latter. Our agreement with Cragwall's work is illustrated in Fig. 1.

Excess recrystallized *p*-aminophenol was added to previously boiled distilled water (to expel dissolved oxygen) in a 200-ml. flask placed in a thermostated oil-bath. The system was again boiled by evacuation (to remove oxygen in the vapor phase), sealed off and allowed to equilibrate with occasional hand agitation. Samples were taken in a tared pipet and weighed, and the amine content was determined by the nitrite procedure.[5]

The solubility of *p*-aminophenol in methyl ethyl ketone (2-butanone) at 58.5° was determined in a manner similar to that above except that no effort was made to exclude oxygen. The solubility was found to be 9.1 and 9.3 weight % by successive determinations.

(5) A 0.5-g. *p*-aminophenol sample was dissolved in 600 ml. of distilled water containing 10 g. of potassium bromide and 25 ml. of concentrated hydrochloric acid. Tenth-normal sodium nitrite was added in 5-ml. portions until indication of an excess (starch–iodide paper), persistent for 15 minutes, was obtained. The solution was then back titrated with 0.1 *N* sulfanilic acid and finally adjusted with more of the 0.1 *N* sodium nitrite. A faint positive starch–iodide test one minute after the last addition was taken as the end-point.

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Preparation of Testosteronephosphoric Acid[1]

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Testosteronephosphoric acid was required for testing as a possible intermediate in the metabolism of testosterone by prostatic tissue. Testosteronephosphoric acid had been obtained before from the reaction of testosterone with phosphorus pentachloride,[2] from 4-androsten-3,17-dione in a four-step sequence[3] and from the phosphorylation of testosterone with phosphorus oxychloride in pyridine.[4] The first two methods, although carefully defined, did not appear particularly attractive, whereas the third method, although of possible value, was published barren of detail. We have now tried the phosphorus oxychloride method and have found it to be satisfactory. A description of this direct phosphorylation, which makes testosteronephosphoric acid readily and conveniently available from testosterone, is given below.

Experimental[5]

Into a 250-ml. round-bottomed flask provided with a magnetic stirrer were placed 1.160 g. (4.00 millimoles) of testosterone, 5 ml. of pure dry pyridine and 50 ml. of sodium-dry ether. With the flask in a bath at −15 to −10° and with continuous stirring, a solution of 0.40 ml. (*ca.* 8.0 millimoles) of freshly distilled phosphorus oxychloride in 25 ml. of sodium-dry ether was added dropwise. The reaction mixture was protected from atmospheric moisture by a calcium chloride tube. After the addition, which required one-half hour, the mixture was stirred at −10° for two hours and was then allowed to come to room temperature (25°) and to stand at this temperature for an additional four hours. Addition of 100 ml. of ice-cold distilled water dissolved the white precipitate. After stirring the hydrolysis mixture for one hour, 50 ml. of ether was added. The ether layer was removed, and was washed with a 50-ml. portion of 0.4% sodium hydroxide solution. The sodium hydroxide washings were combined with the first aqueous phase. Acidification of the aqueous alkaline solution with 2% hydrochloric acid afforded a white precipitate, which was removed by filtration and dried in a desiccator. The crude testosteronephosphoric acid (1.250 g.) was dissolved in approximately 60 ml. of 0.5% aqueous sodium hydroxide, the solution was filtered and the clear filtrate was acidified with 2% hydrochloric acid. The white solids were collected on the filter, and were crystallized twice from approximately 50-ml. portions of 50–60% aqueous methanol. The pure white testosteronephosphoric acid monohydrate so obtained (1.010 g. or 65% yield) melted with vigorous evolution of bubbles at 157–159°. Shrinking and softening was noted at 135–138°, and transformation to an opalescent semi-solid was observed at 138–143°.

Anal. Calcd. for $C_{19}H_{29}O_5P \cdot H_2O$; C, 59.05; H, 8.08; P, 8.01. Found: C, 59.31; H, 8.14.

A 2×10^{-5} *M* solution of the testosteronephosphoric acid in 95% ethanol showed an absorption maximum at 240 mμ (ϵ 1.69×10^4). The material (0.0094 g. in 1.00 ml. of absolute methanol) showed $[\alpha]^{27.6}D$ 72.6°. The melting point of testosteronephosphoric acid monohydrate has been reported before as 160° dec.,[2] 155–157° dec.[3] and 150°,[4] and the specific rotation as $[\alpha]^{20}D$ 71.9°.[3] Dimethyl testosterone phosphate, as a 10^{-4} *M* ethanolic solution, was reported before with λ_{max} 238 mμ and ϵ 1.58×10^4 (approximate values).[3]

A sample of the testosteronephosphoric acid that had been crystallized a third time showed no change in melting point behavior. The material was dried at 50° *in vacuo* for two hours before analysis.

Anal. Found: C, 59.27; H, 7.81; P, 7.80.

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(2) U. Westphal, Yin-Lin Wang and H. Hellmann, *Ber.*, **72**, 1233 (1939).

(3) E. Müller, A. Langerbeck and W. Riedel, *Z. physiol. Chem.*, **281**, 29 (1944).

(4) Soc. pour l'ind. chim. à Bâle, Swiss pat. 201,536 (1939) [*C. A.*, **33**, 8925 (1939)].

(5) Elementary analyses were performed by Dr. Stephen M. Nagy and his staff at the Massachusetts Institute of Technology Microchemical Laboratory, Cambridge, Mass.

Antispasmodics. I. α-Amino-α-phenylacetamides

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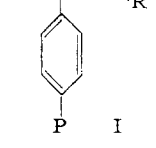
As part of a pharmacological screening program involving various basic phenylacetonitriles and derivatives, a number of amides, represented by the general formula I, where R = alkyl or H, R′ = alkyl, and P = H, CH_3 or OCH_3, were prepared.



P I

The amides recorded in Table I possess musculotropic antispasmodic properties. The *p*-methoxy-substituted compounds are more active than the unsubstituted or *p*-methyl-substituted analogs. α-Dibutylamino-α-(*p*-methoxyphenyl)-acetamide