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Studies of Nitriles. VIII.[1] Reactions of N-Acyl Derivatives of 2-Amino-3,3-dichloroacrylonitrile (ADAN) with Amines. (1). A New Synthesis of 2-Substituted-5-(substituted amino)oxazole-4-carbonitriles and -4-N-acylcarboxamides

Koichi Matsumura, Takahiro Saraie, and Naoto Hashimoto

Chemical Research Laboratories, Central Research Division, Takeda Chemical Industries, Ltd.[2]

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2-Acetylamino-3,3-dichloroacrylonitrile (**1a**) reacted with 2 molar eq. of mercaptides and alkoxides to yield 2-acetylamino-3,3-bis-(substituted mercapto)acrylonitriles (**2**) and 2-acetylamino-3,3,3-trialkoxypropionitriles (**4**), respectively, in high yields. In contrast to these results, we found that the reaction of **1a** with various aliphatic primary and secondary amines including ammonia and hydrazine gave 2-methyl-5-(substituted amino)oxazole-4-carbonitriles (**6**) in almost quantitative yields under mild conditions. Reaction of **1a** with bifunctional amines such as ethylenediamine and aminoethanethiol generated other types of cyclization products, *e.g.*, imidazolidine and thiazolidine derivatives (**8a, b**), as major products. Treating **1** or 2-amino-3,3-dichloroacrylonitrile (ADAN) with various acid anhydrides in the presence of conc. sulfuric acid catalyst resulted in a new one-step synthesis of imidic compounds, 2-acylamino-3,3-dihalogeno-N-acylacrylamides (**21**). The reaction of **21** with aliphatic secondary amines yielded 2-substituted-5-(substituted amino)oxazole-4-N-acylcarboxamides (**32**). The mechanism of the cyclization to oxazoles and the formation of imidic compounds are discussed.

In the preceding paper[1,3] we reported the synthesis and properties of 2-amino-3,3-dichloroacrylonitrile (ADAN), a versatile polyfunctional synthetic intermediate. In this paper, we report the result of investigation of chemical properties of 2-acylamino-3,3-dihalogenoacrylonitriles (**1**), the N-acyl derivatives of ADAN and 2-amino-3,3-dibromoacrylonitrile[1] (**7**).

Although normal substitutions were observed in the reaction of **1a** with alkoxides or mercaptides, **1a** reacted with various aliphatic primary and secondary amines to give 2-substituted-5-(substituted amino)oxazole-4-carbonitriles (**6**) instead of **5**, as expected. After we had published our preliminary results,[3] similar reactions were reported by B.S. Drach and co-workers.[4] Investigation of the scope and limitations of this new cyclization with various N-acyl derivatives and imidic compounds derived from ADAN, and also some mechanistic discussions are presented.

Results and Discussion

Compound (**1a**) reacted readily with excess aqueous methylamine (4 molar eq.) in ethanol at 0° affording 2-methyl-5-methylaminooxazole-4-carbonitrile (**6c**).

The structure of **6c** was confirmed by its nuclear magnetic resonance (NMR) spectrum, which shows a sharp singlet due to three protons at δ 2.28, this indicates considerably more deshielding than that of $NHCO\underline{CH}_3$ protons and can be assigned to the protons of a methyl

1) Part VII: K. Matsumura, T. Saraie, and N. Hashimoto, *Chem. Pharm. Bull.* (Tokyo), **24**, 912 (1976).
2) Location: *Jusohonmachi, Yodogawa-ku, Osaka, 532, Japan.*
3) Part VI: K. Matsumura, T. Saraie, and N. Hashimoto, *Chem. Commun.*, **1972**, 705.
4) *a*) B. S. Drach, É.P. Sviridov, A.A. Kisilenko, and A.V. Kirsanov, *Zh. Org. Khim.*, **9**, 1818 (1973) [*J. Org. Chem. USSR* (Eng. Trans.), **9**, 1842 (1973)]; *b*) B.S. Drach, É.P. Sviridov, and T.Y. Lavrenyuk, *Zh. Org. Khim.*, **10**, 1271 (1974) [*J. Org. Chem. USSR* (Eng. Trans.), **10**, 1278 (1974)].

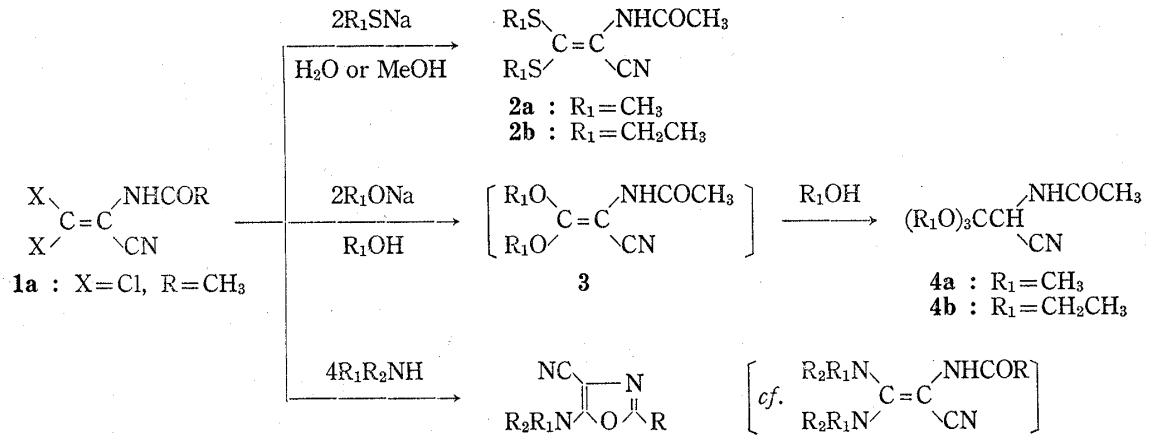
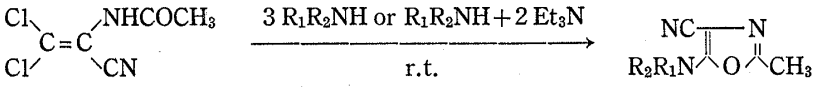


Chart 1

TABLE I. Preparation of 2-Methyl-5-(substituted amino)oxazole-4-Carbonitriles (**6a—p**)



Compd. No.	6 R_1 (R_2=H)	Yield (%)	Reaction conditions: Solv.[a]	Reaction conditions: Method[b]	mp (°C) (lit. mp)	Recryst. solvent[a]
6a	H	22 / 56[c]	E[d]	A[e] / A[f]	152—153 (152.5—154.5)[g]	B
6b[h]	NH_2	88	E	A	163—165 (decomp.)	E
6c	CH_3	98	E-W	A	116—117 (119—121)[i]	B
6d	CH_2CH_3	99	E-W	A	63— 64 (54—56)[i]	H
6e	$CH_2CH_2CH_3$	99	W	A	53—54	H
6f	$CH(CH_3)_2$	99	A	A	45—46	B-H
6g	$CH_2CH=CH_2$	95	A	A	42—43	B-H
6h	CH_2CH_2CN	95	E	B	59—60	ET
6i	$CH_2CH(OEt)_2$	98	E	B	56—57	P
6j	$CH_2CH_2CH_2CH_3$	96	ET	A	oil	—
6k	$CH(CH_3)CH_2CH_3$	98	E	A	41— 42	B-H
6l	$CH_2CH(CH_3)_2$	98	A	A	56— 57.5 (58)[i]	P
6m	$C(CH_3)_3$	55[j]	E	A	88—90	P
6n	$CH_2(CH_2)_4CH_3$	99	E	B	37— 38.5	ET
6o		98	B	A	84— 85	H
6p	CH_2-C_6H_5	96	E	B	82— 83.5 (80—82)[i]	B

r.t.=room temp.
a) A=acetonitrile, B=benzene, E=ethanol, ET=ether, H=*n*-hexane, P=pet. ether, W=water
b) See the experimental section.
c) based on **1a** consumed
d) reaction temperature=80°
e) Gaseous ammonia was used.
f) CH_3COONH_4 was used.
g) *cf.* reference 5)
h) hydrazone derivatives: **6b'**: R_1=N=C$(CH_3)_2$, R_2=H, mp 136—138° (from benzene)
6b'': R_1=N=CH-C_6H_5, R_2=H, mp 202—203° (decomp.) (from benzene)
i) *cf.* reference 4*b*)
j) 63% yield (based on **1a** consumed)

group attached to an aromatic ring together with absorptions at δ 3.03 (d, J=5.0 Hz, CH_3) and δ 5.52 (br, NH) due to the 5-methylamino group. Further structural proof was obtained from elemental analysis and its mass (*m/e* 137, M^+, 100%) and infrared (IR) spectra.

Changing the solvent from ethanol to water, ether, or acetonitrile did not alter the result.

In order to examine the generality of this new cyclization, the reaction of **1a** with various amines including ammonia and hydrazine in ethanol, ether, benzene, acetonitrile, or water as solvent was undertaken.

When **1a** and primary amines, except ammonia, were allowed to react under mild conditions (0—30°), the expected oxazoles (**6b—p**) were obtained in almost quantitative yields after purification by silica gel chromatography (Table I).

Similar excellent results were obtained by treating **1a** both with 3 molar eq. of primary amines (method A) or a mixture of 1 molar eq. of primary amines and 2 molar eq. of triethylamine (method B).

Since **1a** did not react with ammonia at ordinary temperature, the reaction was carried out in refluxing ethanol to give the expected 2-methyl-5-aminooxazole-4-carbonitrile[5] (**6a**), however, the yield of **6a** was as low as 22% due to accompanying decomposition of **1a** under these conditions. A moderately improved yield of **6a** was obtained with excess ammonium acetate in place of gaseous ammonia under similar conditions.

Reaction of **1a** with hydrazine hydrate in ethanol at 0° resulted in a similar cyclization to 2-methyl-5-hydrazinooxazole-4-carbonitrile (**6b**). The structure was confirmed by spectral data, elemental analysis, and also hydrazone (**6b′**, **b″**)-formation with aldehydes.

In the case of *t*-butylamine, even with 3.3 molar eq. of the amine, the yield of **6m** was only 55% and the starting material (**1a**, 21%) was recovered, probably due to steric hindrance.

Similar treatment of **1a** with aliphatic secondary amines such as diethylamine, morpholine, and piperidine yielded 2-substituted-5-(substituted amino)oxazole-4-carbonitriles (**6q—s**) in almost quantitative yields (Table II).

Table II. Preparation of 2-Methyl-5-(substituted amino)-oxazole-4-carbonitriles (**6q—t**)

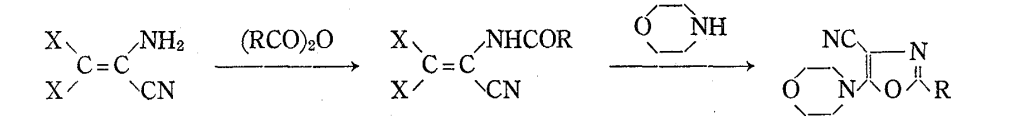
Compd. No.	**6** NR_1R_2	Yield (%)	Reaction conditions Solv.[a]	Method[b]	mp (°C) (lit. mp or bp)	Recryst. solvent[a]
6q	$N(CH_2CH_3)_2$	98	A	A	oil (bp 89—94/0.05)[c]	—
6r		98	A	A	81—82 (77—80)[c]	P
		98	E	B		
6s		97	E	A	46—47 (42—43)[c]	B-H
6t	$NHCH_2CH_2Cl$[d]	36	A	A	54—56	B-H

a) A=acetonitrile, B=benzene, E=ethanol, H=*n*-hexane, P=pet. ether
b) See the experimental section.
c) *cf.* reference 4*a*)
d) Ethylene imine was used as the starting amine. The expected oxazole (NR_1R_2=, **6t′**) was not obtained.

However, reaction of **1a** with ethyleneimine produced only 2-methyl-5-(β-chloroethylamino)oxazole-4-carbonitrile (**6t**) derived from ring opening of the expected aziridino compound (**6t′**).

Further examination of this cyclization was carried out using various 2-acylamino-3,3-dihalogenoacrylonitriles (**1b—g**), prepared almost quantitatively from reactions of ADAN or 2-amino-3,3-dibromoacrylonitrile[1] (**7**) with acylating reagents as shown in Chart 2.

5) J.P. Ferris and L.E. Orgel, *J. Am. Chem. Soc.*, **88**, 3829 (1966).



ADAN: X=Cl
7: X=Br

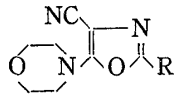
1b : X=Cl, R=H
1c : X=Br, R=CH_3
1d : X=Cl, R=CF_3
1e : X=Br, R=CF_3
1f : X=Cl, R=CH_2CH_3
1g : X=Cl, R=$CH_2CH_2CH_3$

6u : R=H
6r : R=CH_3
6v : R=CF_3
6v : R=CF_3
6w : R=CH_2CH_3
6x : R=$CH_2CH_2CH_3$

Chart 2

When **1b**—**g** were allowed to react with morpholine, which was selected because it often gives crystalline oxazoles, the corresponding 2-substituted-5-morpholinooxazole-4-carbonitriles (**6r**, **u**—**x**) were obtained in excellent yields under similar mild conditions (Table III).

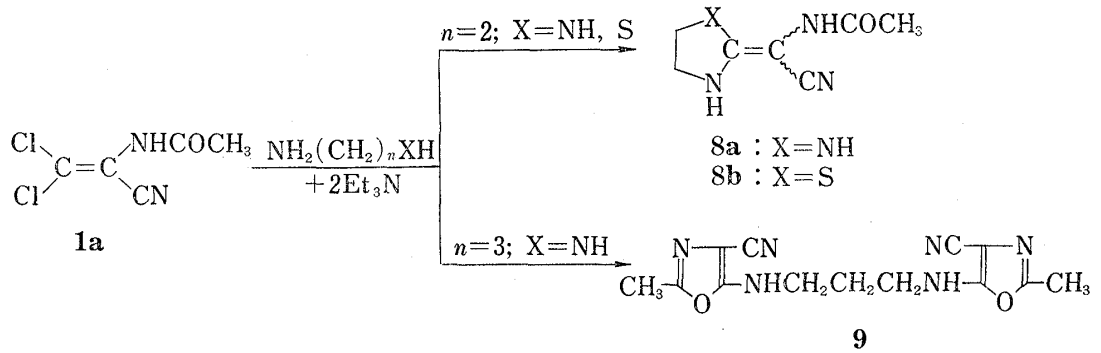
TABLE III. Preparation of 2-Substituted-5-morpholinooxazole-4-carbonitriles (**6r**, **u**—**x**)



Compd. No.	**6** R	Starting material	Yield (%)	mp (°C) (lit. mp)	Recryst. solvent[a]
6u	H	**1b**	90	112—113	B
6r	CH_3	**1c**	99	81—82 (77—80)[b]	P
6v	CF_3	**1d**	98	46—47	P
		1e	97		
6w	CH_2CH_3	**1f**	99	89—91	P
6x	$CH_2CH_2CH_3$	**1g**	98	34— 35	H

a) B=benzene, H=*n*-hexane, P=pet. ether
b) *cf.* reference 4*a*)

When treated with bifunctional amines such as ethylenediamine and aminoethanethiol, **1a** yielded other cyclization products (Chart 3).



1a

8a : X=NH
8b : X=S

9

Chart 3

Thus, the reaction of **1a** with 1 molar eq. of ethylenediamine in the presence of 2 molar eq. of bases (NaOH or triethylamine) afforded a compound, mp 198—212° (decomp.) (from CH_3CN), in moderate to good yields. At first, the compound was considered to be the expected 2-methyl-5-(β-aminoethylamino)oxazole-4-carbonitrile, from the results of its IR spectrum (ν_{max}^{Nujol} cm^{-1}: 3450—3140, 2160, 1660, 1640, and 1520), mass spectrum (*m/e*: 166 (M^+, 25%), 123 (M^+-43, 100%)), and elemental analysis ($C_7H_{10}ON_4$, mol.wt. 166.184). However, the NMR

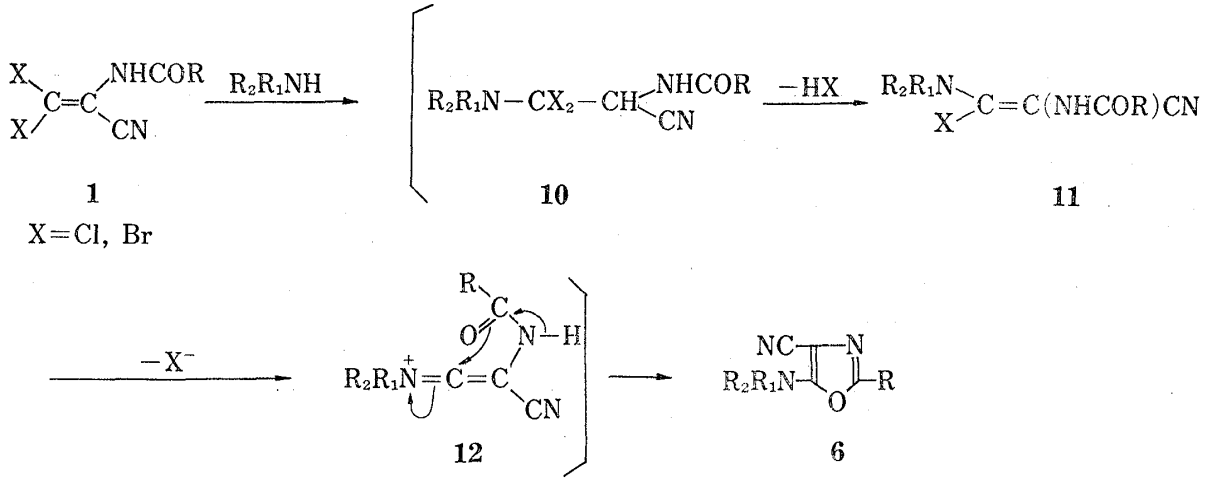
spectrum (d_6-DMSO, δ: 1.84 (3H, s), 3.43 (4H, s), 6.44 (1H, br), 6.55 (1H, br), and 8.14 (1H, br)) did not agree with the structure, because the characteristic absorption[6] (δ 2.2—2.5) of the 2-methyl protons on the oxazole ring was absent and there were absorptions of three different protons. These data indicated the structure, 2-(acetylamino-cyanomethylene)imidazolidine (**8a**), an alternative five-membered cyclic product.

Similarly, 2-(acetylamino-cyanomethylene)thiazolidine (**8b**) was obtained in 81% from **1a** and aminoethanethiol under conditions like those given above. Its structure was ascertained by spectral data and elemental analysis.

With trimethylenediamine, however, a product showing a sharp singlet at δ 2.22 in the NMR spectrum was obtained and identified with the expected oxazole (**9**).

Thin-layer chromatography (TLC) analysis of the reaction mixtures showed that formations of **8a, b** and **9** were almost exclusive, although the presence of two to three by-products was noticed.

These results seem to suggest that the intrinsic nucleophilicity of the amide oxygen is not large and formation of the oxazole requires the presence of a more reactive species than the starting material used.



1 X=Cl, Br **10** **11** **12** **6**

Chart 4

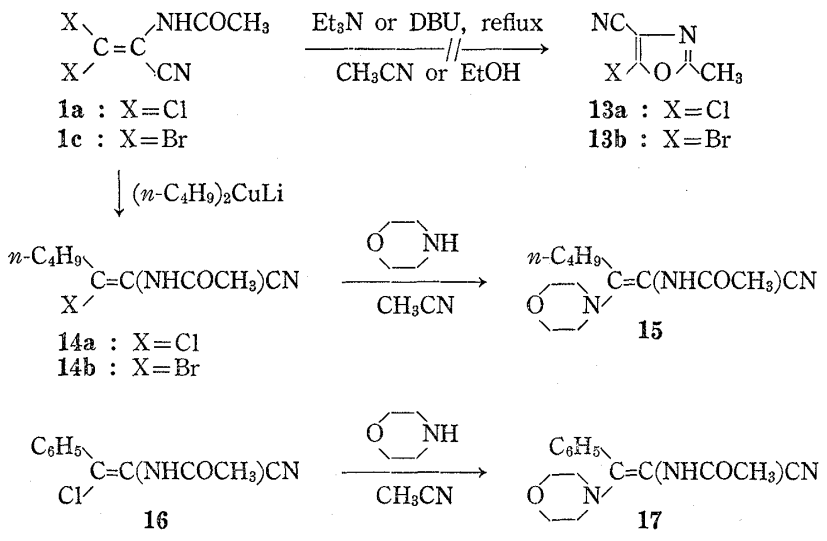


Chart 5

6) R. Lakhan and B. Ternai, "Advance in Heterocyclic Chemistry," Vol. 17, ed. by A.R. Katritzky, and A.J. Boulton, Academic Press, Inc., New York, 1974, pp. 164—168.

We propose a mechanism (Chart 4) which involves the formation of a ketenimmonium salt as a probable reactive intermediate.

To check the validity of this assumption, we tried the following reactions (Chart 5).

When treated with triethylamine or a strong base such as 1,5-diazabicyclo[5,4,0]undecene-5 (DBU), **1a** and **1c** did not give the expected 5-halogenooxazole **13** and the reactions resulted in almost complete recovery of the starting materials.

Next, we tried the reaction of **14a, b** and **16** with morpholine. The starting materials, **14a, b** and **16**, were easily obtained by the action of di-*n*-butylcopperlithium[7] on **1a, c** and by reductive acetylation of 2-imino-3,3-dichloro-3-phenylpropionitrile,[1] respectively. In each case, a single isomer was obtained, although the configuration was not determined. When **14a, b** and **16** were allowed to react with morpholine, only simple substitution products (**15**) and (**17**), respectively, were obtained.

In an attempt to obtain the 3,3-diamino derivative (**19**), 2-diacetylamino-3,3-dichloroacrylonitrile[1] (**18**) was allowed to react with morpholine or cyclohexylamine to give oxazoles (**6o, r**) and N-substituted acetamide (**20a, b**), both in quantitative yields; this revealed the lability of the second acetyl group towards amines (Chart 6).

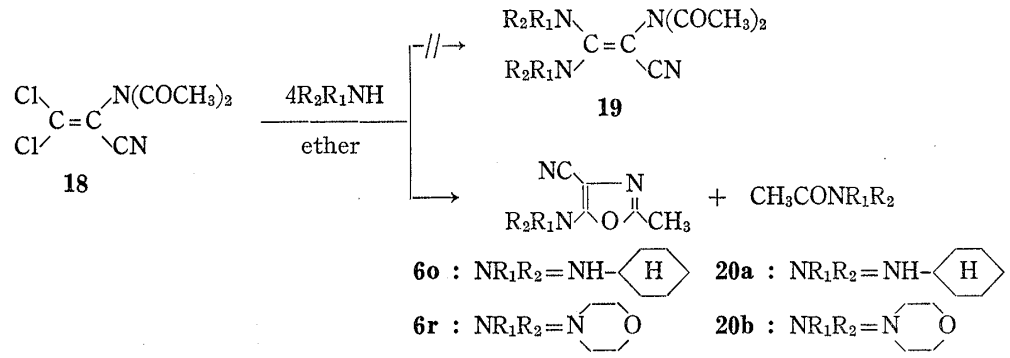


Chart 6

In the previous paper,[1,3] we described the synthesis of N-monoacetyl derivative (**1a**) from ADAN, and N,N-diacetyl derivative (**18**) from ADAN or **1a** depending upon the conditions employed. This time we found that, when treated with acetic anhydride in the presence of a catalytic amount of conc. sulfuric acid, ADAN yields a third acetyl derivative, mp 174—178° (decomp.) (from CH_3CN), in excellent yield. The same compound was prepared by treating **1a** with a mixture of acetic anhydride and acetic acid in the presence of a conc. sulfuric acid catalyst at 80° for a short period.

Although three possible structures **21a, 22, 23** existed for $C_7H_8O_3N_2Cl_2$, according to the results of elemental analysis and mass spectrum (*m/e*, 205, 203 (1:3), M^+-Cl, 6%; 200, 198, 196 (1:6:9), M^+-42, 3%; 163, 161 (1:3), 20%; 158, 156, 154 (1:6:9), 9%; 43, $COCH_3^+$, 100%; 42, 7%), structure (**21a**), namely 2-acetylamino-3,3-dichloro-N-acetylacrylamide, a new imidic compound, was found to be the correct one on the basis of IR and NMR spectra (Chart 7).

Thus, the IR spectrum showed aborptions at 3350—3160 (due to N–H), 1738, 1690sh, 1679 (imido and amido carbonyls), and 1632 cm^{-1} (double bond), and the NMR spectrum (d_6-DMSO) exhibited signals at δ 1.98 (3H, s, $NHCO\underline{CH_3}$), 2.10 (3H, s, $CONHCO\underline{CH_3}$), 9.73 (1H, br, NH), and 11.00 ppm (1H, br, NH).

Treatment of **21a** with conc. sulfuric acid or aqueous potassium carbonate at room temperature produced 2-acetylamino-3,3-dichloroacrylamide (**24**) in good yields. Acetylation

7) G.H. Posner, "Organic Reactions," Vol. 22, ed. by W.G. Dauben, John Wiley & Sons, Inc., New York, 1975, Chapter 2.

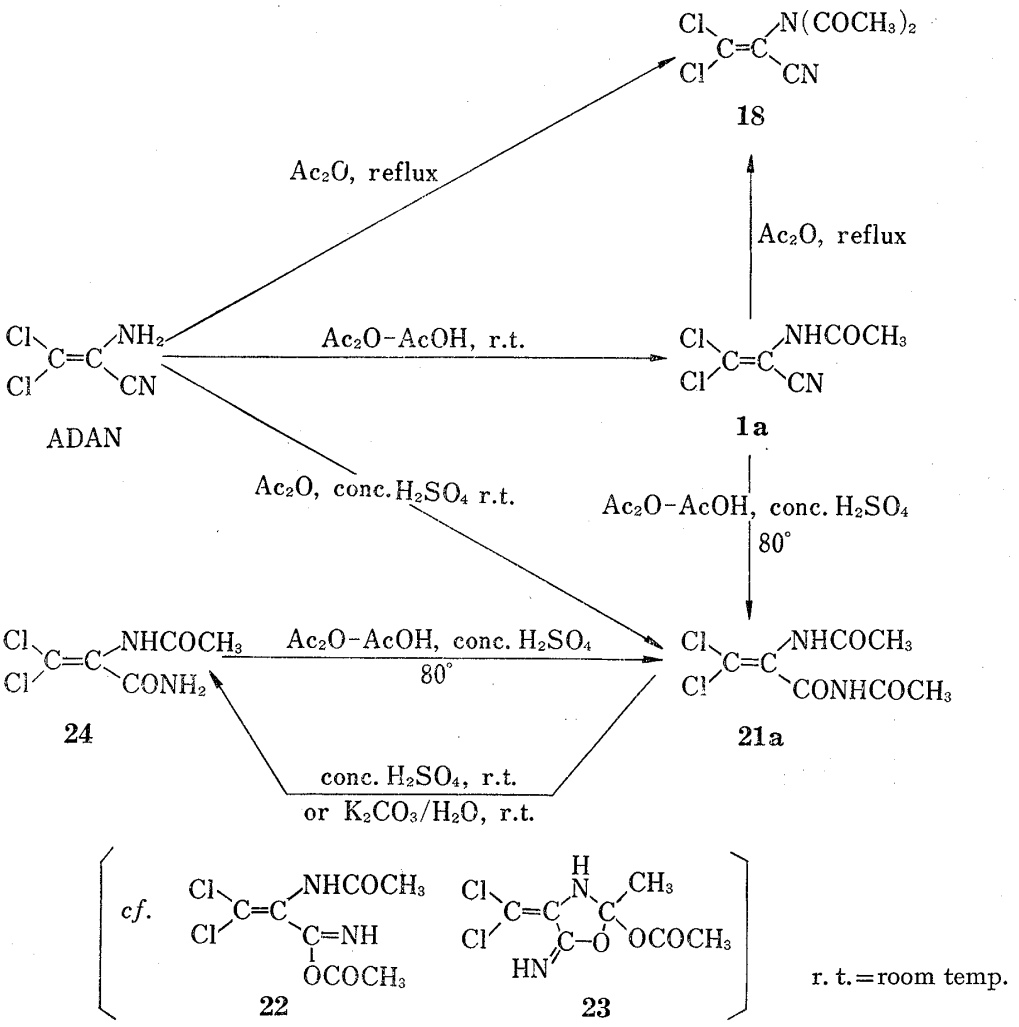


Chart 7

of **24** with acetic anhydride-acetic acid in the presence of a catalytic amount of conc. sulfuric acid at 80°, a known method for acetylation of amides,[8] produced a solid (**21a**).

Although the structure (**22**) also satisfies the IR and NMR spectral data, isoimides such as **22** have only been suggested[8] as intermediates in the preparation of imidic compounds by the reaction of amides with acid anhydrides in the presence of acidic catalyst and indeed, to the best of our knowledge, there has been no precedent of their isolation as stable compounds.

The other structure (**23**), which we had assigned to **21a** in a communication[3] was found to be incorrect. It is difficult to assign the NMR-signals at δ 9.73 or 11.00 to the NH proton in the 3 position of **23**. Furthermore, structure **23** is incompatible with the fact that the compound gives 2-methyl-5-(substituted amino)oxazole-4-N-acetylcarboxamides (**32a—e**; *vide infra*), when treated with secondary amines.

Report of direct conversion of a nitrile into an imidic compound is very rare in literature.[9] In an interconversion of carboxylic acid and nitrile at high temperature,[9a] an imidic compound was suggested as an intermediate, but the reaction

$$\text{R-COOH} + \text{R'-CN} \rightleftarrows \text{R-}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{-}\overset{\overset{\text{H}}{|}}{\text{N}}\text{-}\overset{\overset{\text{O}}{\|}}{\text{C}}\text{-R'} \rightleftarrows \text{R-CN} + \text{R'-COOH}$$

8) O.H. Wheeler and O. Rosado, "The Chemistry of Amides," ed. by J. Zabicky, Interscience Publishers, Inc., London, 1970, Chapter 7.

9) *a*) D.A. Klein, *J. Org. Chem.*, **36**, 3050 (1971); *b*) J.F. Wolfe and Chung-Li C. Mao, *J. Org. Chem.*, **31**, 3069 (1966).

conditions are so different from those for the formation of **21a** from ADAN or **1a** that it seems as though a different mechanism is operating in the latter case.

With acetic anhydride alone and with a mixture of acetic anhydride and acetic acid (3: 1, v/v) at 80° for 30 min, comparable yields of **21a** (68 and 80%, respectively) were obtained. Even with acetic acid in the presence of a catalytic amount of conc. sulfuric acid at 80° for 30 min, 30% of **21a** was obtained together with the recovered starting material (*ca.* 30%) and the corresponding amide (**24**) (*ca.* 30%).

In the direct conversion of ADAN or **1a** into **21a**, participation of the $NHCOCH_3$ group seems very reasonable, because ADAN is easily transformed into the N-monoacetyl derivative (**1a**) under the conditions employed. In fact, when treated with acetic anhydride–acetic acid under similar conditions, 3,3-dichloroacrylonitrile[10] (**25**), a model compound lacking α-acetylamino group, was recovered almost completely, although a trace of the corresponding imidic compound (**27**) was detected by TLC. Compound (**27**) can be prepared by acetylation of 3,3-dichloroacrylamide (**26**) in 94% yield (Chart 8).

In literature, it is known[9b] that some β-ketonitriles can be easily converted into the corresponding β-ketoamides and N-acetyl-β-ketoamides. Wolfe and Mao are pointing out the presence of the neighboring participation of β-keto group in the latter reaction.

Based on the above experimental results, we propose the following mechanism (Chart 9).

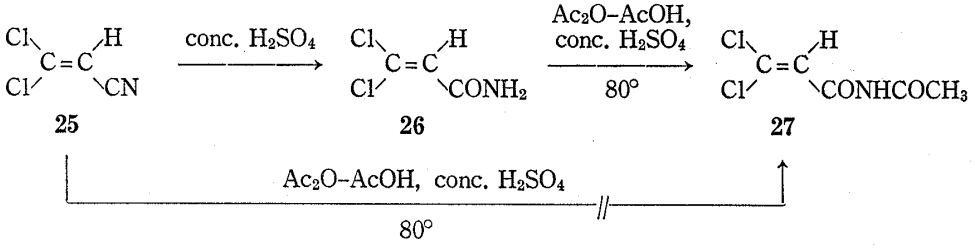


Chart 8

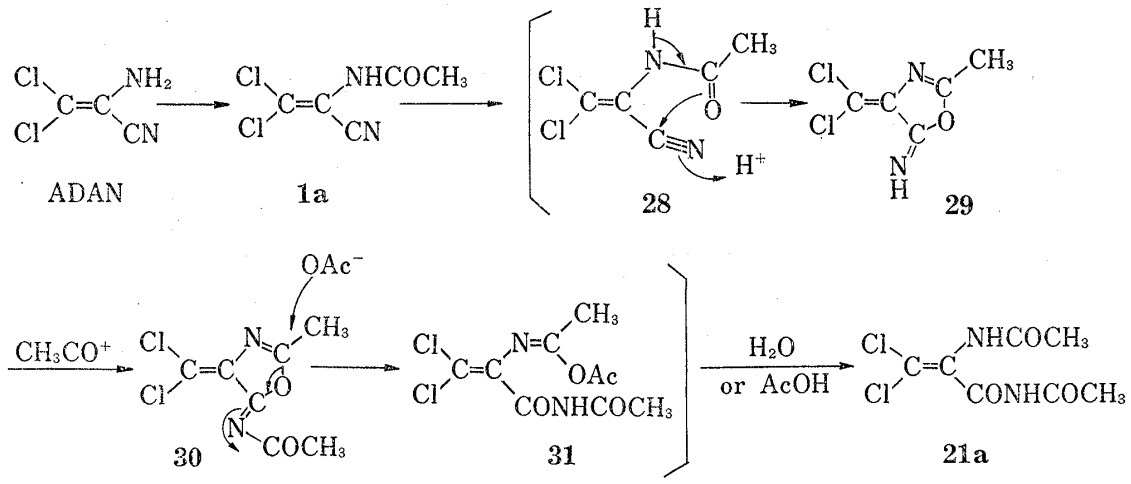


Chart 9

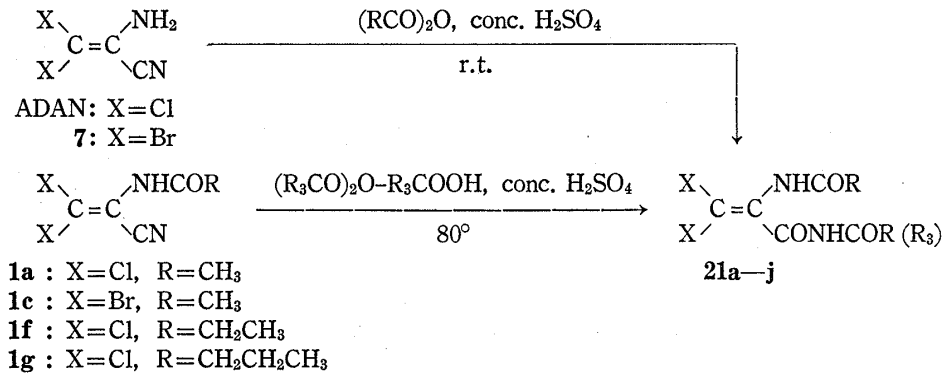
Thus, ADAN is initially converted into N-monoacetyl derivative (**1a**), which cyclizes to oxazoline derivative (**29**) *via* intramolecular nucleophilic attack by the amide oxygen on the

10) *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); *c*) R.L. Souben, D.B. Clifford, F. Grim, and J.A. Johnston, *J. Org. Chem.*, **36**, 3386 (1971).

carbon of the cyano group activated by protonation with sulfuric acid. Acetylation of the imino group of **29** with the existing acylating agent affords the corresponding N-acetyl derivative (**30**). Ring opening of **30** by attack with a nucleophile, followed by hydrolysis, affords the imidic compound (**21a**).

The results summarized in Table IV indicate that this new conversion into imidic compounds is quite general with ADAN, 2-amino-3,3-dibromoacrylonitrile (**7**), and their N-acyl derivatives (**1a—c,f,g**). The structures were confirmed by spectral data and elemental analysis as summarized in Table VII.

Table IV. Preparation of 2-Acylamino-3,3-dihalogeno-N-acylacrylamides (**21a—j**)



Compd. No.	21 X	R	R (R3)	Starting material	Yield (%)	mp[a] (°C)	Recryst. solvent[b]
21a	Cl	CH_3	CH_3	ADAN / **1a**	93 / 95	174—178	A
21b	Br	CH_3	CH_3	**7**	93	167—169	A
21c	Cl	CH_2CH_3	CH_2CH_3	ADAN / **1f**	85 / 92	191—194	A
21d	Cl	$CH_2CH_2CH_3$	$CH_2CH_2CH_3$	ADAN / **1g**	97 / 92	181—182	A
21e	Cl	$CH(CH_3)_2$	$CH(CH_3)_2$	ADAN	94	216—217	A
21f	Cl	$(CH_2)_4CH_3$	$(CH_2)_4CH_3$	ADAN	96	176—178	A
21g	Cl	$(CH_2)_8CH_3$	$(CH_2)_8CH_3$	ADAN	93	158—190	A
21h	Cl	CH_3	CH_2CH_3	**1a**	83	165—170	A
21i	Br	CH_3	CH_2CH_3	**1c**	36	162—163	A
21j	Cl	CH_3	$CH_2CH_3CH_3$	**1c**	85	172—174	A

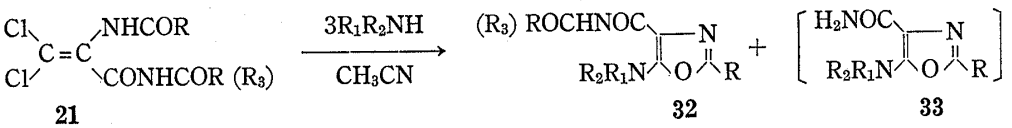
a) decomposition
b) A=acetonitrile

Reaction of these N-acylacrylamides (**21**) with 3 molar eq. of aliphatic secondary amines in acetonitrile at room temperature gave 2-substituted-5-(substituted amino)oxazole-4-N-acylcarboxamides (**32a—e**) in fair to good yields (Table V).

The slightly inferior yields in Table V compared with those in Tables I—III are due to formation of the corresponding carboxamides (**33**) during either reaction or work-up.

In summary, reaction of 2-acylamino-3,3-dihalogenoacrylonitriles (**1**) or N-acylcarboxamides (**21**) with aliphatic amines afforded 2-substituted-5-(substituted amino)oxazole-4-carbonitriles (**6**) or -4-N-acylcarboxamides (**32**) in good to excellent yields.

TABLE V. Preparation of 2-Alkyl-5-(substituted amino)oxazole-4-N-acylcarboxamides (**32a—l**)



21 **32** **33**

Compd. No.	32 R	32 R(R3)	32 NR1R2	Yield (%)	mp (°C)	Recryst. solvent[a]
32a	CH_3	CH_3	$N(CH_2CH_3)_2$	46	101—103	H
32b	CH_3	CH_3	$N(CH_2CH_2CH_3)_2$	51	79— 81	H
32c	CH_3	CH_3		52	108—109	B-H
32d	CH_3	CH_3		87[b]	85— 87	H
32e	CH_3	CH_3		83[c]	130—131	B-H
32f	CH_2CH_3	CH_2CH_3		75	100—101	B-H
32g	$CH_2CH_2CH_3$	$CH_2CH_2CH_3$		76	63— 64	H
32h	$CH(CH_3)_2$	$CH(CH_3)_2$		72	75— 76	H
32i	$(CH_2)_4CH_3$	$(CH_2)_4CH_3$		81	40— 42	H
32j	$(CH_2)_8CH_3$	$(CH_2)_8CH_3$		84	56— 57	H
32k	CH_3	CH_2CH_3		73	129—130	B-H
32l	CH_3	$CH_2CH_2CH_3$		76	86— 88	B-H

a) B=benzene, H=*n*-hexane
b) 2-methyl-5-piperidinooxazole-4-carboxamide (**33d**, mp 122—123°, 4% yield) was also isolated.
c) 2-methyl-5-morpholinooxazole-4-carboxamide (**33e**, mp 147—149°, 9% yield) was also isolated.

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 TMS 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.

2-Trifluoroacetylamino-3,3-dibromoacrylonitrile (1e)——To an ice-cooled solution of 3.0 g (13.3 mmoles) of 2-amino-3,3-dibromoacrylonitrile (7) in 20 ml of ether, 3.0 g (14.3 mmoles) of trifluoroacetic anhydride was added dropwise and the mixture was allowed to stand at room temperature for 2 hr. The solvent was removed *in vacuo* and the resulting solid was washed with a little pet. ether to give 3.95 g (92.5%) of **1e** as a colorless solid. mp 89—90.5° (from *n*-hexane). IR ν_{max}^{Nujol} cm^{-1}: 3250, 3170 sh, 3100, 2240, 1743 sh, 1730, 1588, and 1512. NMR (d_6-DMSO) δ: 9.50 (br). *Anal.* Calcd. for $C_5HON_2Br_2F_3$: C, 18.66; H, 0.31; N, 8.70. Found: C, 18.75; H, 0.24; N, 8.78.

2-Propionylamino-3,3-dichloroacrylonitrile (1f)——A mixture of 2.74 g (20 mmoles) of ADAN in 4 g of propionic anhydride and 1 g of propionic acid was allowed to stand overnight at room temperature. Ice water was added to the almost solidified mixture and the resulting suspension was extracted with ethyl acetate. The extract was washed with aqueous sodium bicarbonate, then with water and dried ($MgSO_4$). The solvent was removed *in vacuo* and the residual solid was chromatographed on silica gel yielding 3.45 g (89.4%) of **1f**. mp 115—117° (from benzene) (*cf.* lit.[4a] mp 111—112°). NMR ($CDCl_3$) δ: 1.22 (3H, t, J=7.2 Hz), 2.38 (2H, q, J=7.2 Hz), and 6.96 (1H, br). Mass Spectrum *m/e* (rel. intensity); 196, 194, 192 (1: 6: 9, M^+, 7%), 167, 165, 163 (1: 6: 9, M^+–C_2H_5, 2%), 159, 157 (1: 3, M^+–Cl, 9%), 140, 138, 136 (1: 6: 9, M^+–CH_3CH=C=O, 20%), 113, 111, 109 (1: 6: 9, Cl_2=C=NH^+, 13%), 57 ($CH_3CH_2CO^+$, 100%). *Anal.* Calcd. for $C_6H_6ON_2Cl_2$: C, 37.33; H, 3.13; N, 14.51. Found: C, 37.34; H, 2.93; N, 14.53.

2-Butyroylamino-3,3-dichloroacrylonitrile (1g)——The reaction of 2.74 g (20 mmoles) of ADAN with 4 g of *n*-butyric anhydride and 1 g of *n*-butyric acid under conditions similar to those given above gave 4.10 g (98.0%) of **1g** as a colorless solid. mp 83—84° (from *n*-hexane). IR ν_{max}^{Nujol} cm^{-1}: 3220, 3150 sh, 3070, 2245, 1670, and 1603. NMR ($CDCl_3$) δ: 0.96 (3H, t, J=*ca.* 7 Hz), 1.50—1.90 (2H, m), 2.18—2.50 (2H, t, J=*ca.* 7 Hz), and 6.80 (1H, br). Mass Spectrum *m/e* (rel. intensity); 210, 208, 206 (1: 6: 9, M^+, 5%), 173, 171 (1: 3,, M^+–Cl, 5%), 167, 165, 163 (1: 6: 9, M^+–C_3H_7, 2%), 140. 138, 136 (1: 6: 9, M^+–$CH_3CH_2CH{=}C{=}O$, 9%), 113, 111 109 (1: 6: 9, $Cl_2C{=}C{=}NH^+$, 8%), 71 ($CH_3CH_2CH_2CO^+$, 95%), 43 ($C_3H_7^+$, 100%). *Anal.* Calcd. for $C_7H_8ON_2Cl_2$: C, 40.60; H, 3.89; N, 13.53. Found: C, 40.50; H, 3.74; N, 13.55.

2-Acetylamino-3,3-bismethylthioacryronitrile (2a)——To an ice-cooled mixture of 20% aqueous CH_3-SNa (120 g, 0.5 mole, Tokyo Chemical Industry Co., Ltd.) and 180 ml of water, 35.8 g (0.2 mole) of **1a** was added and the resulting suspension was stirred overnight at room temperature. The insoluble material was collected by filtration, then dried to give 34.75 g of **2a**. The filtrate was extracted with ethyl acetate and the extract was washed with water, then dried ($MgSO_4$). The solvent was evaporated to give an additional 2.45 g of **2a**, the total yield of which was 37.20 g (92%). mp 122—123.5° (from benzene). IR ν_{max}^{Nujol} cm^{-1}: 3260, 3090, 2210, 1660, 1630 sh, 1565, and 1555 sh. NMR ($CDCl_3$) δ: 2.13 (3H, s), 2.42 (6H, s), and 7.77 (1H, br). *Anal.* Calcd. for $C_7H_{10}ON_2S_2$: C, 41.56; H, 4.98; N, 13.85. Found: C, 41.55; H, 4.85; N, 13.83.

2-Acetylamino-3,3-bisethylthioacrylonitrile (2b)——To an ce-cooled mixture of 5.58 g (90 mmoles) of ethylmercaptan and 3.6 g (90 mmoles) of NaOH in 100 ml of water, 7.16 g (40 mmoles) of **1a** was added and the mixture was stirred under ice-cooling for 5 hr. Compound (**2b**) (8.2 g, 89%) was isolated in a manner similar to that given above. mp 86—87° (from *n*-hexane–benzene). IR ν_{max}^{Nujol} cm^{-1}: 3310, 2230, 1675, and 1565. NMR ($CDCl_3$) δ: 1.27 (3H, t, J=7.8 Hz), 1.31 (3H, t, J=7.8 Hz), 2.12 (3H, s), 2.90 (2H, q, J=7.8 Hz), 2.94 (2H, q, J=7.8 Hz), and 7.38 (1H, br). *Anal.* Calcd. for $C_9H_{14}ON_2S_2$: C, 46.93; H, 6.13; N, 12.16. Found: C, 47.05; H, 6.27; N, 12.25.

2-Acetylamino-3,3,3-trimethoxypropionitrile (4a)——To an ice-cooled methanolic solution of sodium methoxide (0.65 mole), prepared from 15 g of sodium and 500 ml of MeOH, 30 g (0.167 mole) of **1a** was added in portions with stirring, and the mixture was stirred under ice-cooling for 2 hr then overnight at room temperature, and finally at 40—50° for 1 hr. The solvent was evaporated *in vacuo* and 100 ml of ice water was added to the residue. The resulting solid was collected by filtration, then washed with chilled water to give 21.5 g of **4a**. The filtrate was extracted with $CHCl_3$, then the extract was washed with water and dried ($MgSO_4$). The solvent was evaporated to afford 7.5 g of **4a**, bringing the total yield to 29.0 g (86%). mp 91—92° (from benzene). IR ν_{max}^{Nujol} cm^{-1}: 3220, 3050, 2255, 1655, 1640 sh, and 1550. NMR (d_6-DMSO) δ: 1.94 (3H, s), 3.36 (9H, s), 5.22 (1H, d, J=9.0 Hz), and 8.64 (1H, br). Mass Spectrum *m/e* (rel. intensity); 171 (M^+–OCH_3, 30%), 129 (M^+–OCH_3–$CH_2{=}C{=}O$, 24%), 105 ($C(OCH_3)_3^+$, 100%), 59 (21%), 43 (30%). *Anal.* Calcd. for $C_8H_{14}O_4N_2$: C, 47.52; H, 6.98; N, 13.86. Found: C, 47.74; H, 7.01; N, 13.86.

2-Acetylamino-3,3,3-triethoxypropionitrile (4b)——Compound (**4b**) (18.4 g, 79%) was prepared by the reaction of 17.9 g (0.1 mole) of **1a** and 0.3 mole of sodium ethoxide in 500 ml of EtOH under conditions similar to those for the preparation of **4a**. mp 103—105° (*n*-hexane–benzene). IR ν_{max}^{Nujol} cm^{-1}: 3220, 3030, 2255, 1688 sh, 1660, and 1530. NMR ($CDCl_3$) δ: 1.24 (9H, t, J=7.1 Hz), 2.06 (3H, s), 3.71 (6H, q, J=7.1 Hz), 5.14 (1H, d, J=9.0 Hz), 5.90 (1H, br). Mass Spectrum *m/e* (rel. intensity); 199 (M^+–OC_2H_5, 7%), 171 (M^+–C_2H_5-OH–HCN, 13%), 147 ($C(OC_2H_5)_3^+$, 47%), 129 (39%), 119 ($C(OC_2H_5)^+_3$–$CH_2{=}CH_2$, 20%) 102 ($C(OC_2H_5)_2^+$, 39%), 91 (48%), 63 (84%), 43 (100%). *Anal.* Calcd. for $C_{11}H_{20}O_4N_2$: C, 54.08; H, 8.25; N, 11.47. Found: C, 53.86; H, 8.31; N, 11.49.

General Procedure for the Synthesis of 2-Alkyl-5-(substituted amino)oxazole-4-carbonitriles (6d—s and 6u—x)——Reaction conditions, yields, and melting points are shown in Tables I—III. Analytical and physical data are summarized in Table VI. To a slightly cooled solution (or suspension) of 0.01—0.1 mole of 2-acylamino-3,3-dihalogenoacrylonitriles (**1a—g**) in 50—500 ml of EtOH or CH_3CN (or in 100—1000 ml of water, ether or benzene), was added 3.5—4.0 molar eq. of an amine (procedure A) or a mixture of 1 molar eq. of an amine and 2—3 molar eq. of triethylamine (procedure B) with stirring. The reactions were so quick that amine hydrohalogenide formed precipitates almost instantaneously in most cases. After the addition had been completed, the mixture was stirred at room temperature for about 5 hr. The resulting suspension was evaporated *in vacuo* leaving an oil or a semi-solid. The residue was directly chromatographed on a short silica gel column to afford almost pure **6d—s** or **6u—x**. Almost equal results were obtained by extracting the reaction mixture with ether and evaporating the solvent. An analytical sample was obtained by recrystallizing the solid from the solvent listed in Tables I—III.

2-Methyl-5-aminooxazole-4-carbonitrile (6a)——a) Gaseous ammonia was bubbled into a refluxing solution of 1.79 g (10 mmoles) of **1a** in 100 ml of EtOH until the starting material (**1a**) was no longer detected by TLC analysis. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel with $CHCl_3$–5% $(CH_3)_2CO$ to give 0.27 g (22%) of **6a**.

b) A mixture of 1.79 g (10 mmoles) of **1a** and 7.7 g (0.1 mole) of ammonium acetate in 100 ml of EtOH was refluxed for 10 hr. The volatiles were removed *in vacuo* and the brown-black residue was chromatographed on silica gel to give 0.50 g (55.8% based on **1a** consumed) of **6a** and 0.46 g of **1a**.

2-Methyl-5-hydrazinooxazole-4-carbonitrile (6b)——To an-ice-cooled solution of 17.9 g (0.1 mole) of **1a** in 200 ml of EtOH, 25.0 g (*ca.* 0.4 mole) of 80% hydrazine hydrate was added dropwise and the mixture was

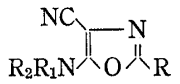
stirred overnight at room temperature. The solvent was evaporated *in vacuo* and the residual oil was diluted with about 20 ml of chilled water, than the mixture was allowed to stand overnight at 0°. The precipitate formed was collected by filtration to give 11.8 g of **6b**. The filtrate was extracted with ethyl acetate, then the extract was washed with water and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to give 0.4 g of **6b**, the total yield of which was 12.2 g (88.4%).

2-Methyl-5-isopropylidenehydrazinooxazole-4-carbonitrile (6b′)——A solution of 1.38 g (10 mmoles) of **6b** in 10 ml of $(CH_3)_2CO$ was refluxed for 10 min. The solvent was evaporated *in vacuo* to dryness and the residual solid was washed with a little *n*-hexane to afford 1.70 g (95%) of **6b′**.

2-Methyl-5-benzylidenehydrazinooxazole-4-carbonitrile (6b″)——A solution of 1.38 g (10 mmoles) of **6b** and 1.1 g (10.4 mmoles) of benzaldehyde in 50 ml of EtOH was heated at 60° for 30 min. The solvent was evaporated *in vacuo* to give a solid which was washed with a mixture of ether and pet. ether to give 2.22 g (98.2%) of **6b″**.

2-Methyl-5-methylaminooxazole-4-carbonitrile (6c)——To a slightly cooled solution of 7.16 g (40 mmoles) of **1a** in 200 ml of EtOH, 15.5 g (*ca.* 0.16 mole) of 30% aqueous methylamine was added and the mixture was stirred overnight at room temperature. The solvent was evaporated *in vacuo*, and the residue was chromatographed on silica gel with $CHCl_3$–3% $(CH_3)_2CO$ to give 5.37 g (98.0%) of **6c**. Almost equal results were obtained with water, ether, or CH_3CN as solvent.

TABLE VI. 2-Substituted-5-(substituted amino)oxazole-4-carbonitriles (**6**)



Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR ($CDCl_3$) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
6a	3300, 3200, 2200, 1660, 1640sh, 1593	2.21 (3H, s), 6.80 (2H, br)[a]	$C_5H_5ON_3$	48.76 (48.78)	3.96 (4.09)	34.49 (34.13)
6b	3300, 3200, 3130sh, 2210, 1650sh, 1630sh, 1605	2.22 (3H, s), 4.63 (2H, br), 8.73 (1H, br)[a]	$C_5H_6ON_4$	43.68 (43.47)	4.26 (4.38)	40.61 (40.56)
6b′	3180, 2220, 1660, 1640, 1600, 1530	1.93 (3H, s), 2.05 (3H, s), 2.34 (3H, s), 8.34 (1H, br)	$C_8H_{10}ON_4$	53.73 (53.92)	5.73 (5.66)	31.76 (31.45)
6b″	3150, 2220, 1652, 1600	2.35 (3H, s), 7.20—7.85 (5H, m), 7.98 (1H, s), 11.35 (1H, br)[a]	$C_{12}H_{10}ON_4$	63.62 (63.70)	4.37 (4.46)	24.72 (24.77)
6c[b]	3200, 3050, 2210, 1660, 1644, 1632sh, 1604, 1550	2.28 (3H, s), 3.03 (3H, d, J=5.0 Hz), 5.52 (1H, br)	$C_6H_7ON_3$	52.65 (52.55)	4.84 (5.15)	30.65 (30.64)
6d	3270, 3230sh, 3100, 2210, 1660, 1642, 1605	1.28 (3H, t, J=7.2 Hz), 2.29 (3H, s), 3.44 (2H, q, J=7.2 Hz), 5.56 (1H, br)	$C_7H_9ON_3$	55.91 (55.61)	5.96 (6.00)	27.73 (27.80)
6e	3260, 3200sh, 3100, 2210, 1655, 1605	0.99 (3H, t, J=6.7 Hz), 1.38—2.00 (2H, m), 2.28 (3H, s), 3.35 (2H, q, J=6.5 Hz), 5.45 (1H, br)	$C_8H_{11}ON_3$	58.31 (58.16)	6.76 (6.71)	25.30 (25.44)
6f	3270, 2200, 1665, 1645, 1603	1.27 (6H, d, J=6.0 Hz), 2.30 (3H, s), 3.58—4.16 (1H, m), 5.02 (1H, br)	$C_8H_{11}ON_3$	58.05 (58.17)	6.51 (6.71)	25.31 (25.44)
6g	3270, 3220sh, 3070, 2200, 1660, 1643, 1602	2.30 (3H, s), 3.96—4.14 (2H, m), 5.08—6.25 (4H, m)	$C_8H_9ON_3$	59.14 (58.88)	5.40 (5.56)	25.83 (25.75)
6h	3300, 3100, 2250, 2200, 1663, 1608	2.33 (3H, s), 2.45—3.20 (3H, m), 3.68 (2H, t, J=6.5 Hz)	$C_8H_8ON_4$	54.41 (54.54)	4.38 (4.58)	31.88 (31.30)
6i	3210, 3050, 2210, 1660sh, 1642, 1605	1.23 (6H, t, J=7.0 Hz), 2.30 (3H, s), 3.37—3.94 (6H, m), 4.62 (1H, t, J=5.0 Hz), 4.96 (1H, br)	$C_{11}H_{17}O_3N_3$	55.23 (55.21)	7.26 (7.16)	17.56 (17.56)
6j	3290, 3050, 2210, 1652, 1608, 1530[c]	0.76—1.10 (3H, m), 1.20—1.80 (4H, m), 2.29 (3H, s), 3.37 (2H, q, J=6.5 Hz), 5.40(1H, br)	$C_9H_{13}ON_3$	60.50 (60.32)	7.36 (7.31)	23.48 (23.45)
6k	3270, 3120, 3075, 2195, 1660, 1608	0.98 (3H, t, J=6.5 Hz), 1.26 (3H, d, J=6.2 Hz), 1.35—1.78 (2H, 2m), 2.29 (3H, s), 3.40—3.92 (1H, m), 5.22 (1H, br)	$C_9H_{13}ON_3$	59.97 (60.32)	7.84 (7.31)	23.37 (23.45)

Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR ($CDCl_3$) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
6l	3250, 3100, 3050, 2210, 1660, 1608	0.98 (6H, d, J=6.2 Hz), 1.50—2.05 (1H, m), 2.29 (3H, s), 3.19 (2H, t, J=6.7 Hz), 5.30 (1H, br)	$C_9H_{13}ON_3$	60.22 (60.32)	7.59 (7.31)	23.75 (23.45)
6m	3280, 3200sh, 2220, 1650, 1600	1.39 (9H, s), 2.34 (3H, s), 4.70 (1H, br)	$C_9H_{13}ON_3$	63.63 (63.74)	8.41 (8.27)	20.11 (20.27)
6o	3190, 3020, 2220, 1642, 1600, 1545	0.90—2.15 (10H, br), 2.28 (3H, s), 3.45 (1H, br), 4.70 (1H, br)	$C_{11}H_{15}ON_3$	64.69 (64.36)	7.56 (7.37)	20.55 (20.47)
6p	3260, 3200sh, 2220, 1655, 1604	2.28 (3H, s), 4.52 (2H, d, J=6.0 Hz), 5.50 (1H, br), 7.35 (5H, s)	$C_{12}H_{11}ON_3$	67.61 (67.59)	5.20 (5.20)	19.69 (19.71)
6q	2220, 1645, 1605[c]	1.24 (6H, t, J=7.0 Hz), 2.29 (3H, s), 3.47 (4H, q, J=7.0 Hz)	$C_9H_{13}ON_3$	60.00 (60.31)	7.12 (7.31)	22.83 (23.45)
6r[d]	2210, 1640, 1595	2.30 (3H, s), 3.40—3.90 (8H, m)	$C_9H_{11}O_2N_3$	56.08 (55.95)	5.66 (5.74)	21.75 (21.75)
6s	2200, 1642, 1597	1.66 (6H, br), 2.29 (3H, s), 3.50 (4H, br)	$C_{10}H_{13}ON_3$	63.04 (62.81)	6.77 (6.85)	22.05 (21.97)
6t[e]	3260, 3040, 2190, 1655sh, 1640, 1600, 1535	2.33 (3H, s), 3.65—3.84 (4H, 2 peaks), 5.70 (1H, br)	$C_7H_8ON_3Cl$	45.09 (45.29)	4.33 (4.34)	22.33 (22.64)
6u	3130, 2220, 1643sh, 1620, 1535	3.40—3.94 (8H, m), 7.24 (1H, s)	$C_8H_9O_2N_3$	53.45 (53.62)	4.84 (5.06)	23.83 (23.45)
6v	2230, 1665sh, 1645, 1630, 1610sh	3.48—3.96 (8H, m)	$C_9H_8O_2N_3F_3$	43.73 (43.73)	3.09 (3.26)	16.89 (17.00)
6w	2220, 1640sh, 1633, 1590	1.26 (3H, t, J=7.0 Hz), 2.60 (2H q, J=7.0 Hz), 3.35—3.90 (8H, m)	$C_{10}H_{13}O_2N_3$	57.75 (57.96)	6.53 (6.32)	20.38 (20.28)
6x	2210, 1645sh, 1634, 1595	0.99 (3H, t, J=6.8 Hz), 1.40—2.04 (2H, m), 2.58 (2H, t, J=7.2 Hz), 3.35—3.95 (8H, m)	$C_{11}H_{15}O_2N_3$	59.83 (59.71)	6.58 (6.83)	19.07 (18.99)

a) in d_6-DMSO
b) mass spectrum *m/e* (rel. intensity): 138 (M^++1, 9%), 137 (M^+, 100%), 122 (M^+-CH_3, 2%), 107 (22%), 80 (52%), 79 (32%), 58 (30%), 53 (84%), 43 (36%), 42 (72%)
c) as liquid film
d) mass spectrum *m/e* (rel. intensity): 193 (M^+, 14%), 192 (100%), 134 (34%), 107 (48%), 79 (32%), 69 (22%), 57 (26%), 56 (22%), 55 (64%), 43 (26%), 42 (54%)
e) mass spectrum *m/e* (rel. intensity): 187, 185 (1:3, M^+, 40%), 137 (8%), 136 (100%), 108 (10%), 107 (78%), 80 (14%), 79 (21%), 63 (13%), 53 (16%), 43 (29%), 42 (17%)

2-Methyl-5-(β-chloroethylamino)oxazole-4-carbonitrile (6t)——To a solution of 3.58 g (20 mmoles) of **1a** in 100 ml of CH_3CN, 3.44 g (80 mmoles) of ethyleneimine was added at room temperature, then the mixture was allowed to stand overnight. The brown-black mixture was evaporated *in vacuo*, and the residue was extracted with $CHCl_3$. The extract was washed with water then dried ($MgSO_4$). The solvent was removed and the resulting oil was chromatographed on silica gel with $CHCl_3$ to give 1.32 g (35.6%) of **6t**.

2-(Acetylamino-cyanomethylene)imidazolidine (8a)——a) To an ice-cooled solution of 8.4 g (0.21 mole) of NaOH and 6.2 g (0.103 mole) of ethylenediamine in 100 ml of water, 17.9 g (0.1 mole) of **1a** was added in portions and the mixture was stirred under ice-cooling for 5 hr and allowed to stand overnight at 0° to −5°. The precipitate formed was collected by filtration, then washed with a small amount of water to yield 8.7 g (52.4%) of **8a**.

b) To an ice-cooled solution of 17.9 g (0.1 mole) of **1a** in 500 ml of EtOH, a mixture of 6.6 g (0.11 mole) of ethylenediamine and 25.3 g (0.25 mole) of triethylamine was added dropwise and the reaction mixture was stirred overnight at room temperature. The solvent was removed *in vacuo* and 50 ml of water was added to the residue. The resulting suspension was allowed to stand at 0° to −5° for 3 days. The precipitate formed was collected by filtration, then washed with a small amount of chilled water to give 11.96 g (72.0%) of **8a** as an almost colorless solid, which was recrystallized from CH_3CN to afford colorless needles of **8a**, mp 198—211° (decomp.). IR ν_{max}^{Nujol} cm^{-1}: 3450, 3270 sh, 3240, 3140, 2160, 1660, 1640, 1628, and 1520. NMR (d_6-DMSO) δ: 1.84 (3H, s), 3.43 (4H, br), 6.44 (1H, br), 6.55 (1H, br), and 8.14 (1H, br). Mass Spectrum *m/e* (rel. intensity); 166 (M^+, 25%), 151 (M^+-CH_3, 4%), 124 (M^+-CH_2=C=O, 23%), 123 (M^+−43, 100%), 44 (76%), 43 (73%), 42 (30%). *Anal.* Calcd. for $C_7H_{10}ON_4$: C, 50.59; H, 6.07; N, 33.71. Found: C, 50.53; H, 5.92; N, 33.73.

2-(Acetylamino-cyanomethylene)thiazolidine (8b)——To an ice-cooled solution of 8.4 g (0.21 mole) of NaOH and 8.5 g (0.11 mole) of aminoethanethiol, 17.9 g (0.1 mole) of **1a** was added in portions with stirring and the mixture was further stirred under ice-cooling for 2 hr. The precipitate formed was collected by

filtration, then washed with chilled water to afford 12.2 g of **8b**. The filtrate was extracted with ethyl acetate, and the extract was washed with water then dried ($MgSO_4$). The solvent was evaporated *in vacuo* and the resulting solid was washed with a little ether to give a further 2.5 g of **8b**. The total yield of **8b** was 14.7 g (80.9%). Recrystallization from CH_3CN gave colorless needles, mp 196—203° (decomp.). The reaction of **1a** with a mixture of 1 molar eq. of aminoethanethiol and 2 molar eq. of triethylamine in EtOH gave almost the same results under conditions similar to those given above. IR ν_{max}^{Nujol} cm^{-1}: 3250, 3130, 2190, 1673 sh, 1660, 1590, and 1565. NMR (d_6-DMSO) δ: 1.86 (3H, s), 3.15—3.90 (4H, m), 7.47 (1H, br), and 8.50 (1H, br). *Anal.* Calcd. for $C_7H_9ON_3S$: C, 45.89; H, 4.95; N, 22.93. Found: C, 45.70; H, 4.80; N, 22.92.

N,N'-Bis(2'-methyl-4'-cyanooxazol-5'-yl)-1,3-propanediamine (9)——To a stirred solution of 17.9 g (0.1 mole) of **1a** in 500 ml of EtOH, a mixture of 4.07 g (0.055 mole) of trimethylenediamine and 22.2 g (0.22 mole) of triethylamine was added dropwise at room temperature, then the mixture was stirred for 2 days. After evaporation of the solvent *in vacuo*, 100 ml of ice water was added to the residual solid. The solid product was collected by filtration, then washed with chilled water to give 12.5 g of crude **9**. Recrystallization from CH_3CN yielded 11.5 g (80.5%) of colorless crystals, mp 173—175°. IR ν_{max}^{Nujol} cm^{-1}: 3280, 3250 sh, 3060, 2205, 1665, 1650 sh, 1616. NMR (d_6-DMSO) δ: 1.40—2.10 (2H, m), 2.22 (6H, s), 2.95—3.50 (4H, m), 7.95 (2H, br). Mass Spectrum *m/e* (rel. intensity); 286 (M^+, 59%), 245 (M^+-CH_3CN, 5%), 244 ($M^+-CH_2=C=O$, 19%), 243 (M^+-CH_3CO, 33%), 203 (8%), 202 (M^+–2 $CH_2=C=O$, 14%), 201 ($M^+-CH_2=C=O-CH_3CO$, 19%), 190 (25%), 164 (36%), 163 (46%), 136 (33%), 127 (22%), 107 ($C_5H_4N_2O^+$, 100%), 79 (46%), 43 (61%). *Anal.* Calcd. for $C_{13}H_{14}O_2N_6$: C, 54.54; H, 4.93; N, 29.35. Found: C, 54.18; H, 4.73; N, 29.48.

2-Acetylamino-3-chloro-3-*n*-butylacrylonitrile (14a)——An ethereal solution of lithium di-*n*-butylcopper was prepared by the known method.[7] To a stirred ethereal solution of *n*-butyl lithium, prepared from 62.4 g (9.0 g atoms) of lithium and 417 g (4.5 moles) of *n*-butyl chloride in 1.3 liters of anhydrous ether, 345 g (1.81 moles) of CuI was added in portions over 10 min at around −30° under nitrogen. The solution was diluted with 1 liter of anhydrous tetrahydrofuran (THF), then cooled to −50°. To this stirred solution, 3.22 g (0.18 mole) of **1a** was added portionwise as a solution in 300 ml of anhydrous THF over 20 min and the mixture was stirred at the same temperature for 10 hr. After addition of aqueous ammonium chloride to the mixture, the Dry Ice-acetone bath was removed, and the brown-black solution was allowed to warm to room temperature over a 3-hr period with stirring. The insoluble material was filtered off using Celite 545, then washed with 500 ml of ether. The filtrate and washings were combined and washed with water, then dried ($MgSO_4$). The solvent was evaporated *in vacuo* and the residual oil (46.8 g) was chromatographed on a silica gel column with $CHCl_3$ to afford 22.8 g (63.1%) of **14a** as a colorless solid. Recrystallization from *n*-hexane yielded fine colorless needles of **14a**, mp 73—75°. IR ν_{max}^{Nujol} cm^{-1}: 3250, 2240, 1665, and 1635 sh. NMR ($CDCl_3$) δ: 0.95 (3H, t), 1.1—2.0 (4H, m), 2.12 (3H, s), 2.38—2.77 (2H, t), and 7.73 (1H, br). Mass Spectrum *m/e* (rel. intensity); 202, 200 (1: 3, M^+, 0.7%), 173, 171 (1: 3, $M^+-C_2H_5$, 1%), 166 (M^++1–Cl, 6%), 165 (M^+–Cl, 64%), 160, 158 (1: 3, $M^+-CH_2=C=O$, 20%), 123 ($M^+-Cl-CH_2=C=O$, 12%), 117, 115 (1: 3, $M^+-CH_2=C=O$–43, 63%), 95 (12%), 81 (17%), 43 (100%). *Anal.* Calcd. for $C_9H_{13}ON_2Cl$: C, 53.87; H, 6.53; N, 13.96. Found: C, 53.62; H, 6.40; N, 13.89.

2-Acetylamino-3-bromo-3-*n*-butylacrylonitrile (14b)——To a cooled (−50°) solution of 0.30 mole of lithium di-*n*-butylcopper in a mixture of 350 ml of ether and 200 ml of THF, prepared from 10.4 g (1.50 g atoms) of lithium, 70 g (0.757 mole) of *n*-butyl chloride, and 57.6 g (0.30 mole) of CuI by the known method, 8.04 g (0.03 mole) of 2-acetylamino-3,3-dibromoacrylonitrile (**1c**) in 100 ml of THF was added dropwise with stirring under nitrogen. After the addition had been completed, the mixture was stirred at the same temperature for 5 hr, then allowed to stand overnight at −70° to −30°. By a work-up similar to that given above, 5.24 g (71.2%) of **14b** was obtained as a colorless solid. Recrystallization from benzene–*n*–hexane yielded fine colorless needles, mp 92—93°. IR ν_{max}^{Nujol} cm^{-1}: 3245, 2240, 1662, and 1630 sh. NMR ($CDCl_3$) δ: 0.7—1.15 (3H, m), 1.15—1.80 (4H, m). 2.18 (3H, s), 2.4—2.8 (2H, t), 8.12 (1H, br). Mass Spectrum *m/e* (rel. intensity); 246, 244 (1: 1, M^+, 1%), 204, 202 (1: 1, $M^+-CH_2=C=O$, 18%), 165 (M^+–Br, 62%), 161, 159 (1: 1, Br_2^+, 33%), 123 (14%), 81 (21%), 43 (100%). *Anal.* Calcd. for $C_9H_{13}ON_2Br$: C, 44.10; H, 5.35; N, 11.43. Found: C, 44.23; H, 5.00; N, 11.19.

2-Acetylamino-3-*n*-butyl-3-morpholinoacrylonitrile (15)——a) A mixture of 2.0 g (10 mmoles) of **14a** and 3.44 g (40 mmoles) of morpholine in 100 ml of EtOH was stirred overnight at room temperature, then heated at 50—60° for 1 hr. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel with $CHCl_3$–3% ethyl acetate yielding 1.83 g (73.2%) of **15** as a colorless solid.

b) A mixture of 1.23 g (5 mmoles) of **14b** and 1.72 g (20 mmoles) of morpholine in 70 ml of EtOH was stirred at room temperature for 3 days. After evaporation of the solvent, the residue was chromatographed on silica gel yielding 0.97 g (77.0%) of **15**. mp 129—130° (from benzene). IR ν_{max}^{Nujol} cm^{-1}: 3240, 2200, 1650, and 1595. NMR ($CDCl_3$) δ: 0.75—1.3 (3H, br), 1.3—1.9 (4H, br), 2.06 (3H, s), 2.3—2.9 (2H, br) 3.1—3.9 (8H, br), and 7.50 (1H, br). *Anal.* Calcd. for $C_{13}H_{21}O_2N_3$: C, 62.13; H, 8.42; N, 16.72. Found: C, 61.93; H, 8.40; N, 16.67.

2-Acetylamino-3-morpholino-3-phenylacrylonitriles (17 *cis*, *trans*)——A mixture of 1.50 g (6.8 mmoles) of 2-acetylamino-3-chloro-3-phenylacrylonitrile[1] (**16**) and 3.56 g (40.9 mmoles) of morpholine in 30 ml of CH_3CN was heated under reflux for 25 hr. The solvent was evaporated *in vacuo* and the residual oil was chromatographed on silica gel yielding 0.35 g (19.0%) of **17** (*cis* or *trans*) as an oil and 1.30 g (70.7%) of **17** (*trans*

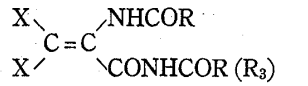
or *cis*) as a colorless solid. That the two products are isomeric with each other was verified by the physical data described below.

Oil: IR $\nu_{max}^{liq.film}$ cm^{-1}: 3250, 2190, 1680 sh, 1660, 1643, and 1585. NMR ($CDCl_3$) δ: 2.00 (3H, s), 3.3—3.8 (8H, br), 7.24 (5H, s), and 7.38 (1H, br). Mass Spectrum *m/e* (rel. intensity); 272 (M^++1, 40%), 271 (M^+, 100%), 229 (M^+–CH_2=C=O, 80%), 228 (M^+−43, 60%).

Solid: mp 181—183° (from CH_3CN). IR I_{max}^{Nujol} cm^{-1}: 3260, 2200, 1660, 1642 sh, 1590, and 1568. NMR (d_6-DMSO) δ: 1.97 (3H, s), 2.8—3.9 (8H, m), 7.3—7.7 (5H, m), and 9.06 (1H, br). *Anal.* Calcd. for $C_{15}H_{17}O_2N_3$: C, 66.40; H, 6.32; N, 15.49. Found: C, 66.36; H, 6.28; N, 16.01.

Reaction of 2-Diacetylamino-3,3-dichloroacrylonitrile (18) with Amines——a) With Cyclohexylamine: To a slightly cooled solution of 4.42 g (20 mmoles) of **18** in 300 ml of anhydrous ether was added dropwise 8.73 g (88 mmoles) of cyclohexylamine with stirring. A white precipitate of cyclohexylamine hydrochloride began to separate almost immediately. The mixture was allowed to stand overnight at room temperature. The insoluble material was filtered off, then washed with ether. The filtrate was evaporated, and the residual oil was chromatographed on slica gel with $CHCl_3$ affording 2.71 g (96.0%) of N-acetylcyclohexylamine, mp 103—104° (from *n*-hexane; lit.[11] mp 104°) and 4.02 g (98.0%) of 2-methyl-5-cyclohexylaminooxazole-4-carbonitrile (**6o**).

TABLE VII. 2-Acylamino-3,3-dihalogeno-N-acylacrylamides (**21a—j**)



Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR (d_6-DMSO) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
21a[a]	3350, 3300sh, 3160, 1738, 1690sh, 1676, 1632	1.98 (3H, s), 2.10 (3H, s), 9.73 (1H, br), 11.00 (1H, br)	$C_7H_8O_3N_2Cl_2$	35.48 (35.17)	3.30 (3.37)	11.49 (11.72)
21b	3275, 3230, 3140, 1734, 1680, 1632	1.98 (3H, s), 2.10 (3H, s), 9.46 (1H, br), 11.02 (1H, br)	$C_7H_8O_3N_2Br_2$	25.75 (25.64)	2.44 (2.46)	8.77 (8.54)
21c	3240, 3160, 1740, 1700, 1665, 1615, 1530, 1500	1.00 (3H, t, J=6.0 Hz), 1.02 (3H, t, J=6.0 Hz), 2.10—2.75 (4H, m), 9.60 (1H, br), 11.03 (1H, br)	$C_9H_{12}O_3N_2Cl_2$	40.30 (40.47)	4.41 (4.53)	10.77 (10.49)
21d	3230, 3150, 1730, 1692, 1660, 1607, 1530, 1500	0.7—1.15 (6H, m), 1.2—2.0 (4H, m), 2.10—2.65 (4H, m), 9.63 (1H, br), 11.00 (1H, br)	$C_{11}H_{16}O_3N_2Cl_2$	44.55 (44.76)	5.20 (5.46)	9.62 (9.49)
21e	3220, 3150sh, 1740, 1690, 1660, 1612, 1530, 1505	1.01 (6H, d, J=6.6 Hz), 1.02 (6H, d, J=6.6 Hz), 2.40—3.0 (2H, m), 9.57 (1H, br), 10.97 (1H, br)	$C_{11}H_{16}O_3N_2Cl_2$	44.68 (44.76)	5.46 (5.46)	9.60 (9.49)
21f	3230, 3160, 1730, 1693, 1658, 1612, 1530, 1502	0.6—1.1 (6H, br), 1.1—1.9 (12H, br), 2.10—2.60 (4H, m), 9.62 (1H, br), 10.98 (1H, br)	$C_{15}H_{24}O_3N_2Cl_2$	51.37 (51.29)	6.81 (6.89)	7.99 (7.97)
21g	3220, 3160, 1732, 1692, 1658, 1610, 1534, 1500	0.70—1.1 (6H, br), 1.1—1.9 (28H, br), 2.20—2.80 (4H, br), 8.75 (1H, br), 9.95 (1H, br)[b]	$C_{23}H_{40}O_3N_2Cl_2$	59.79 (59.60)	8.82 (8.70)	6.09 (6.04)
21h	3250, 3200sh, 3120, 1750, 1708, 1670, 1620, 1550sh, 1530	1.01 (3H, t, J=6.8 Hz), 1.97 (3H, s), 2.43 (2H, q, J=6.8 Hz), 9.63 (1H, br), 10.95 (1H, br)	$C_8H_{10}O_3N_2Cl_2$	38.24 (37.97)	4.05 (3.98)	11.40 (11.07)
21i	3250, 3120, 1758, 1695sh, 1665, 1593, 1510	1.03 (3H, t, J=7.0 Hz), 2.00 (3H, s), 2.15—2.8 (2H, q, J=7.0 Hz), 9.53 (1H, br), 11.00 (1H, br)	$C_8H_{10}O_3N_2Br_2$	27.72 (28.10)	2.84 (2.95)	8.36 (8.19)
21j	3250, 3170, 1735, 1695, 1678sh, 1665, 1610, 1512	0.90 (3H, t, J=7.0 Hz), 1.20—1.95 (2H, m), 1.97 (3H, s), 2.30 (2H, q, J=6.6 Hz), 9.67 (1H, br), 10.97 (1H, br)	$C_9H_{12}O_3N_2Cl_2$	40.75 (40.47)	4.61 (4.53)	10.76 (10.49)

a) mass spectrum *m/e* (rel. intensity): 205, 203 (1:3, M^+−Cl, 6%), 200, 198, 196 (1:6:9, M^+–CH_2=C=O, 3%), 163, 161 (1:3, 20%), 158, 156, 154 (1:6:9, M^+−2 CH_2=C=O, 9%), 43 (100%), 42 (7%)
b) in $CDCl_3$

11) *a*) A. Balyer, *Ann.*, **278**, 88 (1893); *b*) W. Scharvin, *Chem. Ber.*, **30**, 2862 (1897).

b) With Morpholine: To a slightly cooled solution of 4.42 g (20 mmoles) of **18** in 400 ml of anhydrous ether, was added dropwise 7.66 g (88 mmoles) of morpholine and the mixture was allowed to stand overnight at room temperature. A work-up similar to that given above gave 2.60 g (almost quantitative) of N-acetylmorpholine as an oil (IR $\nu_{max}^{liq.film}$ cm^{-1}: 1645—1610) and 3.76 g (97.5%) of 2-methyl-5-morpholinooxazole-4-carbonitrile (**6r**).

Preparation of 2-Acylamino-3,3-dihalogeno-N-acylacrylamide (21a—g)——Yields, and melting points are shown in Table IV. Analytical and spectral data are summarized in Table VII.

a) From 2-Amino-3,3-dihalogenoacrylonitriles (ADAN or **7**): As a typical procedure, the preparation of 2-acetylamino-3,3-dichloro-N-acetylacrylamide (**21a**) is described.

To a solution of 41.1 g (0.3 mole) of ADAN in 70 g of Ac_2O, was added 20 drops of conc. sulfuric acid at room temperature. After an exothermic reaction (around 50°), the mixture was allowed to stand overnight at room temperature. About 100 ml of ice water was added to the almost solidified mixture and the resulting precipitate was collected by filtration to afford 66.0 g of **21a**. The filtrate was extracted with ethyl acetate and the extract was washed with water, then dried ($MgSO_4$). The solvent was evaporated and the residual semi-solid was washed with a little ether to give an additional 0.50 g of **21a**; the total yield was 66.5 g (92.8%) as an almost colorless solid.

b) From 2-Acylamino-3,3-dihalogenoacrylonitriles (**1a—c, e—g**): As a typical procedure, the preparation of 2-acetylamino-3,3-dichloro-N-propionylacrylamide (**21h**) is described.

A suspension of 5.37 g (30 mmoles) of **1a** in a mixture of 10 g (77 mmoles) of propionic anhydride and 2 g of propionic acid was heated at around 80°. To this suspension, was added 10 drops of conc. sulfuric acid and the mixture was heated at the same temperature for 20 min, then allowed to stand overnight at room temperature. Ice water was added and the resulting precipitate was collected by filtration, then washed with pet. ether to afford 6.15 g of **21h**. The filtrate was extracted with ethyl acetate, and the extract was washed with water and dried ($MgSO_4$). The solvent was evaporated *in vacuo*, and the residue was washed with ether to give 0.25 g of **21h**, bringing the total yield to 6.30 g (83.0%).

c) From 2-Acylamino-3,3-dichloroacrylamide (**24**): As a typical procedure, the preparation of 2-acetylamino-3,3-dichloro-N-acetylacrylamide (**21a**) is described.

A suspension of 1.0 g of **24** in a mixture of 3 ml of Ac_2O and 1 ml of AcOH was heated at 80°. To this suspension, 3 drops of conc. sulfuric acid was added and the mixture was heated at the same temperature for an additional 20 min. After cooling, 5 ml of ice water was added and the slurry was allowed to stand overnight at 0°. The solid product was collected by filtration to yield 1.03 g (85.0%) of **21a**.

Hydrolysis of 2-Acetylamino-3,3-dichloro-N-acetylacrylamide (21a)——a) With Acid: A suspension of 5.0 g (20.9 mmoles) of **21a** in 10 ml of conc. sulfuric acid was allowed to stand in a refrigerator for 3 days to give a homogeneous mixture. The mixture was poured onto ice water and the resulting precipitate was collected by filtration, then washed with chilled water to afford 3.2 g of **24**. The filtrate was extracted with ethyl acetate, and the extract was washed with water and dried ($MgSO_4$). The solvent was evaporated and the residual semi-solid was washed with chilled water to give an additional 0.5 g of **24**, the total yield of which was 3.7 g (89.8%).

b) With Base: A suspension of 5.0 g (20.9 mmoles) of **21a** in 100 ml of water containing 5 g (36 mmoles) of K_2CO_3 was stirred at room temperature for 3 days. The insoluble product which separated was collected by filtration, then washed with chilled water to afford 2.90 g (70.4%) of **24**.

3,3-Dichloroacrylamide[12] **(26)**——A solution of 3.6 g of **25**[11] in 10 g of conc. sulfuric acid was stirred at 50° for 3 hr. After cooling, the mixture was poured onto ice water. The resulting suspension was extracted with 500 ml of ethyl acetate, and the extract was washed with 10% aqueous $NaHCO_3$, then with water and dried ($MgSO_4$). The solvent was evaporated *in vacuo* to afford 4.0 g (97%) of **26** as a colorless solid. Recrystallization from benzene yielded pure colorless needles, mp 115—116° (lit.[12] mp 112°). IR ν_{max}^{Nujol} cm^{-1}: 3350, 3290 sh, 3160, 3050, 1670, and 1600. NMR ($CDCl_3$) δ: 6.52 (1H, s), and 6.70—7.60 (2H, br). *Anal.* Calcd. for $C_3H_3ONCl_2$: C, 25.74; H, 2.16; N, 10.01. Found: C, 25.53; H, 1.99; N, 11.00.

3,3-Dichloro-N-acetylacrylamide (27)——A suspension of 2.0 g of **26** in a mixture of 4 ml of Ac_2O and 1 ml of AcOH was heated at 80°. To this suspension, 5 drops of conc. sulfuric acid was added. The mixture became homogeneous immediately. The mixture was heated at the same temperature for an additional 30 min. The volatiles were removed *in vacuo* and 10 ml of ice water was added to the residue. The precipitate formed was collected by filtration, then washed with chilled water to give 2.40 g (92.3%) of **27** as a colorless solid. mp 119—120° (from benzene–*n*-hexane). IR I_{max}^{Nujol} cm^{-1}: 3245, 3150, 3060, 1740, 1697, 1606, and 1540. NMR ($CDCl_3$) δ: 2.37 (3H, s), 6.99 (1H, s), and 9.47 (1H, br). *Anal.* Calcd. for $C_5H_5O_2NCl_2$: C, 33.00; H, 2.77; N, 7.70. Found: C, 32.82; H, 2.86; N, 7.86.

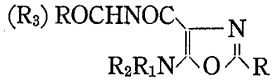
Preparation of 2-Substituted-5-(substituted amino)oxazole-4-N-acylcarboxamides (32)——The procedure for preparation of **32e** is typical. Spectral data and elemental analyses are listed in Table VIII.

2-Methyl-5-morpholinooxazole-4-N-acetylcarboxamide (**32e**): To a stirred suspension of 4.78 g (20 mmoles) of 2-acetylamino-3,3-dichloro-N-acetylacrylamide (**21a**) in 200 ml of anhydrous CH_3CN. 5.74 g (60

12) A. Roedig and F. Hagedorn, *Ann.*, **683**, 30 (1965).

mmoles) of morpholine was added dropwise and the mixture was stirred overnight at room temperature. The solvent was evaporated *in vacuo* and the residue was chromatographed on silica gel with $CHCl_3$–10% $(CH_2)_2$-CO to afford 4.21 g (83.1%) of **32e**, 0.24 g (9.4%) of N-acetylmorpholine and 0.34 g (8.8%) of 2-methyl-5-morpholinooxazole-4-carboxamide (**33e**).

TABLE VIII. 2-Alkyl-5-(substituted amino)oxazole-4-N-acylcarboxamides (**32a—l**)



Compd. No.	IR ν_{max}^{Nujol} cm^{-1}	NMR ($CDCl_3$) δ	Formula	Analysis (%) Found (Calcd.) C	H	N
32a	3340, 1700sh, 1685, 1650, 1575	1.20 (6H, t, J=7.6 Hz), 2.27 (3H, s), 2.47 (3H, s), 3.65 (4H, q, J=7.6 Hz), 9.40 (1H, br)	$C_{11}H_{17}O_3N_3$	55.41 (55.22)	7.14 (7.16)	17.63 (17.56)
32b[a]	3350, 1710, 1692, 1650, 1583	0.90 (6H, t, J=7.6 Hz), 1.20—2.00 (4H, m), 2.26 (3H, s), 2.46 (3H, s), 3.20—3.80 (4H, m), 9.47 (1H, br)	$C_{13}H_{21}O_3N_3$	58.61 (58.41)	7.84 (7.92)	15.80 (15.72)
32c	3340, 1700sh, 1690, 1650	1.70—2.1 (4H, m), 2.29 (3H, s), 2.46 (3H, s), 3.43—3.96 (4H, m), 9.17 (1H, br)	$C_{11}H_{15}O_3N_3$	55.73 (55.69)	6.36 (6.37)	17.72 (17.71)
32d[b]	3310, 1705sh, 1685, 1640, 1575	1.40—1.90 (6H, br), 2.28 (3H, s), 2.48 (3H, s), 3.40—3.80 (4 H, br), 9.33 (1H, br)	$C_{12}H_{17}O_3N_3$	57.48 (57.36)	7.03 (6.82)	16.70 (16.72)
32e[c]	3280, 1705sh, 1682, 1675sh, 1638, 1578	2.30 (3H, s), 2.47 (3H, s), 3.76 (8H, br), 9.30 (1H, br)	$C_{11}H_{15}O_4N_3$	52.04 (52.17)	5.90 (5.97)	16.83 (16.59)
32f	3330, 1706, 1680, 1640, 1574	1.02—1.50 (6H, br), 2.45—3.12 (4H, br), 3.75 (8H, br), 9.37 (1H, br)	$C_{13}H_{19}O_4N_3$	55.53 (55.50)	7.07 (6.81)	14.77 (14.94)
32g	3300, 3160sh, 1695, 1680sh, 1640, 1583	0.70—1.15 (6H, m), 1.35—2.1 (4H, m), 2.30—3.00 (4H, m), 3.74 (8H, br), 9.32 (1H, br)	$C_{15}H_{23}O_4N_3$	57.99 (58.24)	7.57 (7.49)	13.51 (13.58)
32h	3340, 1693, 1637, 1565	1.22 (6H, d, J=7.0 Hz), 1.31 (6H, d, J=7.0 Hz), 2.6—3.6 (2H, m), 3.76 (8H, br), 9.37 (1H, br)	$C_{15}H_{23}O_4N_3$	58.09 (58.24)	7.61 (7.49)	13.46 (13.58)
32i	3300, 1710sh, 1685, 1638, 1574	0.65—1.00 (6H, br), 1.00—2.0 (12H, m), 2.36—2.95 (4H, m), 3.70 (8H, s), 9.30 (1H, br)	$C_{19}H_{31}O_4N_3$	62.54 (62.24)	8.53 (7.49)	11.50 (13.58)
32j	3320, 1710sh, 1690, 1680sh, 1640, 1570	0.60—1.1 (6H, br), 0.95—2.0 (28H, m), 2.2—3.0 (4H, m), 3.6—3.9 (8H, m), 9.36 (1H, br)	$C_{27}H_{47}O_4N_3$	67.67 (67.89)	10.10 (9.92)	8.92 (8.80)
32k	3340, 1710sh, 1690, 1648, 1580	1.20 (3H, t, J=7.0 Hz), 2.30 (3H, s), 2.87 (2H, q, J=7.0 Hz), 3.74 (8H, s), 9.33 (1H, br)	$C_{12}H_{17}O_4N_3$	53.79 (53.92)	6.29 (6.41)	15.75 (15.72)
32l	3350, 1708, 1690, 1640, 1578	0.93 (3H, t, J=7.0 Hz), 1.35—2.0 (2H, m), 2.29 (3H, s), 2.94 (2H, q, J=7.0 Hz), 3.70 (8H, s), 9.27 (1H, br)	$C_{13}H_{19}O_4N_3$	55.30 (55.30)	6.74 (6.81)	15.16 (14.94)

a) mass spectrum *m/e* (rel. intensity): 267 (M^+, 43%), 238 (9%), 225 (3%), 224 (6%), 209 (5%), 208 (5%), 196 (27%), 179 (24%), 167 (19%), 165 (22%), 125 (34%), 110 (13%), 72 (28%), 43 (100%), 42 (21%), 41 (26%)
b) mass spectrum *m/e* (rel. intensity): 251 (M^+, 34%), 209 (5%), 208 (2%), 192 (12%), 191 (6%), 167 (12%), 165 (19%), 151 (15%), 141 (7%), 125 (9%), 123 (9%), 110 (15%), 84 (54%), 83 (100%), 69 (21%), 43 (63%)
c) mass spectrum *m/e* (rel. intensity): 254 (M^++1, 13%), 253 (M^+, 89%), 235 (35%), 211 (10%), 194 (19%), 193 (15%), 167 (21%), 125 (70%), 86 (36%), 85 (50%), 43 (100%)

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