# Heterocyclic Betaines. 19.[1] Unconventional Extended π-Systems Containing Pyridinium and Benzimidazolate Subunits. Synthesis and Characterization

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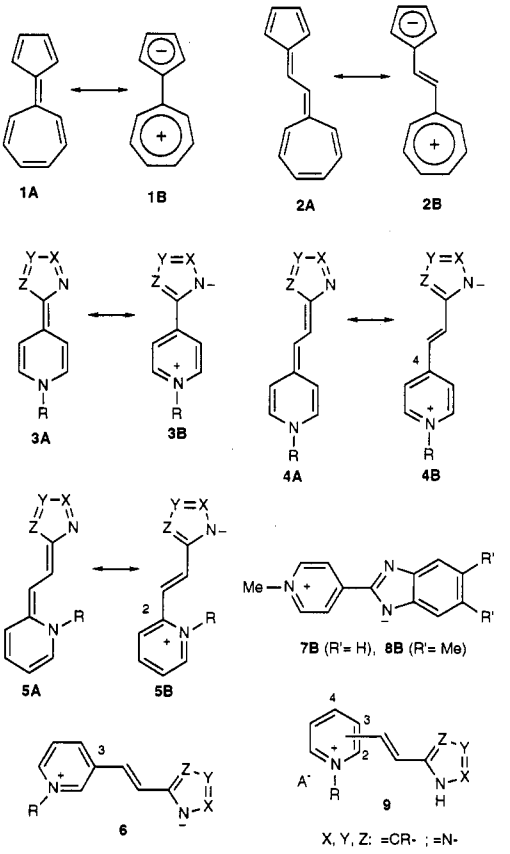
A convenient synthesis and characterization of several examples of (*E*)-2-[2-(1-alkyl-3-pyridinio)-vinyl]benzimidazolate inner salts and (*E*)-1-alkyl-2(or 4)-[2-(benzimidazol-2-ylidene)ethylidene]-dihydropyridines with a betaine character is reported. Their structural aspects are discussed mainly on the basis of the $^1$H NMR data and experimental dipole moment values (11.6–13.0 D). The experimental information available for (*E*)-1-alkyl-2(or 4)-[2-(benzimidazol-2-ylidene)ethylidene]-dihydropyridines (**A** ↔ **B**) is consistent with a betaine character, and the dipolar form (**B**) has been shown to make an important contribution to the ground state.

The background to the extended π-systems offers a fertile area of investigation, and the design of organic substrates with a molecular framework possessing a π-conjugated intramolecular donor–acceptor system is of practical interest.[2] Several push–pull (*E*)-stilbenes and diacetylenes,[3a] phenylpyridylacetylenes,[3b] and pyridinium *N*-phenolate betaines of the Reichardt type[3c] have been reported, and their properties as advanced materials were investigated. Moreover, the photophysical properties[3d,e] and photochemical transformations[3f–h] of (*E*)-stilbenes and their aza analogues are aspects of interest at present. Sesquifulvalene **1** (**A** ↔ **B**)[4a] and its vinylogous **2** (**A** ↔ **B**)[4b] may serve as reference compounds in developing novel cyclic cross-conjugated π-systems with large dipole moments (Chart 1). From the aza analogues of sesquifulvalene **3** (**A** ↔ **B**)[5] were obtained their corresponding vinylogues **4** (**A** ↔ **B**) along with **5** (**A** ↔ **B**) and **6**.

The electronic and molecular structures of several examples of type **3** (**A** ↔ **B**) were studied,[5] and their physicochemical properties indicate a significant contribution of the dipolar resonance structure **3B** to the ground state of **3**, i.e., **7B** and **8B**.[6] In this connection, we have designed[7,8] a novel ensemble of structures **4**–**6** in order to investigate the effect of a vinylene interannular linkage, leading to unconventional extended π-systems[2] with extremely electron-deficient and electron-rich moieties. Structures of type **4** and **5** can be described, at a first approximation, by a covalent resonance form (**A**) and a dipolar one (**B**), whereas structures of type **6** may only exist as betaines. In all cases their immediate precursors are the (*E*)-1-alkyl-2(3 or 4)-[2-(1*H*-azol-2-yl)vinyl]pyridinium salts **9**.[9]

**Chart 1**

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(4) (a) Prinzbach, H.; Knöfel, H.; Woischnik, E. *Aromaticity, Pseudo-Aromaticity, Anti-Aromaticity;* The Jerusalem Symposia on Quantum Chemistry and Biochemistry; The Israel Academy of Sciences: Jerusalem, 1971; Vol. III, p 269. (b) Babsch, H.; Prinzbach, H. *Tetrahedron Lett.* **1978**, 645.

(5) 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 cited therein.

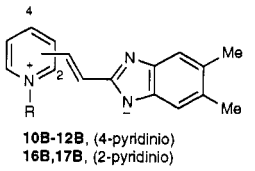
(6) A single-crystal X-ray diffraction analysis of compound **7** showed its betaine character, and the experimental dipole moment values were 9.03 D for **7** and 9.71 D for **8**.[5]

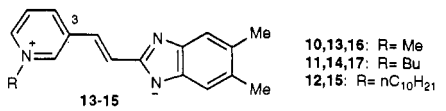
(7) For an earlier report on several examples of compounds **4** and **6**, which can also be considered aza analogues of (*E*)-stilbene, see: Alcalde, E.; Roca, T.; Fayet, J.-P.; Vertut, M.-C. *Chem. Lett.* **1991**, 2151.

(8) For some examples of compounds **4** and **5** in which the π-excessive moiety is an imidazole derivative, see: Alcalde, E.; Roca, T. *J. Org. Chem.* **1992**, *57*, 4834 and references cited therein.

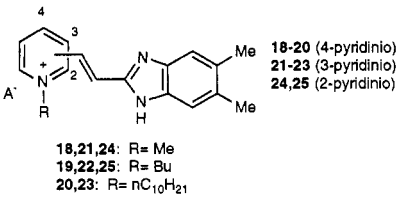
0022-3263/94/1959-0639$04.50/0 

In the present paper,[7] we report on the synthesis of several examples from series **4–6**, the (*E*)-1-alkyl-2(or 4)-[2-(benzimidazol-2-ylidene)ethylidene]dihydropyridines **10–12**, **16**, and **17** (**A** ↔ **B**) and (*E*)-2-[2-(1-alkyl-3-pyridinio)vinyl]benzimidazolate inner salts **13–15**. Their physicochemical properties are discussed mainly on the basis of the $^1$H NMR data, and experimental dipole moment values[7] are in the range of 11.6–13.0 D.



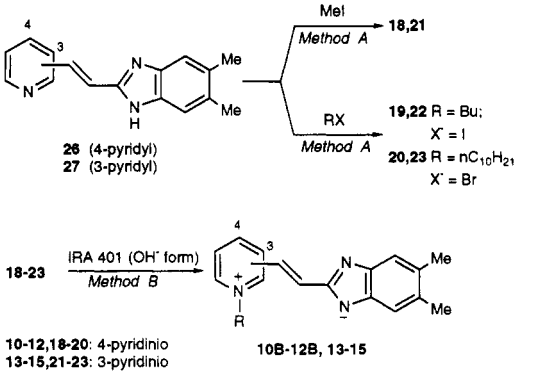

**Synthesis.** The (*E*)-1-alkyl-2(3 or 4)-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]pyridinium salts **18–25** are the immediate precursors of the target compunds **10–17**.




The (*E*)-2-(2-pyridylvinyl)-5,6-dimethyl-1*H*-benzimidazoles **26–28**[10] appeared to be the key intermediates for preparation of compounds **18–25** (see Schemes 1 and 2). By applying Hein's benzimidazole synthesis, compounds **26–28** have been previously reported.[15] The fact that the method could be adapted for synthesis of quaternary pyridinium salts **18–25** (i.e., **18** and **21**)[15] and related compounds[9c] is noteworthy.

The target compounds **10–15** were prepared by a three-step procedure (Scheme 1). Firstly, the intermediates **26** and **27** were obtained.[15] Then, *N*-alkylation under neutral conditions gave the 1-alkyl-4- (**18–20**) and 3-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]pyridinium salts **21–23** as the major products (see later and Experimental Section, method A). Transformation of compounds **18–23** into the (*E*)-1-alkyl-4-[2-(benzimidazol-2-ylidene)-ethylidene]-1,4-dihydropyridines **10–12** (compound **12** was found to be unstable)[16] and the (*E*)-2-[2-(1-alkyl-3-pyridinio)vinyl]benzimidazolate inner salts **13–15** was achieved using an anion-exchange Amberlite IRA-401 resin (OH$^-$ form)[17] giving **10**, **11**, and **13–15** in *ca.* 40% overall yield.

**Scheme 1**




To circumvent the polymethylation byproducts, compounds **18** and **21** were prepared by condensation of the corresponding 3-pyridinium acrylic acids and *o*-arylidenediamine using polyphosphoric acid.[15] In contrast, the reaction of compounds **26** and **27** with iodobutane and bromodecane under neutral conditions gave compounds **19**, **20** and **22**, **23** without problems of isolation or purification. Different reaction conditions in neutral media were assayed, and the best result is described (see Experimental Section, method A).

With regard to the compounds of type **5** (1,2-dihydropyridine ↔ 2-pyridinio), the compound pairs selected were **16**, **17** and **24**, **25**. The unknown (*E*)-1-alkyl-2-[2-(1*H*-benzimidazol-2-yl)vinyl]pyridinium salts **24** and **25** could theoretically be obtained by the method used for synthesis of compounds **18–23** mentioned above. This procedure was applied to the preparation of the 2-substituted pyridine derivatives with the anticipated steric and electronic interference to quaternization[11] of *ortho*-substituted pyridine derivatives.

Starting from (*E*)-2-[2-(2-pyridyl)vinyl]-5,6-dimethyl-1*H*-benzimidazole (**28**), the high selectivity of *N*-alkylation upon treatment with an iodoalkane (i.e., MeI, BuI) led to a single product **29** or **30**, which was then transformed to the neutral 1-alkyl-2-substituted benzimidazole counterpart **31** or **32** (Scheme 2).

Alternatively, Hein's modified protocol[15] for synthesis of compounds **24** and **25** is a reasonable approach. The hitherto unknown (*E*)-1-alkyl-2-(2-carboxyvinyl)pyridinium salts **34** and **35** are the starting materials for this method (Scheme 2). Then, alkylation of (*E*)-3-(2-pyridyl)-acrylic acid (**33**) provided the above-mentioned starting products **34** and **35** (or even **36**). The most representative *N*-alkylation experiments of **33** are collected in Table 1 (see supplementary material and Experimental Section, methods D–F). Condensation of (*E*)-1-alkyl-2-(2-carboxyvinyl)pyridinium salts **34** and **35** with 4,5-dimethyl-1,2-phenylenediamine gave the corresponding (benzimidazolylvinyl)pyridinium tetrafluoroborates **24** and **25**, which

(9) (a) The (*E*)-1-alkyl-2(3 or 4)-[2-(1*H*-azol-2-yl)vinyl]pyridinium salts **9** could also serve as model compounds to test their behavior as enzyme inhibitors, i.e., toward choline acetyltransferase[9b] or (H$^+$-K$^+$)-sensitive ATPase.[9c] (b) Alcalde, E.; Roca, T.; Barat, A.; Ramírez, G.; Goya, P.; Martínez, A. *BioMed. Chem. Lett.* **1992**, 1493. (c) Alcalde, E.; Pérez-García, Ll.; Frigola, J. *Chem. Pharm. Bull.* **1993**, *41*, 614..

(10) The 2-(2-pyridylvinyl)-1*H*-benzimidazoles **26-28** are attractive substrates owing to the presence of three annular nitrogen sp$^2$ atoms to which an alkylating agent[11] may be delivered. Nonetheless, the chemoselectivity on the alkylation of the multiple sites available in **26–28** is beyond the scope of the present study.

(11) Quaternization of aza aromatic molecules[12] (i.e., pyridines[13a]), a subclass of the Menschutkin reaction, and *N*-alkylation of azoles[13b] (i.e., benzimidazoles[14]) has been a matter of extensive investigation.

(12) Gallo, G.; Roussel, Ch.; Berg, U. *Adv. Heterocycl. Chem.* **1988**, *43*, 180–201 and references cited therein.

(13) (a) *Comprehensive Heterocyclic Chemistry*; Katritzky, A. R., Rees, C. W., Eds.; Pergamon Press: Oxford, 1984; Vol. II (Scriven, E.F.V.), pp 174–180. (b) Katritzky, A. R.; Lagowski, J. M. *Ibid.* Vol. V, pp 47–55.

(14) Barni, E.; Savarino, P. *J. Heterocycl. Chem.* **1979**, *16*, 1583 and references cited therein.

(15) Alcalde, E.; Dinarés, I.; Pérez-García, Ll.; Roca, T. *Synthesis* **1992**, 395 and references cited therein.

(16) Using the same procedure[17] (method B) with the (benzimidazolylvinyl)pyridinium salts **20** or **25**, an aliquot of the solid obtained was shown by $^1$H NMR to contain descomposition or alteration products, and the unstable compounds **12** or **17**, respectively, were not detected.

(17) The use of an ion-exchange Amberlite IRA-401 resin (OH$^-$ form) is the method of choice for the preparation of several examples of compounds **3**,[5] **4**,[8,9c] and **5**.[8]

**Scheme 2**

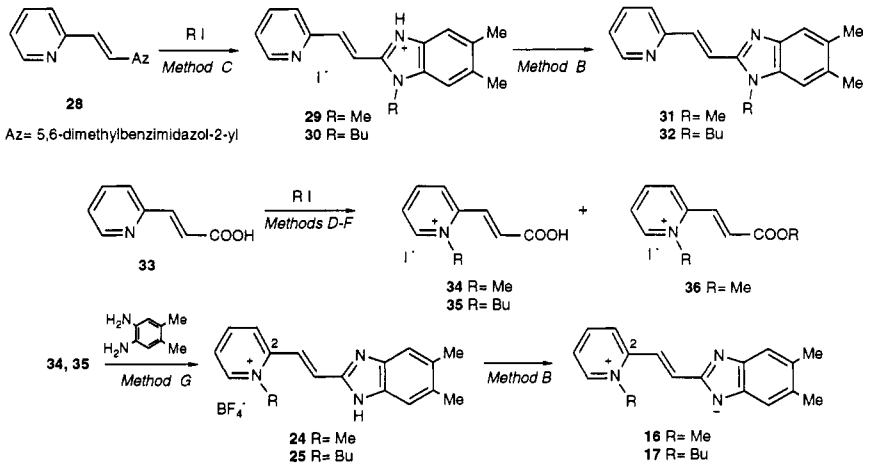



**Table 2. Physical Data of Compounds 10, 11, 13–16, 18–25, 29–32, and 34–36**

| compd[a] | method[b] (yield, %) | reactn time (h) | mp (solvent)[c] |
|---|---|---|---|
| **10** | B(99) | | 237–9 |
| **11** | B(96) | | 206 |
| **13** | B(99) | | 240–2 |
| **14** | B(92) | | 200–2 |
| **15** | B(96) | | 135–7 |
| **16** | B(83) | | 226–7 |
| **18** | A(64) | 33 | 262 (i) |
| **19** | A(42) | 32 | 265 (i) |
| **20** | A(34) | 47 | 232 (ii) |
| **21** | A(30) | 35 | 312–4 (i) |
| **22** | A(41) | 72 | 197 (iii) |
| **23** | A(37) | 120 | 225–6 (iv) |
| **24** | G(22) | 5 | 249–50 |
| **25** | H(34) | 44 | 136–8 |
| **29** | C(55) | 168 | 283–5 (i) |
| **30** | C(27) | 168 | 237–8 (i) |
| **31** | B(97) | | 128–30 |
| **32** | B(96) | | 82–3 |
| **34** | E(37)[d] | 336 | 213–4 |
| **35** | F(71)[d] | 144 | 160 |
| **36** | E(22)[d] | 336 | 163–4 |

[a] Satisfactory microanalysis obtained: C ± 0.4, H ± 0.4, N ± 0.4. [b] Yields were not optimized. [c] Recrystallization solvent: (i) acetonitrile; (ii) dichloromethane; (iii) chloroforme; (iv) ethanol. [d] See Table 1 in supplementary material.

were then deprotonated to afford compound **16**, whereas compound **17** was found to be unstable.[16]

Physical data of compounds **10, 11, and 13–16** and the (*E*)-1-alkyl-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]-pyridinium salts **18–25** are listed in Table 2 (see Experimental Section), and all gave satisfactory elemental analysis. They were characterized mainly on the basis of their $^1$H NMR data (see Tables 3 and 4) (Table 4 in the supplementary material). The title compounds **10, 11,** and **13–16** were air and light sensitive and easily altered or descomposed, even in the solid state.[18]

**Structural Properties.** Selected NMR spectral data for several examples of the new compounds described herein are summarized in Table 3 (Tables 4 and 5 in the supplementary material). Both the $^1$H and $^{13}$C NMR spectra were recorded for the (benzimidazolylvinyl)-pyridinium salts **18–25**, whereas only the $^1$H NMR parameters were available[18a] for the title compounds **10, 11, and 13–16**; individual assignments were made using the appropriate NMR experiments[19] (*vide infra*).

Thus, the $^1$H NMR data for compounds **10, 11,** and **13–16** were important for structural proof of their dipolar nature in solution,[19f,g] as they were for the previously reported examples of compounds of type **3**,[5] **4**,[8,9c] and **5**[8] with a betaine character, or other heterocyclic betaines.[5,20] Comparison of the chemical proton shifts observed[19f,g] of the (*E*)-[(benzimidazolylidene)ethylidene]dihydropyridines **10, 11,** and **16** or (pyridiniovinyl)benzimidazolate inner salts **13–15** with those of their corresponding (benzimidazolylvinyl)pyridinium salts **18, 19, 24,** or **21–23** (see $\Delta\delta$ in Tables 3 and 4) (Table 4 in the supplementary material), reveals a remarkably constant difference irrespective of the substitution pattern between the $\pi$-deficient moiety and the vinylene linkage.

The chemical shifts of the CH protons in the benzimidazole ring moved to lower frequencies (see $\Delta\delta$ H-4 and H-7 in Tables 3 and 4) (Table 4 in the supplementary material), indicating the change of electron density on the $\pi$-excessive nucleus and the anionic nature of the title compounds, in agreement with data reported for anionic species within benzimidazole systems.[5,9c,20] With regard to the $\pi$-deficient moiety of **10, 11,** and **13–16**, the $\delta$H values correspond to quaternary pyridinium structures.[5,8,9c,20]

The NMR results for the (*E*)-vinylene interannular spacer[21] deserve a brief comment. The assignments of the $\alpha$-CH and $\beta$-CH proton signals for (benzimidazolylvinyl)pyridinium salts **18–25** were made using the appropriate NMR techniques. Two-bond heteronuclear selective $^{13}$C{$^1$H} NOE difference[19d] and $^1$H–$^{13}$C heteronuclear shift correlation[19e] would both be expected to show well-resolved correlations. As to the HETNOE method, a

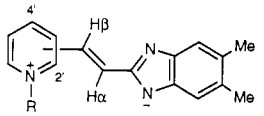
(18) (a) The instability of title compounds **10, 11,** and **13–16** in a solution of $(CD_3)_2SO$ and $CD_3OD$ precluded recording of their $^{13}$C NMR spectra. (b) In contrast, the aza analogues of a sesquifulvalene of type **3** (i.e., **7** and **8**) were quite stable.[5] Furthermore, the imidazole counterparts of type **4** and **5** recently reported[8] were fairly stable but less so than compounds **3**.

(19) (a) Unambiguous assignments have been made by SFORD,[19b] DEPT,[19c] HETNOE,[19d] heteronuclear multiple-quantum coherence (HMQC),[19e] and heteronuclear multiple-bond correlation (HMBC)[19e] techniques. (b) Breitmeier, E.; Voelter, W. *Carbon-13 NMR Spectroscopy*; VHC: Weinheim, 1987; p 47; (c) p 80. (d) Sánchez-Ferrando, F. *Magn. Reson. Chem.* **1985**, *23*, 185. (e) Summers, M. F.; Marzilli, L. G.; Bax, A. *J. Am. Chem. Soc.* **1986**, *108*, 4285. (f) $(CD_3)_2SO$ and $CD_3OD$ were previously dried with an activated molecular sieve (3 Å) to reduce the presence of water in the solvent. (g) The instability of **10, 11, 13–16** in solution precluded recording of their $^1$H NMR spectra in $(CD_3)_2SO$ or $CD_3OD$ with traces of a base (i.e., NaH or $Na^+CD_3O^-$). (h) Fruchier, A.; Pappalardo, L.; Elguero, J. *Anal. Quim.* **1980**, *76*, 79 and references cited therein.

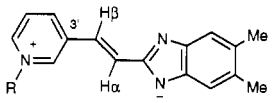
(20) Alcalde, E.; Pérez-Garcia, L.; Miravitlles, C; Rius, J.; Valentí, E. *J. Org. Chem.* **1992**, *57*, 4829 and references cited therein.

(21) Alcalde, E.; Roca, T.; Redondo, J.; Ros, B.; Serrano, J. L.; Rozas, I. *J. Org. Chem.*, following paper in this issue.

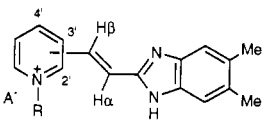
Table 3. Selected $^1$H NMR Data[19] of Compound Pairs 10, 18; 13, 21; and 16, 24[a]



10, 16



13



18, 21, 23

| compd | H-2′ | H-3′ | H-4′ | H-5′ | H-6′ | H-α | H-β | H-4,7 | $R^b$ |
|---|---|---|---|---|---|---|---|---|---|
| 10 | 8.62 | 8.08 | | 8.08 | 8.62 | 7.86 | 7.50[c] | 7.16 | 4.17 |
| 18 | 8.88 | 8.30 | | 8.30 | 8.88 | 7.86 | 7.71 | 7.39 | 4.27 |
| Δδ[d] | −0.26 | −0.22 | | −0.22 | −0.26 | 0.00 | −0.21 | −0.23 | −0.13 |
| 13 | 9.18 | | 8.65 | 7.97 | 8.65 | 7.58 | 7.42 | 7.12 | 4.29 |
| 21[e] | 9.32 | | 8.79 | 8.12 | 8.87 | 7.56 | 7.65 | $H_4$: 7.42<br>$H_7$: 7.31 | 4.36 |
| Δδ[d] | −0.14 | | −0.14 | −0.15 | −0.22 | +0.02 | −0.23 | −0.24[f] | −0.07 |
| 16 | | 8.34 | 8.30 | 7.62 | 8.55 | 7.83 | 7.75[c] | 7.35 | 4.32 |
| 24 | | 8.60 | 8.62 | 8.00 | 8.98 | 7.81 | 8.08[c] | 7.55 | 4.54 |
| Δδ[d] | | −0.26 | −0.32 | −0.38 | −0.43 | +0.02 | −0.33 | −0.20 | −0.22 |

[a] In $(CD_3)_2SO$ except for compounds 16 and 24 in $CD_3OD$. $J_{H\text{-}\alpha,H\text{-}\beta}$ in the range of 15.8–16.8 Hz. [b] Only δ for the α-protons to nitrogen are listed. [c] Assigned by comparison with data from analogous compounds.[8] [d] Δδ: observed chemical shifts difference between betaines or dihydropyridines and their (benzimidazolylvinyl)pyridinium salts. [e] At normal conditions (27 °C), anisochronous signals of benzimidazole H-4 and H-7 protons were observed owing to slow proton exchange between N-1 and N-3. NH proton signal *ca.* 12.7 ppm. [f] From the mean values of δ H-4 and δ H-7 in compound 21.

limiting factor is the narrow range in which the δH-α and δH-β appeared (at 100 MHz) and the difficulty of irradiating one of them. Thus, it was only possible to obtain a suitable HETNOE spectrum for compound 21 (in DMSO–TFAA as solvent, see Table 4 in supplementary material). However, HMBC and HMQC spectroscopy for compounds 19 and 22 clarified the situation; the coupling networks are mapped out in Figure 1 (see supplementary material). Assignment of the olefinic proton signals for the title compounds[18] was achieved by comparison with the spectral aspects of analogous compounds.[1b,8]

The signal of the α-CH proton to the π-excessive ring of compounds 10, 11, and 13–16 appeared in the range of −0.03 to +0.03 ppm, whereas the β-CH proton was shielded in the range of *ca.* −0.22 ppm for compounds 10, 11, and 13–15 and −0.33 for 16 compared with the same positional protons of the corresponding precursors 18, 19, and 21–24 (see $\Delta\delta_{H\text{-}\alpha}$ and $\Delta\delta_{H\text{-}\beta}$ in Tables 3 and 4 (Table 4 in the supplementary material)). Indeed, the nature of the heterocyclic ring systems modulated the overall proton chemical shifts, as shown in Table 3. Evidence of the dipolar nature in solution[19g,h] for the title compounds 10, 11, and 13–16 described herein was obtained from the $^1$H NMR measurements. Unfortunately, these compounds were not suitable for further structural studies due to their intrinsic instability.[18]

The electronic structure of the title compounds could be reflected in the dipole moment values. Owing to the perturbing influence of self-association,[5,8,20] different dipole moment measurements were determined as already described[5] for compounds 11 and 14. The best recorded values were found to be 11.9 D for 11 and 13.0 D for 14.[7] These large experimental dipole moments were extrapolated to extreme dilution[7] to reduce, as far as possible, the perturbing dominance of autoassociation (nonpolar dimers), with consequent decrease in the experimental values. However, the dipole moment observed for 11 (**A** ↔ **B**) is infrequent for organic substrates which are not formal zwitterions or betaines.[22]

Furthermore, the push–pull conjugated systems of type 4–6, and their immediate precursors 9, should present interest for science materials. Among the new molecules synthesized in the present work, compounds 11, 14, and 15 were selected for a preliminary study of their mesogenic behavior.[21] Unfortunately, none showed mesophase(s) deserving further study.

In conclusion, the experimental data for the hitherto unknown (*E*)-2-[2-(1-alkyl-3-pyridinio)vinyl]benzimidazolate inner salts 13–15 show their high dipolar structure in solution[21] (i.e., $\mu_{exp}$ of 14 ≥ 13.0 D). The experimental information available on the hitherto unknown (*E*)-1-alkyl-2(or 4)-[2-(benzimidazol-2-ylidene)ethylidene]dihydropyridines 10, 11, and 16 (**A** ↔ **B**) are consistent with a betaine character of these molecules (i.e., $\mu_{exp}$ of 11 ≥ 11.9 D), and their dipolar canonical forms **10B**, **11B**, and **16B** have been shown to make an important contribution to the ground state, as do other analogues of type 4[8,9c] and 5.[8] The dipolar structural pattern that characterizes these molecules may be used to design related unconventional extended π-systems[21] having two terminal heterocyclic rings with extreme characteristics within heteroaromatic systems: a π-deficient nucleus (cation) and a π-excessive nucleus (anion).

## Experimental Section

**General Methods.** Melting point: CTP-MP 300 hot-plate apparatus with ASTM 2C thermometer (given in Table 2). IR (KBr disks): Perkin-Elmer 1430 spectrophotometer. $^1$H NMR: Varian Gemini 200 and Bruker AM-100 spectrometers (200 MHz and 100 MHz). $^{13}$C NMR: Varian Gemini 200 and Bruker AM-100 spectrometers (50.2 MHz, and 25.1 MHz). SFORD[19b] and HETNOE:[19d] Bruker AM-100 spectrometer. HMQC and HMBC: [19e] Varian VXR-500 spectrometer. NMR spectra were determined in methanol-$d_4$[19f] and dimethyl-$d_6$ sulfoxide,[19f] and chemical shifts are expressed in parts per million (δ) relative to the central peak of methanol-$d_4$ or dimethyl-$d_6$ sulfoxide. TLC: Merck precoated silica gel 60 $F_{254}$ plates; detection by UV light. Flash chromatography (FC): Macherey Nagel silica gel Kiesegel 60. Ion-exchange resin: Amberlite 401 ($OH^-$ form).[8] 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.** (*E*)-2-[2-(4-Pyridyl)vinyl]-5,6-dimethyl-1*H*-benzimidazole (**26**),[15] (*E*)-2-[2-(3-pyridyl)vinyl]-5,6-dimethyl-1*H*-benzimidazole (**27**),[15] (*E*)-2-[2-(2-pyridyl)vinyl]-5,6-dimethyl-1*H*-benzimidazole (**28**),[15] and (*E*)-3-(2-pyridyl)acrylic acid (**33**)[18] were prepared as described in the literature, and 4,5-dimethyl-1,2-phenylenediamine is commercially available.

(22) Among several examples of compounds of type 5 previously reported in which the π-excessive ring is an imidazole,[8] the experimental dipole moment of (*E*)-1-methyl-2-[2-(imidazol-2-ylidene)ethylidene]-1,2-dihydropyridine was found to be ≥11.6 D.[7]

**Preparation of (*E*)-1-Alkyl-2(3 or 4)-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]pyridinium Salts 18–23 (Table 2). Method A.** Iodomethane (1.25 mL, 20 mmol) in dry acetonitrile (10 mL), iodobutane (2.3 mL, 20 mmol), or bromodecane (4.1 mL, 20 mmol) was added dropwise to a stirred solution of (*E*)-2-(2-pyridylvinyl)-5,6-dimethyl-1*H*-benzimidazoles **26** or **27** (1 g, 4 mmol) in dry acetonitrile (250 mL), under an atmosphere of nitrogen, and the mixture was then refluxed for the time specified in Table 2.

The resulting solution was concentrated, and a solid precipitated for compounds **18**, **21**, and **23**. The crude product was filtered and recrystallized twice (Table 2).

The reaction mixture of compounds **19**, **20**, or **22** was evaporated to dryness, and the oily residue was triturated with acetone (20 mL) for **19** and **20** or diethyl ether (20 mL) for **22**. The crude salts **19** and **22** were recrystallized twice (Table 2), while for compound **20** the residue was purified by FC (dichloromethane–ethanol (9.5:0.5)) and the eluates were evaporated to dryness and then recrystallized (Table 2).

**Preparation of (*E*)-1-Alkyl-2(or 4)-[2-(benzimidazol-2-ylidene)ethylidene]dihydropyridines 10, 11, and 16, (*E*)-2-[2-(1-alkyl-3-pyridinio)vinyl]benzimidazolate Inner Salts 13–15, and (*E*)-1-alkyl-2-[2-(2-pyridyl)vinyl]benzimidazoles 31 and 32 (Table 2). Method B.** An aqueous suspension of Amberlite resin IRA-401 hydroxide form was prepared.[8] A column (0.5-in. diameter) was packed with this aqueous suspension of IRA-401 ($OH^-$ form) up to a height of 5 in., and the column bed was equilibrated with the following eluants: 100% water (20 mL), 20% ethanol (20 mL), 70% ethanol (20 mL), and 96% ethanol (20 mL). A solution of (*E*)-1-alkyl-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]pyridinium salts **18–25** (*ca.* 200 mg) in ethanol (50 mL) was passed through the column. The eluates were evaporated to dryness, and the residue was triturated with diethyl ether (20 mL) to give orange to garnet solids of **10**, **11**, and **13–16**, which were air and light sensititve, while compounds **12** and **17** appeared to be unstable.[16]

The fact that lower yields were observed when this transformation was carried out at higher concentrations of the above-mentioned precursors **18–25** is noteworthy.

In similar experimental conditions, the (*E*)-1-alkyl-2-[2-(2-pyridyl)vinyl]-5,6-dimethylbenzimidazolium iodides **29** and **30** were transformed into compounds **31** and **32**, respectively (Table 2).

**Method C.** Iodomethane (2.25 mL, 36 mmol) in dry acetonitrile (10 mL) or iodobutane (3.45 mL, 30 mmol) was added dropwise to a stirred solution of (*E*)-2-[2-(2-pyridyl)vinyl]-5,6-dimethyl-1*H*-benzimidazole (**28**) (1.5 g, 6 mmol) in dry acetonitrile (275 mL), under an atmosphere of nitrogen, and the mixture was then refluxed for 1 week. The progress of the reaction was monitored by TLC (methanol/diethyl ether (8:2)). From the cooled reaction mixture a solid slowly precipitated, which was then concentrated. The crude compounds **29** and **30** were filtered and recrystallized twice (Table 2).

**Alkylation of (*E*)-3-(2-Pyridyl)acrylic Acid (33) (Tables 1 and 2). Method D.** Iodomethane (2.1 mL, 33.5 mmol) in dry methanol (10 mL) was added dropwise to a stirred solution of the (*E*)-3-(2-pyridyl)acrylic acid (**33**) (1 g, 6.7 mmol) in dry methanol (75 mL), under an atmosphere of nitrogen, and the reaction mixture was maintained at 65 °C for the time specified in Table1 (see supplementary material).

Methanol was evaporated (*ca.* 25 mL), and crude **34** slowly precipitated, which was then filtered and purified (Table 2). The filtrate was evaporated to dryness, and the starting pyridylacrylic acid **33** was recovered.

**Method E.** A suspension of compound **33** (2.5 g, 16.8 mmol) and iodomethane (15.7 mL, 252 mmol) or iodobutane (9.5 mL, 83.7 mmol) in dry methanol (50 mL) was kept in a sealed tube, and the reaction mixture was maintained at 55 °C for the time specified in Table 1. The progress of the reaction was monitored by TLC and $^1H$ NMR of aliquots.

From the reaction solution of **34**, methanol was evaporated (*ca.* 25 mL), and a yellow solid of **34** slowly precipitated, which was then filtered and washed in acetone (3 × 25 mL) (see Table 2). The filtrate resulting from the longer reaction (14 days, see Table 1) was evaporated to dryness, and the crude residue was washed in acetone (3 × 75 mL) to give compound **36** (see Table 1).

When the iodoalkane was iodobutane, the resulting reaction mixture was evaporated, and the solid residue was washed and stirred in acetone (50 mL) for 1 h and then filtered to give 1-methylpyridinium iodide **36** in low yield (Table 1). On concentration of the filtrate, an aliquot of the solid obtained was shown by $^1H$ NMR to contain the starting pyridylacrylic acid **33** as the main product. Curiously, no trace of compound **35** was detected by $^1H$ NMR. Owing to the behavior of the (*E*)-3-(2-pyridyl)acrylic acid (**33**) toward iodobutane in methanol, preparation of compound **35** was carried out using forced reaction conditions in DMF as solvent (*vide infra*, method F).

**Method F.** A solution of compound **33** (1 g, 6.7 mmol) and iodobutane (11.5 mL, 100.5 mmol) in dry DMF (30 mL) was kept in a sealed tube at 80 °C for 6 days. The reaction mixture was evaporated to dryness, the residue was dissolved in water (50 mL) and washed in dichloromethane (2 × 50 mL), and the aqueous solution was then evaporated. The crude product **35** was washed in acetone/diethyl ether (1:9) (50 mL), filtered, and dried (Tables 1 and 2).

**Preparation of (*E*)-1-Alkyl-2-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]pyridinium salts 24 and 25 (Table 2). Method G.** In a dry, $N_2$-filled three-necked flask fitted with a stirrer were suspended 4,5-dimethyl-1,2-phenylenediamine (0.31 g, 2.25 mmol) and (*E*)-1-alkyl-2-(2-carboxyvinyl)pyridinium salts **34** ($BF_4^-$)[23] or **35** ($I^-$) (2.25 mmol) in PPA (15 g), and this suspension was heated in a bath at 160 °C for the time specified in Table 2. The cooled mixture was poured into ice–water (50 mL), and the resulting solution was treated with solid $Na_2CO_3$ to pH 8. The suspension was filtered, and the solution was then acidified with 50% $HBF_4/H_2O$ to reach pH 6. Precipitated pyridinium salt **24** or **25** was filtered, washed with water (3 × 10 mL) and dried (Table 2). Compound **25** was very unstable in solution.

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**Supplementary Material Available:** Heteronuclear multiple bond correlation spectra (HMBC) of compounds **19** and **22** (Figure 1), alkylation assays of (*E*)-3-(2-pyridyl)acrylic acid **33** (Table 1), $^1H$ NMR data of compounds **10**, **11**, **13–16**, and **18–25** (Table 4), selected $^{13}C$ NMR data of (*E*)-1-alkyl-2(3 and 4)-[2-(5,6-dimethyl-1*H*-benzimidazol-2-yl)vinyl]pyridinium salts **18–25** (Table 5), selected $^1H$ and $^{13}C$ NMR data of compounds **29–32** in DMSO-$d_6$ (Table 6), and elemental analysis of new compounds (Table 7) (6 pages). This material is contained in 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.

(23) **34**($I^-$) was converted to **34**($BF_4^-$) in order to avoid demethylation of the pyridinium iodide under the reaction conditions required in Hein's benzimidazole synthesis[15] (method G). Then, the (*E*)-2-(2-carboxyvinyl)-1-methylpyridinium iodide (**34**) in ethanol was passed through a column with IRA-401 ($Cl^-$ form). The eluate was treated with a few drops of 50% $HBF_4$–$H_2O$ (to reach pH 6) giving compound **34** as its tetrafluoroborate salt, checked only by IR.