and reaction with maleic anhydride. These reactions led to the isolation of some nine new compounds.

3. Vinylamine behavior may be recognized as an important property of some of the new compounds, especially in connection with their ultraviolet absorption spectra.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, THE UNIVERSITY OF NEW MEXICO[1]]

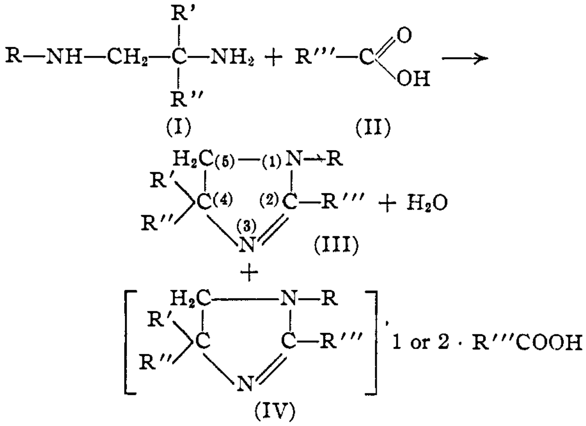
The Synthesis of Imidazolines from 1,2-Diamines and Carboxylic Acids

BY J. L. RIEBSOMER

Chitwood and Reid[2] prepared a series of 2-alkyl-2-imidazolines by distilling or heating the appropriate diacylethylenediamine with sodium, magnesium, zinc, magnesium oxide or sodium hydroxide. Thus 2-methyl-2-imidazoline was produced in 68% yield when diacetylethylenediamine was heated at 270° with magnesium. The yields were less satisfactory with the other inorganic reagents. When ethylenediamine and acetic acid were heated 2-methyl-2-imidazoline was produced in 19% yield and when monoacetylethylenediamine hydrochloride was heated with sodium hydroxide a 26% yield of the imidazoline formed. Hofmann[3] prepared the same imidazoline upon distillation of a sodium acetate and ethylenediamine hydrochloride mixture.

Hill and Aspinall[4] prepared a series of 2-alkyl and 2-aryl substituted imidazolines by heating monoacylethylenediamines.

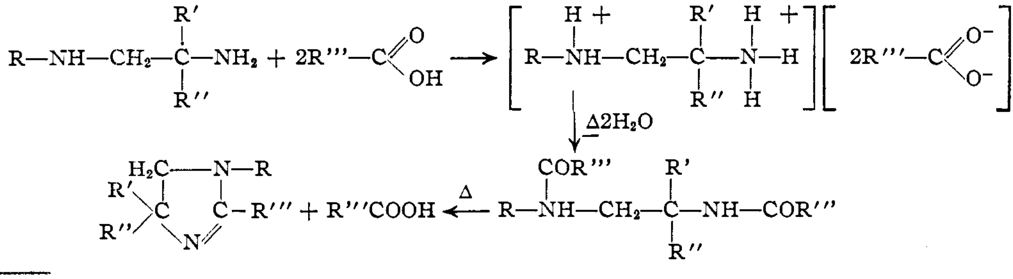
The technique employed for the preparation of the imidazolines reported here was to add benzene to a mixture of the 1,2-diamine and carboxylic acid and to distil the benzene through a four-foot packed column. As the benzene distilled, water formed from the reaction was carried out as an azeotropic mixture. The column was equipped with a suitable head so that the benzene returned and the water was separated. It might have been anticipated that the imidazoline would be the only product formed by this process. In nearly all instances studied, however, a higher boiling substance was produced along with the imidazoline. Indeed in some instances the higher boiling product was formed almost exclusively. The course of most of these reactions may be formulated as



R′ and R″ ′ were H, alkyl, or aryl. R′ and R″ were H or alkyl. The most complete study was made in the case in which R was isopropyl and R′ and R″ were methyl. In this instance R″ was H, alkyl groups from CH_3 to $C_{17}H_{35}$ or aryl.

A few exceptions to the general reaction were noted. When 2,3-dimethyl-2,3-butanediamine reacted with acetic acid none of the expected compounds (III) or (IV) were isolated but a low yield of the diacetate was found. Likewise 1,2-butanediamine and acetic acid reacted to form the diacetyl derivative of the amine along with the imidazoline.

A possible mechanism to account for the formation of the imidazolines by this method may be represented as follows:



The evidence for the existence of the compounds of type (III) seems to be entirely satisfactory. The analyses, neutral equivalents and mode of synthesis all point to the same conclusion.

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[1] Most of this work was completed while the author was at DePauw University, Greencastle, Indiana.

[2] Chitwood and Reid, THIS JOURNAL, 57, 2424 (1935).

[3] Hofmann, *Ber.*, 21, 2332 (1888).

[4] Hill and Aspinall, THIS JOURNAL, 61, 822 (1939).

The non-committal formulation of compounds of type (IV) suggests doubt as to their structures. While most of these compounds gave analyses corresponding to one mole of the imidazoline attached to two moles of the acid, there were a few examples studied in which the molar ratio was one of the imidazoline to one of the acid. These exceptions were found mainly in those instances in which R was aryl. It is also of interest to note that the ratio of (IV) to (III) tended to increase as the chain length of R''' increased.

The examination of the nature of compounds of type (IV) was carried out mainly with the products formed from N-(2-aminoisobutyl)-isopropylamine and acetic and stearic acids. When acetic acid was used in this reaction a 26% yield of 2,4,4-trimethyl-1-isopropyl-2-imidazoline and a 32.7% yield of the complex corresponding to (IV) were obtained. The complex in this instance contained two moles of the acid.

This complex was a colorless, viscous oil when freshly distilled. Upon prolonged standing it turned yellow. It was readily soluble in water and insoluble in ether or petroleum ether suggesting salt-like properties. The fact that it distilled at 124–125° at 16 mm. is not characteristic of salts but does not preclude this possibility. It reacted either with strong acids or strong bases with the evolution of considerable heat, which suggested that it was made up of both acidic and basic constituents not firmly combined chemically. Its neutral equivalent was 258 (using 0.1 normal alkali and phenolphthalein). The end-point was not sharp but this figure indicated the acidic constituent to be of greater influence than the basic constituent.

When this complex was treated with cold aqueous sodium hydroxide solution 2,4,4-trimethyl-1-isopropyl-2-imidazoline was formed in good yield. When this imidazoline was mixed with two molar equivalents of acetic acid the complex was formed in high yield. And finally when one mole of N-(2-aminoisobutyl)-isopropylamine reacted with three moles of acetic acid, the complex was produced in 89% yield while no imidazoline was isolated.

The Raman spectrum for 2,4,4-trimethyl-1-isopropyl-2-imidazoline showed lines which would be expected from —C═N— linkage. When a similar experiment was attempted with the corresponding complex a continuous spectrum was obtained from which no definite conclusions could be drawn.[5]

What has been said for the complex produced from acetic acid and N-(2-aminoisobutyl)-isopropylamine can for the most part be repeated for the analogous product formed from the same diamine and stearic acid. In this instance the complex was formed nearly quantitatively and none of the corresponding imidazoline was isolated.

No evidence has been found to establish unequivocally the structure of compounds of type (IV). One might assume simple salt formation with the acid involving the acceptance of a proton by one or both nitrogen atoms. But this assumption of salt formation is open to the objection that imidazolines always form mono-hydrogen halide salts and they titrate potentiometrically as mono-acid bases. This latter observation makes it clear that one of the nitrogen atoms must be very weakly basic. It would be rather unexpected to find this weakly basic nitrogen capable of accepting a proton from acetic or stearic acid and not capable of doing so from hydrochloric acid. It would, therefore, be reasonable to suggest that most of the compounds of type (IV) may be molecular complexes made up of one mole of the acid and one mole of the salt—the latter being formed by the reaction of one mole of acid with one mole of the imidazoline.

Experimental

The experimental procedure for the preparation of all these compounds was substantially the same. One molar equivalent of the diamine and one molar equivalent of the carboxylic acid were mixed with a little benzene and heated from 140 to 220°. The benzene–water mixture was distilled through a 4′ × $^5/_8$″ helix-packed column which was equipped with a decanter still-head filled with benzene, and arranged to drain off the water layer and to return the benzene to the column. Heating was continued until one molar equivalent of water was removed. In some instances one molar equivalent of the diamine and three of the acid were heated until two molar equivalents of water had been removed. The latter procedure generally gave high yields of compounds of type (IV) and none of (III).

After the reaction was complete the product was usually distilled. In some instances the product was a solid and was crystallized from a suitable solvent.

Two specific examples will suffice to illustrate the preparation of most of the compounds.

Preparation of 2,4,4-Trimethyl-1-isopropyl-2-imidazoline and its Molecular Complex.—A mixture of 130.1 g. (1 mole) of N-(2-aminoisobutyl)-isopropylamine and 60 g. (1 mole) of acetic acid was heated at 190–200° for three hours. During this period 21.5 g. of water was removed. The product was distilled and three main fractions were taken. The first came over at 60–63° (38 mm.), and was shown by its refractive index, density and neutral equivalent to be unreacted N-(2-aminoisobutyl)-isopropylamine, 57.4 g., 44% recovery. The second, which boiled at 94–96° (38 mm.), was the imidazoline, 41 g., 26.6% yield. The third fraction, with b. p. 124–125° (16 mm.), was the complex, 29.9 g., 32.7% yield.

In another experiment, 65 g. (0.5 mole) of N-(2-aminoisobutyl)-isopropylamine and 90 g. (1.5 moles) of acetic acid were mixed and heated to 180–220° for three hours until 18 g. (1 mole) of water was removed. The product, which distilled at 128–130° (19 mm.), was the complex; yield, 89%.

Anal. Calcd. for the complex $C_{13}H_{26}N_2O_4$: N, 10.20. Found: N, 9.89.

No imidazoline (VII) was isolated from the product.

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[5] The author is indebted to Dr. M. J. Murray for the Raman spectra studies.

TABLE A

2-SUBSTITUTED-4,4-DIMETHYL-1-ISOPROPYL-2-IMIDAZOLINES

2-Substituent R =	Yield, %	B. p. °C.	Mm.	d^{20}_{20}	n^{20}_D	Formula	Analyses, % Found C	H	N	Calcd. C	H	N	Neut. equiv. Found	Calcd.
H	13.3	81–82	19	0.8738	1.4525	$C_8H_{16}N_2$	68.13	11.33	19.61	68.52	11.52	19.99	139.6	140.1
CH_3	23.0	72–75	15	.875	1.454	$C_9H_{18}N_2$			18.2			18.1	152	154
C_2H_5	12.9	92	22	.8713	1.4550	$C_{10}H_{20}N_2$	71.62	11.68	16.68	71.37	11.92	16.64	166.3	168.1
C_3H_7	19.0	97–100	20	.8626	1.4549	$C_{11}H_{22}N_2$	71.34	12.04	15.22	72.45	12.11	15.36	179.5	182.1
C_3H_7 (iso)	10.0	88	20	.8522	1.4498	$C_{11}H_{22}N_2$	72.54	11.94	15.11	72.45	12.11	51.36	182.1	182.1
C_4H_9	18.2	112–115	18	.8753	1.4592	$C_{12}H_{24}N_2$	71.43	12.01	14.14	73.41	12.43	14.22	197.5	196.2
C_5H_{11}	15.4	125–128	18			$C_{13}H_{26}N_2$			13.14			13.32	212.9	210.2
$C_{11}H_{23}$[a]		160–162	8			$C_{19}H_{38}N_2$	76.98	12.97	9.34	77.47	13.22	9.51	295.1	294.1
$C_{13}H_{27}$[a]		219–222	18			$C_{21}H_{42}N_2$	77.64	12.98	8.51	78.15	13.13	8.69	327.0	322.2
$C_{15}H_{31}$[a]		183–185	3		1.4691	$C_{23}H_{46}N_2$	78.07	13.26	7.73	78.78	13.25	7.99	361.6	350.3
$C_{17}H_{35}$[a]						$C_{25}H_{50}N_2$	78.97	13.21	7.07	79.33	13.35	7.39	403.7	378.2
Phenyl[a]		163–166	28		1.5210	$C_{14}H_{20}N_2$	77.59	9.50	13.10	77.74	9.33	12.96	215.4	216.1

[a] Obtained by treating the corresponding molecular complexes (IV) with alkali.

TABLE B

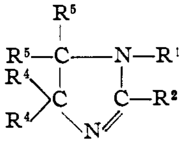
MOLECULAR COMPLEXES OF TYPE (IV) FROM 2-SUBSTITUTED-4,4-DIMETHYL-1-ISOPROPYL-2-IMIDAZOLINES[e]

2-Substituent R =	Yield, %	B. p., °C.	d^{20}_{20}	n^{20}_D	Formula	Analyses, % Found C	H	N	Calcd. C	H	N	Neut.[b] equiv.
H[a]		150–151 (28)			$C_{10}H_{18}N_2O_4$			12.20			12.06	
CH_3	32.7	124–125 (16)	1.026	1.4609	$C_{13}H_{26}N_2O_4$	57.27	9.24	10.04	56.91	9.55	10.20	258[b]
C_2H_5[c]	56.6	129–130 (20)	1.0012	1.4610	$C_{16}H_{32}N_2O_4$	60.17	9.88	8.56	60.73	10.14	8.86	290[b]
C_3H_7[c]	51.8	106–109 (2)	0.9759	1.4600	$C_{19}H_{38}N_2O_4$	63.04	10.67	7.74	63.65	10.68	7.81	356[b]
i-C_3H_7[c]	56.5	128–132 (20)	0.9744	1.4588	$C_{19}H_{38}N_2O_4$	61.94	10.77	7.47	63.65	10.68	7.81	
C_4H_9[c]	64.9	150 (22)	0.9525	1.4607	$C_{22}H_{44}N_2O_4$	65.51	11.18	6.79	65.94	11.10	6.97	
C_5H_{11}[c]	65.2	157–160 (20)		1.4619	$C_{25}H_{50}N_2O_4$	67.91	11.48	6.42	67.81	11.39	6.33	
$C_{11}H_{23}$[c]	87.8	160–162 (1)			$C_{43}H_{86}N_2O_4$	74.33	12.58	4.69	74.27	12.62	4.03	
$C_{13}H_{27}$[c]	92.5	206–209 (6)			$C_{49}H_{98}N_2O_4$	76.16	12.81	3.64	75.51	12.68	3.59	
$C_{15}H_{31}$[c]	Almost	M. p. 43–43.5			$C_{55}H_{110}N_2O_4$	76.30	12.65	3.33	76.48	12.85	3.24	
$C_{17}H_{35}$[c]	quant.	M. p. 54–55			$C_{61}H_{122}N_2O_4$	77.25	13.02	2.82	77.27	13.00	2.96	
Phenyl[d]	73				$C_{28}H_{32}N_2O_4$			6.27			6.15	

[a] Obtained by treating the imidazoline with formic acid. [b] Using phenolphthalein and 0.1 *N* alkali. [c] Reagents mole to mole ratio. [d] One mole of amine allowed to react with 3 moles of the acid. [e] When these complexes were treated with alkali they were converted to the corresponding imidazolines, which had the same properties as when produced directly from the reactions.

TABLE C

SUBSTITUTED IMIDAZOLINES

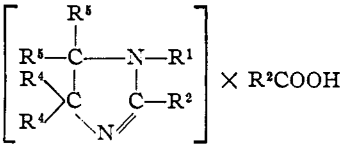


Amine used	R¹	R²	R⁴	R⁵	Formula	B. p. °C.	Mm.	Percentage composition C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found	Neut. equiv. Calcd.	Found
A¹-aniline[a,f]	C_6H_5	CH_3	CH_3	H	$C_{12}H_{16}N_2$[g,o]	144–152	28	76.55	76.22	8.61	8.76	14.88	14.86	...	...
A¹-aniline[a]	C_6H_5	$C_{17}H_{35}$	CH_3	H	$C_{28}H_{48}N_2$[k]	39–40[b]		81.47	81.47	11.73	11.78	6.79	6.77	412.4	412.2
A¹-*m*-toluidine[a,l]	C_7H_7	CH_3	CH_3	H	$C_{13}H_{18}N_2$	155–158	20	77.15	76.16	8.97	9.15	13.85	14.29	202.1	195.5
A¹-*n*-butylamine[a,m]	C_4H_9	CH_3	CH_3	H	$C_{10}H_{20}N_2$[h]	105–108	26	71.34	70.89	11.98	12.35	16.65	16.77	168.2	160.7
A¹-*n*-butylamine[a]	C_4H_9	$C_{17}H_{35}$	CH_3	H	$C_{26}H_{52}N_2$[k]	223–226	3	...	...	...	...	7.13	7.05	392.4	392.2
A¹-*s*-butylamine[a]	C_4H_9	CH_3	CH_3	H	$C_{10}H_{20}N_2$[o,k]	100–102	30	71.34	71.03	11.98	12.50	16.65	17.04	168.2	168.1
A¹-*s*-butylamine[a]	C_4H_9	$C_{17}H_{35}$	CH_3	H	$C_{28}H_{52}N_2$[k]	200–221	3	...	...	...	...	7.13	7.03	...	...
A²-A³[c]	C_6H_{11}	CH_3	CH_3[d]	H	$C_{12}H_{26}N_2$[i,o,k]	131–132	35	74.21	73.74	12.47	12.48	13.32	13.42	210.2	208.4
A²-A³[c]	C_6H_{13}	$C_{17}H_{35}$	CH_3[d]	H	$C_{29}H_{58}N_2$[j,k]	233–235	3	...	...	...	...	6.44	6.46	434.5	432.5
A⁴-2,3-diaminobutane[e]	H	C_5H_{11}	CH_3	CH_3	$C_{12}H_{24}N_2$[k]	143	23	73.39	53.28	12.33	12.21	14.27	14.09	...	...
1,2-Butanediamine[n]	H	CH_3	C_2H_5[p]	H	$C_6H_{12}N_2$	116–118	24	64.23	64.11	10.79	10.88	24.97	23.86	112.3	112.3

[a] A¹ = N-(2-aminoisobutyl)—. [b] Melting point. [c] A² = N-(2-amino-2-methylbutyl); A³ = -1,3-dimethylbutylamine. [d] One R⁴ = ethyl. [e] A⁴ = 2,3-dimethyl. [f] Yield, 87. [g] d^{20}_{20} 1.0143; n^{20}_D 1.5527. [h] d^{20}_{20} 0.8678; n^{20}_D 1.4550. [i] d^{20}_{20} 0.8694; n^{20}_D 1.4568. [j] d^{20}_{20} 0.8573; n^{20}_D 1.4635. [k] Prepared by treatment of molecular complex of type (IV) with alkali. [l] Yield, 76. [m] Yield, 15. [n] Yield, 20. [o] Molar ratio of acid to amine allowed to react was 3 to 1. In other instances equimolecular quantities were used. [p] This compound may be 4- or 5-ethyl.

TABLE D

MOLECULAR COMPLEXES OF IMIDAZOLINES AND ORGANIC ACIDS



Amine used	Yield, %	R¹	R²	R⁴	R⁵	Formula	B. p. °C.	B. p. Mm.	C Calcd.	C Found	H Calcd.	H Found	N Calcd.	N Found
A^1-aniline[a]	94	C_6H_5	$C_{17}H_{35}$	CH_3	H	$C_{46}H_{84}N_2O_2$[b]	40–43[c]		79.23	79.56	12.15	11.99	4.02	4.63
A^1-*m*-toluidine[a]	76	C_7H_7	$C_{17}H_{35}$	CH_3	H	$C_{47}H_{85}N_2O_2$[b]	53–55[c]		79.36	78.07	12.20	12.26	3.94	3.50
A^1-butylamine[a]	28	C_4H_9	CH_3	CH_3	H	$C_{14}H_{28}N_2O_4$[d]	112	2	58.29	59.51	9.80	10.25	9.72	10.32
A^1-butylamine[a]	87	C_4H_9	$C_{17}H_{35}$	CH_3	H	$C_{44}H_{88}N_2O_2$[b]	220–222	2	...	...	...	...	4.13	4.20
A^1-*s*-butylamine[a]	73	C_4H_9	CH_3	CH_3	H	$C_{14}H_{28}N_2O_4$[d]	134–136	26	58.29	58.05	9.83	9.86	9.72	10.02
A^1-*s*-butylamine[a]	84	C_4H_9	$C_{17}H_{35}$	CH_3	H	$C_{52}H_{124}O_4$[d]	213–216	2	77.42	77.14	12.79	13.14	2.91	2.87
A^1-A^2[a,e]	80	C_6H_{13}	CH_3	CH_3	H	$C_{17}H_{34}N_2O_4$[d]	139–140	26	...	...	...	...	8.48	8.48
A^3[f]	..	C_6H_{13}	$C_{17}H_{35}$	CH_3[g]	H	$C_{47}H_{94}N_2O_2$[b]	219–221	2	78.45	78.47	13.18	13.21	3.89	3.94
A^4[h]	67	H	C_5H_{11}	CH_3	CH_3	$C_{24}H_{48}N_2O_4$[d]	168–169	2	67.23	67.95	11.24	11.29	8.97	8.51

[a] A^1 = N-(2-aminoisobutyl)—. [b] X = 1. [c] Melting point. [d] X = 2. [e] A^2 = -1,3-dimethylbutylamine. [f] N-(2-amino-2-methylbutyl)-1,3-dimethylbutylamine. [g] One R^4 is ethyl. [h] 2,3-Dimethyl-2,3-diaminobutane.

Conversion of the Complex to 2,4,4-Trimethyl-1-isopropyl-2-imidazoline.—To 40 g. of the complex was added 70 ml. of 10% aqueous sodium hydroxide. The alkaline solution was extracted with ether, and the ether solution dried over solid potassium hydroxide. The ether was removed and distillation gave a 15 g. fraction, b. p., 78–80° (15 mm.). There was almost no forerun or residue; yield, 72%.

Anal. Calcd. for the imidazoline, $C_9H_{18}N_2$: N, 18.17; neut. equiv., 154.1. Found: N, 18.10; neut. equiv., 159.2.

Conversion of 2,4,4-Trimethyl-1-isopropyl-2-imidazoline to the Complex.—To 3.08 g. (0.02 mole) of the imidazoline was added 2.4 g. (0.04 mole) of acetic acid. The mixture evolved heat. Upon distillation, the entire product boiled at 122–124° (15 mm.), 4.5 g., 90% yield.

Anal. Calcd. for the complex, $C_{13}H_{26}N_2O_4$: N, 10.20. Found: N, 10.11.

Preparation of 4,4-Dimethyl-1-isopropyl-2-heptadecyl-2-imidazoline Molecular Complex with Stearic Acid.—A mixture of 32.5 g. (0.25 mole) of N-(2-aminoisobutyl)-isopropylamine and 71.1 g. (0.25 mole) of stearic acid was heated to 190–200° for three hours. During the heating process 4.5 g. (0.25 mole) of water was removed. The product was transferred to a distillation flask and 13.3 g. of the original diamine (41%) was recovered. A white, solid, undistilled residue remained. After three crystallizations from acetone, it melted at 54–55°; yield of the complex, 95%.

Conversion of the Stearic Acid Complex to 4,4-Dimethyl-1-isopropyl-2-heptadecyl-2-imidazoline.—To 30 g. of the complex was added 150 ml. of 10% potassium hydroxide and the mixture was extracted with ether. The ether solution was dried over solid potassium hydroxide and the ether removed *in vacuo*. The residue was distilled and a fraction boiled at 204–206° (3 mm.); yield of the imidazoline, 8.3 g. The residue remaining from the ether extraction was acidified with hydrochloric acid. A white solid formed which on the basis of its neut. equiv., its melting point (and mixed melting point) was identified as stearic acid.

Conversion of 4,4-Dimethyl-1-isopropyl-2-heptadecyl-2-imidazoline to the Stearic Acid Complex.—A mixture of 1.135 g. (0.003 mole) of the imidazoline and 1.706 g. (0.006 mole) of stearic acid was warmed over steam just long enough to melt the stearic acid. The product melted at 54–55° after recrystallization from acetone. A mixed m. p. with the complex prepared above (m. p. 54–55°) showed no depression.

Similar experiments to those described above were attempted with N-(2-aminoisobutyl)-aniline and benzoic acid, with N-(2-aminoisobutyl)-isopropylamine and trichloroacetic acid and with N-(2-aminoisobutyl)-isopropylamine and *o*-chlorobenzoic acid, but the expected products did not result from any of these examples.

When 2,3-dimethyl-2,3-butanediamine was allowed to react under the usual conditions with acetic acid, none of the expected imidazoline was isolated but only a 10% yield of the diacetate, m. p. 156–157°.

Anal. Calcd. for 2,3-dimethyl-2,3-butanediamine diacetate, $C_{10}H_{24}N_2O_4$: C, 50.84; H, 10.24; N, 11.96. Found: C, 50.84; H, 10.14; N, 11.98.

A 15% yield of diacetyl-1,2-butanediamine, m. p. 150–151°, was obtained from the reaction of 1,2-butanediamine and acetic acid, in addition to a low yield of the expected imidazoline.

Anal. Calcd. for diacetyl-1,2-butanediamine, $C_8H_{16}N_2O_2$: C, 55.79; H, 9.95; N, 16.26. Found: C, 55.88; H, 9.50; N, 16.26.

Acknowledgment.—The author wishes to express his gratitude to Commercial Solvents Corporation for generous support of this project. Thanks are especially due to Dr. P. F. Tryon of that organization who did considerable preliminary work on this problem.

Summary

1. A series of imidazolines has been prepared by heating 1,2-diamines and organic acids under conditions to remove water during the process.

2. Most of these imidazolines react with the acids from which they are formed to produce molecular complexes involving one or two moles of the acid and one mole of the imidazoline.

3. These complexes can be converted to the imidazolines readily by treatment with dilute alkali.

4. When one amino group of the diamine is secondary, the yields are better than when both amino groups are primary.

5. As the molecular weight of the acids becomes larger the yields of the complexes increase and the yields of the imidazolines decrease.

ALBUQUERQUE, NEW MEXICO

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