[Contribution from the Department of Chemistry, the University of New Mexico]

SYNTHESIS OF 2-IMIDAZOLINES AND 2-IMIDAZOLIDONES

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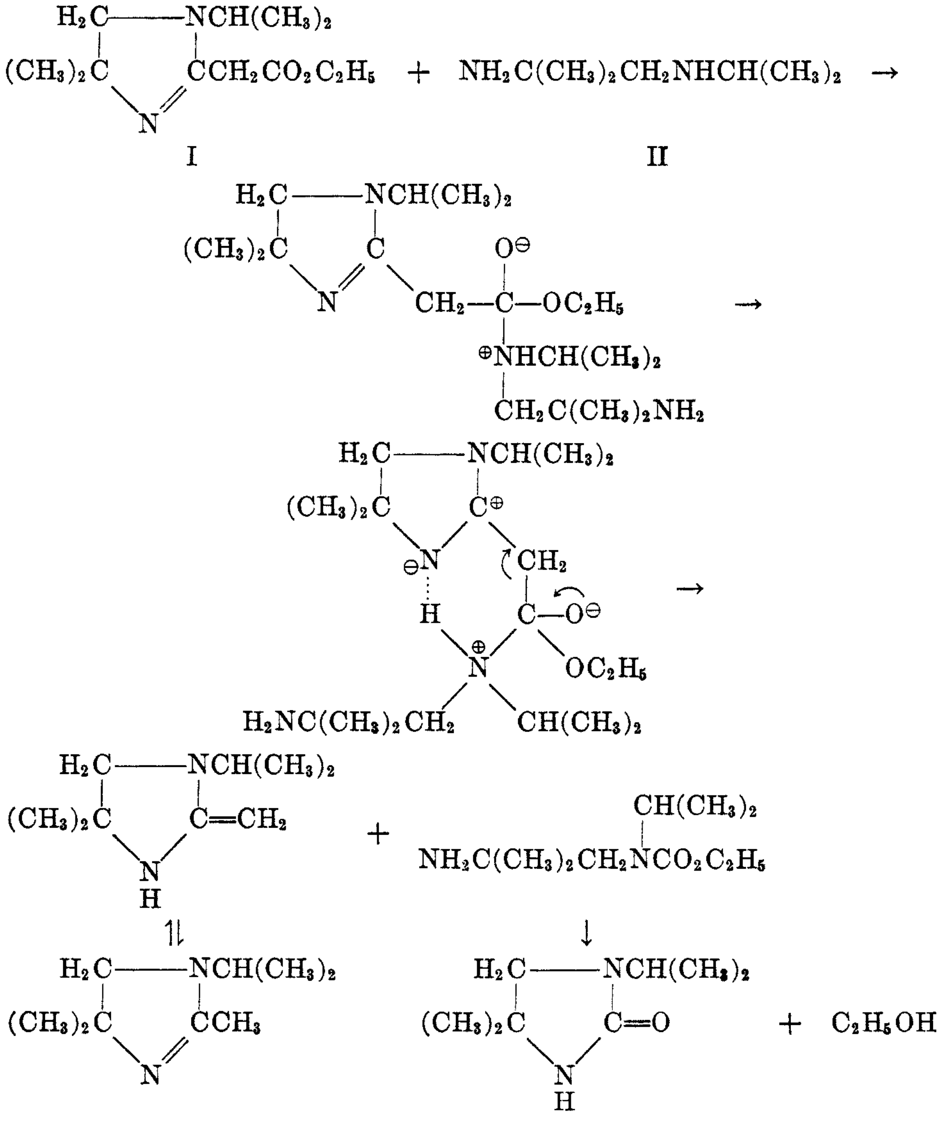
Although 1,2-diamines are widely known (1–4) to react with carboxylic acids or their esters to yield imidazolines, the expected bisimidazoline was not formed



I II III IV

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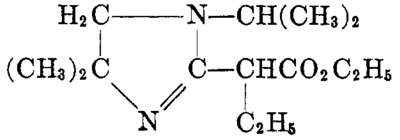
when Pachter and Riebsomer (5) treated ethyl (4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)acetate (I) with *N*-(2-aminoisobutyl)isopropylamine (II). Instead the products were 1-isopropyl-2,4,4-trimethyl-2-imidazoline (III) and 4,4-dimethyl-1-isopropyl-2-imidazolidone (IV). It is believed that this reaction may proceed in the manner shown on preceeding page (page 181) of this article. The formation of the intermediate containing the six-membered ring is not required in this mechanism, but has been suggested from analogy with pyridine compounds, and spectrophotometric studies (6) of 2-imidazoline compounds.

Evidence in agreement with this mechanism was obtained by treating I with diamines identical with II escept for variation of the group attached to the secondary nitrogen atom. Thus when I was treated with *N*-(2-aminoisobutyl)-*p*-toluidine the 2-imidazolidone formed possessed a *p*-tolyl group attached to the ring nitrogen, while the 2-imidazoline retained the isopropyl group of the original 2-imidazoline (I). None of the possible alternate products were formed. The 2-imidazolidones isolated from this type of reaction were readily synthesized by heating the appropriate diamine with urea, which confirms their structures.

It was also found that a substituted 2-imidazoline ester, ethyl α-(4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)butyrate (V) reacted with *N*-(2-aminoisobutyl)isopropylamine in the same manner as shown in the above mechanism for the unsubstituted ester. Again none of the bis-compound was found.



V

EXPERIMENTAL

A. 2-Imidazolidones and 2-imidazolines from 1,2-diamines and ethyl (4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)acetate. A number of these syntheses were carried out following the general procedure of Pachter and Riebsomer (5). Only one is presented here. The data for the 2-imidazolidones obtained are given in Table I, while the 2-imidazoline formed in each case was always 1-isopropyl-2,4,4-trimethyl-2-imidazoline.

Synthesis of 4,4-dimethyl-1-p-tolyl-2-imidazolidone (VI) and 1-isopropyl-2,4,4-trimethyl-2-imidazoline. A mixture of 5.65 g. (0.025 mole) of ethyl (4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)acetate and 4.45 g. (0.025 mole) of *N*-(2-aminoisobutyl)-*p*-toluidine was heated for three hours under a small packed column. The crystals which formed on standing overnight were removed, washed with petroleum ether, and finally dried at room temperature to yield 4.0 g. of (VI). The solvent was removed from the filtrate and the washings *in vacuo*, and the residue distilled under reduced pressure to yield 3.5 g. (91%) of 2,4,4-trimethyl-2-imidazoline, b.p. 89–90°/28 mm. The picrate, m.p. 183°, of the 1-isopropyl-2,4,4-trimethyl-2-imidazoline obtained from this reaction showed no depression in melting point when admixed with an authentic sample. An additional 0.6 g. of VI was recovered from the residue remaining after the distillation of the imidazoline, thus making a total yield of 4.6 g. (90%) m.p. 181–181.5°.

Anal. Calc'd for (VI), $C_{12}H_{16}N_2O$: N, 13.71. Found, 13.38.

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The imidazolidone obtained from this reaction showed no depression in melting point when mixed with the 4,4-dimethyl-1-*p*-tolyl-2-imidazolidone obtained in part *B*.

B. 2-Imidazolidones from 1,2-diamines and urea. All of these compounds were prepared according to the method outlined by Martell and Frost (7). The 2-imidazolidones prepared here were used to identify those obtained in part *A*. While the details of only one example of synthesis are given here, the yields and properties for all of the imidazolidones are presented in Table I.

Synthesis of 4,4-dimethyl-1-p-tolyl-2-imidazolidone. A mixture of 3.75 g. (0.0625 mole) of urea and 8.9 g. (0.050 mole) of *N*-(2-aminoisobutyl)-*p*-toluidine was refluxed for one hour, after which the evolution of ammonia ceased. The brown residue was distilled under reduced pressure to yield 8.8 g. (86%) of 4,4-dimethyl-1-*p*-tolyl-2-imidazolidone, b.p. 206–207° at 5 mm., which upon recrystallization from alcohol melted at 181–181.5°. There was no pre-run and only a small residue. The 2-imidazolidone obtained from this reaction showed no depression in melting point when admixed with a sample of the 2-imidazolidone obtained in part *A*.

TABLE I

2-IMIDAZOLIDONES

IMIDAZOLIDONE	FORMULA	M.P., °C.	B.P., °C/MM.	N		YIELD FROM REACTION WITH THE ESTER[a], %		YIELD OF 2-IMIDAZOLIDONE FROM UREA, %
				Calc'd	Found	2-Imidazolidone	2-Imidazoline[b]	
4,4-Dimethyl-1-isopropyl-2-imidazolidone	$C_8H_{16}N_2O$	164	167–170/27	17.93	17.89	87	65	73
1-*sec*-Butyl-4,4-dimethyl-2-imidazolidone	$C_9H_{18}N_2O$	111–112	176–177/27	16.46	16.42	90	92	91
4,4-Dimethyl-1-phenyl-2-imidazolidone	$C_{11}H_{14}N_2O$	134–135	194–196/5	14.73	14.45	92	70	86
4,4-Dimethyl-1-*p*-tolyl-2-imidazolidone	$C_{12}H_{16}N_2O$	181–181.5	206–207/5	13.71	13.38	90	91	86

[a] Ethyl (4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)-acetate.

[b] The 2-imidazoline obtained in each case from this reaction was 1-isopropyl-2,4,4-trimethyl-2-imidazoline.

C. A 2-imidazolidone and a 2-imidazoline from a 1,2-diamine and ethyl α-(4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)butyrate. Alkylation of ethyl (4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)acetate with ethyl bromide in the presence of sodium hydride was used as a method of preparation of the ethyl α-(4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)butyrate, which has been previously prepared by Shapira (8) in the same manner with the exception that sodium ethoxide was used as the condensing agent.

Synthesis of 4,4-dimethyl-1-isopropyl-2-n-propyl-2-imidazoline (VII) *and 4,4-dimethyl-1-isopropyl-2-imidazolidone* (VIII) *from N-(2-aminoisobutyl)isopropylamine and ethyl α-(4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)butyrate.* A mixture of 7.4 g. (0.029 mole) of ethyl α-(4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)butyrate and 5.66 g. (0.0435 mole) of *N*-(2-aminoisobutyl)isopropylamine was heated under a packed column for a period of eight hours while the temperature was raised slowly to 160°. After the addition of 10 ml. of benzene to the cooled mixture, the temperature was held at 190–200° during an additional eight hours. The reaction mixture was then cooled to room temperature, petroleum ether was added, and after cooling on ice overnight 1.7 g. of 4,4-dimethyl-1-isopropyl-2-imidazolidone, m.p. 164°, was removed by filtration. The solvent was removed *in vacuo* and the remaining liquid distilled under reduced pressure to yield 3.2 g. (60%) of VII, b.p. 97–103° at 21 mm., and an additional 2.0 g. of VIII was obtained from the residue to give a total yield of 3.7 g. (31%).

Anal. Calc'd for (VII), $C_{11}H_{22}N_2$: N, 15.37. Found: N, 15.28.
Calc'd for (VIII), $C_8H_{16}N_2O$: N, 17.93. Found: N, 17.60.

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SUMMARY

1. An explanation for the formation of 2-imidazolidones and 2-imidazolines from the reaction of ethyl (4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)-acetate and 1,2-diamines has been given. A substituted imidazoline ester, ethyl α-(4,4-dimethyl-1-isopropyl-2-imidazolinyl-2)butyrate, was also found to react in the same manner with a 1,2-diamine.

2. Three new 2-imidazolidones have been prepared by two different methods.

ALBUQUERQUE, N. M.

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