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

2-PHENYL-2,1,3-TRIAZOLE-4-CARBOXALDEHYDE AND DERIVATIVES[1]

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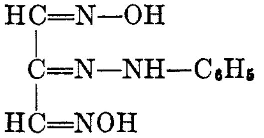
2-Phenyl-2,1,3-triazole-4-carboxaldehyde (I) was first synthesized by von Pechmann (1) who treated the hydrazoxime (II)



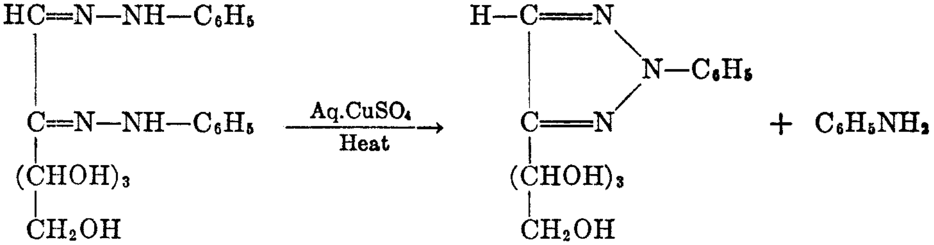
$$\begin{array}{l} \mathrm{HC{=}N{-}OH} \\ \quad | \\ \quad \mathrm{C{=}N{-}NH{-}C_6H_5} \\ \quad | \\ \mathrm{HC{=}NOH} \end{array}$$

(II)

with phosphorus pentachloride, or boiled it with acetic anhydride. These methods produced the oxime of (I) in 20 to 25% yields. An alternative procedure was to heat the monoacetate of (II) with dilute sodium carbonate which produced a 50% yield of the oxime of (I).

A much more satisfactory method was discovered in 1944 by Hann and Hudson (2), who isolated (I) in connection with the proof of structure of "phenyl-D-glucosotriazole" (IV), a product of the action of copper sulfate on phenyl-D-glucosazone (III). The osotriazole showed good crystallizing power and a sharp melting point and was superior to the osazone for the characterization of glucose. Upon oxidation with sodium periodate it gave 2-phenyl-2,1,3-triazole-4-carboxaldehyde (I) in high yield and the latter compound was further identified by oxidation with permanganate to 2-phenyl-2,1,3-triazole-4-carboxylic acid (V).

Hann and Hudson were interested in the osotriazole aldehyde only as an adjunct to the proof of structure of the sugar osotriazoles, of which they subsequently prepared a large number. However, since the aldehyde was not readily available from von Pechmann's method, the relatively direct method of Hann and Hudson seemed to open an avenue by which the chemistry of (I) and (V) might be extended without too much difficulty.



(III) (IV)

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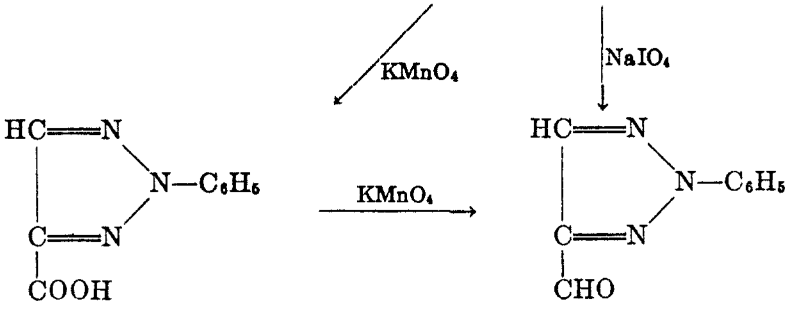
[1] A portion of this publication was abstracted from the thesis presented by Mr. Sumrell to the graduate faculty of the University of New Mexico, in partial fulfilment of the requirements for the M. S. degree.

[2] Revised manuscript, with additional experimental results received July 13, 1948.



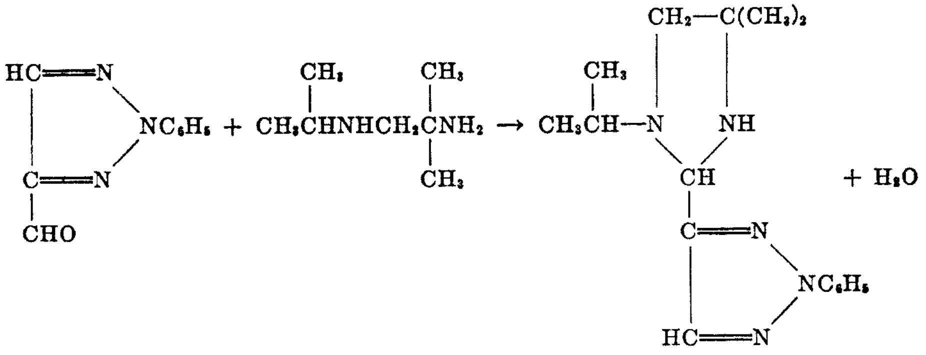
(V) (I)

In the present work it has been shown that the above procedure can be adapted readily to larger scale production of (I) and (V) and that the over-all yield of (I) may be as high as 60%.

The aldehyde (I) was converted readily to some of the common aldehyde derivatives such as its semicarbazone and 2,4-dinitrophenylhydrazone. It reacted with acetophenone to form 2-phenyl-2,1,3-triazole-4-carboxalacetophenone, and with acetone to give bis-(2-phenyl-2,1,3-triazol-4-ylmethylene)-acetone. It is probable that (I) will condense similarly with all methyl ketones.

When the aldehyde (I) was subjected to the usual conditions for the Perkin synthesis a good yield of 2-phenyl-2,1,3-triazol-4-ylmethylene acetic acid was obtained. von Pechmann (3) showed that (I) underwent the Cannizzaro reaction. This work has been corroborated.

Imidazolidines can be prepared from (I) by heating it at relatively low temperatures with 1,2-diamines under conditions to remove water. In a typical example (I) was heated in equimolecular quantity with N-(2-aminoisobutyl)isopropylamine (VI) to produce 1-isopropyl-2-(2′-phenyl-2′,1′,3′-triazol-4′-yl)-4,4-dimethylimidazolidine (VII).



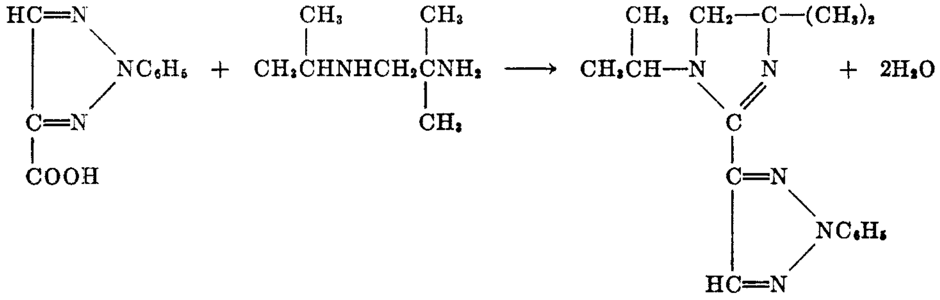
(I) (VI) (VII)

The aldehyde (I) reacted typically with Grignard reagents to form the expected secondary alcohols.

A number of derivatives of (V) have also been prepared. The methyl and ethyl esters and the amide of (V) were prepared previously by von Pechmann.

This work has been repeated. The phenyl and diethylaminoethanol esters have now been produced by conventional methods.

The acid (V) was found to react typically with 1,2-diamines to produce the expected imidazolines. Thus when (V) was heated with (VI) under conditions to remove water, a 93% yield of 1-isopropyl-2-(2′-phenyl-2′,1′,3′-triazol-4′-yl)-4,4-dimethyl-2-imidazoline (VIII) was obtained.



(V) (VI) (VIII)

Thus it is observed that the aldehyde (I) behaves generally like benzaldehyde. One interesting difference has been observed. (I) is soluble in alkali but is not sufficiently acidic to be titrated with a dilute base. Triazoles not possessing an N-substituent are decidedly acidic in character. However, 2-phenyl-2,1,3-triazole is insoluble even in concentrated alkali. Therefore, it would appear that the hydrogen atom attached to the carbonyl carbon of (I) is labile. This would be expected from electronic considerations. The triazole ring is a resonating structure and probably is even more electron attracting than the phenyl group. Consequently, it would be expected that the electrons would tend to be drawn away from the carbonyl carbon and toward the triazole ring and hence the hydrogen atom attached to the carbonyl carbon would be somewhat active.

EXPERIMENTAL

Preparation of 2-phenyl-2,1,3-triazole-4-carboxaldehyde (I). The osazone of glucose was prepared in substantially quantitative yields by standard methods, starting with sucrose and phenylhydrazine hydrochloride. In a typical experiment for the preparation of phenyl-D-glucosotriazole (IV), 260 g. of phenyl-D-glucosazone was suspened in a solution containing 364 g. of cupric sulfate pentahydrate in 15 l. of water. After refluxing 2 hours, the yellow osazone had completely disappeared, and the mixture was dark in color. It was observed that prolonged heating should be avoided, since it resulted in a greater amount of tar formation.

After the reaction was completed, decolorizing charcoal was added, and the hot solution filtered as fast as possible. Upon standing, crystallization took place in the filtrate. More product was obtained by evaporating the filtrate to about one-fifth its original volume. It was necessary to crystallize a second time to obtain a colorless product, with the melting point 195–196°; yield 112 g. (59%).

The conversion of "phenyl-D-glucosotriazole" (IV) to the aldehyde (I) was made by dissolving 607 g. of sodium periodate in 12 l. of water and adding 225 g. of (IV). The mixture was stirred 24 hours at room temperature, and the solid aldehyde was filtered and dried; yield almost quantitative.

Conversion of (I) to 2-phenyl-2,1,3-triazole-4-carboxylic acid (V). To a solution containing 10 g. of potassium hydroxide in 400 ml. of water was added 34.6 g. (0.1 mole) of (I), and while heating over steam and stirring, 41 g. of potassium permanganate was added in small portions. Sodium bisulfite was added to destroy the excess permanganate, the brown manganese dioxide was filtered, and the filtrate acidified with hydrochloric acid. A white precipitate formed which was filtered and dried; yield 33.2 g. (87%), melting point 190–192°. A small portion was recrystallized from water for analysis.

Anal. Calc'd for $C_9H_7N_3O_2$: C, 57.17; H, 3.73; N, 22.16.
Found: C, 57.55; H, 3.52; N, 22.50.

*Conversion of "phenyl-*D*-glucosotriazole" (IV) to 2-phenyl-2,1,3-triazole-4-carboxylic acid (V).* When it became apparent that considerable quantities of (V) would be needed, it was found that it could be prepared directly by permanganate oxidation of (IV), thus eliminating the sodium periodate step. To a mixture of 400 ml. of water, 8 g. of potassium hydroxide, and 23 g. of (IV), was added portionwise 80 g. of potassium permanganate while stirring and warming over steam. Sodium bisulfite was added to destroy the excess of permanganate. The brown manganese dioxide was filtered and the filtrate acidified with hydrochloric acid. A white precipitate of (V) formed, yield 13.3 g. (82%), melting point 191–192°.

Preparation of the 2,4-dinitrophenylhydrazone of (I). A solution was prepared containing 1.73 g. (0.01 mole) of (I) and 1.98 g. (0.01 mole) of 2,4-dinitrophenylhydrazine in 100 ml. 95% ethanol. It was heated to boiling and 20 ml. of concentrated hydrochloric acid was added. A precipitate formed immediately, and the mixture was refluxed 5 minutes. The crystals which formed melted at 198–200°. Crystallization from a chloroform-ethanol mixture did not change the melting point; yield 3.5 g. (almost quantitative).

Anal. Calc'd for $C_{15}H_{11}N_7O_4$: N, 27.74. Found: N, 28.21.

Preparation of the semicarbazone of (I). A solution was prepared containing 2 g. of (I) in 25 ml. of ethanol. Another solution contained 2 g. of semicarbazide hydrochloride and 3 g. of sodium acetate in 20 ml. of water. The two solutions were mixed and warmed over steam 30 minutes. A white solid formed melting at 225–226°, yield 2.6 g. (almost quantitative).

Anal. Calc'd for $C_{10}H_{10}N_6O$: N, 36.52. Found: N, 37.02.

Preparation of 2-phenyl-2,1,3-triazol-4-yl carbinol, by a crossed Cannizzaro reaction. To a suspension of 26 g. (0.15 mole) of (I) in 42.2 ml. (0.60 mole) of 38% formaldehyde was added 18 g. (0.45 mole) of sodium hydroxide in 36 ml. of water. The mixture was agitated occasionally, and sufficient heat was generated by the reaction so that external warming was unnecessary. After the mixture had cooled, it was acidified with hydrochloric acid and then neutralized with sodium carbonate. After cooling, the alcohol was filtered and recrystallized from water containing a little alcohol. The yield was 14.5 g. (55%) and the product melted at 64–65°, which corresponds with the melting point previously reported.

Anal. Calc'd for $C_9H_9N_3O$: N, 23.99. Found: N, 23.90.

Acidification of the sodium carbonate filtrate produced 2.5 g. of 2-phenyl-2,1,3-triazole-4-carboxylic acid, melting point 191–192°. The combined yields of the two products account for 63% of (I).

Reaction of (I) with acetophenone. A solution was prepared containing 1.73 g. (0.01 mole) of (I), 1.2 g. (0.01 mole) of acetophenone in 35 ml. of ethanol. This solution was cooled in an ice-bath and to it was added dropwise with stirring a solution containing 0.5 g. of potassium hydroxide in 5 ml. of water. This mixture was allowed to stand 1.5 hours in the ice-bath. A solid formed which weighed 2.4 g. (87%) and melted at 131–132°. A portion was recrystallized for analysis without raising the melting point.

Anal. Calc'd for $C_{17}H_{13}N_3O$: C, 74.24; H, 4.03; N, 15.28.
Found: C, 74.01; H, 4.52; N, 15.41.

Synthesis of bis-(2-phenyl-2,1,3-triazol-4-ylmethylene)acetone (IX). A solution of 8.7 g. (0.05 mole) of (I) in 135 ml. of ethanol and 1.75 ml. (0.025 mole) of acetone was cooled in an ice-bath and to it was added dropwise a solution of 2.5 g. of potassium hydroxide in

25 ml. of water. The mixture was kept at 0° for 2 hours, and one hour at room temperature. A yellow precipitate formed which was crystallized from a benzene-alcohol mixture. The yield was 4.3 g. (47%) and the product melted at 194–195°.

Anal. Calc'd for $C_{21}H_{16}N_6O$: N, 22.82. Found: N, 23.02.

Preparation of 2-phenyl-2,1,3-triazol-4-ylmethyleneacetic acid. A mixture of 8.5 g. of (I), 2.5 g. of anhydrous sodium acetate, and 7.5 g. of acetic anhydride was heated at 180° for 8 hours. The product was poured into sodium carbonate solution and the insoluble material removed by filtration. The filtrate was acidified with hydrochloric acid, giving a white precipitate which melted at 175–180°; yield 9.4 g. of the crude product (88%). It was recrystallized from hot water. The purified product melted at 179–181°; yield of pure product 6.5 g. (61%).

Anal. Calc'd for $C_{11}H_9N_3O_2$: N, 19.53; Neutr. Equiv., 215.06.
Found: N, 20.33; Neutr. Equiv., 213.6.

Preparation of ethyl-2-phenyl-2,1,3-triazol-4-ylmethylene acetate. A mixture of 50 ml. of absolute ethanol, 13.2 g. of 2-phenyl-2,1,3-triazol-4-ylmethylene acetic acid, and 2 ml. of concentrated sulfuric acid was refluxed ten hours. The excess ethanol was removed *in vacuo* and the residue washed with 5% aqueous sodium carbonate. The ester was dissolved in ether and dried over sodium sulfate. The ether solution was decanted, the ether removed *in vacuo*, and the residue crystallized from methanol; yield 6.7 g., m.p. 64–66°.

Anal. Calc'd for $C_{13}H_{13}N_3O_2$: N, 17.28. Found: N, 17.55.

Attempted synthesis of 2-phenyl-2,1,3-triazol-4-yl-hydroxyacetic acid. A mixture of 17.3 g. (0.10 mole) of (I), 6.5 g. (0.1 mole) of potassium cyanide, and 20 ml. water was treated slowly with stirring and cooling with 30 ml. of sodium bisulfite. During the reaction a semisolid formed and the mixture darkened considerably. This semisolid layer (presumably the cyanohydrin) was refluxed with concentrated hydrochloric acid. The product remaining was a yellow-brown sticky solid from which nothing could be crystallized.

Preparation of 1-isopropyl-2-(2'-phenyl-2',1',3'-triazol-4'-yl)-4,4-dimethylimidazolidine (VII). A mixture of 8.7 g. (0.05 mole) of (I), 6.5 g. (0.05 mole) of N-(2-aminoisobutyl)-isopropylamine, and about 100 ml. of benzene was heated under conditions such that a benzene-water mixture was distilled through a four-foot packed column. The column was fitted with a head so that the benzene was returned and the water separated. The temperature was gradually increased to 100°, resulting in the removal of 0.8 g. of water. An increase of the temperature to 120° caused no more water to separate. The excess of benzene was removed *in vacuo*. Ethanol was added to the residue, and upon cooling, one gram of a white solid (m.p. 197–198°) crystallized. The filtrate from this crystallization was distilled. The entire residue (after a small forerun) boiled at 181–182° at 3 mm.; yield 9.0 g. (63%).

Anal. Calc'd for $C_{16}H_{23}N_5$: N, 24.56. Found: N, 24.22.

Preparation of 1-n-butyl-2-(2'-phenyl 2',1',3'-triazol-4'-yl)-4,4-dimethylimidazolidine (X). A mixture of 8.7 g. (0.05 mole) of (I), 7.2 g. of N-(2-aminoisobutyl) *n*-butylamine, and about 100 ml. of benzene was heated as in the preceding experiment. About 0.8 g. of water was removed. The benzene was removed *in vacuo*, and ethanol was added to the residue. All but about one gram of solid dissolved. This solid was filtered and the filtrate distilled. After the ethanol and a few drops of forerun were removed, the entire product boiled at 196–198° at 4 mm.; yield 11 g. (73%). It was light yellow in color and was redistilled. A middle fraction of 7 g. was taken which was light yellow in color and boiled at 184° at 1 mm.

Anal. Calc'd for $C_{17}H_{25}N_5$: N, 23.39. Found: N, 23.32.

Preparation of 1-phenyl-2-(2'-phenyl-2',1',3'-triazol-4'-yl)-4,4-dimethylimidazolidine (XI). A mixture of 8.7 g. (0.05 mole) of (I) and 8.2 g. (0.05 mole) of N-(2-aminoisobutyl)-aniline, and about 100 ml. of benzene was heated under the same conditions as in the preceding experiment. About 0.8 g. of water was removed. The product upon distillation boiled at 230–235° at 2 mm.; yield 10 g. (62%). The distillation was difficult and some decomposition took place. The distillate partially solidified upon standing, and, was crystallized from ethanol. About 1 g. of solid formed. The filtrate was redistilled and a 5.3-g. middle cut was taken for analysis and testing. It was a thick syrup.

Anal. Calc'd for $C_{19}H_{21}N_5$: N, 21.93. Found: N, 21.44.

Preparation of 1-p-tolyl-2-(2′-phenyl-2′,1′,3′-triazol-4′-yl)-4,4-dimethylimidazolidine (XII). A mixture of 8.7 g. (0.05 mole) of (I), 8.9 g. (0.05 mole) of N-(2-aminoisobutyl)-*p*-toluidine, and about 100 ml. of benzene was heated one hour at 105° as in the preceding experiment to remove water. The benzene was removed *in vacuo* and the residue was purified by crystallization from an alcohol-water mixture. The yield was 6.1 g. (51%) and the product melted at 109–110°.

Anal. Calc'd for $C_{20}H_{23}N_5$: N, 21.09. Found: N, 21.14.

Synthesis of methyl-2-phenyl-2,1,3-triazol-4-yl carbinol. A Grignard reagent was prepared in the usual manner using 16.2 g. (0.17 mole) of methyl iodide and 3.9 g. (0.16 mole) of magnesium. To this Grignard reagent was added 8.5 g. (0.05 mole) of (I) dissolved in 60 ml. of anhydrous ether. The mixture was refluxed 30 minutes, cooled, and poured into ice-water containing 10% sulfuric acid. The ether layer was separated, dried over sodium sulfate, and distilled at 3 mm. The product boiled at 144°; yield 5.5 g. (59%).

Anal. Calc'd for $C_{10}H_{11}N_3O$: N, 22.21. Found: N, 21.86.

Synthesis of ethyl-2-phenyl-2,1,3-triazol-4-yl carbinol. A Grignard reagent was prepared from 13.1 ml. (0.17 mole) of ethyl bromide and 3.9 g. (0.16 mole) of magnesium under the usual conditions. To this Grignard reagent was added 8.5 g. (0.05 mole) of (I) dissolved in 60 ml. of dry ether. After the addition, the mixture was refluxed 30 minutes. It was poured into ice-water containing sulfuric acid, the ether layer was separated, dried over sodium sulfate and distilled. The product boiled at 156° at 3 mm., yield 4.7 g. (47%).

Anal. Calc'd for $C_{11}H_{13}N_3O$: N, 20.68. Found: N, 20.30.

Synthesis of phenyl-2-phenyl-2,1,3-triazol-4-yl carbinol. A Grignard reagent was prepared in the usual manner from bromobenzene (0.17 mole) and magnesium (0.16 mole). To this reagent were added 8.7 g. (0.05 mole) of (I) dissolved in 60 ml. of dry ether. After the addition was complete, the mixture was refluxed 30 minutes and then introduced into ice-water containing sulfuric acid. The ether layer was separated, dried over sodium sulfate, and distilled at 3 mm. It boiled at 214°; yield 7.2 g. (58%).

Anal. Calc'd for $C_{15}H_{13}N_3O$: N, 16.72. Found: N, 17.14.

Conversion of (V) to its acid chloride (XIII). A mixture of 1.89 g. (0.01 mole) of 2-phenyl-2,1,3-triazole-4-carboxylic acid and 2 g. (0.01 mole) of phosphorus pentachloride was warmed gently to start the reaction. The mixture became quite hot and changed to a molten mass, which solidified upon cooling. The product was warmed over steam *in vacuo* to remove the phosphorus oxychloride. A white solid remained which was used for other reactions without purification. In another experiment thionyl chloride was substituted for the phosphorus pentachloride but the results were less satisfactory.

Synthesis of methyl 2-phenyl-2,1,3-triazole-4-carboxylate. About 5 ml. of absolute methanol was added to 0.01 mole of the acid chloride (XIII) prepared in the preceding experiment. The mixture was warmed gently. After a few minutes a white solid began to crystallize, melting point 85–86°. A second crystallization did not raise the melting point; yield 1.6 g. (79%).

Anal. Calc'd for $C_{10}H_9N_3O_2$: C, 59.14; H, 4.47; N, 20.68.
Found: C, 58.90; H, 4.02; N, 20.95.

Synthesis of phenyl-2-phenyl-2,1,3-triazole-4-carboxylate. To 6.2 g. (0.03 mole) of the acid chloride (XIII) was added 3.8 g. of phenol and 15 ml. of pyridine. This mixture was allowed to stand 4 hours and was then refluxed 3 hours. Upon pouring into ice-water a semi-solid appeared. The water was decanted and the semisolid washed with water containing 3% sodium carbonate. The insoluble residue was dissolved in ethanol from which it crystallized; yield 3 g. (50%), melting point 111–112°.

Anal. Calc'd for $C_{15}H_{11}N_3O_2$: N, 15.81. Found: N, 15.92.

Synthesis of the amide of 2-phenyl-2,1,3-triazole-4-carboxylic acid. To 0.01 mole of the acid chloride (XIII) was added 5 ml. of concentrated ammonium hydroxide. The mixture was stirred and warmed gently for 15 minutes. A white solid formed which when crystallized from 95% ethanol melted at 142–143°; yield quantitative.

Anal. Calc'd for $C_9H_8N_4O$: N, 29.77. Found: N, 29.90.

Preparation of the anilide of 2-phenyl-2,1,3-triazole-4-carboxylic acid. To 0.01 mole of the acid chloride (XIII) was added 1.86 g. (0.02 mole) of aniline dissolved in anhydrous ether. A heavy white precipitate formed at once. The mixture was stirred and warmed gently 15 minutes. The ether was removed and water added to dissolve the aniline hydrochloride. The solid was filtered and crystallized from 95% ethanol; yield 1.9 g. (73%), melting point 154–155°. A second crystallization did not raise the melting point.

Anal. Calc'd for $C_{15}H_{12}N_4O$: N, 21.20. Found: N, 21.72.

Synthesis of the hydrochloride of the diethylaminoethanol ester of 2-phenyl-2,1,3-triazole-4-carboxylic acid. To 14.5 g. (0.07 mole) of the acid chloride (XIII) was added 40 g. of diethylaminoethanol. Much heat was evolved. After the reaction subsided, the mixture was warmed over steam 2 hours, and added to about 1 liter of 2% sodium carbonate solution. An oil came to the top which was extracted with ether, washed with water, and dried over sodium sulfate. The ether solution was decanted and treated with anhydrous hydrogen chloride. The slightly colored hydrochloride formed, upon crystallizing twice from ethanol was colorless, and melted at 189–190°; yield 11.8 g. (51%).

Anal. Calc'd for $C_{15}H_{21}ClN_4O_2$: N, 17.25; Cl, 10.96.
Found: N, 17.17; Cl, 10.92.

Nitration of 2-phenyl-2,1,3-triazole-4-carboxylic acid. A mixture of 4.2 g. of the acid (V) and 6.6 ml. of concentrated sulfuric acid was cooled in an ice-salt bath and 3.3 ml. of concentrated nitric acid was added dropwise with stirring. After the addition was complete the mixture was allowed to stand at room temperature 30 minutes and then poured into 50 ml. of cold water. The solid which formed was crystallized from 95% ethanol; yield 3.1 g. (60%), melting point 236–238°.

Anal. Calc'd for $C_9H_6N_4O_4$: N, 23.92. Found: N, 24.16.

The position of the nitro group has not been proved, but it is reasonable to expect it to appear in the 4-position.

Synthesis of 1-isopropyl-2-(2'-phenyl-2',1',3'-triazol-4'-yl)-4,4-dimethyl-2-imidazoline (VIII). A mixture of 17 g. of 2-phenyl-2,1,3-triazole-4-carboxylic acid, 11.7 g. of N-(2-aminoisobutyl)isopropylamine, and about 100 ml. of benzene was heated under the usual conditions to remove the water formed from the reaction as an azeotropic mixture. No water was driven over until the temperature reached about 200°. From 200–230° 1.4 g. of water came over. After cooling, the product was washed with 200 ml. of 5% sodium hydroxide. The oil remained undissolved, was extracted once with benzene and once with ether. The combined extracts were dried over solid potassium hydroxide, and distilled. After a small forerun the entire product boiled at 190° at 4 mm., yield 11.7 g. (93%). This yield is based upon the fact that 3 g. of the acid was recovered from the sodium hydroxide washing.

Anal. Calc'd for $C_{16}H_{21}N_5$: N, 24.72. Found: N, 24.82.

Synthesis of 1-n-butyl-2-(2'-phenyl-2',1',3'-triazol-4'-yl)-4,4-dimethyl-2-imidazoline (XIV). A mixture of 18.9 g. (0.1 mole) of (V), 14.4 g. (0.1 mole) of N-(2-aminoisobutyl)*n*-butylamine, and 100 ml. of benzene was heated at 245° for one hour under the usual conditions to remove water. The product was washed with 5% sodium hydroxide and the oil which remained was extracted once with benzene and once with ether. The combined ether and benzene extracts were dried over solid potassium hydroxide and distilled. The main product boiled at 196° at 4 mm. The yield of XIV was 18.8 g. (77%). This calculation of the percentage yield considered the fact that 3.2 g. of (V) was recovered by acidifying the alkaline extract.

Anal. Calc'd for $C_{17}H_{23}N_5$: N, 23.52. Found: N, 23.26.

The picrate of (XIV) was prepared by refluxing a solution of 1.9 g. of (XIV) and 1.6 g. of picric acid in 10 ml. of ethanol for 15 minutes. A yellow solid formed upon cooling, which upon purification by crystallization from ethanol melted at 141–143°.

Anal. Calc'd for $C_{23}H_{26}N_8O_7$: N, 21.28. Found: N, 21.41.

The hydrochloride of XIV was prepared by dissolving 2 g. in dry ether and adding excess dry hydrogen chloride. The white solid hydrochloride was filtered and purified by crystallization from a benzene-acetone mixture. It melted at 220–222°.

Anal. Calc'd for $C_{17}H_{24}ClN_5$: N, 20.98. Found: N, 20.78.

PHARMACOLOGICAL STUDIES

The semicarbazone of 2-phenyl-2,1,3-triazole-4-carboxaldehyde, 2-phenyl-2,1,3-triazole-4-carboxylic acid, and 2-phenyl-2,1,3-triazol-4-ylmethyleneacetic acid proved to be ineffective in the treatment of tetanus toxemia, *Streptococcus hemolyticus*, influenza virus, and rabic virus infected mice. The latter compound had no bactericidal, bacteriostatic, fungicidal, or fungistatic action toward common organisms.

The hydrochloride of the diethylaminoethyl ester of 2-phenyl-2,1,3-triazole-4-carboxylic acid was ineffective as an antispasmodic and had little antihistamine activity. Likewise it was ineffective as a local anesthetic.

1-Isopropyl-2-(2′-phenyl-2′,1′,3′-triazol-4′-yl)-4,4-dimethyl-2-imidazoline proved ineffective against tuberculosis. The same can be said for 1-isopropyl-2-(2′-phenyl-2′,1′,3′-triazole-4′-yl)-4,4-dimethylimidazolidine and 1-*n*-butyl-2-(2′-phenyl-2′,1′,3′-triazol-4′-yl)-4,4-dimethylimidazolidine.

1-Phenyl-2-(2′-phenyl-2′,1′,3′-triazol-4′-yl)-4,4-dimethylimidazolidine was not effective against tuberculosis or as an antimalarial. No appreciable bactericidal, bacteriostatic, fungicidal, or fungistatic action was observed for any of the other imidazolines or imidazolidines reported above.

ACKNOWLEDGMENT

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SUMMARY

1. Twenty-seven derivatives of 2-phenyl-2,1,3-triazole-4-carboxaldehyde have been prepared.

2. Some of these compounds have been examined for therapeutic value but none has proved to be effective.

Albuquerque, New Mexico

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(2) Hann and Hudson, *J. Am. Chem. Soc.*, **66**, 735 (1944).

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