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SYNTHESIS OF ALKYL- AND PHENYL-SUBSTITUTED 4-AMINOMETHYL-2-BUTEN-4-OLIDES

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UDC 547.391.4'724.466.3:543.422:541.63

4-Aminomethyl-2-buten-4-olides, 5-hydroxy-5,6-dihydro-2-pyridone, and isomeric 8,9-dihydro-4-cyano-2-oxofuro[2,3-c]piperidines were obtained by the base-catalyzed cyclization of 5-amino-4-hydroxy-4-alkyl-2-pentenoic acid esters. 5-Dimethylamino-3-methyl-4-oxovaleric acid ester and 4-dimethylamino-2-buten-4-olide, respectively, were isolated by isomerization of 5-dimethylamino-3-methyl-4-hydroxy-2-pentenoic acid ester and 4-dimethylamino-2-penten-5-olide in the presence of sodium isopropoxide.

γ-Heteromethyl-substituted unsaturated γ-lactones are members of the series of natural compounds and substances with high biological activity, and they are also used in organic synthesis [1-8]. The hydrolysis of derivatives of 4,5-epoxy-2-alkenoic acids, which are synthesized in the form of mixtures of Z,E isomers by olefination of acyloxiranes by the Wittig–Horner method [3, 8-11], has been used extensively in recent years to obtain γ-hydroxymethyl-substituted butenolides [3, 8, 9]; the yield of the lactone is limited by the percentage of the Z isomer of the substrate in the mixture, since the preponderant E isomer usually does not undergo lactonization under conditions of acid-catalyzed hydrolysis [3, 9].

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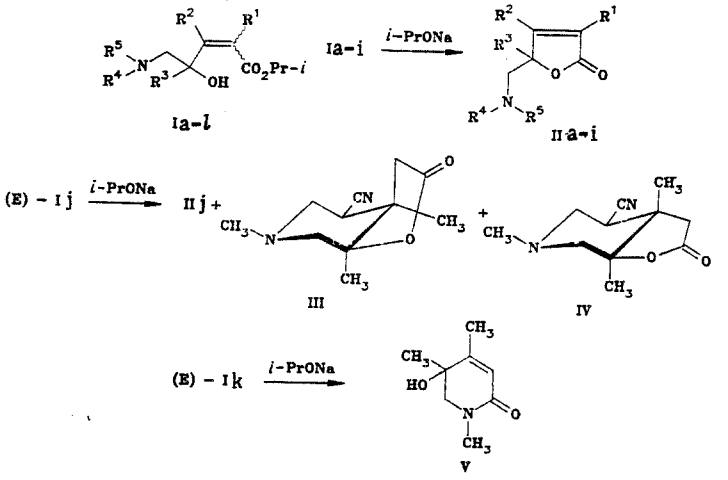
0009-3122/87/2310-1049 $12.50

We have previously reported the formation of 5-amino-4-hydroxy-2-pentenoic acid esters I by the reaction of 4,5-epoxy-2-pentenoic acid esters with alkyl- and dialkylamines [12]. It seemed of interest to study the possibility of the lactonization of Ia-ℓ under the conditions of basic catalysis.

It was found that isopropyl esters of both the individual E isomers and mixtures of the Z,E isomers of alkyl- and phenyl-substituted 5-dialkylamino-4-hydroxy-2-pentenoic acids (Ia-i) form the previously unknown 4-dialkylaminomethyl-2-buten-4-olides (IIa-i, Table 1) when they are refluxed in toluene in the presence of sodium isopropoxide. The cyclization of the E isomers of Ia-i proceeds via the reversible addition of the alkoxide anion to the activated double bond; the characteristic (for glycidic esters) isomerization of Ia-i with the participation of the α-hydrogen atoms [13] is not observed in this case, as indicated by the synthesis, under the conditions presented, of α-substituted lactone Id in high yield.

The use in the investigated transformation of functionally substituted (in the dialkylamino group) esters with structure I opens up a new approach to the synthesis of piperidinecarbolactones, which are of definite interest as biologically active substances [14, 15]. Thus, as a result of the treatment of isopropyl (E)-5-[N-methyl-N-(2-cyanoethyl)amino]-4-hydroxy-3,4-dimethyl-2-pentenoate (Ij) with sodium isopropoxide under the conditions indicated above, we isolated chromatographically a small amount of the corresponding butenolide IIj and products of Michael intramolecular addition – isomeric cyano-substituted piperdinecarbolactones III and IV in a ratio of 3.8:1 (the overall yield of the latter was 76%). Individual lactone IV, under the reaction conditions, is probably converted to III via recyclization of the piperidine ring; this makes it possible to assume trans fusion of the rings in lactone IV, since two-ring carbolactones with similar structures readily undergo base-catalyzed isomerization to cis-fused structures [6]. In the case of prolonged exposure of the reaction mixture with a close-to-equimolar amount of the catalyst the only product of transformation of ester Ij is lactone III; however, its yield is low because of significant resinification.



Ia—ç,e—ℓ, IIa—c,e—j R^1=H; Id, IId R^1=CH_3; I, II a R^2=R^3=R^4=R^5=CH_3; b R^2=R^3=CH_3, R^4=R^5=C_2H_5; c, d R^2=R^3=CH_3, R^4—R^5=$(CH_2)_5$; e R^2=R^3=CH_3, R^4—R^5=$(CH_2)_6$; f R^2=R^3=CH_3, R^4—R^5=$(CH_2)_2O(CH_2)_2$; g R^2=H, R^3=p-Pr, R^4=R^5=CH_3; h R^2=Ph, R^3=R^4=R^5=CH_3; i R^2=Ph, R^3=CH_3, R^4—R^5=$(CH_2)_5$; j R^2=R^3=R^4=CH_3, R^5=CH_2CH_2CN; Ik R^2=R^3=R^4=CH_3, R^5=H; Iℓ R^2=R^4=R^5=CH_3, R^3=H

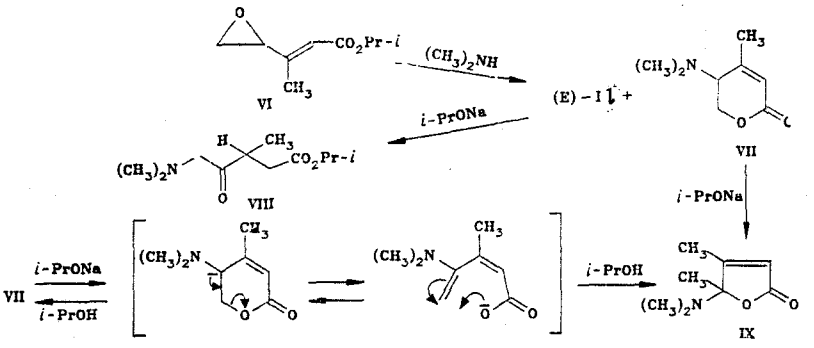
Ester (E)-Ik, which contains a secondary amino group, forms 5-hydroxyl-1,4,5-trimethyl-5,6-dihydro-2-pyridone (V) in high yield; this is associated with the greater nucleophilicity of the amino group as compared with the hydroxy group and is in agreement with our data on the transformation of γ-methylaminomethylbutyrolactones to δ-lactams [12].

In order to synthesize aminomethylbutenolides that do not contain an alkyl group in the γ position (II, R^3 = H) we studied the reaction of isopropyl 3-methyl-4,5-epoxy-2-pentenoate (VI, Z:E = 2:1) [17] with dimethylamine; in addition to ester (E)-Iℓ, we isolated, in low yield, a cyclic product of opening of the oxirane ring in VI counter to the Krasuskii rule, viz., 4-dimethylamino-3-methyl-2-penten-5-olide (VII). Compound Iℓ, in contrast to its analogs Ia-i, upon treatment with sodium isopropoxide does not undergo lactonization, but, as a

result of protrotropic rearrangement, which was previously observed in a series of aryl-substituted γ-hydroxycrotonic acids [18], is converted to isopropyl 5-dimethylamino-3-methyl-4-oxovalerate (VIII). Under the same conditions, unsaturated lactone VII undergoes isomerization to 4-dimethylamino-3,4-dimethyl-2-buten-4-olide (IX), which is probably formed via deprotonation of VII at the 4-CH group, opening of the ring as a result of a Michael retroreaction, and competitive (with respect to δ-lactonization) irreversible 5-exo-trig addition of the carboxylate anion to the conjugated enamine.

The structures of the compounds obtained were confirmed spectrally and by the results of elementary analysis, as well as by alternative synthesis of lactone IIc via the method that we previously proposed [6].

Absorption bands of C=O and C=C groups at 1750-1770 and 1640-1650 cm^{-1}, respectively, are observed in the IR spectra of unsaturated lactones IIa-c, e, f, j and IX; this is characteristic for unsaturated lactones. In the spectrum of α-substituted lactone IId the absorption band of the C=C bond is shifted to the short-wave region, and conjugation with the phenyl group (lactones IIh, i) leads to a decrease in the absorption frequency of the double bond. A lower $\nu_{C=O}$ value is characteristic for δ-lactone VII, while the band of carbonyl absorption in the spectra of bicyclic γ-butyrolactones III and IV is observed at 1785 cm^{-1}. A distinctive feature of the IR spectrum of δ-lactam V is the presence of absorption bands of OH groups at 3310 and 3357 cm^{-1} and a shift of the absorption bands of the C=O and C=C groups to 1660 and 1605 cm^{-1}, respectively.



A doublet of a 3-CH_3 group and the presence of a quartet of 2-H proton, as well as a significant difference in the chemical shifts of the 3-CH_3 and 4-CH_3 groups in lactones IIa-f, j, and IX, are characteristic for the PMR spectra of lactones IIa-c, e, f, j, V, and IX. In the PMR spectra of piperidinecarbolactones III and IV the spin-spin coupling constants (SSCC) of the 4-H proton indicate its axial orientation and, consequently, the equatorial orientation of the adjacent cyano group. The configuration of III was established on the basis of a study of the PMR spectra with recourse to the method of the Overhauser nuclear effect (the differential method). Saturation of the resonance signals of both the 8-CH_3 and 9-CH_3 groups leads to an increase in the intensity of the signal of the methyl groups, which is possible in the case of their, respectively, axial and equatorial orientations.

A molecular-ion peak is observed in the mass spectra of all of the synthesized compounds. The most intense peaks in the mass spectra of IIa-j and VIII correspond to $[R^4R^5NCH_2]^+$ ions; we have previously observed this in series of halogen-substituted aminobutenolides [6].

A study of the biological activity of the hydrochlorides of 4-aminomethyl-2-buten-4-olides IIa-c, e, i, which was made in the Central Scientific-Research Laboratory of the Minsk Medical Institute, showed that all of the investigated compounds display a significantly less pronounced diuretic action as compared with the previously obtained α-halo-substituted analogs [6].

EXPERIMENTAL

The IR spectra of solutions (0.1 mole/liter) of the substances in CCl_4 (layer thickness 0.01 cm) were recorded with a Specord 75-IR spectrometer. The PMR spectra of solutions in CCl_4 and in $CDCl_3$ were measured with Tesla BS-467 (60 MHz) and Bruker MW-360 (360 MHz) spectrometers with hexamethyldisiloxane (HMDS) as the internal standard. The mass spectra were obtained with a Varian MAT-311 spectrometer with a system for direct introduction of the

TABLE 1. Characteristics of the Synthesized Compounds

Compound	Tmp [bp (3 hPa)],* °C		IR spectrum, ν, cm⁻¹	PMR spectrum,† δ, ppm (J, Hz)	Found, %			Empirical formula	Calc., %			Yield, %‡
	base	hydrochloride			C	H	N		C	H	N	
IIa	35—36	165—166	1650 (C=C), 1765 (C=O)	1,3 (3H, s, CH_3); 1,98 (3H, d, J=1,5, CH_3); 2,18 [6H, s, $N(CH_3)_2$]; 2,32; 2,62 (2×1H, 2 d, J=14, CH_2); 5,51 (1H, q, J=1,5, CH=C)	63,8	8,7	8,3	$C_9H_{15}NO_2$	63,9	8,9	8,3	65 [85]
IIb	[87—88]	158—159	1650 (C=C), 1760 (C=O)	0,87 [6H, t, J=7, $(CH_2CH_3)_2$]; 1,28 (3H, s, CH_3); 1,95 (3H, e, J=1,5, CH_3); 2,47; 2,73 (2×1H, 2 d, J=14, CH_2); 2,51 [4H, q, $(CH_2CH_3)_2$; J=7]; 5,53 (1H, q, J=1,5, CH=C)	67,1	9,4	7,2	$C_{11}H_{19}NO_2$	67,0	9,7	7,1	50
IIc	53—54	208—209	1650 (C=C), 1760 (C=O)	1,17—1,60 [6H, m, $(CH_2)_3$]; 1,27 (3H, s, CH_3); 1,93 (3H, d, J=1,5, CH_3); 2,23—2,50 [4H, m, $N(CH_2)_2$]; 2,29; 2,58 (2×1H, 2 d, J=14, CH_2); 5,52 (1H, q, J=1,5, CH=C)	69,0	9,2	6,8	$C_{12}H_{19}NO_2$	68,9	9,2	6,7	58
IId	34—35	209—210	1680 (C=C), 1750 (C=O)	1,07—1,57 [6H, m, $(CH_2)_3$]; 1,26 (3H, s, CH_3); 1,70; 1,83 (2×3H, 2 q, J=1,5, CH_3); 2,23—2,50 [4H, m, $N(CH_2)_2$]; 2,23; 2,57 (2×1H, 2 d, J=14, CH_2)	70,1	9,5	6,3	$C_{13}H_{21}NO_2$	69,9	9,5	6,3	[82]
IIe	33—34	161—162	1645 (C=C), 1765 (C=O)	1,27 (3H, s, CH_3); 1,45 [8H, br. s, $(CH_2)_4$]; 1,93 (3H, d, J=1,5, CH_3); 2,52—2,85 [4H, m, $N(CH_2)_2$]; 2,60; 2,90 (2×1H, 2 d, J=14, CH_2); 5,53 (1H, q, J=1,5, CH=C)	70,0	9,4	6,4	$C_{13}H_{21}NO_2$	69,9	9,5	6,3	65
IIf	77—78	173—174	1645 (C=C), 1760 (C=O)	1,30 (3H, s, CH_3); 1,92 (3H, d, J=1,5, CH_3); 2,31—2,57 [4H, m, $N(CH_2)_2$]; 2,38; 2,62 (2×1H, 2 d, J=14, CH_2); 3,38—3,65 [4H, m, $O(CH_2)_2$]; 5,52 (1H, q, J=1,5, CH=C)	62,7	8,0	6,5	$C_{11}H_{17}NO_3$	62,5	8,1	6,6	49
IIg	[79—80]	154—155	1610 (C=C), 1755 (C=O)	0,78—1,90 (7H, m, C_3H_7); 2,17 [6H, s, $N(CH_3)_2$]; 2,33; 2,62 (2×1H, 2 d, J=14, CH_2); 5,93; 7,27 (2×1H, 2 d, J=6, CH=CH)	65,5	9,2	7,5	$C_{10}H_{17}NO_2$	65,5	9,4	7,6	56
IIh	Oil	164—165	1610 (C=C), 1760 (C=O)	1,53 (3H, s, CH_3); 2,14 [6H, s, $N(CH_3)_2$]; 2,53; 2,80 (2×1H, 2 d, J=14, CH_2); 6,15 (1H, s, CH=C); 7,38—7,62 (5H, m, C_6H_5)	72,9	7,6	6,0	$C_{14}H_{17}NO_2$	72,7	7,4	6,1	70
IIi	58—59	176—177	1610 (C=C), 1750 (C=O)	1,22—1,58 [6H, m, $(CH_2)_3$]; 1,58 (3H, s, CH_3); 2,23—2,57 [4H, m, $(CH_2)_2$]; 2,55; 2,82 (2×1H, 2 d, J=14, CH_2); 6,22 (1H, s, CH=C); 7,35—7,62 (5H, m, C_6H_5)	75,2	7,8	5,1	$C_{17}H_{21}NO_2$	75,3	7,8	5,2	79

IIj	Oil	—	1640 (C=C), 1750 (C=O), 2240 (C≡N)	1,50 (3H, s, CH_3); 1,77 (3H, d, J=1,5, CH_3); 2,03—2,63 [4H, m, $(CH_2)_2CN$]; 2,12 (3H, s, NCH_3); 2,25; 2,57 (2×1H, 2 d, J=14, CH_2); 5,67—5,72 (1H, q, J=1,5, CH=C)	63,5	7,6	13,4	$C_{11}H_{16}N_2O_2$	63,4	7,7	13,5	3
III	104—105	255—256	1785 (C=O), 2240 (C≡N)	1,31; 1,45 (2×3H, 2 s, CH_3); 2,18 (1H, d, J=12, 7a-H); 2,30 (1H, d, J=16,8, 3-H); 2,33 (3H, s, NCH_3); 2,37 (1H, t, $J=J_{5a,4a}$=11,0, 5a-H); 2,76 (1H, dd, $J_{7e,5e}$=1,8, J=12,0, 7e-H); 2,85 (1H, dd, $J_{4a,5e}$=4,8, $J_{4a,5a}$=11,0, 4a-H); 2,97 (1H, d, J=16,8, 3-H); 2,99 (1H, d.d.d. $J_{5e,7e}$=1,8, $J_{5e,4a}$=4,8, J=11,0, 5e-H)	63,6	7,6	13,5	$C_{11}H_{16}N_2O_2$	63,4	7,7	13,5	60
IV	126—127	—	1780 (C=O), 2240 (C≡N)	1,35; 1,37 (2×3H, 2 s, CH_3); 2,31 (1H, d, J=13,0, 7a-H); 2,34 (3H, s, CH_3); 2,46 (1H, dd $J_{5a,4a}$=10,5, J=13,2, 5a-H); 2,55; 2,68 (2×1H, 2 d, J=18,1, 3-CH_2); 2,85 (1H, d.d., $J_{7e,5e}$=1,8, J=13,0, 7e-H); 2,87 (1H, d.d.d. $J_{5e,7e}$=1,8, $J_{5e,4a}$=4,1, J=13,2, 5e-H); 2,97 (1H, dd $J_{4a,5e}$=4,1, $J_{4a,5a}$=10,5, 4a-H)	63,5	7,5	13,4	$C_{11}H_{16}N_2O_2$	63,4	7,7	13,5	16
V	115—116	—	1606 (C=C), 1660 (C=O), 3310, 3570 (OH)	1,26 (3H, s, CH_3); 1,88 (3H, d, J=1,5, CH_3); 2,92 (3H, s NCH_3); 3,18; 3,45 (2×1H, 2 d, J=12, CH_2); 4,33 (1H, br.s OH); 5,48 (1H, q, J=1,5, CH=C)	61,9	8,2	9,1	$C_8H_{13}NO_2$	61,9	8,4	9,0	70
VII	[87—88]	212—213	1645 (C=C) 1735 (C=O)	2,00 (3H, d, J=1,5; CH_3); 2,32 [6H, s, $N(CH_3)_2$]; 2,95—3,17 (1H, m, NCH); 4,10—4,77 (2H, m, CH_2); 5,73 (1H, br.s, CH=C)	62,1	7,9	9,2	$C_8H_{12}NO_2$	62,3	7,8	9,1	16
VIII	Oil	—	1720, 1735 (C=O)	0,98 (3H, d, J=7, CH_3); 1,11 [6H, d, J=7, $CH(CH_3)_2$]; 1,78—2,48 (2H, m, CH_2); 2,66—3,06 (1H, m, $CHCH_3$); 2,22 [6H, s, $N(CH_3)_2$]; 3,00 (2H, s, CH_2); 4,83 [1H, septet, J=7, $CH(CH_3)_2$]	61,5	9,8	6,5	$C_{11}H_{21}NO_3$	61,4	9,8	6,5	23
IX	42—43	—	1655 (C=C), 1750 (C=O)	1,48 (3H, s, CH_3); 1,92 (3H, d, J=1,5, CH_3); 2,24 [6H, s, $N(CH_3)_2$]; 5,50 (1H, q, J=1,5, CH=C)	62,0	8,6	9,1	$C_8H_{13}NO_2$	61,9	8,4	9,0	88

*Compound IIb had n_D^{20} 1.4726, IIg had n_D^{20} 1.4645, IIh had n_D^{20} 1.5615, VII had n_D^{20} 1.4930, and VIII had n_D^{20} 1.4582.

†The PMR spectrum of a solution of IIj in pyridine was recorded, while the PMR spectra of III and IV in $CDCl_3$ and V in $CHCl_3$ were recorded.

‡The yield of the product from the E isomer is given in parentheses.

samples; the ionizing-electron energy was 70 eV, and the ion-source temperature was 100-150°C. The course of the reactions and the purity of the compounds obtained were monitored by means of TLC on activity of II Al_2O_3 (development with iodine vapors).

The characteristics and yields of the compounds obtained are presented in Table 1.

Isopropyl 3-Methyl-4,5-epoxy-2-pentenoate (VI). This compound was obtained by the method in [17]. Esters Ia-c, e-i in the form of mixtures of Z and E isomers were obtained by the reaction of esters of alkyl- and phenyl-substituted 4,5-epoxypentenoic acids with secondary amines [12] and were subjected to lactonization without isolation from the reaction mixtures. The individual E isomers of esters Ia, d, k were isolated by crystallization of their hydrochlorides [12]. The E isomer of ester Ij was obtained by crystallization from a mixture of the isomers. The yield was 42%, and the product had mp 49-50°C [hexane–isopropyl alcohol (10:1)]. PMR spectrum (CCl_4): 1.13 [6H, d, j = 6 Hz, $CH(C\underline{H}_3)_2$], 1.13 (3H, s, 4-CH_3), 1.96 (3H, d, J = 1 Hz, 3-CH_3), 2.22 (3H, s, NCH_3), 2.27-2.83 [6H, m, $CH_2N(CH_2)_2$], 3.23 (1H, broad s, OH), 4.82 [1H, septet, J = 6 Hz, $C\underline{H}(CH_3)_2$], and 5.92 ppm (1H, broad s, CH=C). IR spectrum (CCl_4): 1630 (C=C), 1700 (C≡O), 2240 (C≡N), and 3430 cm^{-1} (OH). Found, %: C 62.5; H 9.2; N 10.3. $C_{14}H_{24}N_2O_3$. Calculated, %: C 62.7; H 9.1; N 10.4.

4-Dialkylaminomethyl-2-buten-4-olides IIa-i. A solution of 10 mmole of sodium metal in 10 ml of dry isopropyl alcohol was added to a solution of 100 mmole of ester Ia-c, e-i in the form of a mixture of Z and E isomers or the E isomer of Ia, d, k, j in 50 ml of toluene, and the mixture was refluxed for 1 h with slow removal of 20-30 ml of a mixture of alcohol and toluene. Water (10 liters) and 10 mmole of acetic acid were added, and the mixture was extracted with ether. The ether extracts were dried with sodium sulfate, the ether was removed, and the residue was fractionated in vacuo or crystallized from pentane–ether (10:1). No melting-point depression was observed for a mixture of a sample of lactone IIc with the sample obtained by the method in [6]. The hydrochlorides of IIa-g, i were obtained by passing hydrogen chloride into solutions of lactones IIa-g, i in dry ether; the precipitates were separated and crystallized from acetone–methanol (5:1).

Cyclization of Isopropyl (E)-5-[N-Methyl-N-(2-cyanoethyl)amino]-4-hydroxy-3,4-dimethyl-2-pentenoate (Ij). A solution of 2.68 g (10 mmole) of ester Ij in 30 ml of toluene and 0.05 g (2 mmole) of sodium in 3 ml of isopropyl alcohol was refluxed for 2 h with removal of a mixture of toluene and alcohol. The reaction mixture was then worked up as indicated above, and the ether was removed. The residue was chromatographed with a column packed with Al_2O_3 by elution with ether to give, successively, 1.25 g of 8,9-dihydro-6e,8a,9e-trimethyl-4e-cyano-2-oxofuro[2,3-c]piperidine (III), 0.06 g of 4-[N-methyl-N-(2-cyanoethyl)aminomethyl]-3,4-dimethyl-2-buten-4-olide (IIj), and 0.33 g of 8,9-dihydro-6e,8a,9a-trimethyl-4e-cyano-2-oxofuro[2,3-c]piperidine (IV).

Similarly, 0.3 g (15%) of lactone III was obtained as a result of refluxing the same amount of ester Ij with 0.68 g (8 mmole) of sodium isopropoxide in toluene for 3 h.

Isomerization of Lactone IV. Similarly, 1.48 g (71%) of a mixture of lactones III and IV in a ratio of 2:1 (according to the PMR spectrum) were obtained from 2.08 g (10 mmole) of lactone IV and 0.082 g (1 mmole) of sodium isopropoxide by refluxing for 1 h.

5-Hydroxy-1,4,5-trimethyl-5,6-dihydro-2-pyridone (V). A solution of 2.15 g (10 mmole) of ester Ik in 50 ml of toluene and 0.41 g (5 mmole) of sodium isopropoxide in isopropyl alcohol were refluxed as indicated above for 1 h, after which 10 ml of water was added to the reaction mixture, and the aqueous mixture was neutralized with 0.3 g (5 mmole) of acetic acid. This mixture was extracted with methylene chloride, and the extract was dried with sodium sulfate. The methylene chloride was removed, and the residue was crystallized from hexane–isopropyl alcohol (3:1) to give 1.1 g of lactam V.

Reaction of Isopropyl 3-Methyl-4,5-epoxy-2-pentenoate (VI) with Dimethylamine. A solution of 17 g (100 mmole) of ester VI and 5.4 g (120 mmole) of dimethylamine in 50 ml of isopropyl alcohol was allowed to stand at 18-20°C for 7 days, after which the alcohol was evaporated, and the residue was dissolved in dry ether. Dry hydrogen chloride was passed through the solution. Fractional crystallization of the liberated oil from acetone–methanol (5:1) gave 3.06 g (16%) of the hydrochloride of lactone VII and 10 g (40%) of the hydrochloride of ester Iℓ with mp 151-152°C. Free bases VII and Iℓ were isolated by treatment of the aqueous solutions of their hydrochlorides with potassium carbonate and subsequent extraction of the products with ether. The ether extracts were dried with sodium sulfate, the ether was re-

moved, and the residue was fractionated in vacuo. Ester Iℓ had bp 82-83°C (3 hPa) and n_D^{20} 1.4693. PMR spectrum (CCl_4): 1.13 [6H, d, J = 6 Hz, $CH(C\underline{H}_3)_2$], 1.93 (3H, d, J = 1 Hz, 3-CH_3), 2.17 [6H, s, $N(CH_3)_2$], 2.08-2.33 (2H, m, CH_2), 3.72-4.03 (1H, m, C<u>H</u>OH), 3.83 (1H, broad s, OH), 4.80 [1H, septet, J = 6 Hz, $C\underline{H}(CH_3)_2$], and 5.75 ppm (1H, q, J = 1.5 Hz, 2-H). Found, %: C 61.5; H 9.9; N 6.6. $C_{11}H_{21}NO_3$. Calculated, %: C 61.4; H 9.8; N 6.5.

5-Dimethylamino-3-methyl-4-oxovaleric Acid Isopropyl Ester (VIII). A 2.15-g (10 mmole) sample of Iℓ and 0.16 g (2 mmole) of sodium isopropoxide were refluxed in isopropyl alcohol for 3 h, after which the alcohol was removed, and the residue was chromatographed with a column packed with Al_2O_3 by elution with ether to give 0.5 g (23%) of ester VIII.

4-Dimethylamino-3,4-dimethyl-2-buten-4-olide (IX). A solution of 1.55 g (10 mmole) of lactone VII and 0.082 g (1 mmole) of sodium isopropoxide in isopropyl alcohol was refluxed for 1 h, after which the alcohol was removed, and the residue was chromatographed with a column packed with SiO_2 by elution with ether—isopropyl alcohol (10:1) to give 0.91 g (88% based on the amount of starting compound that underwent the reaction) of lactone IX and 0.52 g (34%) of starting lactone VII.

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