5-Anilino-1,2,3,4-thiatriazole (V). Following the above procedure, the reaction mixture of similar quantities of III with aniline (in ethanol) gave a crude yellow precipitate after 16 hr. Recrystallization from dry ethanol gave 0.7 g. (40%), m.p. 136°, of colorless rod-shaped crystals identified as V by mixture melting point with an authentic specimen.

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Syntheses of Some 1-(2-Phenylethyl)benzimidazoles

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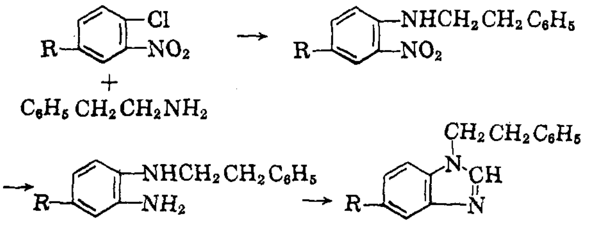
The preparation of several 1-(2-phenylethyl)-benzimidazoles, whose adrenergic properties are being evaluated, and their intermediate nitroanilines and *o*-phenylenediamines are described in this note. The diamines were isolated only in those cases where they were new compounds.



R = H, Cl, $COOC_2H_5$, COOH, $CONH_2$, $CONHNH_2$

EXPERIMENTAL

All melting points were determined in an apparatus described by Wagner and Meyer[1] using silicone oil and internal electrical heating. The values are uncorrected. Some of the compounds reported did not have sharp melting points even though they were obtained analytically pure. In these cases they were recrystallized to a constant melting point range before analysis.

Preparation of o-nitrophenylethylaminobenzenes. The general method is illustrated with the preparation of 2-nitrophenylethylaminobenzene.

N-(2-Phenylethyl)-2-nitroaniline (I). 1-Chloro-2-nitrobenzene (78.8 g., 0.5 mole) was dissolved in 100 ml. of xylene and 121.2 g. (1 mole) of β-phenylethylamine was added. The solution was refluxed for 6 hr., cooled to room temperature, and the β-phenylethylamine hydrochloride removed by filtration. The solid was washed with xylene. The filtrate plus the washings were distilled *in vacuo* to give an oil that was solidified by treating with petroleum ether (b.p. 30–60°). The product was recrystallized from 95% ethyl alcohol and obtained as orange crystals, yield 54%, m.p. 71.5–72.5°.

Anal. Calcd. for $C_{14}H_{14}N_2O_4$: C, 69.40; H, 5.82; N, 11.57. Found: C, 69.35; H, 6.09; N, 11.42.

N-(2-Phenylethyl)-2-nitro-4-chloroaniline (II). Compound II was prepared from 1,4-dichloro-2-nitrobenzene and β-phenylethylamine. The product was recrystallized several times from 95% ethyl alcohol, yield 50%, m.p. 89–92° (orange crystals).

Anal. Calcd. for $C_{14}H_{13}ClN_2O_2$: C, 60.76; H, 4.73; Cl, 12.81; N, 10.13. Found: C, 61.00; H, 4.56; Cl, 12.73; N, 10.13. Found: C, 61.00; H, 4.46; Cl, 12.73; N, 10.18.

N-(2-Phenylethyl)-2-nitro-4-carbethoxyaniline (III). This compound was prepared from ethyl 3-nitro-4-chlorobenzoate by the procedure used for compound I. The product was recrystallized repeatedly from 95% ethyl alcohol, yield 69%, m.p. 100–105° (orange crystals).

Anal. Calcd. for $C_{17}H_{18}N_2O_4$: C, 64.95; H, 5.77; N, 8.91. Found: C, 65.12; H, 5.78; N, 8.93.

N-(2-Phenylethyl)-o-phenylenediamine (IV). *N*-(2-Phenylethyl)-2-nitroaniline (24.2 g., 0.1 mole) was hydrogenated over 0.3 g. of platinum oxide. After removing the catalyst, 17 ml. of concd. hydrochloric acid was added to the filtrate. The dark solution was concentrated *in vacuo* to give an oil which solidified on standing under dry ether overnight. The dihydrochloride was washed with ether and dried, yield 57%. The product was sufficiently pure for subsequent reactions.

The free base was obtained by dissolving the dihydrochloride in water and neutralizing the solution with ammonium hydroxide. The oil, which formed, solidified on standing overnight. After drying, the product was recrystallized from petroleum ether (b.p. 30–60°) m.p. 53–55°.

Anal. Calcd. for $C_{14}H_{16}N_2$: C, 79.20; H, 7.60; N, 13.20. Found: C, 79.11; H, 7.56; N, 13.37.

N-(2-Phenylethyl)-2-amino-4-chloroaniline (V). To an intimate mixture of 27.6 g. (0.1 mole) of compound II and 59.7 g. of stannous chloride, 95 ml. of concd. hydrochloric acid was gradually added. After the reaction had subsided, the mixture was heated on a steam bath for 15 min. On cooling, a gel formed. An equal volume of ethanol was added and a vacuum distillation was carried out. This process was repeated until the precipitate became crystalline. It was then treated with 50% sodium hydroxide in the cold. The resulting oil was extracted with diethyl ether and the extract dried over anhydrous potassium carbonate. The ether was removed under reduced pressure in an atmosphere of nitrogen. The residual oil was dissolved in petroleum ether (b.p. 30–60°), treated with decolorizing carbon and the solution allowed to stand overnight. The solid product so obtained was recrystallized from petroleum ether (b.p. 30–60°), yield 65%, m.p. 48–50°.

Anal. Calcd. for $C_{14}H_{15}ClN_2$: C, 68.14; H, 6.13; Cl, 14.37; N, 11.36. Found: C, 68.08; H, 6.20; Cl, 14.17; N, 11.46.

1-(2-Phenylethyl)benzimidazole (VI). *N*-(2-Phenylethyl)-*o*-phenylenediamine (14.3 g., 0.05 mole) was dissolved in 150 ml. of 98% formic acid and the solution refluxed for 3 hr. The solution was concentrated to about 25 ml. *in vacuo* and neutralized with ammonium hydroxide. The product was removed, washed with water and dried. It was recrystallized from a mixture of diethyl ether and petroleum ether (b.p. 30–60°) with the aid of decolorizing carbon, yield 78%, m.p. 74–75°.

Anal. Calcd. for $C_{15}H_{14}N_2$: C, 81.05; H, 6.35; N, 12.61. Found: C, 80.90; H, 6.21; N, 12.61.

1-(2-Phenylethyl)-5-chlorobenzimidazole (VII). Compound VII was prepared from *N*-(2-phenylethyl)-2-amino-4-chloroaniline by the method used for compound VI. Neutralization with ammonium hydroxide gave an oil which was dissolved in diethyl ether and dried over anhydrous potassium carbonate. A solid was obtained when the ether was removed. Otherwise the procedure was the same as the one used for VI. The yield was 75%, m.p. 74°.

Anal. Calcd. for $C_{15}H_{13}ClN_2$: C, 70.17; H, 5.10; Cl, 13.81; N, 10.91. Found: C, 70.34; H, 5.21; Cl, 13.75; N, 10.96.

1-(2-Phenylethyl)-5-carbethoxybenzimidazole (VIII). *N*-(2-Phenylethyl)-2-nitro-5-carbethoxyaniline (15.7 g., 0.05 mole) in 100 ml. of ethanol was hydrogenated over 0.3 g. of platinum oxide. After removing the catalyst, dry hydrogen chloride was passed into the filtrate. The precipitated hydrochloride was washed with dry ether. Fifteen grams of the hydrochloride was refluxed in 100 ml. of 98% formic acid for 5 hr. The solution was concentrated *in vacuo* to about 25

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(1) E. C. Wagner and J. Meyer, *Ind. Eng. Chem., Anal. Ed.*, 10, 584 (1938).

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 *p*H 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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[1] (1) Present address: Goodrich-Gulf Chemical Company, Institute, W. Va.

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

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

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

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

[6] (6) All melting points are uncorrected.