cooled (liquid N_2/EtOH) to -75 °C. Dry hexamethylphosphoric triamide (HMPT, 5 mL) was then introduced into the stirred solution followed by excess precooled tri-*n*-butyl borate (4.5 mL, 16.68 mmol). The cooling bath was replaced with a solid CO_2/acetone bath and the mixture was left for 3 h at -60 to -65 °C. The HMPT which had solidified slowly melted at that temperature. The yellow solution was then allowed to warm up slowly to room temperature and then MeOH/H_2O (1:1, 20 mL) was added. Partial evaporation of the organic phase was followed by addition of H_2O (20 mL), and the pH of the solution was adjusted to 3 with AG 50 WX 2 (H^+) resin. The resin was filtered and washed with H_2O and the filtrate was extracted 3 times with $CHCl_3$ (50 mL) to remove HMPT. TLC ($CHCl_3$-EtOH, 2:1) of the aqueous layer revealed two major components [R_f 0.13 (product); 0.34 (2'-deoxyuridine, dUrd)]. 5-Bromo-2'-deoxyuridine could not be detected by TLC. Partial evaporation (10 mL) of the aqueous layer under reduced pressure furnished on cooling a white solid which was shown to be inorganic salts. Evaporation of the aqueous layer to dryness gave a residue which was loaded onto a silica column (300 g). Elution with $CHCl_3$-EtOH (2:1) initially afforded fractions which contained dUrd followed by fractions rich in product but still containing dUrd. The latter were pooled and evaporated to dryness, and the residue was dissolved in MeOH (8 mL). The light-brown solution was then fractionally crystallized in that solvent at room temperature. Initially, crops of almost pure dUrd (mp 163-165 °C) were recovered from the solution (545 mg). Two crops of compound **3** (326 mg, 18%) were then obtained. HPLC revealed that these had about a 5% impurity of dUrd and that these two samples did not contain any detectable traces of 5-bromo-2'-deoxyuridine. Recrystallization twice from MeOH afforded chromatographically pure compound **3** as white prisms: 208 mg, yield 12%; mp 226-227 °C dec; NMR [$(CD_3)_2SO$] δ 2.12 (m, 2, 2'-H), 3.54 (m, 2, 5'-CH_2), 3.80 (m, 1, 4'-H), 4.22 (bs, 1, 3'-H), 4.95 (t, J = 5.3 Hz, 1, 5'-OH), 5.28 (d, J = 3.5 Hz, 1, 3'-OH), 6.14 (t, J = 6.6 Hz, 1, 1'-H), 8.12 [s, 2, $B(OH)_2$], 8.13 (s, 1, 6-H), 11.67 (s, 1, NH); ^{11}B NMR δ -41.84 (bs); UV (0.01 N HCl) λ_{max} 268 nm (ϵ 12 500), λ_{min} 236 (ϵ 2310); UV (0.01 N NaOH) λ_{max} 265 nm (ϵ 10 200), λ_{min} 236 (ϵ 4350); IR ν (KBr, cm^{-1}) 3450 m, 3350 s, 3150 w, 3100 w, 3020 w, 2945 w, 2820 w, 1740 s, 1675 vs, 1620 w, 1475 s, 1415 m, 1375 m, 1310 m, 1280 s, 1230 vw, 1205 m, 1193 sh, 1150 w, 1123 m, 1100 s, 1092 sh, 1075 m, 1060 w, 1040 sh, 1030 s, 980 w, 950 sh, 940 m, 918 vs, 882 w, 848 w, 802 s, 787 m. Anal. Calcd for $C_9H_{13}BN_2O_7$: C, 39.75; H, 4.78; B, 3.98; N, 10.30. Found: C, 40.04; H, 5.03; B, 4.01; N, 10.64. Omitting HMPT or diglyme from the reaction reduced the yield to 7%. However, replacement of HMPT by diglyme (5 mL) did not significantly increase the yield of product.

5-(Trimethylsilyl)-2'-deoxyuridine (17). Substituting trimethylchlorosilane (3 mL, 23.6 mmol) for tri-*n*-butyl borate in the above experiment afforded on addition of MeOH/H_2O (1:1) an acidic solution. Partial evaporation of the solvents was followed by addition of H_2O and then the pH of the solution was adjusted to 5.5 with 1 M NaOH. Extraction of the aqueous layer twice with EtOAc and evaporation of the organic phase under reduced pressure furnished an oil which was loaded onto a silica column. Elution with $CHCl_3$-EtOH (9:1) and evaporation under high vacuum of the early fractions containing the desired product, afforded an amorphous white solid: 517 mg, yield 26%, mp 62-64 °C; NMR [$(CD_3)_2SO$] δ 0.16 [s, 9, $Si(CH_3)_3$] 2.11 (m, 2, 2'-H), 3.34 (m, 2, 5'-CH), 3.80 (bs, 1, 4'-H), 4.25 (m, 1, 3'-H), 5.02 (m, 1, 5'-OH), 5.25 (d, J = 3.5 Hz, 1, 3'-OH), 6.22 (m, 1, 1'-H), 7.73 (s, 1, 6-H), 11.18 (s, 1, NH); MS, m/e 300 (M^+), 184 (base), 169 (base - Me); TLC ($CHCl_3$-EtOH, 4:1) R_f 0.48; UV (0.01 N HCl) λ_{max} 266 nm (ϵ 9430), λ_{min} 236 (ϵ 2900); UV (0.01 N NaOH) λ_{max} 266 (ϵ 8460), λ_{min} 237 (ϵ 3210). Anal. Calcd for $C_{12}H_{20}N_2O_5Si \cdot 0.25\ H_2O$: C, 47.27; H, 6.78; N, 9.19. Found: C, 47.08; H, 6.56; N, 8.94. This compound can also be successfully prepared by using diglyme instead of HMPT.

High-Pressure Liquid Chromatography. The high-pressure liquid chromatograph used to determine the purity of the nucleosides was an Altex Model 110. The conditions used were as follows: Zorbax C-8 Column (Dupont), 25 cm × 4.6 mm id; ambient temperature; isocratic; mobile phase: 0.1 M sodium phosphate, pH 5.5; flow rate 0.5 mL/min; UV detection at 280 and 254 nm. The retention time (min) for the compounds analyzed measured at 280 nm were as follows: 2'-deoxyuridine, 9.2; 5-bromo-2'-deoxyuridine, 24.0; 5-(dihydroxyboryl)-2'-deoxyuridine, 16.6; 5-(trimethylsilyl)-2'-deoxyuridine, 9.1. The reproducibility was found to be within ±2%. Limit of detection, measured by relative ϵ_{280} for 5-bromo-2'-deoxyuridine was about 0.005%.

Registry No. **1**, 70523-22-7; **2**, 70523-23-8; **3**, 70577-63-8; **4**, 41244-53-5; **5**, 70523-24-9; **6**, 70523-25-0; **7**, 70523-26-1; **9**, 70523-27-2; **10**, 36847-11-7; **11**, 94706-32-8; **12**, 70523-28-3; **13**, 94706-33-9; **15**, 34279-86-2; **17**, 70523-31-8; 5-bromo-2,4-dichloropyrimidine, 36082-50-5; tributyl borate, 688-74-4; diethanolamine, 111-42-2; barbituric acid, 67-52-7; 5-bromo-2'-deoxyuridine, 59-14-3.

Nucleophilic Additions to *N*-Propargylpyridinium and *N*-Allenylpyridinium Salts and to 1,3-Propenediylbis(pyridinium) Salts

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Benzyl mercaptan adds to *N*-propargylpyridiniums to give *N*-[β-(benzylthio)allyl]pyridiniums, probably via an initial rearrangement to *N*-allenylpyridinium intermediates. Thiophenol reacts similarly, except that the 1-propargyl-4-(dimethylamino)pyridinium gives the *N*-[*cis*-γ-(phenylthio)allyl]pyridinium analogue. 2-Propene-1,3-diylbis(pyridinium) salts with 1 or 2 mol of thiol react by addition–elimination to form *N*-[1-(phenylthio)propen-2-yl]-, *N*-[3-(phenylthio)propen-2-yl]-, or *N*-[1,3-bis(phenylthio)propan-2-yl]pyridinium salts. *N*-(Oxiranylmethyl)pyridinium salts are prepared and converted into (2-hydroxypropane-1,3-diyl)bis(pyridinium) salts and corresponding propene-1,3-diylbis(pyridiniums). Semiquantitative studies of the base-catalyzed hydrogen–deuterium exchange of some of these compounds are reported, and the relative stability of the six possible isomeric 1-[(phenylthio)propenyl]pyridinium cations is discussed.

Pyridinium salts with unsaturated N substituents have recently received attention.[1-3] We reported on *N*-vinyl-,[1] *N*-propargyl-,[2] and *N*-propadienylpyridinium salts.[2] *N*-Vinylpyridinium cations act as Michael-type acceptors.[3]

We now describe the addition of sulfur nucleophiles to multiple bonds activated by an adjacent pyridinium moiety. A major aim of our work was to prepare as many of the possible isomers of the 1-[(phenylthio)propenyl]-pyridinium cation as possible and to study their relative stability. Additionally we were interested in the structural influences of the pyridinio substituent toward nucleophilic

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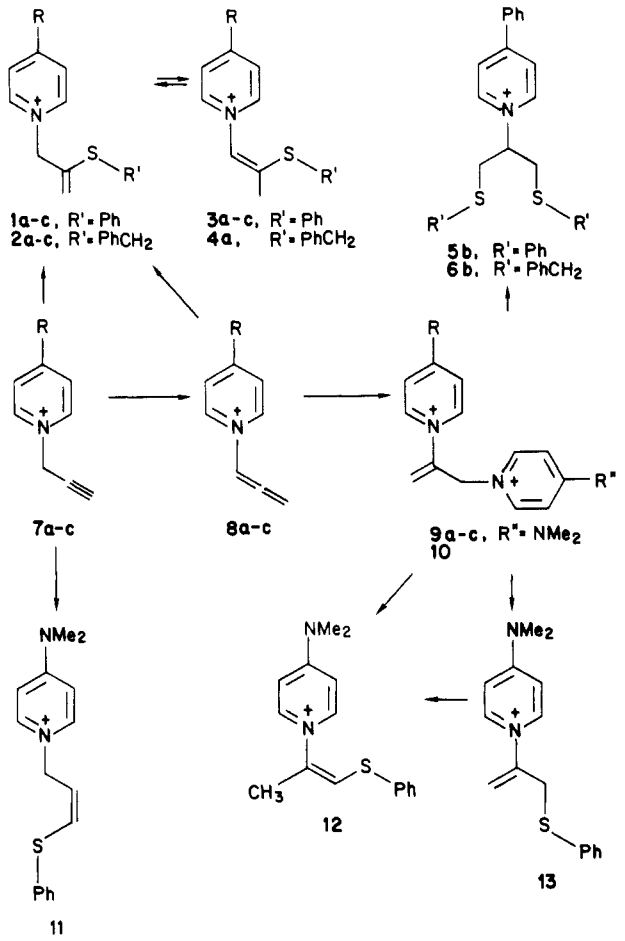
Scheme I[a]



[a] Series a, R = NMe_2; b, R = Ph; c, R = CH_3; all anions ClO_4^-.

addition to double bonds. From previous work propargyl and allenyl groups activated by an electron-withdrawing group are expected to add nucleophiles to give different products. Allenes should suffer nucleophilic attack at the central C-2 atom[4] and propargyl derivatives at the terminal C-3 atom.[5] As previously reported,[2] base-catalyzed rearrangement readily transforms propargylpyridinium salts **7a–c** to the corresponding allenes **8a–c**.

Addition to 4-(Dimethylamino)pyridinium (DMAP) Derivatives. Addition of thiophenol in EtONa/EtOH to 4-(dimethylamino)-1-propadienylpyridinium perchlorate (**8a**) occurred at the C-2 to form the vinyl sulfide **1a**. The ^1H NMR spectrum confirmed the proposed structure, exhibiting broad singlets for the olefinic hydrogens at 5.30 and 5.60 ppm and for the methylene group adjacent to the pyridinium ring at 4.95 ppm.

However, with the 4-(dimethylamino)-1-propargylpyridinium perchlorate (**7a**), thiophenol under the same conditions as above underwent addition to C-3 leading to the vinyl sulfide **11**. The product showed on olefinic proton at 6.90 ppm of characteristic multiplicity (doublet of triplets) in the ^1H NMR. The vicinal olefinic coupling constant of 9.6 Hz pointed to a cis configuration of the double bond, arising from trans addition of thiophenol in agreement with the "trans-addition rule" proposed by Truce[6] for similar systems. A radical mechanism is unlikely as the presence of a radical inhibitor (1,3-dinitrophenol) did not effect the production of **11**, and with a radical initiator (di-*tert*-butyl peroxide) instead of base, no reaction occurred.

With benzyl mercaptan instead of thiophenol under otherwise identical conditions as above, the propargyl derivative **7a** gave only the C-2 addition product **2a** and none of the C-3 product as with thiophenol. The allene **8a** formed mixtures of the tautomers **2a** and **4a** resulting from the addition of the thiolate ion to C-2.

Addition to 4-Phenyl- and 4-Methylpyridinium Derivatives. Under analogous conditions as above, reacting allene **8b** or the propargylpyridinium salts **7b,c** with benzyl mercaptan as well as with thiophenol, attack at C-2 was observed exclusively leading to the vinyl sufides **2b,c** and **1b,c**, respectively.

The fact that we found addition to the triple bond only with the DMAP derivative **8a** and thiophenoxide as nucleophile can be explained by a competition between addition and base-catalyzed propargyl–allene rearrangement. The use of the stronger base benzyl mercaptan (p*K*a 9.43 vs. p*K*a 6.50 of thiophenol in water[7]) or propargylpyridinium salts such as **7b** and **7c** with a more acidic methylene group favored rearrangement over addition to the triple bond.

Hydrolysis and Isomerization of the Vinyl Sulfides 1a–c and 2a–c. All the vinyl sulfides **1a–c** and **2a–c** described are sensitive to acid hydrolysis to the corresponding 1-acetonylpyridinium salts, similar to previously reported systems.[2]

On heating in EtONa/EtOH (0.1 equiv), the vinyl sulfides underwent partial isomerization. After 16 h, the isomer ratios found did not change on further heating (up to 48 h) or by the use of higher base concentrations (0.2 or 1.0 equiv). The equilibrium ratios thus obtained (mean values of at least three runs, determined from integrated ^1H NMR) were for **1a** ⇄ **3a**, 35:65; for **1b** ⇄ **3b**, 65:35; and for **2a** ⇄ **4a**, 55:45.

Under analogous conditions **11** was recovered unchanged. In no case could we separate the mixture of the two isomers. We confirmed the structure of the 1-propenyl derivatives **3a,b** and **4a** by their ^1H and ^{13}C NMR spectra by recording the spectrum of the particular mixture and subtracting the spectrum of the starting material. Thus we found for **3a** the expected singlets for the vinyl proton at 6.55 and for the methyl group at 1.90 ppm. The isomer mixtures gave correct C, H, N, analyses.

Addition of Bis(pyridinium) Salts. The bis(pyridinium) salts **9b,c** were prepared by a method similar to that recently reported[2] for **9a** and **10**. Treating the diDMAP compound **9a** with thiophenol in EtONa/EtOH (0.1 equiv) gave the vinylpyridinium **13**; even with large excess of thiophenol, no second addition was observed. However, the use of a mole of base led to the rearranged isomeric vinyl sulfide **12**. As expected, isolated **13** isomerized in EtONa/EtOH to **12**.

Under analogous conditions the 4-phenyl-4′-(dimethylamino)bis(pyridinium) diperchlorate (**9b**) yielded the dithioethers **5b** and **6b**. In contrast to **9a**, no pyridinium thioether analogous to **13** was detected even when only 0.9 equiv of thiophenol was used.

An addition–elimination–addition sequence is suggested for the formation of the dithioethers **5b** and **6b** via intermediates of type **13**, which in the case of the more strongly activated 4-phenyl derivatives undergo addition

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Table I. 1-(β-Substituted-Thioallyl)pyridinium Salts. Analytical and Spectroscopic Data

					^{1}H NMR[a]			^{13}C NMR			UV[b]	
no.	method	yield, %	mp, °C	mol form.[d]	N^+CH_2		$C{=}CH_2$	N^+CH_2	CCH_2	$C{=}CH_2$	λ_{max}	ϵ
1a	A	81	113–115	$C_{16}H_{19}ClN_2O_4S$	4.90	5.85	5.55	60.0	130.6	127.4	291	24 000
1b	A, B	67	118–119	$C_{20}H_{18}ClNO_4S$	5.45	6.05	5.60	63.1	130.5	124.1	302	22 000
1c	A, B	76	115–116	$C_{15}H_{16}ClNO_4S$	5.32	6.08	5.62	63.1	130.4	123.7	249	9000
2a	A,[c] B	76	139–141	$C_{17}H_{21}ClN_2O_4S$	4.95	5.60	5.30	60.6	139.1	115.1	291	25 000
2b	A, B	58	125–128	$C_{21}H_{20}ClNO_4S$	5.25	5.93	5.43	63.5	137.2	117.9		
2c	A	64	99–101	$C_{15}H_{18}ClNO_4S$	5.25	5.92	5.45	63.6	137.7	117.8		

[a] In $CDCl_3$, except for **1b** and **2a** in $Me_2SO/CDCl_3$. [b] In EtOH. [c] Gave 55:45 mixture with tautomer **4a**. [d] Satisfactory analytical data (±0.4% for C, H, N) were reported for all compounds.

of a second mole of thiol. Reaction of the bis(4-phenylpyridinium) salt **10b** with thiophenol also yielded **5b**, which demonstrates that 4-phenylpyridine can also act as a leaving group.

1,3-Propenediylbis(pyridinium) Salts. In order to compare the reactivity and stability of the 1,2- to the 1,3-substituted propenes, we looked for a general route to synthesize the 1,3-substituted products, as nucleophilic addition to propargylpyridinium salts as described above gave the desired substitution pattern only in the case of **11**.

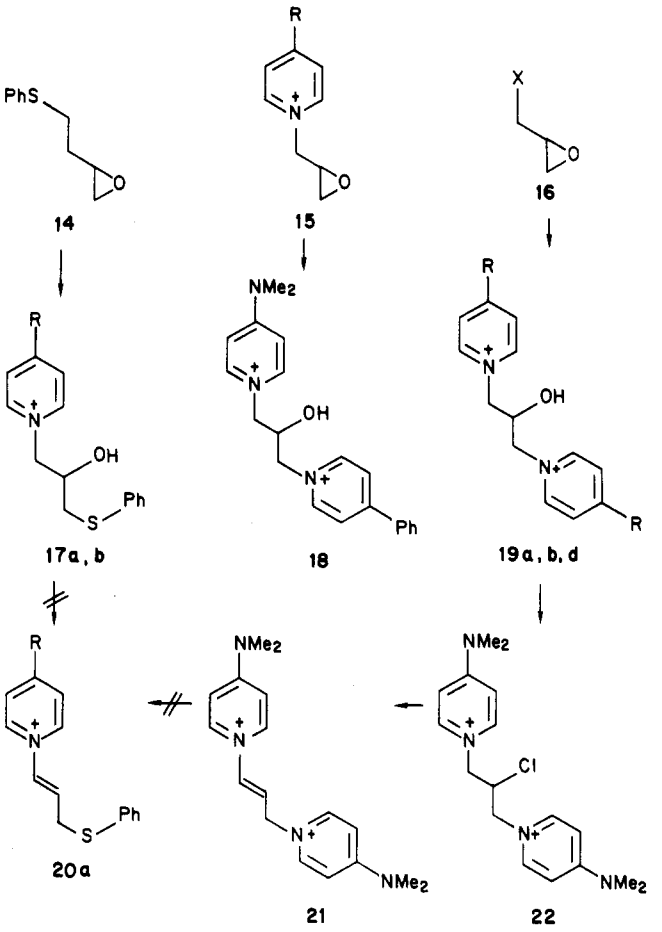
Nucleophilic ring opening of [(phenylthio)methyl]oxirane (**14**)[8] was accomplished with DMAP/DMAP·HCl to give **17a** (59%) or with 4-phenylpyridine/4-phenylpyridine hydroperchlorate to give **17b** (42%) (use of hydrochlorides gave low yields). Attempts to use 4-picoline or pyridine in place of 4-phenylpyridine gave as the only isolated products the chloro- and bromohydrins resulting from HX addition to the starting **14**, indicating that the halogen ions are stronger nucleophiles than the pyridines under these conditions. Attempts to convert (with $SOCl_2$, $SOCl_2/ZnCl_2$, $HCl/ZnCl_2$) the hydroxy derivatives **17a,b** to the corresponding chloro compounds failed, as did direct dehydration to **20**.

(2-Hydroxypropane-1,3-diyl)pyridinium salts **19** should yield the 1,3-disubstituted propenes **21** by elimination from the corresponding 2-chloro compounds. The only published[9] procedure for compunds of type **19** is the reaction of the corresponding pyridine with 1,3-dibromo-2-propanol which gives poor yields. We now find that reaction of molar amounts of a pyridine, the corresponding pyridine hydrochloride, and epichlorohydrin give **19a,b,d**. The strongly nucleophilic pyridines, DMAP, and 4-pyrrolidinopyridine, give **19a,d** in high yields. The 4-phenyl analogue **19b** was obtained in moderate yield by replacing epichloro- with epibromohydrin. 4-Picoline gave only tar.

Ring opening of heterocyclic epoxides of type **15** with pyridine hydrochlorides should give unsymmetrical bis(pyridinium) salts **18**. The strongly nucleophilic DMAP and 4-pyrrolidinopyridine reacted with epibromohydrin to form **15a,d** under conditions similar to those reported[10] for aliphatic amines. Ring opening of the epoxide **15a** with 4-phenylpyridine indeed gives **18**.

The DMAP hydroxy product **19a** was readily converted into the chloro compound **22** with $SOCl_2$. The 4-phenyl derivatives **18** and **19b** on reaction with $SOCl_2$ were recovered under mild conditions (40 °C, dilution with $CHCl_3$) and underwent decomposition under more vigorous conditions. Elimination of HCl in **22** with aqueous NaOH

Scheme II[a]



[a] Series a, R = NMe_2; b, R = Ph; d, R = pyrrolidino; anions ClO_4^- unless otherwise stated.

yielded the 1,3-disubstituted propene **21**. This was envisaged as a precursor for **20a**, but repeated attempts under various conditions to react thiolate nucleophiles with **21** failed to yield defined products.

UV Spectra of Vinyl Sulfides (Table I). Compounds **1a** and **1b** exhibited slight bathochromic shifts (5 and 7 nm) and increased extinction coefficients (24 000 and 22 000) in relation to the correspondingly 4-substituted pyridinium methyl iodides. [UV spectra (λ_{max}; ϵ) of 4-(dimethylamino)-1-methylpyridinium iodide (286.5 nm; 22 000) and 1-methyl-4-phenylpyridinium iodide (295 nm; 19 000) were recorded for comparison.] The UV absorption maxima and extinction coefficients of **3a** and **12** are very similar to those of the 4-(dimethylamino)-1-vinylpyridinium cations,[1] showing no significant modification by the sulfide group.

NMR Spectra. ^{1}H and ^{13}C NMR spectra have been recorded for all compounds. Chemical shifts of the various *N*-propenyl and *N*-propargyl substituents are reported in

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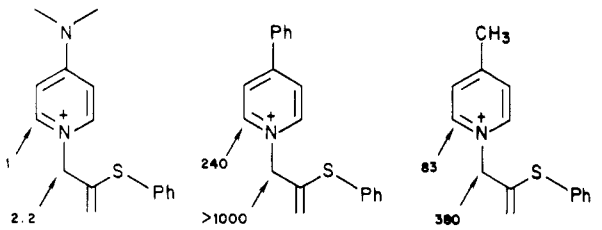
Table II. 1-(β-Substituted-Thiovinyl)pyridinium Salts. Analytical and Spectroscopic Data

			^{1}H NMR[c]		^{13}C NMR[d]		
no.	ratio[a]	mol form.[b]	NCH=	CH_3	NCH=	=CSPh	CH_3
3a[e]	35:65	$C_{16}H_{19}ClN_2O_4S$	6.70	1.95	127.9	132.9	17.1
3b	55:45	$C_{20}H_{18}ClNO_4S$	6.80	1.95	122.3	137.0	17.1
4a	65:35	$C_{17}H_{21}ClN_2O_4S$	6.80	1.95	125.9	140.3	17.2

[a] Compound:starting material. [b] Satisfactory analytical values were reported for all of the isomeric mixtures. [c] In $CDCl_3/Me_2SO$-d_6; signals are broadened by allylic coupling of ~1 Hz. [d] In Me_2SO-d_6. [e] UV (EtOH) λ_{max} 306 nm (ε 25000) obtained after substraction of UV of 1a in the UV of the mixture.

Chart I. Relative H-D Exchange Rates



the Experimental Section and in Tables I–III. The configuration of the double bond substituents in **11** and **21** have been assigned due to their coupling constants and in **3a,b**, **4a**, and **12** by the chemical shifts of their single olefinic hydrogen, on the basis of recently published[1] data for substituted *N*-vinylpyridinium cations. As the differences of the calculated chemical shifts for the *E* and *Z* conformers are small, the assignments are tentative.

Hydrogen–Deuterium Exchange. Semiquantitative relative rates of base-catalyzed H–D exchange of various pyridinium compounds in Me_2SO/D_2O at 25 °C were obtained by using ^{1}H NMR (see Experimental Section). While these experiments do not provide highly precise kinetics data, the relative orders of reactivity shown in Chart I seem secure.

With the vinyl sulfides **1a–c**, H–D exchange was observed at the α-position of the pyridinium ring and at the C-1 methylene group, with the latter always being faster. Under the conditions employed no detectable exchange of the other annular positions or the C-3 methylidene hydrogens was found. Even after 1 h at 80 °C (complete exchange of C-α and C-1 protons), and C-3 protons were unchanged.

Relative Stability of the Isomeric 1-[(Phenylthio)-propenyl]pyridinium Cations. In the 4-DMAP series of the 1-[(phenylthio)propenyl)pyridinium cations there are six possible isomers which fall into three sets of tautomeric pairs: **1a** ⇄ **3a**; **12a** ⇄ **13a**; and **11a** ⇄ **20a**. Of these compounds we characterized five. The equilibrium data of the base-catalyzed isomerizations (reported above) reflect the relative thermodynamic stability of the corresponding tautomers.

Isomerization studies of the effect of functional groups on the stability of olefins have been extensive.[11-13] Electron-withdrawing substituents increase the mobility of the methylene protons in $RCH{=}CHCH_2X$ and thus the rate of equilibration, but such substituents stabilize the resulting vinyl form $RCH_2CH{=}CHX$ only if they also display a mesomeric (M) effect.[12] In particular, while SCH_3 (–I, +M) stabilizes relative to CH_2SCH_3,[13] a simple ammonium group, NR_3^+ (–I, but no M effect), favors the allylic over the vinylic isomer.[14] However, as we reported recently,[15] *N*-allylpyridinium cations are isomerized into the *N*-(1-propenyl) derivatives.

The tautomerism in **12a** ⇄ **13a** favors the former: isolated **13** isomerized completely to **12**. The increased stability of the vinyl sulfide **12** as compared to the allyl sulfide substructure **13** is expected. Of the tautomeric pair **11** ⇄ **20a** we could prepare only **11**. Treatment with EtONa/EtOH (0.1 equiv) left **11** unaffected: it is expected to be more stable than the allyl sulfide **20a**.

In the equilibrium **1a** ⇄ **3a**, the latter predominates by a ratio of 35:65 corresponding to a ΔG of some –0.5 kcal/mol. In the corresponding 4-phenyl series the allylpyridinium cation **1b** is some 0.5 kcal/mol more stable than the vinyl compound **3b**, and in the 4-picoline series only **1c** was detected by NMR, hence **1c** is ≥2 kcal/mol more stable than **3c** (assuming 10% would have been detected). This indicates that the importance of conjugation between the double bond and the pyridine ring increases in the order **3c** ≪ **3b** < **3a**, presumably because of less charge spreading in the unconjugated tautomers.

No evidence was obtained for significant nucleophilic attack on the pyridinium ring in any of the work described in this paper.

Experimental Section

Melting points were determined with a Kofler hot-stage microscope and are uncorrected. Spectra were recorded with the following instruments: ^{1}H NMR with a Varian Model EM 360 L spectrometer using Me_4Si as internal standard, ^{13}C NMR with a JEOL Model JNM-FX 100 spectrometer, referring to the center signal of $CDCl_3$ (77.00) and of Me_2SO-d_6 (39.50), respectively, and UV with a Perkin-Elmer Model 330 spectrometer. Elemental analyses were carried out at the department by Dr. R. W. King. All reactions with perchlorate salts were carried out in a fume hood using appropriate safety precautions.

Addition of Thiophenol or Benzyl Mercaptan to 1-(2-Propynyl)- and 1-Propadienylpyridinium Salts 1a–c, 2a–c. General Procedure. Method A. Ethanolic 1 M sodium ethoxide (0.1 mmol) was added to the 4-substituted 1-propadienylpyridinium perchlorate (1 mmol) and the thiol (1.1 mmol) in dry ethanol (25 mL) and heated under reflux for 2 h. The solution was concentrated to 5 mL and the residue treated with ether (5 mL). The precipitated product was recrystallized from EtOH/EtOAc.

Method B. The reaction was performed as above but with 4-substituted 1-propargylpyridinium perchlorate instead of the 1-propadienyl derivative.

Physical data and spectral properties of the products **1a–c** and **2a–c** are recorded in Table I.

4-(Dimethylamino)-1-[3-(phenylthio)-2-propenyl]-pyridinium perchlorate (11) following method B: 82%; mp 156–159 °C; ^{1}H NMR ($CDCl_3$), 8.20 (2 H, d, 8 Hz), 7.50 (5 H, s), 7.02 (2 H, d, 8 Hz), 6.82 (1 H, d, 9.6 Hz), 5.95 (1 H, dt, 9.6 Hz, 6.6 Hz), 4.98 (2 H, d, 6.6 Hz), 3.35 (6 H, s). Anal. Calcd for $C_{16}H_{19}ClN_2O_4S$: C, 51.82; H, 5.16; N, 7.55. Found: C, 51.41; H, 5.30; N, 7.16.

Isomerization of Products 1a,b and 2a. General Procedure. Ethanolic 0.1 M sodium ethoxide (0.1 mmol or 0.2 mmol) was added to the pyridinium perchlorate (1 mmol) in dry ethanol (25 mL) and refluxed for the appropriate time. The solvent was

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Table III. (2-Hydroxypropane-1,3-diyl)bis(pyridinium) Salts. Analytical and Spectroscopic Data

					^{1}H NMR[a]		^{13}C NMR[a]		
no.	method	yield, %	mp, °C	mol form.[b]	CH_2	CHOH	CH_2	CHOH	CH_2
18d	B	74	111–112	$C_{21}H_{25}Cl_2N_3O_9$		5.2–4.4, 5 H, m	59.3	69.4	62.7
19a	A	77	301–303	$C_{17}H_{26}Cl_2N_2O_9$		4.8–4.1, 5 H, m	59.6	71.1	59.6
19b	A	38	224–226	$C_{25}H_{24}Cl_2N_2O_9$		5.4–4.7, 5 H, m	62.5	70.5	62.5
19d	A	68	230–232	$C_{21}H_{30}Cl_2N_4O_9$	4.8–4.1, 4 H, m	3.9–3.4, 1 H, m	59.6	69.3	59.6

[a] In Me_2SO-d_6. [b] Satisfactory analytical values were reported for all compounds.

removed in vacuo (40 °C (20 mmHg)), and the residue treated with ether and filtered. Recrystallization from ethanol afforded the isomeric mixtures. For spectral data of compounds **3a,b** and **4a**, see Table II.

Addition of 4-Substituted Pyridines to 4-(Dimethylamino)-1-propadienylpyridinium Perchlorate (8a). 4-(Dimethylamino)-1-propadienylpyridinium perchlorate (0.27 g, 1.05 mmol), 4-phenylpyridine (1 mmol), and 4-phenylpyridine hydrochloride (1 mmol) were heated under reflux in dry ethanol (25 mL) for 4 h. The solution was concentrated to 5 mL, and an excess of aqueous $NaClO_4$ was added. The precipitate was filtered off and recrystallized from $EtOH/H_2O$ (8:2) to yield **9b** as colorless needles (70%): mp 229 °C; ^{1}H NMR ($CDCl_3$/TFA) 9.20 (2 H, d, 7 Hz), 8.60 (2 H, d, 7 Hz), 8.5–7.8 (7 H, m), 7.10 (2 H, d, 7 Hz), 6.20 (1 H, d, 3.5 Hz), 5.85 (1 H, d, 3.5 Hz), 5.55 (2 H, s), 3.38 (6 H, s). Anal. Calcd for $C_{21}H_{23}Cl_2N_3O_8$: C, 48.85; H, 4.49; N, 8.14. Found: C, 49.12; H, 4.33; N, 7.81. In a similar manner **9c** was prepared from 4-picoline (75%): mp 235–236 °C; ^{1}H NMR ($CDCl_3$/TFA) 9.00 (2 H, d, 7 Hz), 8.35 (2 H, d, 7 Hz), 8.20 (2 H, d, 7 Hz), 7.12 (2 H, d, 7 Hz), 6.18 (1 H, d, 4 Hz), 5.85 (1 H, d, 4 Hz), 5.50 (2 H, s), 3.38 (6 H, s), 2.85 (3 H, s). Anal. Calcd for $C_{16}H_{21}Cl_2N_3O_8$: C, 42.31; H, 4.66; N, 9.25. Found: C, 42.29; H, 4.65; N, 8.77.

Addition of Thiophenol and Benzyl Mercaptan to 4-Substituted 2-Propenediylbis(pyridinium) Diperchlorates 9a–c and 10. The bis(pyridinium) salt **9b** (0.52 g, 1 mmol), thiophenol (0.5 g, 2.2 mmol) and 1 M ethanolic sodium ethoxide (1 mL, 1 mmol) were heated under reflux in dry ethanol (15 mL) for 5 h. The solution was concentrated to 5 mL and the products were precipitated with ether. The resulting crystals were filtered and recrystallized from EtOAc/EtOH to yield **5b** as colorless needles (0.42 g, 82%): mp 140–141 °C; ^{1}H NMR ($CDCl_3$) 8.75 (2 H, d, 7 Hz), 7.98 (2 H, d, 7 Hz), 7.70 (5 H, bs), 7.25 (10 H, bs), 4.65 (1 H, m), 3.80 (4 H, m). Anal. Calcd for $C_{26}H_{24}ClNO_4S_2$: C, 60.75; H, 4.71; N, 2.72. Found: C, 60.83; H, 4.74; N, 2.64. In a similar manner **6b** was prepared from **9b** and benzyl mercaptan (65%): mp 130–131 °C; ^{1}H NMR (Me_2SO-d_6) 9.20 (2 H, d, 7 Hz), 8.50 (2 H, d, 7 Hz), 8.3–7.2 (15 H, m), 5.2–4.7 (1 H, m), 4.80 (4 H, s), 3.1 (4 H, bd). Anal. Calcd for $C_{28}H_{28}ClNO_4S_2$: C, 62.04; H, 5.21; N, 2.58. Found: C, 61.63; H, 5.27; N, 2.50.

4-(Dimethylamino)-1-[1-(phenylthio)-1-propen-2-yl]-pyridinium Perchlorate (12). The reaction was performed as in the above procedure starting with **9a** to yield product **12** (78%) as colorless prisms: mp 146–148 °C; ^{1}H NMR ($CDCl_3$) 8.20 (2 H, d, 8 Hz), 7.48 (5 H, bs), 7.12 (2 H, d, 8 Hz), 6.66 (1 H, s), 3.30 (6 H, s), 2.32 (3 H, s); UV (EtOH) λ_{max} 310 nm (ϵ 22 000). Anal. Calcd for $C_{16}H_{19}ClN_2O_4S$: C, 51.82; H, 5.16; N, 7.55. Found: C, 51.71; H, 5.21; N, 7.60.

4-(Dimethylamino)-1-[1-(phenylthio)-2-propen-2-yl]-pyridinium Perchlorate (13). Bis(pyridinium) salt **9a** (0.48 g, 1 mmol), thiophenol (0.12 g, 1 mmol), and sodium ethoxide (0.1 mL 1 N in ethanol, 0.1 mmol) were heated in dry ethanol (15 mL) under reflux for 15 h and cooled to 0 °C. Product **13**, contaminated with 50% DMAP perchlorate (360 mg, 61%), separated. Recrystallization from ethanol was not effective: ^{1}H NMR ($CDCl_3$/TFA) 7.95 (2 H, d, 8 Hz), 7.40 (5 H, bs), 6.92 (2 H, d, 8 Hz), 5.32 (2 H, s), 4.00 (2 H, s), 3.30 (6 H, s); peaks from co-crystallizing product: 8.30 (2 H, d, 8 Hz), 6.92 (2 H, d), 3.30 (6 H, s).

Preparation of 4-Substituted 1-(Oxiranylmethyl)-pyridinium Salts 15a,b. 4-(Dimethylamino)-1-(oxiranylmethyl)pyridinium Bromide (15a). DMAP (5 g, 41 mmol) and epibromohydrin (6.17 g, 45 mmol) were stirred in dry THF (40 mL) at 25 °C for 36 h. The resulting crystals were filtered and washed with THF and ether to yield **15a** (8.5 g, 80%) as colorless needles: mp 181–182 °C; ^{1}H NMR ($CDCl_3$/Me_2SO-d_6) 8.55 (2 H, d, 8 Hz), 7.20 (2 H, d, 8 Hz), 5.11 and 4.16 and 3.6–3.4 (ABX, J_{AB} = 15 Hz, J_{AX} = 1.7 Hz, J_{BX} = 8.5 Hz), 3.35 (6 H, s), 3.6–3.4 and 2.92 and 2.70 (ABX system: J_{AB} = 5.0 Hz, J_{AX} = 4.1 Hz, J_{BX} = 1.9 Hz); the 2-CH is X in both ABX systems.

4-(1-Pyrrolidinyl)-1-(oxiranylmethyl)pyridinium Perchlorate (15d). The reaction was performed as above for **15a**. The obtained pyridinium bromide was dissolved in a little methanol and precipitated with an excess of aqueous $NaClO_4$ to give **15d**, which was recrystallized from 1,2-dichloroethane (60%, colorless needles): mp 150–152 °C: ^{1}H NMR (Me_2SO-d_6) 8.40 (2 H, d, 7 Hz), 7.00 (2 H, d, 7 Hz), 4.51 and 4.44 (ABX, J_{AB} = 15 Hz, J_{AX} = 2.8 Hz, J_{BX} = 6.2 Hz), 3.9–3.3 (9 H, m), 2.81 and 2.76 (ABX, J_{AB} = 4.4 Hz, J_{AX} = 4.4 Hz, J_{BX} = 2.3 Hz), 2.4–2.0 (8 H, m); X of both ABX systems is hidden under NCH_2 signal (3.9–3.3) of the pyrrolidine substituent, the center is at 3.45 ppm (found by irradiation experiments). Anal. Calcd for $C_{12}H_{17}ClN_2O_5$: C, 47.30; H, 5.62; N, 9.19. Found: C, 47.37; H, 5.65; N, 9.07.

Preparation of 4-Substituted 1-[2-Hydroxy-3-(phenylthio)propanyl]pyridinium Perchlorates 17a,b. In a typical example a solution of DMAP (3 g, 24.6 mmol), DMAP hydrochloride (3.89 g, 24.6 mmol), and [(phenylthio)methyl]oxirane (4.1 g, 24.6 mmol) were refluxed in dry ethanol (60 mL) for 20 h. The solvent was removed in vacuo (50 °C (15 mmHg)), an excess of aqueous $NaClO_4$ was added, and the product was filtered to yield **17a**, which was recrystallized twice from $EtOH/CHCl_3$ (9:1): 5.6 g (59%, colorless needles); mp 98–99 °C; ^{1}H NMR ($CDCl_3$/TFA) 8.00 (2 H, d, 8 Hz), 7.45 (5 H, bs), 6.82 (2 H, d, 8 Hz), 4.6–3.9 (3 H, m), 3.25 (6 H, s), 3.3–3.1 (2 H, m). Anal. Calcd for $C_{16}H_{21}ClN_2O_5S$: C, 49.41; H, 5.44; N, 7.20. Found: C, 48.98; H, 5.54; N, 6.98.

Identically, **17b** was prepared from 4-phenylpyridine (23%, colorless needles): mp 138–141 °C; ^{1}H NMR ($CDCl_3$/TFA) 8.83 and 8.31 (4 H, AB q, J_{AB} = 7 Hz), 8.0–7.7 (5 H, m), 7.5–7.3 (5 H, m), 5.1–4.3 (3 H, m), 3.30 (2 H, bd, 6 Hz). Anal. Calcd for $C_{20}H_{20}ClNO_5S$: C, 56.94; H, 4.78; N, 3.32. Found: C, 56.55; H, 4.77; N, 3.19.

When 4-phenylpyridine hydroperchlorate was used instead of the hydrochloride under otherwise identical conditions, the yield of **17b** was greatly improved (42%).

Preparation of 4,4′-Disubstituted 1,1′-(2-Hydroxypropane-1,3-diyl)bis(pyridinium) Diperchlorates 19a,b,d and 18. Method A. The 4-substituted pyridine (20 mmol), the corresponding pyridine hydrochloride (20 mmol), and epichlorohydrin (20 mmol) (epibromohydrin in the case of 4-phenylpyridine) were refluxed for 16 h in dry ethanol (50 mL). The solution was concentrated (10 mL) and an excess of aqueous $NaClO_4$ added. The crude precipitate was recrystallized from $EtOH/H_2O$ (8:2).

Method B. 4-(Dimethylamino)-1-(oxiranylmethyl)pyridinium bromide (10 mmol) and the 4-substituted pyridine hydrochloride in dry ethanol (30 mL) were refluxed for 16 h. The solvent was removed in vacuo (50 °C (20 mmHg)) and the oily residue treated with an excess of aqueous $NaClO_4$. The product was filtered and recrystallized from $EtOH/H_2O$ (9:1).

For physical properties of spectral data of compounds **19a,b,e** and **18**, see Table III.

1,1′-(2-Chloropropane-1,3-diyl)bis[4-(dimethylamino)-pyridinium] Diperchlorate (22). Compound **19a** (13.5 g, 28.6

mmol) was refluxed in $SOCl_2$ (40 mL) for 2 h. The solvent was removed by distillation (80 °C (760 mmHg)), and the resulting solid was treated with ether and filtered. Recrystallization from $EtOH/H_2O$ (8:2) yielded the chloro compound **22** (11.2 g, 80%) as colorless needles: mp 294–297 °C; ^1H NMR (Me_2SO-d_6) 8.37 (4 H, d, 7 Hz), 7.20 (4 H, d, 7 Hz), 5.1–4.2 (5 H, m), 3.25 (12 H, s). Anal. Calcd for $C_{17}H_{25}Cl_3N_4O_8$: C, 39.28; H, 4.85; N, 10.78; Found: C, 39.16; H, 4.93; N, 10.71.

1,1′-(1-Propene-1,3-diyl)bis[4-(dimethylamino)pyridinium] Diperchlorate (21). A suspension of finely powdered chloro compound **22** (4 g, 8.16 mmol) in ethanol (50 mL) was treated with aqueous NaOH (2.5 N, 3.9 mL, 9.8 mmol) and stirred for 24 h. The reaction mixture was acidified with $HClO_4$ (70%) and concentrated to a third of its volume, yielding **21** as colorless crystals, recrystallized from $EtOH/H_2O$ (8:2) (2.5 g, 76%, needles): mp 274–275 °C; ^1H NMR ($CDCl_3$/TFA) 8.35 (2 H, d, 8 Hz), 8.25 (2 H, d, 8 Hz), 7.45 (1 H, d, 14 Hz), 7.10 (2 H, d, 8 Hz), 7.05 (2 H, d, 8 Hz), 6.55 (1 H, dt, 14 Hz, 7 Hz), 5.05 (2 H, d, 7 Hz), 3.40 (6 H, s), 3.35 (6 H, s). Anal. Calcd for $C_{17}H_{24}Cl_2N_4O_8$: C, 42.25; H, 5.01; N, 11.59. Found: C, 42.08; H, 5.07; N, 11.49.

Hydrogen–Deuterium Exchange. Due to the low solubility of pyridinium perchlorates in D_2O, it took us several attempts to develop working conditions for the H–D exchange. The exchange experiments were conducted at 25 °C in Me_2SO-d_6–D_2O (v/v 3:2) saturated with dry K_2CO_3; substrate concentration 0.075 mmol in 0.4 mL solvent. In all cases the H_2O concentration was below 5%. Rates were calculated from five to eight points by applying first-order kinetics, after following at least 1.5 half-lives.

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Registry No. **1a**, 94821-09-7; **1b**, 94821-11-1; **1c**, 94821-13-3; **2a**, 94821-15-5; **2b**, 94821-17-7; **2c**, 94821-19-9; **3a**, 94821-21-3; **3b**, 94821-23-5; **4a**, 94821-25-7; **5b**, 94821-27-9; **6b**, 94821-29-1; **7a**, 93288-50-7; **7b**, 93288-56-3; **7c**, 94821-31-5; **8a**, 93288-65-4; **8b**, 93288-69-8; **8c**, 93288-67-6; **9a**, 93288-58-5; **9b**, 94821-33-7; **9c**, 94821-35-9; **10b**, 94821-37-1; **11**, 94843-11-5; **12**, 94821-39-3; **13**, 94843-13-7; **14**, 94821-40-6; **15a**, 94821-42-8; **15b**, 94821-44-0; **15d**, 94821-46-2; **16** (X = Cl), 106-89-8; **16** (X = Br), 3132-64-7; **17a**, 94821-48-4; **17b**, 94821-50-8; **18**, 94821-52-0; **19a**, 94821-54-2; **19b**, 94821-56-4; **19d**, 94843-15-9; **21**, 94821-58-6; **22**, 94821-60-0; DMAP, 1122-58-3; DMAP·HCl, 71561-71-2; thiophenol, 108-98-5; 4-phenylpyridine hydrochloride, 16663-69-7; 4-picoline, 1333-41-1; 4-phenylpyridine hydroperchlorate, 94821-61-1; 4-pyrrolidinopyridine, 2456-81-7; 4-pyrrolidinopyridine hydrochloride, 94821-62-2; 4-(dimethylamino)-1-(oxiranylmethyl)pyridinium bromide, 94821-63-3; benzyl mercaptan, 100-53-8; 4-phenylpyridine, 939-23-1.

Heterocyclic Ynammonium Salts

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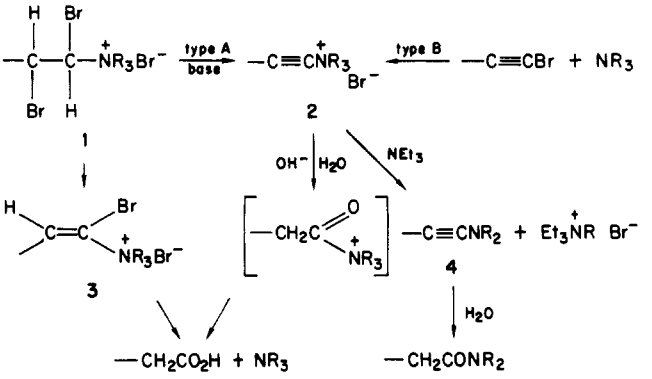
9(10*H*)-Acridinone anion reacts with ethynyl bromides to give 10-ethynyl-9(10*H*)-acridinones which are converted by phenyllithium to the corresponding 9-phenyl-9-hydroxy-10-ethynylacridinanes. The latter are converted by acid into 10-ethynylacridinium salts. ^{13}C NMR spectra are obtained, assigned, and discussed for all compounds mentioned.

Ynamines **4**, first described some 20 years ago,[1] are now familiar and versatile synthons. Their chemistry has been reviewed recently.[2,3] By contrast, there are few reports of ynammonium salts **2**. The first synthesis, claimed[4] in 1892, was disproved by Klages[5] in 1940. Ynammonium intermediates **2** have been postulated[6,7] in reactions of type A and B (Scheme I). Babayan et al.[6] studied the elimination of HBr from the dibromide **1** and suggested that intermediate **2** underwent addition of a hydroxide ion to form the acid and tertiary amine which were isolated. However, reaction of hydroxide ion with a vinyl bromide intermediate (**3**) would lead to the same products.

In reactions of the type B (Scheme I) Viehe[8] and Miller[7] also postulated the same unstable intermediates **2** which, by a transalkylation similar to a von Braun degradation, gave the ynamines **4** (or amide hydrolysis products) that were actually isolated.

Dumont[9] reported some diynammonium salts, but without physical data. The only ynammonium salt **2** that

Scheme I



has been isolated and adequately characterized is *N,N,N*-triethylethynylammonium bromide (**5**) by Miller.[10] Under

$$HC{\equiv}CBr + NEt_3 \rightarrow HC{\equiv}C^+NEt_3Br^-$$

analogous conditions but using pyridine, quinoline, or acridine (in place of NEt_3) and (bromoethynyl)benzene, Miller[10] observed only tar formation. Thus, as far as we are aware, no heterocyclic ynammonium salts have previously been reported.

However, heterocyclic ynammonium salts should be considerably more stable than aliphatic analogues, as transalkylation is precluded. We attempted their prepa-

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