Reaction of Pyridines with Tetrachlorocyclopropene. A New Synthesis of Indolizines

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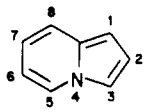
Pyridines react with tetrachlorocyclopropene, TCCP, to give indolizine products in high yields. A mechanism is suggested in which successive nucleophilic reactions by the pyridine nitrogen lead to a cyclopropyl anion that undergoes electrocyclic ring-opening to the corresponding allyl anion. Cyclization followed by elimination gives the indolizine products **2** and **3**. In addition, the chemistry of the pyridinium–indolizine products formed in this reaction is found to be dominated by the pyridinium functionality.

Indolizines, **1**, show a wide range of biological activity,[1] and indeed, the saturated indolizine system (*d*-coniceine) is found in many naturally occuring alkaloids.[2] The



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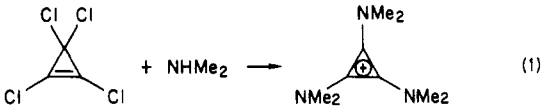
primary method available for synthesizing indolizines is that of Tschitschibabin[3] in which an α-picoline is treated with an α-halocarbonyl compound to give the corresponding 2-substituted indolizine. Another synthesis[4] involves reaction of dimethyl acetylenedicarboxylate with pyridine. In general, these syntheses are limited by the availability of appropriate precursors and by the modest yields often obtained. Moreover, it has been difficult to generate stable indolizines with halogens on the 1, 2, or 3 positions. 3-Chloroindolizine, for example, decomposes in air.[5] One of the few stable such haloindolizines is 1-acetyl-2-methyl-3-chloroindolizine.[6]

The reactivity of tetrachlorocyclopropene, TCCP,[7] toward nucleophiles has been noted by many researchers.[8] In particular, secondary amines react with TCCP to give cyclopropenium ions, **2**.[8a] Similarly, mercaptans react with TCCP to give the corresponding tris(alkylthio)cyclopropenium cations.[8b,c] The only reference, prior to our communication,[9] of reaction between TCCP and heteroaromatics was a notation that an insoluble material is formed on mixing pyridine with TCCP.[7b]



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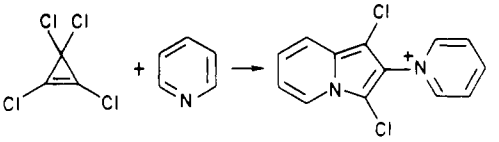
In this paper we describe a new synthesis of indolizines based on the reaction of pyridines with TCCP,[9] a plausible mechanism is proposed, and the reactivity of the products is discussed.

Results and Discussion

Reaction of Pyridines with TCCP. Pyridine reacts with TCCP to give the indolizines **3** and **4** in a ratio (**3**:**4**) of about 1:3.5–5. This ratio is almost independent of the



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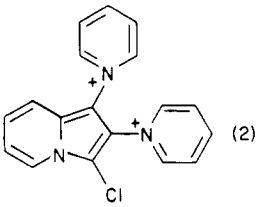

(2)

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pyridine concentration used. The combined yield of products is essentially quantitative, with pyridine being the limiting reagent. Considerably lower yields of purified materials were obtained in practice due to difficulties in separating the two products. The substitution about the pyrrole ring of **3** and **4** shows only the isomers indicated.

The structure of **3** can be deduced partially from ^{1}H NMR (Table II) and UV–vis spectral data (Table I). The UV–vis spectrum of **3** shows a component at 282 nm (log ϵ = 4.20) which is similar to an absorption for indolizine at 281 nm (3.49).[10] The ^{1}H NMR shifts and coupling constants for protons at C-5 through C-8 of **3** are similar to those for indolizine itself (Table II).[10] The proposed

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(8) (a) Yoshida, Z.; Tawara, Y. *J. Am. Chem. Soc.* **1971**, *93*, 2573. (b) Gompper, R.; Jersak, U. *Tetrahedron Lett.* **1973**, 3409. (c) Yoshida, Z.; Yonada, S.; Miyamoto, T.; Miki, S. *Tetrahedron Lett.* **1974**, 813. (d) Mock, W. L.; Sprecher, C. M.; Stewart, F. F.; Northolt, M. G. *J. Am. Chem. Soc.* **1976**, *94*, 2015.

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Table I. Ultraviolet-Visible Spectral Data

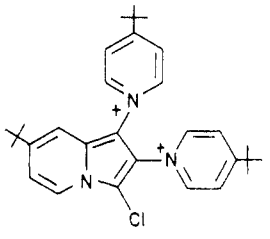
compd	solvent	λ_{max} (log ϵ)
indolizine[10]	H_2O	232 (4.47), 292.5 (3.58), 274 (3.33), 281 (3.49), 337 (3.26)
3[a]	EtOH	260 (4.21), 267 (4.25), 274 (4.24), 282 (4.20)
4	H_2O	219 (4.36), 264 (3.96), 390 (3.42)
5	H_2O	225 (4.60), 266 (4.23), 395 (3.74)
19	CH_3CN	263 (4.42), 348 (3.66)
PyHCl[10]	H_2O	261 (3.53)

[a] As the tetraphenylborate salt.

structure was confirmed by single-crystal X-ray crystallographic analysis on the tetraphenylborate salt. Information concerning the crystallographic collection is found in Table III. The structure obtained along with selected bond distances and angles are shown in Figure 1 (note that the atom numbering for the crystal structure is not the same as the IUPAC numbering system employed elsewhere in this paper). Additional bond angles, distances, and thermal parameters are available as supplementary material. The structure consists of well-separated BPh_4 anions and closely associated $C_{13}H_9N_2Cl_2$ cation pairs stacked in sheets in the *b*–*c* plane. A stereoprojection of the cation pair arrangement is available as supplementary material. The indolizine pairs are separated by 3.39 Å. The six-membered ring of the indolizine shows alternating single and double bonds, but the bonds on the five-membered ring are essentially equal and of a length characteristic of aromatic bonds. The pyridinium-1-yl ring is twisted from the plane of the indolizine by 53.3°.

The structure of **4** is inferred largely from UV–vis (Table I) and ^1H NMR data (Table II). A long-wavelength UV–vis component at 390 nm (log ϵ = 3.42) can be compared to 337 nm (3.26) for indolizine.[10] The ^1H NMR chemical shifts and coupling constants for H-5 through H-8 of **4** are comparable to those for **3**. The chemical shifts for H-5, H-6, and H-7 of **4** appear slightly downfield from the same positions of **3**: however, H-8 is shifted upfield. This shift is presumably caused by shielding from a pyridinium group at C-1 and suggests the structure for **4** shown.

When TCCP is treated with 4-methylpyridine (γ-picoline), 4-*n*-propylpyridine, or 4-*tert*-butylpyridine, the bis-pyridinium indolizine product is found to dominate. With 4-*tert*-butylpyridine, more than 95% of the product corresponds to the bis-substituted indolizine **5**. Com-



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pounds with electron-withdrawing groups appear either not to react with TCCP (such as 2,2′-biquinolyl) or to give

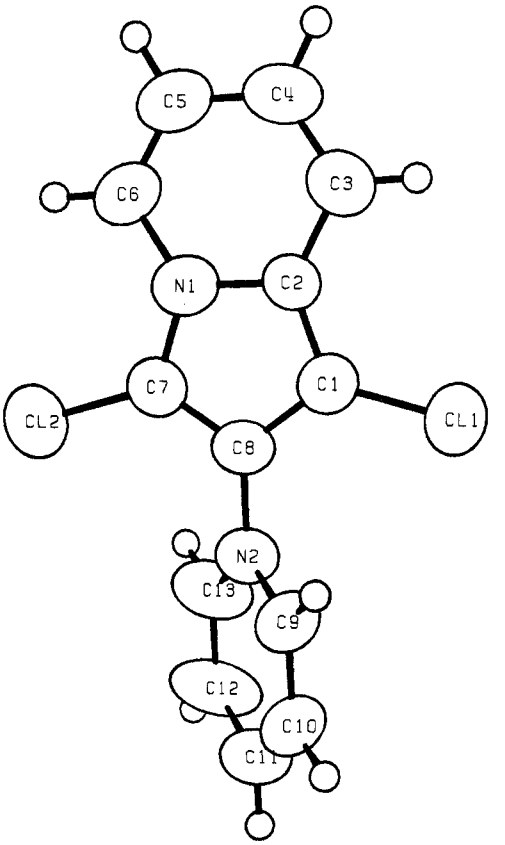
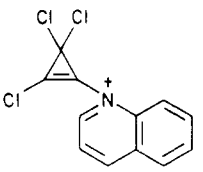


Figure 1. Structure of **3**. Bond distance (Å): Cl–Cl1, 1.70; N1–C2, 1.39; N1–C7, 1.38; N1–C6, 1.40; C7–C8, 1.37; C8–C1, 1.39; C1–C2, 1.38; C2–C3, 1.40; C3–C4, 1.35; C4–C5, 1.41; C5–C6, 1.33; C8–N2, 1.43. Bond angles (degrees): N1–C7–C8, 107.3; C7–C8–C1, 108.8; C8–C1–C2, 107.5; C2–N1–C7, 108.8; N1–C2–C3, 118.9; C2–C3–C4, 119.5; C3–C4–C5, 120.6; C4–C5–C6, 121.2; C5–C6–N1, 118.9; C2–C1–Cl1, 124.6.

unstable adducts (uncharacterized), perhaps trichlorocyclopropene compounds such as **6** and **7**. 2,4,6-Collidine



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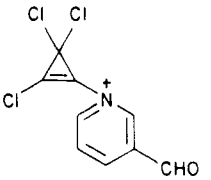

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and 2,6-lutidine also react with TCCP to give products which hydrolyze readily; no indolizines are formed.

Tetrabromocyclopropene[7] reacts with pyridine to give only the bis-adduct **8**.

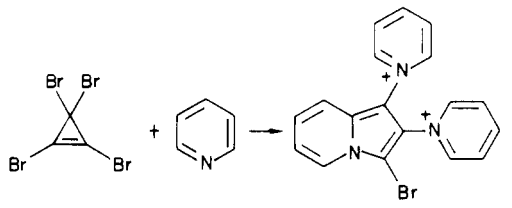
Mechanism. These results suggest a mechanism consisting of the following steps (see Charts I–III).

1. **Addition–Elimination of the Pyridine.** Pyridine can attack TCCP as a nuclephile to give an intermediate cyclopropyl anion. The anion can eliminate Cl^- to give a mono-pyridinium cyclopropene. There is some debate in

Table II. ^1H NMR Spectral Data

		δ				J, Hz					
compd	solvent	H_5	H_6	H_7	H_8	5,6	5,7	5,8	6,7	6,8	7,8
indolizine[10]	CCl_4	7.76	6.31	6.50	7.25	6.8	1.0	1.2	6.4	1.0	8.9
3[a]	D_2O	8.21	7.05	7.18	7.63	7.0	0.9		6.5	1.1	9.2
4	D_2O	8.33	7.15	7.32	7.51	7.1	0.9		6.9	0.9	9.1
5	CD_3OD	8.45	7.41		7.52	7.5		0.8		1.8	
19	$CDCl_3$	7.82	6.76		7.09	7.5				1.0	
20	D_2O	8.21	7.01		7.23	7.8				1.8	

[a] As the chloride salt.



(3)

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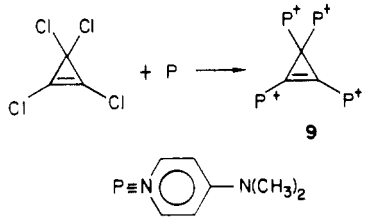
the literature as to the nature of nucleophilic attacks on TCCP.[8d,10] We favor the carbanion mechanism shown in Chart I since, as shown below, a cyclopropyl anion is almost certainly involved in a later stage of the reaction. In addition, the mono-pyridinium indolizine product **3** most likely involves 1-(pyridinium-1-yl)-2,3,3-trichlorocyclopropene as an intermediate since the 3-pyridinium isomer would lead to a product not observed in the reaction (see Chart I). If the reaction were to go through an S_N2 or S_N2' type of mechanism, the 3-pyridinium isomer would be involved. An S_N1 mechanism seems unlikely due to the large amount of positive charge in the system at later stages of the reaction.

With electron-attracting substituents on the pyridine, no further reaction occurs. With pyridine or pyridines bearing electron-donating substituents, the addition–elimination is repeated to give 1,3-bis(pyridinium-1-yl)-2,3-dichlorocyclopropene. The second addition must occur through the ylide intermediate rather than by placing both pyridiniums on the same carbon since the latter process would again yield a product not observed in the reaction (see Chart I). These substitution reactions are consistent with our reported isolation of 1,2,3,3-tetrakis(4-(dimethylamino)pyridinium-1-yl)cyclopropene **9** from reaction of (dimethylamino)pyridine (DMAP) with TCCP.[11]



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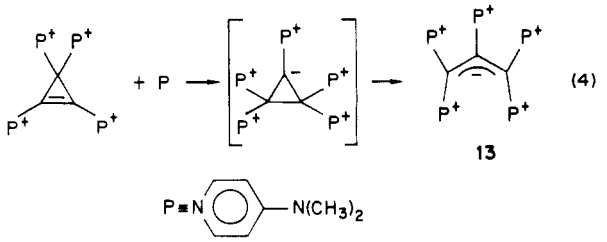
2. Electrocyclic Ring-Opening of the Cyclopropyl Ring. Competitive with elimination of halide ion is electrocyclic ring opening of the bis-pyridinium cyclopropyl anion, **10**, to give a positively charged allyl anion **11** (Chart II). Addition of a pyridine to the bis-pyridinium cyclopropene produces a cyclopropyl anion which can also electrocyclicly ring-open to give the allyl anion **12**. Such a step is also consistent with the observation that **9** goes to the allylide **13** upon addition of excess DMAP.[11]



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Starting with **10**, the anion involved in the formation of **3** (Chart I), only one pathway for further addition leads to **4** (Chart III). Pyridines with electron-donating groups destabilize the cyclopropyl anion intermediate and, therefore, promote elimination. Further substitution can then occur leading to products with more pyridinium groups. Ring opening only occurs when the cyclopropyl anion intermediate is sufficiently stabilized by pyridiniums to survive long enough for the electrocyclic reaction to occur. In the case of DMAP, the destabilization by the

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Table III. Crystal and Data Collection Parameters

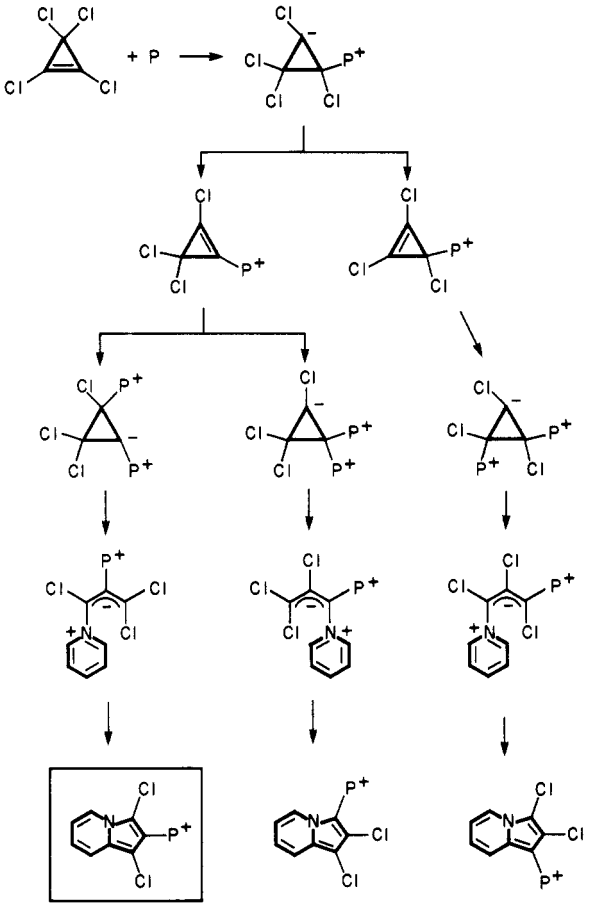
A. Crystal Parameters at 25 °C

a = 16.3668 (11) Å	space group = $P2_1/c$
b = 10.0669 (19) Å	z = 4
c = 18.5781 (24) Å	d(calcd) = 1.279
α = 90°	μ(calcd) = 2.411
β = 98.170 (8)°	size = 0.26 × 0.38 × 0.50 mm
γ = 90°	v = 3029.9 (12)

B. Data Measurement Parameters

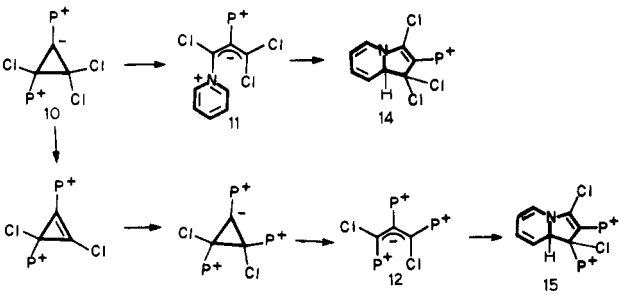
diffractometer	Enraf-Nonius CAD-4
radiation	Mo Kα (λ = 0.71073 Å)
no. of ref collected	4373
no. of unique reflections	3940

Chart I[a]



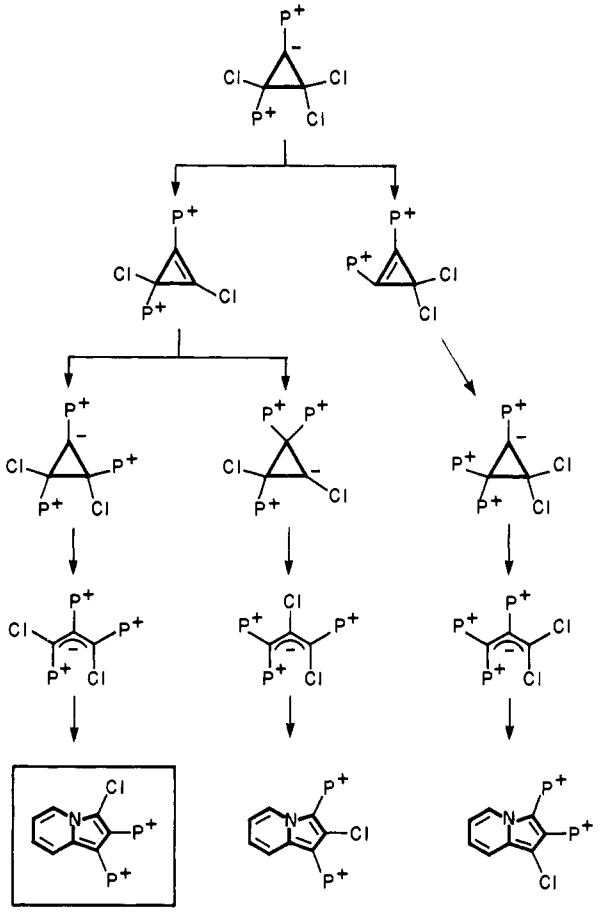
[a] P = pyridine.

Chart II[a]



[a] P = pyridine.

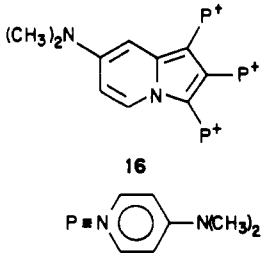
Chart III[a]



[a] P = pyridine.

electron-donating dimethylamino group is so great that this ring opening does not occur until five pyridiniums are on the cyclopropyl ring.[11]

3. Cyclization of the Allylide. Pyridinium-1-yl allylides are known to cyclize to dihydroindolizines.[12] We can expect an analogous reaction with **11** or **12** to give **14** or **15**, respectively (assuming rotation of the allylide to the proper conformation), as shown in Chart II. That cyclizations of this type occur readily without a pyridinium-1-yl moiety at the allyl C-2[12] makes it unlikely that this step controls the selective formation of **3** and **4**. The reaction of 4-*tert*-butylpyridine with TCCP was monitored by UV–vis spectroscopy. Reaction at 0 °C in chloroform showed that a blue intermediate (λ_{max} = 560 nm) is formed rapidly and then decays in a much slower process as the absorptions characteristic of the product grow in. Presumably, the blue intermediate is **12**. As a comparison, 1,1,3,3-tetraphenylallyl anion has a long-wavelength absorption at 563 nm.[13] This reaction was also monitored by using ^{1}H NMR spectroscopy; at −20 °C in chloroform, resonances attributable to the pyridine declined with the corresponding growth of resonances attributable to pyridiniums. No indolizine peaks appeared at this temperature. At 0 °C, the product peaks slowly grew in as the peaks for the intermediate declined. These data indicate that the barrier to cyclization is much greater than that for electrocyclic ring opening. This is more dramatically seen by the fact that **13** only goes to the corresponding indolizine **16** on heating to 170 °C.[11]



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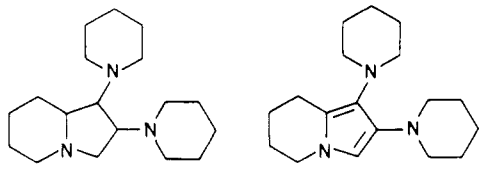
4. Elimination. Elimination of HCl or pyridine hydrochloride could occur from **15** to give the two products of the reaction, **3** and **4**. Such elimination could be stereospecific, presumably anti, and then the relative proportions of bis- and mono-pyridinium indolizine products would depend only on the relative amounts of the two dihydroindolizines (cis and trans) present. These, in turn, would depend on the conformations of the allylide at the time of cyclization. Such a sequence would explain the insensitivity of the ratio of bis- to mono-pyridinium indolizine products (**3** to **4**) to the concentration of pyridine, but it does not explain the dominance of bis-substituted product with pyridines having electron-donating groups. Alternatively, **3** can be formed by loss of HCl from a mono-pyridinium dihydroindolizine. This would necessitate ring opening of a bis-pyridinium cyclopropyl anion followed by cyclization. The fact that reaction of pyridine with tetrabromocyclopropene gives only bis-substituted product is then explained by the greater propensity for elimination of bromide ion relative to electrocyclic ring opening of the bromo analogue of the cyclopropyl anion **10**. The bis(pyridinium-1-yl)cyclopropene formed reacts with a third pyridine to give the bis-pyridinium indolizine product **8**. For these reasons, we favor the separate pathway through **12** to give **4** (Chart II); however, we note also that pyridinium hydrochloride can be eliminated in the cyclization to the indolizine since such a pathway is required in the formation of **16** from **13**.[11]

5. Summary. Reaction 2 occurs through a mechanism involving first repeated addition of pyridine followed by elimination of chloride ion. When a choice of sites for addition exists, the preferred path is apparently that which results in the formation of a pyridinium ylide and avoids the placement of two pyridiniums on the same carbon. Elimination of chloride occurs in such a way as to place a pyridinium group on the double bond (an *N*-vinylpyridinium cation). This preference is probably due to π-conjugation between the pyridinium moiety and the cyclopropene double bond. At the bis(pyridinium-1-yl)cyclopropyl anion stage, electrocyclic ring-opening competes with loss of halide ion and further substitution by the pyridine. Pyridines with more electron-donating substituents or a cyclopropene with a better leaving group (bromide) favor elimination followed by additional substitution and ring-opening to the appropriate allyl anion. In the extreme case of DMAP, ring-opening does not occur until the system is fully substituted.[11] Once the allylide is formed, it can cyclize and eliminate HCl to give the observed reaction products.

Reactivity of Pyridinium-Substituted Indolizines. The chemistry of the pyridinium-substituted indolizines is dominated by the pyridinium moiety. For example, hydrogenation of **4** gave a mixture of **17** and **18**. These two compounds were recovered from a complex mixture of products formed during the hydrogenation. No product could be isolated with the indolizine intact, and no chlorine was found in these products. Reaction of **4** with excess $NaBH_4$ lead to reduction to the fully saturated system,

(12) (a) Sasaki, T.; Kanematsu, K.; Kakehi, A.; Ito, G. *Tetrahedron* **1972**, *28*, 4947. (b) Pohjala, E. *Tetrahedron Lett.* **1972**, 2585.
(13) Streitwieser, A., Jr.; Ciuffarin, E.; Hammons, J. H. *J. Am. Chem. Soc.* **1967**, *89*, 63.



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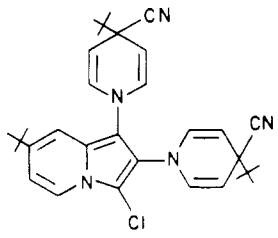
presumably because of the activation of the hydride on complexation with the basic nitrogens of the partially reduced indolizines (an IR spectrum of what may be the amine–borohydride complex has absorptions at 2250 and 1150 cm^{-1}). With less $NaBH_4$, unstable products were obtained.

Reaction of **4** or **5** with iodide ion showed only exchange of the counterions; no displacement of the ring-bound chlorine occurred. With cyanide ion, **5** reacted to give the bis-dihydropyridine derivative **19**. The product of the



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reaction is a neutral compound with corresponding properties unlike those of the other indolizines produced in reaction 2. For example, it is soluble in such organic solvents as ether and acetone. In acid, **19** gave only **5** plus HCN; no hydrolytic cleavage of the dihydropyridine function occurred.

Conclusion

Reaction 2 represents a new route to novel indolizines. The products contain rare examples of halogen-substituted and unprecedented examples of pyridinium-1-yl substituents on the pyrrole part of the indolizine ring. The yields are high and involve readily available starting materials. The products are subject to some reactions (reduction, nucleophilic attack), although the chemistry appears to be dominated by the pyridinium groups.

The mechanism shown is consistent with the data presented. This mechanism involves successive nucleophilic attacks of pyridines on TCCP to displace chlorides (probably via a carbanion intermediate). This anion can ring-open in an electrocyclic reaction. The allyl anion formed cyclizes to give the dihydroindolizine derivative which can in turn eliminate HCl to give the products of the reaction.

Experimental Section

General Methods. Chloroform used in these reactions was shaken with H_2SO_4, washed with H_2O, and distilled from P_2O_5 prior to use. GC analyses were run on a Hewlett Packard 5880A gas chromatograph. Elemental analyses were done by the University of California Analytical Services Laboratory, Berkeley. All melting points are reported uncorrected. UV–vis data are reported as λ_{max} (log ϵ). IR data are in cm^{-1}, and NMR data are presented in ppm downfield from Me_4Si (number of hydrogens, multiplicity, coupling constants in Hz). Mass spectra are reported as m/e (percent of base).

Tetrachlorocyclopropene (TCCP). The procedure of Tobey and West[7a] was used with the modification that the emulsion formed with the aqueous base and the TCCP was broken by diluting to twice the volume with cold water (containing NaCl, for some runs). Distillation gave 70–80% of TCCP of purity >95% by GC (the remainder being DME). No differences were found in experiments using TCCP having some DME and those in which the TCCP was pure. ^{13}C NMR ($CDCl_3$) δ 62.27, 122.58.

Tetrabromocyclopropene. The procedure of Tobey and West[7a] gave product as reported. ^{13}C NMR ($CDCl_3$) δ 24.0, 120.9.

Reaction of TCCP with Pyridine. In a typical reaction, a 0 °C solution of pyridine (0.797 g, 10.1 mmol) in 10.0 mL of $CHCl_3$ was added in a slow, dropwise fashion to a stirred solution of 25.0 mL of $CHCl_3$ containing TCCP (0.9448 g, 5.04 mmol). After 10 min (at which point the solution had turned from purple to green), the solution was stirred at room temperature for 14 h. Solvent and unreacted TCCP were removed by vacuum transfer to yield a bright golden-green solid (2.00 g) which was washed with cold CH_3CN. The washed solid was essentially pure 1,2-bis(pyridinium-1-yl)-3-chloroindolizine dichloride (**4**) (0.910 g; 23%) which could be recrystallized from hot acetonitrile plus 1% water to give yellow sheets: mp > 270 °C dec. The washings were dried under vacuum (0.496 g) and dissolved in water. A solution of 1.5 g of Ph_4BNa in 20 mL of H_2O was added with stirring. After filtration and recrystallization from acetone, 0.31 g (3%) of 2-(pyridinium-1-yl)-1,3-dichloroindolizine tetraphenylborate (dec >150 °C) was recovered. The relative molar ratio of the bis- to the mono(pyridinium)indolizine was found to be 5.0–3.2 over a range of TCCP/pyridine equal to 12.0 to 10^{-2} according to ^1H NMR integrated ratios. With excess pyridine, all of the TCCP reacted to give 75–85% of the bis-adduct and 25–15% of the monoadduct. Similar results were obtained at dilutions of a factor of 6 times the sample reaction. Reactions were also carried out in the following solvents to give the same products in roughly the same ratios: CH_2Cl_2, CH_3CN, THF, ether, toluene, EtOH, and neat. The reaction in toluene was carried out in a high dilution.

1,2-Bis(pyridinium-1-yl)-3-chloroindolizine dichloride (4): IR (KBr) 3460, 3110, 3050, 3020, 1625, 1617, 1450, 1352, 1328, 1263, 1152, 1012, 790, 779, 763, 696, 677; ^1H NMR (D_2O) δ 8.97 (2, d, J = 6.7), 8.92 (2, d, J = 6.7), 8.72 (1, t of t, J = 7.9, 1.2), 8.63 (1, t of t, J = 7.9, 1.1), 8.33 (1, d of d, J = 7.1, 0.9), 8.16 (2, t), 8.11 (2, t), 7.51 (1, dd, J = 9.1, 0.9), 7.32 (1, ddd, J = 1, 6.9, 0.9), 7.15 (1, ddd, J = 7.1, 6.9, 0.9); ^{13}C NMR (D_2O) δ 174.4, 149.5, 148.2, 146.8, 129.9, 129.0, 127.8, 126.4, 116.2, 115.0, 114.0, 94.7; UV–vis (H_2O) 219 (4.36), 264 (3.96), 390 (3.42).

Anal. Calcd for $C_{18}H_{14}N_3Cl_3 \cdot H_2O$: C, 54.50; H, 4.06; N, 10.59; Cl, 26.81. Found: C, 54.35; H, 4.07; N, 10.55; Cl, 26.58.

1,2-Bis(pyridinium-1-yl)-3-bromoindolizine dibromide (8): ^{13}C NMR (D_2O, CH_3OH as reference) δ 148.9, 147.5, 146.2, 129.3, 128.4, 127.0, 125.8, 124.5, 122.9, 115.5, 114.1, 94.0.

2-(Pyridinium-1-yl)-1,3-dichloroindolizine tetraphenylborate: IR (KBr) 3110, 3095, 3068, 3050, 1625, 1575, 1455, 1423, 1357, 1308, 1268, 1242, 1211, 1164, 1144, 1062, 1053, 1027, 1016, 957, 845, 796, 758, 735 (strong), 705, 665, 600; ^1H NMR ($CDCl_3$) δ 8.79 (2, d, J = 6.8), 8.72 (1, t of t, J = 7.9, 1.4), 8.21 (1, dd, J = 7.0, 0.9), 8.20 (2, t), 7.63 (1, dd, J = 9.2, 1.1), 7.32 (1, dd, J = 9.2, 0.9), 7.27 (8, br s), 7.05 (1 dd, J = 7.0, 1.1), 6.97 (8, t, J = 7.5), 6.82 (4, t); ^{13}C NMR (CD_3CN) δ 146.0, 144.8, 136.1, 133.9, 126.0 (J_{B-C} = 2.6), 123.9, 122.0, 119.7, 114.5; UV–vis (EtOH) 260 (4.21), 267 (4.25), 274 (4.24), 282 (4.20).

Anal. Calcd for $C_{66}H_{54}N_3ClB_2$: C, 76.18; H, 5.01; N, 4.80; Cl, 12.15. Found: C, 76.11; H, 5.08; N, 4.82; Cl, 12.03.

1,2-Bis(4-*tert*-butylpyridinium-1-yl)-3-chloro-7-*tert*-butylindolizine Dichloride (5). To a stirred solution of 0.276 g (1.55 mmol) of TCCP in 20 mL of chloroform at 0 °C was added 1.55 g (1.05 mmol; 5.0 equiv) of 4-*tert*-butylpyridine. The solution turned intensely purple after a few seconds. The solution was stirred at 0 °C for 20 min and then allowed to warm to room temperature and stir for 15 h. The solution at this time appeared to be a homogeneous yellow color. The solvent was removed on a rotary evaporator. The crude product was dissolved in 5 mL of methanol and precipitated from solution with ether, filtered, and dried under vacuum to give essentially pure product (0.778 g; 92%). This material was recrystalized from acetonitrile to give 0.393 g (46%) of yellow crystals, mp >300 °C dec; ^1H NMR (CD_3OD) δ 1.37 (s, 9), 1.49 (s, 18), 7.41 (dd, 1, J = 1.80, 7.54), 7.52 (dd, 1, J = 1.7, 0.98), 8.29 (d, 2, J = 7.02), 8.37 (d, 2, J = 7.04), 8.45 (dd, 1, J = 0.7, 7.45), 9.12 (d, 2, J = 6.95), 9.20 (d, 2, J = 7.05); ^{13}C NMR ($CDCl_3$) δ 174.0, 173.2, 149.0, 148.7, 148.1, 127.4, 125.4, 125.1, 122.2, 121.8, 115.0, 108.1, 37.1, 35.0, 29.9; UV–vis (H_2O) 225 (4.60), 266 (4.23), 395 (3.74); vis (MeOH) 389 (3.61); ($CHCl_3$) 389 (3.48).

Anal. Calcd for $C_{30}H_{38}N_3Cl_3 \cdot 2.5H_2O$: C, 60.86; H, 7.27; N, 7.10; Cl, 18.01. Found: C, 60.70; H, 6.93; N, 7.04; Cl, 18.14.

1,2-Bis(4-propylpyridinium-1-yl)-3-chloro-7-propylindolizine dichloride (20): ^1H NMR (D_2O) δ 8.77 (2, dd, J = 6.7, 2.3), 8.69 (2, dd), 8.21 (1, d, J = 7.8), 7.94 (4, dd), 7.23 (1, br s), 7.01 (1, dd, J = 1.8); ^1H NMR ($CDCl_3$) δ 10.27 (4, m), 8.08 (1, d), 7.92 (4, d), 6.95 (1, d), 6.90 (1, s), 2.90 (4, t), 2.61 (2, t), 1.76 (6, m), 1.04 (9, m); ^{13}C NMR ($CDCl_3$) δ 194.5, 194.0, 166.0, 165.1, 148.5, 141.0, 128.1, 127.2, 122.4, 121.9, 117.3, 111.9, 98.5, 38.0, 37.2, 37.0, 23.2, 22.3, 13.8.

1,2-Bis(pyridinium-1-yl)-3-chloroindolizine Diiodide. A solution of **4** (0.50 g, 1.3 mmol) in water was added to LiI (0.84 g, 6.3 mmol) in water resulting in a color change from yellow to orange. Extraction with $CHCl_3$ and removal of the solvent under vacuum gave a crystalline solid, mp 281–283 °C dec: ^1H NMR ($CDCl_3$) superimposable with that of **4**.

Anal. Calcd for $C_{18}H_{14}N_3ClI_2 \cdot H_2O$: C, 37.30; H, 2.78; N, 7.25. Found: C, 37.29; H, 2.57; N, 7.26.

1,2-Bis(4-*tert*-butylpyridinium-1-yl)-3-chloro-7-*tert*-butylindolizine Diiodide. To a stirred solution of 0.927 g (1.57 mmol) of the corresponding chloride **5** in 60 mL of water was added 2.6 g of potassium iodide (15.9 mmol) in 30 mL of water. A bright yellow precipitate formed immediately. The product was extracted from solution with methylene chloride. The organic layer was dried over magnesium sulfate and evaporated to dryness on a rotary evaporator to give 1.060 g (1.38 mmol, 86.8%) of the bright yellow solid (mp >300 °C); ^1H NMR ($CDCl_3$) δ 1.38 (s, 9), 1.54 (s, 18), 7.09 (s, 1), 7.19 (d, 1), 7.24 (d, 1), 8.20 (m, 4), 10.20 (m, 4).

Anal. Calcd for $C_{30}H_{38}N_3ClI_2 \cdot H_2O$: C, 47.04; H, 5.49; N, 5.49; I, 33.16. Found: C, 46.93; H, 5.28; N, 5.47; I, 33.30.

1,2-Bis(4-*tert*-butyl-4-cyanodihydropyridin-1-yl)-3-chloro-7-*tert*-butylindolizine (19). To a stirred solution of 0.791 g of **5** (1.34 mmol) in 50 mL of methanol was added 0.30 g of sodium cyanide (6.1 mmol) in 10 mL of methanol. The solution immediately turned from yellow to orange. After 1 h, a white precipitate formed and was filtered and washed with additional methanol. The solid was crystallized twice from anhydrous ether to give 0.312 g (0.59 mmol, 43.5%) of the product, mp 170–172 °C; IR ($CHCl_3$) 2900, 1680, 1605, 1520, 1480, 1370, 1320, 1025, 925; UV–vis (CH_3CN) 263 (4.42), 348 (3.66); ^1H NMR ($CDCl_3$) δ 1.07 (s, 9), 1.10 (s, 9), 1.30 (s, 9), 4.67 (d, 2, J = 8.1), 4.70 (d, 2, J = 7.7), 6.11 (d, 2, J = 7.9), 6.21 (d, 2, J = 8.1), 6.76 (dd, 1, J = 7.4, 1.6), 7.09 (d, 1, J 0.5), 7.82 (d, 1, J = 7.6); mass spectrum (chemical ionization) 500 (0.21), 475 (0.75), 465 (0.28).

Anal. Calcd for $C_{32}H_{38}N_5Cl$: C, 72.80; H, 7.20; N, 13.27; Cl, 6.73. Found: C, 72.98; H, 7.20; N, 13.28; Cl, 6.77.

1,2-Bis(piperidin-1-yl)-5,6,7,8-tetrahydroindolizine (17) and 3,4-Bis(piperidin-1-yl)dihydroindolizine (18). A mixture of **4** (0.500 g, 1.26 mmol) and 50 mg of PtO_2 in 20 mL of ethanol was placed under H_2 (48 psi) and shaken at room temperature for 36 h. The resulting light-yellow solution was filtered and the solvent was removed to yield 380 mg of a yellow oil containing many compounds by TLC. Column chromatography (silica gel; 95% $CHCl_3$, 5% CH_3OH) yielded 132 mg of the product mixture in a ratio of fully saturated to partially reduced compound of 0.39 (by NMR and mass spectroscopy): ^1H NMR ($CDCl_3$) δ 6.97 (s), 3.35–3.95 (br m), 3.15 (br m), 1.4–2.2 (br m); ^{13}C NMR ($CDCl_3$) δ 110.4, 106.0, 56.2, 53.2, 52.3, 51.4, 47.5, 45.6, 44.3, 37.1, 26.7, 26.0, 24.3, 23.6, 22.3; LRMS, m/e (relative intensity) 291 (2.9), 288 (7.7), 287 (37.4), 204 (12.1), 193 (22.5), 124 (18.2), 97 (base), 84 (61.2), 69 (33.4).

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Supplementary Material Available: Crystallographic data, bond lengths and angles, and thermal parameters for **3** (24 pages). Ordering information is given on any current masthead page. Structure factor tables are available from the authors.

Ozonolysis of Enol Ethers. Formation of 3-Alkoxy-1,2-dioxolanes by Concerted Addition of a Carbonyl Oxide to an Enol Ether

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The ozonolyses of methyl vinyl ether, ethyl vinyl ether, and ethyl isopropenyl ether were studied in a variety of solvents. Alkoxy-1,2,4-trioxolanes and alkoxy-1,2-dioxolanes were the main products in pentane and ester solvents. These products arose from the carbonyl oxide (H_2COO) produced upon ozonolysis undergoing 1,3-cycloaddition reactions with esters and activated olefins (enol ethers). From additional trapping experiments, the following relative dipolarophilicities toward the carbonyl oxide were inferred: aldehydes > enol ethers > esters ≃ ketones. Ozonolysis of stereolabeled ethyl vinyl-2-d_1 ether gave ethoxy-1,2-dioxolane with retention of the alkene configuration at the –CHDCH(OEt)– linkage. This is the first example where stereospecificity, implying concertedness, has been directly observed for a reaction of a carbonyl oxide with a substrate. These results are consistent with the Criegee mechanism and extend it to the ozonolysis of enol ethers.

In previous papers, we reported the synthesis of 3-methoxy-1,2,4-trioxolane (**3a**) from the ozonolysis of styrene in methyl formate[1] or the ozonolysis of methyl vinyl ether (**1a**).[2] The latter reaction also produced unexpectedly high yields of 3-methoxy-1,2-dioxolane (**2a**). It was postulated that the synthesis of alkoxy-1,2,4-trioxolanes **3** and alkoxy-1,2-dioxolanes **2** could be rationalized by cycloaddition reactions of the carbonyl oxide (H_2COO) which is produced upon breakdown of a primary ozonide (Scheme I). This would extend the Criegee ozonolysis mechanism[3] to include cycloaddition of a car-

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