azolate inner salts 5-10 and their corresponding (azolylmethyl)pyridinium salts 17-22 (Table V), ^{13}C NMR spectroscopic data of methylenepyridinium azolate inner salts 5-10 and their corresponding (azolylmethyl)pyridinium salts 17-22 (Table VI), ^{1}H NMR spectroscopic data of methyleneimidazolium azolate inner salts 11-16 and their corresponding (azolylmethyl)-imidazolium salts 23-28 (Table VII), ^{13}C NMR spectroscopic data of methyleneimidazolium azolate inner salts 11-16 and their corresponding (azolylmethyl)imidazolium salts 23-28 (Table VIII), selected conformers of 2-(1-pyridiniomethyl)benzimidazolate 5, heats of formation, torsion angles (θ_A and θ_B), and dipole moments (Table XI), bond angles (Å) with esd's in parentheses (Table XII), final positional parameters ($\times 10^4$) for non-hydrogen atoms and equivalent isotropic temperature coefficients (Å^2) with esd's in parentheses (Table XIII), positional parameters ($\times 10^4$) of the H atoms (Table XIV), thermal anisotropic coefficients ($\times 10^4$) for non-H atoms with their esd's (Table XV), elemental analyses of compounds 5-28 (Table XVI), AM1 and MNDO data of betaines 5, 7, 9, 10, 13, 16, 32, and 33 AM1 and MNDO Mulliken charges and dipole direction of betaines 5, 7, 9, 10, 13, 16, 32, and 33 (58 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

Heterocyclic Betaines. 14.[1] (*E*)-1-Alkyl-[2-(imidazol-2-ylidene)ethylidene]dihydropyridines with a Betaine Character. An Improved Protocol for a Knoevenagel-Type Condensation for Synthesis of (*E*)-1-Alkyl-[2-(1*H*-imidazol-2-yl)vinyl]pyridinium Salts

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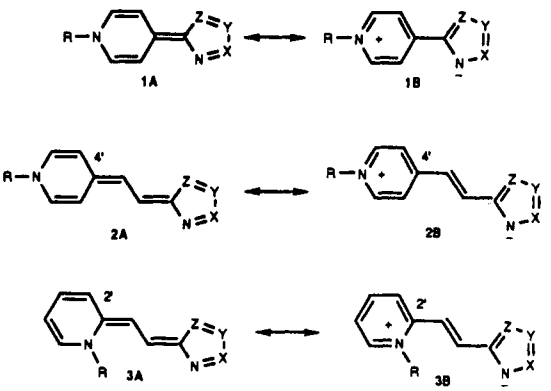
A novel class of aza analogues of (*E*)-stilbene, the (*E*)-1-alkyl-[2-(imidazol-2-ylidene)ethylidene]dihydropyridines **4A ↔ 4B, 5A ↔ 5B**, have been studied. They were synthesized by a convenient two-steps procedure. In each of the steps, the necessary basic reaction medium has been generated by a strong basic ion-exchange resin (OH^- form). Thus, a modified protocol of the Knoevenagel condensation has been applied to preparation of the title (imidazolylvinyl)pyridinium salts, deprotonation of which yields several examples of compounds **4** and **5**. The betaine character of **4** and **5** is well reflected by their physicochemical properties and reactivity toward electrophiles (MeI).

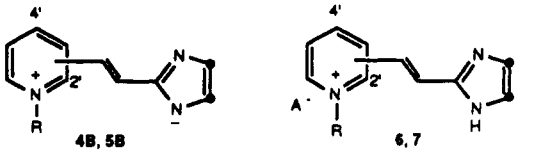
Introduction

Pursuing our research project in the quest for novel organic substrates with a dipolar character in the context of heterocyclic betaines and molecules with a betaine character, we have recently studied[2] an unusual class of aza analogues of sesquifulvalene, the 1-alkyl-4-azolylidene-1,4-dihydropyridines **1 (A ↔ B)**. Their electronic and molecular structure are consistent with the betaine character of these compounds. A logical extension of the preceding study leads to the development of a novel ensemble of aza analogues of (*E*)-stilbene, the (*E*)-1-alkyl-[2-(azol-2-ylidene)ethylidene]dihydropyridines **2(A ↔ B)** and **3(A ↔ B)** in which both rings are linked by a vinylene group leading to an extended π-system which contains extremely π-deficient and π-excessive moities.[3]

This paper describes the first synthesis and characterization of several examples of the title compounds **4(A ↔ B)** and **5(A ↔ B)** with a dipolar nature. Furthermore their immediate precursors, the (*E*)-1-alkyl-[2-(1*H*-imidazol-2-yl)vinyl]pyridinium salts **6** and **7** have been prepared by



an efficient modification of Knoevenagel condensation.



4, 6 (4-pyridinio)
5, 7 (2-pyridinio)

Results and Discussion

Synthesis. The unknown (*E*)-(imidazolylvinyl)-pyridinium salts **6** and **7**, a priori could not be prepared in a satisfactory yield using existing methodologies for preparation of (*E*)-stilbazolium salts, (*E*)-stilbazoles, and

(1) (a) Part 13: Alcalde, E.; Pérez-García, Ll.; Miravitlles, C.; Rius, J.; Valentí, E. *J. Org. Chem.* previous paper in this issue. (b) Abstracted from the Ph.D. Thesis of Tomás Roca, Facultad de Farmacia, Universidad de Barcelona, 1992.

(2) Alcalde, E.; Dinarés, I.; Frigola, J.; Jaime, C.; Fayet, J.-P.; Vertut, M.-C.; Miravitlles, C.; Rius, J. *J. Org. Chem.* **1991**, *56*, 4223 and references quoted therein.

(3) For an earlier report on several examples of compounds **2** and **3**, see: Alcalde, E.; Roca, T.; Fayet, J.-P.; Vertut, M.-C. *Chem. Lett.* **1991**, 2151.

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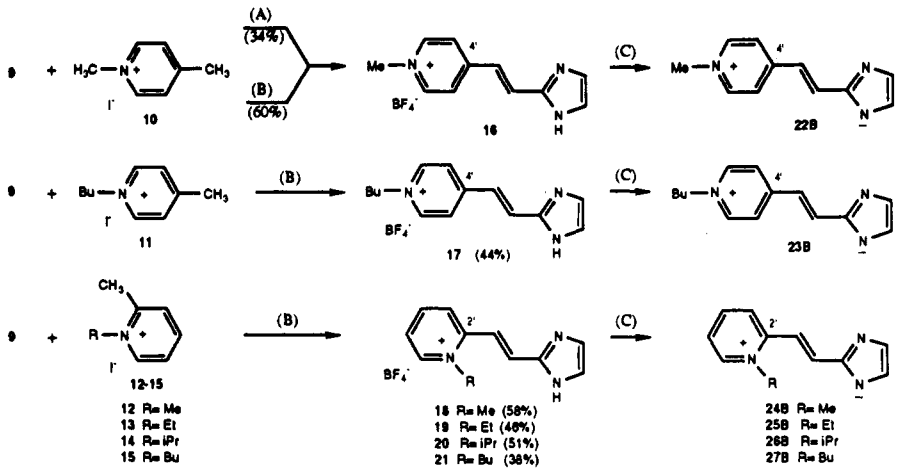
Scheme I[a]



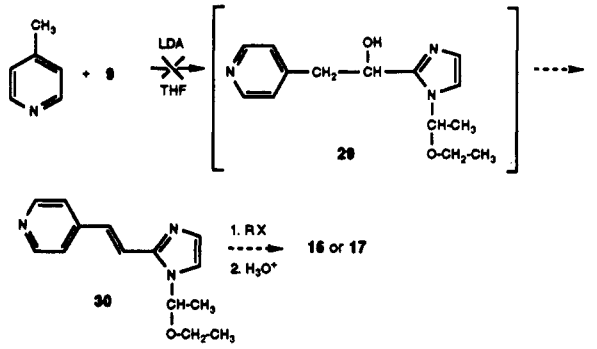
[a] Reagents and conditions: (A) Method A. (1) Piperidine, MeOH, reflux, 4 h; (2) 0.5 N HBF_4–H_2O to pH ≈ 3, 50 °C, 4 h; (3) 2 N Na_2CO_3 to pH ≈ 6. (B) Method B. (1) A solution of compounds **10**, **11**, **12**, **13**, **14**, or **15** in methanol previously treated with Amberlite IRA-401 (OH^- form) was transferred into a solution of 1-(1-ethoxyethyl)-2-imidazolecarbaldehyde (**9**)[9] in methanol under an atmosphere of nitrogen; (2) room temperature, 0.25–0.5 h; (3) 0.5 N HBF_4–H_2O to pH ≈ 3, 50 °C, 4 h; (4) 2 N Na_2CO_3 to reach pH ≈ 6. (C) Method C. Anion-exchange Amberlite IRA 401 (OH^- form), yield 82–100%.

(*E*)-stilbenes. Among these, a widely-used procedure, the Knoevenagel Condensation,[4] would not appear to be an efficient method for synthesis of compounds **6** and **7** since the starting azole derivatives are less reactive (e.g. than aromatic aldehydes) and are difficult to obtain. Another method used, addition of (lithiomethyl)pyridine to aldehydes, could be used.[5] Both classical procedures have been applied to preparation of (*E*)-(imidazolylvinyl)-pyridinium salts **6** and **7**. In all cases they either proceeded to give disappointingly low yields or no reaction was observed; when the reaction conditions were forced only decomposition products were found.

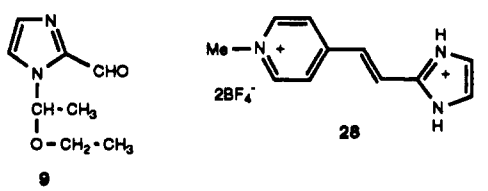
As for Knoevenagel condensation,[6] (*E*)-4-(2-phenylvinyl)-1-methylpyridinium iodide (**8**) was conveniently prepared—using piperidine as catalyst—as described in the literature[8] (80% yield). Almost the same reaction conditions were applied for preparation of (*E*)-4-[2-(1*H*-imidazol-2-yl)vinyl]-1-methylpyridinium iodide (**16**) from 1*H*-2-imidazolecarbaldehyde and compound **10**, yields being rather low (no more than 10%, see the Experimental Section). After trying of a variety of conditions, and using the 1-(1-ethoxyethyl)-2-imidazolecarbaldehyde **9**,[9] the tetrafluoroborate of **16** was obtained in 34% yield (Scheme I, method A).

We herein report an improved protocol for a Knoevenagel-type reaction using a strong basic ion-exchange resin, IRA-401 (OH^- form), which provides a simple entry into a variety of (*E*)-(imidazolylvinyl)pyridinium salts **6** and **7**, with excellent yields for this type of reaction.[10] Six

Scheme II



(*E*)-(imidazolylvinyl)pyridinium tetrafluoroborates **16**–**21** were prepared (Scheme I, method B). The selection of the ion-exchange resin is probably the key point in the process.[11] It is noteworthy that the later treatment with 2 N Na_2CO_3 to reach pH ≈ 6[12] was important in order to obtain the title salts **16**–**21**. Thus, at pH ≈ 3 it was possible to isolate pure 2-[2-(1-methyl-4-pyridinio)vinyl]-imidazolium ditetrafluoroborate **28**, the positively charged imidazolium counterpart of compound **16** (see the Experimental Section, method D).



(4) (a) Jones, G. *Organic Reactions*; John Wiley & Sons, Inc.: New York, 1967; Vol. 15, Chapter 2. (b) *Ibid.* p 204. (c) *Ibid.* p 265.

(5) Wakefield, B. J. *Organolithium Methods*; Academic Press: London, 1988; pp 67–69. (b) *Ibid.* p 108.

(6) In general, the Knoevenagel condensations are catalyzed by weak bases under homogeneous conditions.[4b] However, several basic solid catalyst[7] (i.e. xenolite *tert*-butoxide) have been conveniently used in Knoevenagel condensations.

(7) Lazlo, P. *Acc. Chem. Res.* **1986**, *19*, 121 and references quoted therein.

(8) Phillips, A. P. *J. Org. Chem.* **1949**, *14*, 302.

(9) Manoharan, T. S.; Brown, R. S. *J. Org. Chem.* **1988**, *53*, 1107.

(10) (a) A wide range of aromatic aldehydes are known and easily accessible. On the contrary, the less common 1*H*-2-imidazolecarbaldehydes[10b] are difficult to obtain, and this could prove to be a limiting factor for method. (b) A search by CAS ONLINE (1967 to date) brought to light 17 compounds closely related to 1*H*-2-imidazolecarbaldehyde and contained in 16 references, as well as 43 references for 1*H*-2-imidazolecarbaldehyde itself.

(11) (a) In fact, the use of ion-exchange resins as catalyst in base-promoted reactions was been reported,[11b] and just a few Knoevenagel condensations were been performed with weakly basic ion-exchange resins[4c] (Amberlite IR-4B and Dowex 3). (b) Arrad, O.; Sasson, Y. *J. Org. Chem.* **1989**, *54*, 4993.

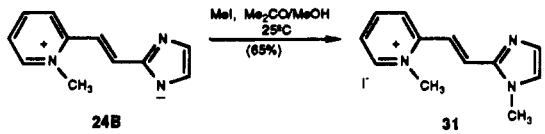
(12) (a) Imidazole is the most basic of the azoles.[13a,b] (b) A similar situation holds for 1-alkyl-(1*H*-benzimidazol-2-yl)pyridinium salts with several interannular moieties previously reported.[13c,e] (c) Alcalde, E.; Dinarès, I.; Pérez-Garcia, Ll.; Roca, T. *Synthesis* **1992**, 395. (d) Alcalde, E.; Pérez-Garcia, Ll.; Dinarès, I.; Frigola, J. *J. Org. Chem.* **1991**, *56*, 6516.

(13) (a) *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Peragamon Press: Oxford, 1984; Vol. 5. (b) Grimmett, M. R. In *Ibid.* Vol. 5, pp 383–385. (c) Grimmett, M. R.; In *Ibid.* Vol. 5, pp 387–390. (d) Ulf, B. C. In *Ibid.* Vol. 2, pp 329–335. (e) Grimmett, M. R. *Adv. Heterocycl. Chem.* **1980**, *27*, 241.

Table I. Physical Data of (*E*)-1-Alkyl[2-(1*H*-imidazol-2-yl)vinyl]pyridinium Tetrafluoroborates 16–21, (*E*)-1-Alkyl[2-(imidazol-2-ylidene)ethylidene]dihydropyridines 22–27, and Compound 28

compd[a]	alkyl	method	yield, %[b]	mp, °C (solvent)
16	Me	A	34	227–9 (*c*)
16	Me	B	60	227–9 (*c*)
17	*n*-Bu	B	44	130–1 (*c*)
18	Me	B	58	183–5 (*c*)
19	Et	B	46	160–1 (*d*)
20	*i*-Pr	B	51	81–3 (*d*)
21	*n*-Bu	B	38	119–20 (*e*)
22	Me	C	90	85–7
23	*n*-Bu	C	82	158–60
24	Me	C	100	*f*
25	Et	C	88	*f*
26	*i*-Pr	C	95	50–2
27	*n*-Bu	C	100	210–2
28	Me	D	49	223–5

[a] Satisfactory analytical data (±0.4% for C, H, N) were obtained for all new compounds. [b] Yields were not optimized. [c] Water. [d] Methanol. [e] Water/acetone (3:1). [f] At 130 °C was transformed into a gummy solid and the mp was precluded.



24B 31

An alternative route to (*E*)-1-alkyl-4-[2-(1*H*-imidazol-2-yl)vinyl]pyridinium salts **16** or **17** was explored. Thus, 4-(lithiomethyl)pyridine, generated by standard procedure,[14] was added to 1-(1-ethoxyethyl)-2-imidazolecarbaldehyde (**9**), and several attempts were carried out. Neither of the addition compounds, **29** or **30**, was formed. By using forced reaction conditions, 1*H*-2-imidazolecarbaldehyde and decomposition products were observed by ^{1}H NMR and TLC, and these were not further investigated (Scheme II).

Finally, the title (*E*)-1-alkyl-[2-(imidazol-2-ylidene)-ethylidene]dihydropyridines **22–27** were obtained by deprotonation of their corresponding (*E*)-(imidazolylvinyl)-pyridinium salts **16–21**, using the above-mentioned anion-exchange Amberlite resin IRA-401 (OH^- form), a successful procedure previously described and also applied to the preparation of several examples of compounds **1**.[2]

Physical data of (*E*)-(imidazolylvinyl)pyridinium salts **16–21** and (*E*)-1-alkyl-[2-(imidazol-2-ylidene)ethylidene]-dihydropyridines **22–27** are listed in Table I. The title vinylogues, compounds **22–27**, were fairly stable[15] but less so than the previously reported compounds **1**.

Reactivity toward Electrophiles (MeI). Heterocyclic mesomeric betaines of pyridinium benzimidazolate[17a] and imidazolium benzimidazolate[17b] react with methyl iodide as an electrophile under neutral and mild conditions (yield ≥80%) due to their highly dipolar structures. Further, it is well established that following N-alkylation of the azole nucleus by alkyl halides under neutral (but not usually mild) conditions the yields are restricted to around 50%[13] (e.g. imidazole[13c,e]).

(*E*)-1-Methyl-2-[2-(imidazol-2-ylidene)ethylidene]-1,2-dihydropyridine (**24**) did indeed react with methyl iodide/acetone–methanol at room temperature to afford the (*E*)-1-methyl-2-[2-(1-methylimidazol-2-yl)vinyl]pyridinium iodide (**31**) (yield 65%). This result reflects the dipolar nature of the title compounds **4** and **5** (see below).

Structural Assignments. The structures of the new (*E*)-1-alkyl-[2-(imidazol-2-ylidene)ethylidene]dihydropyridines **22–27** and their precursors **16–21** have been unambiguously characterized on the basis of their spectroscopic data and all gave satisfactory elemental analysis. IR spectra of compounds **16–21** showed absorptions in the range of 3500–3400 cm^{-1} (ν NH) and 1100–1000 cm^{-1} (ν BF_4^-). These bands were absent for compounds **22–27**. Table II summarizes the selected ^{1}H and ^{13}C NMR data of compounds **16–21** and **22–27**; individual assignments were made using the appropriate NMR techniques,[18] but detailed description of the results is beyond the scope of this paper.[19] The ^{1}H and ^{13}C parameters for all new compounds described are given in Tables III–VI (see the supplementary material).

Compounds **22–27** can be described to a first approximation by covalent resonance (**A**) or dipolar resonance structure (**B**). Their ^{1}H and ^{13}C NMR parameters were crucial for structural proof and for providing evidence of charge distribution within the molecule. As shown in Table II, the ^{1}H and ^{13}C NMR chemical shifts of the π-excessive moiety, the ring protons of **22–27** were shifted to lower frequencies than the protons of their corresponding precursors **16–21**, and the δC values of the carbon atoms were in good agreement with data for the imidazolate ion itself.[20a] With regard to the π-deficient moiety of **22–27**, the NMR signals correspond to quaternary pyridinium structures.[2]

Inspection of the ^{1}H and ^{13}C NMR data[18] for the (*E*)-vinylene interannular linkage for compounds **22–27** and their corresponding (imidazolylvinyl)pyridinium salts **16–21** shows that these chemical shift values differences are the most affected (see $\Delta\delta$ in Table II). The change observed in the position of C-β resonances is in agreement with the β-substituent effects in the ^{13}C NMR chemical shifts of a series of β-heteroaryl styrenes.[20b] The overall NMR results, therefore, provide evidence of the dipolar nature in solution[18f] for compounds **22B–27B**.

Unfortunately, the title compounds **22–27** were not suitable for further structural studies, e.g. a single-crystal X-ray analysis[15] and dipole moment measurements.[3] In this connection, a theoretical study by semiempirical methods (i.e. AM1 SCF-MO) was not performed for **22–27** because the results are insufficient for such semiempirical calculations.[16]

In our previous structural studies on heterocyclic betaines or organic substrates with a dipolar nature,[1a] it was pointed out that *extreme* dilution of the *anhydrous* sample was necessary for the measurement of the electric dipolar moments due to the perturbing influence of self-association

(14) Tomioka, K.; Koga, K. *Tetrahedron Lett.* **1988**, *14*, 4351.

(15) It has not been possible to obtain suitable single crystals of **22–27** for an X-ray structure analysis under standard crystallization techniques. Compounds **22–27** are air- and light-sensitive as well as quite instables in the appropriate recrystallization solvents.

(16) Streitwieser, A. *J. Org. Chem.* **1990**, *55* (19), 7A.

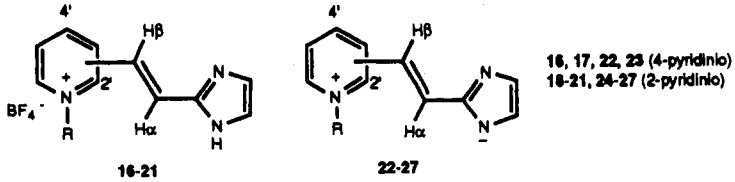
(17) (a) Alcalde, E.; Dinarés, I.; Elguero, J.; Frigola, J.; Osuna, A.; Castanys, S. *Eur. J. Med. Chem.* **1990**, *25*, 309. (b) Alcalde, E.; Dinarés, I. *J. Org. Chem.* **1991**, *56*, 4233.

(18) (a) Unambiguous assignments have been made by SFORD,[18b] DEPT,[18c] HETNOE,[18d] heteronuclear multiple-quantum coherence (HMQC)[18e] and heteronuclear multiple-bond correlation (HMBC)[18e] techniques. (b) Breitmeier, E.; Voelter, W. In *Carbon-13 NMR Spectroscopy*; VHC: Weinheim, 1987; p 47, (c) p 80. (d) Sánchez-Ferrando, F. *Magn. Reson. Chem.* **1985**, *23*, 1072. (e) Summers, M. F.; Marzilli, L. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285. (f) Methanol-d_4 was previously dried with activated molecular sieve 3A to reduce the presence of water from the solvent. (g) Compounds **22–27** are instable in dimethyl sulfoxide.

(19) Alcalde, E.; Redondo, J.; Roca, T. Unpublished results.

(20) (a) Pugmire, R. J.; Grant, D. M. *J. Am. Chem. Soc.* **1971**, *93*, 1880. (b) Aun, C. E.; Clarkson, T. J.; Happer, D. A. R. *J. Chem. Soc., Perkin Trans. 2* **1990**, 645 and references quoted therein.

Table II. Selected ^1H and ^{13}C NMR Data[18] of Compounds 22–27 and 16–21[a]



compd	H-2′	H-3′	H-4′	H-5′	H-6′	H-α	H-β	H-4,5	R[b]	Cα	Cβ	C-2
16	8.86	8.24		8.24	8.86	7.76	7.50	7.40	4.43	129.0	125.3	145.5
22	8.39	7.88		7.88	8.39	7.67	7.09	7.32	4.12	136.6	117.4	152.4
Δδ[c]	−0.47	−0.36		−0.36	−0.47	−0.09	−0.41	−0.08	−0.31	+7.6	−7.9	+6.9
17	8.90	8.23		8.23	8.90	7.75	7.48	7.38	4.63	129.0	125.2	145.3
23	8.52	7.94		7.94	8.52	7.75	7.17	7.32	4.39	136.2	118.0	152.2
Δδ[c]	−0.38	−0.29		−0.29	−0.38	0.00	−0.31	−0.06	−0.24	+7.2	−7.2	+6.9
18		8.50	8.55	7.93	8.87	7.69	7.74	7.40	4.46	131.0	119.1	145.0
24		8.35	8.21	7.50	8.46	7.77	7.35	7.31	4.25	139.0	109.6	152.6
Δδ[c]		−0.15	−0.34	−0.43	−0.41	+0.08	−0.39	−0.09	−0.21	+8.9	−9.5	+7.6
19		8.55	8.60	8.00	8.96	7.71	7.81	7.43	4.84	131.3	118.8	145.0
25		8.38	8.25	7.58	8.58	7.84	7.44	7.34	4.69	139.5	108.9	152.9
Δδ[c]		−0.17	−0.35	−0.42	−0.38	+0.13	−0.37	−0.09	−0.15	+8.2	−9.9	+7.9
20		8.45	8.58	8.08	9.10	7.61	7.88	7.42	5.45	131.0	120.0	144.7
26		8.30	8.28	7.78	8.73	7.65	7.48	7.31	5.33	138.3	112.1	153.0
Δδ[c]		−0.15	−0.30	−0.30	−0.37	+0.04	−0.40	−0.11	−0.12	+7.3	−7.9	+8.3
21		8.55	8.60	7.99	8.95	7.70	7.79	7.43	4.79	131.3	118.8	145.3
27		8.42	8.28	7.62	8.61	7.83	7.45	7.35	4.65	139.4	109.3	152.7
Δδ[c]		−0.13	−0.32	−0.37	−0.34	+0.13	−0.34	−0.08	−0.14	+8.1	−9.5	+7.7

[a] In CD_3OD.[18f] $J_{H\alpha,H\beta}$ in the range of 15.3–16.4 Hz. [b] Only δ for the α-protons to nitrogen are listed. [c] Δδ: observed chemical shifts difference between compounds 22–27 and their (imidazolylvinyl)pyridinium salts 16–21.

(nonpolar dimers), and this effect was not completely eliminated. A similar situation holds for the (*E*)-1-alkyl-4-[2-(imidazol-2-ylidene)ethylidene]-1,4-dihydropyridines **22** and **23**, and the experimental dipole moments could not be measured accurately.[3] It was, however, possible to record the dipole moment of compound **24**, which was found to be 11.66 D,[3] quite unusual for organic molecules which are not formal zwitterions or betaines.[21]

Conclusions

A convenient protocol for a Knoevenagel type Condensation using Amberlite IRA-401 (OH^- form) resin allows a facile entry to (*E*)-(imidazolylvinyl)pyridinium salts **16–21**, deprotonation of which by the same type of strong basic ion-exchange resin (OH^- form) affords the title compounds **22–27**. All the experimental data available on the hitherto unknown (*E*)-1-alkyl[2-(imidazol-2-ylidene)-ethylidene]dihydropyridines **22–27** (**A** ↔ **B**) are consistent with a betaine character of these compounds. Accordingly, their dipolar canonical forms **22B–27B** can make an important contribution to the ground state. Owing to the potential aromaticity of the rings attached to the vinylene interannular group both the pyridinium cation and imidazolate anion are stable heteroaromatic electronic systems.

Experimental Section

General Methods. Melting point: CTP-MP 300 hot-plate apparatus in ASTM 2C thermometer. IR (KBr disks): Perkin-Elmer 1430 spectrophotometer. ^1H NMR: Varian Unity 300 and Varian Gemini 200 spectrometer (300 and 200 MHz). ^{13}C NMR: Varian Unity 300 and Varian Gemini 200 spectrometer (75.4 and 50.2 MHz). SFORD[18b] and HETNOE:[18d] Varian Unity 300 spectrometer. HMQC and HMBC:[18e] Varian VXR-500 spectrometer. NMR spectra were determined in methanol-d_4[18f] and dimethyl-d_6 sulfoxide, and chemical shifts are expressed in parts per million (δ) relative to central peak of methanol-d_4 or dimethyl-d_6 sulfoxide. TLC: Merck precoated silica gel 60 F_{254} plates; solvent system, diethyl ether–methanol (2:8); detection by UV light. Flash chromatography (FC): Macherey Negel silica gel Kiesegel 60. Ion-exchange resin: Amberlite IRA-401 OH^- form (See, Method C). When a rotary evaporator was used, the bath temperature was 25 °C. In general, the compounds were dried by heating overnight at 25 °C in a vacuum oven. Microanalyses (Table VII) were performed on a Carlo Erba 1106 analyzer.

Materials. (*E*)-1-Methyl-4-(2-phenylvinyl)pyridinium iodide (**8**)[8] 1-(1-ethoxyethyl)-2-imidazolecarbaldehyde (**9**),[9] 1,4-dimethylpyridinium iodide (**10**),[22a] 1-butyl-4-methylpyridinium iodide (**11**),[22b] 1,2-dimethylpyridinium iodide (**12**),[22a] 1-ethyl-2-methylpyridinium iodide (**13**),[23] and 1-butyl-2-methylpyridinium iodide (**15**)[24] were prepared as in literature, and 2-methylpyridine, 4-methylpyridine, and 1*H*-2-imidazolecarbaldehyde are commercially available.

Preparation of 1-Isopropyl-2-methylpyridinium Iodide 14. To a stirred solution of 2-methylpyridine (17.4 mM) in anhyd acetone (25 mL) was added isopropyl iodide (16.10 mL, 135 mM) dropwise at room temperature, under an atmosphere of nitrogen, and the mixture was refluxed for 8 days. The progress of the reaction was monitored by TLC (methanol–diethyl ether, 8:2) and by ^1H NMR of aliquots.

The precipitate product was filtered, washed with anhyd acetone (3 × 20 mL), and dried to afford compound **14** in a pure state (1.92 g, 42% yield, mp 150–2 °C). ^1H and ^{13}C NMR data (see Table V and VI of the supplementary material).

Preparation of (*E*)-1-Alkyl-[2-(1*H*-imidazol-2-yl)vinyl]-pyridinium Tetrafluoroborates 16–21 (Table I). Method A. A stirred solution of 1-(1-ethoxyethyl)-2-imidazolecarbaldehyde (**9**) (0.4 g, 2.38 mM), 1,4-dimethylpyridinium iodide (**10**) (0.56 g, 2.38 mM), and piperidine (0.12 mL, 1.19 mM) in anhyd methanol (50 mL), was refluxed for 4 h under a nitrogen atmosphere. To the cooled reaction mixture was added 0.5 N $HBF_4 \cdot H_2O$ to pH 3, and the mixture was maintained at 50 °C for 4 h. Then, 2 N Na_2CO_3 was added to reach pH 6, the resultant solid was filtered,

(21) For a casual terminology of *dipolar ions*, see: Nickon, A.; Silversmith, E. F. In *Organic Chemistry: The Name Game*; Pergamon Press: New York, 1987; p 196.

(22) (a) Kosower, E. M.; Klinedinst, P. E. *J. Am. Chem. Soc.* **1956**, *78*, 3493. (b) Takahashi, T.; Sato, K. *J. Pharm. Soc. Jpn.* **1956**, *76*, 195.

(23) Katcka, K.; Urbanski, T. *Bull. Acad. Pol. Sci. Ser. Sci. Chim.* **1967**, *15*, 413.

(24) Compound **15** (Br^-): Boyd, G. V.; Ellis, A. W.; Harms, M. D. *J. Chem. Soc., Chem. Commun.* **1970**, 800.

and the filtrate was evaporated to dryness. The residue was recrystallized from water to give 0.22 g (34% yield) of **16** (BF_4^-): mp 227–9 °C.

A solution of the N-unsubstituted 1*H*-2-imidazolecarbaldehyde (0.5 g, 5 mM), 1,4-dimethylpyridinium iodide (**10**) (1.17 g, 5 mM), and piperidine (0.25 g, 2.5 mM) in anhyd methanol (80 mL), under an atmosphere of nitrogen, was refluxed for 30 min. The reaction mixture was concentrated, and a white solid was filtered to give 2-(1-piperidylmethylidene)imidazole (0.21 g, 25% yield): mp 180 °C; ^{1}H NMR ($CDCl_3$) δ 7.07–6.83 (2 H, H-4,5), 5.58 (1 H, =CH), 2.41 (4 H, H-2′,6′), 1.43 (6 H, H-3′,4′,5′). Anal. Calcd for $C_9H_{13}N_3$: C, 66.2; H, 8.0; N, 25.7. Found: C, 66.3; H, 8.1; N, 25.7.

The filtrate was evaporated to dryness, acetone/methanol (9.5:0.5; 25 mL) was added to the residue, and the resulting solid washed with chloroform (2 × 10 mL) and then recrystallized from acetonitrile/methanol (9:1) to afford 0.16 g (10% yield) of **16** (I^-): mp 251–2 °C.

Method B. A mixture of 1-alkylpyridinium iodides **10–15** (8.9 mM) in anhyd methanol (75 mL) and ion-exchange Amberlite resin IRA 401 (OH^- form) (5.8 g, 22.2 mM), previously filtered from its aqueous suspension (see later, method C) and washed with anhyd methanol, was energetically stirred at room temperature under an atmosphere of nitrogen for 5–15 min. The solution was transferred via cannula to a solution of compound **9** (1.5 g, 8.9 mM) in anhyd methanol (60 mL) under an atmosphere of nitrogen. The reaction mixture was stirred at room temperature for 15–30 min, and for compound **20** for 2.5 h. Then 0.5 N aqueous fluoboric acid was added to pH ≈ 3 and maintained at 50 °C for 4 h.

To the resulting solution was added 2 N Na_2CO_3 to reach pH ≈ 6, and on concentrating the solution a yellow solid precipitated for compounds **16–18**. The crude product was filtered and recrystallized (Table I).

In a similar manner the yellow solution (pH ≈ 6) of compound **19** was evaporated to dryness, the residue was treated with anhyd acetonitrile (3 × 20 mL), and the insoluble materials were removed by filtration. The filtrate was evaporated to dryness and the solid residue recrystallized (Table I).

From the yellow solution (pH ≈ 6) of compound **20** and **21** methanol was evaporated, and the aqueous solution was extracted with dichloromethane (5 × 50 mL). The combined extracts were dried (anhyd Na_2SO_4) and evaporated to dryness. The oily residue was triturated with dichloromethane/diethyl ether (1:3) or ethyl acetate/methanol (9:1) respectively, filtered, and recrystallized (Table I).

Control Runs To Determine the Stability of the 1-Alkylpyridinium Salts 10–15 after Treatment with Amberlite IRA-401 OH^- Form (See Method B). To a solution of 1-alkylpyridinium salts **10–14** or **15** (50 mg) in methanol-d_4 (ca. 0.5 mL) was added Amberlite IRA-401 resin, hydroxide form (ca. 100 mg), previously washed with anhyd methanol. The mixture was vigorously stirred at room temperature and under an atmosphere of nitrogen for 5–15 min. Then, the solution was transferred to a NMR tube and the ^{1}H NMR spectrum was recorded; in all cases hydrogen–deuterium exchange was observed in the C_2-Me or C_4-Me side chain,[25] but not alteration or decomposition of the substrate (see Table V in the supplementary material).

Preparation of (*E*)-1-Alkyl-[2-(imidazol-2-ylidene)-ethylidene]dihydropyridines 22–27 (Table I). Method C. A column packed with anion-exchange Amberlite IRA-401 resin chloride form was converted to the hydroxide form. The resin (50 g) was washed with aqueous 10% NaOH (ca. 4 L) until it was free of halide ion ($AgNO_3$–HNO_3 test) with water until the eluant was no longer alkaline (pH 7) and then stored in water.

A column (0.5-in. diameter) was packed with an aqueous suspension of Amberlite IRA-401 (OH^- form) up to a height of 5 in., and the column bed equilibrated with the following eluants: H_2O (20 mL), 20% ethanol (20 mL), 70% ethanol (20 mL), and ethanol (20 mL). A solution of (*E*)-1-alkyl-[2-(1*H*-imidazol-2-yl)vinyl]pyridinium tetrafluoroborates **16–21** (200 mg) in ethanol (50 mL) was passed through the column. The neutral eluates were evaporated to dryness, and the residue washed with diethyl ether (20 mL) to afford a garnet solid[15] of **22–27** (Table I).

2-[2-(1-Methyl-4-pyridinio)vinyl]imidazolium Ditetrafluoroborate (28) (Table I). Method D. Reaction of compound **9** and 1,4-dimethylpyridinium iodide (**10**) was carried out following the above-mentioned protocol for the Knoevenagel condensation (method B). Then, the resulting yellow solution without neutralization was concentrated (ca. 30 mL). On standing at −10 °C a white solid of **28** slowly precipitated. Compound **28** was filtered, washed with acetone/chloroform (2:1) (3 × 10 mL), and dried (Table I). ^{1}H and ^{13}C NMR data (see, Table III and IV, supplementary material).

Attempted Preparation of 1-(1-Ethoxyethyl)-2-[2-(4-pyridyl)vinyl]imidazole (29) (Scheme II). To a stirred solution of diisopropylamine (0.38 mL, 2.71 mM) and anhyd THF (10 mL) at −75 °C under an atmosphere of nitrogen was transferred via cannula BuLi (ca. 1.6 M in hexane, 2.71 mM), and the mixture was stirred at 0 °C for 30 min. A solution of 4-methylpyridine (0.24 mL, 2.47 mM) in anhyd THF (4 mL) was added at −75 °C during 10 min.[15] The resulting orange solution was stirred at −75 °C for 45 min, and a solution of 1-(1-ethoxyethyl)-2-imidazolecarbaldehyde (**9**) (0.5 g, 2.97 mM) in anhyd THF (5 mL) was added. The resulting solution was stirred at 25 °C for 16 h, water was added, and it was extracted with dichloromethane (5 × 40 mL). The combined organic layers were dried and concentrated to dryness. The residue was chromatographed by FC: A, diethyl ether; B, dichloromethane–methanol, 9:1; C, methanol; and D, methanol–diethylamine. The eluates were evaporated to dryness, and from the first fractions (diethyl ether) only 40 mg of the starting imidazolecarbaldehyde was recovered. From the remaining fractions, only unidentified products of decomposition or alteration were found, which were not further investigated.

Preparation of (*E*)-1-Methyl-2-[2-(1-methylimidazol-2-yl)vinyl]pyridinium Iodide (31) (Scheme III). Methyl iodide (0.50 mL, 8.0 mM) was added at 0–5 °C to a solution of (*E*)-1-methyl-2-[2-(imidazol-2-ylidene)ethylidene]-1,2-dihydropyridine (**24**) (0.29 g, 1.56 mM) in dry acetone/methanol (9.5:0.5) (90 mL) under an atmosphere of nitrogen, and stirring was continued at 25 °C for 8.5 h. The progress of the reaction was monitored by ^{1}H NMR of aliquots. The resulting solution was concentrated, and the solid precipitated was filtered and washed with dry acetone to afford **31** (0.33 g, yield 65%): mp 220–2 °C; ^{1}H NMR (CD_3OD) δ 4.03 (s, 3 H, Me-N), 4.49 (s, 3 H, Me-N^+), 7.32 (s, 1 H, H-5), 7.44 (s, 1 H, H-4), 7.82 (d, 1 H, H-α, J = 15.7 Hz), 7.95 (d, 1 H, H-β, J = 15.7 Hz), 7.97 (m, 1 H, H-5′), 8.58 (m, 1 H, H-4′), 8.71 (d, 1 H, H-3′, J = 8.2 Hz), 8.93 (d, 1 H, H-6′, J = 5.9 Hz); ^{13}C NMR (CD_3OD) δ 33.8 (CN), 46.9 (CN^+), 119.8 (C-β), 126.6 (C-3′), 127.0 (C-4,5), 128.6 (C-5′), 131.3 (C-α), 145.2 (C-2), 146.1 (C-4′), 147.6 (C-6′), 154.1 (C-2′).

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Supplementary Material Available: ^{1}H NMR data of compounds **16–27** and **28** (Table III), ^{13}C NMR data of compounds **16–27** and **28** (Table IV), ^{1}H NMR data of 1-alkylpyridinium iodides **10–15** (Table V); ^{13}C NMR data of 1-alkylpyridinium iodides **10–15** (Table VI), and elemental analyses of new compounds (Table VII) (6 pages). This material is contained in many libraries on microfiche, immediately follows this article in the microfilm version of the journal, and can be ordered from the ACS; see any current masthead page for ordering information.

(25) Pyridinium anhydrobases are implicated in many reactions of pyridinium cations.[13d,26]

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