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Studies of Nitriles. VII.[1] Synthesis and Properties of 2-Amino-3,3-dichloroacrylonitrile[2] (ADAN)

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2-Amino-3,3-dichloroacrylonitrile (ADAN), a versatile polyfunctional synthetic intermediate, was prepared in 96% yield by addition of HCN to the C–N triple bond of dichloroacetonitrile (**11a**). The structural proof for ADAN, an enamino nitrile, comes from comparison of the spectral data with those of 2-imino-3,3,3-trichloropropionitrile (**15**), a model compound for α-imino nitrile. Similarly, 2-amino-3,3-dibromoacrylonitrile (**13**) was prepared from dibromoacetonitrile (**11b**) and HCN in 82% yield. ADAN, although relatively unstable in air at room temperature, can be stored without detectable change for a long period in nitrogen or ether vapor atmosphere at low temperatures. 2-Amino-3,3-bis(substituted mercapto)acrylonitriles (**18a—c**), mercapto-analogues of ADAN, were prepared from ADAN or its N-acyl derivatives (**16**, **19**) by nucleophilic substitution of the chlorine atoms with mercaptides, and in the latter case, with subsequent hydrolysis of the N-acyl group. Hydrolysis of the cyano group of N-acyl derivatives (**16**, **21**, **22**) gave the corresponding carboxamides (**23**), carboxylic acids (**24**), and N-*t*-butylcarboxamides (**26**) in good yields.

There are several general methods for preparing α-amino acids from aldehydes, but only a few from nitriles.[4] We are interested in the synthesis of α-amino acids from α-imino nitriles (**1**) which can be formed from nitriles by the addition of HCN to the C–N triple bond of the nitrile group. Thus, reduction of the imino group and subsequent hydrolysis of the cyano group may be a general synthetic route to α-amino acids (Eq. 1).

$$\mathrm{R\text{-}C{\equiv}N \xrightarrow{HCN} R\text{-}C(=NH)(CN)} \longrightarrow \mathrm{R\text{-}CH(NH_2)(CN)} \longrightarrow \mathrm{R\text{-}CH(NH_2)(COOH)} \qquad \text{Eq. 1}$$

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α-Imino nitriles (**1**) are known to be formed by addition of HCN to the C–N triple bond of the nitrile group when the cyano group is activated by one or more, usually more than two, strongly electron-withdrawing groups on the α-carbon atom, as in CCl_3CN,[5] CH_3CCl_2CN,[5] some perfluoronitriles,[6] and cyanogen.[7] Similar addition of HCN to the C–N triple bond is assumed to take place in the syntheses of diaminomaleonitrile[8] (DAMN, HCN tetramer) and

1) Part VI: K. Matsumura, T. Saraie, and N. Hashimoto, *Chem. Comm.*, **1972**, 705.
2) A part of this paper was presented at the 24th Annual Meeting of the Chemical Society of Japan, Osaka, April, 1971.
3) Location: *Jusohonmachi, Yodogawa-ku, Osaka, 532, Japan.*
4) *a*) H.E. Baumgarten, J.E. Dirks, J.M. Peterson, and R.L. Zey, *J. Org. Chem.*, **31**, 3708 (1966); *b*) W.H. Graham, *Tetrahedron Letters*, **1969**, 2223; *c*) Y. Wolman and S.L. Miller, *Tetrahedron Letters*, **1972**, 13; *d*) U.E. Diner and M. Worsley, *Tetrahedron Letters*, **1972**, 3145; *e*) Y. Nogami, Y. Kawazoe, and T. Taguchi, *Yakugaku Zasshi*, **93**, 1058 (1973); *f*) K. Ogura and G. Tsuchihashi, *J. Am. Chem. Soc.*, **96**, 1960 (1974).
5) Röhm and Haas, Ger. Patent 1053500 (1959) [*C.A.*, **55**, 9286*d* (1961)].
6) W.J. Middleton and C.G. Krespan, *J. Org. Chem.*, **33**, 3625 (1968).
7) R.W. Begland, A. Cairncross, D.S. Donald, D.R. Harter, W.A. Sheppard, and O.W. Webster, *J. Am. Chem. Soc.*, **93**, 4953 (1971).
8) *a*) H. Bredereck, G. Schmötzer, and E. Oehler, *Ann. Chem.*, **600**, 81 (1956); *b*) D.W. Woodward, U.S. Patent 2499441 (1950) [*C.A.*, **44**, 5898*i* (1950)]; *c*) P.S. Robertson and J. Vaughan, *J. Am. Chem. Soc.*, **80**, 2691 (1958); *d*) J.P. Ferris and L.E. Orgel, *J. Am. Chem. Soc.*, **87**, 4976 (1965); *ibid.*, **88**, 3829 (1966); *e*) J.P. Ferris and R.A. Sanchez, "Organic Syntheses," Vol. 48, ed by P. Yates, John Wiley and Sons, Inc., New York, 1968, p. 60.

adenine[9] (HCN pentamer) by oligomerization of HCN itself, and is considered to be closely related to the prebiotic syntheses of organic molecules and the origin of life.[10]

In spite of all our efforts, we failed in the direct synthesis of the α-imino nitrile from phenylacetonitrile, which may be the key intermediate according to Eq. 1 ($R=C_6H_5$) to phenylalanine, one of the essential amino acids. However, hydrogen cyanide was added smoothly to the C≡N group of α,α-dichlorophenylacetonitrile (**2**), where the C≡N group is activated by two chlorine atoms on the α-carbon to yield a new α-imino nitrile (**3**), which was found to give a new enamino nitrile (**5**) instead of the expected **4**, when subjected to reduction (Chart 1).

Based on this information, 2-amino-3,3-dichloroacrylonitrile (ADAN), a novel enamino nitrile, was prepared from dichloroacetonitrile (**11a**) and HCN in excellent yield.

In this paper, we describe our fundamental study on the reactivity of ADAN and its derivatives.

Results and Discussion

As expected, the addition of HCN to α,α-dichlorophenylacetonitrile (**2**) gave α-imino nitrile (**3**) in high yield under mild conditions. The reduction of **3** with zinc powder in ethanol and water, and chromatographic purification gave an unstable compound, with only one chlorine atom according to the correct mass spectrum, *m/e* 180, 178 (1:3) (M^+, 100%), in 12% yield in place of the expected product **4**. The infrared (IR) spectrum of the product shows absorptions at 3200, 3375, 3475 (NH_2), 2250 (C≡N), and 1620 cm^{-1} (C=C) in contrast to that of the starting material (**3**), at 3260 (=NH), 2250 (C≡N), and 1630 cm^{-1} (C=N). The nuclear magnetic reasonance (NMR) spectrum ($CDCl_3$) of the compound shows bands at δ 4.14 (2H, br, NH_2) and 7.30—7.70 (5H, m, phenyl ring), differing from those of **3** at δ 11.30 and 11.65 (7:2, 1H, br, NH *syn*, *anti*), and 7.30—7.90 (5H, m, phenyl ring).

These spectral data indicate that one of the two chlorine atoms in the starting material is replaced by hydrogen, and the resulting compound exists preferably in its enamino nitrile form (**5**) rather than the imino nitrile form (**6**) (Chart 1).

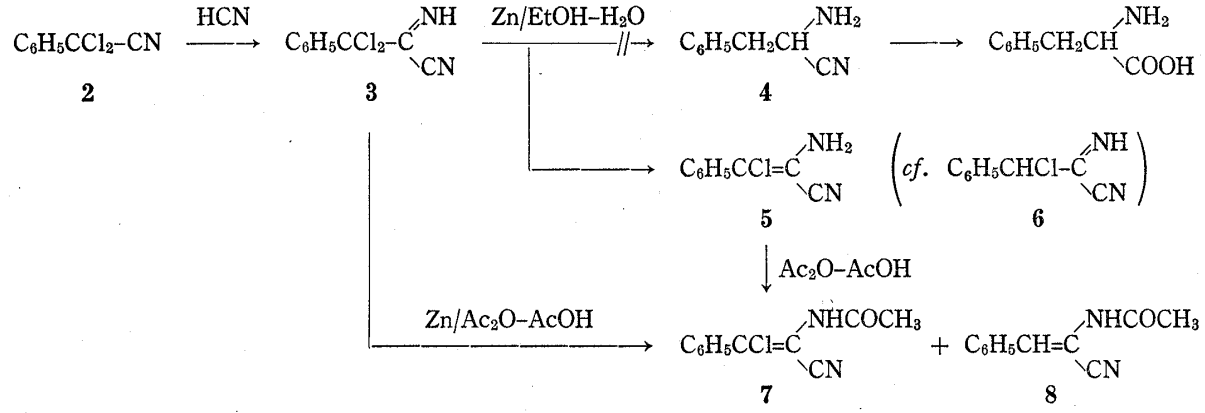


Chart 1

Further, reductive acetylation of α-imino nitrile (**3**) with Zn/Ac_2O–AcOH gave two products. The major one was 2-acetylamino-3-chloro-3-phenylacrylonitrile (**7**, 12% yield from **2**), which agrees with the monoacetylation product of **5**. The minor one was 2-acetylamino-3-phenylacrylonitrile (**8**), a further reduced product of **7** (5% yield from **2**).

9) *a*) J. Oró and A.P. Kimball, *Arch. Biochem. Biophys.*, **94**, 217 (1961); *b*) H. Wakamatsu, Y. Yamada, T. Saito, I. Kumashiro, and T. Takenishi, *J. Org. Chem.*, **31**, 2035 (1966).

10) *a*) J.P. Ferris, D.B. Donner, and W. Lotz, *J. Am. Chem. Soc.*, **94**, 6968 (1972); *b*) For a recent review see R.M. Lemmon, *Chem. Rev.*, **70**, 95 (1970).

These results suggested that the addition of HCN to the C–N triple bond of nitriles having at least one hydrogen atom at the α-position will lead to enamino nitriles (**10**) as a result of isomerization of the initially formed α-imino nitriles. The enamino nitriles are perhaps more suitable and interesting intermediates for the syntheses of amino acids.

Next, the addition of HCN to several halogenated nitriles (**9**) was investigated in the presence of base catalyst in acetonitrile at temperatures between 0° and 50°, but without success, because of the formation of side reaction products or the inactiveness of the starting nitriles (Eq. 2).

$$\underset{\mathbf{9}}{RCHX\text{-}CN} \xrightarrow{HCN} \left[RCHX\text{-}C(=NH)\text{-}CN\right] \longrightarrow \underset{\mathbf{10}}{RXC{=}C(NH_2)CN} \qquad \text{Eq. 2}$$

R=C_6H_5 (X=Cl, Br); R=H, CH_2Cl, $CHCl_2$, CCl_3 (X=Cl); R=H (X=Cl, Br, F)

In cases of dichloroacetonitrile (**11a**) and dibromoacetonitrile (**11b**), however, 1:1 adducts, based on mass spectral and elemental analyses, were isolated in high yields. Thus, the reaction of dichloroacetonitrile (**11a**) and HCN (1.1 molar eq.) in the presence of a catalytic amount of NaCN in acetonitrile at room temperature gave a 1:1 adduct as colorless needles (mp 61°) in 96% yield. Similarly, dibromoacetonitrile (**11b**) reacted with HCN to give a 1:1 adduct (**13**, mp 76—77°) in 82% yield, based on the starting material consumed. When dichloroacetonitrile (**11a**) was treated with excess HCN (3 molar eq.) under similar conditions, a 1:2 adduct (**14**) was also isolated. The reaction of the 1:1 adduct (ADAN) with HCN did not give the 1:2 adduct (**14**) under similar conditions (Chart 2).

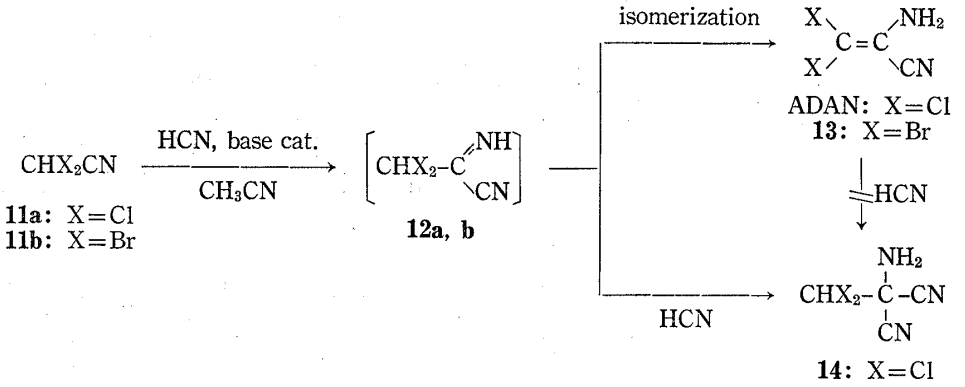


Chart 2

As expected, the structures of 1:1 adducts have been proved to be enamino nitriles (ADAN, **13**) by comparison of their IR, NMR, and ultraviolet (UV) spectra with those[11] of 2-imino-3,3,3-trichloropropionitrile[5] (**15**), prepared from trichloroacetonitrile and HCN by the known method,[5] as **a** model compound of α-imino nitrile (Table I).

That is, the IR spectrum of **15** shows absorptions at 3230 (=NH), 2250 (C≡N) and 1634 cm^{-1} (C=N), in contrast to those of ADAN, and **13**; three bands attributable to the NH_2 group between 3480 and 3170 cm^{-1}, a single sharp peak at around 2250—2235 cm^{-1} (C≡N), and almost a single peak at around 1620—1590 cm^{-1} (C=C) depending upon the difference of recording conditions. The NMR spectrum of **15** shows two peaks at δ 11.30 and 11.84 (2:1, br, *syn* and *anti* imino protons), but those of 1:1 adducts (ADAN, **13**), only one at δ 3.76 (br, NH_2), and 3.86 (br, NH_2), respectively. The UV spectrum of **15** ($CHCl_3$) shows absorption at 260.0 nm (ε=177) due to the n-π^* transition of the imino group, where 1:1 adducts (ADAN, **13**) absorb at almost the same wavelength, 260.5 nm (ε=9300) and 264.5 nm (ε=9660), respectively. But the ε-values are markedly higher than that of **15**, being ascribable to the π-π^* transition of the C=C double bonds.

11) The spectral data were measured in our laboratories.

Table I. Comparison of Spectral Data of Imino Nitrile (**15**) and Enamino Nitriles (ADAN, **13**)

	$CCl_3-C(=NH^{a})-CN$ (**15**)	$Cl_2C=C(NH_2)-CN$ (ADAN)	$Br_2C=C(NH_2)-CN$ (**13**)
mp or bp (°C)	bp 24/0.3 mmHg	mp 61	mp 76—77
IR ν_{max} cm^{-1}	(liq. film)	(Nujol)	(Nujol)
	3230, 2250, 1634[b]	3400, 3320, 3190, 2250, 1610	3450, 3340, 3200, 2250, 1610, 1594sh
		($CHCl_3$)	($CHCl_3$)
		3480, 3380, 3200, 2245, 1616	3470, 3360, 3170, 2235, 1606
		(KBr)	(KBr)
		3435, 3300, 3170, 2240, 1612	3480, 3330, 3170, 2235, 1606, 1590sh
NMR ($CDCl_3$) δ	11.36, 11.84[b] (2: 1, br)	3.67 (br)	3.86 (br)
UV λ_{max} nm (ε)	($CHCl_3$)	($CHCl_3$)	($CHCl_3$)
	260.0 (177)[b]	260.5 (9300)	264.5 (9660)
		(EtOH)	
		265.5 (8950)	
		(*n*-hexane)	
		253.0 (9880)	

a) *cf.* reference 5)
b) *cf.* reference 11)

This assignment was supported by the following observation. When the UV spectrum of ADAN was recorded in *n*-hexane, a more non-polar solvent than chloroform, a hypsochromic shift (λ_{max} 253.0 nm) was observed. In ethanol, a more polar solvent than chloroform, a bathochromic shift (λ_{max} 265.5 nm) resulted.

The formation of 1: 1 adducts (ADAN, **13**) may be rationalized by assuming the addition of HCN to the C–N triple bond of dihalogenoacetonitrile (**11a, b**), followed by proton migration. The formation of 1: 2 adduct (**14**) may also be rationalized by the addition of HCN to initially formed α-imino nitrile (**12a**), based on the fact that the 1: 1 adduct once formed (ADAN), did not react with HCN under similar conditions.

Although even the formation of ADAN and **13** was recognized in the absence of added NaCN or KCN, basic materials such as K_2CO_3, CH_3COONa, KF, triethylamine, N-methylmorpholine, and 2-methylimidazole are generally satisfactory as catalysts for the reaction according to extensive studies of about thirty neutral, acidic, and basic substances. The combination of acetone cyanohydrin and basic materials, such as KCN, NaCN, or K_2CO_3 or metal salts of HCN and acids, may be successfully employed instead of liq. HCN.

Subsequent experiments were carried out using ADAN, because ADAN is superior to **13** from the viewpoint of preparation and purity, *i.e.*, it allows higher yield, greater stability, and accessibility of starting material.

ADAN, although rather unstable, can be easily purified by recrystallization from pet. ether as colorless needles, mp 61°; it is soluble in ether, benzene, chloroform and alcohol, and insoluble in *n*-hexane, pet. ether, and water. Material sufficiently pure for synthetic use is obtained by merely washing the crude reaction product with a mixture of ether and pet. ether.

Although, ADAN begins to decompose in a few days at room temperature in air and changes completely into a deep brown mass in about a week, it can be stored without appreciable change in air at low temperatures around −20° for a few months. For longer storage, it should be kept in a nitrogen or ether vapor atmosphere, or in an ether solvent at low temperatures (around −20°).

As an alternative route to ADAN, we tried reducing 2-imino-3,3,3-trichloropropionitrile (**15**) with zinc without success, but reductive acetylation of the same material gave N-mono-

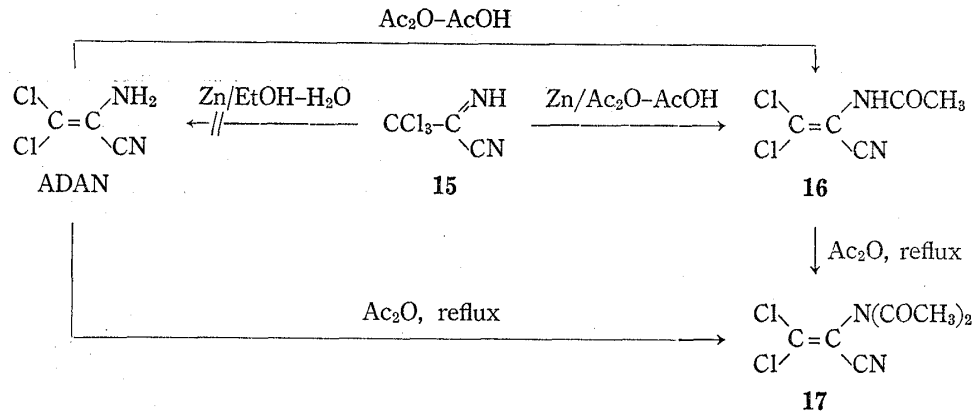


Chart 3

acetyl derivative[12] (**16**, 58% yield), also derived from ADAN by mild acetylation with acetic anhydride and acetic acid at room temperature in 98% yield (Chart 3).

N,N-Diacetyl derivative (**17**) of ADAN was prepared in almost quantitative yield by the reaction of ADAN or N-monoacetyl derivative (**16**) with acetic anhydride at reflux temperature. After isolation using silica gel chromatography, however, the yield of **17** was reduced to around 70%. The sensitivity of **17** toward moisture gave rise to an appreciable amount of **16** during the purification step.

The reactions of ADAN with some nucleophilic reagents were investigated and the results are summarized in Chart 4.

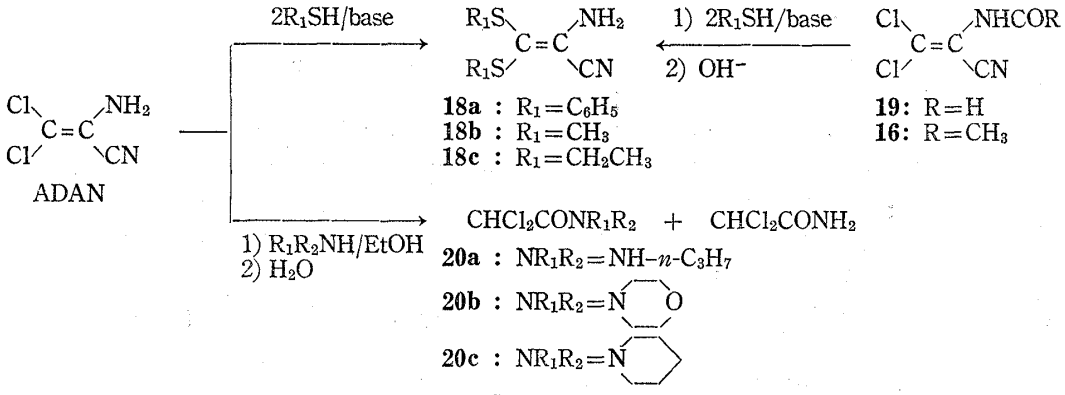


Chart 4

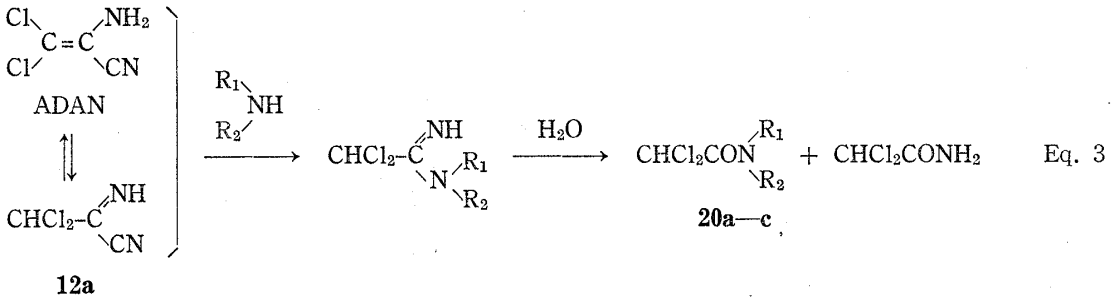
2-Amino-3,3-bisphenylthioacrylonitrile (**18a**), a new enamine, was obtained in 82% yield by the reaction of ADAN with 2 molar eq. of thiophenol in the presence of base at room temperature. Compound **18a** was also obtained from **16** by nucleophilic substitution of the chlorine atoms with $C_6H_5S^-$, followed by hydrolysis of the N-acyl group. Compound **18a** is much more stable than ADAN, and no detectable decomposition was observed upon storage for a long period even in air at room temperature.

On the other hand, the reaction of ADAN with aliphatic mercaptans in the presence of base did not proceed with ease as with aromatic mercaptans, and the expected mercapto-substituted products (**18b, c**) were obtained only in low yield, together with a complex mixture of unidentified by-products. In these cases, acylation of the amino group of ADAN was found to be a necessary detour in order to obtain the compounds (**18b, c**) in good yields. For example, the N-formyl derivative (**19**), prepared in 98% yield by treating ADAN with acetic-formic anhydride at room temperature and hydrolyzed more easily than N-acetyl derivative

12) *a*) V.V. Dovlatyan and É.N. Ambartsumyan, *Arm. Khim. Zh.*, **22**, 137 (1969); *b*) B.S. Drach and É.P. Sviridov, *Zh. Obsch. Khim.*, **44**, 348 (1974) [*J. Gen. Chem. USSR*, **44**, 330 (1974)].

(**16**), was allowed to react with excess mercaptan in the presence of base in water at room temperature to give 2-amino-3,3-bis-(substituted mercapto)acrylonitrile (*e.g.*, **18b**,**c**) in good yield in a substantially one-step procedure. That the compounds (**18a—c**) exist in the enamino nitrile form was proved by IR and NMR spectra.

Without substituting the chlorine atoms of ADAN, primary and secondary amines, which are less reactive nucleophiles than S-nucleophiles, reacted with ADAN in ethanol at room temperature giving N-dichloroacetylamines (**20a—c**) and dichloroacetamide. The formation of these products is rationalized by the attack of N-nucleophiles on the carbon-bearing cyano group giving amidines which are hydrolyzed in the reaction (Eq. 3).



The cyano groups of the three acyl derivatives (**16, 21, 22**) from ADAN and **13** were hydrolyzed to the corresponding amides smoothly and in excellent yields with the aid of conc. sulfuric acid both in the absence or presence of added carbonium ion source, in the latter case leading to N-substituted amides (**26a, b, c**) (Chart 5).

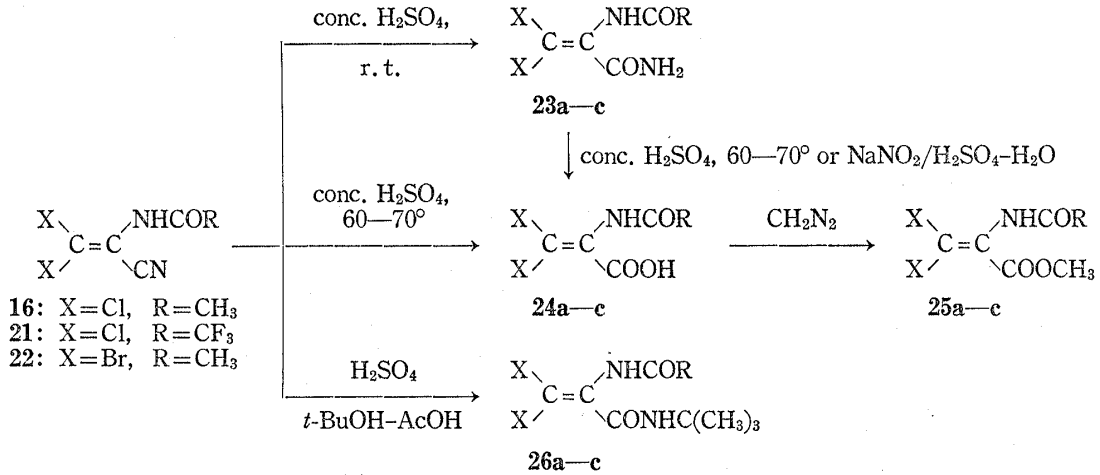


Chart 5

When heated in conc. sulfuric acid, compounds **16**, **21** and **22** were converted into the corresponding carboxylic acid derivatives **24a**, **24b**, and **24c**, respectively. The same compounds were also obtained by treating **23** with $NaNO_2$ in sulfuric acid.[13] The reaction of carboxylic acids **24a, b, c** with 1 eq. of diazomethane yielded the corresponding methyl esters (**25a, b, c**) in almost quantitative yields. The yields, melting points, and recrystallization solvents are shown in Table II.

13) P. Strehlke, *Chem. Ber.*, **106**, 721 (1973).

Table II. Preparation of 2-Acylamino-3,3-dihalogenoacrylonitriles and Their Derivatives

Compd. No.	X	R	Y	Yield (%)	mp (°C)	Recryst.[a] solvent
16	Cl	CH_3	CN	98	128—130[b]	B
21	Cl	CF_3	CN	98	76— 77	B–H
22	Br	CH_3	CN	93	172—173 (decomp.)	B
23a	Cl	CH_3	$CONH_2$	76	201—203 (decomp.)	AC
23b	Cl	CF_3	$CONH_2$	83	128—129 (decomp.)	B–EA
23c	Br	CH_3	$CONH_2$	86	190—192 (decomp.)	A
24a	Cl	CH_3	COOH	76 (from **23a**) 80 (from **16**)	185—189 (decomp.)	B–AC
24b	Cl	CF_3	COOH	77 (from **23b**) 18 (from **21**)	171—173 (decomp.)	B
24c	Br	CH_3	COOH	90 (from **23c**) 90 (from **22**)	160—164 (decomp.)	B–AC
25a	Cl	CH_3	$COOCH_3$	99	100—102	B–H
25b	Cl	CF_3	$COOCH_3$	97	71— 72	H
25c	Br	CH_3	$COOCH_3$	95	98—100	B–H
26a	Cl	CH_3	$CONHC(CH_3)_3$	73	220—222 (decomp.)	A
26b	Cl	CF_3	$CONHC(CH_3)_3$	54	192—194	C
26c	Br	CH_3	$CONHC(CH_3)_3$	68	165—168 (decomp.)	B

a) A=acetonitrile, AC=acetone, B=benzene, C=chloroform, EA=ethyl acetate, H=*n*-hexane
b) lit. mp 133—135° (*cf.*reference 11))

Experimental

Melting points were determined in open capillary tubes and are uncorrected. IR spectra were recorded on a Hitachi EPI-S2 spectrophotometer. NMR spectra were recorded on a Varian A-60 or T-60 spectrometer. Chemical shifts are given in parts per million (δ) down field from tetramethylsilane (TMS) as an internal standard. UV spectra were obtained with a Perkin-Elmer 450 spectrophotometer. Mass spectra were obtained at 70 eV with a Hitachi RMU-6D mass spectrometer. Vapor phase chromatography was performed on a Hitachi KGL-2B instrument. The following abbreviations are used; sh=shoulder, s=singlet, d=doublet, t=triplet, m=multiplet, and br=broad.

Materials——Monobromoacetonitrile, and monofluoroacetonitrile were prepared by the dehydration of the corresponding acid amides with phosphorus pentoxide.[14] α-Chlorophenylacetonitrile,[15] α-bromophenylacetonitrile,[16] 2,3-dichloropropionitrile,[17] and 2,3,3-trichloropropionitrile[17] were prepared according to the literature.

2,3,3,3-Tetrachloropropionitrile was prepared in 88% yield by the reaction of 20 g of 3,3-dichloroacrylonitrile[18] with *ca.* 10 ml of liquid chlorine in a 50-ml steel bomb overnight at room temperature. bp 56—58° (5 mmHg). IR $\nu_{max}^{liq.film}$ cm^{-1}: 2950, 1040, 953, 821, and 752. NMR ($CDCl_3$) δ: 5.18 (s). *Anal.* Calcd. for C_3HNCl_4: C, 18.68; H, 0.52. Found: C, 18.94; H, 0.75.

14) *a*) W. Steinkopf, *Chem. Ber.*, **38**, 2694 (1903); *b*) F.J. Buckle, R. Heap, and B.C. Saunders, *J. Chem. Soc.*, **1949**, 912.
15) A.J. Buckle and F. William Kay, *J. Soc. Chem. Ind.*, **54**, 98T (1935).
16) C.M. Robb and E.M. Schultz, "Organic Syntheses," Coll. Vol. III, ed. by A.H. Blatt, John Wiley and Sons, Inc., New York, 1955, p. 347.
17) H. Brintzinger, K. Pfannstiel, and H. Koddebusch, *Angew. Chem.*, **60**, 311 (1948).
18) *a*) B. Miller and M.V. Kalnins, *Tetrahedron*, **23**, 1145 (1967); *b*) N. Hashimoto, Y. Kawano, and K. Morita, *J. Org. Chem.*, **35**, 828 (1970).

2-Imino-3,3-dichloro-3-phenylpropionitrile (3)——To an ice-cooled mixture of 9.3 g (50 mmoles) of α,α-dichlorophenylacetonitrile[19] (2), 1.8 g (65 mmoles) of HCN and 20 ml of anhydrous CH_3CN in a 100 ml steel bomb, 0.41 g (10 mmoles) of NaCN was added. The vessel was closed, then the mixture was magnetically stirred at room temperature for 10 hr, and at 40° for 3 hr. The volatiles were removed *in vacuo* and the residual oil was chromatographed on silica gel (Merck) with $CHCl_3$ to give 8.2 g (83.2%) of **3** and 0.7 g of the starting material (**2**). A pure colorless product was obtained by a preparative gaschromatographic technique. Vapor phase chromatography (VPC) analysis of the oil showed only one single peak. The column was silicon DC 550 (25%) on 60—80 mesh celite 545. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3260, 3060, 2250, 1630, and 1585. NMR ($CDCl_3$) δ: 7.30—7.90 (5H, m, phenyl ring), and 11.30 and 11.65 (7: 2, 1H, br, =NH). Mass Spectrum *m/e* (rel. intensity): 216, 214, 212 (1: 6: 9, M^+, 3%), 163, 161, 159 (1: 6: 9, M^+–NH=C–CN, 100%). *Anal.* Calcd. for $C_9H_6N_2Cl_2$: C, 50.73; H, 2.84; N, 13.15. Found: C, 50.99; H, 2.93; N, 12.80.

2-Amino-3-chloro-3-phenylacrylonitrile (5)——To a stirred solution of 2.13 g (10 mmoles) of 2-imino-3,3-dichloro-3-phenylpropionitrile (3) in 50 ml of 95% EtOH, 2.0 g of zinc powder (Merck) was added at room temperature and the mixture was stirred for 1 hr, then refluxed for 1 hr. The reaction mixture was filtered to remove insoluble inorganic materials. The filtrate was evaporated under reduced pressure at room temperature to give a residue which was extracted with ether. The extract was dried, the solvent evaporated, and the residual oil was chromatographed on silica gel using $CHCl_3$ as solvent to yield 0.22 g (12%) of unstable solid (**5**), together with phenylacetonitrile and α-chlorophenylacetonitrile. Attempts to purify **5** by recrystallization were unsuccessful. IR ν_{max}^{Nujol} cm^{-1}: 3470, 3370, 3210, 3050, 2250, and 1620, NMR ($CDCl_3$) δ: 4.14 (2H, br, NH_2), and 7.30—7.70 (5H, m, phenyl ring). Mass Spectrum *m/e* (rel. intensity): 180, 178 (1: 3, M^+, 100%), 153, 151 (1: 3, M^+–HCN, 17%), 143 (M^+–Cl, 51%), 142 (M^+–HCl, 25%), 116 (M^+–Cl–HCN, 44%),115 (23%), 91 (39%).

2-Acetylamino-3-chloro-3-phenylacrylonitrile (7)——a) To a stirred solution of 75 g of crude **3**, prepared from 55.8 g (0.3 mole) of **2** and 12 g (0.445 mole) of HCN in the presence of NaCN in 200 ml of CH_3CN, in 100 g of Ac_2O and 40 g of AcOH, 50 g of zinc powder (Merck) was added portionwise at 0° over 30 min. The mixture was stirred overnight at room temperature and filtered, ice water was added to the filtrate, and the product was extracted with 600 ml of $CHCl_3$. Removal of the solvent *in vacuo* left a residue which was chromatographed on 450 g of silica gel with $CHCl_3$–5% acetone to yield 7.6 g (12% yield from **2**) of **7** and 2.6 g (5% yield from **2**) of **8**.

b) A solution of 70 mg of **5** in 1 ml of Ac_2O and 0.2 ml of AcOH was allowed to stand overnight at room temperature. The mixture was treated with ice water, and extracted with 100 ml of $CHCl_3$. The extract was dried and removed *in vacuo* to give a residue which was chromatographed on silica gel to yield 74 mg (86%) of **7**. Compound **7**; mp 161—163° (from benzene), IR ν_{max}^{Nujol} cm^{-1}: 3260, 3200sh, 3060, 2240, 1690sh, 1680, 1670, and 1612. NMR ($CDCl_3$) δ: 2.12 (3H, s), 7.25—7.80 (5H, m), 8.20 (1H, br). Mass Spectrum *m/e* (rel. intensity): 222, 220 (1: 3, M^+, 2%), 185 (M^+–Cl, 48%), 180, 178 (1: 3, M^+–CH_2=C=O, 100%), 143 (M^+–CH_2=C=O–Cl, 15%), 142 (M^+–CH_2=C=O–HCl, 9%), 126, 124 (1: 3, $C_6H_5CCl^+$, 4%), 89 ($C_6H_5C^+$, 14%), 43 (CH_3CO^+, 63%). *Anal.* Calcd. for $C_{11}H_9ON_2Cl$: C, 59.88; H, 4.11; N, 12.70. Found: C, 60.06; H, 4.02; N, 12.74. Compound **8**; mp 131—133° (from $CHCl_3$), IR ν_{max}^{Nujol} cm^{-1}: 3300, 3200sh, 2235, 1690, 1680, 1652sh, 1618, 1597, and 1573. NMR ($CDCl_3$) δ: 2.11 (3H, s), 7.28—7.70 (6H, m), and 8.42 (1H, br). Mass Spectrum *m/e* (rel. intensity): 186 (M^+, 3%), 144 (M^+–CH_2=C=O, 70%), 143 (M^+–CH_3CO, 14%), 117 (C_6H_5CH=C=NH^+, 16%), 90 (11%), 89 ($C_6H_5C^+$, 16%), 77 ($C_6H_5^+$, 4%), 43 (CH_3CO^+, 100%). *Anal.* Calcd. for $C_{11}H_{10}ON_2$: C, 70.95; H, 5.41; N, 15.05. Found: C, 70.67; H, 5.36; N, 14.91.

2-Amino-3,3-dichloroacrylonitrile (ADAN)——a) To a stirred solution of 22 g (0.2 moles) of dichloroacetonitrile[20] (**11a**) and 6.0 g (0.22 mole) of HCN in 100 ml of anhydrous CH_3CN, 0.49 g (10 mmoles) of NaCN was added in portions at 0° under nitrogen, and the mixture was stirred at 0° for 2 hr and further overnight at room temperature. The volatiles were removed under reduced pressure to give a brown solid which was chromatographed on silica gel with $CHCl_3$ to yield 26.3 g (96.0%) of ADAN as a slightly tan solid.

b) To a solution of 220 g (2.0 moles) of dichloroacetonitrile and 187 g (2.2 moles) of acetone cyanohydrin in 800 ml of CH_3CN and 200 ml of ether, 2.6 g (40 mmoles) of KCN was added with vigorous stirring at 0°, and the mixture was stirred at 0° for 10 hr. The volatiles were removed *in vacuo* to give a brown to black semi-solid. To the solid, 500 ml of ether and about 5 g of activated charcoal were added and the mixture was filtered. The filtrate was evaporated *in vacuo* and the resulting yellow to orange solid was washed with a small amount of a mixture of ether and pet. ether to give 240 g (88%) of practically pure ADAN as a pale yellow solid suitable for synthetic use. Recrystallization from pet. ether afforded pure ADAN, mp 61°. IR ν_{max}^{Nujol} cm^{-1}: 3400, 3320, 3190, 2250, 1610, 1330, 1170, 960, 883, 810, and 720. NMR ($CDCl_3$) δ: 3.67 (br). Mass Spectrum *m/e* (rel. intensity): 140, 138, 136 (1: 6: 9, M^+, 100%), 113, 111, 109 (1: 6: 9, M^+–HCN, 19%), 103, 101, (1: 3, M^+–Cl, 58%), 102, 100 (1: 3, M^+–HCl, 22%), 73 (M^+–HCN–HCl, 38%), 66 (M^+–2Cl, 28%),53 (M^+–$CHCl_2$, 51%). *Anal.* Calcd. for $C_3H_2N_2Cl_2$: C, 26.30; H, 1.47; N, 20.45. Found: C, 26.07; H, 1.30; N, 20.33.

2-Amino-2-cyano-3,3-dichloropropionitrile (14)——To a solution of 1.1 g (10 mmoles) of dichloroaceto-

19) L.M. Iagupol'skii and R.V. Belinskaia, *J. Gen. Chem. USSR*, **28**, 750 (1958).
20) H. Bauer, *Ann.*, **229**, 163 (1885).

nitrile (**11a**) and 0.83 g (30 mmoles) of HCN in 5 ml of CH_3CN placed in a 50-ml steel bomb, 0.1 g of aluminum isopropoxide was added and the vessel was closed. The mixture was stirred overnight at room temperature. After removal of the volatiles, the residue was chromatographed on silica gel with $CHCl_3$ to give 183 mg (13%) of ADAN and 148 mg (9%) of **14** as an oil. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3350, 3290, 2250, and 1615. NMR ($CDCl_3$) δ: 2.53 (2H, br), and 5.84 (1H, s). Mass Spectrum *m/e* (rel. intensity): 141, 139, 137 (1: 6: 9, M^+–CN, 5%), 140, 138, 136 (1: 6: 9, M^+–HCN, 11%), 103, 101 (1: 3, M^+–HCN–Cl, 14%), 87, 85, 83 (1: 6: 9, $CHCl_2^+$, 100%), 80 (M^+–$CHCl_2$, 99%), 53 (M^+–$CHCl_2$–HCN, 60%).

2-Amino-3,3-dibromoacrylonitrile (13)——To a stirred solution of 1.99 g (10 mmoles) of dibromoacetonitrile[21] (**11b**) and 1.7 g (20 mmoles) of acetone cyanohydrin in 10 ml of anhydrous CH_3CN, 0.325 g (5 mmoles) of KCN was added at 0° under nitrogen, and the mixture was stirred overnight, the temperature being kept at below 10°. The volatiles were removed under reduced pressure at room temperature and the residue was chromatographed on silica gel to give 1.18 g (82.5% yield based on the **11b** consumed) of **13** as an unstable solid together with 0.73 g of **11b**. The physical data are presented in Table I. *Anal.* Calcd. for $C_3H_2N_2Br_2$: C, 15.95; H, 0.89; N, 12.40. Found: C, 15.89; H, 0.64; N, 12.36.

2-Acetylamino-3,3-dichloroacrylonitrile[12] (16)——a) A solution of 13.7 g (0.1 mole) of ADAN in 20.4 g (0.2 mole) of Ac_2O and 3.0 g (0.05 mole) of AcOH was allowed to stand overnight at room temperature. Ice water was added, and the mixture was extracted with 500 ml of $CHCl_3$. The extract was washed with water, then dried ($MgSO_4$). The solvent was evaporated *in vacuo* and the residueal solid was washed with chilled ether to give 17.5 g (98%) of **16**. Recrystallization from benzene yielded pure **16**, mp 128—130° (lit.[12] mp 133—135°).

b) To a stirred solution of 4.5 g of **15**, prepared from trichloroacetonitrile and HCN according to the known method,[5] in 20 ml of Ac_2O and 10 ml of AcOH, 7.5 g of zinc powder was added in portions, and the mixture was stirred overnight at room temperature. After addition of ice water, the mixture was extracted with 300 ml of $CHCl_3$. The extract was washed with water, dried, then the solvent was removed and the residue chromatographed on silica gel to give 2.70 g (58%) of **16**. IR ν_{max}^{Nujol} cm^{-1}: 3250, 3180 sh, 3080, 2230, 1690 sh, 1678, 1655 sh, and 1603. NMR ($CDCl_3$) δ: 2.15 (3H, s), and 7.36 (1H, br). Mass Spectrum *m/e* (rel. intensity): 182, 180, 178 (1: 6: 9, M^+, 2%), 145, 143 (1: 3, M^+–Cl, 3%), 140, 138, 136 (1: 6: 9, M^+–CH_2=C=O, 22%), 113, 111, 109 (1: 6: 9, M^+–CH_2=C=O–HCN, 3%), 53 (4%), 43 (100%). *Anal.* Calcd. for $C_5H_4ON_2Cl_2$: C, 33.55; H, 2.25; N, 15.65. Found: C, 33.86; H, 2.13; N, 15.78.

2-Diacetylamino-3,3-dichloroacrylonitrile (17)——a) A solution of 27.4 g (0.2 mole) of ADAN in 300 ml of Ac_2O was refluxed for 8 hr, and the volatiles were evaporated *in vacuo*. The residue was chromatographed on silica gel to yield 31.7 g (72%) of **17** as an oil and 8.2 g (23%) of **16**. Compound **17** is rather sensitive to moisture and was hydrolyzed to **16** to some extent during the chromatographic purification.

b) A solution of 17.9 g (0.1 mole) of **16** in 300 ml of Ac_2O was refluxed for 8 hr. By a work-up similar to that given above, 17.7 g (almost quantitative yield based on **16** consumed) of **17** and 3.9 g (22%) of **16** were obtained. IR $\nu_{max}^{liq.film}$ cm^{-1}: 2245, 1740, 1724, and 1589. NMR ($CDCl_3$) δ: 2.33 (s). Mass Spectrum *m/e* (rel. intensity): 187, 185 (1: 3, M^+–Cl, 19%), 182, 180, 178 (1: 6: 9, M^+–CH_2=C=O, 50%), 155, 153, 151 (1: 6: 9, M^+–CH_2=C=O–HCN, 8%), 145, 143 (1: 3, M^+–CH_2=C=O–Cl, 13%), 140, 138, 136 (1: 6: 9, M^+–$2CH_2$=C=O, 28%), 43 (100%). *Anal.* Calcd. for $C_7H_6O_2N_2Cl_2$: C, 38.04; H, 2.74; N, 12.67. Found: C, 38.18; H, 2.66; N, 12.81.

2-Amino-3,3-bisphenylthioacrylonitrile (18a)——a) To a cold solution of 10.1 g (0.084 mole) of thiophenol and 3.36 g (0.084 mole) of NaOH in 100 ml of water, 5.48 g (0.04 mole) of ADAN was added. The mixture was stirred overnight at room temperature under nitrogen. The resulting mixture was extracted with 300 ml of ether. The extract was washed, dried and evaporated *in vacuo*. The residual solid was chromatographed on silica gel to yield 9.31 g (82%) of **18a**.

b) To a stirred solution of 2.20 g (20 mmoles) of thiophenol and 1.20 g (30 mmoles) of NaOH in 20 ml of MeOH, 1.79 g (10 mmoles) of **16** was added, and the mixture was stirred at 50° for 1 hr. The resulting orange solution was evaporated under reduced pressure leaving an orange solid, which was chromatographed on silica gel to give 2.0 g (70%) of **18a**. mp 88—90° (recrystallized from *n*-hexane). IR ν_{max}^{Nujol} cm^{-1}: 3425, 3310, 3150, 3050, 2240, 1603, 1580, and 1557. NMR ($CDCl_3$) δ: 4.46 (2H, br), and 7.10—7.40 (10H, br s). Mass Spectrum *m/e* (rel. intensity): 284 (M^+, 100%), 175 (M^+–SC_6H_5, 12%), 174 (M^+–C_6H_5SH, 9%), 148 (M^+–SC_6H_5–HCN, 12%), 142 (44%), 121 ($C_6H_5SC^+$, 43%), 110 ($C_6H_5SH^+$, 9%), 109 ($C_6H_5S^+$, 9%), 77 ($C_6H_5^+$, 17%). *Anal.* Calcd. for $C_{15}H_{12}N_2S_2$: C, 63.38; H, 4.26; N, 9.86. Found: C, 63.58; H, 4.23; N, 9.85.

2-Amino-3,3-bismethylthioacrylonitrile (18b)——a) To 170 ml of an aqueous solution containing 0.3 mole of CH_3SNa, 16.5 g (0.1 mole) of **19** was added at room temperature with stirring under nitrogen. Compound **19** dissolved gradually and 2-formylamino-3,3-bismethylthioacrylonitrile, the substitution product of the chlorine atoms of **19**, separated out in about 30 min. Without isolation of the precipitate, the reaction mixture was further stirred at room temperature for 3 days, during which the formylamino group was hydrolyzed. The resulting orange solution was extracted with 500 ml of ether. The extract was washed, dried and evaporated to give 12.3 g of orange oil, which was chromatographed on silica gel to yield 9.4 g (59%) of

21) J.W. Wilt and J.L. Diebold, "Organic Syntheses," Vol. 38, ed. by A.H. Blatt, John Wiley and Sons, Inc., New York, 1958, p. 16.

18b as an oil.

b) To a solution of 9.6 g (40 mmoles) of 20% aqueous CH_3SNa and 100 ml of water, 1.37 g (10 mmoles) of ADAN was added under nitrogen, and the mixture was stirred overnight at room temperature. The mixture was extracted with 100 ml of ether. The extract was washed with water, dried, and evaporated *in vacuo* to give a residue. The residual oil was chromatographed on silica gel to yield 192 mg (12%) of **18b**, together with 500 mg of an unidentified oily mixture. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3420, 3310, 3170, 2210, 1600, and 1558. NMR ($CDCl_3$) δ: 2.30 (3H, s), 2.32 (3H, s), and 4.34 (2H, br). Mass Spectrum *m/e* (rel. intensity): 160 (M^+, 100%), 145 (M^+–CH_3, 52%), 128 (M^+–S, 12%), 113 (M^+–SCH_3, 9%), 101 (M^+–S–HCN, 23%), 99 (10%), 98 (29%), 91 (56%), 45 (60%). *Anal.* Calcd. for $C_5H_8N_2S_2$: C, 37.47; H, 5.03; N, 17.48. Found: C, 37.82; H, 5.41; N, 17.54.

2-Amino-3,3-bisethylthioacrylonitrile (18c)——Treating 16.5 g (0.1 mole) of **19** with a solution of 18.6 g (0.3 mole) of ethylmercaptan and 13.2 g (0.33 moles) of NaOH in 300 ml of water under conditions similar to those given above and purifying the ether extract through a silica gel column gave 17.5 g (93%) of **18c** as an oil. IR $\nu_{max}^{liq.film}$ cm^{-1}: 3450, 3340, 3200, 2220, 1602, and 1568. NMR ($CDCl_3$) δ: 1.24 (6H, t, J=7.2 Hz), 2.55—3.10 (4H, m), and 4.44 (2H, br). Mass Spectrum *m/e* (rel. intensity): 188 (M^+, 100%), 159 (M^+–C_2H_5, 41%), 127 (M^+–SC_2H_5, 19%), 105 (19%), 99 (21%), 98 (M^+–SC_2H_5–C_2H_5, 54%). *Anal.* Calcd. for $C_7H_{12}N_2S_2$: C, 44.65; H, 6.42; N, 14.88. Found: C, 44.05; H, 6.20; N, 14.43.

2-Formylamino-3,3-dichloroacrylonitrile (19)——To 5 ml of acetic-formic anhydride,[22] prepared *in situ* from Ac_2O and formic acid, 2.74 g (20 mmoles) of ADAN was added at room temperature. ADAN dissolved rapidly with heat evolution and **19** crystallized out in a few minutes. Three hours later, ice water was added, and the resulting mixture was extracted with 500 ml of ethyl acetate. The extract was washed, dried, evaporated and the residue was washed with chilled ether to give 3.2 g (97%) of **19**. Recrystallization from benzene gave colorless needles, mp 148—150°. IR ν_{max}^{Nujol} cm^{-1}: 3200, 3150, 3050, 2245, 1694 sh, 1665, and 1602. NMR (d_6-DMSO) δ: 8.23 (1H, br), and 10.46 (1H, br). Mass Spectrum *m/e* (rel. intensity): 168, 166, 164 (1: 6: 9, M^+, 43%), 140, 138, 136 (1: 6: 9, M^+–CO, 100%), 131, 129 (1: 3, M^+–Cl, 28%), 113, 111, 109 (1: 6: 9, M^+–CO–HCN, 77%), and 103, 101 (1: 3, M^+–CO–Cl, 45%). *Anal.* Calcd. for $C_4H_2ON_2Cl_2$: C, 29.12; H, 1.22; N, 16.98. Found: C, 29.20; H, 0.90; N, 17.03.

Reaction of ADAN with *n*-Propylamine——To a solution of 2.74 g (20 mmoles) of ADAN in 20 ml of EtOH, 5.66 g (96 mmoles) of *n*-propylamine was added, and the mixture was stirred at room temperature for three days. The solvent was removed and the residual oil was chromatographed on silica gel to give 1.16 g (34%) of N-*n*-propyl-dichloroacetamide (mp 49—50°, from *n*-hexane; lit.[23] mp 50°) and 0.82 g (32%) of dichloroacetamide (mp 98°, from *n*-hexane; lit.[24] mp 97.5—99.5°).

Reaction of ADAN with Morpholine——The reaction of 2.74 g (20 mmoles) of ADAN with 8.35 g (96 mmoles) of molpholine under conditions similar to those given above gave 0.37 g of dichloroacetamide and 0.48 g (12%) of dichloroacetomorpholide (mp 61—62°, from *n*-hexane). IR ν_{max}^{Nujol} cm^{-1}: 1660. NMR ($CDCl_3$) δ: 3.71 (8H, s), and 6.23 (1H, s). *Anal.* Calcd. for $C_6H_9O_2NCl_2$: C, 36.39; H, 4.58; N, 7.07. Found: C, 36.38; H, 4.75; N, 7.00.

Reaction of ADAN with Piperidine——The reaction of 685 mg (5 mmoles) of ADAN with 1.70 g (20 mmoles) of piperidine under conditions similar to those given above gave 185 mg (19%) of dichloroacetopiperidide (mp 43°,[25] from *n*-hexane; lit.[26] mp 51°) and 200 mg (31%) of dichloroacetamide.

2-Trifluoroacetylamino-3,3-dichloroacrylonitrile (21)——To a cold solution of 13.7 g (0.1 mole) of ADAN in 100 ml of ether, 23.1 g (0.11 mole) of trifluoroacetic anhydride was added dropwise, and the mixture was allowed to stand overnight at room temperature. The volatiles were evaporated and the residue was washed with a mixture of ether and pet. ether to give 22.8 g (98%) of **21**, as colorless needles; mp 76—77° (from *n*-hexane–benzene). IR ν_{max}^{Nujol} cm^{-1}: 3250, 3100, 2240, 1745—20, and 1604. NMR ($CDCl_3$) δ: 8.11 (br). Mass Spectrum *m/e* (rel. intensity): 236, 234, 232 (1: 6: 9, M^+, 7%), 199, 197 (1: 3, M^+–Cl, 49%), 167, 165, 163 (1: 6: 9, M^+–CF_3, 12%), 113, 111, 109 (1: 6: 9, M^+–$COCF_3$–HCN, 54%), 69 (CF_3^+, 100%). *Anal.* Calcd. for $C_5HN_2Cl_2F_3$: C, 25.78; H, 0.43; N, 12.02. Found: C, 26.18; H, 0.39; N, 11.87.

2-Acetylamino-3,3-dibromoacrylonitrile (22)——A mixture of 2.26 g (10 mmoles) of **13b** in 4 ml of Ac_2O and 1 ml of AcOH was allowed to stand overnight at room temperature. After addition of ice water, the mixture was extracted with 300 ml of ethyl acetate. The extract was washed, dried, and the solvent was evaporated. The residue was washed with ether to give 2.50 g (93%) of **22**, as colorless needles; mp 172—173° (decomp.) (from benzene). IR ν_{max}^{Nujol} cm^{-1}: 3240, 3160 sh, 3060, 2235, 1670, and 1590. NMR (d_6-DMSO)

22) V.C. Mehlenbacher, *Org. Analysis*, **1**, 37 (1953).
23) A.D. Swensen and W.E. Weaver, *J. Am. Chem. Soc.*, **70**, 4060 (1948).
24) J.R. Clark, W.J. Shibe, and R. Connor, "Organic Syntheses," Coll. Vol. III, ed. by A.H. Blatt, John Wiley and Sons, New York, 1955, p. 260.
25) The melting point of dichloroacetopiperidide was lower than the reported one, but the structure was identified unambiguously by the following data. IR ν_{max}^{Nujol} cm^{-1}: 1655. NMR ($CDCl_3$) δ: 1.63 (6H, br), 3.58 (4H, br), and 6.28 (1H, s). *Anal.* Calcd. for $C_7H_{11}ONCl_2$: C, 42.88; H, 5.65; N, 7.14. Found: C, 42.61; H, 5.64; N, 7.20.
26) Y. Ursy and M. Paty, *Compt. Rend.*, **252**, 3812 (1961).

δ: 2.08 (3H, s), and 7.47 (1H, br). Mass Spectrum *m/e* (rel. intensity): 270, 268, 266 (1: 2: 1, M^+, 13%), 228, 226, 224 (1: 2: 1, $M^+-CH_2=C=O$, 97%), 189, 187 (1: 1, M^+-Br, 13%), 43 (100%). *Anal.* Calcd. for $C_5H_4ON_2Br_2$: C, 22.41; H, 1.51; N, 10.46. Found: C, 22.42; H, 1.38; N, 10.57.

2-Acetylamino-3,3-dichloroacrylamide (23a)——To 18 g of conc. sulfuric acid, 5.0 g of **16** was added in portions with ice cooling and the resulting mixture was allowed to stand at around 5° for three days. The homogeneous mixture obtained was poured onto ice and the precipitate was collected by filtration to give 3.8 g of **23a**. The filtrate was extracted with 300 ml of ethyl acetate. The extract was washed with water, dried, and the solvent was evaporated *in vacuo*. The residual solid was chromatographed on silica gel with $CHCl_3$–10% ethyl acetate to give 0.45 g (8%) of the corresponding acid **24a** and 0.35 g of **23a**. The total yield of **23a** was 4.15 g (76%). Recrystallization from acetonitrile gave fine colorless needles; mp 201—203° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3450, 3320, 3150, 3070, 1685 sh, 1650, 1640 sh, 1598, and 1510. NMR (d_6-DMSO) δ: 1.97 (3H, s), 7.3—7.9 (2H, br), and 9.53 (1H, br). Mass Spectrum *m/e* (rel. intensity): 200, 198, 196 (1: 6: 9, M^+, 1%), 163, 161 (1: 3, M^+-Cl, 10%), 158, 156, 154 (1: 6: 9, $M^+-CH_2=C=O$, 55%), 114, 112, 110 (1: 6: 9, $Cl_2C=C=NH_2^+$, 6%), 113, 111, 109 (1: 6: 9, $Cl_2C=C=NH^+$, 16%). *Anal.* Calcd. for $C_5H_6O_2N_2Cl_2$: C, 30.48; H, 3.07; N, 14.22. Found: C, 30.34; H, 2.87; N, 14.19.

2-Trifluoroacetylamino-3,3-dichloroacrylamide (23b)——To 80 g of conc. sulfuric acid, 30 g (0.129 mole) of **21** was added in portions with ice cooling and the mixture was allowed to stand at room temperature for 1 week. The resulting homogeneous mixture was poured onto ice and the precipitate formed was collected by filtration and washed with chilled water to give 22.0 g of **23b**. The filtrate was extracted with ethyl acetate, the solvent was removed and the residue was washed with ether to give 4.8 g of **23b**. The total yield of **23b** was 26.8 g (83%). IR ν_{max}^{Nujol} cm^{-1}: 3450, 3410, 3340, 3170, 3120 sh, 1715, 1670, 1610, and 1534. NMR (d_6-DMSO) δ: 7.5—8.2 (2H, br), and 11.1 (1H, br). Mass Spectrum *m/e* (rel. intensity): 254, 252, 250 (1:6:9, M^+, 2%), 217, 215 (1: 3, M^+-Cl, 6%), 200, 198 (1: 3, $M^+-Cl-17$, 31%), 114, 112, 110 (1: 6: 9, $Cl_2=C=NH_2^+$, 33%), 113, 111, 109 ($Cl_2=C=NH^+$, 44%), 69 (CF_3^+, 97%), 44 ($CONH_2^+$, 100%). *Anal.* Calcd. for $C_5H_3O_2N_2Cl_2F_3$: C, 23.93; H, 1.20; N, 11.16. Found: C, 23.99; H, 1.18; N, 11.34.

2-Acetylamino-3,3-dibromoacrylamide (23c)——The reaction of 3.0 g (11.2 mmoles) of **22** with 15 g of conc. sulfuric acid under conditions similar to those for the preparation of **23a** gave 2.75 g (86%) of **23c**. IR ν_{max}^{Nujol} cm^{-1}: 3460, 3380, 3330, 3200, 3150 sh, 3080, 1695 sh, 1655, and 1600. NMR (d_6-DMSO) δ: 1.98 (3H, s), 7.2—7.8 (2H, br), and 9.35 (1H, br). *Anal.* Calcd. for $C_5H_6O_2N_2$: C, 21.00; H, 2.12; N, 9.80. Found: C, 21.07; H, 2.04; N, 9.63.

2-Acylamino-3,3-dihalogenoacrylic Acids (24a—c)——The following procedure for the preparation of **24a** is typical.

a) A solution of 1.97 g (10 mmoles) of **23a** in 5 ml of conc. sulfuric acid was stirred at 60° for 1 hr, poured onto ice and the product was extracted with 200 ml of ethyl acetate. The extract was washed with water, then dried. The solvent was evaporated and the residue was washed with a mixture of ether and pet. ether to give 1.50 g (76%) of **24a**.

b) To a stirred solution of 5.0 g (25.3 mmoles) of **23a** in 20 ml of conc. sulfuric acid, a solution of 3.0 g of $NaNO_2$[13] in 4.3 ml of water was added in portions at below 5°. Next, the mixture was further stirred at the same temperature for 2 hr and allowed to stand overnight at room temperature. The mixture was poured onto ice, and the product was collected and washed with a small amount of chilled water to give 3.3 g of **24a**. The filtrate was extracted with ethyl acetate. The extract was washed with water, dried, and the solvent was evaporated *in vacuo* to give 0.50 g of **24a**, the total yield of which was 3.80 g (76%).

c) A mixture of 10 g (0.0559 mole) of **16** in 20 ml of conc. sulfuric acid was stirred at between 60° and 70° for 2 hr. The cooled mixture was poured onto ice, and the precipitate formed was collected and washed with a small amount of chilled water to give 7.3 g of **24a**. The filtrate was extracted with ethyl acetate. The extract was washed with water, dried, and the solvent was removed *in vacuo* to give 1.50 g of **24a**, the total yield of which was 8.80 g (80%). IR ν_{max}^{Nujol} cm^{-1}: 3290, 2900—2350, 1725, 1714 sh, 1660 sh, 1640, 1612, 1595 sh, 1530 sh, and 1514. NMR (d_6-DMSO) δ: 1.98 (3H, s), 9.72 (1H, br), and 12.23 (1H, br). Mass Spectrum *m/e* (rel. intensity): 201, 199, 197 (1: 6: 9, M^+, 3%), 164, 162 (1: 3, M^+-Cl, 3%), 159, 157, 155 (1: 6: 9, $M^+-CH_2=C=O$, 30%), 113, 111, 109 (1: 6: 9, $Cl_2C=C=NH^+$, 34%), 86, 84, 82 (1: 6: 9, CCl_2^+, 16%), 43 (100%). *Anal.* Calcd. for $C_5H_5O_3NCl_2$: C, 30.33; H, 2.55; N, 7.07. Found: C, 30.22; H, 2.36; N, 7.05.

2-Trifluoroacetylamino-3,3-dichloroacrylic Acid (24b)——IR ν_{max}^{Nujol} cm^{-1}: 3250, 3130, 3050, 2850—2400, 1718, 1690 sh, 1602, and 1530. NMR (d_6-DMSO) δ: 11.0 (1H, br), and 11.3 (1H, br). Mass Spectrum *m/e* (rel. intensity): 255, 253, 251 (1: 6: 9, M^+, 6%), 218, 216 (1: 3, M^+-Cl, 29%), 200, 198 (1: 3, $M^+-Cl-18$, 79%), 114, 112, 110 (1: 6: 9, $Cl_2=C=NH_2^+$, 20%), 113, 111, 109 (1: 6: 9, $Cl_2=C=NH^+$, 42%), 69 (CF_3^+, 100%). *Anal.* Calcd. for $C_5H_2O_3NCl_2F_3$: C, 23.83; H, 0.80; N, 5.56. Found: C, 23.93; H, 0.73; N, 5.79.

2-Acetylamino-3,3-dibromoacrylic Acid (24c)——IR ν_{max}^{Nujol} cm^{-1}: 3260, 2850—2300, 1728, 1703 sh, 1640, 1595, and 1510. NMR (d_6-DMSO) δ: 1.94 (3H, s), 7.76 (1H, br), and 9.65 (1H, br). *Anal.* Calcd. for $C_5H_5O_3NBr_2$: C, 20.93; H, 1.76; N, 4.88. Found: C, 21.11; H, 1.63; N, 4.84.

Methyl-2-acylamino-3,3-dihalogenoacrylate (25a—c)——The procedure for the preparation of **25a** is typical. To a cold solution of 10.0 g of **24a** in 150 ml of tetrahydrofuran (THF) and 50 ml of ether, an etheral solution of diazomethane was added in portions. Completion of the reaction was confirmed by the cessation of nitrogen evolution and thin-layer chromatography (TLC). The solvent was evaporated to give 10.55 g

(99%) of **25a**. IR ν_{max}^{Nujol} cm^{-1}: 3210, 1730, 1650, 1640 sh, 1630 sh, and 1610. NMR ($CDCl_3$) δ: 2.14 (3H, s), 3.97 (3H, s), and 7.68 (1H, br). Mass Spectrum *m/e* (rel. intensity): 215, 213, 211 (1: 6: 9, M^+, 3%), 184, 182, 180 (1: 6: 9, M^+-OCH_3, 12%), 173, 171, 169 (1: 6: 9, $M^+-CH_2=C=O$, 87%), 114, 112, 110 (1: 6: 9, $Cl_2C=C=NH_2^+$, 10%), 113, 111, 109 (1: 6: 9, $Cl_2C=C=NH^+$, 52%), 43 (100%). *Anal.* Calcd. for $C_6H_7O_3NCl_2$: C, 33.98: H, 3.33; N, 6.61. Found: C, 33.82; H, 3.16; N, 6.61.

Methyl 2-Trifluoroacetylamino-3,3-dichloroacrylate (25b)——IR ν_{max}^{Nujol} cm^{-1}: 3260, 3050, 1725, 1690 sh, 1610, and 1522. NMR ($CDCl_3$) δ: 3.86 (3H, s), and 8.14 (1H, br). *Anal.* Calcd. for $C_6H_4O_3NCl_2F_3$: C, 27.09; H, 1.52; N, 5.27. Found: C, 27.08; H, 1.32; N, 5.40.

Methyl 2-Acetylamino-3,3-dibromoacrylate (25c)——IR ν_{max}^{Nujol} cm^{-1}: 3240, 1730, 1660, and 1594. NMR ($CDCl_3$) δ: 2.07 (3H, s), 3.82 (3H, s), and 7.43 (1H, br). *Anal.* Calcd. for $C_6H_7O_3NBr_2$: C, 23.95; H, 2.34; N, 4.65. Found: C, 23.88; H, 2.39; N, 4.53.

2-Acylamino-3,3-dihalogeno-N-*t*-butylacrylamide (26a—c)——The procedure for the preparation of **26a** is typical.

2-Acetylamino-3,3-dichloro-N-*t*-butylacrylamide (26a)——To a stirred solution of 4.55 g of *t*-butanol, 10 ml of AcOH and 10 ml of 95% sulfuric acid, 5.0 g of **16** was added and the mixture was stirred at below 10° for 2 days. The mixture was poured onto ice, and the resulting solution was extracted with ethyl acetate. The extract was washed with water, then dried. The solvent was evaporated and the residue was washed with a small amount of ether to give 5.20 g (73%) of **26a**. IR ν_{max}^{Nujol} cm^{-1}: 3270, 3200 sh, 3090, 1680 sh, 1658, 1640 sh, 1608, 1565, and 1520. NMR (d_6-DMSO) δ: 1.27 (9H, s), 1.96 (3H, s), 7.90 (1H, br), and 9.36 (1H, br). *Anal.* Calcd. for $C_9H_{14}O_2N_2Cl_2$: C, 42.70; H, 5.58; N, 11.07. Found: C, 42.64; H, 5.53; N, 11.08.

2-Trifluoroacetylamino-3,3-dichloro-N-*t*-butylacrylamide (26b)——IR ν_{max}^{Nujol} cm^{-1}: 3250, 3080, 1728, 1720, 1663, 1618, 1570 sh, 1560, and 1530. NMR ($CDCl_3$) δ: 1.42 (9H, s), 6.18 (1H, br), and 9.61 (1H, br). *Anal.* Calcd. for $C_9H_{11}O_2N_2Cl_2F_7$: C, 35.20; H, 3.61; N, 9.12. Found: C, 34.93; H, 3.63; N, 8.77.

2-Acetylamino-3,3-dibromo-N-t-butylacrylamide (26c)——IR ν_{max}^{Nujol} cm^{-1}: 3250, 3200 sh, 3090, 1660, 1598, 1560, and 1517. NMR (d_6-DMSO) δ: 1.27 (9H, s), 1.96 (3H, s), 9.23 (1H, br), and 9.60 (1H, br). *Anal.* Calcd. for $C_9H_{14}O_2N_2Br_2$: C, 31.60; H, 4.13; N, 8.19. Found: C, 30.93; H, 3.78; N, 7.85.

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