ml. and neutralized with solid sodium bicarbonate. The solid was removed, washed with water, and dried. It was recrystallized from hexane, yield 70%, m.p. 99–100°.

Anal. Calcd. for $C_{18}H_{18}N_2O_2$: C, 73.45; H, 6.16; N, 9.52. Found: C, 73.39; H, 6.22; N, 9.51.

1-(2-Phenylethyl)-5-carboxybenzimidazole (IX). The acid was prepared from the ester (VIII) by refluxing with 10% aqueous sodium hydroxide solution. The resulting solution was adjusted to pH 5 and the solid which separated was removed and dried. It was then recrystallized from aqueous ethyl alcohol, m.p. 219.5–220.5°.

Anal. Calcd. for $C_{16}H_{14}N_2O_2$: C, 72.16; H, 5.30; N, 10.52. Found: C, 71.98; H, 5.20; N, 10.47.

1-(2-Phenylethyl)-5-carboxamidobenzimidazole (X). 1-(2-Phenylethyl)-5-carboxybenzimidazole (11.7 g.) was suspended in 160 ml. of chloroform and 40 ml. of thionyl chloride added slowly with stirring. The mixture was refluxed for 4 hr. in which time it became homogeneous. The chloroform and excess thionyl chloride were removed *in vacuo*. The resulting solid was cooled and treated with 300 ml. of concd. ammonium hydroxide. After stirring for 30 min., the mixture was heated on the steam bath for 1 hr. The solid was removed, washed with cold water and recrystallized from aqueous alcohol, yield 74%, m.p. 230–231°.

Anal. Calcd. for $C_{16}H_{15}N_3O$: C, 72.43; H, 5.70; N, 15.84. Found: C, 72.26; H, 5.88; N, 15.69.

1-(2-Phenylethyl)-5-benzimidazolecarboxyhydrazide (XI). The acid chloride of IX, prepared as before, was dissolved in dry pyridine and the solution added gradually to a slight excess of 95% hydrazine with stirring. After 24 hr., the liquid was removed by distillation *in vacuo* and the resulting solid was washed with water and dried. The product was recrystallized from aqueous ethyl alcohol, yield 17%, m.p. 209–211°.

Anal. Calcd. for $C_{16}H_{16}N_4O_2$: C, 68.55; H, 5.75; N, 19.99. Found: C, 68.72; H, 5.88; N, 19.82.

1,2-Bis-1-[(2-phenylethyl)-5-benzimidazolecarboxy]hydrazide (XII). The acid chloride of IX was cooled and a cold 24% aqueous solution of hydrazine was slowly added with stirring. The mixture was finally heated for 1 hr. on a steam bath. The solid was removed, washed with water and dried. It was recrystallized from 95% ethyl alcohol, yield 49%, m.p. 278–278.5°.

Anal. Calcd. for $C_{32}H_{28}N_6O_2$: C, 72.71; H, 5.34; N, 15.90. Found: C, 72.70; H, 5.56; N, 15.97.

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Synthesis of 1,2,3,2*H*-Triazoles with Side Chains in the 4-Position

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Previous communications in the 2-phenyl-1,2,3,-2*H*-triazole system have stressed compounds in which the side-chain consisted of only one carbon atom and with substituents on the benzene ring.[3-5] This report deals with the extension of the side chain in the 4-position to two, three, and four carbon atoms and with the preparation and determination of the properties of suitable derivatives of these new compounds. More specifically, 2-phenyl-1,2,3,2*H*-triazol-4-ylacetic acid, β-2-phenyl-1,2,3,2*H*-triazol-4-ylpropionic acid, γ-2-phenyl-1,2,3,2*H*-triazol-4-ylbutyric acid, and some of their simple derivatives have been synthesized.

EXPERIMENTAL[6]

2-Phenyl-1,2,3,2H-triazol-4-ylcarbinol (I). A 3-l., three-necked flask equipped with stirrer was flame dried and swept with dry nitrogen. To the flask was added 19 g. (0.5 mole) of lithium aluminum hydride and 800 ml. of anhydrous ether. To this mixture was added dropwise with stirring 40.6 g. (0.2 mole) of methyl-2-phenyl-1,2,3,2*H*-triazol-4-carboxylate[3] dissolved in 400 ml. of anhydrous ether. The rate of addition was such that a gentle reflux was maintained. After the addition was completed, the reaction mixture was stirred and refluxed for an additional 30 min. The mixture was cooled and water was added cautiously to destroy the excess lithium aluminum hydride. The contents of the flask were poured into 400 ml. of ice water, and 200 ml. of 10% sulfuric acid was then added to the mixture. The layers were separated and the aqueous layer extracted with more ether. The ether extracts were washed with water and dried with anhydrous sodium sulfate. Upon evaporation of the ether, a white solid residue of 2-phenyl-1,2,3,2*H*-triazol-4-ylcarbinol remained, weighing 29.5 g. (84% yield). After two crystallizations from benzene, colorless needles were obtained, m.p. 70.5–72°.

Anal. Calcd. for $C_9H_4N_3O$: C, 61.70; H, 5.18; N, 23.99. Found: C, 61.48; H, 5.28; N, 23.70.

2-Phenyl-1,2,3,2H-triazol-4-ylmethyl bromide (II). To 250 ml. of 48% aqueous hydrobromic acid solution was added 28 g. (0.16 mole) of (I) and the mixture was refluxed 1 hr. Upon cooling, the product which solidified was filtered, washed with cold water, and air-dried. The light yellow 2-phenyl-1,2,3,2*H*-triazol-4-ylmethyl bromide (II) weighed 30.8 g. (81% yield). When purified by three crystallizations from cyclohexanol, colorless crystals were obtained, m.p. 45–46° (previously reported 37–38°).

Anal. Calcd. for $C_9H_8N_3Br$: C, 45.40; H, 3.39; N, 17.65. Found: C, 45.60; H, 3.69; N, 17.33.

2-Phenyl-1,2,3,2H-triazol-4-ylacetonitrile (III). A solution of 6.5 g. (0.13 mole) of sodium cyanide in 60 ml. of water was placed in a 250-ml., three-necked flask. A solution of 21.5 g. (0.09 mole) of II in 70 ml. of acetone was added with stirring to the sodium bromide solution during a period of 45 min. During the addition, the mixture was refluxed gently; after all of II was added, refluxing was continued for 4 hr. Benzene was added to the cooled reaction mixture and the organic layer was washed thoroughly with water. The water was removed from the benzene solution by azeotropic distillation. The 2-phenyl-1,2,3,2*H*-triazol-4-ylacetonitrile (III) was purified by crystallization from benzene and weighed 7.0 g. (42% yield), m.p. 65–67° (previously reported 53–54°).

Anal. Calcd. for $C_{10}H_8N_4$: C, 65.20; H, 4.38; N, 30.42. Found: C, 65.51; H, 4.49; N, 30.21.

2-Phenyl-1,2,3,2H-triazol-4-ylacetic acid (IV). Six and nine-tenths grams (0.04 mole) of the nitrile (III) was refluxed for 4 hr. with 50 ml. of 70% aqueous sulfuric acid solution. After the reaction mixture had cooled, it was poured onto cracked ice. The resulting precipitate was filtered, washed with water, and air-dried. The 2-phenyl-1,2,3,-

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[2] Abstracted from the thesis presented by Mr. Collier in partial fulfillment of the requirements for the M. S. degree.

[3] J. L. Riebsomer, *J. Org. Chem.*, **13**, 815 (1948).

[4] J. L. Riebsomer and G. Sumrell, *J. Org. Chem.*, **13**, 807 (1948).

[5] J. L. Riebsomer and D. A. Stauffer, *J. Org. Chem.*, **16**, 1643 (1951).

[6] All melting points are uncorrected.

2*H*-triazol-4-ylacetic acid weighed 6.2 g. (76.5% yield). Two crystallizations from ethyl acetate afforded colorless rods, m.p. 110–111°.

Anal. Calcd. for $C_{10}H_9N_3O_2$: C, 59.10; H, 4.46; N, 20.68; neut. equiv., 203. Found: C, 59.34; H, 4.67; N, 20.28; neut. equiv., 205.

Methyl 2-phenyl-1,2,3,2H-triazol-4-ylacetate (V). Absolute methyl alcohol (25 ml.) was saturated with dry hydrogen chloride and to this solution was added 0.2 g. (0.001 mole) of the acid (IV). The solution was refluxed 10 hr. on a steam bath, after which the excess methanol was removed by distillation under reduced pressure. The residue of methyl 2-phenyl-1,2,3,2*H*-triazol-4-ylacetate was taken up in ether and washed thoroughly with cold aqueous 5% sodium carbonate, followed by washing with water. Colorless plates, m.p. 44–45°, remained after evaporation of the dried ether solution over a steam bath. The yield was 0.19 g. (92%).

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.35. Found: C, 61.16; H, 5.02; N, 19.52.

1-Isopropyl-2-(2'-phenyl-1',2',3',2'H-triazol-4'-ylmethyl)-4,4-dimethyl-2-imidazoline (VI). The apparatus for this preparation was a 3-ft. vacuum-jacketed Vigreux type 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. A mixture of 1.5 g. (0.007 mole) of V and 1 g. (0.007 mole) of *N*-(2-aminoisobutyl)isopropylamine dissolved in 5 ml. of benzene was heated over a temperature range of 210–230° for 5 hr. A small quantity of water was removed during the heating period. After cooling, the reaction mixture was dissolved in ether and the ether solution was washed with cold 5% aqueous sodium hydroxide, followed by washing with water and finally dried over potassium hydroxide pellets. After evaporation of the ether, a light brown oil remained, which upon cooling afforded 0.7 g. (32.5% yield) of VI. Three crystallizations from ligroin (b.p. 30–60°) and treatment with Norit produced pale yellow crystals, m.p. 83–85°.

Anal. Calcd. for $C_{17}H_{23}N_5$: C, 68.65; H, 7.80; N, 23.55; neut. equiv., 297. Found: C, 68.62; H, 8.04; N, 23.96; neut. equiv., 285.

β-2-Phenyl-1,2,3,2H-triazol-4-ylacrylic acid (VII). A mixture of 15 g. (0.09 mole) of 2-phenyl-1,2,3,2*H*-4-carboxaldehyde and 9.5 g. (0.09 mole) of malonic acid was dissolved in 150 ml. of pyridine containing a trace of piperidine. The solution was warmed over steam until the evolution of carbon dioxide had ceased. The mixture was cooled and poured into water containing enough hydrochloric acid to react with the pyridine and to leave a slight excess acidity. The precipitate which formed was filtered with suction, washed with water, and air-dried, affording 15 g. (79% yield) of VII. The material was purified by crystallizing from benzene, giving colorless crystals, m.p. 178–179°.

Anal. Calcd. for $C_{11}H_9N_3O_2$: C, 61.39; H, 4.22; N, 19.53; neut. equiv., 215. Found: C, 61.40; H, 4.42; N, 19.57; neut. equiv., 215.

The acid (VII) was previously reported[4] as prepared *via* the Perkin reaction starting with 2-phenyl-1,2,3,2*H*-triazol-4-ylcarboxaldehyde.

β-2-Phenyl-1,2,3,2H-triazol-4-ylpropionic acid (VIII). At atmospheric pressure 13 g. (0.06 mole) of the unsaturated acid (VII) dissolved in 500 ml. of ethanol was reduced in the presence of 0.9 g. of Adams catalyst. After 13 hr. at room temperature 96% of the theoretical quantity of hydrogen had been absorbed. Upon filtration of the catalyst and evaporation of the alcohol, a nearly colorless oil remained, which crystallized upon cooling. The yield was nearly quantitative. Crystallization of this material from ethyl acetate afforded colorless needles, m.p. 75–75.5°.

Anal. Calcd. for $C_{11}H_{11}N_3O_2$: C, 60.82; H, 5.10; N, 19.35; neut. equiv., 217. Found: C, 60.96; H, 5.22; N, 19.40; neut. equiv., 219.

Methyl β-2-phenyl-1,2,3,2H-triazol-4-ylpropionate (IX). Into 50 ml. of absolute methanol, which had been saturated in the cold with dry hydrogen chloride, was placed 2.5 g. (0.01 mole) of the acid (VIII) and the mixture was refluxed overnight. After removal of the solvent under reduced pressure, the residue was dissolved in ether and washed several times with cold 5% aqueous sodium carbonate solution, followed by washing with water and the ether solution dried over anhydrous magnesium sulfate. After evaporation of the ether, there remained 2.1 g. (91% yield) of IX as a colorless oil which crystallized upon cooling, m.p. 32.5-33.5°.

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.32; H, 5.67; N, 18.17. Found: C, 62.54; H, 5.87; N, 18.52.

β-2-Phenyl-1,2,3,2H-4-ylpropanamide (X). A mixture of 0.3 g. (0.001 mole) of IX and 5 ml. of concd. ammonium hydroxide was placed in a test tube and shaken vigorously for 30 min. The resultant mixture was allowed to stand overnight, during which time a crystalline product formed. The crystals were filtered with suction, washed with cold water, and air-dried. There remained 0.16 g. (73% yield) of X, which upon crystallization from benzene afforded colorless crystals, m.p. 137–138°.

Anal. Calcd. for $C_{11}H_{12}N_4O$: C, 61.09; H, 5.59; N, 25.91. Found: C, 61.40; H, 5.77; N, 26.14.

1-Hydroxy-3-(2'-phenyl-1',2',3',2'H-triazol-4'-yl)propane (XI). To a mixture of 2.5 g. (0.07 mole) of lithium aluminum hydride and 100 ml. of anhydrous ether was added dropwise 10 g. (0.04 mole) of the ester (IX) dissolved in 100 ml. of anhydrous ether. After refluxing for 30 min. and cooling, water was added cautiously to destroy the excess of lithium aluminum hydride. The reaction mixture was poured into water and acidified with 10% aqueous sulfuric acid. The aqueous layer was extracted with ether and the combined ether extracts were added to the organic layer. After washing with water and drying over anhydrous sodium sulfate, evaporation of the ether afforded 8.4 g. (96% yield) of XI as an almost colorless oil. The oil solidified after standing and upon two crystallizations from a benzene-ligroin mixture produced colorless plates, m.p. 45.5–47°.

Anal. Calcd. for $C_{11}H_{13}N_3O$: C, 65.00; H, 6.45; N, 20.68. Found: C, 65.15; H, 6.69; N, 20.67.

1-Bromo-3-(2'-phenyl-1',2',3',2'H-triazol-4'-yl)propane (XII). A solution of 7.5 g. (0.03 mole) of the alcohol (XI) in 75 ml. of 48% hydrobromic acid was refluxed for 2 hr. The cooled reaction mixture was diluted with water and extracted with ether. The ether extracts were washed with water, 20% sulfuric acid, 5% sodium carbonate solution and again with water, in that order. The organic layer was dried over Drierite, after which the ether was evaporated on the steam bath. The oily residue of XII weighed 9.4 g. (95% yield), b.p. 195–200° at 0.25 mm. No satisfactory analysis of this material was obtained and it was used in the next step in the impure state.

γ-2-Phenyl-1,2,3H-triazol-4-yl-n-butyronitrile (XIII). A solution of 4.9 g. (0.1 mole) of sodium cyanide in 50 ml. of water was introduced into a 250-ml., three-necked flask equipped with ground glass joints and fitted with a condenser, a dropping funnel, and a rubber sealed stirrer. To the solution was added dropwise with stirring 9 g. (0.03 mole) of XII dissolved in 50 ml. of acetone. The mixture was refluxed for 4 hr. and cooled. Benzene was added and the organic layer was washed with water. The benzene solution was dried by azeotropic distillation and the benzene was removed on the steam bath, leaving 7.1 g. (98% yield) of XIII as a pale yellow oil, b.p. about 205° at 0.5 mm. An acceptable analysis of this compound was not obtained and the crude material was used in the next step.

γ-2-Phenyl-1,2,3,2H-triazol-4-ylbutyric acid (XIV). A mixture of 6.7 g. (0.03 mole) of the nitrile (XIII) and 15 ml. of concd. sulfuric acid diluted to twice its volume with water was refluxed for 1 hr. The reaction mixture was cooled and poured onto cracked ice. The resultant precipitate was filtered with suction, washed with water, and air-dried. The light tan γ-2-phenyl-1,2,3,2*H*-triazol-4-ylbutyric acid (XIV) weighed 6.3 g. (85% yield). Crystallization from benzene-m.p. 72–73.5°.

Anal. Calcd. for $C_{12}H_{13}N_3O_2$: C, 62.32; H, 5.67; N, 18.17; neut. equiv., 231. Found: C, 62.43; H, 5.84; N, 18.31; neut. equiv., 234.

Methyl γ-2-phenyl-1,2,3,2H-triazol-4-ylbutyrate (XV). Six tenths of a gram (0.002 mole) of the acid (XIV) was dissolved in 25 ml. of absolute methyl alcohol which had been saturated with dry hydrogen chloride in the cold and the solution was refluxed overnight. After removal of the solvent under reduced pressure, the residue was dissolved in ether and washed thoroughly with 5% sodium carbonate solution, followed by water. The ether solution was dried over anhydrous sodium sulfate and the ether was evaporated on the steam bath, leaving an analytical sample of XV as an almost colorless oil. The sample weighed 0.4 g. (80% yield), too small an amount for the determination of the boiling point.

Anal. Calcd. for $C_{13}H_{15}N_3O_2$: C, 63.65; H, 6.16; N, 17.13. Found: C, 63.98; H, 6.52; N, 17.32.

γ-2-Phenyl-1,2,3,2H-triazol-4-ylbutyramide (XVI). Into a test tube was placed 0.1 g. (0.0004 mole) of XV and 5 ml. of concd. ammonium hydroxide. The contents of the test tube were shaken periodically for several days, after which time crystals formed. The crystals were filtered with suction, washed with water, and air-dried, yielding 0.075 g. (83% yield) of XVI. Crystallization from benzene afforded fine colorless needles, m.p. 105–106°.

Anal. Calcd. for $C_{12}H_{14}N_4O$: C, 62.59; H, 6.13; N, 24.33. Found: C, 62.21; H, 5.89; N, 23.79.

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Hydrogenation of the Imidazole Ring. Formation of Diacetylimidazolidine and of Diacetylbenzimidazoline[1]

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The remarkable resistance of the imidazole ring to catalytic hydrogenation is well established.[2] The only exception that has been described is the hydrogenation of lophine and of amarine which was catalyzed by a suspension of platinum black in glacial acetic acid.[3] In the work reported here it was found that hydrogenation of the imidazole ring proceeded smoothly at room temperature and at atmospheric pressure when acetic anhydride was used as the solvent and platinum oxide as the catalyst. In this way, two hitherto unknown compounds were prepared: diacetylimidazolidine was formed by the hydrogenation of imidazole; diacetylbenzimidazoline was formed by the hydrogenation of benzimidazole, leaving the benzene ring unchanged.

EXPERIMENTAL

Acetic anhydride (150 ml., 1.47 moles) was shaken with hydrogen and 1.0 g. of platinum oxide at room temperature and ordinary pressure until the uptake of hydrogen stopped. About 400–470 ml. of hydrogen (corr.) were absorbed.[4] To this pretreated suspension of platinum black in acetic anhydride, 2.04 g. (0.03 mole) of imidazole were added and the shaking continued until no further hydrogen was absorbed. The calculated amount of hydrogen (0.06 mole of hydrogen) was consumed in about 7 hr. The acetic anhydride solution was decomposed with ice water and evaporated to dryness *in vacuo* (20 mm.). The remaining oil was mixed with a small amount of absolute ethanol and ether. Upon storage in the cold room beautiful crystals of diacetylimidazolidine were formed; the yield was 3.77 g. (80%), m.p. 95°.

Anal. Calcd. for $C_7H_{12}N_2O_2$: C, 53.83; H, 7.75; N, 17.94. Found: C, 53.85; H, 7.50; N, 17.88.

Diacetylimidazolidine is very soluble in water and in ethanol, soluble in acetone and in hot benzene, and sparingly soluble in ether. It can be recrystallized from ethanol-ether. Determination of the acetyl groups: Calcd. as CH_3-COOH: 76.89. Found: 76.97.

Boiling with 2*N* hydrochloric acid for 45 min. split the imidazolidine ring with the formation of formaldehyde (detected by the fuchsin-sulfurous acid reaction) and ethylenediamine (detected with ninhydrin spray after chromatography in *n*-propyl alcohol, 75, 28% NH_4OH, 1.5, water, 23.5). At room temperature, at the other hand, only a trace of formaldehyde was detected after 18 hr. in 2*N* hydrochloric acid.

Benzimidazole (2.36 g., 0.02 mole) was hydrogenated the same way in acetic anhydride and consumed the calculated amount of hydrogen (0.02 mole) in about 7 hr. After recrystallization from absolute ethanol the yield of diacetylbenzimidazoline was 3.51 g. (86%). The melting point was 168–170°.

Anal. Calcd. for $C_{11}H_{12}N_2O_2$: C, 64.69; H, 5.92; N, 13.72. Found: C, 64.60; H, 6.10; N, 13.60.

Diacetylbenzimidazoline is soluble in ethanol, sparingly in cold water, soluble in hot water, soluble in acetone and in benzene; it is almost insoluble in ether.

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(2) K. Hofmann, *Imidazole and Its Derivatives*, Interscience Publishers, New York, 1953, p. 16.

(3) E. Waser and A. Gratsos, *Helv. Chim. Acta*, 11, 944 (1928).

(4) This amount of hydrogen represents approximately 220 ml. (0.01 mole) more than that calculated for the reduction of platinum oxide to platinum black. The mechanism of this partial reduction of the acetic anhydride is unclear. Similar findings have been reported by C. Mannich and A. H. Nadelmann, *Ber.*, 63B, 796 (1930), who found that at room temperature and ordinary pressure, in the presence of palladium black as the catalyst, acetic anhydride consumed a small amount of hydrogen with the formation of aldehyde and a little ethyl acetate.

Preparation of 5(6)-Iodobenzimidazole and 4(7)-Iodobenzimidazole

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During the course of some work concerning a comparative study of the physical properties of