version that may occur when the two sugars are heated together during the course of the reaction, we have studied the reaction rates of mixtures of glucose and fructose in which only one of the sugars was labeled with carbon-14. By purification of the resultant osazone and determination of its specific activity, and by knowing the specific activity of the osazone derived from the labeled hexose alone, we can calculate the relative contributions of glucose and fructose to the osazone. Table I gives the calculated ratios of F/G in the osazone formed from the various mixtures. Plotting F/G in the reaction mixture against the calculated F/G in the osazone gave Fig. 2.

We have demonstrated that 2.0 to 2.2 molecules of fructose react per molecule of glucose under the conditions specified. It should be noted, however, that during the early course of the reaction, before the concentrations of the substrates become limiting, fructose reacts 2.5 to 2.6 times as fast as glucose. A maximum yield of phenylglucosazone from glucose of 50% was the highest ever obtained under our conditions, whereas fructose was quantitatively converted to the osazone under the same conditions.

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Some Physical Properties of *p*-Aminophenol

BY S. A. DUNN

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During the development of an improved process for the production of *p*-aminophenol, it became necessary either to check or to determine for the first time some of the physical properties of the compound.

Melting Point.—The m.p. was determined under nitrogen on two recrystallized samples of *p*-aminophenol. In each case *p*-aminophenol (assaying 99.1% by Kjeldahl, m.p. 189–190° under N_2) was recrystallized once from alcohol and once from water, oxygen being carefully excluded. Samples were placed in m.p. tubes (soft glass) and the tubes were four times evacuated to about 1 mm. pressure and flushed with nitrogen. The tubes were then sealed off, bound to a 76 mm. immersion thermometer and placed in a preheated silicone oil-bath (estimated accuracy ±0.3) equipped with mechanical agitation. Both samples melted 191 to 192° (uncorrected) without visible signs of decomposition. Two other samples of *p*-aminophenol were sublimed (110°, 0.3 mm. pressure), and their melting points were determined in the same manner: 189.6 to 190.2° and 189.8 to 190.6°. The latter range could be repeated on the same sample by lowering and raising the temperature. All of these values are appreciably higher than those variously reported in the literature,[1,2] which average around 185° and are in each case accompanied by decomposition. Our higher values are undoubtedly the result of rigorous exclusion of oxygen.

Vapor Pressure.—The vapor pressure of a small sample of sublimed *p*-aminophenol (m.p. 190°) was determined in an isoteniscope at temperatures of from 130 to 186°. Table I lists the observed vapor pressures, corrected for that of mercury, as a function of temperature.

TABLE I

VAPOR PRESSURE OF *p*-AMINOPHENOL

t, °C.	*p*, mm.	*t*, °C.	*p*, mm.
130.2	0.3	159.6	5.1
143	2.2	167.0	8.0
145	2.2	171.1	9.9
150	3.0	176.5	14.9
151.1	3.2	185.3	26.7
157.5	4.7	284	*ca.* 760

A value of 22 kcal./mole for the heat of sublimation can be obtained from these data. The b.p., included above, was determined during distillation under a blanket of nitrogen; there was approximately 7% decomposition during distillation, as determined on the solid distillate by nitrite absorption.[5] The pressure measurement at 185.3° was complicated by the slow evolution of a second gas, correction for which was made by extrapolation to zero time. This gas evolution was probably caused by oxidative decomposition of *p*-aminophenol, since approximately 0.05 mm. partial pressure of air remained from the initial evacuation of the system.

Solubility.—The solubility of *p*-aminophenol in water was checked in order to clear up discrepancies between the values reported by Sidgwick and Callow[2,3] and found by Cragwall.[4] At nearly all temperatures, solubilities determined by the former authors are nearly twice as great as those of the

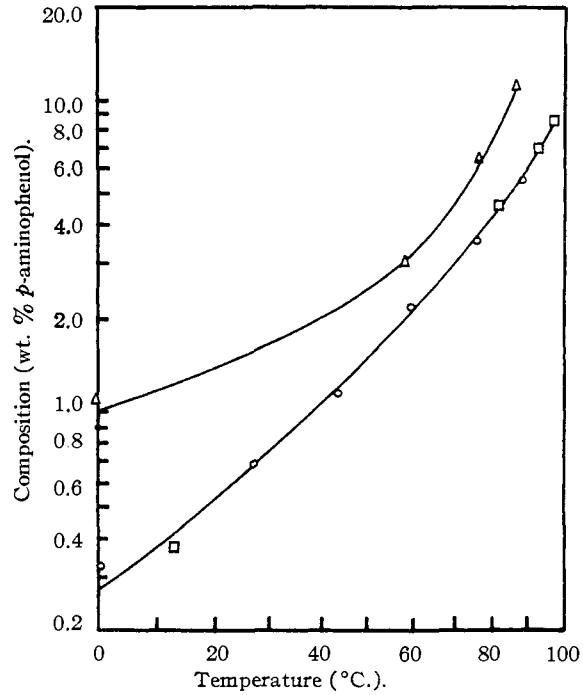

Fig. 1.—Solubility of *p*-aminophenol in water: △, ref. 2; ○, ref. 4; □, present work.

(1) "Beilstein," Vol. 13, p. 427.
(2) N. V. Sidgwick and R. K. Callow, *J. Chem. Soc.*, **125** 522 (1924).
(3) A. Seidell, "Solubilities of Organic Compounds," 3rd Edition, Vol. 2, D. Van Nostrand Co., Inc., New York, N. Y., 1941, p. 421.
(4) G. O. Cragwall, Jackson Laboratory work.

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]

BY WALTER J. GENSLER AND A. P. MAHADEVAN

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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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(1) This work was supported by an Institutional Grant from the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council, and was carried out as part of a coöperative program on cancer, with the Departments of Chemistry and Biology and the Boston University Medical School participating.

(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

BY PAUL A. J. JANSSEN

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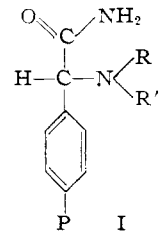
As part of a pharmacological screening program involving various basic phenylacetonitriles and derivatives, a number of amides, represented by the general formula I, where R = alkyl or H, R′ = alkyl, and P = H, CH_3 or OCH_3, were prepared.



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