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Studies of Nitriles. XI.[1] Preparation and Chemistry of Schiff Bases of ADAN, 2-Amino-3,3-dichloroacrylonitrile.[2] A highly Effective Conversion into 2-Substituted-4(5)-chloroimidazole-5(4)-carbaldehydes

Koichi Matsumura, Masaaki Kuritani, Hiroshi Shimadzu, and Naoto Hashimoto

Chemical Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd.[3]

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Schiff bases of 2-amino-3,3-dichloroacrylonitrile (ADAN) have been prepared in excellent yields by condensation of ADAN with various aldehydes under mild conditions. These Schiff bases (**2**, **3**, **4**) are highly reactive polyfunctional compounds and useful synthetic intermediates: the chlorine atoms of Schiff base **2e** react with various nucleophiles such as alkoxides, mercaptides, and primary and secondary amines giving the corresponding 3,3-dialkoxy-,3,3-bis(substituted mercapto)-, and 3,3-bis(substituted amino)-derivatives (**7**, **8**, and **10**), respectively. Reduction of Schiff base **2e** with zinc powder under mild conditions resulted in formation of the monochloro derivative **5**. With anhydrous hydrogen chloride in ether, these Schiff bases underwent smooth cyclization to new 4(5)-chloro-5(4)-dichloromethylimidazoles **11**, which in turn were converted into 4(5)-chloroimidazole-5(4)-carbaldehydes **12** in excellent yields upon hydrolysis.

ADAN, 2-amino-3,3-dichloroacrylonitrile,[2] produced almost quantitatively by the reaction of dichloroacetonitrile with HCN in the presence of a base, is a versatile polyfunctional synthetic intermediate for the syntheses of heterocycles and also amino acids. Although ADAN, having an amino and a reactive dichloromethylene group, is somewhat unstable and decomposes gradually in air at room temperature (r.t.), it can be stored at lower temperature for long periods. But, the N-protected derivatives of ADAN are much more stable and also useful synthetic intermediates of amino acids or heterocycles. In paper VIII[4] and IX,[5] we described the N-acyl derivatives and their reactivities. We now report on the synthesis and reactivities of Schiff bases from ADAN as well as their highly effective conversion into 2-substituted-4(5)-chloroimidazole derivatives.

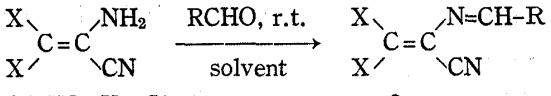
Results and Discussion

ADAN condenses with aliphatic and aromatic aldehydes at room temperature in a solvent such as benzene or ether giving the corresponding Schiff bases **2**. However, many difficulties arose in the purification of 2-alkylideneamino-3,3-dichloroacrylonitriles (**2a—c**) due to their instability, the structural proof being based on their spectral data only. While, the Schiff bases **2e—y** from aromatic aldehydes are stable compounds and easily obtained in excellent yields.

Similarly, 2-amino-3,3-dibromoacrylonitrile[2] (**1**) reacted with benzaldehyde to give 2-benzylideneamino-3,3-dibromoacrylonitrile (**2d**) in 93% yield.

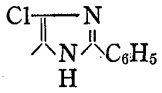
1) Part X: K. Matsumura, O. Miyashita, H. Shimadzu, and N. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), **24**, 948 (1976).
2) Part VII: K. Matsumura, T. Saraie, and N. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), **24**, 912 (1976).
3) Location: *Jusohonmachi, Yodogawa-ku, Osaka, 532, Japan.*
4) Part VIII: K. Matsumura, T. Saraie, and N. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), **24**, 924 (1976).
5) Part IX: K. Matsumura, H. Shimadzu, O. Miyashita, and N. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), **24**, 941 (1976).

TABLE I. Preparation of Schiff Bases of ADAN



ADAN: X=Cl
1 : X=Br

2a—y

Compd. No.	**2** X	R	Reaction conditions Solvent[a]	Method[b]	Yield (%)	mp (°C)	Recryst. solvent[a]
2a	Cl	CH_2CH_3	E	A	*ca.* 50	unstable solid	—
2b	Cl	$CH{=}CH_2$	B	A	*ca.* 69	unstable solid	—
2c	Cl	$CH(CH_3)_2$	E	A	*ca.* 52	oil	—
2d	Br	C_6H_5	B	A	93	97— 98	H
2e	Cl	C_6H_5	B	A	95	78— 79	P
2f	Cl	*p*-$CH_3C_6H_4$	M	B	92	99—100	M
2g	Cl	*o*-ClC_6H_4	B	A	96	89— 91	B-H
2h	Cl	*p*-ClC_6H_4	B	A	97	132—134	H
2i	Cl	*p*-BrC_6H_4	M	B	87	131—133	M
2j	Cl	*o*-$CH_3OC_6H_4$	B	A	82	115—117	B-H
2k	Cl	*m*-$CH_3OC_6H_4$	B	A	96	102—104	B-H
2l	Cl	*p*-$CH_3OC_6H_4$	B-C	A	91	141—142	B-H
2m	Cl	*m*, *p*-$(CH_3O)_2C_6H_3$	B-C	A	95	143—144	M
2n	Cl	*m*,*p*-OCH_2O-C_6H_3	B-C	A	96	141—142	M
2o	Cl	*o*-OHC_6H_4	B-C	A	95	124—125	H
2p	Cl	*p*-OH-*m*-$CH_3OC_6H_3$	B-C	A	96	150—152	B-H
2q	Cl	*o*-$NH_2C_6H_4$	B-C	A	82	131—134	B-H
2r	Cl	*p*-$N(CH_3)_2C_6H_4$	B-C	A	97	127—128	B-H
2s	Cl	*o*-$NO_2C_6H_4$	C	A	96	130—132	B
2t	Cl	*m*-$NO_2C_6H_4$	AC	A	92	146—149	M
2u	Cl	*p*-$NO_2C_6H_4$	AC-C	A	94	170—172	M
2v	Cl	α-naphthyl	M	B	96	121—122	M
2w	Cl		B	A	90	123—124	B-H
2x	Cl		B	A	94	108—110	B-H
2y	Cl		B-C	A	86	178—180	M

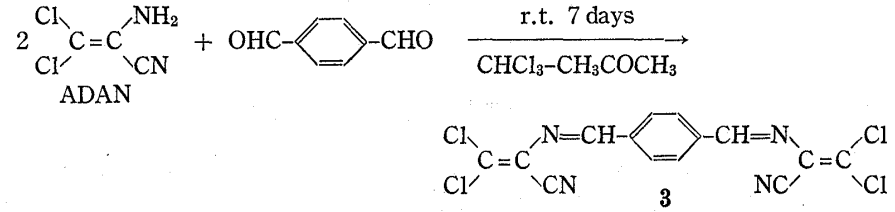
a) AC=acetone, B=benzene, C=chloroform, E=ether, H=*n*-hexane, M=methanol, P=pet. ether
b) See the experimental section.

Addition of anhydrous magnesium sulfate to the reaction mixture was found to be effective. Yields, melting points, and solvents for recrystallization are summarized in Table I.

Schiff bases **2d—y** derived from aromatic aldehydes can be easily purified by recrystallization and preserved at room temperature for years without any detectable change, except for compounds **2r** and **2y** which show photosensitivity and should be stored in the dark.

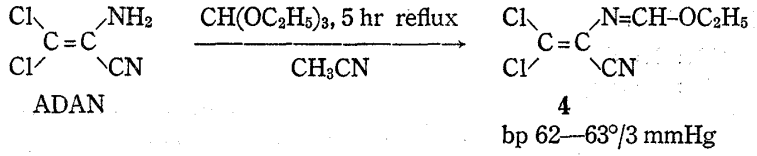
The yields were not affected markedly by the species and the position of the substituents on the phenyl moiety of benzaldehydes. Schiff bases **2v—y** from aldehydes bearing naphthalene, furan, thiophene, or imidazole ring were also prepared in excellent yields under similar conditions.

Schiff base **3** was also prepared without difficulty as shown in Eq. 1.



Eq. 1

2-Ethoxymethyleneamino-3,3-dichloroacrylonitrile (**4**) was prepared by the reaction of ADAN with ethyl orthoformate in refluxing acetonitrile in 96% yield (Eq. 2).



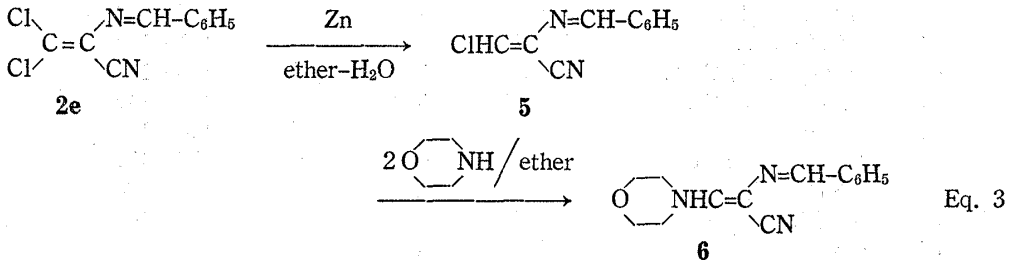
ADAN — **4**, bp 62—63°/3 mmHg

Eq. 2

The structures of Schiff bases **2**, **3**, and **4** were confirmed by the disappearance of signals due to the amino group of ADAN and **1** in the infrared (IR) and nuclear magnetic resonance (NMR) spectra and the appearance of the signal due to the proton of the –N=CH– moiety in the δ 8.10—9.10 ppm range of the NMR spectra together with the results of mass spectra and elemental analyses (Table IV).

Next, the reactivities of 2-benzylideneamino-3,3-dichloroacrylonitrile (**2e**), as a representative, towards reducing agent and various O-, S-, N-nucleophiles were investigated.

Reduction of **2e** with zinc powder in a mixture of ether and water gave the monochloro compound **5** as confirmed by IR, NMR, and mass spectra and elemental analysis (Eq. 3).



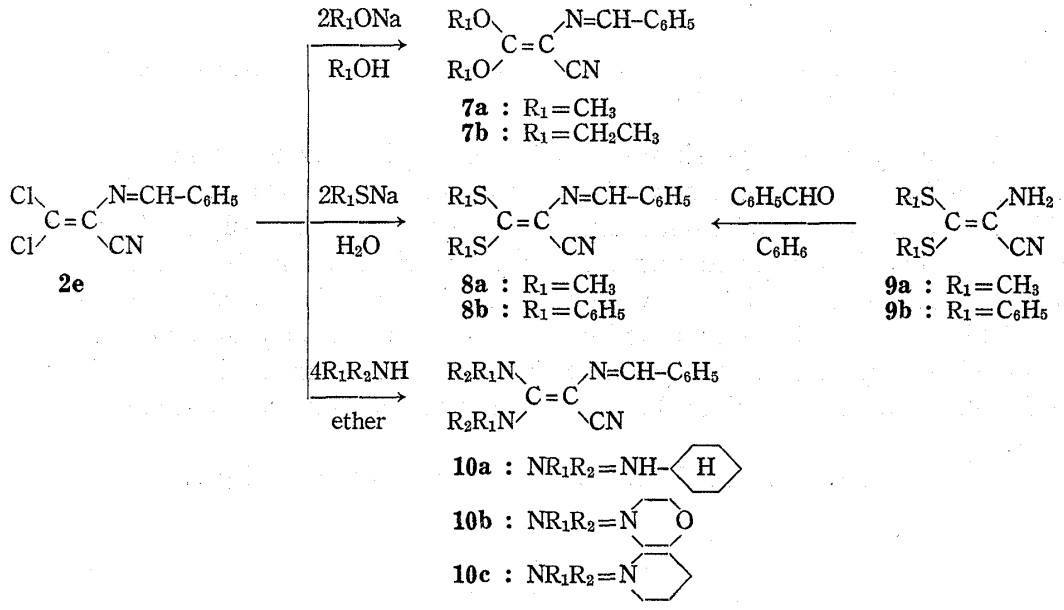
2e — **5** — **6**

Eq. 3

When treated with 2 molar eq. of morpholine in ether at room temperature, **5** yielded 2-benzylideneamino-3-morpholinoacrylonitrile (**6**) quantitatively.

That **5** and **6** showed only one singlet due to –N=CH– proton at δ 8.56 and δ 8.20 ppm, respectively, suggested that only one isomer was obtained selectively in the reduction of **2e**.

The reactions of **2e** with various O-, S-, and N-nucleophiles are shown in Chart 1 and the reaction conditions, yields, and melting points are summarized in Table II.



2e

Chart 1

Thus, **2e** reacted with 2 molar eq. of alkoxides to give 2-benzylideneamino-3,3-dialkoxyacrylonitriles (**7a, b**) in good yields. Further addition of alcohol to the C–C double bond of

TABLE II. Preparation of Various Schiff Bases (**7**, **8**, and **10**)

Compd. No.	Starting material	Yield (%)	mp (°C)	Recryst. solvent[a]
7a	**2e**	67	89— 90	B-H
7b	**2e**	84	72— 74	M
8a	**2e** / **9a**	87 / 82	57— 59	M
8b	**2e** / **9b**	88 / 91	140—141	M
10a	**2e**	79	121—123	M
10b	**2e**	82	145—146	M
10c	**2e**	91	106—109	H

a) B=benzene, H=*n*-hexane, M=methanol

7 was not observed even with excess alkoxide, which was the case[4] with 2-acetylamino-3,3-dichloroacrylonitrile,[2] an N-acyl derivative of ADAN.

Similarly, treatment of **2e** with 2 molar eq. of mercaptides afforded 2-benzylideneamino-3,3-bis(substituted mercapto)acrylonitriles (**8a, b**) in excellent yields. The same compounds **8a, b** were prepared alternatively by the condensation of 2-amino-3,3-bis(substituted mercapto)-acrylonitriles[2] (**9a, b**) with benzaldehyde under conditions similar to those mentioned above.

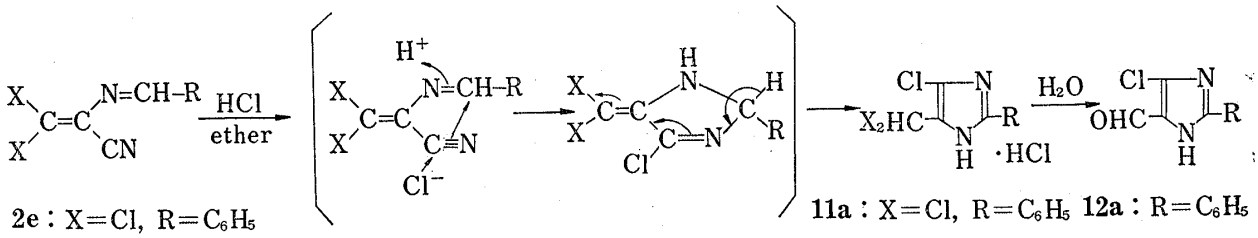
When **2e** was allowed to react either with 4 molar eq. of amines (primary and secondary) or with 2 molar eq. of the amines and 2 molar eq. of triethylamine, the normal substitution products **10a**—**c**, were obtained.

The structures of these products, **7**, **8**, and **10** were ascertained on the basis of spectroscopic evidence together with elemental analysis (Table IV).

These new Schiff bases derived from ADAN serve as versatile intermediates especially for the synthesis of heterocycles.

For example, when treated with gaseous HCl in anhydrous ether, **2e** readily underwent Hartke cyclization[6] to give colorless crystals which melted at 185—195° (decomp.) and were almost insoluble in many organic solvents. The crystals showed absorption bands at 3250—3000, 2750—2200, 1630, and 1550 cm^{-1} in the IR spectrum. The NMR spectrum (d_6-dimethyl sulfoxide (DMSO)) showed δ 14.15 (2H, br) and 9.77 (1H, s), both exchangeable with deuterium, together with peaks at δ 8.00—8.30 (2H, m), and δ 7.35—7.60 (3H, m) due to the phenyl-ring protons. The mass spectrum (*m/e* 228, 226, 224 (1: 6: 9), M^+-2HCl, 50%), and elemental analysis together with the above data revealed that the compound was the expected 2-phenyl-4(5)-chloro-5(4)-dichloromethylimidazole hydrochloride (**11a**).

The dichloromethyl group in **11a** was easily hydrolyzed into formyl group, *e.g.* 2-phenyl-4(5)-chloroimidazole-5(4)-carbaldehyde (**12a**) was obtained from **11a** when the latter was heated briefly in water (*cf.* Chart 2).

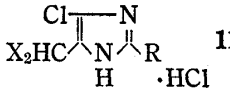


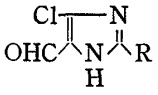
2e : X=Cl, R=C_6H_5 **11a** : X=Cl, R=C_6H_5 **12a** : R=C_6H_5

Chart 2

6) K. Hartke and B. Seib, *Pharmazie*, **30**, 517 (1970).

Table III. Preparation of 4(5)-Chloroimidazole Derivatives (**11** and **12**)


11


12

X	R	Compd. No.	Yield[a] (%)	Compd. No.	Yield (%)	mp (°C)	Recryst. solvent[b]
Cl	C_6H_5	**11a**	84[c]	**12a**	98	169—171	E-W
Br	C_6H_5	**11b**	66		97		
Cl	*o*-ClC_6H_4	**11c**	90	**12c**	99	245—249 (decomp.)	B
Cl	*p*-BrC_6H_4	**11d**	87	**12d**	96	264—266 (decomp.)	A
Cl	*o*-$NO_2C_6H_4$	**11e**	90	**12e**	98	163—164	B
Cl	*o*-OHC_6H_4	**11f**	93	**12f**	99	245—247 (decomp.)	E-W
Cl	*m,p*-OCH_2O-C_6H_3	**11g**	94	**12g**	93	234—235 (decomp.)	B
Cl	α-naphthyl	**11h**	87	**12h**	94	204—205	B
Cl		**11i**	91	**12i**	97	211—212	A

a) of the crude product
b) A=acetonitrile, B=benzene, E=ethanol, W=water
c) mp 185—195° (decomp.)

Similarly, imidazole derivatives **11b—i** and **12a—i** were obtained from **2** in excellent yields (Table III).

All the imidazoles **11, 12** obtained are new compounds. IR spectra of **12** show absorptions at 1670—1630 cm^{-1} due to the carbonyl group and also at 3250—3150 cm^{-1} due to the NH group. Absorptions of the aldehyde and NH protons are observed at δ 9.67—9.80 ppm as a sharp singlet and δ 13.9—14.2 ppm as a very broad peak, respectively, in the NMR spectra (d_6-DMSO) (Table V).

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 Me_4Si as an internal standard. Ultraviolet (UV) spectra were obtained with a Perkin-Elmer 450 spectrophotometer. Mass spectra were obtained at 70 eV with a Hitachi RMU-6D mass spectrometer. The following abbreviations are used; sh=shoulder, s=singlet, d=doublet, t=triplet, m=multiplet, and br=broad.

Yields, melting points, and reaction conditions are shown in Table I—III. Analytical and spectral data are summarized in Table IV, V.

2-Alkylideneamino-3,3-dichloroacrylonitriles (2a—c)——As a typical procedure, the preparation of 2-propylideneamino-3,3-dichloroacrylonitrile (**2a**) is described. To a solution of 5.48 g (40 mmoles) of ADAN and 2.44 g (42 mmoles) of propionaldehyde in 100 ml of ether, was added 1 g of anhydrous $MgSO_4$. The mixture was allowed to stand at around 10° for 10 days. The thin-layer chromatography (TLC) showed a new spot with a larger *Rf* value than that of ADAN due to **2a** and a small spot of remaining ADAN. The insoluble material was removed by filtration and the filtrate was evaporated *in vacuo*. The resulting semi-solid was successively washed with a little pet. ether and ether to give 3.54 g (*ca.* 50%) of **2a** as a solid. The TLC of the solid showed several spots other than that of **2a**. Attempted purification of the product **2a** by passing it through a silica gel column or by recrystallization from several solvents was unsuccessful due to its instability. The solid decomposed completely in a day at room temperature.

General Procedures for the Preparation of 2-Arylideneamino-3,3-dichloro- and 3,3-dibromoacrylonitriles (2d—y)——Method A: To a solution of 0.1 mole of ADAN or 2-amino-3,3-dibromoacrylonitrile (**1**) and 0.105—0.11 mole of an aromatic aldehyde in about 100—600 ml of the solvent listed in Table I, was added about 3 g of anhydrous $MgSO_4$. The mixture was allowed to stand at room temperature for 3—10 days. The insoluble inorganic material was filtered, and washed with a solvent such as benzene, $CHCl_3$, and ethyl acetate. The combined filtrate and washings were evaporated to dryness, and the residual solid was washed with a

small amount of cold MeOH to give practically pure **2d—y** suitable for synthetic use. An analytically pure sample was obtained by recrystallization from the solvent listed in Table I.

Method B: A solution of 0.1 mole of ADAN and 0.105—0.11 mole of an aromatic aldehyde in about 300 ml of MeOH was allowed to stand at room temperature for about 1 week. The mixture, which in most cases contained the precipitated product as fine needles, was concentrated *in vacuo* to a volume of around 50 ml. After cooling, the precipitate was collected by filtration to obtain a condensation product of high purity.

2,2′-(N,N′-*p*-Phenylenedimethine)diamino-3,3,3′,3′-tetrachlorodiacrylonitrile (3)——A mixture of 0.85 g (50 mmoles) of ADAN and 3.35 g (25 mmoles) of terephthalaldehyde and 3 g of anhydrous $MgSO_4$ in 300 ml of $CHCl_3$ and 100 ml of acetone was allowed to stand at room temperature for 1 week. The insoluble material was filtered, then washed with 200 ml of acetone. The combined filtrate and washings were evaporated to dryness and the residual solid was recrystallized from benzene to give 6.80 g (73.2%) of **3**. mp 218—221°. IR ν_{max}^{Nujol} cm^{-1}: 2200, 1593, and 1550 sh. NMR ($CDCl_3$) δ: 8.03 (4H, s), and 8.65 (2H, s). *Anal.* Calcd. for $C_{14}H_6N_4Cl_4$: C, 45.20; H, 1.63; N, 15.06. Found: C, 45.50; H, 1.39; N, 15.04.

2-Methoxymethyleneamino-3,3-dichloroacrylonitrile (4)——A solution of 41.1 g (0.3 mole) of ADAN and 48.9 g (0.33 mole) of triethyl orthoformate in 400 ml of CH_3CN was heated under reflux for 3 hr. After evaporation of the volatiles *in vacuo*, the residual oil was distilled to give 55.6 g (96%) of **4** as a colorless oil, bp 62—63°/3 mmHg.

2-Benzylideneamino-3-chloroacrylonitrile (5)——a) To a stirred solution of 9.0 g (40 mmoles) of **2e** in 300 ml of ether and 15 ml of water was added 5.24 g of zinc powder (Merck) at room temperature and the mixture was further stirred overnight. Vapor-phase chromatography (column, 15% Thermol-3 on 60—80 mesh Shimalite × 1 m; column temperature, 180°) of the reaction mixture revealed that about 50% of the starting material had been consumed at this stage. The insoluble material was removed by filtration and the filtrate washed with water, then dried. After evaporation of the solvent under reduced pressure, the residual oil was chromatographed on silica gel with $CHCl_3$–30% *n*-hexane yielding 1.94 g (43.2% based on **2e** consumed) of **5** and 3.72 g of starting material **2e**.

b) To a solution of 9.0 g (40 mmoles) of **2e** in 100 ml of dioxane and 3 ml of water was added 7.86 g of zinc powder (Merck) at room temperature. The mixture was stirred at room temperature for 2 days. By a work up similar to that given above, 1.91 g (25.1% from **2e** consumed) of **5** and 0.35 g of starting material were isolated.

Attempts to improve the yield of **5** using several commercially available zinc powders or sands were unsuccessful. Compound **5** is rather unstable and should be kept in a refrigerator. mp 65—66° (from pet. ether). IR ν_{max}^{Nujol} cm^{-1}: 3060, 2240, 1613, and 1570. NMR ($CDCl_3$) δ: 7.34 (1H, s), 7.3—7.6 (3H, m), 7.6—8.0 (2H, m), and 8.56 (1H, s). Mass spectrum *m/e* (rel. intensity): 192, 190 (1: 3, M^+, 75%), 155 (M^+—Cl, 100%), 128 (M^+—Cl—HCN, 31%), 104 (35%), 89 (9%), 77 (34%). *Anal.* Calcd. for $C_{10}H_7N_2Cl$: C, 63.01; H, 3.70; N, 14.70. Found: C, 63.10; H, 3.72; N, 14.66.

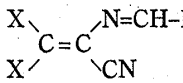
2-Benzylideneamino-3-morpholinoacrylonitrile (6)——To a solution of 0.15 g (0.79 mmole) of **5** in 7 ml of ether was added 0.14 g (1.61 mmoles) of morpholine at room temperature. The mixture was stirred for 1 hr at the same temperature. The insoluble salt was filtered, and washed with ether. The combined filtrate and washings were washed with water, then dried over anhydrous $MgSO_4$. After evaporation of the solvent, the residue was chromatographed on silica gel to yield 183 mg (96%) of **6**. mp 130—131° (from benzene–*n*-hexane). IR ν_{max}^{Nujol} cm^{-1}: 2200, 1633, 1590, and 1568. NMR ($CDCl_3$) δ: 3.15—3.50 (4H, m), 3.58—3.93 (4H, m), 7.27 (1H, s), 7.27—7.80 (5H, m), and 8.20 (1H, s). Mass Spectrum *m/e* (rel. intensity): 241 (M^+, 67%), 240 (100%), 183 (78%), 182 (92%), 164 (19%), 155 (31%), 77 (33%). *Anal.* Calcd. for $C_{14}H_{15}ON_3$: C, 69.69; H, 6.27; N, 17.42. Found: C, 69.73; H, 6.28; N, 17.57.

2-Benzylideneamino-3,3-dialkoxyacrylonitriles (7a, b)——As a typical procedure, the preparation of 2-benzylideneamino-3,3-dimethoxyacrylonitrile (**7a**) is described. To a stirred solution of 10.0 g (44.4 mmoles) of **2e** in 200 ml of MeOH was added dropwise at 0° a methanolic solution of sodium methoxide, prepared from 2.14 g (93 mg atoms) of sodium and 100 ml of MeOH. Next, the mixture was stirred at the same temperature for 3 hr and further allowed to stand overnight at room temperature. The solvent was evaporated *in vacuo* and the resulting solid was extracted with 500 ml of ether. The extract was washed with water then dried. After evaporation of the solvent, the residue was chromatographed on silica gel with $CHCl_3$ giving 6.4 g (66.7 %) of **7a**.

2-Benzylideneamino-3,3-bis(substituted mercapto)acrylonitriles (8a, b)——a) As a typical procedure, the preparation of 2-benzylideneamino-3,3-bisphenylthioacrylonitrile (**8b**) is described. To a stirred solution of 2.25 g (10 mmoles) of **2e** in 200 ml of ether was added a solution of 2.31 g (21 mmoles) of thiophenol and 2.12 g (21 mmoles) of triethylamine in 10 ml of ether. The mixture was stirred overnight at room temperature. The mixture was washed with water, then dried. After evaporation of the solvent, the resulting solid was washed with a little MeOH to give 3.28 g (88.2%) of **8b** as a yellow solid.

b) To a solution of 2.84 g (10 mmoles) of **9b**[2] and 1.12 g (10.5 mmoles) of benzaldehyde in 50 ml of benzene was added 1 g of anhydrous $MgSO_4$. The mixture was allowed to stand at room temperature for 7 days. The insoluble inorganic material was removed by filtration and washed with benzene. The combined filtrate and washings were evaporated *in vacuo* and the resulting solid was washed with a little amount of MeOH to afford 3.39 g (91.3%) of **8b**.

Table IV. Schiff Bases of ADAN and Their Derivatives

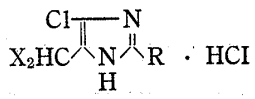

(**2**,**4**,**7**,**8**, and **10**)

Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR ($CDCl_3$) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
2a	2240, 1600	1.00 (3H, t, J=7.0 Hz), 2.30—2.80 (2H, m), 8.10 (1H, t, J=4.0 Hz)	$C_6H_6N_2Cl_2$	—	—	—
2b	2200, 1620, 1580, 1560, 1545	5.80—7.06 (3H, m), 8.17 (1H, d, J=9.0 Hz)	$C_6H_4N_2Cl_2$	—	—	—
2c	2225, 1628, 1600[a]	—	$C_7H_8N_2Cl_2$	—	—	—
2d[b]	2230, 1600, 1572	7.38—8.00 (5H, m), 8.58 (1H, s)	$C_{10}H_6N_2Br_2$	38.41 (38.25)	1.75 (1.93)	9.21 (8.92)
2e[c]	2220, 1612, 1573	7.40—8.05 (5H, m), 8.56 (1H, s)	$C_{10}H_6N_2Cl_2$	53.24 (53.36)	2.47 (2.69)	12.51 (12.45)
2f	2200, 1605, 1560	2.36 (3H, s), 7.23 (2H, d, J=8.0 Hz), 7.76 (2H, d, J=8.0 Hz), 8.47 (1H, s)	$C_{11}H_8N_2Cl_2$	55.12 (55.26)	3.21 (3.37)	11.79 (11.72)
2g	2230, 1600sh, 1592 1556	7.20—7.50 (3H, m), 8.02—8.28 (1H, m), 9.00 (1H, s)	$C_{10}H_5N_2Cl_3$	46.62 (46.28)	1.95 (1.94)	10.72 (10.80)
2h	2220, 1615, 1598. 1568, 1557	7.48 (2H, d, J=9.0 Hz), 7.90 (2H, d, J=9.0 Hz), 8.48 (1H, s)	$C_{10}H_5N_2Cl_3$	46.48 (46.28)	1.83 (1.93)	10.79 (10.79)
2i	2200, 1610, 1590, 1552	7.46—7.94 (4H, m), 8.50 (1H, s)	$C_{10}H_5N_2BrCl_2$	39.56 (39.51)	1.66 (1.66)	9.22 (9.22)
2j	3060, 2210, 1600, 1556	3.94 (3H, s), 6.80—8.30 (3H, m), 9.01 (1H, s)	$C_{11}H_8ON_2Cl_2$	51.88 (51.79)	2.90 (3.16)	11.01 (10.98)
2k	3050, 2210, 1613, 1578	3.80 (3H, s), 6.80—7.50 (4H, m), 8.47 (1H, s)	$C_{11}H_8ON_2Cl_2$	51.91 (51.79)	3.06 (3.16)	11.07 (10.98)
2l	2200, 1608, 1570, 1555	3.85 (3H, s), 6.95 (2H, d, J=9.0 Hz), 7.86 (2H, d, J=9.0 Hz), 8.46 (1H, s)	$C_{11}H_8ON_2Cl_2$	51.60 (51.79)	3.33 (3.16)	11.09 (10.98)
2m	2220, 1605, 1600, 1580, 1560, 1512	3.91 (6H, s), 6.76—7.60 (3H, m), 8.30 (1H, s)	$C_{12}H_{10}O_2N_2Cl_2$	51.02 (50.72)	3.50 (3.52)	9.65 (9.79)
2n	2205, 1620sh, 1612, 1590	6.12 (2H, s), 7.00—7.75) (3H, m), 8.27 (1H, s)	$C_{11}H_6O_2N_2Cl_2$	48.95 (49.10)	2.09 (2.25)	10.56 (10.41)
2o[e]	3500—3300, 2240, 1620, 1605, 1572, 1560	6.80—7.50 (4H, m), 8.62 (1H, s), 11.79 (1H, br)	$C_{10}H_6ON_2Cl_2$	50.19 (49.82)	2.14 (2.51)	11.63 (11.62)
2p	3500, 3080, 2230, 1613, 1592	3.83 (3H, s), 6.75—7.60 (3H, m)[d]	$C_{11}H_8O_2N_2Cl_2$	48.82 (48.73)	2.79 (2.97)	10.32 (10.33)
2q[f]	3450, 3300, 2225, 1623, 1598, 1550	6.35 (2H, br), 6.50—6.85 (2H, m), 7.07—7.40 (2H, m), 8.56 (1H, s)	$C_{10}H_7N_3Cl_2$	50.45 (50.02)	2.92 (2.94)	17.51 (17.50)
2r	2210, 1613, 1595, 1530	3.03 (6H, s), 6.64 (2H, d, J=8.5 Hz), 7.70 (2H, d, J=8.5 Hz), 8.34 (1H, s)	$C_{12}H_{11}N_3Cl_2$	53.50 (53.75)	4.09 (4.14)	15.67 (15.67)
2s[g]	2235, 1608, 1568, 1520	7.60—8.30 (4H, m), 9.07 (1H, s)	$C_{10}H_5O_2N_3Cl_2$	44.98 (44.47)	1.46 (1.87)	15.71 (15.56)
2t	3060, 2210, 1612, 1579, 1522	7.58—8.80 (4H, m), 8.64 (1H, s)	$C_{10}H_5O_2N_3Cl_2$	44.21 (44.47)	1.70 (1.87)	15.62 (15.56)
2u	3100, 2210, 1615, 1593, 1560, 1520	8.05 (2H, d, J=9.0 Hz), 8.34 (2H, d, J=9.0 Hz), 8.63 (1H, s)	$C_{10}H_5O_2N_3Cl_2$	44.40 (44.47)	1.86 (1.87)	15.40 (15.56)
2v	3050, 2200, 1622, 1600, 1583, 1510	7.15—8.10 (6H, m), 8.67—9.27 (1H, m), 8.90 (1H, s)	$C_{14}H_8N_2Cl_2$	61.11 (61.12)	2.79 (2.93)	10.27 (10.18)
2w	3110, 3050, 2215, 1640sh, 1615, 1545	6.57 (1H, q, J=3.8 Hz, J=2.0 Hz), 7.12 (1H, d, J=3.8 Hz), 7.69 (1H, d, J=2.0 Hz), 8.30 (1H, s)	$C_8H_4ON_2Cl_2$	44.55 (44.68)	1.54 (1.88)	13.00 (13.03)
2x	3080, 2230, 1600, 1556	7.10 (1H, t, J=4.4 Hz), 7.38—7.70 (2H, m), 8.57 (1H, s)	$C_8H_4N_2SCl_2$	41.68 (41.58)	1.61 (1.74)	12.15 (12.12)
2y	3250, 2230, 1610, 1590sh, 1550	7.20—8.40 (5H, m), 8.34 (1H, s), 13.67 (1H, br)[d]	$C_{13}H_7N_4Cl_3 \cdot 1/2H_2O$	46.70 (46.67)	2.19 (2.41)	17.03 (16.74)
4	2240, 1630, 1583[a]	1.37 (3H, t, J=9.0 Hz), 4.35 (2H, q, J=9.0 Hz), 8.03 (1H, s)	$C_6H_6ON_2Cl_2$	37.33 (37.33)	3.05 (3.13)	14.62 (14.51)

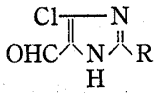
Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR ($CDCl_3$) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
7a	3050, 2200, 1610, 1587, 1570sh	3.88 (3H, s), 4.44 (3H, s), 7.20—7.80 (5H, m), 8.12 (1H, s)	$C_{12}H_{12}O_2N_2$	66.98 (66.65)	5.70 (5.59)	12.99 (12.96)
7b	3050, 2180, 1608, 1580, 1565	1.20—1.66 (6H, t×2, J=7.0 Hz, J=7.2 Hz), 4.20 (2H, q, J=7.0 Hz), 4.90 (2H, q, J=7.2 Hz), 7.20—7.82 (5H, m), 8.10(1H, s)	$C_{14}H_{16}O_2N_2$	68.81 (68.83)	6.80 (6.60)	11.46 (11.47)
8a	3050, 2180, 1598, 1570, 1560	2.54 (3H, s), 2.61 (3H, s), 7.30—8.05 (5H, m), 8.46 (1H, s)	$C_{12}H_{12}N_2S_2$	58.26 (58.03)	4.72 (4.87)	11.31 (11.28)
8b	3050, 2190, 1605, 1572	6.80—8.04 (15H, m), 8.52(1H, s)	$C_{22}H_{16}N_2S_2$	70.77 (70.94)	4.18 (4.33)	7.66 (7.52)
10a	3270, 3070, 2200, 1595, 1570, 1550, 1530	0.7—2.35 (20H, br), 3.00—3.90 (2H, br), 4.18 (1H, br d, J=*ca.* 9 Hz), 5.97 (1H, br d, J=*ca.* 10 Hz), 7.20—7.75 (5H, m), 7.97 (1H, s)	$C_{22}H_{30}N_4$	75.21 (75.39)	8.67 (8.63)	16.12 (15.98)
10b	3050, 2190, 1608, 1586, 1570	3.20—3.54 (8H, m), 3.60—3.96 (8H, m), 7.20—7.80 (5H, m), 8.12 (1H, s)	$C_{18}H_{22}O_2N_4$	65.95 (66.24)	7.05 (6.79)	17.02 (17.17)
10c[h]	3050, 2180, 1590, 1568, 1515	1.50—1.86 (12H, br), 3.14—3.50 (8H, br), 7.20—7.80 (5H, m), 8.08 (1H, s)	$C_{20}H_{26}N_4$	74.55 (74.49)	7.99 (8.13)	17.31 (17.38)

a) as liquid film
b) Mass Spectrum *m/e* (rel. intensity): 316, 314, 312 (1:2:1, M$^+$, 100%), 235, 233 (1:1, 55%), 154 (93%), 127 (53%), 104 (70%), 103 (34%), 89 (30%), 77 (70%), 51 (97%), 50 (48%)
c) Mass Spectrum *m/e* (rel. intensity): 228, 226, 224 (1:6:9, M$^+$, 90%), 227, 225, 223 (1:6:9, 40%), 191, 189 (1:3, 100%), 164, 162 (1:3, 16%), 153 (20%), 104 (33%), 89 (11%), 77 (30%), 51 (28%)
d) in d_6-DMSO
e) Mass Spectrum *m/e* (rel. intensity): 244, 242, 240 (1:6:9, M$^+$, 45%), 207, 205 (1:3, 100%), 120 (29%)
f) Mass Spectrum *m/e* (rel. intensity): 243, 241, 239 (1:6:9, M$^+$, 56%) 206, 204 (1:3, 17%), 169 (4%), 143 (15%), 119 (100%), 92 (15%)
g) Mass Spectrum *m/e* (rel. intensity): 273, 271, 269 (1:6:9, M$^+$, 63%), 256, 254, 252 (1:6:9, 57%), 189, 187 (89%), 165, 163, 161 (1:6:9, 58%), 134 (85%), 104 (100%)
h) Mass Spectrum *m/e* (rel. intensity): 323 (M$^+$+1, 26%), 322 (M$^+$, 100%), 238 (26%), 84 (99%)

TABEL V. 2-Substituted-4(5)-chloro-5(4)-dihalogenomethylimidazole Hydrochlorides (**11**) and 2-Substituted-4(5)-chloroimidazole-5(4)-carbaldehydes (**12**)



11



12

Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR (d_6-DMSO) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
11a[a]	3250—3000, 2800—2150, 1700, 1630, 1550	7.35—7.60 (3H, m), 8.00—8.30 (2H, m), 9.77 (1H, s), 14.15 (2H, br)	$C_{10}H_8N_2Cl_4$	39.97 (40.30)	2.57 (2.71)	9.36 (9.40)
11b[b]	3250—3000, 2800—2100, 1690, 1630, 1545	7.32—7.70 (3H, m), 7.98—8.35 (2H, m), 9.75 (1H, s), 13.20 (2H, br)	$C_{10}H_8N_2Br_2Cl_2$	—	—	—
11c[c]	3300—3000, 2750—2150, 1700, 1630, 1545	7.35—7.85 (4H, m), 9.76 (1H, s), 13.90 (2H, br)	$C_{10}H_7N_2Cl_5$	—	—	—
11d	3250—3000, 2800—2100, 1700, 1630, 1555	—	$C_{10}H_7N_2BrCl_4$	—	—	—
11e	—	—	$C_{10}H_7O_2N_3Cl_4$	—	—	—
11f[d]	3350—3000, 2800—2200, 1630, 1610, 1600sh, 1550	6.65—7.60 (3H, m), 8.00—8.22 (1H, m), 9.82 (1H, s), 13.42 (3H, br)	$C_{10}H_8ON_2Cl_4$	—	—	—

Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR (d_6-DMSO) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
11g	3300—3000, 2800—2150, 1632, 1610sh, 1555	—	$C_{11}H_8O_2N_2Cl_4$	—	—	—
11h	3250—3000, 2800—2100, 1620, 1590, 1540	—	$C_{14}H_{10}N_2Cl_4$	—	—	—
11i	—	—	$C_8H_6N_2SCl_4$	—	—	—
12a[e]	3220, 3150sh, 1650, 1620, 1555, 1510	7.35—7.60 (3H, m), 7.95—8.28 (2H, m), 9.71 (1H, s), 13.90 (1H, br)	$C_{10}H_7ON_2Cl$	58.14 (58.12)	3.25 (3.41)	13.56 (13.56)
12c	3260, 3060, 1672, 1600, 1570, 1510	7.30—7.85 (4H, m), 9.77 (1H, s), 14.00 (1H, br)	$C_{10}H_6ON_2Cl_2$	49.45 (49.82)	2.42 (2.51)	11.28 (11.62)
12d	3250, 3160sh, 3090, 1648, 1630sh, 1600, 1510	7.50 (2H, d, J=9.0 Hz), 7.97 (2H, d, J=9.0 Hz), 9.75 (1H, s), 14.05 (1H, br)	$C_{10}H_6ON_2BrCl$	41.71 (42.07)	1.98 (2.12)	9.75 (9.81)
12e	3200—3000, 1668, 1630, 1555, 1520	7.60—8.24 (4H, m), 9.73 (1H, s), 14.20 (1H, br)	$C_{10}H_6O_3N_3Cl$	47.92 (47.73)	2.15 (2.40)	16.35 (16.70)
12f[f]	3230, 3150sh, 3080, 1650, 1628sh, 1590, 1520	3.44 (1H, br). 6,76—7.56 (3H, m), 7.94—8.20 (1H, m), 9.80 (1H, s), 14.10 (1H, br)	$C_{10}H_7O_2N_2Cl$	54.09 (53.95)	3.19 (3.17)	12.66 (12.58)
12g	3245, 3180sh, 3070, 1650, 1620, 1605sh, 1520	6.06 (2H, s), 6.95 (1H, d, J=9.5 Hz), 7.55—7.85 (2H, m), 9.67 (1H, s), 13.60 (1H, br)	$C_{11}H_7O_3N_2Cl$	52.65 (52.71)	2.64 (2.82)	11.12 (11.18)
12h	3200—3000, 1675, 1580, 1552, 1513	7.35—8.20 (6H, m), 8.40—8.60 (1H, m), 9.83 (1H, s), 14.03 (1H, br)	$C_{14}H_9ON_2Cl$	65.64 (65.51)	3.13 (3.53)	10.81 (10.91)
12i	3210, 3150sh, 3075, 1642, 1590, 1580, 1526	7.13 (1H, t, J=4.0 Hz), 7.67 (1H, d, J=4.0 Hz), 7.90 (1H, d, J=4.0 Hz), 9.67 (1H, s), 14.00 (1H, br)	$C_8H_5ON_2SCl$	45.21 (45.18)	2.28 (2.37)	13.24 (13.17)

a) Mass Spectrum *m/e* (rel. intensity): 228, 226, 224 (1: 6: 9, M^+-2 HCl, 50%), 191, 189(1: 3, $M^+-2HCl-Cl$, 100%), 104 (13%), 103 (7%), 77 (17%)

b) Mass Spectrum *m/e* (rel. intensity): 272, 270, 268 (1: 4: 3, $M^+-HCl-HBr$, 9%), 236, 234 (1: 1, 3%), 235, 233 (1: 1, 16%), 228, 226, 224 (1: 6: 9, 38%), 191, 189 (1: 3, 100%), 128 (16%), 104 (37%), 103 (19%), 82,80 (1: 1, 44%), 77 (40%)

c) Mass Spectrum *m/e* (rel. intensity): 303, 301, 299, 295, 293 (1: 12: 54: 108: 81, $M^+-HCl-H$, 2%) 265, 263, 261, 259 (1: 9: 27: 27, 24%), 264, 262, 260, 258 (1: 9: 27: 27, 33%), 228, 226, 224 (1: 6: 9, 13%), 227, 225, 223 (1: 6: 9, 100%), 164, 162 (1: 3, 7%), 140, 138 (1: 3, 13%), 113, 111 (1: 3, 7%), 102 (12%)

d) Mass Spectrum *m/e* (rel. intensity): 245, 243, 241 (1: 6: 9, $M^+-HCl-H$, 13%), 244, 242, 240 (1: 6: 9, 100%), 208, 206 (1: 3, 99%)

e) Mass Spectrum *m/e* (rel. intensity): 209, 207 (1: 3, M^++1, 13%), 208, 206 (1: 3, M^+, 100%), 205 (31%), 180, 178 (1: 3, 2%), 179, 177 (1: 3, 3%), 171 (36%), 152, 150 (1: 3, 40%), 116 (19%), 104 (25%), 103 (9%), 89 (25%), 77 (20%)

f) Mass Spectrum *m/e* (rel. intensity): 225, 223 (1: 3, M^++1, 14%), 224, 222 (1: 3, M^+, 100%), 223, 221 (1: 3, 8%), 196, 194 (1: 3, 3%), 195, 193 (1: 3, 2%), 187 (20%), 186 (17%), 132 (14%)

2-Benzylideneamino-3,3-bis(substituted amino)acrylonitriles (10a—c)——As a typical procedure, the preparation of 2-benzylideneamino-3,3-biscyclohexylaminoacrylonitrile (**10a**) is described. To a stirred solution of 22.5 g (0.1 mole) of **2e** in 500 ml of ether was added dropwise, with ice cooling, a mixture of 20.8 g (0.21 mole) of triethylamine. The mixture was stirred at room temperature for 3 hr. The insoluble material was removed by filtration and washed with ether. The combined filtrate and washings were evaporated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$ yielding 27.6 g (78.8%) of **10a** as a pale yellow solid.

General Procedure for the Preparation of 2-Substituted-4(5)-chloro-5(4)-dichloromethylimidazole Hydrochlorides (11a—i)——Anhydrous hydrogen chloride was bubbled through a solution of 20 mmoles of **2** in 200 ml of anhydrous ether with ice-cooling until saturation. The HCl-saturated solution was allowed to stand at room temperature for 3 days. The resulting precipitate was collected by filtration and washed with a small amount of cold ether to obtain **11**, as an almost colorless solid.

General Procedures for the Preparation of 2-Substituted-4(5)-chloroimidazole-5(4)-carbaldehydes (12a—i)——a) A slurry of 10 g of **11** in 250 ml of EtOH–H_2O (1: 1, v/v) was heated until all the solid dissolved. The mixture was cooled and the precipitate formed was collected by filtration to give **12** as colorless needles. The filtrate was concentrated *in vacuo* to a volume of about 50 ml. The resulting solid was filtered off and washed with water to afford a further crop of **12**.

b) A suspension of 40 mmoles of **11** in 200 ml of water was heated at around 90° for 30 min. The mixture was cooled and filtered to give **12** in almost quantitative yield.

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