Isobutane was used as the chemical ionization (protonating) agent unless otherwise noted. All compounds were obtained commercially and were used without further purification.

Typical operating conditions for the MIKES instrument include a source pressure of 200 mtorr, an ion kinetic energy (collision energy) of 7000 eV, and a source temperature of 420 K. Air was used as the collision gas at a pressure of 2×10^{-5} torr which corresponds to single collision conditions. (Some of the high-energy experiments were repeated on a similar instrument [VG-Analytical Ltd ZAB-2F] and the results were in agreement with the MIKES results.)

Typical operating conditions for the Finnigan triple quadrupole instrument include a source pressure of 450 mtorr, a collision energy of 10eV, and a source temperature of 420 K. Argon was used as the collision target at a pressure of 0.2 mtorr which corresponds to single collision conditions. A series of experiments was performed on selected compounds in which the operating conditions for the triple quadrupole were varied over the ranges shown below; these changes did not cause the domiant reaction pathway to become a minor pathway (or vice versa) in any case.

collision energy	5–25 eV
collision pressure	0.2–2.0 mtorr
source temperature	360–440 K
source pressure	200–900 mtorr

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Appendix

Estimates of ΔH values were made through use of eq 1 where $[M + H]^+$ represents the protonated molecule, $-PA_M$ = negative of the proton affinity (PA) of species M, $\Delta H_f(M)$ represents the heat of formation of neutral M (calculated by using the method of group additivity, ref 22), and $\Delta H_f([H]^+) = 1530$ kJ/mol.[28]

$$\Delta H_f([M + H]^+) = -PA_M + \Delta H_f(M) + \Delta H_f[(H]^+) \quad (1)$$

Calculations for open chain, protonated forms were completed by using monofunctional proton affinity values without correction for substituent effects of the second functional group (for a precedent, see ref 21). Monofunctional PA values for the linear and cyclic amines, the alcohols, the acids, and the cyclic ethers were available from ref 29 with the exception of the PA of 5-aminopentanol which was estimated from ref 30. The PA's of the lactones and lactams of Figure 3 were not available and had to be estimated. The PA's of the lactones were estimated based on PA values for linear esters[29] in conjunction with the PA's of appropriate cyclic ketones and ethers,[29] and the PA's of the lactams were estimated by using PA values of amides[29] in conjuction with values for *N*-methyl lactams.[31] PA values for the amino alcohols (cyclic, protonated form) were available from ref 20. PA values for the chelated amino acids were not available and no attempt was made to estimate these values.

Registry No. 1, 13325-10-5; $HO(CH_2)_2NH_2$, 141-43-5; $HO(CH_2)_3NH_2$, 156-87-6; $HO(CH_2)_5NH_2$, 2508-29-4; $H_2N(CH_2)_2CO_2H$, 107-95-9; $H_2N(CH_2)_3CO_2H$, 56-12-2; $H_2N(CH_2)_4CO_2H$, 660-88-8; $H_2NCH_2CO_2H$, 56-40-6.

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Scope, Limitations, and Mechanism of the Homoconjugate Electrophilic Addition of Hydrogen Halides

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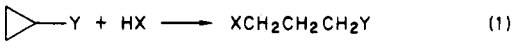
Hydrogen halides (HCl, HBr, HI) add by a homoconjugate 1,5 mechanism to cyclopropanes carrying certain electron-withdrawing substituents. When the substituent is $COCH_3$, COC_6H_5, CO_2H, or CN, the reaction gives the 1,3-disubstituted propane in high yield. Addition of DCl gives a product with deuterium only in the position α to the substituent. The order of rates is not in agreement with a mechanism whereby the cyclopropane ring is protonated initially, since the rate of such a process should be slowed by electron-withdrawing groups. The ketones, however, react much more rapidly than benzylcyclopropane, a model for the direct protonation mechanism. The homoconjugate mechanism involves rapid protonation of the side chain, followed by nucleophilic attack on the cyclopropane ring. The reaction is limited to substrates that can be protonated on the side chain to produce an intermediate with charge ajacent to the cyclopropane ring. This charge must be able to be transmitted by resonance to the unsubstituted ring positions in order to facilitate the nucleophilic step.

The addition of the elements of hydrogen halide (HX, X = Cl, Br, I) to cyclopropane bearing an electron-withdrawing group Y has been known for a century[2] (eq 1).



(1)

Because the mechanistic effects of the group Y have not been fully explored, we have carried out and report herein a survey of this reaction. Two general mechanisms have received support in the literature.[3] Initial protonation of

(1) This work was supported by the National Science Foundation (Grant CHE83-12285).

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the cyclopropane ring would form an edge-protonated, corner-protonated, or open cation. Nucleophilic attack would then give the product. Alternatively, initial protonation could take place on the substituent Y, followed by nucleophilic attack on the ring and tautomerization to the product. If Y has a carbonyl, nitrile, or imine group attached directly to the ring, the elements of HX would add in a 1,5 fashion by this mechanism, and the addition may be termed homoconjugate, by analogy with 1,4 conjugate addition to α,β-unsaturated ketones.

In cyclopropane and its alkylated derivatives, there is ample evidence that the ring is protonated initially, since there is no sufficiently basic site on the side chain.[4] For carboxyl-substituted cyclopropanes, other authors have favored the homoconjugate addition mechanism.[3d] Deno et al.[3c] offered three criteria for proving initial ring protonation: (1) hydrogen–deuterium exchange, whcih leads to multiple introduction or removal of deuterium; (2) scrambling of deuterium or carbon label in the 1-propyl products; (3) formation of 1,1 and 1,2 as well as 1,3 addition products. In this paper we examine a wide range of substituents (Y = $COCH_3$, COC_6H_5, CO_2H, CN, SCH_3, $SOCH_3$, SO_2CH_3, $CONH_2$, CHO, CO_2Et, NO_2, CH_2OH, and $CH_2C_6H_5$). We first establish the scope and limitations of the reaction by determining which of these substrates give clean addition of HX to the cyclopropane ring. Then, by use of Deno's criteria and other mechanistic tools, we attempt to establish the mechanism for those substrates that give addition.

Results

Addition of hydrogen chloride was carried out with heating in water, methanol, or 2-propanol and without solvent. Addition of hydrogen bromide was carried out under aqueous and neat conditions. Hydrogen iodide was added only under aqueous conditions.

Cyclopropanecarboxylic Acid. Anhydrous addition of HCl or HBr afforded a high yield of only one product, the 4-halobutyric acid. Under aqueous conditions γ-butyrolactone also was formed. Under the aqueous conditions, 4-chlorobutyric acid is converted smoothly to the lactone, so the primary product presumably was the open-chain acid of eq 1. Furthermore, a vinylcyclopropane-like rearrangement directly from protonated substrate to lactone[3b] is eliminated, since the lactone does not go to the 4-halobutyric acid. It was not possible to add the elements of water directly to form the hydroxy acid. Qualitatively, HI added fastest and HCl most slowly.

Addition of DCl in D_2O to the substrate in which CO_2H had been previously converted to CO_2D gave 4-chlorobutyric acid with deuterium fully and exclusively at the α-position, i.e., $ClCH_2CH_2CD_2CO_2D$.[5]

Cyclopropyl Methyl Ketone and Cyclopropyl Phenyl Ketone. Addition of HX occurred smoothly under neat, aqueous, and methanolic conditions at temperatures much lower than for the acid, to give only a single product, 5-halo-2-pentanone or 4-halobutyrophenone, respectively. Again the elements of water (aqueous conditions with a catalytic amount of HCl) failed to add, in contrast to the case for α,β-unsaturated ketones. In D_2O, DCl added to cyclopropyl methyl ketone to give 5-chloro-2-pentanone with deuteration at only the α-positions.[5] Similar results were obtained with cyclopropyl phenyl ketone. The starting ketones were heated alone under reaction conditions without undergoing ring opening, so that thermal ring opening followed by HX addition has not occurred. Addition of HCl to the phenyl ketone was attempted in benzene, in which HCl is poorly ionized. After 48 h at room temperature only a small amount of product had formed.

Cyclopropanecarbonitrile. Additions to this substrate have not previously been reported. Addition of HCl or HBr occurred without solvent to give a high yield of the 4-halobutyronitrile. Under aqueous conditions hydrolysis of the nitrile group competed with addition.

Cyclopropyl Phenyl Sulfoxide and Cyclopropyl Phenyl Sulfone. Both these substrates failed to react under all reaction conditions. Starting materials were recovered even after heating for 24 h at 120 °C. The sulfoxide apparently was protonated, since an exothermic reaction clearly occurred upon addition, but ring opening did not follow.

Benzylcyclopropane. Addition occurred smoothly to give 1-phenyl-2-halobutanes. Addition of DCl in D_2O gave the product deuterated in the 4-position ($C_6H_5CH_2CHClCH_2CH_2D$), without scrambling.[5]

Other Substrates. All other substrates followed alternative reaction pathways. Methyl cyclopropanecarboxylate gave ester hydrolysis under most conditions. Cyclopropanecarboxaldehyde yielded only polymers on exposure to HCl and HBr. Cyclopropanecarboxamide gave inorganic ammonium salts. Nitrocyclopropane gave polymeric materials even at room temperature. Cyclopropyl phenyl sulfide gave thiophenol, analogous to ether cleavage. Cyclopropylcarbinol gave 4-halo-1-butene by a cyclopropylcarbinyl/allylcarbinyl rearrangement.

Kinetics. Although the kinetics of conjugate addition to α,β-unsaturated ketones and analogous species have been under study for some time,[6] only a few attempts have been made to study the kinetics for the analogous cyclopropyl compounds.[7]

Kinetics were determined titrimetrically by following the loss of HX as the reaction proceeded. The ketones were studied most extensively. The carboxylic acid, the nitrile, and the hydrocarbon were only examined for relative rates. Initially, we assumed that the reaction of HCl with the methyl ketone was first order in ketone and second order in HCl, by analogy with various alkenes.[5] A plot of $[HCl]^{-2}$ vs. $(t - t_0)$ should then give a linear plot with slope of $2k$. From rates calculated in this fashion for HCl addition at 40, 50, and 60 °C (all correlation coefficients were at least 0.99), activation parameters at 25 °C were measured to be E_a = 17.4 kcal/mol, $\Delta H^{\ddagger}$ = 16.9 kcal/mol, $\Delta S^{\ddagger}$ = −28 eu, and $\Delta G^{\ddagger}$ = 25.1 kcal/mol. These results are in fair agreement with those by Bus et al. for 1,1-cyclopropanedicarboxylic acid.[6] Similar results were obtained at 40 °C for HBr addition, with a rate faster by about 55. Analogous kinetics for the phenyl ketone at 50, 60, and 69 °C gave activation parameters at 25 °C of E_a = 23.9 kcal/mol, $\Delta H^{\ddagger}$ = 23.4 kcal/mol, $\Delta S^{\ddagger}$ = −10 eu, and $\Delta G^{\ddagger}$ = 26.3 kcal/mol. The runs with HBr at 50 °C again were faster by a factor of 48.

Plots were also reasonably linear for overall second-order reactions, so concentration studies were carried out to

(3) For leading references, see (a) Lee, C. C. *Prog. Phys. Org. Chem.* **1970**, *7*, 140–145. (b) Pittman, C. U., Jr.; McManus, S. P. *J. Am. Chem. Soc.* **1969**, *91*, 5915–5918. (c) Deno, N. C.; Billups, W. E.; LaVietes, D.; Scholl, P. C.; Schneider, S. *Ibid.* **1970**, *92*, 3700–3703. (d) Cristol, S. J.; Harrington, J. K.; Morrill, T. C.; Greenwald, B. E. *J. Org. Chem.* **1971**, *36*, 2773–2776.

(4) See references in Lambert, J. B.; Schulz, W. J., Jr.; Mueller, P. H.; Kobayashi, K. *J. Am. Chem. Soc.* **1984**, *106*, 792–793.

(5) Product structures and ^1H NMR chemical shifts are reported in detail in Napoli, J. J. Ph.D. Dissertation, Northwestern University, Evanston, IL, 1972; p 79.

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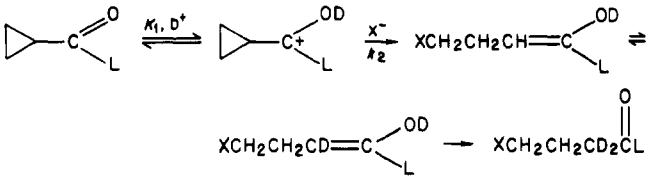
Table I. Temperatures for Half Reaction of HCl with Monosubstituted Cyclopropanes[a]

substituent	σ_m[b]	temp, °C
$COCH_3$	0.38	26
COC_6H_5		64
$CH_2C_6H_5$	−0.07[c]	120
CO_2H	0.37	135
C≡N	0.56	145[d]
$SOCH_3$	0.52	>150
SO_2CH_3	0.60	>150

[a] Reaction for one half-life between equivalent amounts of 12 M aqueous HCl and the substrate, heated in a sealed tube for 5 h. [b] Swain, C. G.; Lupton, E. C., Jr. *J. Am. Chem. Soc.* **1968**, *90*, 4328. [c] The value is actually for CH_2CH_3. [d] Adjusted from a value of 135 °C observed under anhydrous conditions.

Scheme I



clarify the order of the reaction. It was found that the reaction with HCl in methanol is first order in substrate for both the methyl and the phenyl ketones. The order in HCl, however, is nonintegral and possibly fractional. This result indicates multiple kinetic roles for HCl, as has been commonly found in electrophilic additions to alkenes.[6]

Relative rates were obtained by NMR integration for several systems by determining the temperature required for loss of half of the starting material in 5 h (Table I). All values are for aqueous reaction, except the nitrile. The listed temperature for the nitrile (145 °C) is 10 °C higher than the measured temperature under neat conditions, to allow for the expected solvent effect.

Discussion

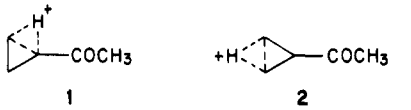
For those substrates that undergo HX addition, all evidence points toward the homoconjugate (1,5) mechanism (Scheme I) rather than direct protonation of the cyclopropane ring. This conclusion follows from a number of lines of argument.

If direct protonation of the ring were rate determining, the reaction rate would decrease as the substituent becomes more electron withdrawing. The data in Table I do not follow this trend. The ketonic substituents actually accelerate the reaction, in comparison with the hydrocarbon. This order is not possible for direct protonation of all three substrates.

Deuterium scrambling was not observed, and neither 1,1 nor 1,2 addition products of DX were formed. Thus two of Deno's criteria for protonated cyclopropanes are not met. The introduction of more than one deuterium atom occurred only at positions next to carbonyl groups or their equivalent and may be explained as the result of enolic-type equilibration.

Each compound with an electron-withdrawing group (Y = $COCH_3$, COC_6H_5, CO_2H, CN) gave ring opening with nucleophilic attack at the less substituted carbon. The hydrocarbon (Y = $CH_2C_6H_5$) gave ring opening with nucleophilic attack at the more substituted carbon (standard Markownikoff addition).

If direct protonation occurred, ions **1** and **2** could be formed from edge attack. It might be argued that the protonated cyclopropanes do not equilibrate, in order to explain the deuterium labeling results. The observed

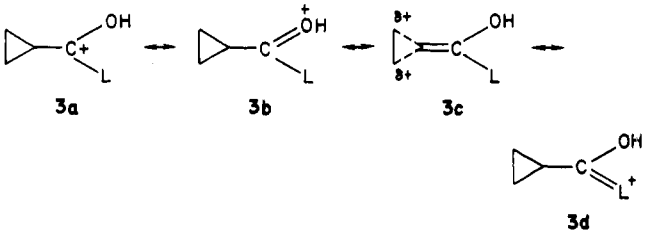


1 **2**

product, however, must then derive from the less stable cation **1** rather than from the more stable cation **2**, in whch the charge is further from the electron-withdrawing group. If protonation occurred to give **2** first, followed by equilibration to the product-forming cation **1**, deuterium scrambling should have occurred, contrary to observation. Lee[3a] did not include the homoconjugate mechanism in his discussion, but only considered the less stable cation **1** and the analogous open-chain cation. Our results exclude both these pathways.

If the reaction proceeds by protonation of the side chain followed by rate-determining nucleophilic attack on the ring, the observed rate constants should be K_1k_2; K_1 is the equilibrium constant for initial protonation, and k_2 is the rate constant for nucleophilic attack by halide ion (Scheme I). The overall rate therefore will be sensitive to structural effects on both K_1 and k_2. The relative rates in part parallel side-chain basicity, which would influence K_1. Thus the nitrile is much slower than the carbonyl compounds.

The order of substrates is also sensitive to k_2. The rate of nucleophilic attack will be enhanced by delocalization of charge from the α-carbon into the three-membered ring, as represented by **3c**. Any factor that reduces this do-



3a **3b** **3c**

3d

nation would also reduce k_2. Thus when L is phenyl rather than methyl (see Scheme I; Y = $COCH_3$ or COC_6H_5 in eq 1), delocalization of positive charge into the phenyl ring (δ^+ is now on L too, **3d**) reduces delocalization into the cyclopropyl ring. Consequently, nucleophilic attack occurs more slowly and the overlall rate is reduced (Table I). The hydroxyl substituent in the acid (L = OH in Scheme I; Y = CO_2H in eq 1) is even more effective at withdrawing positive charge (**3d**, L = OH), so that the rate of electrophilic addition to cyclopropanecarboxylic acid is much slower than those of the ketones. Direct observation of the protonated forms of the carboxylic acid and the two ketones confirms the location of initial protonation, and chemical shift analysis confirms our interpretation of the relative abilities of charge delocalization into the cyclopropane ring ($COCH_3 > COC_6H_5 > CO_2H$).[8]

The pair of sulfur compounds (Y = $SOCH_3$, SO_2CH_3) provides an interesting contrast. Cyano and sulfonyl have about the same electron-withdrawing abilities (see σ constants in Table I), but only the nitrile substrate goes to product. The sulfone is recovered unreacted. Direct protonation of the cyclopropane rings should have occurred at about the same rate for Y = CN and SO_2CH_3. The nitrile functionality, however, is protonated (favorable K_1), whereas the sulfone is not. Thus the low reactivity of the sulfone is the result of a low value of K_1 (little side chain protonation) combined with a low value of k_2 (no charge delocalization since there is no protonation). The sulfoxide

(8) Pittman, C. U., Jr.; Olah, G. A. *J. Am. Chem. Soc.* **1965**, *87*, 5123–5132.

on the other hand seems to be protonated, as judged by the observation of an exothermic reaction when the substrate dissolved. Positive charge on sulfur is not readily transmitted to carbon orbitals; i.e., **3c** is not an important resonance contributor in this case. As a result, nucleophilic attack is slow (low k_2).

Benzylcyclopropane probably reacts by direct protonation of the cyclopropane ring, followed by isomerization to the open nonbenzylic carbocations, $CH_3CH_2C^+HCH_2C_6H_5$, without deuterium scrambling.[4] The absence of scrambling is explained by the higher stability of an open secondary carbocation than of edge- or corner-protonated cations. The structure of the product indicates that hydride shift does not take place to form the benzylic cation. Alternatively, the protonated cyclopropane may react with nucleophile faster than hydrogen shifts occur. The failure of Deno's criteria for the hydrocarbon may be caused by differences in media. The conclusion that the homoconjugate mechanism is preferred for the substrates with $COCH_3$, COC_6H_5, CO_2H, and CN is based primarily on the relative rates. The absence of deuterium scrambling and of rearranged products may not be reliable criteria in the present media.

The acid sensitive side chains (Y = SC_6H_5, CH_2OH, NO_2, CO_2Et, CHO, $CONH_2$) gave rise to alternative mechanisms that are not of interest in this study.

Summary and Conclusions

Addition of HX (eq 1, X = Cl, Br, I) to cyclopropane rings bearing electron-withdrawing groups takes place primarily by a 1,5 homoconjugate mechanism. For Y = $COCH_3$, COC_6H_5, CO_2H, and CN, the only product is the adduct $XCH_2CH_2CH_2Y$ in high yield, although under aqueous condition the carboxylic acid gives some lactone and the nitrile hydrolyzes. The ketones react more rapidly than the hydrocarbon model, Y = $CH_2C_6H_5$. This order of reactivity and the lack of deuterium scrambling among the methylene groups is not in agreement with a mechanism involving direct protonation of the cyclopropane ring. The homoconjugate mechanism involves protonation of the side chain followed by attack of the nucleophile at the unsubstituted cyclopropane carbons. Homoconjugate addition occurs only when the side chain has a basic site for protonation and when the positive charge thus formed on the α atom (**3a**) can be delocalized to the unsubstituted cyclopropane carbons (**3c**). Low basicity of the cyano and sulfone groups explains the low reactivity of the nitrile and the complete absence of reactivity of the sulfone. The phenyl ring in the phenyl ketone and the hydroxy group in the carboxylic acid remove some of the positive charge from the α-carbon, so that less charge may be delocalized into the ring. The progressively lower reactivity for the phenyl ketone and the carboxylic acid results from lower charge in the cyclopropane ring and hence slower nucleophilic attack (k_2). Homoconjugate addition is aided by stronger acids and better nucleophiles, so that HI reacts faster than HBr, which reacts faster than HCl.

It is possible that the direct protonation mechanism may become important in solvents of very high acidity and low nucleophilicity, such as concentrated sulfuric acid. Under these conditions, ring protonation may follow or compete with side chain protonation. Such experiments have already been reported for the reaction of some substrates in 98% H_2SO_4.[3b,c]

Although our results document the importance of charge delocalization from the α carbon into the ring, as represented by **3c**, they have no bearing on the actual structure of **3c** and the nature of charge delocalization. There are a number of viable alternative representations.

Experimental Section

Infrared spectra were recorded on a Beckman IR-5 spectrometer. Proton magnetic resonance spectra were obtained on a Varian Associates T-60 spectrometer. Cyclopropyl phenyl ketone, cyclopropanecarbonitrile, and benzylcyclopropane were purchased from Aldrich Chemical Co.

Cyclopropanecarboxylic Acid-*O*-*d*. A mixture of 5 g (0.058 mol) of cyclopropanecarboxylic acid (Aldrich), 20 mL of diethyl ether, and 5 mL of D_2O was stirred for 5 min. The procedure was repeated with two fresh portions of D_2O, and the combined aqueous layers were extracted three times with 10-mL portions of ether. The combined organic portions were dried ($MgSO_4$), and the ether was evaporated to give the deuterated acid: NMR (neat) δ 1.37 (m, 1, α-proton), 0.80 (m, 4, ring protons).

Cyclopropyl-*1*-*d* Methyl-d_3 Ketone.[9] A mixture of 5 g (0.06 mol) of cyclopropyl methyl ketone (Aldrich), 5.0 mL of D_2O, 0.95 g of NaCl, and 0.10 g of K_2CO_3 was heated to 95 °C and stirred for 24 h. The procedure was repeated with five fresh D_2O solutions. The combined aqueous portions were extracted three times with 20-mL portions of ether, and the combined ether layers were dried ($MgSO_4$). Evaporation of the ether yielded the deuterated ketone: NMR (neat) δ 0.55 (m, 4, ring protons).

Methyl cyclopropanecarboxylate was prepared by treatment of cyclopropanecarboxylic acid with diazomethane in 70% yield: bp 114–117 °C; IR (film) 3030 (w), 2963 (w), 1735 (s), 1458 (m), 1447 (s), 1390 (m), 1183 (s) cm^{-1}; NMR (neat) δ 3.42 (s, 3, OCH_3), 1.35 (m, 1, α-proton), 0.67 (m, 4, ring protons).

Cyclopropanecarboxamide[10] was prepared by treatment of cyclopropanecarbonitrile with 30% hydrogen peroxide: IR (KBr) 3380 (s), 3220 (s), 2813 (w), 1653 (s), 1447 (s), 1303 (m), 827 (s) cm^{-1}; NMR (neat) δ 6.55 (br s, 2, NH_2), 1.23 (m, 1, α-proton), 0.50 (m, 4, ring protons).

Cyclopropylcarbinol[11,12] was prepared by reduction of cyclopropanecarboxylic acid with lithium aluminum hydride in 67% yield: bp 122–124 °C (lit.[11] 122–123 °C); NMR (neat) δ 4.87 (br s, 1, OH), 3.23 (d, 2, methylene), 0.83 (m, 1, methine), 0.28 (m, 4, ring protons).

Cyclopropanecarboxaldehyde[11] was prepared by reduction of cyclopropanecarbonitrile with lithium aluminum hydride at −78 °C in 41% yield: bp 97–102 °C (lit.[11] bp 97–99 °C); IR (film) 3030 (w), 2838 (w), 2760 (w), 1708 (s), 1638 (w), 1438 (w), 1178 (w) cm^{-1}; NMR (neat) δ 8.34 (d, 1, CHO), 1.23 (m, 1, α-proton), 0.58 (d, 4, ring protons).

Nitrocyclopropane was prepared in three steps from 1-bromo-3-chloropropane according to the method of Lampman et al.:[13] bp 53–60 °C (15 mm) (lit.[13] 77–81 °C (58 mm)); NMR (CCl_4) δ 4.12 (m, 1, α proton), 1.32 (m, 4, ring protons).

Cyclopropyl phenyl sulfide was prepared in two steps by the method of Truce et al.:[14] bp 62–63 °C (1.0 mm)); IR (film) 3075 (w), 3020 (w), 1586 (m), 1480 (m), 1286 (m), 1100 (m), 737 (s) cm^{-1}; NMR ($CDCl_3$) δ 7.18 (m, 5, phenyl), 2.03 (m, 1, CHS), 0.76 (m, 4, ring protons).

Cyclopropyl phenyl sulfone was prepared in two steps by the method of Zimmerman and Thyagarajan:[15] NMR ($CDCl_3$) δ 7.57 (m, 5, phenyl), 2.35 (m, 1, α proton), 0.93 (m, 4, ring protons).

Anhydrous Hydrogen Halide Additions. For product studies, a sample of the cyclopropyl compound was placed in a Carius tube, and the tube was cooled in a dry ice/acetone bath. The anhydrous hydrogen halide (HCl or HBr) (Matheson) was bubbled through the cyclopropyl compound (neat or alcoholic solution) until an equimolar amount of the acid was trapped (about 1 M). The Carius tube then was sealed and placed in a preheated oven (see Table I for temperature) for the appropriate amount of time, as determined by NMR analysis of preliminary

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runs, typically 1–2 days. The tube was cooled, the contents were rinsed out with ether, and the resulting solution was dried ($MgSO_4$). Evaporation of the solvent and distillation of the residue then yielded the ring-opened products. The products were identified by NMR spectroscopy.

Aqueous Hydrogen Halide Additions. The cyclopropyl compound and the aqueous hydrogen halide (HCl, HBr, and HI) were placed in a Carius tube. The tube was sealed and placed in a preheated oven (Table I) for the appropriate length of time, then cooled, and opened. The aqueous mixture was neutralized and extracted with ether, and the combined ether portions were dried ($MgSO_4$). Evaporation of the solvent and distillation of the residue yielded the ring-opened products, which were identified by NMR spectroscopy.

Generation of Deuterium Chloride in D_2O. A fourfold excess of D_2O was added to a sample of succinyl chloride, and the mixture was stirred with heating for several hours. The hydrolysis product, succinic acid, was then filtered, and the remaining aqueous solution was used in additions to the cyclopropyl compounds.

Kinetic Studies. Alcoholic HCl or HBr solutions were prepared by bubbling the gaseous acid through anhydrous methanol or 2-propanol. The solutions were standardized by diluting an aliquot (2–5 mL) in 50 mL of H_2O and titrating to a phenolphthalein endpoint with standardized KOH with a Metrohm Dosimat E415 piston burette (Brinkmann Instruments). A series of tubes was prepared that contained known amounts of the cyclopropyl substrate and the required amount of HX. Concentrations varied from 0.0057 to 2.64 M. The tubes were sealed, placed in a constant temperature bath, and removed at appropriate intervals. The tube was immediately immersed in a dry ice/acetone bath and opened, and the reaction was quenched by adding the tube contents to an excess of a KOH solution of known quantity. Back titration with standard aqueous HCl to a phenolphthalein endpoint gave the amount of HCl remaining in the reaction mixtures.

Half-Life Determinations. A sample of the cyclopropyl compound and an equimolar amount of concentrated aqueous HCl (2 N) were placed in a Carius tube. The tube was sealed, placed in a preheated bath for 5 h, and cooled. The contents of the tube were rinsed out with $CHCl_3$ or CCl_4, and the extent of reaction was determined by NMR intensities. The γ-methylene protons were compared with the cyclopropane ring protons, and the temperature was varied until the NMR spectrum gave an intensity ratio of 2:5 for these two sets of protons.

Registry No. HCl, 7647-01-0; HBr, 10035-10-6; HI, 10034-85-2; DCl, 7698-05-7; acetylcyclopropane, 765-43-5; benzoylcyclopropane, 3481-02-5; benzylcyclopropane, 1667-00-1; cyclopropanecarboxylic acid, 1759-53-1; cyclopropanecarbonitrile, 5500-21-0; cyclopropyl methyl sulfoxide, 79306-50-6; cyclopropyl methyl sulfone, 79306-51-7; cyclopropanecarboxylic acid-*O*-*d*, 59472-46-7; cyclopropyl-1-*d* methyl-d_3 ketone, 95249-93-7; methyl cyclopropanecarboxylate, 2868-37-3; cyclopropanecarboxamide, 6228-73-5; cyclopropylcarbinol, 2516-33-8; cyclopropanecarboxaldehyde, 1489-69-6; nitrocyclopropane, 13021-02-8; cyclopropyl phenyl sulfide, 14633-54-6; cyclopropyl phenyl sulfone, 17637-57-9; cyclopropyl phenyl sulfoxide, 50337-59-2; succinyl chloride, 543-20-4.

Notes

Cyanic Acid Esters. 36.[1] 1,2,4-Thiadiazoles from Amino-1,2,3,4-thiatriazoles and Cyano Compounds

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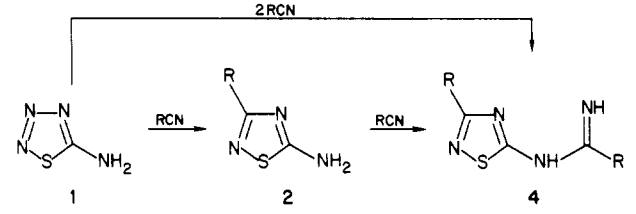
Since 1975 4-alkyl-5-imino-1,2,3,4-thiatriazoles have been subjected to thorough investigation, particularly in cycloaddition and ring-transformation reactions with systems bearing multiple bonds.[2,3] The parent compound, 5-amino-1,2,3,4-thiatriazole,[4,5] has been much less investigated, although known since the turn of the century.[6] This compound and its 5-alkylamino and 5-arylamino derivatives are readily available from thiosemicarbazides and nitrous acid.[6,7]

Dimethyl sulfate methylates 5-(arylamino)thiatriazoles at the amino group,[8] whereas diazomethane methylates these compounds and 5-[(arylsulfonyl)amino]thiatriazoles primarily at the 4 position.[8,9] In the presence of pyridine, 5-aminothiatriazole is converted into 2,5-diaryl-3,4-dioxa(dithia or diarylaza)-3aλ^4-thia-1,6-diazapentalenes by aroyl or thioaroyl chlorides or arylimido chlorides.[10,11] Acetyl chloride does not react similarly but affords 3,5-diacetamido-1,2,4-thiadiazole.[11] With isocyanates 5-(alkyl- and arylamino)thiatriazoles react under elimination of nitrogen to give (3-oxo-Δ^4-1,2,4-thiadiazolin-5-yl)ureas.[12] We here report on the reaction of 5-aminothiatriazole and

Table I



1 2 4

	R	yield, %	mp, °C	crystallizn solvent
2a	C_6H_5O	60	138–140[a]	C_6H_6
2b	2-ClC_6H_4O	39	166–167	C_6H_5Cl
2c	3-$CH_3C_6H_4O$	65	144–145	C_6H_6
2e	4-$CH_3OC_6H_4O$	54	178–180	C_6H_6/MeOH
2f	Cl_3C	92	193–194	C_6H_5Cl
4a	C_6H_5O	35	229–230	dioxane/H_2O
4d	4-$CH_3C_6H_4O$	48	255–256	DMF/H_2O
4e	4-$CH_3OC_6H_4O$	42	247–248	DMF/H_2O

[a] Reference 16.

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