The Stereochemistry of Addition of Trialkylammonium and Pyridinium Tetrafluoroborate Salts to Activated Acetylenes. Preparation of Novel Dienophiles for Diels–Alder Reactions[1]

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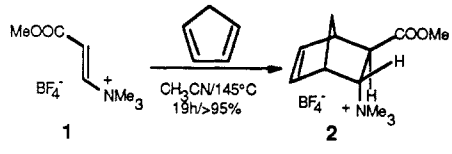
Abstract: The preparation of a new class of dienophiles, alkenylammonium and -immonium tetrafluoroborate salts, for Diels–Alder cycloadditions is described. The reactions between trialkylammonium and pyridinium tetrafluoroborate salts with activated acetylenes show an unusual stereochemical dependence upon steric factors, solvent, and the nature of the activating group. A reasonable mechanism for the reaction which accounts for the observed stereochemistry based on the different rates of equilibration of the various intermediate vinyl anions is presented. Thus acetylenic ketones give exclusively *E*-isomers (thermodynamic control) and acetylenic nitriles afford only *Z*-isomers (kinetic control), while acetylenic esters and amides generally furnish mixtures of *E*- and *Z*-isomers. The addition of hindered 2-substituted pyridinium salts gives only the less stable *Z*-isomers due to steric hindrance to protonation leading to the more stable *E*-isomers.

We recently reported that alkenyltrialkylammonium salts such as **1** and alkenylimmonium salts such as **3** underwent Diels–Alder reactions with dienes such as cyclopentadiene to afford the endo adducts **2** and **4**, respectively, in excellent yields.[4-5] (see eq 1 and 2). During the course of these investigations, we required a facile



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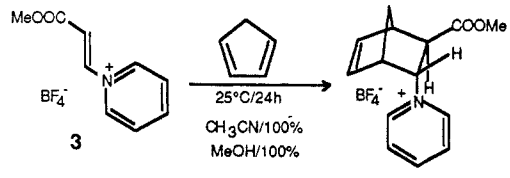
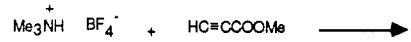


3 4 (2)

preparation of several alkenylammonium and -immonium tetrafluoroborate salts in stereochemically homogeneous form. There have been several reports in the recent literature of the reaction of methyl propiolate with various trialkylammonium halide salts to yield primarily *trans*-(2-methoxycarbonylvinyl)trialkylammonium salts. For example, Herkes and Simmons[6] reported that various trialkylammonium or pyridinium bromides react with equimolar amounts of methyl propiolate in warm aqueous dioxane to afford exclusively *trans*-(2-methoxycarbonylvinyl)trialkylammonium salts. Unfortunately, the yields were modest at best (21–50%). McCulloch and McInnes[7] discovered that triethylammonium chloride reacts with equimolar amounts of methyl propiolate in refluxing methanol to give a mixture of *cis*- and *trans*-(2-methoxycarbonylvinyl)triethylammonium chlorides in an approximately 1.2:1 ratio in 80% yield. Interestingly, if 2 equiv of methyl propiolate were employed, the ratio increased to 91% of the trans isomer.

Our experience with these halide salts in Diels–Alder cycloadditions indicate that they suffer from facile thermal N-dealkylation. Furthermore they are often very hygroscopic, requiring special handling. We subsequently discovered that the tetrafluoroborate salts are advantageous for three reasons: (1) they are stable, nonhygroscopic, crystalline solids; (2) they have increased solubility in aprotic organic solvents (e.g., acetonitrile), and (3) they do not suffer thermal N-dealkylation at temperatures below 200 °C. Although exchange of halide for tetrafluoroborate can be achieved with silver tetrafluoroborate or more economically via ion exchange chromatography, we felt it expeditious to develop a simple, one-pot procedure for the synthesis of these compounds. Additionally, there are virtually no reports in the literature concerning the addition of trialkylammonium salts with complex counterions to activated acetylenes. We now report the results of our investigation in this area.

Table I. Addition of Trimethylammonium Fluoroborate to Methyl Propiolate



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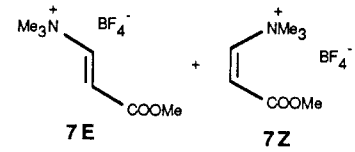

7E 7Z

time	solvent	temp (°C)	yield (%)	*E*:*Z* ratio
5 min	MeOH	65	64	54:46
15 min	MeOH	65	79	57:43
25 min	MeOH	65	87	53:47
40 min	MeOH	65	92	55:45
1 h	MeOH	65	>95	56:44
2 h	MeOH	65	>95	55:45
2.5 h	MeOH	65	99	57:43
10 min	MeOH	25	5	56:44
0.5 h	MeOH	25	11	47:53
1 h	MeOH	25	17	47:53
19 h	MeOH	25	49	62:38
10 min	CH_3CN	75	70	82:18
0.5 h	CH_3CN	75	80	78:22
1 h	CH_3CN	75	85	82:18
19 h	CH_3CN	75	88	85:15
15 min	CH_3CN	25	8	86:14
18 h	CH_3CN	25	100	90:10

Results and Discussion

Following the lead of McCulloch and McInnes,[7] we treated trimethylammonium tetrafluoroborate **5** with 1.2 equiv of methyl propiolate **6** in refluxing methanol for 2.5 h (Table I). Examination of the reaction product (crude yield 100%) by ^1H NMR revealed a mixture of (*E*- and *Z*)-(2-methoxycarbonylvinyl)trimethylammonium tetrafluoroborate salts in a 57:43 ratio. A single recrystallization from MeOH/Et_2O afforded analytically pure

(1) Abstracted in part from the Ph.D. Thesis of K.R.B., University of California, Los Angeles, October, 1987.
(2) UCLA Gold Shield Faculty Awardee, 1986–1988; UCLA Glenn T. Seaborg Awardee, 1987.
(3) Saul Winstein Dissertation Awardee, 1986–1987.
(4) Jung, M. E.; Buszek, K. R. *J. Org. Chem.* **1985**, *50*, 5440.
(5) Jung, M. E.; Buszek, K. R. *Tetrahedron Lett.* **1986**, *27*, 6165.
(6) McCulloch, A. W.; McInnes, A. G. *Can. J. Chem.* **1974**, *52*, 3569.
(7) Herkes, F. E.; Simmons, H. E. *J. Org. Chem.* **1973**, *38*, 2845.

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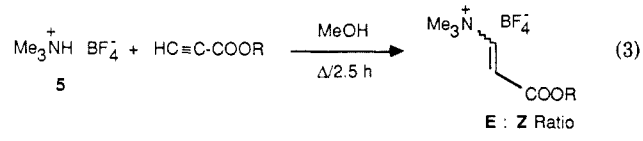
E-isomer **7E** (J = 14 Hz). The mother liquor was further recrystallized (MeOH/Et_2O) to yield nearly pure *Z*-isomer **7Z** (J = 8 Hz). When 2 or more equiv of methyl propiolate was used, essentially no change in product distribution was observed. Since this result is not consistent with the results obtained with halide salts in protic solvents and also differs with respect to primary and secondary amine additions to activated acetylenes,[8] we decided to investigate further the factors controlling the stereochemistry of such additions.

It is probable that the kinetically favored product results from trans addition of the ammonium salt to the triple bond resulting in overall cis stereochemistry.[9] This initial compound may then isomerize to the trans product during the course of the reaction. However, examination of the reaction mixture at intervals between 5 min and 2.5 h reveals essentially no change in product ratio (Table I). Either a rapid equilibrium is established very early in the reaction or else the factors controlling E/Z ratios are independent of time. The same reaction performed at 25 °C reveals a similar result, although the rate of reaction is now much slower.

If, however, a polar aprotic solvent such as acetonitrile is used, then the yield of *E*-isomer is significantly increased, to nearly 80% in refluxing acetonitrile and almost 90% at ambient temperature. Presumably protic solvents such as methanol promote a higher proportion of the products of kinetic control, whereas polar aprotic solvents such as acetonitrile afford more of the products of thermodynamic control. One would expect the product of kinetic control to be the *Z*-product, namely that resulting from the well-known trans addition of the nucleophile, in this case the ammonium salt, to the acetylene.[9] The thermodynamic product would be expected to be the *E*-isomer with the large trialkylammonium group trans to the ester. Indeed, the addition of trimethylammonium tetrafluoroborate **5** to increasingly hindered propargylic acid esters **6**, **8–10** in methanol results in ever greater amounts of the *E*-isomers **7E**, **11E–13E** (eq 3). Thus it seems

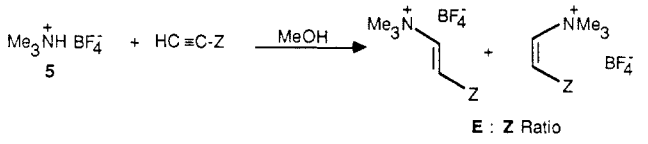


(3)

	E : Z Ratio
6 R = Me	**7** 57:43
8 R = Et	**11** 70:30
9 R = iPr	**12** >76:<24
10 R = 2,6-$(CH_3)_2C_6H_3$	**13** >95:<5

that with esters, a fast equilibrium is established with the initial kinetic product, the *Z*-isomer, isomerizing rapidly to give the more stable *E*-isomer.

The reactions with acetylenes activated by other electron-withdrawing groups show some rather dramatic results (eq 4).



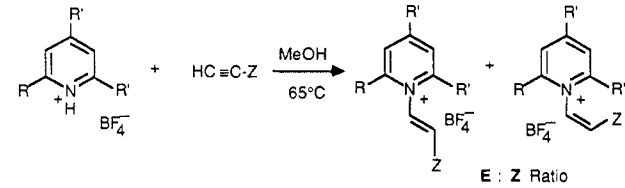
		E : Z Ratio
14 Z=$COCH_3$	25°C/8h	**17** 100:0
15 Z=CONHEt	65°C/2.5h	**18** 64:36
6 Z=COOMe	65°C/2.5h	**7** 57:43
16 Z=CN	25°C/8h	**19** 0:100

(4)

Reaction with 3-butyn-2-one (**14**) afforded only the *E*-isomer **17E**, while similar reaction with propiolonitrile (**16**) yielded only the *Z*-isomer **19Z**. As expected, the reaction with these substrates is much faster than with the esters due to the greater electron-withdrawing ability of the substituents. The amide **15** reacted more sluggishly and produced a 64:36 mixture of *E*- and *Z*-isomers, **18EZ**.

Since the product **19Z** is only slightly soluble in the reaction medium, an initial conjecture was that the kinetic cis nitrile preferentially crystallized from solution. However, examination of the mother liquor from this reaction revealed no other product; furthermore, when the reaction was carried out with a large excess of solvent to prevent crystallization, the same results were obtained. Additionally, reaction temperature was determined to not be a factor. In this case it is not obvious that there would be a large difference in the thermodynamic stability of the *E*- and *Z*-isomers since steric interaction would be small in the *Z*-isomer, which might be slightly stabilized electronically. In any event, one would not expect the *Z*-isomer **19Z** to be the sole product on a thermodynamic basis, and thus it must be the kinetic product.

Finally we decided to investigate the stereochemistry of the addition of various pyridinium tetrafluoroborates **23a–d** to methyl propiolate (**6**), 3-butyn-2-one (**14**), and propiolonitrile **16** (eq 5).



				E : Z Ratio
23a	R=R'=H		**14** Z=$COCH_3$	**24** 100:0
23a	R=R'=H		**16** Z=CN	**25** 0:100
23a	R=R'=H		**6** Z=COOMe	**26** 44:56
23b	R=CH_3	R'=H	**6** Z=COOMe	**27** 0:100
23c	R=CH_2OAc	R'=H	**6** Z=COOMe	**28** 0:100
23d	R=R'=Me		**6** Z=COOMe	**29** 0:100

(5)

The unsubstituted pyridinium tetrafluoroborate **23a** reacts with both **14** and **16** in dry methanol at room temperature for 8 h to afford exclusively the *E*-ketone **24E** and the *Z*-nitrile **25Z**, respectively, in excellent yields. Also, **23a** adds to methyl propiolate (**6**) to give a 44:56 mixture of **26E**:**26Z**. This is consistent with our earlier observations with the trialkylammonium salts. However, in sharp contrast, 2-monosubstituted or 2,4,6-trisubstituted pyridinium tetrafluoroborates **23b–d** give only the *Z*-isomers (**27Z–29Z**) when treated with 2.0 equiv of methyl propiolate (**6**) in refluxing methanol for 24 h. Clearly, these very sterically hindered compounds must be kinetic products, with no cis–trans isomerization having occurred. In all cases the stereochemistry of the compounds was assigned on the basis of ^1H, ^{13}C, and, especially, nuclear Overhauser effect (NOE) magnetic resonance experiments. In general, the coupling constants of the trans hydrogens in the *E*-adducts, e.g., **26E**, were about 14 Hz, while the corresponding cis hydrogens in the *Z*-isomers had J = 8.5 Hz. The use of different NOE measurements helped confirm the structure determination for compounds such as **29Z**. Irradiation of the methyl signals α to the pyridine nitrogen (δ 2.56) caused an enhancement of 15% in the β-hydrogen (δ 7.32) but had no effect on the α-hydrogen (δ 6.61), thus indicating the trans arrangement of the α-hydrogen and the pyridinium group. Under all reaction conditions no evidence of any equilibration of the *Z*-isomers **27Z–29Z** with their presumably more stable *E*-isomers was obtained.

These somewhat confusing results can be explained by the following hypotheses. One would expect in all cases that the kinetic product would be that arising from trans addition of the ammonium salt to the acetylene, namely the *Z*-isomers due to the well-known preference for trans addition of nucleophiles to activated acetylenes.[9] Mechanistically the reaction probably proceeds as shown in Scheme I. The small amount of free tertiary amine **30** present in the solution of the salt **31** should add to the acetylene **32** to give **33Z** rather than **33E** as the major isomer. If the equilibrium between **33Z** and **33E**, which proceeds via the allenic form **34**, is slow versus protonation, one would expect **35Z** to predominate over **35E**. When equilibration is fast, one should

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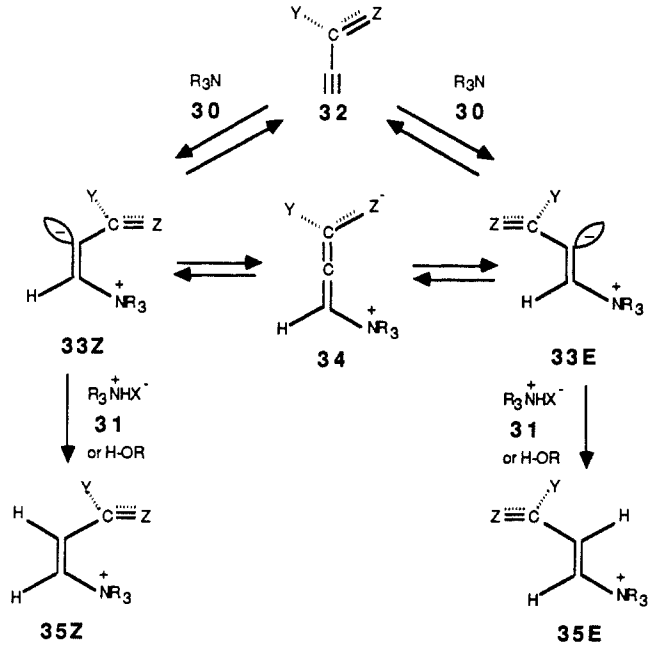
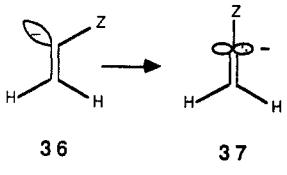
Scheme I



obtain the thermodynamically more stable product. One can estimate the rate of equilibration between **33Z** and **33E** via **34** as a function of the ability of the activating group to stabilize an anion by resonance with ketones being more readily equilibrated, esters and amides intermediate, and nitriles (which stabilize α-carbanions mainly by induction)[10] least easily equilibrated. This hypothesis is supported by the calculations of Houk on the influence of electron-withdrawing substituents on the barriers to inversion of vinyl anions.[11] The calculations show that the barrier to inversion (e.g., **36** → **37**), (see eq 6) for the α-cyanovinyl anion



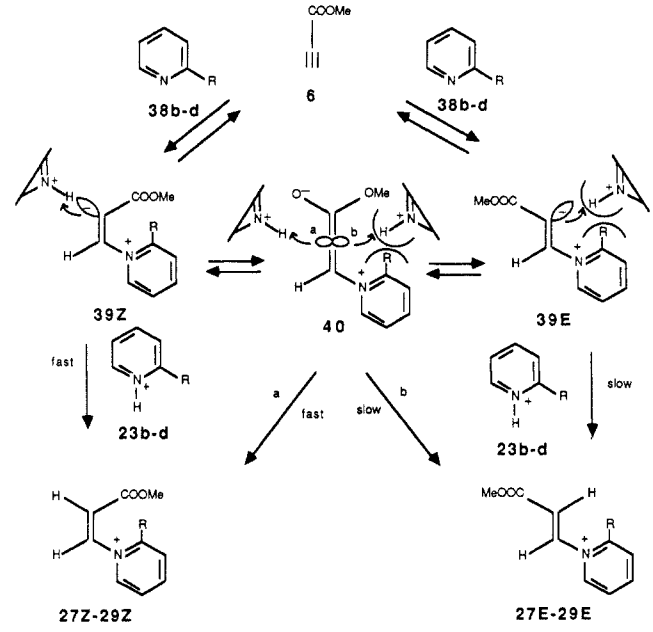
		$E_{linear} - E_{bent}$ (kcal/mole)	
a	Z=CN	+ 10.3	(6)
b	Z=COOMe	+ 5.0	
c	Z=CHO	- 5.7	
d	Z=COMe	—	

36a to be 10 kcal/mol, that for the α-carbomethoxyvinyl anion **36b** 5 kcal/mol, and that for the α-formylvinyl anion **36c** to be −6 kcal/mol (i.e., it should be more stable as the linear form **37** rather than the bent form **36**). No calculations were done for the corresponding α-acetylvinyl anion **36d**, but one would estimate it to be about midway between the ester and aldehyde, say 0 kcal/mol. Thus the stereochemistry of the adducts is determined by the rate of protonation of the vinyl anions **33Z** and **33E** versus the rate of equilibration between **33Z** and **33E** via **34**. For the reaction of the trialkylammonium tetrafluoroborates with the methyl ester **6** in acetonitrile equilibration is presumably more rapid than protonation, and a highly thermodynamic mixture is obtained. In methanol, protonation of the kinetically formed anion **33Z** now competes somewhat with equilibration, and thus a higher proportion of **35Z** is produced (Table I). The more hindered the ester function is, the higher the proportion of *E*-isomer **35E** formed (eq 3). The same holds true for the amide **15**, namely a nearly 1:1 mixture of *E*- and *Z*-isomers is obtained. In fact the rate of protonation for the anion from the methyl ester **6** must be very similar to the rate of equilibration in methanol to give a nearly 1:1 mixture of the *E*- and *Z*-isomers, slightly favoring the *E*-isomer. Since the anion from the ketone **14** should be much more easily equilibrated (~5 kcal/mol lower barrier to inversion) than

(10) (a) Walborsky, H. M.; Motes, J. M. *J. Am. Chem. Soc.* **1970**, *92*, 2445. (b) Motes, J. M.; Walborsky, H. M. *Ibid.* **1970**, *92*, 3697. (c) Walborsky, H. M.; Turner, L. M. *Ibid.* **1972**, *94*, 2273.

(11) Caramella, P.; Houk, K. N. *Tetrahedron Lett.* **1981**, 819.

Scheme II



the ester, one would expect only the thermodynamic *E*-isomer to be formed and this is the case. In contrast, since the anion from the nitrile **16** should be much less readily equilibrated (~5 kcal/mol higher barrier to inversion) than the ester, one would expect only the kinetic *Z*-isomer to be produced and again this is observed.

The same arguments hold for the addition of the pyridinium tetrafluoroborate salt itself **23a** to the ketone **14**, nitrile **16**, and ester **6** with respectively the thermodynamic *E*-isomer **24E**, kinetic *Z*-isomer **25Z**, and an approximate 1:1 mixture **26EZ** being formed. However, there is clearly a breakdown in the simple mechanistic picture for addition of the 2-substituted and 2,4,6-trisubstituted pyridinium salts (**23b–d**) to the ester **6**. In the absence of other effects, one would have expected mixtures of *E*- and *Z*-isomers with the more thermodynamically stable *E*-isomers being the major products. However only the *Z*-isomers are obtained. This can be explained by invoking the following argument. We assume that the rates of protonation of the intermediate vinyl anions resulting from addition of the trialkylamine to the acetylenes **33EZ** leading to **35EZ** are essentially identical. However this should no longer be the case for the 2-substitued and 2,4,6-trisubstituted pyridines. Now protonation of **39Z** should be much faster than protonation of **39E** or **40** due to the large steric hindrance associated with protonation cis to the large 2-substituted pyridinium group. Thus formation of the *E*-isomers **27E–29E** is favored by a kinetic protonation of the equilibrium mixture of anions **39ZE** and **40** from the less hindered direction (see Scheme II).

Conclusion

We have carried out extensive studies on the factors governing the stereochemistry of the addition of trialkylammonium salts and pyridinium salts to activated acetylenes. In general the stereochemistry observed is directly related to the rate of equilibrium of the derived vinylanions with ketones giving *E*-isomers (thermodynamic control), nitriles giving *Z*-isomers (kinetic control), and esters and amides giving mixtures of *E*- and *Z*-isomers. In the case of the addition of the very hindered 2-substituted pyridinium salts, only the kinetic *Z*-isomers are observed due to steric hindrance to protonation leading to the more stable *E*-isomers.

Experimental Section

General Methods. For specific information on general experimental details, see the Ph.D. thesis of Keith R. Buszek, UCLA, 1987. Low resolution fast atom bombardment (FAB) mass spectroscopy was performed on a KRATOS model MS902 mass spectrophotometer employing a 5 kV xenon source at 25 °C in a glycerol matrix. Propiolic acid and 3-butyn-2-one were purchased from Aldrich Chemical Co. and were

distilled immediately prior to use. Boron trifluoride etherate was obtained from Alfa Products and purified according to literature procedures.[12] The trialkylammonium and pyridinium tetrafluoroborate salts were obtained by mixing an excess of the appropriate amine with 48% aqueous fluoboric acid in methanol, followed by evaporation to dryness and recrystallization from methanol or methanol/ether.

Methyl Propiolate (6). To a solution of freshly distilled propiolic acid (25 g, 0.37 mol) in dry methanol (200 mL) was added via syringe freshly distilled boron trifluoride etherate (93 mL, 0.76 mol). The solution was refluxed for 1.5 h and further stirred at room temperature for 4 h. Water (200 mL) was added, and the mixture was extracted with dichloromethane (100 mL). The organic layer was removed, and the aqueous portion was further extracted with 3 × 100 mL of dichloromethane. The combined organic layers were washed sequentially with 200 mL of water and 100 mL of brine. The organic solution was dried over magnesium sulfate, the solvent was removed, and the residue was distilled in vacuo to give pure **6** (18.7 g, 60%): bp 42–44 °C/30 mmHg, lit.[13] bp 102 °C/742 mmHg; ^{1}H NMR (200 MHz) ($CDCl_3$) δ 3.85 (3 H, s), 2.97 (1 H, s); IR (neat) 3270, 2960, 2110, 1715, 1435, 1250, 990, 860, 760 cm^{-1}.

***N*-(*E*)- and -(*Z*)-(2-Methoxycarbonylvinyl)trimethylammonium Tetrafluoroborate (7*E* and *Z*).** Trimethylammonium tetrafluoroborate **5** (3.02 g, 21 mmol) and methyl propiolate **6** (2.1 g, 25 mmol) were heated in dry methanol (200 mL) at reflux for 2.5 h. Upon cooling to room temperature, a small amount of **7E** crystallized from solution. The solvent was removed in vacuo, and the residue (*E*:*Z* ratio 57:43 by ^{1}H NMR) recrystallized from methanol/ether to afford pure **7E** (1.52 g, 50%) as white crystals: mp 265–266 °C; ^{1}H NMR (200 MHz) (CD_3CN) δ 7.22 (1 H, d, *J* = 14.2 Hz), 6.47 (1 H, d, *J* = 14.2 Hz), 3.80 (3 H, s), 3.31 (9 H, s); ^{13}C NMR (50 MHz) (CD_3CN) δ164.7, 149.0, 120.4, 55.6, 53.4; IR (Nujol mull) 1730, 1665, 1330, 1245, 1205, 1185, 1040, 960, 940, 780, 725 cm^{-1}; FAB MS (*m*/*e*), calcd for $C_7H_{14}NO_2BF_4$ 231, found 231. Anal. Calcd for $C_7H_{14}NO_2BF_4$: C, 36.40; H, 6.11. Found: C, 36.43; H, 6.06.

Further recrystallization of the mother liquor from methanol/ether gave nearly pure **7Z** (1.35 g, 45%) as white needles: mp 92–94 °C; ^{1}H NMR (200 MHz) (CD_3CN) δ 6.49 (1 H, d, *J* = 10.2 Hz), 6.16 (1 H, bd, *J* = 10.2 Hz), 3.81 (3 H, s), 3.46 (9 H, s); ^{13}C NMR (50 MHz) (CD_3CN) δ 164.3, 144.8, 120.4, 57.1, 53.9; IR (Nujol mull) 1715, 1665, 1305, 1270, 1240, 1215, 1050, 970, 940, 925, 880, 820, 775, 720 cm^{-1}; FAB MS (*m*/*e*), calcd for $C_7H_{14}NO_2BF_4$ 231, found 231. Anal. Calcd for $C_7H_{14}NO_2BF_4$: C, 36.40; H, 6.11. Found: C, 36.47; H, 6.02.

Ethyl Propiolate (8). Prepared as described for **6** in 60% yield: bp 50–52 °C/30 mmHg, lit.[13] bp 119 °C/745 mmHg; ^{1}H NMR (200 MHz) ($CDCl_3$) δ 4.27 (2 H, q, *J* = 7 Hz), 2.88 (1 H, s), 1.33 (3 H, t, *J* = 7 Hz); IR (neat) 3260, 2955, 2120, 1715, 1440, 1245, 990, 860, 775 cm^{-1}.

Isopropyl Propiolate (9). Prepared as described for **6** in 56% yield: bp 65 °C/35 mmHg; ^{1}H NMR (200 MHz) ($CDCl_3$) δ 5.12 (1 H, septet, *J* = 6 Hz), 2.90 (1 H, s), 1.30 (6 H, d, *J* = 6 Hz); IR (neat) 3275, 3250, 2975, 2115, 1720, 1435, 1245, 995, 860, 760 cm^{-1}.

2,6-Dimethylphenoxy Propiolate (10). To a suspension of oil-free sodium hydride (0.83 g, 35 mmol) in ether (300 mL) at room temperature was added in 1 portion 2,6-dimethylphenol (3.0 g, 31 mmol). Stirring was continued for 0.5 h at which time gas evolution ceased, and the solution developed a green color. After cooling to −78 °C, propiolic acid chloride[14] (3.0 g, 34 mmol) was added dropwise via syringe over 15 min. The now yellow reaction mixture was stirred an additional 30 min at this temperature and then gradually warmed to room temperature. The reaction was quenched with water (100 mL). The organic layer was removed, and the aqueous portion was further extracted with 3 × 50 mL of ether. The combined organic layers were washed with 100 mL of brine and then dried over magnesium sulfate. The solvent was removed, and the residue was chromatographed (75% petroleum ether/ether) to afford **10** (5.1 g, 94%) as a low melting yellow solid: ^{1}H NMR (200 MHz) ($CDCl_3$) δ 7.20 (3 H, s), 3.07 (1 H, s), 2.22 (6 H, s); ^{13}C NMR (50 MHz) ($CDCl_3$) δ 150.3, 147.2, 129.9, 128.7, 126.5, 76.6, 74.0, 16.1; IR (neat) 2140, 1735, 1480, 1210, 1165, 1095, 980, 920, 780 cm^{-1}; high resolution MS (*m*/*e*), calcd for $C_{11}H_{10}O_2$ 174.202, found 174.201.

***N*-(*E*)- and -(*Z*)-(2-Carbethoxyvinyl)trimethylammonium Tetrafluoroborate (11E and Z).** Prepared in analogous fashion to **7E** and **Z** by using dry ethanol at 70 °C as the solvent. The residue (E:Z ratio 70:30 by ^{1}H NMR) was recrystallized from methanol/ether to give pure **11E** in 67% yield: mp 187–188 °C; ^{1}H NMR (200 MHz) (CD_3CN) δ 7.22 (1 H, d, *J* = 14 Hz), 6.44 (1 H, d, *J* = 14 Hz), 4.26 (2 H, q, *J* = 7 Hz), 3.31 (9 H, s), 1.29 (3 H, t, *J* = 7 Hz); ^{13}C NMR (125 MHz) (CD_3CN) δ 164.2, 148.9, 120.8, 62.9, 55.7, 14.4; IR (Nujol mull) 3080, 3060, 1720, 1410, 1290, 1225, 1060, 960, 940, 930, 885, 780, 725 cm^{-1}; high resolution MS (*m*/*e*), calcd for $C_8H_{16}NO_2$ 158.223, found 158.227. Anal. Calcd for $C_8H_{16}NO_2BF_4$: C, 39.22; H, 6.58. Found: C, 39.28; H, 6.42.

***N*-(*E*)- and -(*Z*)-(2-Isopropoxycarbonylvinyl)trimethylammonium Tetrafluoroborate (12E and Z).** Prepared in analogous fashion to **7E** and **Z**. The residue (E:Z ratio >76:<24 by ^{1}H NMR) was recrystallized from methanol/ether to give nearly pure **12E** in 76% yield: mp 159–162 °C; ^{1}H NMR (200 MHz) (CD_3CN) δ 7.19 (1 H, d, *J* = 14.4 Hz), 6.41 (1 H, d, *J* = 14.4 Hz), 5.11 (1 H, septet, *J* = 6.0 Hz), 3.29 (9 H, s), 1.29 (6 H, d, *J* = 6.0 Hz); IR (Nujol mull) 3070, 3050, 1715, 1430, 1285, 1225, 1190, 1045, 970, 950, 920, 850, 775 cm^{-1}; high resolution MS (*m*/*e*), calcd for $C_9H_{18}NO_2$ 172.249, found 172.050. Anal. Calcd for $C_9H_{18}NO_2BF_4$: C, 41.73; H, 7.00. Found: C, 41.73; H, 7.06.

***N*-(*E*)-[2-(2,6-Dimethylphenoxy)carbonylvinyl]trimethylammonium Tetrafluoroborate (13E).** Prepared in analogous fashion to **7E** and **Z**. The residue (E:Z ratio >95:<5 by ^{1}H NMR) was recrystallized from methanol/ether to give pure **13E** in 97% yield: mp 115–120 °C; ^{1}H NMR (200 MHz) (CD_3CN) δ 7.44 (1 H, d, *J* = 14.1 Hz), 7.14 (3 H, s), 6.73 (1 H, d, *J* = 14.1 Hz), 3.37 (9 H, s), 2.15 (6 H, s); ^{13}C NMR (50 MHz) (CD_3CN) δ 162.3, 150.1, 147.2, 131.2, 129.7, 127.5, 119.9, 55.6, 16.3; IR (Nujol mull) 3090, 1735, 1665, 1320, 1235, 1180, 1160, 1060, 965, 935, 830, 810, 775, 770 cm^{-1}. Anal. Calcd for $C_{14}H_{20}NO_2BF_4$: C, 52.36; H, 6.28. Found: C, 52.28; H, 6.49.

Propiolamide. Prepared by a modification of the procedure by Moureu and Bongrand.[15] To a vigorously stirred solution of concentrated aqueous ammonia (14 mL) cooled to −30 °C was added dropwise **6** (4.2 g, 50 mmol) over 10 min. Stirring was continued for an additional 20 min, after which time the solvent was removed in vacuo at room temperature. The residual oil was triturated with dry ether (30 mL). The mixture was gravity filtered, and the solvent was removed in vacuo. Upon cooling to 0 °C, off-white crystals of propiolamide formed (3.0 g, 87%): mp 55–56 °C, lit. 61–62 °C;[15] ^{1}H NMR (200 MHz) (CD_3CN) δ 7.8–5.2 (2 H, br s), 3.23 (1 H, s); IR (Nujol mull) 3400–3000, 2110, 1650, 1580, 1130, 805, 770, 720 cm^{-1}.

Propiolonitrile (16). Prepared by a modification of the procedure by Moureu and Bongrand.[15] Phosphorus pentoxide (2.35 g, 0.165 mol) and propiolamide (5.4 g, 0.078 mol) were thoroughly mixed in a 100-mL boiling flask under a stream of dry argon. The flask was connected to a short-path distillation apparatus, and the system was purged with argon. The reaction flask was heated at 180 °C for 0.5 h during which time the product **16** was distilled (3.28 g, 83%), bp 42–45 °C (lit.[15] 42.5 °C), and collected at −78 °C. No further purification was necessary. The product was stored under argon at −30 °C until further use. *Caution*: This compound is a severe vesicant, causing extremely painful burns of several hours to days duration, and should be handled with great care. This product will pentrate surgical gloves with ease. It is also a potent lachrymator: ^{1}H NMR (200 MHz) ($CDCl_3$) δ 2.60 (1 H, s).

***N*-(*E*)-(2-Acetylvinyl)trimethylammonium Tetrafluoroborate (17E).** To a stirred solution of freshly distilled 3-butyn-2-one (1.0 g, 15 mmol) in dry methanol (125 mL) at room temperature was added trimethylammonium tetrafluoroborate **5** (1.80 g, 12.2 mmol) in 1 portion. Stirring was continued for 8 h at room temperature during which time 1.5 g (58%) of **17E** had crystallized from solution. The mother liquor was evaporated, and the residue was examined by ^{1}H NMR. No *Z*-isomer was present. Recrystallization of the residue from methanol/ether afforded another 0.92 g (35%) of **17E** for a total yield of 93%. A small sample was further recrystallized to give analytically pure **17E**: mp 169.5–170.5 °C; ^{1}H NMR (500 MHz) (CD_3CN) δ 7.08 (1 H, d, *J* = 14.3 Hz), 6.61 (1 H, d, *J* = 14.3 Hz), 3.29 (9 H, s), 2.33 (3 H, s); ^{13}C NMR (50 MHz) (CD_3CN) δ 196.9, 147.9, 126.9, 55.5, 29.0; IR (Nujol mull) 3100, 3050, 1680, 1290, 1255, 1220, 1040, 950, 930, 765 cm^{-1}; FAB MS (*m*/*e*), calcd for $C_7H_{14}NO$ 128, found 128. Anal. Calcd for $C_7H_{14}NOBF_4$: C, 39.11; H, 6.56. Found: C, 39.35; H, 6.71.

***N*-(*E*)- and -(*Z*)-(2-*N*-Ethylcarbamidovinyl)trimethylammonium Tetrafluoroborate (18E and Z).** A solution of *N*-ethylpropiolamide[16] (0.33 g, 3.4 mmol) and trimethylammonium tetrafluoroborate **5** (0.50 g, 3.4 mmol) in methanol (40 mL) was refluxed for 4.5 h. The solvent was removed in vacuo, and the residue (E:Z ratio 45:55 by ^{1}H NMR) was recrystallized 3 times from methanol/ether. The product **18E** was obtained as a low melting solid in 43% yield: ^{1}H NMR (200 MHz) (CD_3CN) δ 7.06 (1 H, d, *J* = 14.5 Hz), 6.50 (1 H, d, *J* = 14.5 Hz), 6.20 (1 H, br s), 3.45 (2 H, q, obscured), 3.33 (9 H, s), 1.12 (3 H, t, *J* = 7 Hz); ^{13}C NMR (50 MHz) (CD_3CN) δ 163.0, 141.8, 123.5, 57.0, 35.3, 14.3; IR (Nujol mull) 3380, 3060, 1680, 1640, 1540, 1245, 1045, 945,

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895, 830, 800, 725 cm^{-1}; FAB MS (*m/e*), calcd for $C_8H_{17}N_2O$ 157, found 157.

***N*-(*Z*)-(2-Cyanovinyl)trimethylammonium Tetrafluoroborate (19Z).** To a stirred solution of propiolonitrile **16** (1.73 g, 34 mmol) in dry methanol (170 mL) at room temperature was added trimethylammonium tetrafluoroborate **5** (4.07 g, 27.7 mmol) in 1 portion. After 15 min, crystals of **19Z** appeared. Stirring was stopped, and the solution was allowed to stand for 12 h. The crystals were collected in vacuo, washed with a small portion of cold methanol, and air dried for 1 day to give **19Z** (4.5 g, 82%) as slightly beige prisms: mp 225–227 °C; ^1H NMR (200 MHz) (CD_3CN) δ 6.80 (1 H, d, J = 10.3 Hz), 6.08 (1 H, br d, J = 10.3 Hz), 3.46 (9 H, s); ^{13}C NMR (50 MHz) (CD_3CN) δ 150.2, 113.0, 98.9, 56.5; IR (Nujol mull) 3070, 2220, 1290, 1030, 945, 930, 880, 745 cm^{-1}; FAB MS (*m/e*), calcd for $C_6H_{11}N_2$ 111, found 111. Anal. Calcd for $C_6H_{11}N_2BF_4$: C, 36.40; H, 5.60. Found: C, 36.46; H, 5.81.

***N*-(*E*)-(2-Acetylvinyl)pyridinium Tetrafluoroborate (24E).** To a stirred solution of 3-butyn-2-one (1.00 g, 14.7 mmol) in dry methanol (75 mL) at room temperature was added in 1 portion pyridinium tetrafluoroborate **23a** (2.05 g, 12.3 mmol) and 3 drops of freshly distilled pyridine. Stirring was continued for 8 h. The solvent was removed in vacuo, and the residue (only the *E*-isomer is present by ^1H NMR) was recrystallized from methanol/ether to yield **24E** (2.5 g, 86%) as beige needles: mp 129–131 °C; ^1H NMR (200 MHz) (CD_3CN) δ 8.95 (2 H, d, J = 6.1 Hz), 8.74–8.58 (2 H, m), 8.20–8.03 (2 H, m), 7.02 (1 H, d, J = 14.0 Hz), 2.44 (3 H, s); IR (Nujol mull) 3150, 3090, 1700, 1625, 1460, 1280, 1225, 1045, 845, 775, 720 cm^{-1}; FAB MS (*m/e*), calcd for $C_9H_{10}NO$ 148, found 148. Anal. Calcd for $C_9H_{10}NOBF_4$: C, 46.00; H, 4.29. Found: C, 46.12; H, 4.52.

***N*-(*Z*)-(2-Cyanovinyl)pyridinium Tetrafluoroborate (25Z).** To a stirred solution of propiolonitrile **16** (0.56 g, 11 mmol) in a 1:1 mixture (by volume) of methanol/ethanol at room temperature was added in 1 portion pyridinium tetrafluoroborate **23a** (1.67 g, 10 mmol). Stirring was continued for 12 h, during which time white crystals were deposited on the side of the reaction flask. The crystals were filtered and air-dried to give analytically pure **25Z** (1.84 g, 84%) as colorless needles: mp 140.5–142 °C; ^1H NMR (200 MHz) (CD_3CN) δ 8.94 (2 H, d, J = 6.4 Hz), 8.74 (1 H, t, J = 7.8 Hz), 8.24 (2 H, distorted dd), 7.94 (1 H, d, J = 9.2 Hz), 6.39 (1 H, d, J = 9.2 Hz); ^{13}C NMR (125 MHz) (CD_3CN) δ 150.6, 145.9, 144.5, 129.8, 113.3, 103.2; IR (Nujol mull) 3130, 3070, 2230, 1625, 1475, 1295, 1240, 1050, 820, 790, 765, 730, 670 cm^{-1}; low resolution MS (*m/e*), calcd for $C_8H_7N_2$ 131, found 131. Anal. Calcd for $C_8H_7N_2BF_4$: C, 44.09; H, 3.24. Found: C, 44.26; H, 3.12.

***N*-(*E*)- and -(*Z*)-(2-Methoxycarbonylvinyl)pyridinium Tetrafluoroborate (26E and Z).** Pyridinium tetrafluoroborate **23a** (8.35 g, 50 mmol) and methyl propiolate **6** (4.62 g, 55 mmol) were heated in dry methanol (500 mL) at reflux for 9 h. The solvent was removed in vacuo, and the residue (E:Z ratio 44:56 by ^1H NMR) was recrystallized from methanol/ether to give pure **26E** (1.4 g, 11%) as white needles: mp 157–159 °C; ^1H NMR (200 MHz) (CD_3CN) δ 8.95 (2 H, d, J = 6.7 Hz), 8.68 (1 H, t, J = 7.9 Hz), 8.21 (1 H, d, J = 14.3 Hz), 8.16 (2 H, distorted dd), 6.85 (1 H, d, J = 14.3 Hz), 3.84 (3 H, s); IR (KBr) 3080, 3030, 1720, 1650, 1620, 1475, 1425, 1330, 1220, 1190, 1065, 975, 955, 935, 865, 840, 790, 770, 660 cm^{-1}; high resolution MS (*m/e*), calcd for $C_9H_{10}NO_2$ 164.186, found 164.341. Anal. Calcd for $C_9H_{10}NO_2BF_4$: C, 43.07; H, 4.02. Found: C, 43.00; H, 4.15.

***N*-(*Z*)-(2-Methoxycarbonylvinyl)-2-methylpyridinium Tetrafluoroborate (27Z).** To dry methanol (25 mL) at room temperature was sequentially added purified 2-methylpyridine[12] (0.94 g, 10 mmol), 48% aqueous fluoboric acid (0.91 g, 5 mmol), and methyl propiolate **6** (1.26 g, 15 mmol). The solution was refluxed for 1 h, at which time the solution acquires a wine-red color. The solvent was removed in vacuo. The residue was determined by ^1H NMR to be the single isomer **27Z**. Recrystallization twice from absolute ethanol/ether affords **27Z** (1.02 g, 78%) as pink crystals: mp 104–105 °C; ^1H NMR (200 MHz) (CD_3CN) δ 8.56 (1 H, d, J = 6.2 Hz), 8.50 (1 H, overlapping dd), 7.98 (1 H, d, J = 8.1 Hz), 7.89 (1 H, overlapping dd), 7.53 (1 H, d, J = 8.8 Hz), 6.60 (1 H, d, J = 8.8 Hz), 3.62 (3 H, s), 2.70 (3 H, s); ^{13}C NMR (125 MHz) (CD_3CN) δ 163.5, 156.4, 148.4, 145.9, 139.5, 130.1, 126.0, 124.8, 53.2, 20.7; IR (Nujol mull) 3080, 1720, 1625, 1490, 1260, 1220, 1185, 1170, 1050, 980, 835, 820, 805, 775, 645 cm^{-1}; low resolution MS (*m/e*), calcd for $C_{10}H_{12}NO_2$ 178, found 178. Anal. Calcd for $C_{10}H_{12}NO_2BF_4$: C, 45.32; H, 4.56. Found: C, 45.54; H, 4.63.

***N*-(*Z*)-(2-Methoxycarbonylvinyl)-2-acetoxymethylpyridinium Tetrafluoroborate (28Z).** To dry methanol (10 mL) at room temperature was added sequentially 2-(acetoxymethyl)pyridine[17] (302 mg, 2.0 mmol), 48% aqueous fluoboric acid (183 mg, 1.0 mmol), and methyl propiolate **6** (252 mg, 3.0 mmol). The solution was refluxed for 22 h, during which time the solution acquired a deep-red color. Following solvent removal in vacuo, ^1H NMR analysis of the gummy residue revealed a single isomer **28Z** to be present. Recrystallization of the gum from methanol/ether at 0 °C gave **28Z** (210 mg, 65% unoptimized) as reddish crystals: mp 115–116 °C; ^1H NMR (200 MHz) (CD_3CN) δ 8.67 (1 H, d, J = 7.0 Hz), 8.64 (1 H, overlapping dd), 8.20 (1 H, d, J = 7.9 Hz), 8.07 (1 H, distorted dd), 7.66 (1 H, d, J = 8.9 Hz), 6.66 (1 H, d, J = 8.9 Hz), 5.33 (2 H, s), 3.62 (3 H, s), 2.12 (3 H, s); ^{13}C NMR (125 MHz) (CD_3CN) δ 170.8, 163.4, 152.5, 149.3, 147.0, 138.3, 128.7, 127.9, 125.9, 61.4, 53.4, 20.7; IR (Nujol mull) 3040, 1740, 1720, 1625, 1240, 1220, 1180, 1060, 1030, 1010, 985, 825, 810, 785 cm^{-1}; high resolution MS (*m/e*), calcd for $C_{12}H_{14}NO_4$ 236.251, found 236.092. Anal. Calcd for $C_{12}H_{14}NO_4BF_4$: C, 44.62; H, 4.37. Found: C, 44.68; H, 4.49.

***N*-(*Z*)-(2-Methoxycarbonylvinyl)-2,4,6-trimethylpyridinium Tetrafluoroborate (29Z).** To a solution of 2,4,6-trimethylpyridinium tetrafluoroborate **23d** (209 mg, 1.0 mmol) in dry methanol (5 mL) was added in sequence purified 2,4,6-trimethylpyridine (121 mg, 1.0 mmol) and methyl propiolate **6** (160 mg, 2.0 mmol). The solution was heated to reflux to 16 h, during which time the solution acquires a deep-red color. After having been cooled to room temperature, ether was added to the methanol solution until no more precipitate forms. The solution was filtered to remove the tacky red residue, and the mother liquor was set aside for 24 h at room temperature. During this time, long colorless needles of **29Z** (59 mg, 20%), mp 85–86 °C, formed. The tacky residue was repeatedly recrystallized from methanol/ether in the manner described to afford another 147 mg of **29Z** for a combined yield of 70%. ^1H NMR analysis of all the mother liquors revealed none of the *E*-isomer to be present: ^1H NMR (200 MHz) (CD_3CN) δ 7.64 (2 H, s), 7.32 (1 H, d J = 8.5 Hz), 6.61 (1 H, d, J = 8.5 Hz), 3.62 (3 H, s), 2.56 (9 H, s); ^{13}C NMR (125 MHz) (CD_3CN) δ 163.6, 161.3, 154.9, 137.6, 128.0, 125.8, 53.2, 22.0, 21.3; IR (Nujol mull) 3080, 1720, 1635, 1320, 1285, 1260, 1245, 1220, 1175, 1060, 855, 830 cm^{-1}; FAB MS (*m/e*), calcd for $C_{12}H_{16}NO_2$ 206, found 206. Anal. Calcd for $C_{12}H_{16}NO_2BF_4$: C, 49.18; H, 5.50. Found: C, 49.34; H, 5.55.

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Registry No. 5, 16970-98-2; **6**, 922-67-8; **6** (acid), 471-25-0; **7*E***, 99476-55-8; **7*Z***, 99476-53-6; **8**, 623-47-2; **9**, 96088-62-9; **10**, 114251-41-1; **11*E***, 99476-63-8; **11*Z***, 114251-43-3; **12*E***, 114251-45-5; **12*Z***, 114251-47-7; **13*E***, 114251-49-9; **13*Z***, 114251-51-3; **14**, 1423-60-5; **15**, 2682-33-9; **16**, 1070-71-9; **17*E***, 114251-53-5; **18*E***, 114251-55-7; **18*Z***, 114251-57-9; **19*Z***, 99476-64-9; **23a**, 505-07-7; **23d**, 89954-97-2; **24*E***, 114251-59-1; **25*Z***, 110128-93-3; **26*E***, 110128-79-5; **26*Z***, 110128-81-9; **27*Z***, 110128-89-7; **28*Z***, 114251-61-5; **29*Z***, 114251-63-7; 2,6-dimethylphenol, 576-26-1; propiolic acid chloride, 50277-65-1; propiolamide, 7341-96-0; 2-(acetoxymethyl)pyridine, 1007-49-4.

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