

Table IV.—Assay of Desiccated Thyroid

Thyroid	U. S. P. XI	U. S. P. XI, 5 Years Previous	B. and W.	Proposed	MnO ₂
No. 1.	0.237	0.236	0.230	0.237	0.234
Max. var.	0.002 (3)	0.006 (6)	0.007 (4)	0.004 (4)	0.001 (3)
No. 4.	0.191	0.201	0.187	0.196	0.193
Max. var.	0.003 (3)	0.006 (6)	0.002 (2)	0.008 (5)	0.003 (4)
No. 5.	0.199	0.203	0.196	0.199	0.200
Max. var.	0.006 (4)	0.004 (6)	0.001 (2)	0.000 (5)	0.003 (4)
No. 13.	0.217	0.233	0.209	0.219	0.218
Max. var.	0.011 (4)	0.001 (3)	0.006 (4)	0.003 (5)	0.002 (4)

SUMMARY

A simplified method is presented for the determination of iodine in desiccated thyroid. The procedure involves ignition in an alkaline fusion mixture free from oxidizing agents. Interference by the hypochlorite and nitrate employed in the U. S. P. XI procedure is eliminated. Recovery of 97–99 per cent of the iodine is indicated by analysis of mixtures of standardized diiodotyrosine and casein.

The final titration should be performed at a pH within the range of 2.20–2.50, and the assays of thyroid by the proposed procedure fall within this range.

The stable iodine content of desiccated thyroid, stored in the laboratory for five years with no special precautions having been taken, is worthy of note.

Acknowledgment.—The authors are indebted to C. R. Szalkowski for the analyses made in 1935; also to E. Koozin Johnson, and to E. R. Frederick of the Iodine Educational Bureau for collaboration in the analyses. The authors are grateful for the interest and advice of George D. Beal, Assistant Director of Mellon Institute.

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New Pyrazolone Derivatives

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Of the hundreds of pyrazolone derivatives that are described in the literature, relatively few contain substituted phenyl groups and none have acetamino or ethoxy radicals on the phenyl. Since acetophenetidine is used in medicine like antipyrine, the introduction of these two radicals into the latter seemed a promising field of investigation. Accordingly, we started out to make some of the ten possible compounds derived by placing (EtO)(AcNH)C₆H₃ for C₆H₅ in antipyrine. While none of these has as yet been produced, several new intermediates have been prepared, as well as a nitrophenylpyrazolone.

EXPERIMENTAL

4-Acetamino-3-nitrophenetole (1).—To a cooled solution of acetophenetidine (0.1 mol) in 50 cc. of glacial acetic acid was added gradually a mixture of 6.3 cc. (0.1 mol) of concentrated nitric acid and an equal volume of acetic anhydride. After standing thirty minutes, the whole was poured into 300 cc. of cold water. The lemon-yellow precipitate, after being filtered and dried, had a melting point of 103–104°. Yield 90% of theory.

4-Amino-3-nitrophenetole.—The product from the first experiment (0.1 mol) was dissolved in boiling alcohol, and a solution of 12 Gm. of sodium hydroxide in 15 cc. of water was added. The mixture was boiled under reflux for one hour and poured into 500 cc. of cold water. The red precipitate, after recrystallization from alcohol, melted at 109–110°. Yield 91.8% of theory.

3,4-Dinitrophenetole.—To 35 Gm. (0.192 mol) of 4-amino-3-nitrophenetole were added 88 cc. of fluoboric acid (2), and to the well-cooled mixture, stirred mechanically, was gradually added a cold solution of 13.2 Gm. of sodium nitrite (0.192 mol). The precipitated diazonium fluoborate, suspended in

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150 cc. of water, was added gradually with stirring to a mixture of 153.6 Gm. of sodium nitrite, 30 Gm. of powdered copper and 300 cc. of water. The resulting precipitate was filtered off, washed with a solution of sodium hydroxide and then with water, and dried at 110°. After recrystallization from alcohol, the buff-colored product melted at 76°. Yield very poor. Per cent of nitrogen found, 13.69; calc., 13.21.

4-Acetamino-3-aminophenetole.—A thin paste of 44.8 Gm. (0.2 mol) of 4-acetamino-3-nitrophenetole and 265 cc. of hot water was poured in a thin stream into a boiling solution of 388 Gm. of ferrous sulfate in 750 cc. of water. Stronger ammonia water was then added with vigorous shaking to definite alkalinity. After boiling the mixture for five minutes, it was filtered and the filtrate was cooled in ice-water to produce 16.6 Gm. of product melting at 139–140°. Concentration of the mother liquor gave more to bring the total to 22.1 Gm., a yield of 54.3%. The reduction was also performed with aluminum amalgam, with ammonium sulfide and with sodium hydrosulfite, but the yield in each case was smaller. Per cent of nitrogen found, 13.97; calc., 14.43. Hydrolysis of the compound by usual methods gave 3,4-diaminophenetole melting at 71–72°.

3,4-Diacetaminophenetole.—A small quantity of 4-acetamino-3-aminophenetole was heated with an excess of acetic anhydride for a few minutes, then an equal volume of water was added, and the mixture was boiled to expel excess of acid. Upon cooling, white crystals were deposited that melted at 186°. Hydrolysis of these, as in the previous experiment, gave 3,4-diaminophenetole melting at 71–72°.

2-Amino-4-nitrophenetole (3).—*o*-Phenetidine (30 cc.) was acetylated with acetic anhydride in the usual way. The product was dissolved in 40 cc. of glacial acetic acid, and 87 cc. of sulfuric acid were added gradually with cooling. To the mixture at 0° was added in small portions a solution of 24 cc. of nitric acid in 36 cc. of sulfuric acid. The whole was then poured into 600 cc. of water, and the resulting precipitate of the acetamino compound, after filtering and washing, was hydrolyzed by heating with hydrochloric acid. This brownish yellow hydrochloride was identified by converting to the amine, melting at 97°.

2-Ethoxy-5-nitrophenylhydrazine.—To 35.7 cc. of 2-amino-4-nitrophenetole hydrochloride (0.164 mol), mixed with 30 cc. of hydrochloric acid and 20 Gm. of ice, were added slowly with stirring 11.8 Gm. of sodium nitrite in 24 cc. of water. The diazonium mixture was added to a cold solution of 114 Gm. of sodium sulfite in 246 cc. of water, previously saturated with sulfur dioxide. The mixture was heated at 60–70° and then for an equal period after adding 26 cc. of hydrochloric acid. After standing over night and further heating, the solution was filtered and an excess of sodium hydroxide was added to precipitate the base, yellow crystals melting at 124.5–125.5°. Yield 30.8% of theory. Per cent of nitrogen found, 19.95; calc., 21.32. Benzaldehyde

2-ethoxy-5-nitrophenylhydrazone, glistening orange crystals melting at 169–169.5°. Acetone 2-ethoxy-5-nitrophenylhydrazone, minute orange crystals melting at 123.5–124°.

1-(2-Ethoxy-5-nitrophenyl)-3-methyl-5-pyrazolone.—A mixture of 6.5 Gm. of 2-ethoxy-5-nitrophenylhydrazine and 6 cc. of acetoacetic ester was heated on a water bath for thirty minutes. The dark red solution solidified on standing to a brown mass, from which 8 Gm. of yellowish crystals were separated, melting at 82–83.5°. Yield 89% of theory. The analysis for nitrogen gave very low results and it is probable that the product is contaminated.

SUMMARY

In attempts to make acetaminoethoxyphenyl derivatives of antipyrine, the following new compounds were prepared: 3,4-dinitrophenetole, m. p. 76°; 4-acetamino-3-aminophenetole, m. p. 139–140°; 3,4-diacetaminophenetole, m. p. 186°; 2-ethoxy-5-nitrophenylhydrazine, m. p. 124.5–125.5°; benzaldehyde hydrazone of the latter, m. p. 169–169.5°; acetone hydrazone m. p. 123.5–124°; 1-(2-ethoxy-5-nitrophenyl)-3-methyl-5-pyrazolone, m. p. 82–83.5°.

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Some of the Constituents of the Tuber of Coqui (*Cyperus rotundus* L.). II. The Volatile Oil

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The volatile oil present in the tuber of *Cyperus rotundus* L. is the only constituent of this plant to have been studied chemically in the past. Goebel-Kunze (1) in 1830 reported the presence of a volatile oil in the tuber. The distillation of this oil has been carried out in the Sudan, India and Japan. Its use as a fixative in perfumery has been suggested (2).

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