δ 8.45 (d, 1, J = 8.5 Hz), 8.10 (d, 1, J = 8.5 Hz), 7.88 (d, 1, J = 8.5 Hz), 7.71 (d, 1, J = 8.5 Hz), 7.60-7.69 (m, 2), 6.30 (s, 1), 2.50 (s, 3); IR (KBr) 1650, 1635 $cm^{-1}$.

Similar dehydrogenation of the other chromanones and flavanones gave the analogous chromones and flavones. **8a** (eluted with 2% acetone in $CH_2Cl_2$) (51%): mp 123-124 °C (95% ethanol) (lit.[17] mp 125 °C); NMR δ 8.45 (d, 1, J = 8.6 Hz), 8.13 (d, 1, J = 8.9 Hz), 8.02 (d, 1, J = 6.2 Hz), 7.91 (d, 1, J = 8.6 Hz), 7.75 (d, 1, J = 8.9 Hz), 7.63-7.70 (m, 2), 6.49 (d, 1, J = 6.2 Hz); IR (KBr) 1630, 1560 $cm^{-1}$. **8c** (65%): mp 153-155 °C (MeOH) (lit.[21] mp 154 °C); NMR δ 8.58-8.62 (m, 1), 8.16 (d, 1, J = 8.9 Hz), 7.98-8.03 (m, 2), 7.91-7.93 (m, 1), 7.77 (d, 1, J = 8.9 Hz), 7.67-7.71 (m, 2), 7.53-7.58 (m, 3), 6.85 (s, 1); IR (KBr) 1650, 1640, 1580 $cm^{-1}$. **16a** (28%): mp 207-209 °C (95% ethanol); NMR δ 8.83 (s, 1), 8.58 (d, 1, J = 10.0 Hz), 8.13-8.22 (m, 4), 7.95-8.07 (m, 3), 6.56 (d, 1, J = 6.8 Hz); IR (KBr) 1640, 1630 $cm^{-1}$. Anal. Calcd for $C_{19}H_{10}O_2$: C, 84.43; H, 3.73. Found: C, 84.56; H, 3.90. **16b** (40%): mp 212-214 °C (95% ethanol); NMR δ 8.74 (s, 1), 8.49 (d, 1, J = 10.0 Hz), 8.09-8.17 (m, 3), 7.90-8.02 (m, 3), 6.36 (s, 1), 2.59 (s, 3); IR (KBr) 1640 $cm^{-1}$. Anal. Calcd for $C_{20}H_{12}O_2$: C, 84.49; H, 4.25. Found: C, 84.38; H, 4.38. **16c** (84%): mp 231-232 °C (ethanol); NMR δ 8.86 (s, 1), 8.71 (d, 1, J = 7.5 Hz), 7.95-8.23 (m, 8), 7.57-7.63 (m, 3), 7.03 (s, 1); IR (KBr) 1635, 1600, 1580, 1560 $cm^{-1}$. Anal. Calcd for $C_{25}H_{14}O_2$: C, 86.69; H, 4.07. Found: C, 86.63; H, 3.99. **16d** (eluted with 15:1 $CH_2Cl_2/CHCl_3$) (44%): mp 188-189 °C (ethanol); NMR δ 8.90 (s, 1), 8.63 (dd, 1, J = 1.5 and 9.7 Hz), 8.22 (d, 2, J = 8.7 Hz), 8.17 (d, 1, J = 7.4 Hz), 8.12 (s, 1), 8.07 (t, 1, J = 8.7 Hz), 8.04 (d, 1, J = 7.4 Hz), 7.98 (dd, 1, J = 1.5 and 9.7 Hz), 2.23 (s, 3); IR (KBr) 1650, 1630, 1610 $cm^{-1}$. Anal. Calcd for $C_{20}H_{12}O_2$: C, 84.48; H, 4.26. Found: C, 84.19; H, 4.34. The second fraction was collected, evaporated and passed through a column of neutral alumina (activity 1), and eluted with $CHCl_3$ to give **17** (27%); mp 236-237 °C (ethanol); NMR δ 8.81 (s, 1), 8.58 (d, 1, J = 10.9 Hz), 8.48 (d, 1, J = 8.9 Hz), 8.25 (d, 1, J = 8.9 Hz), 8.10 (s, 1), 8.02 (d, 1, J = 10.9 Hz), 7.95 (d, 1, J = 8.9 Hz), 7.88 (d, 1, J = 8.9 Hz), 2.21 (s, $CH_3$); IR (KBr) 1635, 1595 $cm^{-1}$; MS 363 (100, $M^+$). **16d** was also prepared by catalytic dehydrogenation of **13d** (0.11 g, 0.4 mmol) over 10% Pd/C (100 mg) in refluxing triethylene glycol dimethyl ether (8 mL) for 5 h under nitrogen. The solution was cooled and filtered, and the filtrate was poured into ice-water to give **16d** as a yellow powder (65 mg, 58%) whose NMR spectrum matched that of an authentic sample.

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**Registry No.** **2**, 7382-37-8; **3a**, 129986-82-9; **3b**, 129986-81-8; **3c**, 129986-83-0; **4a**, 129986-90-9; **4b**, 129986-88-5; **4c**, 129986-92-1; **5a**, 129986-91-0; **5b**, 129986-89-6; **5c**, 129987-13-9; **6a**, 16563-51-2; **6b**, 21568-05-8; **6c**, 6051-86-1; **7a**, 129987-00-4; **7b**, 129986-99-8; **7c**, 125574-15-4; **8a**, 3528-23-2; **8b**, 54965-49-0; **9**, 115560-65-1; **10a**, 129986-84-1; **10b**, 129986-85-2; **10c**, 129986-86-3; **10d**, 129986-87-4; **11a**, 129986-93-2; **11b**, 129986-95-4; **11c**, 129986-97-6; **11d**, 129986-98-7; **12a**, 129986-94-3; **12b**, 129986-96-5; **13a**, 129987-01-5; **13b**, 129987-03-7; **13c**, 129987-04-8; **13d**, 129987-06-0; **14a**, 129987-02-6; **14c**, 129987-05-9; **14d**, 129987-07-1; **15**, 129987-08-2; **16a**, 129987-09-3; **16b**, 129987-10-6; **16c**, 129987-11-7; **16d**, 129987-12-8; **17**, 129987-14-0; $H_2C$=CHCHO, 107-02-8; (*E*)-PhCH=CHCHO, 14371-10-9; $H_2C$=$C(CH_3)$CHO, 78-85-3; 1-acetylpyrene, 3264-21-9; 1-acetoxypyrene, 78751-40-3; 1-hydroxypyrene, 5315-79-7; 1-naphthol, 90-15-3; (*E*)-crotonaldehyde, 123-73-9.

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# Preparation and Reactivity of Methyl 3,3-Bis(4-(dimethylamino)pyridinium-1-yl)propenoate Dichloride

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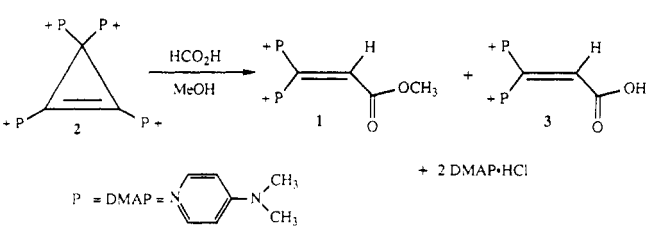
The preparation, structure, and reactivity of methyl 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoate dichloride (**1**) are discussed. 1,2,3,3-Tetrakis(4-(dimethylamino)pyridinium-1-yl)cyclopropene tetrachloride (**2**) was converted to **1** with formic or acetic acid in methanol. A mechanism for the conversion of **2** to **1** is suggested. Hydrolysis of **1** under basic conditions gave 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoic acid (**3**), which has a $pK_a$ of 2. The X-ray structure of **1** shows that the pyridinium rings are both twisted with respect to the double bond; the resulting high steric hindrance prevent Diels-Alder reactions with dienes despite the electrophilic nature of the system.

We have recently reported the preparation and some reactions of 1,2,3,3-tetrakis(4-(dimethylamino)-pyridinium-1-yl)cyclopropene tetrachloride (**2**).[1,2] Compound **2** has been shown to undergo nucleophilic attack at the double bond followed by ring opening to give allyl anions substituted with *N*-pyridinium cations, which in some cases undergo electrocyclic ring closure to give indolizines.[1-4] In this paper we report the conversion of **2** to 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoic acid, **3**, and its esters, along with the properties of this unique acrylic system.

## Results and Discussion

Compound **2** was found to react with formic or acetic acids in methanol to give **1** and **3**. The reaction produces 2 equiv of 4-(dimethylamino)pyridine hydrochloride, DMAP·HCl. The reaction of **2** as the chloride salt with




formic acid in ethanol gave ethyl 3,3-bis(4-dimethylamino)pyridinium-1-yl)propenoate, **4**, DMAP·HCl, and **3**. The ratio of acrylic acid to ester is dependent both on the

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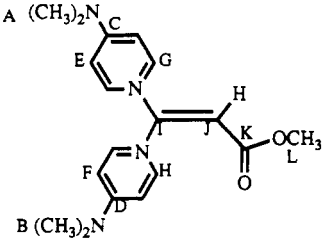
0022-3263/90/1955-6166$02.50/0 

**Table I. $^{13}C$ DEPT Experiment on 1 and 9[a]**




| | | 1 | | | | 9 | | |
|---|---|---|---|---|---|---|---|---|
| signal | δ | 45° | 90° | 135° | δ | 45° | 90° | 135° |
| A | 43.0 | ↑ | – | ↑ | 42.0 | ↑ | – | ↑ |
| B | 43.0 | ↑ | – | ↑ | 42.0 | ↑ | – | ↑ |
| C | 160.1 | – | – | – | 159.8 | – | – | – |
| D | 160.2 | – | – | – | 159.9 | – | – | – |
| E | 111.1 | ↑ | ↑ | ↑ | 110.8 | ↑ | ↑ | ↑ |
| F | 110.6 | ↑ | ↑ | ↑ | 110.5 | ↑ | ↑ | ↑ |
| G | 141.2 | ↑ | ↑ | ↑ | 141.6 | ↑ | ↑ | ↑ |
| H | 143.1 | ↑ | ↑ | ↑ | 142.9 | ↑ | ↑ | ↑ |
| I | 147.9 | – | – | – | 142.3 | – | – | – |
| J | 113.7 | ↑ | ↑ | ↑ | | – | – | – |
| K | 166.5 | – | – | – | 169.1 | – | – | – |
| L | 55.7 | ↑ | – | ↑ | | | | |

[a] ↑ stands for a positive signal, – stands for a nulled signal. Note that A can be exchanged for B, C for D, E for F, and G for H.

alcohol used and the amount of water present during reaction. Some formation of **3** is unavoidable due to the 6.5 equiv of water associated with **2**.

When **2** was treated with formic acid, used as a 95% aqueous solution, in absolute ethanol, 42% of the ethyl ester **4** and 58% of the corresponding acrylic acid **3** was detected by $^1H$ NMR spectroscopy. Substituting glacial acetic acid for formic acid in ethanol with the hexafluorophosphate salt of **2** gave a 57:43 ester:acid ratio.

Compound **I** gave a $^1H$ NMR with two types of 4-(dimethylamino)pyridinium groups in addition to a singlet at 6.47 ppm, area 1, corresponding to the vinylic proton and a singlet at 3.57 ppm, area 3, corresponding to the methyl ester protons. As shown in Table I, the $^{13}C$ NMR spectrum of **1** also shows two types of DMAP units along with signals at 166.5 ppm, corresponding to the carbonyl carbon, 147.9 ppm for the quaternary vinylic carbon, 113.7 ppm for the other vinylic carbon, and the methoxy methyl carbon at 55.7 ppm. The carbon multiplicities were verified by a DEPT experiment, as shown in Table I. In addition, this structure was confirmed by single-crystal X-ray analysis; a structure diagram is shown in Figure 1.[5,6]

An interesting feature shown in the X-ray analysis of **1** is that the two pyridinium moieties are twisted 72° with respect to each other. The entire system is twisted so that there is virtually no conjugation between the carbon–carbon double bond, the ester functionality, and the two pyridinium moieties. The bond distance between the ring carbon and the dimethylamino nitrogen is 1.32 Å, which is between that of a carbon nitrogen double bond and a carbon nitrogen single bond, indicating that a substantial amount of the positive charge is delocalized onto the dimethylamino group. The chloride counterions, not shown in Figure 1, are heavily solvated by the four waters of crystallization and are relatively far removed from the dicationic molecule. Some additional structural parameters are summarized in Table II. In Figure 1 note that some of the *N*-methyl groups show rotational disorder.

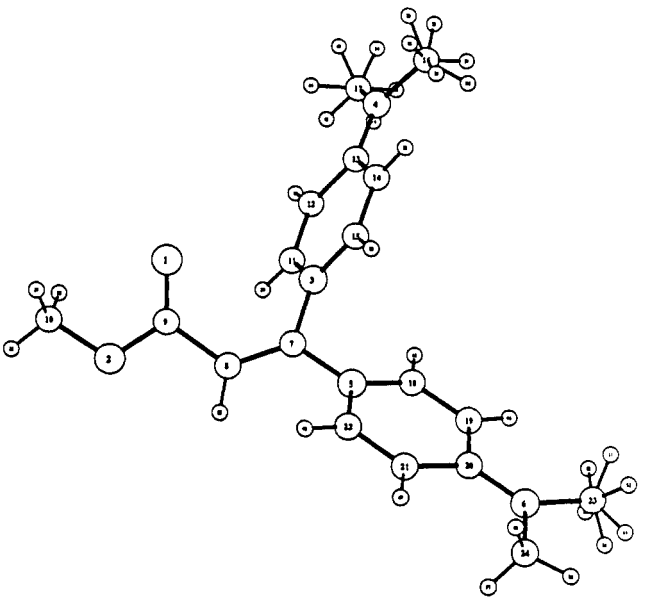


**Figure 1.**

**Tabled II. Some Structural Parameters for 1[a]**

| | | | |
|---|---|---|---|
| C(7)–C(8) | 1.316 Å | C(7)–N(5) | 1.432 Å |
| C(8)–C(9) | 1.480 Å | C(13)–N(4) | 1.325 Å |
| C(9)–O(1) | 1.204 Å | C(20)–N(6) | 1.320 Å |
| C(9)–O(2) | 1.330 Å | N(3)–C(7)–N(5) | 111.7° |
| C(7)–N(3) | 1.426 Å | C(7)–C(8)–C(9) | 122.1° |

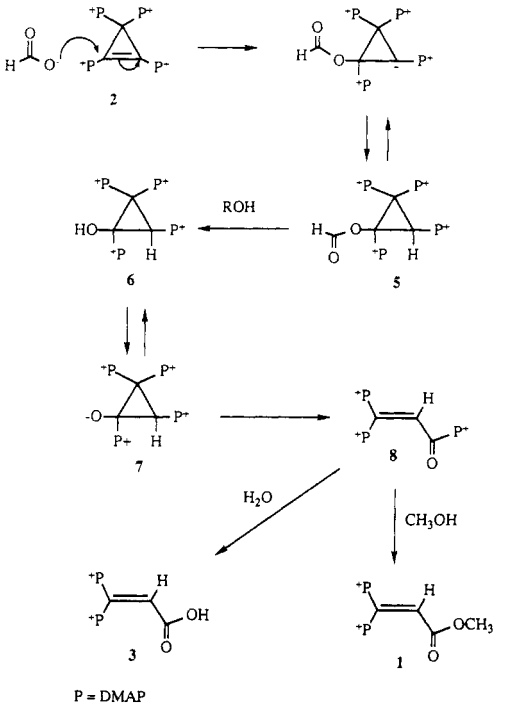
[a] Numbers refer to atom labels in Figure 1.

The mechanism in Scheme I provides a reasonable rationalization for the conversion of **2** to **1** and **3**. Formic acid is sufficiently strong in methanol that a substantial amount of formate ion would be present. Since **2** is known to undergo nucleophilic attack at the double bond, reaction with formate ion would give a cyclopropyl anion, which, in acidic solution would be expected to protonate rapidly to give **5** rather than undergo electrocyclic ring opening.[2] In the presence of methanol, **5** would be expected to un-

(5) The structure was solved at the University of California, Berkeley, Chemistry Department X-ray Crystallographic Facility (CHEXRAY) under the supervision of Dr. Fred Hollander.

(6) A unit cell figure is given in Waterman, K. C. Dissertation, University of California, Berkeley, 1985.

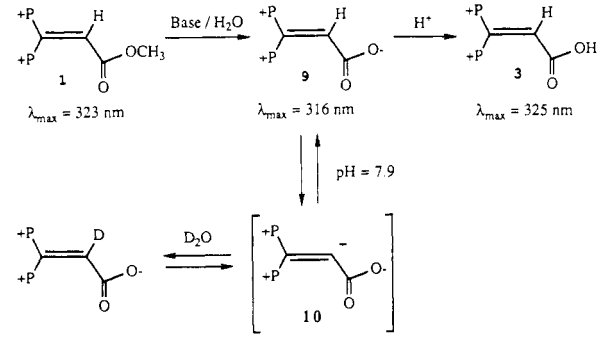
**Scheme I. Proposed Mechanism for Conversion of 2 to 1**




dergo solvolysis to give methyl formate and **6**. Detection of methyl formate was not attempted, since methyl formate would already be present to some extent in a solution of formic acid in methanol. The cyclopropanol **6** is expected to be rather acidic because of the nearby pyridinium cation groups and the corresponding alkoxide **7** should be in significant concentration even in acidic solution. Ring opening with concurrent loss of DMAP gives the $\alpha,\beta$-unsaturated acrylamide **8**, which would quickly solvolyze to give **1** or **3**. Other pyridinium amides are known,[7-12] and some are used as acylating agents.[12] An alternative pathway involving a cyclopropanone intermediate by loss of DMAP from **7** is considered less likely. The ring strain inherent in a cyclopropanone would facilitate nucleophilic addition, so that a strong solvent dependence should not be observed for the ratio of **1** to **3**, but such a path cannot be rigorously excluded.

The decrease in the ratio of acrylic acid to ethyl ester when changing from formic to acetic acid can be explained by the substantial increase in the amount of water present when using formic acid, thus increasing the amount of hydrolysis of the proposed intermediate **8** relative to alcoholysis. Compound **2** does not hydrolyze to **3** in neutral or acidic solution. Apparently, the presence of two positive charges makes acidic hydrolysis unlikely. Thus **3** must be formed from the intermediate **8**. When **2** was treated with formic acid in the presence of methanol, 71% of the methyl acrylate ester and 29% of the acrylic acid was observed, but when the reaction was carried out in 2-propanol only the acrylic acid was detected. This indicates that the intermediate **8** is formed prior to the formation of **1** and must live long enough to compete between hydrolysis and alcoholysis. When **2** was subjected to a catalytic amount

**Scheme II. Hydrolysis of 1**



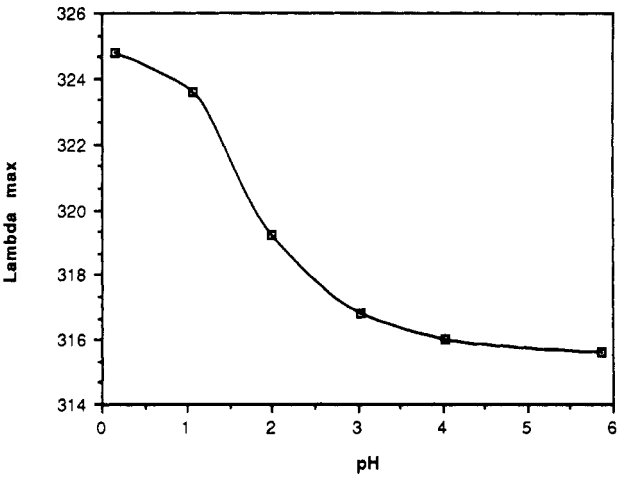




**Figure 2.**

of formic acid in methanol, mostly starting material was recovered, so an excess of acid was routinely used.

This reaction was originally discovered when a solution of **2** in methanol was treated with ozone and the products isolated were **1**, **3**, and DMAP·HCl. However, **2** was found to be stable to ozone in aprotic nonnucleophilic solvents as well as to 2-propanol and to water. From the reaction of **2** with carboxylic acids it would seem that the role of ozone was to oxidize some methanol to formic acid which then reacted with **2** to give **1**.

Hydrolysis of an aqueous solution of **1** ($\lambda_{max}$ = 323 nm) occurs rapidly under mildly basic conditions to yield the zwitterion cation (**9**) ($\lambda_{max}$ = 316 nm) as shown in Scheme II. The $^1H$ NMR in $D_2O$ shows that the methoxy peak at 3.57 ppm has shifted to that of methanol, 3.2 ppm. In addition to hydrolysis, the vinylic proton at 6.47 ppm exchanges in $D_2O$. Upon protonation, **3** was isolated, which has $\lambda_{max}$ = 325 nm in an aqueous solution of pH <1, and a vinylic proton at 6.5 ppm. When **3** is taken up in $H_2O$ $\lambda_{max}$ = 316 nm, and the $^1H$ NMR in $D_2O$ shows no sign of the carboxylate proton, but the signal due to the vinylic proton is present. It can be deduced that the change in $\lambda_{max}$ from 316 to 325 nm is due to the protonation of the carboxyl group. In 5 M KOH, **3** decomposes to DMAP. There was no notable change in $\lambda_{max}$ related to the disappearance of the vinylic proton in the $^1H$ NMR.

When **3** was taken up in a solution of pH 7.9 the vinylic proton slowly exchanged. Attempts to trap the vinylic anion with methyl iodide in water failed; upon workup only the corresponding acrylic acid was isolated. A broadband decoupled $^{13}C$ NMR and a DEPT sequence were run on both **1** and the zwitterion **9**, as shown in Table I. The signal for the vinylic carbon attached to the vinylic proton disappeared upon addition of carbonate even when scanning to 260 ppm. This, and the fact that there seems to

(7) Tamura, T. *Jpn. Kokai Tokkyo Koho* **1982**, *57*, 146, 741; *Chem. Abstr.* **1983**, *98*, 154884w.
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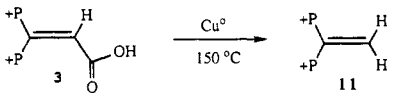
**Scheme III. Decarboxylation of 3**




be no observed change in $\lambda_{max}$ corresponding to the loss of the vinylic proton, indicates rapid exchange of the vinyl hydrogen but only a small concentration of the corresponding vinyl anion, **10**, a neutral species. This result still indicates a relatively high acidity for the vinylic proton, undoubtedly from stabilization of the anionic charge by the pyridinium cations.

The extinction coefficient, $\epsilon$, for **3** is 54 600 and that of **9** is 47 400. Since these $\epsilon$ are similar, a plot of $\lambda_{max}$ vs pH should provide a good approximation to the $pK_a$. Six points were measured and the $pK_a$ of **3** was found to be about 1.7, as shown in Figure 2. A more precise determination is not feasible because of ionic effects on $\lambda_{max}$; that is, both $\lambda_{max}$ and $\epsilon$ may be different in the different buffer mixtures used. For example it was noted that the $\lambda_{max}$ rose to 326 nm in 3 M HCl.

An aqueous solution of **2** was also found to undergo hydrolysis over several weeks to give **3**. The hydrolysis mechanism is undoubtedly analogous to that with formic acid.

Compound **3** was found to be unreactive toward nucleophilic attack. When **1** was treated with nucleophiles, hydrolysis to **3** occurred and hence no addition was observed. A variety of cycloadditions were also attempted with no reaction noted even at 15 Kbar. Jung has reported that methyl 3-(pyridinium-1-yl)propenoate tetrafluoroborate undergoes cycloaddition with cyclopentadiene to give the corresponding *endo*- and *exo*-norbornenes.[13] The positive substituent on the dienophile is expected to accelerate reactions with dienes. When **1** was treated with cyclopentadiene under a variety of conditions, no reaction occurred, even when heated at 60 °C at 15 Kbar, or at 180 °C in acetonitrile in a sealed tube. Cycloaddition reactions with 1,3-butadiene and **1** were also attempted under the same conditions with no reaction.

The acid **3** can be decarboxylated to give 1,1-bis(4-(dimethylamino)pyridinium-1-yl)ethylene dichloride (**11**) by heating to 150 °C in the presence of copper, but the yield was low. The product showed a singlet at 6.07 ppm that integrates to two protons and one new DMAP resonance. The singlet at 6.07 ppm is upfield of the vinylic proton of **1** or **3**, 6.56 and 6.50 ppm, respectively, an expected change due to absence of the electron-withdrawing carboxyl group. The $^{13}C$ NMR of **11** shows one type of DMAP along with a signal at 74 ppm, which was confirmed to be a methylene by the DEPT experiment.

The formation of 3,3-bis(4-pyrrolidinopyridinium-1-yl)propenoic acid dichloride and methyl 3,3-bis(4-pyrrolidinopyridinium-1-yl)propenoate dichloride from 1,2,3,3-tetrakis(4-pyrrolidinopyridinium-1-yl)cyclopropene tetrachloride[14] was also successful although pure crystalline material was not obtained. The $^1H$ NMR shows two overlapping pyrrolidinopyridines in addition to small singlets at 6.49 and 6.44 ppm corresponding to the acid and ester vinylic proton, respectively. The two integrate to one proton compared to the four protons of the pyridine ring. There is also a singlet at 3.64 ppm corresponding to the methyl of the methyl ester. The singlet at 3.64 ppm overlaps somewhat with the downfield pyrrolidino protons at 3.54 ppm so separate integration was not possible; however, the combined integration works out to be roughly 9 hydrogens compared to 8 for the upfield protons of the pyrrolidino ring, indicating that substantially more acid is formed than ester.

(13) Jung, M. E.; Buszek, K. R. *J. Org. Chem.* **1985**, *50*, 5440.
(14) This sample was prepared by Drew V. Speer.

## Conclusion

In many reactions of **2** with nucleophiles the intermediate cyclopropyl anion undergoes electrocyclic ring opening to the allyl anion. Alternatively, we now find that in acidic solutions the intermediate cyclopropyl anion can be protonated. If the nucleophile is a carboxylate ion, the intermediate **5** can hydrolyze and ring open to give acrylates such as **1** and **3**.

The ease with which **1** hydrolyzes under basic conditions limits its use as a Michael acceptor, since **3** is too sterically hindered to allow attack at the $\beta$-position and the carboxyl group is deprotonated and retards reaction at the carboxyl group. Compound **1** is also too sterically hindered to undergo cycloaddition reactions, although the two positive moieties should activate the dienophile.

## Experimental Section

**General.** Unless otherwise indicated, all materials were obtained from commercial suppliers and used without purification. Melting points and decomposition points (Pyrex capillary) are uncorrected. $^1H$ spectra were determined at 180, 200, or 250 MHz; $^{13}C$ spectra were obtained at 50.75 MHz on superconducting FT spectrometers equipped with Cryomagnets, Inc., magnets and Nicolet Model 1180 data collection systems. Chemical shifts are reported in ppm, referenced to TMS indirectly by the resonance of the solvent or added acetonitrile. All positive values indicate a downfield shift from TMS. All $^1H$ data is tabulated in order: number of protons, multiplicity (s, singlet; d, doublet; t, triplet; q, quartet; m, multiplet), coupling constants are given in hertz. UV–vis spectra were obtained using an IBM 9430 spectrophotometer. Infrared spectra were obtained from a Perkin-Elmer 297 spectrophotometer (s = strong, m = medium, w = weak, br = broad, sh = sharp). The gegenion anions are chloride unless stated otherwise.

**Anion Exchange of 2 to the Hexafluorophosphate Salt.** To a solution of 2.32 g (3.18 mmol) of **2**[2] in 10 mL of $H_2O$ was added 2.39 g (14.23 mmol) of $NaPF_6$ in 15 mL of $H_2O$, to give 3.05 g (2.76 mmol) of 1,2,3,3-tetrakis(4-(dimethylamino)-pyridinium-1-yl)cyclopropene tetrakishexafluorophosphate (87%): IR (KBr) 3720 (sh, w), 3470 (br, s), 3150 (sh, w), 2950 (br, w), 2700 (br, w), 2500 (br, w), 1920 (br, w), 1650 (sh, s), 1590 (sh, s), 1440 (sh, w), 1400 (sh, s), 1350 (sh, s), 1260 (sh, m), 1210 (sh, s), 1150 (sh, s), 1060 (sh, w), 940 (br, w), 840 (br, s), 790 (sh, w), 740 (sh, s), 720 (sh, w), 700 (sh, w), 690 (sh, w), 640 $cm^{-1}$ (sh, w).

**Preparation of Methyl 3,3-Bis(4-(dimethylamino)-pyridinium-1-yl)propenate Dichloride, 1. By Reaction of 2 with Formic Acid in Methanol.** To a solution of 393 mg (0.502 mmol) of **2** in 8 mL of methanol at 0 °C was added 1 mL (26.5 mmol) of 95% formic acid in water. The solution was allowed to stir for 3 min at 0 °C and then gradually warmed to 22 °C. Excess formic acid and methanol were removed via vacuum transfer. $^1H$ NMR of the crude products showed formic acid, DMAP·HCl, and a 71:29 ratio of **1** to **3**. The mixture was recrystallized from methanol and acetonitrile to yield 127 mg (0.277 mmol, 55%) of **1**: UV ($H_2O$) $\lambda$ 322.8 ($\epsilon$ 54 000); IR (KBr) 3410 (br, s), 3045 (sh, s), 1630 (br, s), 1590 (sh, s), 1500 (sh, w), 1410 (sh, w), 1370 (sh, m), 1350 (sh, w), 1330 (sh, w), 1290 (sh, m), 1160 (br, s), 1020 (sh, w), 870 (sh, m), 830 (sh, m), 790 (sh, w), 750 (sh, w), 730 (sh, w), 700 (br, w), 670 $cm^{-1}$, (sh, w); $^1H$ NMR ($D_2O$, $CH_3CN$ standard) 7.88 (2 H, d, $J$ = 8.0), 7.85 (2 H, d, $J$ = 7.9), 6.89 (2 H, d, $J$ = 8.1), 6.84 (2 H, d, $J$ = 7.9), 6.50 (1 H, s), 3.57 (3 H, s), 3.18 (6 H, s), 3.16 (6 H, s); $^{13}C$ ($D_2O$, sodium 3-(trimethylsilyl)-1-propanesulfonate, TMSPSA) 166.5, 160.2, 160.1, 147.9, 143.1, 141.2, 113.7, 111.1, 110.6, 55.7, 43.12, 43.08. $^{13}C$ DEPT, 45° pulse, 143.1, 141.2, 113.7, 111.1, 110.6, 55.7, 43.10, 43.06; 90° pulse, 143.1, 141.2, 113.7, 111.1, 110.6 (55.7, 43.10, and 43.06 significantly decreased).

**By Reaction of 2 with Ozone in Methanol.** Ozone was bubbled through a solution of 1.211 g (1.55 mmol) of **2** in 30 mL of MeOH at 0 °C for 5 min followed by $N_2$ for 30 min to remove excess $O_3$. After removal of the solvent under high vacuum and recrystallizations from 2-PrOH followed by recrystallization from acetonitrile, a white crystalline product was obtained: yield 0.435 g (0.99 mmol, 64%); mp 180 °C dec; UV ($H_2O$) λ 322.8 (ε 54 000); $^1$H NMR as above. Counterions were exchanged to $PF_6^-$ by dissolving 1.235 g (2.78 mmol) of **1** ($Cl^-$ salt) in 5 mL of $H_2O$ and adding a solution containing 1.399 g (8.33 mmol) of $NaPF_6$ in 5 mL of $H_2O$. The mixture was allowed to sit for 30 h before collecting 1.504 g (2.36 mmol) of **1** ($PF_6^-$ salt): yield 85%; $^1$H NMR (acetone-$d_6$) 8.40 (2 H, d, $J$ = 8.1), 8.36 (2 H, d, $J$ = 8.1), 7.30 (2 H, d, $J$ = 8.1), 7.28 (2 H, d, $J$ = 8.2), 6.92 (1 H, s), 3.75 (3 H, s), 3.51 (6 H, s), 3.49 (6 H, s). Anal. Calcd for $C_{18}H_{24}N_4F_{12}O_2P_2$: C, 34.96; H, 3.91; N, 9.06. Found: C 34.91; H, 3.92; N, 9.03.

**By Reaction of 2 with Acetic Acid in Methanol.** To a solution containing 3.385 g (3.97 mmol) of **2** ($Cl^-$ salt) in 40 mL of $CH_3OH$ was added 5 mL (87 mmol) of acetic acid that was distilled from $P_2O_5$. The mixture was allowed to stand for 30 min before acetic acid and methanol were removed in vacuo. Recrystallization from hot acetonitrile gave 1.60 g (3.57 mmol, 90%) of **1**. $^1$H NMR as above.

**Crystal Structure.** Crystals were prepared by dissolving a pure sample of **1** in boiling 2-propanol, gravity filtering the hot solution, and allowing to cool to room temperature. The mixture was filtered through a fritted disk, and the crystals were washed with cold 2-propanol. A white needle was cut to appropriate size with a razor blade. Crystal parameters at 25 °C: $a$ = 7.9861 (10) Å, $b$ = 11.1273 (13) Å, $c$ = 26.7361 (42) Å, $\beta$ = 90.737 (11)°, $V$ = 2375.7 (10) Å$^2$, space group $P2_1/c$, $z$ = 4, $d_c$ = 1.32 g cm$^{-3}$, $\mu_{calcd}$ = 3.10 cm$^{-1}$, size of crystal 0.20 × 0.26 × 0.38 mm. Data measurement parameters: radiation, Mo Kα (λ 0.710 73 Å), number of reflections collected 3545, number of unique reflections 3099. Atomic coordinates are available from the corresponding author.

**Reaction of 2 with Acetic Acid in Ethanol.** To a solution of 270 mg (0.242 mmol) of **2** ($PF_6^-$ salt) in 30 mL of 67% ethanol in $CH_3CN$ (distilled from $CaH_2$ and stored over 4-Å sieves) at 22 °C was added 4 mL of acetic acid. The solution was allowed to stand for 30 min before excess acetic acid and solvents were removed via vacuum transfer. $^1$H NMR (acetone-$d_6$) of the crude reaction mixture showed 2 parts of DMAP·$HPF_6$, 0.43 parts of **3**, and 0.57 parts of its ethyl ester, ethyl 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoate, **4**, as determined by integration of the methylene protons of the ethyl group (4.2 ppm) relative to the combined integration of the dimethylamino protons of the ethyl group (4.2 ppm) relative to the combined integration of the dimethylamino protons of the ethyl ester and **3** (3.5 ppm). Multiple recrystallizations from acetone/ethanol removed 80% of the DMAP·$HPF_6$ and increased the ratio of **4**/**3** to 71/29. $^1$NMR (acetone-$d_6$, numbers of H are reported as relative to combined vinylic protons of **3** and its ethyl ester (6.90, 6.89 ppm)): 8.34 (complex m of all pyridinium α-H, 4.77 H), 7.28 (complex m of **3** and **4** pyridinium β-H, 4 H), 7.12 (d, $J$ = 7.7, DMAP·$HPF_6$, 0.77 H), 6.90 and 6.89 (overlapping s, 1 H), 4.20 (quartet, $J$ = 7.1, 1.4 H), 3.52 (s, dimethylamino of **3**, 3.5 H), 3.48 (s, dimethylamino of **4**, 8.5 H), 3.35 (s, dimethylamino of DMAP·$HPF_6$, 2.4 H), 1.23 (t, $J$ = 7.1, 2.2 H).

**Reaction of 2 with Formic Acid in Ethanol.** To a solution of 20 mg (0.026 mmol) of **2** in 1.5 mL of absolute ethanol at 22 °C was added 3 drops of 95% formic acid in water. The solution was stirred for 5 min before removing the excess formic acid and ethanol via vacuum transfer. $^1$H NMR ($D_2O$, $CH_3CN$ standard) showed 2 parts of DMAP·HCl to 0.42 parts of ethyl 3,3-bis(4-(dimethylamino)pyridinium-1-yl)propenoate and 0.58 parts of **3**, $^1$H NMR as above except 4.10 (0.84 H, q), 1.09 (1.26 H, t).

**Reaction of 2 with Formic Acid in 2-Propanol.** To a solution of 20 mg (0.026 mmol) of **2** in 6 mL of 2-propanol at 22 °C was added 0.5 mL of 95% formic acid in water while stirring for 30 min. Excess formic acid and solvent were removed by vacuum transfer: $^1$H NMR ($D_2O$, $CH_3CN$ standard) 7.92 (4 H, overlapping doublets), 7.87 (4 H, d (DMAP·HCl)), 6.93 (4 H, d), 6.75 (4 H, d (DMAP·HCl)), 6.50 (1 H, s), 3.22 (12 H, overlapping singlets), 3.05 (12 H, s, (DMAP·HCl)).

**3,3-Bis(4-(dimethylamino)pyridinium-1-yl)propenoic Acid Dichloride, 3. By Hydrolysis of 2.** A solution of **2** in $D_2O$ was maintained at room temperature for several weeks. The $^1$H NMR spectrum showed the presence of **2** and DMAP·HCl. The DMAP·HCl could also be detected by TLC: $^1$H NMR ($D_2O$, $CH_3CN$ standard), 7.92 (4 H, overlapping doublets), 7.87 (4 H, d (DMAP·HCl)), 6.93 (4 H, d), 6.75 (4 H, d (DMAP·HCl)), 6.50 (1 H, s), 3.22 (12 H, overlapping singlets), 3.05 (12 H, s, (DMAP·HCl)).

**By Hydrolysis of 1.** To a solution of 1.60 g (3.57 mmol) of **1** in 5 mL of $H_2O$ at 25 °C was added 2.466 g (17.8 mmol) of $K_2CO_3$ in 5 mL of $H_2O$. The resulting yellow solution was neutralized with 0.5 M HCl and pumped to dryness under vacuum. The resulting solid was dissolved in MeOH and filtered. After removal of the MeOH under vacuum, 1.340 g (0.309 mmol, 86%) of white product was obtained: mp 217 °C dec; UV ($H_2O$) $\lambda_{max}$ 315 nm (ε 54 600); IR (KBr) 3450 (br, s), 3080 (sh, w), 1715 (sh, m), 1645 (sh, s), 1585 (sh, m), 1410 (sh, m), 1370 (sh, m), 1290 (sh, m), 1210 (sh, m), 1185 (sh, m), 1155 (sh, m), 905 (sh, w), 875 (sh, w), 830 cm$^{-1}$ (sh, m); $^1$H NMR ($D_2O$, $CH_3CN$ standard) 7.92 (4 H, overlapping doublets), 6.93 (4 H, d, $J$ = 8.1), 6.50 (1 H, s), 3.22 (12 H, overlapping singlets); $^{13}$C (methanol-$d_4$) 169.1, 159.9, 159.8, 142.9, 142.3, 141.6, 110.8, 110.5, 51.5, 42.9, 42.8; $^{13}$C DEPT, 45° pulse, 142.9, 141.6, 110.8, 110.5, 51.5, 42.9, 42.8; 90° pulse, 142.9, 141.6, 110.8, 110.5; 135° pulse, 142.9, 141.6, 110.8, 110.5; 135° pulse, 142.9, 141.6, 110.8, 110.5, 51.5, 42.9, 42.8. Analysis was complicated by the deliquescent nature of **2**. The chloride was low possibly due to the presence of **2** as a zwitterion. The presence of sodium even after several reprecipitations may result from either NaCl or the sodium salt of the carboxylate. Anal. Calcd for $C_{17}H_{22}N_4Cl_2O_2$: C, 53.00; H, 5.76; N, 14.54; Cl, 18.40. Calcd for $C_{17}H_{21}N_4Cl_1O_2$: C, 58.54; H, 6.07; N, 16.06; Cl, 10.16. Calcd for $C_{17}H_{21}N_4Cl_2O_2Na$: C, 53.13; H, 5.51; N, 14.58; Cl, 18.45; Na, 5.98. Found: C, 46.76; H, 5.71; N, 12.80, Cl, 16.52; Na, 1.98.

**Determination of the p$K_a$ of 3.** The extinction coefficients for the protonated species (ε 54 600) and the unprotonated species (ε 47 400) are close enough so that a plot of $\lambda_{max}$ vs pH should give a reasonable approximation to the p$K_a$. Six points were taken using Fisher buffer solutions at pH 5.86, 4.03, 3.03, 2.00, 1.07. The pH values were confirmed with a Fisher Accumet, Model 805 MP, pH meter using a two point calibration. A pH 0.16 buffer solution was prepared by adding 6 M HCl to the Fisher pH 1.07 buffer solution.

**Vinyl Hydrogen Exchange of 3.** Deuteriobuffer solutions were prepared by taking 2.00 mL of a standard pH 10.00 buffer solution, containing boric acid, potassium chloride, and sodium hydroxide and removing water via high vacuum. The resulting solid was taken up in 0.5 mL of $D_2O$ and dried under high vacuum. The solid was then transferred to a 2.00-mL volumetric flask and diluted to 2.00 mL with $D_2O$. The pH of the solution was determined to be 10.98 using a Fisher Accumet Model 805 MP pH meter. To 1 mL of the buffer solution was added 10 mg (0.023 mmol) of **3**: $^1$H NMR 7.89 (2 H, d, $J$ = 8), 7.32 (2 H, d, $J$ = 8), 6.85 (4 H, d, $J$ = 8), 3.17 (12 H, s); $^{13}$C NMR ($D_2O$, TMSPSA standard) 169.1, 159.9, 159.8, 142.9, 142.3, 141.6, 110.8, 110.5, 42.0, 42.0; $^{13}$C DEPT ($D_2O$, TMSPSA standard) 45° pulse 142.9, 141.6, 110.8, 110.5, 42.0, 42.0; 90° pulse 142.9, 141.6, 110.8, 110.5; 135° pulse 142.9, 141.6, 110.8, 110.5, 42.0, 42.0. A pH 7.9 deuteriobuffer solution was prepared as described above using a standard pH 7.00 buffer solution containing potassium phosphate monobasic and sodium hydroxide. $^1$H NMR analysis showed the gradual disappearance of vinylic proton at 6.47 ppm over 2 days.

**Decarboxylation of 3.** To a mixture of 1.340 g (3.09 mmol) of **3** partly dissolved in 30 mL of *N*-methylpyrrolidone (M-pyrol) was added 1.0 g (16 mmol) of $Cu^0$ powder, and the reaction mixture was stirred at 114 °C for 20 h. To the reaction mixture was added 200 mL of $Et_2O$, and the resulting sludge was separated from solution via centrifugation and extracted three times with 50 mL of saturated NaCl solution and three times with 50 mL of $H_2O$. Water from the extract was removed via high vacuum, and the compound was extracted from the resulting solid with $CH_3OH$. Methanol was removed in vacuo, and the resulting solid was taken up in 4 mL of $H_2O$ and added to 2 mL of saturated aqueous $NaPF_6$ solution. The resulting oil was triturated until solid. Recrystallization from acetonitrile/methanol/water gave 86 mg (0.0.194 mmol, 6.3%) of **11**: $^1$H NMR ($CD_3CN$) 8.03 (4 H, d, $J$ = 7.9), 6.89 (4 H, d, $J$ = 7.9), 6.06 (2 H, s), 3.20 (12 H, s); $^1$c NMR ($CD_3CN$) 158.09, 141.78, 109.30, 73.90, 41.10; $^{13}$C DEPT ($CH_3CN$) 135° pulse

141.78, 109.30, 73.90 (down), 41.10. Anal. Calcd for ($C_{16}H_{22}N_4P_2F_{12}$·$H_2O$): C, 33.23; H, 4.18; N, 9.69. Found: C, 32.80; H, 4.00; N, 9.54.

**Preparation of DMAP·HCl.** To a solution of 150 mg (1.23 mmol) of DMAP in 5 mL of $H_2O$ at 0 °C was added 3 mL of 6 M HCl. The excess HCl and water were removed via vacuum transfer: UV ($H_2O$) $\lambda_{max}$ 280 nm; $^1H$ NMR ($D_2O$, $CH_3CN$ standard) 7.86 (2 H, d, $J$ = 7.7), 6.71 (2 H, d, $J$ = 7.7), 3.04 (6 H, s ($CD_3OD$)), 8.02 (2 H, d, $J$ = 7.3), 6.90 (2 H, d, $J$ = 7.3), 3.13 (6 H, s ($CD_3)_2CO$)), 8.19 (2 H, d, $J$ = 7.5), 7.04 (2 H, d, $J$ = 7.6), 3.32 (6 H, s); $^{13}C$ NMR ($CD_3OD$) 158.6, 139.6, 108.2, 40.7.

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**Registry No.** 1·2$Cl^-$, 130146-51-9; 1·2$PF_6^-$, 130146-54-2; 2·4$Cl^-$, 90432-32-9; 2·4$PF_6^-$, 114692-31-8; 3·2$Cl^-$, 106538-37-8; 4, 130146-52-0; DMAP·$HPF_6$, 130146-53-1; DMAP·HCl, 71561-71-2; DMAP, 1122-58-3.

# Reductive Radical Cyclizations of Haloalkenes Promoted by Samarium Diiodide. Sequential Cyclization/Intermolecular Carbonyl Addition Reactions

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A sequential radical cyclization/intermolecular carbonyl addition process promoted by samarium(II) iodide ($SmI_2$) is reported. Treatment of appropriate haloalkenes with $SmI_2$ in the presence of a variety of ketones leads to products resulting from cyclization followed by intermolecular addition of the resultant anion to the carbonyl electrophiles. Although several mechanisms can be envisioned, this process is most likely initiated by $SmI_2$-induced formation of a hexenyl radical. Intramolecular addition of this radical to the tethered alkene leads to generation of a new alkyl radical, which can be reduced in situ to the corresponding organosamarium species. This organosamarium adds to the carbonyl electrophile, completing the tandem process. In this study, 2-(allyloxy)ethyl iodide and 2-(allyloxy)-1-iodobenzene were the most thoroughly examined radical precursors. The anion intermediates ultimately derived from these starting materials were trapped with a range of ketones to yield the corresponding heterocyclic derivatives.

Intramolecular radical cyclization reactions have proven to be an efficient means for the generation of heterocyclic compounds. Although such radical cyclization processes have found widespread use in recent years,[2] the currently available methods are not without some drawbacks and limitations. We have recently developed an efficient and mild route to a variety of heterocyclic compounds which complements these more traditional protocols. The method involves a sequential radical cyclization/intermolecular carbonyl addition reaction which leads to functionalized heterocycles.

Perhaps the most commonly utilized means of radical generation involves treatment of a halide with $R_3SnH$. Generally, the radicals produced in the $R_3SnH$-mediated cyclization process are terminated by hydrogen abstraction, usually from the $R_3SnH$ present in the reaction mixture. This process, however, results in a net loss of functionality in proceeding from the starting material to the products of the reaction. In addition, the removal of tin-containing byproducts from the reaction mixture is not always a trivial matter.[3] Alternative methods for radical cyclization/termination, including atom-transfer reactions,[4] electrochemical processes,[5] oxidative free-radical cyclization processes,[6] and other miscellaneous reactions,[7] have been developed which involve entrapment or further reaction of intermediate radical species. These processes tend to provide products with greater or at least comparable functionality in the products as compared to that found in the starting material. Although reaction sequences have also been developed in which radical cyclization precedes a second (radical) carbon–carbon bond-forming reaction, care must be taken in these transformations to tune each substrate in order to avoid polymerization and other undesirable side reactions.[8]

Other reductive processes provide useful alternatives to the aforementioned reactions for further elaboration of the cyclized radical intermediates.[9] Previously, Kagan dem-

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