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Syntheses of 4-Alkylidene- and 4-Aralkylidene-2-chloromethyl-5-oxazolones and *N*-(Chloroacetyl)dehydroamino Acids

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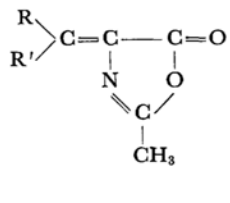
Treatment of *N*-dichloroacetyl amino acids with acetic anhydride at a temperature between 85°C and 130°C yielded 4-alkylidene- and 4-aralkylidene-2-chloromethyl-5-oxazolones, which were readily hydrolyzed to give 2-(2-chloroacetamido)-2-alkenoic acids, *i. e.*, *N*-(chloroacetyl)-dehydroamino acids.

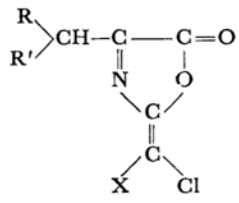
Several synthetic methods of 2-(2-chloroacetamido)-2-alkenoic acid, *i. e.*, *N*-(chloroacetyl)dehydroamino acid have been known, since the acid can be used as one of the most convenient intermediates for dehydropeptide synthesis.[1] Greenstein and his coworkers reported the preparation of several *N*-(chloroacetyl)dehydroamino acids by treating a mixture of α-keto acids and chloroacetonitrile with dry hydrogen chloride.[2] The reaction with pyruvic acid leads to the substantially quantiative formation of 2-(2-chloroacetamido)-acrylic acid, *i. e.*, *N*-(chloroacetyl)dehydroalanine in a pure state,[2a] which can be also prepared by the condensation of pyruvic acid with chloroacetamide in 30% yield.[3] In the condensations of other α-keto acids, such as α-ketovaleric acid or α-ketocaproic acid, with chloroacetonitrile, however, the yields of the products are low and the isolation and purification are difficult.[2b,c] Bergmann and his coworkers described that *N*-(chloroacetyl)phenylserine could be dehydrated under carefully controlled conditions by the action of acetic anhydride to give 4-benzylidene-2-chloromethyl-5-oxazolone, which, upon hydrolysis with dilute alkali, afforded α-2-(chloroacetamido)-cinnamic acid, *i. e.*, *N*-(chloroacetyl)dehydrophenylalanine.[4] Sheehan and Duggins reported the formation of α-(2-chloroacetamido)cinnamic acid in the treatment of *N*-(dichloroacetyl)phenylalanine with acetic anhydride in the presence of pyridine.[5] The formation has been explained by the initial cyclization of *N*-(dichloroacetyl)phenylalanine into 4-benzylidene-2-chloromethyl-5-oxazolone, followed by a hydrolytic fission of the oxazolone ring.

This paper deals with the preparation and characterization of 4-alkylidene- and 4-aralkylidene-2-chloromethyl-5-oxazolones and those transformations into *N*-(chloroacetyl)dehydroamino acids.

The treatment of *N*-(chloroacetyl)phenylalanine or *N*-(chloroacetyl)leucine with acetic anhydride has been known to form readily 4-benzylidene- or 4-isobutylidene-2-methyl-5-oxazolone (I, R=C_6H_5 or *i*-C_3H_7; R′=H) by the elimination of one molecule each of water and hydrogen chloride.[6] On the other hand, the recent report by Steglich *et al.* showed that *N*-trichloroacetyl amino acids, upon treatment with dicyclohexylcarbodiimide or phosphorus trichloride in the presence of pyridine, gave 2-dichloromethylene-pseudo-5-oxazolones (II, X=Cl).[7]



I



II

When *N*-dichloroacetyl-L-leucine (IIIb) was heated in acetic anhydride at 85—90°C for 1 hr, 2-chloromethyl-4-isobutylidene-5-oxazolone (IVb) was obtained in 74% yield. The structure of IVb was determined by its elemental analysis and spectral studies as well as the hydrolysis reaction. The infrared spectrum showed a strong, broad band at 1800 cm^{-1} (C=O), a strong sharp band at 1670 (C=N) and a weak band at 1615 (C=C). The

1) a) J. P. Greenstein and M. Winitz, "Chemistry of Amino Acids," Vol. 2, John Wiley and Sons, Inc., New York (1961), pp. 838—860; b) J. P. Greenstein, "Advances in Enzymology," Vol. 8, F. F. Nord, Ed., Interscience Publishers, Inc., New York (1948), p. 117.

2) a) V. E. Price and J. P. Greenstein, *J. Biol. Chem.*, **171**, 477 (1947); b) A. Meister and J. P. Greenstein, *ibid.*, **195**, 849 (1952); c) L. Levintow, S.-C. J. Fu, V. E. Price and J. P. Greenstein, *ibid.*, **184**, 633 (1950).

3) T. Wieland, G. Ohnacker and W. Ziegler, *Chem. Ber.*, **90**, 194 (1957).

4) M. Bergmann, V. Schmidt and A. Miekeley, *Z. Physiol. Chem.*, **187**, 264 (1930).

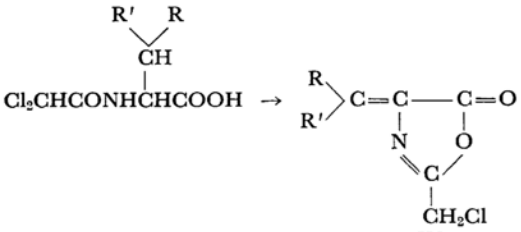
5) J. C. Scheehan and W. E. Duggins, *J. Am. Chem. Soc.*, **74**, 2475 (1950).

6) a) M. Bergmann and F. Stern, *Ann.*, **448**, 20 (1926); b) D. G. Doherty, J. E. Tiezman and M. Bergmann, *J. Biol. Chem.*, **147**, 617 (1943).

7) W. Steglich, H. Tanner and R. Hurnaus, *Chem. Ber.*, **100**, 1824 (1967).

NMR spectrum exhibited a doublet at τ 3.44, a singlet at 5.64, a multiplet centered at 6.8, and a doublet at 8.85. The peak areas were in the ratio 1.0 : 2.3 : 1.0 : 6.0 (theory 1 : 2 : 1 : 6). The peak pattern corresponds not to the pseudo-oxazolone structure II (R=*i*-C_3H_7; R'=H; X=H), but to 2-chloromethyl-4-isobutylidene-5-oxazolone structure IVb.

Analogous treatments of several *N*-dichloroacetyl amino acids (III) with actic anhydride resulted in the formation of the corresponding 4-alkylidene- and 4-aralkylidene-2-chloromethyl-5-oxazolones (IV). The yields of the oxazolones IV were affected sensitively with the reaction temperature, probably owing to the thermo-unstability of IV. After much repeated experiments under various conditions, the best yields could be obtained only at the temperature described in Experimental. Sheehan and Duggins demonstrated that the treatment of *N*-(dichloroacetyl)phenylalanine (IIId) with acetic anhydride at 100°C for seventy-five min led only to recovery of the starting material.[5] In our experiment, however, 4-benzylidene-2-chloromethyl-5-oxazolone (IVd) was obtained in 61% yield by the treatment at 130°C for 1 hr.



	R	R'
IIIa	CH_3	CH_3
b	*i*-C_3H_7	H
c	C_2H_5	CH_3
d	C_6H_5	H
e	*p*-HO-C_6H_4	H

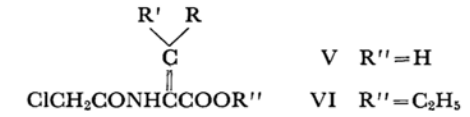
IV

IVf R=*p*-AcO-C_6H_4, R'=H

4-Alkylidene-2-chloromethyl-5-oxazolones were susceptible to undergo hydrolysis. Even when left to stand at room temperature, the oily oxazolones were partially hydrolyzed by atmospheric moisture to afford the crystalline product. Treatment of 2-chloromethyl-4-isopropylidene-5-oxazolone (IVa) with water at room temperature gave 2-(2-chloroacetamido)-3-methylcrotonic acid, *i. e.*, *N*-(chloroacetyl)dehydrovaline (Va) in 80% yield.

In a similar fashion, *N*-(chloroacetyl)dehydroleucine (Vb), *N*-(chloroacetyl)dehydroisoleucine (Vc) and *N*-(chloroacetyl)dehydrophenylalanine (Vd) were prepared by the hydrolysis of the oxazolones (IVb, IVc, IVd). The acids V were characterized by elemental analyses and infrared spectra.[8] In turn, the formation of V also supported the structure of the parent oxazolone IV.

When 2-chloromethyl-4-isopropylidene-5-oxazolone (IVa) was refluxed in ethanol, the ethanolysis product, ethyl 2-(2-chloroacetamido)-3-methylcrotonate (VIa) was obtained in 17% yield. The ester VIa was also obtained in 39% yield by the esterification of the acid Va in the presence of



V R''=H

VI R''=C_2H_5

sulfuric acid and *p*-toluenesulfonic acid. The NMR analysis revealed that the ester has an *N*-acyl-enamine structure VIa and not the tautomeric *N*-acyl-imine structure (see Experimental).

The amination of the crude 2-(2-chloroacetamido)-2-alkenoic acids V with ammonia has been known to give *N*-(glycyl)dehydroamino acids.[2b,c] In order to study the reactivity of the chloroacetyl group, the reactions of *N*-(chloroacetyl)dehydroleucine (Vb) with several amines were carried out.

Piperidine (pK_a=11.22) reacted with Vb immediately at room temperature to afford 4-methyl-2-(2-piperidinoacetamido)-2-pentenoic acid hydrochloride. Analogously, L-leucine ethyl ester (pK_a=7.66) treated smoothly with Vb within half an hour to give 4-methyl-2-[2-(1-ethoxycarbonyl-3-methylbutylamino)acetamido] - 2 - pentenoic acid hydrochloride, while the reaction of Vb with pyridine (pK_a=5.23) occurred in acetonitrile at the refluxing temperature to yield the corresponding pyridinium chloride. The reaction with aniline (pK_a=4.6) was attempted in refluxing tetrahydrofuran or acetonitrile, but the starting materials were recovered.

N-(Chloroacetyl)dehydrophenylalanine (Vd) was again treated with acetic anhydride under the same condition as for the preparation of IVd, but this reaction gave 4-benzylidene-2-methyl-5-oxazolone in 74% yield, instead of the parent oxazolone IVb. The formation of the dechlorinated oxazolone is possibly explained by an exchange of the chloroacetyl group of Vd with acetyl group, followed by the cyclization of the resultant α-acetamidocinnamic acid.

N-Dichloroacetyl amino acids (III) were prepared by treatment of amino acids with dichloroacetyl chloride in ethyl acetate[9] or in aqueous sodium hydroxide.

Treatment of DL-valine with 1.2—1.3 equiv. of dichloroacetyl chloride in refluxing ethyl acetate afforded not only *N*-dichloroacetyl-DL-valine (IIIa), but also *N*-(chloroacetyl)dehydrovaline (Va). The formation of Va could be easily rationalized by transformation of IIIa with dichloroacetyl chloride into the oxazolone IVa, followed by hydrolysis of IVa.

8) There has been no description about the constants of *N*-chloroacetyl derivatives of dehydrovaline, dehydroleucine, and dehydroisoleucine, owing to the difficulties in the purification of the products from the reactions of α-keto acids with chloroacetonitrile.[2b,c]

9) E. Ronwin, *J. Org. Chem.*, **18**, 1546 (1953).

TABLE 1. YIELDS OF PRODUCTS IN THE REACTION OF AMINO ACIDS WITH DICHLOROACETYL CHLORIDE

Amino acid	Method[a]	Yield of III %	Yield of V %
DL-Valine	A-1	33	12
	A-2	44	Trace
	B	32	—
L-Leucine	A-2	46	0
	B	54	—
DL-Isoleucine	A-1	48	0
	A-2	45	0
	B	69	—
DL-Phenylalanine	A-1	38	16
	A-2	48	Trace
	B	62	—
L-Tyrosine	A-1	42	Trace
	B	41	—

a) A-1 means the reaction in ethyl acetate where the amino acid and dichloroacetyl chloride were used in the mole ratio 1 : 1.2—1.3. A-2 means the reaction in ethyl acetate where the amino acid and dichloroacetyl chloride were used in the mole ratio 1 : 0.5—0.7. B means the reaction in aqueous sodium hydroxide. (See Experimental)

Analogous treatment of other amino acids with dichloroacetyl chloride in ethyl acetate led to the results summarized in Table 1.

Experimental[10]

Dichloroacetyl chloride was prepared by using the technique of Boshard *et al.*[11] for trichloroacetyl chloride. A mixture of dichloroacetic acid (162 m*l*, 247 g, 1.92 mol), thionyl chloride (160 m*l*, 259 g, 2.18 mol) and dimethylformamide (20 m*l*, 18.5 g, 0.25 mol) was heated at 70—85°C for 4 hr, and then distilled to give a colorless liquid (214 g, 76%), bp 104—109°C (lit.[12] bp 105—107°C).

***N*-Dichloroacetyl Amino Acids (III).** *A) Reaction in Ethyl Acetate.* The procedure was modified from the method of Ronwin.[9] To a suspension of an amino acid (25 g) in ethyl acetate (300 m*l*) was added the appropriate equiv. of dichloroacetyl chloride, and the mixture was refluxed for 30 min in the case of DL-valine, L-leucine and DL-isoleucine, or for 1 hr in the case of DL-phenylalanine and L-tyrosine. After the removal of the insoluble substance, the resultant solution was concentrated and the residue was treated with a small amount of ether in the case of DL-valine, DL-isoleucine, DL-phenylalanine and L-tyrosine, or with a small amount of carbon tetrachloride in the case of L-leucine: thereby the dichloroacetyl amino acid separated as a crystalline product, which was collected and washed with the same solvent as that of the filtrate.[13] The product was characterized by the melting point[5,9] and the infrared spectrum, which exhibited four characteristic sharp bands at 3300—3250, 1730—1715, 1680—1660 and 1560 cm^{-1}. The yields were summarized in Table 1.

The combined filtrate and washing were concentrated to yield *N*-(chloroacetyl)dehydroamino acid in the yield shown in Table 1. The product was characterized by comparison (mp and infrared spectrum) with a sample obtained by the method described below, except *N*-(chloroacetyl)dehydrotyrosine.

B) Reaction in Aqueous Sodium Hydroxide. The procedure was modified from the method for the preparation of *N*-dichloroacetyl-DL-phenylalanine described by Sheehan and Duggins.[5] To a solution of an amino acid (0.2 mol) in 1 N sodium hydroxide (200 m*l*) were added dropwise, with stirring, dichloroacetyl chloride (30 g) and 1 N sodium hydroxide (210 m*l*) below 0°C. After the additions had been completed, the mixture was stirred for several hr, while being allowed to warm to room temperature. The insoluble substance was removed and the filtrate was acidified to pH 1 with concentrated hydrochloric acid. The crystalline solid was collected, dissolved in ethyl acetate and dried over anhydrous sodium sulfate. Evaporation of the ethyl acetate afforded the *N*-dichloroacetyl amino acid[13] in the yield shown in Table 1. In the case of L-tyrosine, analogous directions were followed to the procedure for the preparation of *N*-chloroacetyl-L-tyrosine described by Fisher.[14]

4-Isopropylidene-2-chloromethyl-5-oxazolone (IVa). A suspension of *N*-dichloroacetyl-DL-valine (11.7 g) in acetic anhydride (35 m*l*) was heated at 95—105°C for 1 hr. The resultant red-brown solution was concentrated and the residual oil was distilled to give a pale yellow oil (6.9 g, 78%), bp 93—103°C/2 mmHg.[15] A colorless fraction, bp 103.5°C/2.5 mmHg, obtained from the redistillation was submitted to analysis.[15] IR (liquid film): 1800, 1670, 1615 cm^{-1}. NMR ($CDCl_3$): τ 5.65 (s, 2H), 7.62 (s, 3H), 7.71 (s, 3H).

Found: C, 47.50; H, 4.36; N, 7.76%. Calcd for $C_7H_8NO_2Cl$: C, 48.41; H, 4.61; N, 8.07%.

4-Isobutylidene-2-chloromethyl-5-oxazolone (IVb). In a manner analogous to the case of IVa, dichloroacetyl-L-leucine (10 g) was treated with acetic anhydride (60 m*l*) at 85—90°C for 1 hr to give a pale yellow oil (5.7 g, 74%), bp 90—102°C/3 mmHg.[13] A colorless fraction, bp 90°C/1 mmHg, obtained from the redistillation was submitted to analysis. The spectra data were described in the text.

Found: C, 50.97; H, 5.54; N, 7.66%. Calcd for $C_8H_{10}NO_2Cl$: C, 51.20; H, 5.33; N, 7.47%.

4-*s*-Butylidene-2-chloromethyl-5-oxazolone (IVc). In a manner analogous to the case of IVa, *N*-dichloroacetyl-DL-isoleucine (17 g) was treated with acetic anhydride (30 m*l*) at 115—125°C for 1—1.5 hr to

10) All concentrations and evaporations were carried out by rotary evaporation under reduced pressure. All melting points were determined in a liquid bath, and those and boiling points are uncorrected.

11) H. H. Boshard, R. Mory and H. Zollinger, *Helv. Chim. Acta*, **42**, 1653 (1959).

12) H. C. Brown, *J. Am. Chem. Soc.*, **60**, 1326 (1938).

13) The product was sufficiently pure to be used for a next reaction without further purification.

14) E. Fisher, *Chem. Ber.*, **37**, 2494 (1904).

15) The analytical results were outside the generally accepted limits for C and H, possibly owing that the oxazolone IVa is too sensitive towards atmospheric moisture to be microanalyzed. But the formation was characterized by the spectral data and by the conversion to *N*-(chloroacetyl)dehydrovaline (Va).

give a pale yellow oil (8.9 g, 67%), bp 90—102.5°C/0.8 mmHg.[13] A colorless fraction, bp 113—115°C/3.5 mmHg, obtained from the redistillation was submitted to analysis. IR (liquid film): 1800, 1670, 1615 cm^{-1}.

Found: C, 50.83; H, 5.02; N, 7.84%. Calcd for $C_8H_{10}NO_2Cl$: C, 51.20; H, 5.33; N, 7.47%.

4-Benzylidene-2-chloromethyl-5-oxazolone (IVd). A mixture of *N*-dichloroacetyl-DL-phenylalanine (18.5 g) and acetic anhydride (80 m*l*) was heated at 130°C for 1 hr. The resultant red-brown solution was concentrated and the crystalline residue was treated with methanol (20 m*l*). The collected yellow product was washed twice with methanol (4 m*l*×2). Yield: 8.9 g (61%).[13] A part of the product was recrystallized from ethanol to give yellow plates, mp 109—110°C (lit.[4] mp 114°C). IR: 1785, 1660, 1605 cm^{-1}. NMR ($CDCl_3$): τ 2.0 and 2.7 (m, 6H), 5.65 (s, 2H).

4-(*p*-Acetoxybenzylidene)-2-chloromethyl-5-oxazolone (IVf). In a manner analogous to the case of IVd, *N*-dichloroacetyl-L-tyrosine (5.2 g) was treated with acetic anhydride (20 m*l*) at 105—115°C for 1 hr to give IVf as yellow crystals (3.9 g, 78%). Recrystallization from carbon tetrachloride afforded orange crystals, mp 123.5°C (after sintered at 110°C). IR (KBr): 1790, 1760, 1655, 1605 cm^{-1}.

Found: C, 55.57; H, 3.27; N, 4.95%. Calcd for $C_{13}H_{10}NO_4Cl$: C, 55.81; H, 3.58; N, 5.01%.

The oxazolone IVf is soluble easily in ethyl acetate and tetrahydrofuran, moderately in carbon tetrachloride and slightly in water, ether, benzene and ethanol.

2-(2-Chloroacetamido)-3-methylcrotonic Acid (*N*-(Chloroacetyl)dehydrovaline, Va). A mixture of IVa (7.7 g) and water (15 m*l*) was left to stand at room temperature overnight: thereby the oily oxazolone had been hydrolyzed to give Va as a crystalline solid. The crystals were collected (6.5 g), and the filtrate was concentrated to give additional crystals (0.3 g). Total yield was 6.8 g, 80%.[13] An analytical sample was obtained by recrystallization from acetone, as colorless needles, mp 166—166.5°C (decomp.). IR (KBr): 3250, 1690, 1670, 1640, 1530 cm^{-1}.

Found: C, 44.00; H, 5.32; N, 7.28%. Calcd for $C_7H_{10}NO_3Cl$: C, 43.86; H, 5.22; N, 7.31%.

The acid Va is soluble easily in tetrahydrofuran, ethanol and acetone, moderately in hot acetonitrile, hot ethyl acetate and hot water, and slightly in ether, carbon tetrachloride and benzene.

2-(2-Chloroacetamido)-4-methyl-2-pentenoic Acid (*N*-(Chloroacetyl)dehydroleucine, Vb). The same directions were followed as for Va. From IVb (6.2 g) and water (10 m*l*) there was obtained Vb (5.7 g, 83%). Recrystallization from water afforded colorless needles, mp 128—129°C (decomp.). IR (KBr): 3250, 1695, 1670, 1625, 1525 cm^{-1}.

Found: C, 46.34; H, 5.84; N, 6.61%. Calcd for $C_8H_{12}NO_3Cl$: C, 46.72; H, 5.84; N, 6.81%.

2-(2-Chloroacetamido)-3-methyl-2-pentenoic Acid (*N*-(Chloroacetyl)dehydroisoleucine, Vc). The same directions were followed as for Va. From IVc (5.1 g) and water (15 m*l*) there was obtained Vc (4.1 g, 73%). Recrystallization from ethyl acetate afforded colorless needles, mp 149.5—150°C (decomp.). IR (KBr): 3250, 1690, 1675, 1630, 1530 cm^{-1}.

Found: C, 46.75; H, 5.67; N, 6.82%. Calcd for $C_8H_{12}NO_3Cl$: C, 46.72; H, 5.84; N, 6.81%.

α-(2-Chloroacetamido)cinnamic Acid (*N*-(Chloroacetyl)dehydrophenylalanine, Vd). A solution of IVd (8.86 g) and water (10 m*l*) in tetrahydrofuran (120 m*l*) was refluxed for 3 hr and then left to stand at room temperature overnight. The tetrahydrofuran was evaporated and the residue was treated with ether (50 m*l*) to give an almost colorless crystalline product (8.15 g, 86%).[13] Recrystallization from isopropyl alcohol afforded colorless needles, mp 194—195°C (decomp.) (lit. mp 204.5—206°C,[5] 207°C[4]). IR (KBr): 3250, 1690, 1665, 1635, 1525 cm^{-1}. NMR (CF_3COOH): τ1.35 (s, 1NH), 2.11 (s, 1H), 2.54 (m, 5H), 5.71 (s, 2H).

α-(2-Chloroacetamido)-*p*-hydroxycinnamic Acid (*N*-(Chloroacetyl)dehydrotyrosine, Ve). This compound was obtained from the reaction of DL-tyrosine with dichloroacetyl chloride in ethyl acetate, as described above. Recrystallization from acetonitrile afforded pale yellow needles, mp 185°C (decomp.). IR (KBr): 3375, 3200, 1675 (broad), 1635, 1515 cm^{-1}.

Found: C, 51.82; H, 3.74; N, 5.75%. Calcd for $C_{11}H_{10}NO_4Cl$: C, 51.66; H, 3.91; N, 5.48%.

The acid Ve is soluble easily in tetrahydrofuran, ethanol, hot acetonitrile and hot water, and slightly in ethyl acetate and ether.

4-Methyl-2-(2-piperidinoacetamido)-2-pentenoic Acid Hydrochloride. Colorless needles (from ethyl acetate), mp 110—111°C.

Found: C, 53.72; H, 7.96; N, 9.79%. Calcd for $C_{13}H_{23}N_2O_3Cl$: C, 53.70; H, 7.92; N, 9.64%.

4-Methyl-2-[2-(1-ethoxycarbonyl-3-methylbutylamino)acetamido]-2-pentenoic Acid Hydrochloride. Colorless plates (from ethyl acetate), mp 134—135°C.

Found: C, 53.06; H, 8.09; N, 7.57%. Calcd for $C_{16}H_{29}N_2O_5Cl$: C, 52.67; H, 7.96%; N, 7.68%.

[*N*-(1-Carboxy-3-methyl-1-butenyl)carbamoylmethyl]pyridinium Chloride. Colorless crystals (from isopropyl alcohol), mp 222—223°C (decomp.).

Found: C, 55.25; H, 5.90; N, 9.55%. Calcd for $C_{13}H_{17}N_2O_3Cl$: C, 54.83; H, 5.98; N, 9.84%.

Ethyl 2-(2-Chloroacetamido)-3-methylcrotonate (VIa). *A) From IVa.* A solution of IVa (bp 89—98°C/1.5 mmHg, 6.9 g) in ethanol (20 m*l*) was refluxed for 4 hr. After evaporation of the ethanol, the residue was dissolved in ether and washed successively with a small amount of aqueous sodium bicarbonate and with water. The ethereal layer was dried over anhydrous sodium sulfate and evaporated to give the ester, which was treated with *n*-dibutyl ether and collected (1.45 g, 17%, mp 115—116°C). Recrystallization from water-methanol (11 : 9) and then from *n*-dibutyl ether gave colorless long needles, mp 118—119°C. IR (KBr): 3200, 1715, 1665, 1535 cm^{-1}. NMR ($CDCl_3$): τ 2.07 (s, 1H), 5.77 (q, 2H), 5.86 (s, 2H), 7.80 (s, 3H), 8.15 (s, 3H), 8.72 (t, 3H).

Found: C, 49.41; H, 6.24; N, 6.09%. Calcd for $C_9H_{14}NO_3Cl$: C, 49.20; H, 6.38; N, 6.38%.

B) From Va. A mixture of Va (2 g), ethanol (15 m*l*), benzene (20 m*l*), *p*-toluenesulfonic acid (0.5 g) and concentrated sulfuric acid (0.5 g) was refluxed for 5 hr. After concentration of the solution, ether and water were added to the resultant oily residue. The ethereal layer was spearated and the aqueous layer was extracted further twice with ether. The combined extracts were dried over anhydrous sodium sulfate and concentrated to give the ester (0.9 g, 39%), mp 109—

110°C. Recrystallization raised the mp to the value described in A method. The product was identical (mp and infrared spectrum) with the above sample.

Treatment of Vd with Acetic Anhydride. A suspension of Vd (1 g) in acetic anhydride (30 m*l*) was heated at 120—130°C for 1 hr. After concentration of the resultant solution, the crystalline residue was treated with ethanol (10 m*l*) and collected (0.58 g). Recrystallization from ethanol gave pale yellow needles, mp 152.5°C, which was identical in mp and infrared spectrum with authentic 4-benzylidene-2-methyl-5-oxazolone, mp 151—153°C (lit.[6a] mp 151—152°C).