1660, 1460, 1340 (SO_2N), 1305, 1220, 1155 (SO_3), 1115 (SO_2N), 1045 (SO_3), 945, 855, 760, 655 (SO_3) cm^{-1}; ^1H NMR (DMSO-d_6) δ 2.23 (s, 3 H, CH_3), 4.48 (s, 2 H, CH_2), 7.19 (d, 2 H, Ar *H*, *J* = 8.1 Hz), 7.27-7.46 (m, 7 H, Ar*H*), 7.57 (d, 1 H, Ar *H*, *J* = 7.8 Hz), 7.87 (d, 1 H, Ar *H*, *J* = 8.4 Hz), 7.90 (d, 2 H, Ar *H*, *J* = 8.0 Hz), 8.27 (d, 1 H, Ar *H*, *J* = 7.3 Hz), 8.95 (br s, 2 H, NH_2), 9.20 (br s, 2 H, NH_2), 12.82 (s, 1 H, N*H*); ^{13}C NMR (DMSO-d_6) δ 20.9, 34.3, 116.0, 120.9, 124.4, 124.5, 125.6, 127.5, 128.0, 128.1, 128.9, 129.0, 129.2, 131.9, 133.6, 134.9, 135.9, 136.6, 141.7, 143.0, 169.0. Anal. Calcd for $C_{25}H_{25}N_3O_5S_3$: C, 55.23; H, 4.63; N, 7.73. Found: C, 55.26; H, 4.67; N, 7.75.

Acknowledgment. We acknowledge generous support from the National Science Foundation for Grant CHE 8308245 to K.K.A. and for Grants CHE 7908399 and CHE 86 14606 enabling purchase of UV and NMR spectrometers, respectively; from the U.S. Department of Defense for Grant US DOD DAAL03-88-G-0100 enabling purchase of a mass spectrometer; and from the Central University Research Fund of the University of New Hampshire to G.J.H. We thank Dr. Achim Gerhard for assistance in conducting the high pressure kinetics experiments and Professor Dr. R. van Eldik of the University of Witten/Herdecke, Germany, for access to the instrument and for hospitality (C.D.H.).

Registry No. **1a**, 107555-82-8; **1b**, 136061-81-9; **1c**, 136061-82-0; **1d**, 136061-83-1; **1e**, 136061-84-2; **1f**, 136061-85-3; **1g**, 136061-86-4; **b**, 3897-39-0; **7**, 70376-37-3; **8a**, 136061-87-5; **8b**, 136061-96-6; **9**, 136061-92-2; **10**, 136061-95-5; **11**, 136061-98-8; **12**, 109593-01-3; **13**, 603-72-5; **14**, 136061-97-7; **15a**, 136088-51-2; **19**, 130955-98-5; **19**·$PhCH_2SC{=}NH(NH_2)$, 136061-99-9; **28**, 136061-93-3; **29**, 136061-94-4; **30**, 81256-17-9; SO_2Cl_2, 7791-25-5; C_6H_5Li, 591-51-5; CH_3Li, 917-54-4; CH_3NH_2, 74-89-5; *t*-$BuNH_2$, 75-64-9; CH_3ONa, 124-41-4; KF, 7789-23-3; $C_6H_5SO_2C_6H_4$-4-CH_3, 640-57-3; $CH_2(S{-}O_2C_6H_4$-4-$CH_3)_2$, 15310-28-8; $C_6H_5OSO_2NHC_6H_5$, 85599-60-6; $C_6H_5CH_2SC{=}NH(NH_2)$·HCl, 538-28-3; *N*-(2-hydroxy-5-methylphenyl)-4-toluenesulfonamide, 81256-11-3; *N*-(5-*tert*-butyl-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-88-6; *N*-(5-bromo-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-89-7; *N*-(5-chloro-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-90-0; *N*-(5-acetyl-2-hydroxyphenyl)-4-toluenesulfonamide, 136061-91-1; *N*-(2-hydroxy-5-nitrophenyl)-4-toluenesulfonamide, 91956-17-1; *N*-(2-hydroxy-4-nitrophenyl)-4-toluenesulfonamide, 91956-16-0; 1-naphthylamine-8-sulfonic acid, 82-75-7.

An Efficient Synthesis of 2-Vinylbenzimidazoles from 1-(2-Benzimidazol-2-ylethyl)pyridinium Salts Using an Anion-Exchange Resin

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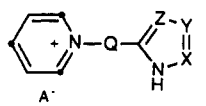
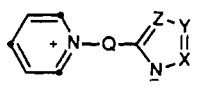
Transformation of several 1-(2-benzimidazol-2-ylethyl)pyridinium salts, obtained by two different procedures, into their corresponding 2-vinylbenzimidazoles either using an anion-exchange resin (OH^- form) or in the solid state is described. This approach now allows a facile entry into the almost unknown 2-vinylbenzimidazole monomers.

As part of an ongoing research project in the quest for novel organic substrates with large dipole moments, we have reported[1,2] the transformation of *N*-azolylpyridinium **1** and (azolylmethyl)pyridinium salts **2** into their corresponding heterocyclic betaines **3** and **4**.[3] A logical extension of the preceding studies is to consider an ethylene moiety as the interannular linkage, leading to the (azolylethyl)pyridinium salts **5**, potential precursors of ethylenepyridinium azolate inner salts **6**.



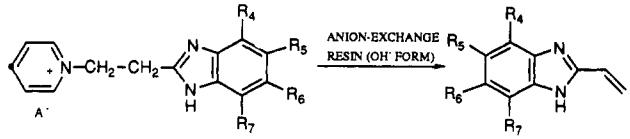


1 Q: -
2 Q: CH_2
5 Q: CH_2CH_2

3 Q: -
4 Q: CH_2
6 Q: CH_2CH_2

X, Y, Z: = CR-; =N-
•: = CR-

During the course of this investigation it became apparent that the almost unknown title pyridinium salts **7** could be efficiently prepared by two methods which have sufficient flexibility to allow conveniently substituted benzimidazoles to be generated from a variety of *o*-arylenediamines. Once synthesis was achieved, this class of pyridinium salts **7** was quantitatively transformed at room temperature into the corresponding 2-vinyl-1*H*-benzimidazoles **8** using an anion-exchange resin (OH^- form).



7 **8**

To the best of our knowledge, only three 2-vinyl-1*H*-benzimidazoles and a few 1-alkyl derivatives have been described since the work of Bachman,[4] seeking 2-vinyl

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(1) (a) Alcalde, E.; Dinarés, I.; Elguero, J.; Fayet, J.-F.; Vertut, M. C.; Miravitlles, C.; Molins, E. *J. Org. Chem.* **1987**, *52*, 5009. (b) Alcalde, E.; Dinarés, I.; Elguero, J.; Frigola, J.; Osuna, A.; Castanys, S. *Eur. J. Med. Chem.* **1990**, *25*, 309.

(2) Alcalde, E.; Pérez, L.; Fayet, J.-P.; Vertut, M.-C. *Chem. Lett.* **1991**, 845.

(3) The method of choice for this transformation was found to be the use of an anion-exchange Amberlite IRA-401 resin (OH^- form) in over 90% yield and also applied to other betaines or compounds with a betaine character.

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Scheme I. Method A

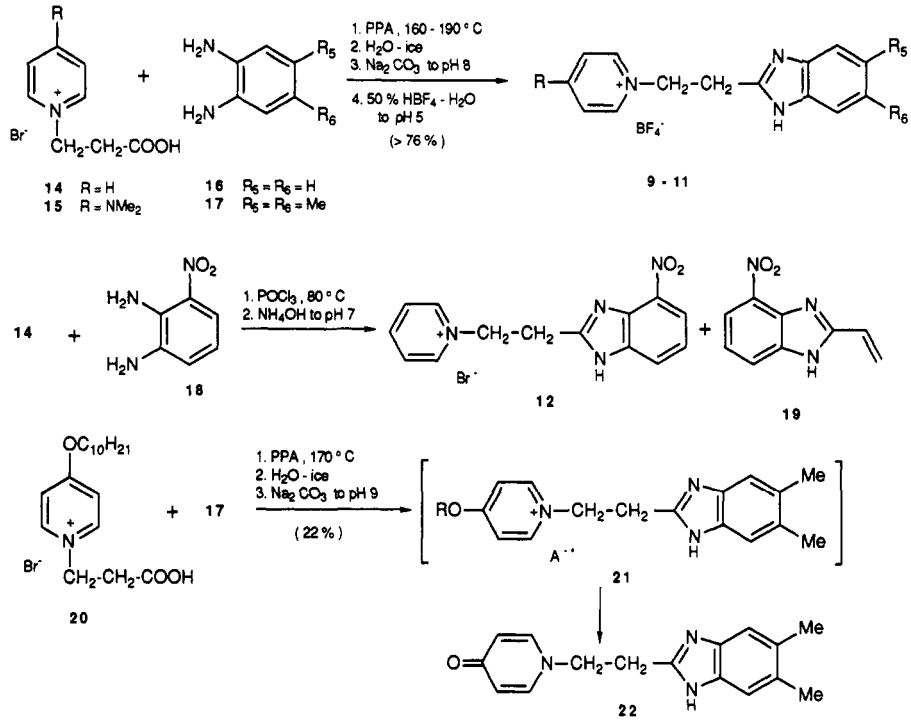


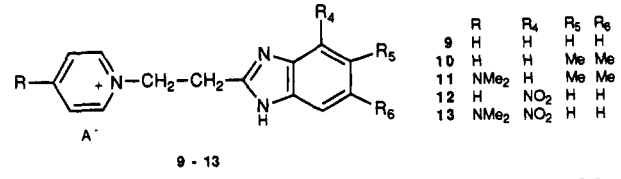
Table I. Physical Data of 1-(2-1*H*-Benzimidazolylethyl)pyridinium Salts 9–13 and 2-Vinyl-1*H*-benzimidazoles 19, 31, and 32

compd[a]	R	R_4	R_5	R_6	A^-	method[b] (yield, %)	mp[c] (°C)	reaction time (h)	TLC[d]
9	H	H	H	H	BF_4^-	A (71)	183–4	4	A
10	H	H	Me	Me	BF_4^-	A (82)	161–3	4	A
11	NMe_2	H	Me	Me	BF_4^-	A (80)	189–90	28	A
12	H	NO_2	H	H	Cl^-	B (20)	218–20	2	B
13	NMe_2	NO_2	H	H	Cl^-	B (39)	220	4	B
31		H	H	H		C (95)	203–4		B
						D (59)[e]	184	3	B
32		H	Me	Me		C (99)	174–5		B
19		NO_2	H	H		C (d)	*d*		B

[a] Satisfactory analytical data (±0.4% for C, H, N) were obtained for new compounds. [b] Yields were not optimized. [c] 2-Vinylbenzimidazole (31) has been described, mp 186–7 °C.[5b] [d] See Experimental Section. [e] Overall yield (see Experimental Section).

derivatives of π-excessive heteroaromatic compounds and their polymeric materials. This fact is probably due to their lability, which prevents isolation as monomers. For a successful synthesis of the thermolabile 2-vinylbenzimidazoles it is necessary to avoid conditions which allow polymerization, i.e., by means of a Wittig reaction from 2-(chloromethyl)benzimidazoles.[5a] In contrast, the chemistry of quaternary pyridinium compounds has been widely studied.[6,7]

Synthetic methods leading to 2-substituted benzimidazoles by reaction of *o*-arylenediamines with carboxylic acids—Phillips synthesis[8-10]—are widely applicable, whereas the use of an acyl chloride, instead of the carboxylic acid, is limited to only a few examples.[8] We selected both procedures for synthesis of the new 1-(2-1*H*-benzimidazol-2-ylethyl)pyridinium salts **9–13**.



A convenient modification of the Phillips method has been applied[8] to preparation of the new benzimidazolyl-

(4) Bachman, B. G.; Heisey, L. V. *J. Am. Chem. Soc.* **1949**, *71*, 1985 and references quoted therein.

(5) (a) Popov, I. I.; Narezhnaya, V. N.; Zubenko, A. A. *Khim. Geterotsikl. Soedin.* **1978**, 1104 and references cited therein. (b) Popov, I. I.; Simonov, A. M.; Zubenco, A. A. *Khim. Geterotsikl. Soedin.* **1976**, 1145.

(6) The use of pyridines as leaving groups.[7] Studies of the reactions of N-substituted pyridinium salts,[7] e.g., nucleophilic attack, formation of olefins.

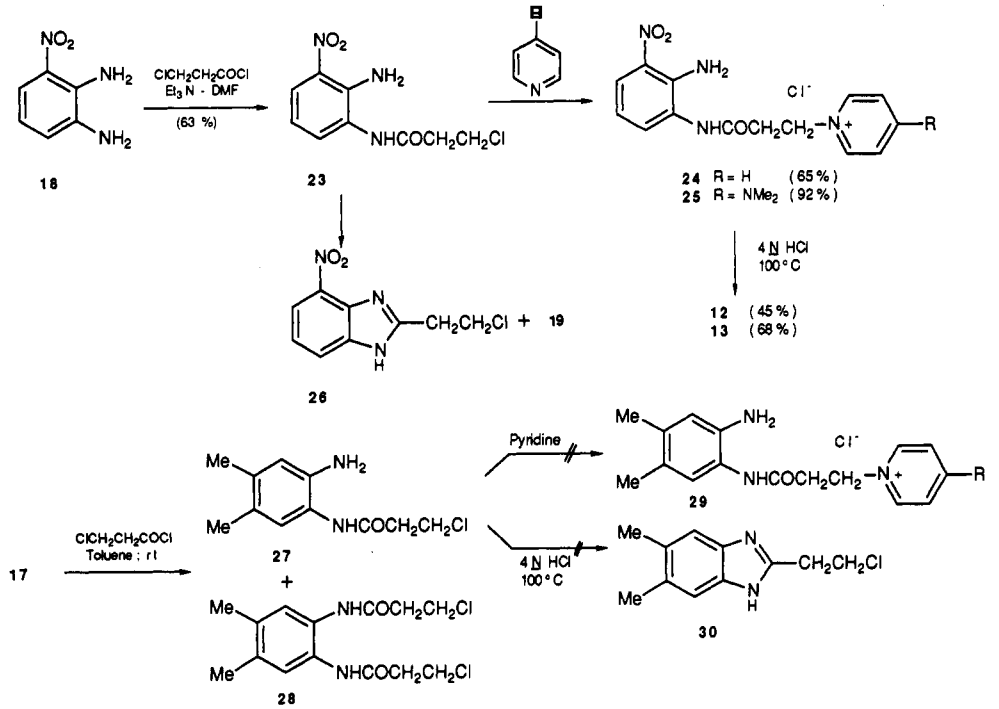
(7) (a) Katritzky, A. R.; Musumarra, G. *Chem. Soc. Rev.* **1984**, *13*, 47. (b) Katritzky, A. R.; El-Mowafy, A. M. *J. Chem. Soc., Chem. Commun.* **1981**, 96. (c) Gallo, G.; Roussel, Ch.; Berg, U. *Adv. Heterocycl. Chem.* **1988**, *43*, 278. (d) Katritzky, A. R.; Marson, Ch. M. *Angew. Chem., Int. Ed. Engl.* **1984**, *23*, 420. (e) Dorofeenko, G. N.; Zvezdina, E. A.; Zhdonova, M. P.; Barchan, I. A. *Khim. Geterotsikl. Soed.* **1973**, 1682.

(8) (a) Preston, P. N. *Chem. Heterocycl. Compds.* **1981**, *40*(1), 6–13 and references cited therein. (b) Since the work of Hein et al., there are several reports of the use of polyphosphoric acid (PPA) as the catalyst and solvent in condensations of the type found in Phillips synthesis.[8a] Nonetheless, there is an obvious lack of literature precedents where an ammonium quaternary salt moiety is present in the carboxylic acid derivative,[8c] as is the case for compounds **14** and **15**. (c) Venkataramu, S. D.; Macdonell, G. D.; Purdum, W. R.; Dilbeck, G. A.; Barlin, K. D. *J. Org. Chem.* **1977**, *42*, 2195 and references cited therein.

(9) It was previously reported[10] for synthesis of two 1-[2-(1*H*-benzimidazol-2-yl)ethyl]-4-methylpyridinium bromides using 2 N hydrobromic acid (yield ca. 21%), although the Phillips method results in a low overall yield.

(10) Elguero, J.; Katritzky, A. R.; El-Osta, B. S.; Harlow, R. L.; Simonsen, S. H. *J. Chem. Soc., Perkin Trans. 1* **1976**, 312 and references cited therein.

Scheme II. Method B

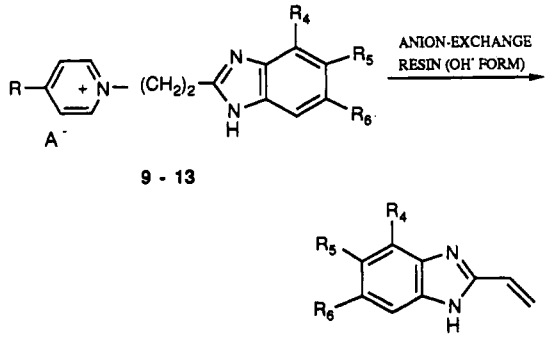


pyridinium salts **9–11**, but not to the 4-nitrobenzimidazole derivatives,[11] i.e., **12**. The reaction conditions leading to compounds **9–11** in satisfactory yields are shown in Scheme I. The choice of the basic medium and posterior treatment with 50% HBF_4–H_2O are the most critical points of the process.

With regard to the reaction of 1-(2-carboxyethyl)-4-(decyloxy)pyridinium bromide (**20**) and *o*-arylenediamine **17** in similar experimental conditions, at 170 °C, as for the above-mentioned compounds **9–11** (see Scheme I and Experimental Section), this proceeded with formation of the 4-pyridone **22** along with decomposition products. Unfortunately, the (benzimidazolylethyl)pyridinium salt **21** was not isolated, and these were therefore not further studied.[12]

Alternatively, the preparation of [(4-nitrobenzimidazolyl)ethyl]pyridinium salts **12** and **13** was performed by the three-step procedure shown in Scheme II. This approach is mostly limited to a handful of *o*-arylenediamines, one of which is compound **18** used in the present study. The key intermediates **24** and **25** were treated with 4 N hydrochloric acid (classical Phillips conditions)[13] and afforded compounds **12** (45%) and **13** (68%). An aliquot of the reaction mixture was shown by ^1H NMR to contain compound **12** or **13** as the main product along with 2-vinyl-4-nitrobenzimidazole (**19**) and unidentified products.

Scheme III



	R_4	R_5	R_6
19	NO_2	H	H
31	H	H	H
32	H	Me	Me

On the other hand, the *o*-aminobenzanilide **23** was treated with 4 N hydrochloric acid to give a mixture of compound **19** and the unstable 2-(2-chloroethyl)-4-nitro-1*H*-benzimidazole (**26**), which was slowly transformed to **19** in the solid state and quite easily upon recrystallization (see Experimental Section).

In contrast, reaction of the *o*-arylenediamine **17** with 3-chloropropionyl chloride gave a mixture of the corresponding monoacyl **27** and diacylamides **28**. Their isolation was very difficult and took place in low yields (see Experimental Section). Moreover, the *o*-aminobenzanilide **27** was not cyclodehydrated to 2-(2-chloroethyl)-5,6-dimethyl-1*H*-benzimidazole (**30**) or transformed to the key intermediate **29** in the same experimental conditions as for *o*-aminobenzanilide **23**. Only decomposition products could be detected by ^1H NMR spectroscopy and TLC, and these were not further studied.

Finally, transformation of the aforementioned (benzimidazolylethyl)pyridinium salts **9–13** using an anion-exchange IRA-401 resin (OH^- form) afforded the 2-vinylbenzimidazoles **19**, **31**, and **32** in quantitative yields (see Scheme III and Experimental Section). Furthermore,

(11) Only polymeric material was isolated, even when the reaction was carried out at 100 °C, probably due to the oxidative effect of the nitro group under the reaction conditions.[8] Using $POCl_3$ at 80 °C as the cyclodehydrating agent (Scheme I) formation of compounds **12** and **19** was detected (in a small proportion) along with secondary products.

(12) Formation of 4-pyridone **22** shows that method A is suitable for generation of the benzimidazole nucleus. Nonetheless, the alkoxypyridinium salt **21** is unstable under the reaction conditions (acid medium and high temperatures) and transformed to compound **22** by a *O*-alkyl cleavage which is acid promoted.

(13) For other examples of preparation of 2-substituted benzimidazoles from *o*-aminobenzanilides, see: (a) Morgan, K. J.; Turner, A. M. *Tetrahedron* **1969**, *25*, 915. (b) Le Bris, M.-T. *Bull. Soc. Chim. Fr.* **1967**, 3411. (c) Shcheltsyn, V. K.; Kaminskii, A. Ya.; Shapirovskaya, T. P.; Vaisman, I. L.; Andrianov, V. F.; Gitis, S. S. *Khim. Geterosikl. Soed.* **1973**, 115. (d) Malichenko, N. A.; Krasnoshchek, A. P.; Medvedeva, T. P.; Yagupolskii, L. M. *Khim. Geterosikl. Soed.* **1976**, 1262.

Table II. Selected ^1H NMR Data of Compounds 9–13 and 19, 31, and 32[a]

compd	H-2,6	H-3,5	H-4	CH_2	CH_2–N^+	H-4′,7′	H-6′,5′
9	9.04	8.19	8.65	3.61	5.09	7.78	7.50
10	9.00	8.18	8.64	3.77	5.06	7.55	
11	8.17	7.03		3.61	4.63	7.57	
12	9.18	8.15	8.61	3.76	5.17	H-7′: 8.04	H-5′: 8.14
							H-6′: 7.42
12[b]	9.19	8.31	8.83	4.27	5.46	H-7′: 8.27	H-5′: 8.35
							H-6′: 7.75
13	8.37	7.02		3.61	4.74	H-7′: 8.08	H-5′: 8.16
							H-6′: 7.45
13[b]	8.03	6.79		3.70	4.79	H-7′: 8.09	H-5′: 8.35
							H-6′: 7.69
				=CH	$=CH_2$		
31				6.77	6.24	7.13	7.52
					5.62		
32				6.72	6.18	7.29	
					5.59		
32[c]				6.83	6.23	7.35	
					5.55		
19				6.96	6.55	H-7′: 8.06	H-5′: 8.10
					5.79		H-6′: 7.39

[a] In DMSO-d_6. [b] In D_2O. [c] In $CDCl_3$.

these pyridinium salts, especially the unsubstituted pyridinium derivatives **9**, **10**, and **12**, were slowly transformed in the solid state to their corresponding 2-vinylbenzimidazoles.[14]

Physical data of the title compounds **9–13** and **19**, **31**, and **32** are listed in Table I. The structures of all of them have been unambiguously characterized on the basis of their spectroscopic data and for new compounds gave satisfactory elemental analysis. Selected ^1H NMR chemical shifts are shown in Table II. The ^1H and ^{13}C NMR data for all new compounds described are given in Tables III–V (see supplementary material). Moreover, in some instances the carbon-13 chemical shifts were very important for elucidating their structure, i.e., compound **24**.

In conclusion, these results illustrate an example of the versatile use of simple *N*-pyridinium salts as leaving groups, in a special type of β-elimination under mild conditions and at room temperature. This approach allows a practical synthesis of the almost unknown 2-vinylbenzimidazole monomers.

Experimental Section

General Methods. Melting point (uncorrected): CTP-MP 300 hot-plate apparatus (given in Table I). IR (KBr discs): Perkin-Elmer 1430 spectrophotometer. ^1H NMR: Varian XL-200, Bruker AM-100, or Perkin-Elmer R-24B spectrometer (200, 100 and 60 MHz, respectively). ^{13}C NMR: Bruker AM-100 Fourier transform spectrometer (25.1 MHz). NMR spectra were determined in dimethyl-d_6 sulfoxide, and chemical shifts are expressed in parts per million (δ) relative to TMS as internal standard or the central peak of dimethyl-d_6 sulfoxide. EIMS: Finnigan TSQ-70 and Hewlett-Packard 5988A spectrometer. Distillation: Büchi GKR-50 Kugelrohr apparatus. TLC: Merck silica gel 60 F_{254} plates; solvent systems, A, methanol–water (1:1); B, chloroform–methanol (8:2); detection by UV light. Flash chromatography (FC): Macherey Nagel silica gel Kiesegel 60. Ion-exchange chromatography: Amberlite IRA-401 (OH^- form).[1] If necessary, the compounds were dried by heating overnight at 25 °C in a vacuum oven. Where microanalyses are indicated by symbols of the elements, the analytical results were within ±0.4% of the theoretical values (see Table V); they were performed on a Carlo Erba 1106 analyzer by the Centro de Investigación y Desarrollo, CSIC, Barcelona.

Materials. 4-Chloropyridine hydrochloride, 1,2-diaminobenzene (**16**), and 1,2-diamino-4,5-dimethylbenzene (**17**) are commercially available. 1,2-Diamino-3-nitrobenzene (**18**)[15] and 2-(chloromethyl)-1*H*-benzimidazole (**33**)[16] were prepared as in the literature.

Preparation of 1-(Carboxyethyl)pyridinium Bromides 14 and 15. A stirred solution of pyridine or 4-(dimethylamino)-pyridine (3.27 mM) and 3-bromopropionic acid (3.27 mM) in anhydrous acetonitrile (8 or 65 mL) was refluxed under an atmosphere of nitrogen for 4.5 or 30 h.

A white solid was obtained after cooling (**15**) or by addition of acetone (20 mL) to the resulting solution (**14**). The crude product was filtered, washed with acetone (2 × 10 mL) or diethyl ether (3 × 10 mL), and dried to give 7.0 g (91%) of **14** or 7.5 g (83%) of **15**. Compound **14**: mp 138–9 °C (lit.[17] mp 145–6 °C). Compound **15**: mp 177 °C.

Preparation of 1-(2-1*H*-Benzimidazol-2-ylethyl)-pyridinium Salt 9–13 and 2-Vinyl-1*H*-benzimidazoles 19, 31, and 32 (Table I). Method A. A stirred suspension of *o*-arylenediamine **16** or **17** (8.6 mM) and 1-(2-carboxyethyl)-4-substituted pyridinium bromide **14** or **15** (8.6 mM) in PPA (20g) under an atmosphere of nitrogen was heated at 160–90 °C (bath temperature) for the time specified in Table I. The cooled mixture was poured into ice–water (200 mL), and the resulting solution was treated with solid sodium carbonate to reach pH 8. This solution was then acidified with 50% HBF_4–H_2O to pH 5, and the solid was filtered, washed with water (2 × 25 mL), and dried (Table I).

Following the same experimental procedure, equimolecular amounts of compounds **14** and **18** in PPA were heated at 100 °C for 24 h. The reaction mixture was worked up and only polymeric material was isolated.

Method B. 3-Chloropropionyl chloride (0.62 mL, 6.5 mM) was added dropwise at 5 °C to a solution of 1,2-diamino-3-nitrobenzene (**18**; 1.0 g, 6.5 mM) and triethylamine (0.62 mL, 6.5 mM) in anhydrous DMF (15 mL) under an atmosphere of nitrogen, and stirring was continued at rt for 4 h. The reaction mixture was filtered to remove insoluble materials, and the filtrate was evaporated at 50 °C (1.33 mbar) to dryness. The oily residue was triturated with water (30 mL), and the crude orange product **23** was filtered, washed with water (2 × 15 mL), and dried to give 1.0 g (63%) of **23**; mp 128–30 °C.

A stirred solution of compound **23** (2.0 g, 8.2 mM) in anhydrous pyridine (2.6 mL, 32.8 mM) under an atmosphere of nitrogen was heated in a bath at 100 °C for 10 h. After the solution was cooled, acetone (20 mL) was added and the mixture triturated to give

(14) The instability of the salts **9–12** in solution (e.g., alcohols, acetonitrile, DMSO) precluded their recrystallization. Under these conditions they were transformed into either the 2-vinyl derivatives **19**, **31**, or **32** or their polymeric materials.

(15) Rabinowitz, J. L.; Wagner, E. C. *J. Am. Chem. Soc.* **1951**, *73*, 3030.
(16) Lettré, H.; Fritsch, W.; Porath, J. *Chem. Ber.* **1958**, 719.
(17) De Berre, A.; Delacroix, A. *Bull. Soc. Chim. Fr.* **1973**, 2404.

an orange solid which was then filtered, washed with acetone (2 × 5 mL), and dried. Recrystallization from acetonitrile afforded 1.6 g (65%) of **24**: mp 180 °C.

To a stirred solution of compound **23** (1g, 4.1 mM) in anhydrous DMF (4 mL) was added dropwise anhydrous DMAP (1.5 g, 12.3 mM) under an atmosphere of nitrogen and the mixture heated in a bath at 100 °C for 1 h. The resulting orange precipitate was filtered, washed with diethyl ether (2 × 10 mL), and dried. Recrystallization from acetonitrile–ethanol (5:1) provided 1.38 g (92%) or **25**; mp 235 °C.

A suspension of compound **24** or **25** (3.8 mM) in 4 N HCl (11.4 mL, 45.6 mM) was heated in a bath at 100 °C for the time specified in Table I. The resulting solution was concentrated to dryness, and acetone (10 mL) was then added. The precipitate was filtered and washed with acetone (2 × 5 mL). The crude product **12** was washed several times with anhydrous acetonitrile and ethanol, and the crude product **13** was recrystallized from ethanol (Table I).

Method C. A column packed with anion-exchange Amberlite resin IRA-401 was used, and the chloride form was converted to the hydroxide form.[1] A solution of the (benzimidazolylethyl)-pyridinium tetrafluoroborates **9**, **10**, or **11** (0.5 mM) in 80% ethanol (50 mL) was passed through the column. The neutral eluates were concentrated in a rotary evaporator at 25 °C to give a solid, which was then washed with diethyl ether (3 × 2 mL) and filtered to give the corresponding 2-vinyl-1*H*-benzimidazole **31** or **32** (Table I).

Using the same procedure with the (benzimidazolylethyl)-pyridinium chloride **12**, an aliquot of the solid obtained was shown by ^{1}H NMR to contain 4-nitro-2-vinyl-1*H*-benzimidazole (**19**) as the main product (ca. 34%), along with decomposition or alteration products.[18] Unfortunately, compound **19** could not be isolated analytically pure after several attempts of recrystallization.

Method D. A solution of the 2-(chloromethyl)-1*H*-benzimidazole (**33**; 5.0 g, 3.0 mM) and triphenylphosphine (7.9 g, 30 mM) in anhydrous dioxane (70 mL) was refluxed under an atmosphere of nitrogen for 14 h. After being cooled, the resulting white precipitate was filtered, washed with dioxane (15 mL), and dried to give 11.1 g (86%) of the phosphonium salt **34**; mp 285 °C.[5b]

A solution of 10% sodium carbonate (13.6 mL, 12.8 mM) was added to a solution of compound **34** (5.0 g, 11.7 mM) in chloroform (60 mL), followed by a 10% aqueous solution of formaldehyde (7 mL, 23.3 mM), and stirring was continued at rt for 3 h. The chloroformic layer was separated and extracted with 5 N hydrochloric acid (3 × 10 mL). The acid extract was neutralized with solid sodium carbonate and the precipitate filtered, washed with water (2 × 5 mL), and dried. Recrystallization from chloroform afforded 1.35 g (80%) of **31**; mp 184 °C.[5b]

Reaction of 1-(2-Carboxyethyl)pyridinium Bromide (14) with 1,2-Diamino-3-nitrobenzene (18) Using $POCl_3$ as Cyclocondensation Agent (Scheme I). A stirred solution of 1,2-diamino-3-nitrobenzene (**18**; 7.3 g, 47.4 mM) and 1-(2-carboxyethyl)pyridinium bromide (**14**; 11.0 g, 47.4 mM) in phosphorus oxychloride (187 mL) was heated on a bath at 80 °C for 96 h. The cooled solution was carefully poured into ice–water (100 mL) and then slowly neutralized with a solution of concentrated ammonium hydroxide to pH 7. The precipitate was filtered, washed with water (2 × 10 mL), and dried. It was shown by ^{1}H NMR to contain a mixture of (benzimidazolylethyl)pyridinium salt **12** (ca. 5%) and 4-nitro-2-vinyl-1*H*-benzimidazole (**19**; ca. 13%) along with unidentified products.

1-(Carboxyethyl)-4-(decyloxy)pyridinium Bromide (20). Metallic sodium (5.6 g, 0.24 M) was dissolved in decanol (110 mL, 0.57 M) by heating at 130 °C for 2 h, then 4-chloropyridine hydrochloride (15.0 g, 0.1 M) was added at 110 °C, and stirring continued for 52 h. The reaction mixture was neutralized with 5 N HCl, and decanol was distilled off (50 °C (4 mbar)). The residue was chromatographed, and pure 4-(decyloxy)pyridine (17.6 g, 75%) was obtained by FC (dichloromethane–methanol (9.9:0.1)), mp 30 °C. A subsequent FC (dichloromethane–methanol (9:1)) afforded pure 4-(decyloxy)pyridine hydrochloride (2.87 g, 11%), mp 112–4 °C.

A stirred solution of 4-(decyloxy)pyridine (3.6 g, 15.3 mM) and 3-bromopropionic acid (2.3 g, 15.3 mM) in anhydrous acetonitrile (40 mL) was refluxed under an atmosphere of nitrogen for 25 h. The reaction mixture was evaporated to dryness and the oily residue triturated with diethyl ether (50 mL). The solid was filtered, washed with diethyl ether (3 × 10 mL), and dried to give 4.3 g (73%) of **20**, mp 161–3 °C.

5,6-Dimethyl-2-[2-(4-oxo-1,4-dihydro-1-pyridyl)ethyl]-1*H*-benzimidazole (22). A stirred suspension of 1,2-diamino-4,5-dimethylbenzene (**17**; 0.70 g, 5.15 mM) and 1-(2-carboxyethyl)-4-(decyloxy)pyridinium bromide (**20**; 2.0 g, 5.15 mM) in PPA (20 g) under an atmosphere of nitrogen was heated on a bath at 170 °C for 1.5 h. The cooled mixture was poured into ice–water (200 mL) and the resulting solution treated with solid sodium carbonate to pH 9. The resulting white solid was filtered and digested in chloroform (500 mL) for 5 d. The insoluble materials were removed by filtration and the filtrate dried ($MgSO_4$) and evaporated to dryness to afford 0.3 g (22%) of compound **22** mp 182–3 °C.

Attempted Isolation of 2-(2-Chloroethyl)-4-nitro-1*H*-benzimidazole (26) (Scheme II). A stirred suspension of compound **23** (0.5 g, 2.1 mM) in 4 N HCl (6.3 mL, 25.0 mM) was heated in a bath at 100 °C for 1 h. The resulting solution was cooled and carefully neutralized with solid sodium carbonate and then concentrated in a rotary evaporator at 25 °C to 1 mL.

The brown precipitate was filtered, washed with water (1 mL), and dried to afford 0.13 g of brown solid which was then identified by ^{1}H NMR (DMSO-d_6) as a mixture of 2-(2-chloroethyl)-4-nitro-1*H*-benzimidazole (**26**) and 4-nitro-2-vinyl-1*H*-benzimidazole (**19**), the relative proportions of which were 1:1, respectively. Several attempts of recrystallization have been made using different solvents, and the unstable compound **26** was easily transformed to **19** along with products of alteration or decomposition which were not further investigated because the unstable chloroethyl derivative **26** is not a suitable intermediate for preparation the title compounds **12** and **13** (see Scheme II).

Curiously, the mixture of compounds **26** + **19** (ratio 1:1) was slowly transformed in the solid state. Thus, after 6 months the brown solid was shown by ^{1}H NMR to contain **26** (40%) and **19** (60%).

Reaction of 1,2-Diamino-4,5-dimethylbenzene (17) with 3-Chloropropionic Chloride. 3-Chloropropionyl chloride (2.82 mL, 29.36 mM) was added dropwise at 5 °C during 3 h to a solution of compound **17** (4.0 g, 29.36 mM) in anhydrous toluene (400 mL) under an atmosphere of nitrogen, and stirring was continued at rt for 14 h. The resulting solid was filtered and washed with toluene (5 × 5 mL), and then water (200 mL) was added and the suspension treated with solid sodium carbonate to pH 8. The precipitate was filtered and washed with water (25 mL) and then dissolved in dichloromethane (50 mL). The organic solution was washed with 2 N HCl (3 × 25 mL), dried ($MgSO_4$), and evaporated to dryness to give 1.09 g (12%) of compound **28**, mp 190–200 °C. The aqueous filtrate was neutralized with Na_2CO_3 to pH 8, dichloromethane was added (4 × 25 mL), and the organic phase was separated, dried ($MgSO_4$), and evaporated to dryness to give 2.41 g (30%) of compound **27**, mp 142–3 °C.

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Registry No. **9**, 136642-47-2; **10**, 136616-50-7; **11**, 136642-49-4; **12**-Br$^-$, 136616-52-9; **13**, 136616-53-0; **14**, 19604-98-9; **15**, 89389-94-6; **16**, 95-54-5; **17**, 3171-45-7; **18**, 3694-52-8; **19**, 136616-54-1; **20**, 136616-55-2; **22**, 136616-56-3; **23**, 136616-57-4; **24**, 136616-58-5; **25**, 136616-59-6; **26**, 136616-60-9; **27**, 136616-61-0; **28**, 136616-62-1; **31**, 14984-26-0; **12**-Cl$^-$, 136616-51-8; **32**, 136616-63-2; **33**, 4857-04-9; **34**, 60912-44-9; amberlite resin IRA 401, 9002-25-9; pyridine, 110-86-1; 4-(dimethylamino)pyridine, 1122-58-3; 3-bromopropionic acid, 590-92-1; 1-decanol, 112-30-1; 4-chloropyridine hydrochloride, 7379-35-3; 4-(decyloxy)pyridine, 75125-02-9;

(18) Concerning the transformation of some 4-nitro-1*H*-benzimidazol-2-ylpyridinium salts **1** into their corresponding betaines **3**, the use of a strong base anion-exchange resin (OH^- form) proceeded with rather low yield probably due to the presence of a nitro group in the abovementioned salts **1**.

4-(decyloxy)pyridine hydrochloride, 136616-64-3; 3-chloropropionyl chloride, 625-36-5.

Supplementary Material Available: Selected ^1H NMR data of compounds **15**, **20**, and **22–28** (Table III); selected ^{13}C NMR spectroscopic data of compounds **9–13**, **19**, **31**, and **32** (Table IV); selected ^{13}C NMR spectroscopic data of compounds **15**, **20**, **22–24**, and **26–28** (Table V); elemental analyses of new compounds (Table VI) (4 pages). Ordering information is given on any current masthead page.

Conformational Study of (*R*)-(−)-2,2,2-Trifluoro-1-(9-anthryl)ethanol (Pirkle's Alcohol) by Dynamic NMR

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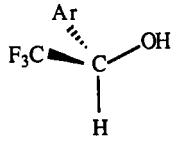
Observation of anisochronous ^1H and ^{13}C NMR signals in (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol at low temperature indicates that restricted rotation around the C(sp^2)–C(sp^3) bond occurs. From the coalescence temperature data and the corresponding chemical shift difference, the free energy of activation for rotation was evaluated to be 14.5 kcal mol^{-1} at 320 K in deuteriochloroform. These results, together with MM2 calculations, indicate that the ground-state conformation is that in which the trifluoromethyl group is almost orthogonal to the anthracene ring. The transition state will correspond then to the conformation in which the CF_3 group eclipses the aromatic nucleus. Complete ^1H and ^{13}C NMR assignments of the system at the frozen ground state (340 K) were made by homo- and heteronuclear COSY experiments and NOE difference spectroscopy.

Introduction

Enantiomerically pure (+)- and (−)-1-aryl-2,2,2-trifluoroethanols **1**, also known as Pirkle's alcohols, have been widely applied as optically active NMR reagents and as chiral stationary phases in chromatography.[1]



a, Ar = phenyl

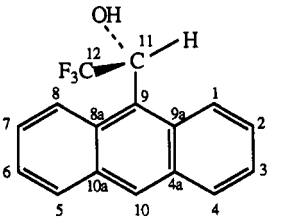
b, Ar = α-naphthyl

c, Ar = 9-anthryl

1

Even though **1a** and **1b** have been the most frequently used for the NMR determination of enantiomeric purity and absolute configuration, it has been proved that **1c**, despite its modest solubility, induces greater spectral nonequivalence between enantiomeric solutes than either **1a** or **1b**; it is not uncommon to observe nonequivalence magnitudes of 0.1 ppm.[2] Resolved (*R*)-(−)-fluoro alcohol **1c** was used throughout this study without other precaution than to protect it from light and oxygen.[3]

In spite of the general uses of **1c** in organic chemistry, a detailed description of its NMR properties has never been reported in the literature.[4] This situation prompted us to perform a systematic ^1H and ^{13}C NMR study of (*R*)-(−)-2,2,2-trifluoro-1-(9-anthryl)ethanol at several temperatures in order to facilitate its NMR applications as a chiral reagent. We report here evidence for restricted rotation involving an sp^2–sp^3 bond (C_9–C_{11}) connecting the trifluoroethanol group to the anthracene ring in Pirkle's alcohol **1c**, and also the application of molecular mechanics (MM2) calculations to this molecule.



R-(−)- **1c**

MM2 Theoretical Calculations

MM2 Theoretical Calculations

Although compound **1c** has a π electron system, it does not electronically interact with the substituent at C_9; therefore, MM2 calculations[5] treating the anthracene moiety mechanically have been undertaken. From them, it appears that **1c** assumes a ground-state conformation in which the trifluoromethyl group is almost orthogonal to the aryl group. The calculations have been performed considering the variety of intermediate conformations obtained by extensive drive of C_{9a}–C_9–C_{11}–OH and C_9–C_{11}–O–H bonds from 180 to −180° at 15° steps. According

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(3) Complete structural characterization of the isolated head-to-tail photodimer from **1c** by recrystallization in ethanol without protection from oxygen and light is now in progress.

(4) To our knowledge only Pirkle, W. H. *et al.* (Pirkle, W. H. et al. *J. Org. Chem.* **1977**, *42*, 384) describe the ^1H NMR of **1c** in carbon tetrachloride: δ (in ppm) = 3.42 (d, 1 H, exchangeable OH, J = 5.2 Hz), 6.28 (d of q, 1 H, J_d = 5.2 Hz, J_q = 8.0 Hz), 7.15–7.45 (m, 4 H), 7.62–7.85 (m, 2 H), 7.6–9.1 (m, very broad, 2 peri H), and 8.20 (s, 1 ArH at position 10).

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