1449, 840, 810, 778, 764, 756, 728, 718 cm^{-1}; MS (CI) MH^+, *m/e* 441 (31), 275 (17), 247 (100). Anal. Calcd. for $C_{34}H_{32}$: C, 92.68; H, 7.32. Found: C, 92.64; H, 7.36.

8,15,23,30-Tetramethyl[2.1.2.1]metacyclophane-*trans*,-*trans*-1,16-diene (11C). $NaBH_4$ (2.7 mg, 0.07 mmol) was added to a solution of cyclophane **2B** (minor isomer)[2] (15.9 mg, 0.035 mmol) in wet THF (50 mL) and the mixture heated at reflux for 12 h. After the mixture had cooled, dilute HCl was added and then dichloromethane. The organic layer was washed, dried, and evaporated, and the residue was mixed thoroughly with powdered $NaBH_4$ (13.5 mg, 0.35 mmol) and added in portions to CF_3COOH (30 mL) at 0 °C under N_2 with vigorous stirring. After a further 20 min, aqueous $NaHCO_3$ solution was added and then dichloromethane. The organic layer was washed, dried, and evaporated, and the residue was recrystallized from cyclohexane/hexane to give 12.5 mg (81%) of colorless crystals of **11C**: mp 305–307 °C; ^1H NMR (90 MHz) δ 7.38–7.06 (m, 12 H, Ar H), 6.49 (s, 4 H, —CH=), 4.20 (s, 4 H, CH_2), 1.14 (s, 12 H, Ar CH_3); IR (KBr) 1458, 965 (*trans*-CH=CH), 848, 779, 769, 759, 710 cm^{-1}; MS (CI) MH^+, *m/e* 441 (10), 425 (10), 275 (20), 249 (39), 247 (100). Anal. Calcd. for $C_{34}H_{32}$: C, 92.68; H, 7.32. Found: C, 92.70; H, 7.30.

Hydrogenation of Dienes 2C and 11C to 8C (12G). 30% Pd/C (3 mg) was added to a solution of the cyclophanediene **2C** or **11C** (15 mg) in dry benzene (10 mL), which was then stirred under 1 atm of H_2 at 20 °C for 24 h. Removal of catalyst and then solvent yielded in both cases quantitative samples of **8C (12G)** identical with the previously obtained samples (mp, ^1H NMR, MS).

Registry No. 1A, 90133-68-9; **1B**, 75404-52-3; **1C**, 90133-67-8; **2A**, 90133-71-4; **2B**, 90133-70-3; **2C**, 90133-69-0; **8A**, 90133-73-6; **8B**, 90133-72-5; **8C**, 75397-87-4; **11A**, 90133-74-7; **11B**, 90133-75-8; **11C**, 90133-76-9.

Supplementary Material Available: Full variable temperature NMR data for compounds **12** and figures S1–S10 (10 pages). Ordering information is given on any current masthead page.

Charge-Shift Probes of Membrane Potential. Synthesis

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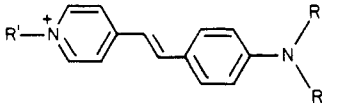
We are reporting two general synthetic approaches to a number of (aminostyryl)pyridinium dyes and their heterocyclic analogues which are of interest as electrochromic probes for membrane potential. The two routes which involve palladium-catalyzed coupling or aldol condensation permit considerable structure variations to be introduced in the dyes. Some spectral properties of the dyes are discussed.

The synthesis of cyanine, merocyanine, and styryl dyes has been based largely on a key condensation step between the heterocyclic nuclei. These dyes are especially useful as sensitizers in the photographic industry, and their syntheses have been thoroughly reviewed.[1] Hundreds of these dyes are commercially available.

Cohen[2] and Tasaki[3] were the first to discover voltage-dependent changes in fluorescence or transmittance characteristics of the squid giant axon which had been stained with a variety of dyes. It soon became apparent that the electrical properties of a variety of cell and membrane preparations could be studied in this way.[4]

We have been interested in the styryl class of dyes because of the possibility that they would respond to membrane potential changes by an electrochromic mechanism.[5,6] The latter requires that the dyes should provide a response time which is able to follow the fastest of physiological events, and should be operative on a wide variety of membrane preparations.

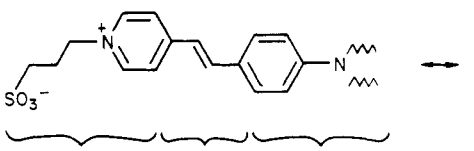
A number of (*p*-aminostyryl)pyridinium dyes **1** have



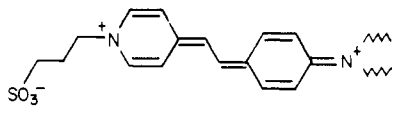
1

been tested on model membrane systems and do indeed appear to respond to voltage pulses via electrochromism.[7,8] Such electrochromic dyes are amenable to theoretical design and are of intrinsic physical-chemical interest apart from the biological applications. The synthesis of these dyes has closely followed the aldol condensation strategy.[9] In an effort to explore chromophores with more extended π-systems and dyes with unusual side chains it has become necessary to expand the aldol condensation methodology as well as to develop other general dye syntheses.

The chromophoric system that has been most useful in our studies of membrane potential probes is exemplified by structure **1a**. These molecules possess at their polar



A



B

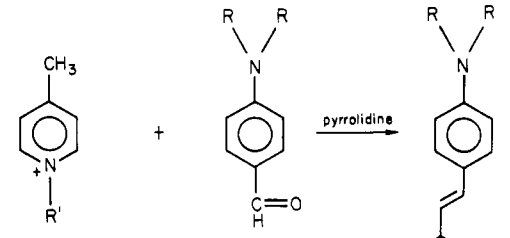
1a

hydrophilic end a pyridinium salt moiety preferably in the form of an electrically neutral zwitterion sulfonate (part a). This heterocyclic moiety is conjugated via an unsatu-

(1) Hamer, F. M. In "The Cyanine Dyes and Related Compounds"; Wiley, New York, 1964.
(2) Cohen, L. B.; Salzberg, B. M.; Davilla, H. V.; Ross, W. N.; Landowne, D.; Waggoner, A. S.; Wang, C. H. *J. Membr. Biol.* **1974**, *19*, 1.
(3) Tasaki, I. *Ann. N. Y. Acad. Sci.* **1974**, *227*, 247.
(4) Freedman, J. C.; Laris, P. C. *Int. Rev. Cytol. Suppl.* **1981**, *12*, 177.
(5) Loew, L. M.; Bonneville, G. W.; Surow, J. *Biochemistry* **1978**, *17*, 4065.
(6) Loew, L. M. *J. Biochem. Biophys. Meth.* **1982**, *6*, 243.
(7) Loew, L. M.; Scully, S.; Simpson, L.; Waggoner, A. S. *Nature (London)* **1979**, *281*, 497.
(8) Loew, L. M.; Simpson, L. *Biophys. J.* **1981**, *34*, 353.
(9) Loew, L. M.; Simpson, L.; Hassner, A.; Alexanian, V. *J. Am. Chem. Soc.* **1979**, *101*, 5439.

0022-3263/84/1949-2546$01.50/0

Scheme I



2a, R = $(CH_2)_3SO_3^-$ 3a, R = *n*-hexyl
b, R = $(CH_2)_4SO_3^-$ b, R = *n*-butyl
c, R = CH_3

1a, R = *n*-hexyl; R′ = $(CH_2)_3SO_3^-$
b, R = *n*-hexyl; R′ = $(CH_2)_4SO_3^-$
c, R = *n*-hexyl; R′ = CH_3
d, R = *n*-butyl; R′ = $(CH_2)_3SO_3^-$
e, R = *n*-butyl; R′ = $(CH_2)_4SO_3^-$
f, R = *n*-butyl; R′ = CH_3

rated chain (part b) to an anilino group which possesses medium-length carbon chains attached to nitrogen (part c) to provide the lipophilic end of the molecule. Upon excitation, such a molecule, which binds to a membrane in an orientation perpendicular to the membrane surface,[8,9] undergoes a shift of the positive pole from one end of the molecular to the other.[5,8] Put simply, resonance structure A is the major contributor to the ground state whereas B more closely describes the first excited state.

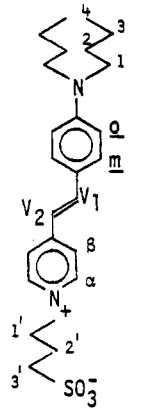
The electrical response of these molecules is dependent in part on their absorption maxima. Hence it was of interest to synthesize a series of related molecules in which parts a–c can be structurally altered and to test the effect of structure on the spectral properties of these molecules.

Synthetic Methodology

1. The Aldol Approach. The general approach toward dyes of type 1 is to link a heterocyclic unit a with an aromatic unit c via one or more double bonds (unit b), the latter preferably with an *E* stereochemistry. To this end we have employed the aldol strategy shown in Scheme I and the palladium-catalyzed coupling (Heck reaction)[10] described in the following section.

Scheme I requires a pyridinium derivative or analogous heterocycle capable of activating a properly positioned alkyl substituent toward base-catalyzed aldol condensation with an amino-substituted aromatic aldehyde.[11] The pyridinium salts **2** were prepared from 4-picoline with sultones or methyl iodine. The aldehydes **3** were obtained by Vilsmeier reaction of the corresponding N,N-disubstituted anilines. In addition to the synthesis of the orange-red **1a–d**, we have used the strategy of Scheme I to obtain a variety of dyes as summarized in Tables I and II.

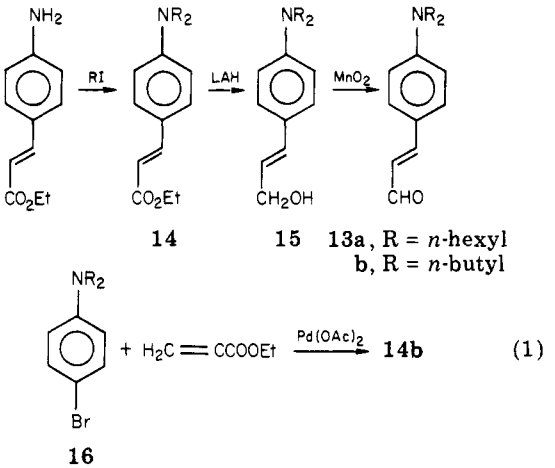
The red diene-linked dyes, **5**, presented some stereochemical problems. While the stereochemistry of the double bonds in most compounds obtained by the aldol route are *E* (trans) as indicated by NMR coupling (Figure



8.74 α (d,2H,J=6.6 Hz)
7.84 β (d,2H,J=6.6 Hz)
7.7 V_2 (d,2H,J=15.9 Hz)
7.53 o (d,2H,J=8.7 Hz)
6.92 V_1 (d,2H,J=15.9 Hz)
6.66 m (d,2H,J=8.8 Hz)
4.79 1′ (t,2H,J=6.2 Hz)
3.39 1 (t,4H,J=7.6 Hz)
2.74 3′ (t,2H,J=6.1 Hz)
2.58 2′ (m,2H)
1.59 2 (m,4H)
1.38 3 (m,4H)
0.58 4 (t,6H,J=7.3 Hz)

Figure 1. ^1H NMR (δ at 360 MHz) spectral assignments for **1d**.

1), the diene **5b** is formed as two stereoisomers, one red and one pink-violet, separable by column chromatography. The pink-violet isomer (λ_{max}^{EtOH} 517 nm) is identical with "RH162" reported by Grinvald et al.[12] and is presumably the *E,E* isomer, while the red isomer (λ_{max}^{EtOH} 495 nm), with the same R_f value on TLC, most likely has the *E,Z* structure. The starting aminocinnamaldehydes **13** were obtained from ethyl *p*-aminocinnamate as outlined in eq 1. Ester **14b** was also obtained in a more convenient



14 15 13a, R = *n*-hexyl
b, R = *n*-butyl

16 (1)

manner (50% yield) by Pd coupling of **16** with ethyl acrylate. Coupling of **16** with CH_2=$CHCH(OMe)_2$, on the other hand, proceeded only in very poor yield (~10%).

Also worthy of note in Table II is that activation of methyl substituents in quinolinium salts is possible not only in the pyridine ring but also in the nonheterocyclic aromatic ring as evidenced by the synthesis of **10**.

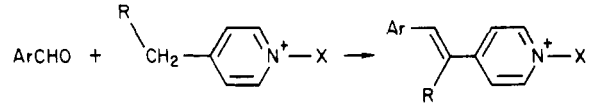
2. Pd-Catalyzed Coupling. A more versatile method of synthesis for these dyes proved to be palladium-catalyzed coupling of olefins with aromatic halides. Conceptually this can be accomplished either via the heterocyclic olefin **18** (Scheme IIa) or via the 4-vinylaniline **19** (Scheme IIb) to produce **20**; however, only route a is practical because **19** polymerizes too readily. The neutral intermediate **20** can be converted conveniently into a variety of quaternary derivatives **1**, making it unnecessary to prepare different pyridinium derivatives **2** as required for the aldol condensation.

In this manner, the readily obtainable 4-bromoaniline **16** (formed on bromination of N,N-disubstituted aniline)

(10) Heck, R. F. *Accs. Chem. Res.* **1979**, *12*, 146.
(11) The alternative condensation of an amino-substituted toluene with a pyridinecarboxaldehyde cannot be achieved. Neither does the aldol condensation proceed smoothly with nonquaternized 4-methylpyridine and the aminobenzaldehyde.

(12) Grinvald, A.; Hildesheim, R.; Farber, I. C.; Anglister, L. *Biophys. J.* **1982**, *39*, 301.

Table I. Styrylpyridinium Dyes by Aldol Condensation



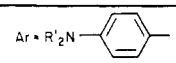
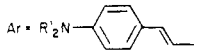
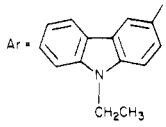
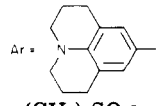
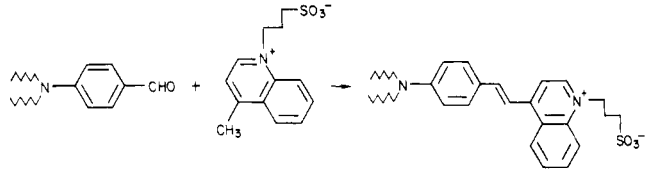
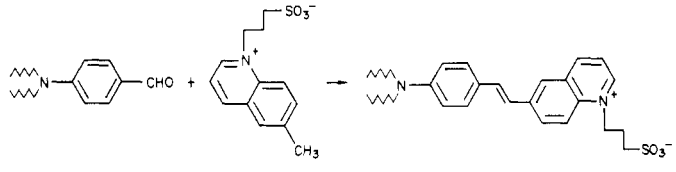
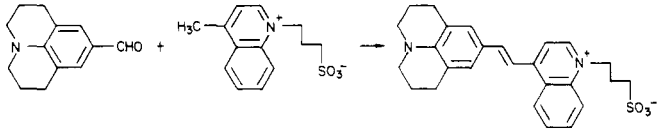
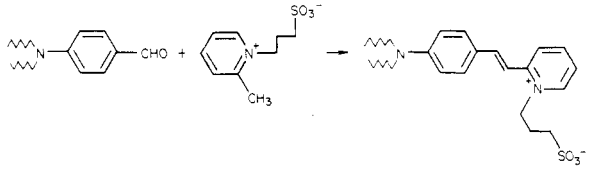
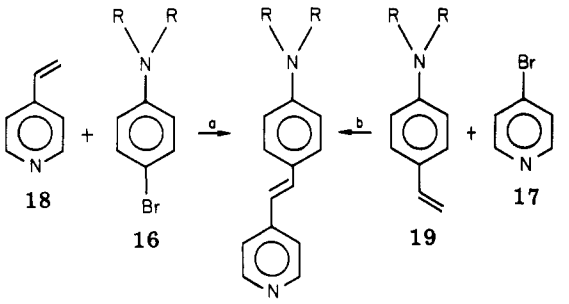
no.	R	R′	X	yield (%)	mp (°C)	λ_{max}^{EtOH} (nm)
						
1a	H	*n*-hexyl	$(CH_2)_3SO_3^-$	65	261–263	496
1b	H	*n*-hexyl	$(CH_2)_4SO_3^-$	60	310–312	495
1c	H	*n*-hexyl	$CH_3(I^-)$	34	149–150	495
1d	H	*n*-butyl	$(CH_2)_3SO_3^-$	75	265–267	492
4a	CH_3	*n*-hexyl	$(CH_2)_3SO_3^-$	50	190–192	478
4b	CH_3	*n*-butyl	$(CH_2)_3SO_3^-$	73	221–223	475
						
5a	CH_3	*n*-hexyl	$(CH_2)_3SO_3^-$	12	gum	495
5b	H	*n*-butyl	$(CH_2)_3SO_3^-$	34	230–232	517, 495
5c	CH_3	*n*-butyl	$(CH_2)_3SO_3^-$	45	144–147	495
5d	H	*n*-hexyl	$(CH_2)_3SO_3^-$	12	gum	505
						
6	H		$(CH_2)_3SO_3^-$	86	282–284	446
						
7a	H		$(CH_2)_4SO_3^-$	91	>320	440
7b	H		$(CH_2)_3SO_3^-$	88	>330	440
7c	CH_3		$(CH_2)_3SO_3^-$	87	302–304	422
						
8	H		$(CH_2)_3SO_3^-$	86	81–82	523

Table II. Aldol Condensations with Other Heterocyclic Reagents

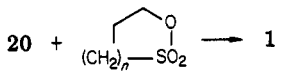
	yield (%)	mp (°C)	λ_{max}^{EtOH} (nm)
 **9**	65	222–226	565
 **10**	65	187–195	465, 540
 **11**	87	232–234	605
 **12**	76	203–210	485

Scheme II



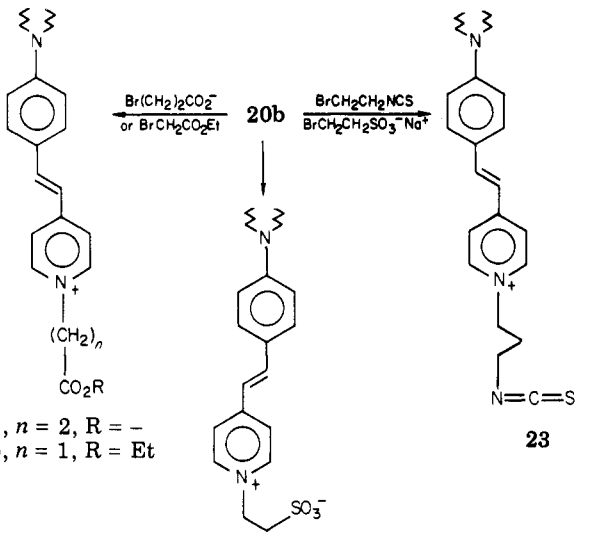
20a, R = *n*-hexyl
b, R = *n*-butyl

was heated with a 25% excess of commercially available 4-vinylpyridine (**18**), 0.01 molar equiv of palladium acetate, and 0.02 equiv of tri-*o*-tolylphosphine in dry triethylamine at 110 °C for 72 h to produce **20b** in 85% yield. Only the *E* isomer was observed.[13] Transformation of **20a** or **20b** into **1a–f** (identical with the dyes obtained via the aldol



21a, *n* = 1
b, *n* = 2

method) occurred smoothly on treatment with sultones **21** or methyl iodide, respectively. More important, **20b** could be converted into several positively charged (e.g., **22b**, **23**)

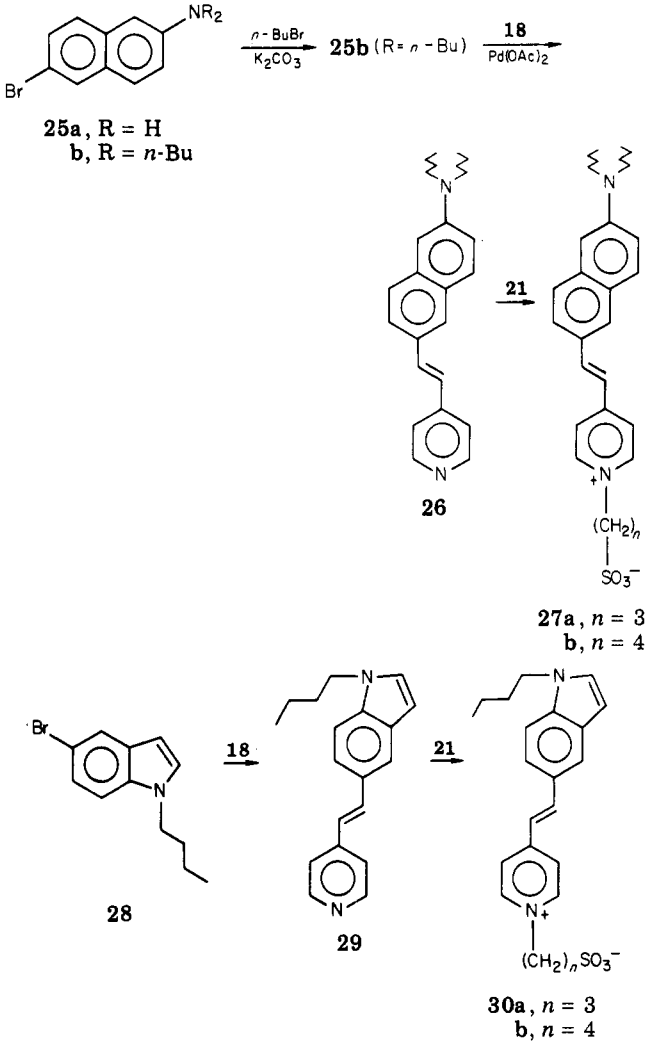


22a, *n* = 2, R = –
b, *n* = 1, R = Et

23

24

or neutral pyridinium dyes (e.g., **24a**, **24**) stressing the versatility of this route. All quaternization reactions proceeded with preferential reaction at the less hindered pyridine nitrogen. An extension of this methodology to aminonaphthalenes leads to the highly conjugated dye **26** (in 77% yield) from which the deep purple dyes **27a** and **27b** were obtained. This illustrates the advantage of the Pd-coupling route since the aminonaphthalene carboxaldehyde required for the aldol method is difficult to prepare. The Pd catalysis procedure was also applied to the coupling of 5-bromo-1-butylindole (**28**) with vinylpyridine which led to **29** and from there to the weakly conjugated dyes **30**. Apparently further delocalization of the electron pair from the indole nitrogen is counteracted by its involvement in the indole resonance and these dyes possess only yellow color. A more highly conjugated dye such as **34** was obtained by two consecutive palladium-coupling reactions. Thus, the more reactive iodoaniline **16c** was coupled with *p*-bromostyrene (**31**) to produce **32** in 60% yield. The latter was further coupled with 4-vinylpyridine (**18**) to produce the red dye **33** in 85% yield. The red-black dye **34** resulted on quaternization with sultone **21a**.



25a, R = H
b, R = *n*-Bu

26

27a, *n* = 3
b, *n* = 4

28

29

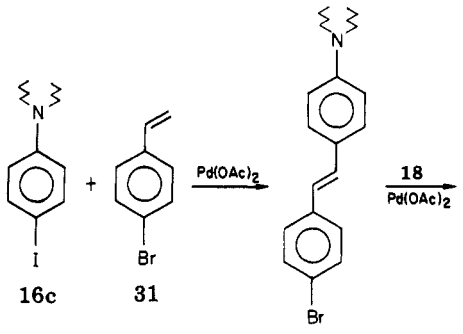
30a, *n* = 3
b, *n* = 4

Spectral Properties

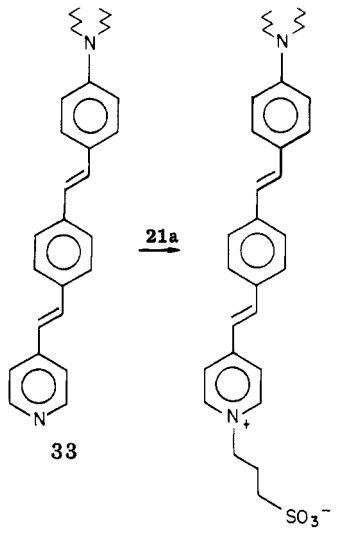
In all cases cited elemental analyses and NMR data were consistent with the structures shown. The trans $J_{H,H}$ coupling of the double bond is not discernable at 60 MHz, but the spectrum of the Pd-coupling product **20b** or of the dye **1d** at 360 MHz clearly shows all the relevant protons (see Figure 1). For instance, the olefinic protons in **1d** display a simple AB pattern centered at 7.31 ppm with a coupling of 15.9 Hz, characteristic of a trans configuration. Though the dyes are difficult to purify because of their low solubility, chromatography usually produced pure crystalline compounds. The UV spectra of the dyes synthesized showed a characteristic large red shift (75–100 nm) compared to the nonquaternized precursors (e.g., **20b** has λ_{max}^{EtOH} 387 nm (ϵ 3.9 × 10^4) while the quaternized **1d** showed a λ_{max}^{EtOH} 492 nm (ϵ 5.5 × 10^4).

It is interesting to compare the UV spectrum of the julolidine dyes **8** and **11** with the dialkylamino analogue

(13) Stilbenes have been prepared via the Wittig reaction (see: Becker, K. B. *Synthesis* **1983**, 341), but in many cases a mixture of *E* and *Z* isomers result.



16c 31 32



33 34

1 or 9. Thus, 11 has λ_{max}^{EtOH} at 605 nm, while its analogue 9 shows λ_{max}^{EtOH} at 565 nm. Similar phenomena have been observed for 2-(*p*-aminostyryl)pyridinium dyes.[14] The mass spectra showed significant $M^{+\cdot}$ peaks. In the *N,N*-dibutyl series there were usually strong $(M - C_3H_2)^+$ fragment ions, whereas in the *N,N*-dihexyl series there were strong $(M - C_5H_{11})^+$ ions present.

Many of these dyes are stable at room temperature in the solid state or in solution, even in the presence of light for several years. The detailed absorption and fluorescence spectra as well as binding characteristics to model membranes and response to membrane potential will be discussed in a forthcoming paper.

Experimental Section

Melting points were obtained on a Büchi melting point apparatus and are uncorrected. Infrared spectra were obtained with a Perkin-Elmer Model 700 or a Beckman IR8 spectrophotometer. The 60-MHz NMR spectra were obtained on a Varian EM360A spectrometer. The Syracuse University High Field NMR Facility provided ^1H spectra at 360 MHz. Elemental microanalyses were performed by Atlantic Microlab, Inc., Atlanta, GA. Although most of the dyes are hygroscopic salts or betaines and did not always furnish completely acceptable elemental analyses, they were always homogeneous by TLC.

General Procedure of Pd-Catalyzed Coupling. Synthesis of *trans*-4-[*p*-(Di-*n*-butylamino)styryl]pyridine (20b). A mixture of 5.68 g (0.02 mole) of *p*-bromo-*N,N*-dibutylaniline, 2.63 g (0.025 mol) of 4-vinylpyridine, 45 mg (0.0002 mol) of palladium diacetate, 120 mg (0.004 mol) of tri-*o*-tolylphosphine, and 10 mL of dry triethylamine was heated at 110 °C for 72 h in a capped heavy-wall Pyrex tube that was flushed with dry N_2. To the cooled mixture was added water and chloroform (all solids dissolved). The water layer was extracted with chloroform (2 × 100 mL), and the combined chloroform solutions were washed with water, dried over $MgSO_4$, and evaporated. The crystalline product **20b** was recrystallized from cold hexane; yield 86%, mp 80–81 °C. Alternatively, purification of the product was carried out by chromatography on silica gel by using hexane–CH_2Cl_2 as eluent: NMR ($CDCl_3$) δ 7.1 (d, d, J = 15.9 Hz); MS, m/e (relative intensity) 308 (42, M^+), 265 (100, $M - C_3H_7$); λ_{max}^{EtOH} 387 nm (ϵ 3.9 × 10^4).

Anal. Calcd for $C_{21}H_{28}N_2$: C, 81.82; H, 9.09; N, 9.09. Found: C, 81.79; H, 9.19; N, 9.11.

β-[2-(Di-*n*-butylamino)-6-napthyl]-4-vinylpyridine (26). Following the general procedure, 6.68 g (0.020 mol) of 6-bromo-2-(di-*n*-butylamino)naphthalene (**25b**) and 2.625 g (0.025 mol of 4-vinylpyridine (**18**) were converted into 5.5 g of **26**: 77% yield, mp 105–107 °C; NMR δ 8.35 (d, 2 H), 6.7–7.4 (10 H), 3.3 (t, 4 H); λ_{max}^{EtOH} 396 nm (ϵ 3.51 × 10^4).

Anal. Calcd for $C_{25}H_{30}N_2$: C, 83.75; H, 8.43; N, 7.81. Found: C, 83.33; H, 8.33; N, 7.31.

4-Bromo-4′-(di-*n*-butylamino)stilbene (32a) was prepared in 60% yield as a yellow powder from 4.2 g (0.013 mol) of *p*-iodo-*N,N*-dibutylaniline (**16c**) and 3 g (0.0164 mol) of 4-bromostyrene (**31**) at 115 °C for 16 h: mp 218–220 °C; MS, m/e (relative intensity), 385/387 (44.8/42.3, M^+), 342/344 (65.1/62.6, $M - C_3H_7$).

4-Bromo-4′-(di-*n*-hexylamino)stilbene (32b) was prepared in 51% yield from *p*-iodo-*N,N*-di-*n*-hexylaniline as for **32a** except that the reaction time was 28 h: MS, m/e (relative intensity) 441/443 (62.6/64.8, M^+), 370/372 (100/99.2, $M - C_5H_{11}$).

4-[β-[*p*′-(Di-*n*-butylamino)-*p*-stilbenyl]vinyl]pyridine (33). Following the general procedure, 2 g (0.005 mol) of **32** and 1 g (0.0095 mol) of **18** were converted at 125 °C and 16 h to 1.8 g (85%) of **33**: mp 222–224 °C; MS, m/e (relative intensity) 410 (83.5, M^+), 367 (56.4, $M - C_3H_7$); $\lambda_{max}^{CH_2Cl_2}$ 412 nm (ϵ 4.06 × 10^4).

Anal. Calcd for $C_{29}H_{34}N_2$: C, 84.88; H, 8.29; N, 6.83. Found: C, 84.03; H, 8.38; N, 6.61.

4-[β-(1-*n*-Butyl-5-indolyl)vinyl]pyridine (29). Following the general procedure, 5.04 g (0.020 mol) of 5-bromo-1-butylindole (**28**) and 2.675 g (0.025 mol) of **18** were converted to 2.2 g (40%) of **29**: mp 108–109 °C; MS, m/e (relative intensity) 276 (57.4, M^+), 233 (88.4, $M - C_3H_7$); λ_{max}^{EtOH} 341 nm (δ 2.72 × 10^4).

Anal. Calcd for $C_{19}H_{20}N_2$: C, 82.57; H, 7.29; N, 10.14. Found: C, 82.45; H, 7.34; N, 10.10.

6-Bromo-2-(di-*n*-butylamino)naphthalene (25b). A mixture of 10.7 g (0.048 mol) of 6-bromo-2-naphthyl amine[15] (**25a**), 60 mL of dry dimethylformamide, 31.2 g (0.17 mol) of 1-iodobutane, and 10 g (0.072 mol) of anhydrous potassium carbonate was heated at 130 °C for 20 h. Water was added to the cooled mixture, which was then extracted 3 times with 100 mL of $CHCl_3$. The organic layer was dried over $MgSO_4$ and evaporated to give the product, eluted with hexane from silica gel: 11.2 g (70%); bp 195 °C (0.1 torr); MS, m/e (relative intensity) 333/335 (83/83, M^+); NMR ($CDCl_3$) δ 7.67 (s, 1 H); 7.3–7.44 (m, 3 H), 7.02 (d, 1 H), 6.82 (br s, 1 H), 3.83 (t, 4 H), 0.88 (6 H).

Anal. Calcd for $C_{18}H_{29}NBr$: C, 64.67; H, 7.19; N, 4.19. Found: C, 64.78; H, 7.19; N, 4.16.

General Procedure for Formation of Pyridinium Betaines from Sultones 21. A mixture of 0.5 g (0.0016 mol) of **20b**, 3 mL of 1,4-butanesultone (**21b**) was heated at 120 °C for 1 h and then placed in a refrigerator overnight. The product was filtered and crystallized from ethanol–hexane (10:1). Alternatively, pure **1e** was obtained by chromatography over silica gel and elution with ethyl acetate–ethanol (1:1); yield 0.5 g (70%); mp 296–297 °C.

Anal. Calcd for $C_{25}H_{36}N_2SO_3$: C, 67.57; H, 8.11. Found: C, 67.70; H, 8.20.

1-(4-Sulfonatobutyl)-4-[β-[2-(di-*n*-butylamino)-6-naphthyl]vinyl]pyridinium betaine (27b) was prepared from **26** and the sultone **21b** as described for **1e**. The product **27b** (82%) was crystallized from methanol–ether: mp 246–248 °C; λ_{max}^{EtOH} 495 nm (Δ 4.05 × 10^4).

Anal. Calcd for $C_{29}H_{38}N_2SO_3$: C, 70.40; H, 7.74; N, 5.66. Found: C, 70.12; H, 7.78; N, 5.57.

1-(Sulfonatobutyl)-4-[β-(1-*n*-butyl-5-indolyl)vinyl]pyridinium betaine (30b) was prepared from **29** and sultone **21b** in 82% yield, mp 307–309 °C, as a yellow powder crystallized from

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(15) **25a** was prepared from 6-bromo-2-naphthol by the Bucherer reaction.

methanol–ether: λ_{max}^{EtOH} 417 nm (ϵ 3.42 × 10^4).

Anal. Calcd for $C_{23}H_{28}N_2SO_3$: C, 66.99; H, 6.80; N, 6.80. Found: C, 66.26; H, 6.87; N, 6.54.

1-(3-Sulfonatopropyl)-4-[β-(1-*n*-butyl-5-indolyl)vinyl]pyridinium betaine (30a) was prepared from **29** and sultone **21a** in 70% yield: mp 248–250 °C; λ_{max}^{EtOH} 427 nm (ϵ 3.12 × 10^4).

1-(3-Sulfonatopropyl)-4-[β-[2-(di-*n*-butylamino)-6-naphthyl]vinyl]pyridinium Betaine (27a). To 1 g (0.008 mol) of 1,3-propanesultone in 5 mL of CH_2Cl_2 was added 1 g (0.028 mol) of **26** and the mixture was stirred for 24 h at 20 °C. Upon cooling for 24 h, **26** precipitated as a red solid and was crystallized from methanol–ether or purified by chromatography on silica gel: 0.75 g (56%); mp 122–124 °C; λ_{max}^{EtOH} 495 nm (ϵ 3.05 × 10^4).

Anal. Calcd for $C_{28}H_{36}N_2SO_3$: C, 69.97; H, 7.55. Found: C, 69.74; H, 7.58.

1-(3-Sulfonatopropyl)-4-[β-[p'-(di-*n*-butylamino)-*p*-stilbenyl]vinyl]pyridinium betaine (34) was prepared in 46% yield by refluxing 1,3-propanesulftone (**21a**) and pyridine **33** in CH_2Cl_2 for 16 h; **34** crystallized as a black solid: mp >300 °C; λ_{max}^{EtOH} 482 nm (ϵ 3.83 × 10^4).

Anal. Calcd for $C_{32}H_{40}N_2SO_3$: C, 72.18; H, 7.52; N, 5.26. Found: C, 70.96; H, 7.64; N, 5.11.

1-(2-Carboxyethyl)-4-[*p*-(di-*n*-butylamino)styryl]pyridinium betaine (22a) was obtained by refluxing 1 g (0.0032 mol) of **20b** and 0.7 g (0.004 mol) of sodium 3-bromopropanoate in 30 mL of absolute ethanol for 16 h. Chromatography of the resulting oil on silica gel and elution with ethyl acetate–ethanol (6:4) gave 0.6 g of **22a** (48%) as a red solid: mp 156–157 °C; MS, *m/e* (relative intensity) 308 (51.1, M – $C_3H_4O_2$), 265 (100, 308 – C_3H_7); λ_{max}^{EtOH} 486 nm (ϵ 3.92 × 10^4). The identical product (**22a**) was obtained by reaction of **20b** with β-propiolactone.

1-(Carbethoxymethyl)-4-[*p*-(di-*n*-butylamino)styryl]pyridinium bromide (22b) was prepared in 51% yield by refluxing **20b** with 1.2 equiv of ethyl bromoacetate in dry benzene and crystallization from ethanol–hexane: mp 160–162 °C; λ_{max}^{EtOH} 507 nm (ϵ 5.31 × 10^4).

Anal. Calcd for $C_{25}H_{25}N_2O_2Br$: C, 63.15; H, 7.42; N, 5.89. Found: C, 61.96; H, 7.27; N, 5.85.

1-[γ-(Isothiocyanato)propyl]-4-[*p*-(dibutylamino)-styryl]pyridinium Bromide (23). A solution of 1 g (0.0032 mol) of **20b** and 2 mL of 3-bromopropylisothiocyanate in 50 mL of acetone (analytical grade) was allowed to stand for 16 h. The red solid was crystallized from acetone–hexane to give 0.95 g (60%) of **23**: mp 148–150 °C; IR 2100 cm^{-1} (N=C=S); λ_{max}^{EtOH} 500 nm (ϵ 5.28 × 10^4).

Anal. Calcd for $C_{25}H_{34}N_3BrS$: C, 61.47; H, 6.97; N, 8.61. Found: C, 59.94; H, 7.49; N, 8.46.

General Procedure for Aldol Coupling. Synthesis of 1-(4-Sulfonatobutyl)-4-[*p*-(di-*n*-hexylamino)styryl]pyridinium Betaine (1b). A solution of 3 g (0.01 mol) of 4-(di-*n*-hexylamino)benzaldehyde (**3a**), 3 g (0.013 mol) of 1-(4-sulfonatobutyl)-4-picolinium betaine (**2b**) and 1 mL of pyrrolidine in 30 mL of absolute ethanol was refluxed for 16 h. After cooling at 5 °C for 1 h, the orange solid was filtered and then purified by chromatography on silica gel (elution with ethyl acetate–ethanol (1:1) to furnish 3 g (60%) of **1b**: mp 310–312 °C; λ_{max}^{EtOH} 495 nm (ϵ 3.41 × 10^4).

Anal. Calcd for $C_{29}H_{44}N_2SO_3$: C, 69.56; H, 8.86; N, 5.59. Found: C, 69.41; H, 8.88; N, 5.52.

The other compounds in Tables I and II were prepared by this procedure and gave satisfactory analyses. The nmr spectrum of *1d* is described in Figure 1 and indicates an *E* (trans) stereochemistry about the double bond.

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Registry No. **1a**, 77673-49-5; **1b**, 90133-77-0; **1c**, 86691-58-9; (*E*)-**1d**, 90133-78-1; **1e**, 83683-58-3; **2a**, 15626-30-9; **2b**, 90133-79-2; **2c-I**, 2301-80-6; **3a**, 90133-80-5; **4a**, 90133-81-6; **4b**, 90133-82-7; **5b**, 83668-96-6; **5c**, 90133-83-8; **5d**, 90133-84-9; **6**, 90133-85-0; **7a**, 90133-86-1; **7b**, 90171-25-8; **7c**, 90133-87-2; **8**, 90133-88-3; **9**, 90133-89-4; **10**, 90133-90-7; **11**, 90133-91-8; **12**, 90133-92-9; **16** (R = Bu), 53358-54-6; **16c**, 90133-93-0; **18**, 100-43-6; (*E*)-**20b**, 90133-94-1; **21a**, 1120-71-4; **22a**, 90133-95-2; **22b**, 90133-96-3; **23**, 90133-97-4; **25a**, 7499-66-3; **25b**, 90133-98-5; **26**, 90133-99-6; **27a**, 90134-00-2; **27b**, 90134-01-3; **28**, 90134-02-4; **29**, 90134-03-5; **30a**, 90134-04-6; **30b**, 90134-05-7; **32a**, 90134-06-8; **32b**, 90134-07-9; **33**, 90134-08-0; *p*-iodo-*N*,*N*-di-*n*-hexylaniline, 90134-09-1; sodium 3-bromopropanoate, 43165-24-8; 4-(dibutylamino)benzaldehyde, 90134-10-4; 4-(dibutylamino)cinnamaldehyde, 90134-11-5; 4-(dihexylamino)cinnamaldehyde, 90134-12-6; 9-ethyl-3-formylcarbazole, 7570-45-8; 9-formyl-2,3,6,7-tetrahydro-[1*H*,5*H*]benzo[*ij*]quinolizine, 33985-71-6; 1-(3-sulfopropyl)-4-ethylpyridinium, 90134-13-7; 1-(3-sulfopropyl)-4-methylquinolinium, 56405-66-4; 1-(3-sulfopropyl)-6-methylquinolinium, 90134-14-8; 1-(3-sulfopropyl)-2-methylpyridinium, 56405-61-9; 4-bromostyrene, 2039-82-9; 3-bromopropyl isothiocyanate, 2799-73-7; 1-methylpyrrole-2-carboxaldehyde, 1192-58-1.

Solvomercuration–Demercuration. 11. Alkoxymercuration–Demercuration of Representative Alkenes in Alcohol Solvents with the Mercuric Salts Acetate, Trifluoroacetate, Nitrate, and Methanesulfonate

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The alkoxymercuration–demercuration of seven representative olefins with the mercuric salts acetate, trifluoroacetate, nitrate, and methanesulfonate, in methyl, ethyl, isopropyl, and *tert*-butyl alcohols was examined. Mercuric acetate was effective only in methanol and ethanol. On the other hand, mercuric trifluoroacetate was effective in all four solvents, giving in most cases high yields of the corresponding ethers. Both mercuric nitrate and mercuric methanesulfonate were effective in methanol, ethanol, and 2-propanol. However, in several cases poor selectivity for the ether was observed, as evidenced by the formation of significant amounts of side products. Both electronic and steric effects are important factors in the reaction. Moreover, the structure of the olefin has a pronounced effect, both on the types of oxymercurials formed and on their stability to the reaction conditions.

The oxy(solvo)mercuration of olefins has been extensively studied since the turn of the century.[1-3] The major thrust of the work has been mechanistically oriented. This reaction became a major synthetic tool when it was dis-

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