the *N*-ylides **1** and **2**[1] and their homologues **3** and **4**,[2] and also applied to other analogous compounds.[5]
5) E.Alcalde, L. Pérez-García, J.M. Pons, and T. Roca, *Chem. Lett.*, **1992**, 1779.
6) The imidazolium quaternary moiety has proved to be stable in 3-alkyl-1-(1*H*-benzimidazol-2-yl)imidazolium salts[1] and their homologues,[2] as well as other analogous systems.[5]
7) Both procedures were conveniently applied for synthesis of several 1-(2-benzimidazol-2-ylethyl)pyridinium salts **7**.[3]
8) A column (0.5-in. diameter) was packed with anion-exchange resin IRA-401 (OH^- form)[1,2] up to a height of 5 in. *Method C* : A solution of compounds **16-19** (*ca.* 0.13 mmol) in 80% ethanol (40 ml) was passed through the column (*ca.* 10 mg/min). The eluates were evaporated to dryness at *ca.* 15 °C to give the corresponding inner salts **10-13**. *Method D* : A solution of compounds **20**, **21** (*ca.* 0.3 mmol) in 80% ethanol (30 ml) was passed through the column (*ca.* 1.7 mg/min). The eluates were evaporated to dryness at *ca.* 15 °C to afford the corresponding inner salts **14** and **15**.
9) ^1H and ^{13}C spectra were recorded on a Varian Gemini-200, Varian Unity 300, and Varian VXR-500 spectrometers. The spectra were taken in $(CD_3)_2SO$ for compounds **10-21**, CD_3OD for compounds **16-21** and $Na^+ CD_3O^-$ /CD_3OD for the inner salts **10-15**.
10) A.R. Katritzky, C.H. Watson, Z. Dega-Szafran, and J.R. Eyler, *J. Am. Chem. Soc.*, **112**, 2479 (1990), and references quoted therein.
11) Following a similar protocol described by Katritzky and co-workers[12] for preparation of the 1,5-diazocine system **32** from 1-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)ethyl]-4-methylpyridinium bromide: its structure was unambiguously elucidated.
12) J. Elguero, A.R. Katritzky, and B.S. El-Osta, *J. Chem. Soc., Perkin Trans. 1*, **1976**, 312.
13) A.R. Katritzky and B.E. Brycki, *Chem. Soc. Rev.*, **19**, 83 (1990).

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