The *p*-phenylphenacyl ester prepared in the usual way[4] was the derivative of lactic acid.

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Several Derivatives of Acetyl-*dl*-phenylalanine[1]

BY VIVIAN GOLDENBERG, HARRY GOLDENBERG[2] AND A. D. McLAREN

In a recent communication, MacAllister and Niemann[3] reported for the first time the hydrolysis of a hydrazide, *viz.*, nicotinyl-*l*-tyrosylhydrazide, by the proteolytic enzyme chymotrypsin. We are prompted to submit the preparation of another hydrazide, plus a thio ester, both of which are selectively attacked by beef chymotrypsin.

Experimental

Acetyl-*dl*-phenylalanine Hydrazide (APH).—APH was derived from acetyl-*dl*-phenylalanine ethyl ester (APEE),[4,5] prepared in turn by the condensation of acetic anhydride and *dl*-phenylalanine ethyl ester. APEE (1.5 g.) was dissolved in 5 ml. of absolute alcohol to which was added 0.62 ml. of 100% hydrazine hydrate. The solution was permitted to remain in a stoppered flask for 24 hours at room temperature, after which time 1.25 g. of the desired compound, m. p. 160.1–160.2° (uncor.), was precipitated out with a mixture of ether and petroleum ether. It was recrystallized from ethanol, from which it separated as needles.

Anal. Calcd. for $C_{11}H_{15}O_2N_3$: C, 59.70; H, 6.83; N, 18.99. Found: C, 59.64; H, 6.68; N, 18.79.

Unlike nicotinyl-*l*-tyrosylhydrazide, APH is hydrolyzed slowly by chymotrypsin under the conditions observed. After a 20-hr. incubation at 24.6° of an aqueous solution (*p*H 7.3) consisting of APH (0.1 *M*) and chymotrypsin (0.470 mg. nitrogen/ml.) in 0.05 *M* phosphate buffer, the extent of hydrolysis was found to be 24.2% by titration of the carboxyl groups liberated.[6] This value is based on an effective substrate concentration of 0.05 *M*, *i. e.*, it is presumed the *d*-form is not hydrolyzed. Blanks showed complete stability of APH, in the absence of enzyme, for a period of at least one day.

Acetyl-*dl*-phenylalanine Thio Ethyl Ester (APTEE).—Acetyl-*dl*-phenylalanine (5 g., 0.024 mole), thoroughly dried in a vacuum desiccator for a week over phosphorus pentoxide, was suspended in about 30 ml. of acetyl chloride. Phosphorus pentachloride (5.1 g., 0.024 mole) was added. The flask was immediately stoppered tightly and placed in an ice-bath, whereupon the acetyl-*dl*-phenylalanine rapidly dissolved. After the solution had remained at room temperature for three hours, it was vacuum distilled to dryness with total exclusion of moisture. Anhydrous ether was quickly poured on the residue, and the solution was again vacuum distilled to remove acetyl chloride and phosphorus oxychloride. The crude acyl halide was further evacuated by pump for half an hour. Then about 40 ml. of ethyl mercaptan was added rapidly. Immediately a vigorous ebullition developed, and the residue went into solution. By the next day, some white material had precipitated out. The entire mixture was taken to dryness. The residue was slightly yellow and very hygroscopic. Water was added, the resulting suspension was chilled, made alkaline with bicarbonate, and stirred for five minutes with ether. The mixture separated into two layers; the ether layer was removed and dried over magnesium sulfate. The ether was removed by vacuum distillation to give a residue which still appeared somewhat yellow and hygroscopic. It was dried in a vacuum desiccator for several days. The residue was then washed with petroleum ether several times to remove the colored hygroscopic impurity. The crude thio ester (yield 3.2 g. or 53%) was dissolved in boiling ethanol, the solution cooled, and diluted with water. On standing in the ice-box, white needles crystallized out, m. p. 92–93° (uncor.).

Anal.[7] Calcd. for $C_{13}H_{17}O_2NS$: C, 62.13; H, 6.82; S, 12.76. Found: C, 62.05; H, 6.78; S, 12.89.

APTEE (0.03 *M*) and chymotrypsin[8] (0.048 mg. nitrogen/ml.) were incubated at 25° and an initial *p*H of 7.6 in a 50% alcoholic solution containing 0.006 *M* phosphate buffer. Within one minute an intense odor of ethyl mercaptan developed, accompanied by a drop in *p*H due to liberated carboxyl groups. The presence of mercaptan was confirmed by a positive nitroprusside test, which was carried out in weakly basic solution to avoid hydrolysis of APTEE. No spontaneous hydrolysis of the substrate could be detected in the absence of enzyme.

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(1) From the M.Sc. (June, 1949) and Ph.D. (November, 1949) Theses of Vivian Goldenberg and Harry Goldenberg, respectively, of the Polytechnic Institute of Brooklyn, New York.

(2) National Institutes of Health Predoctoral Fellow, 1947–1949.

(3) R. V. MacAllister and C. Niemann, THIS JOURNAL, **71**, 3854 (1949).

(4) APEE, m. p. 68.0–68.6°, was synthesized in excellent yield and high purity according to the directions of E. Fischer (*Ber.*, **37**, 2496 (1904)) for the preparation of the related compound, chloroacetyl-*l*-tyrosine ethyl ester.

(5) E. Cherbuliez and P. Plattner (*Helv. Chim. Acta*, **12**, 324 (1929)) reported a m. p. of 68°.

(6) W. Grassmann and W. Heyde, *Z. physiol. Chem.*, **183**, 32 (1929).

(7) Microanalyses of APH and APTEE by F. Schwarzkopf, Elmhurst, L. I.

(8) Once crystallized chymotrypsin was used to study the catalyzed hydrolysis of both APH and APTEE.

The Hydration of 2-Heptyne[1]

BY G. F. HENNION AND C. J. PILLAR[2]

The hydration of an unsymmetrically situated non-terminal carbon–carbon triple bond has been studied previously in only three cases. Stearolic acid[3] was reported to form 9-keto- and 10-keto-stearic acids, by treatment with sulfuric acid, in a ratio of 42.4:57.6. In the same way, 9-undecynoic acid yielded 59% 9-keto and 41% 10-keto product; hydration with acetic acid and mercuric acetate altered the ratio considerably, giving the 9-keto and 10-keto isomers in a ratio of 46:54.[4] 2-Pentyne (the only hydrocarbon reported) yielded 2- and 3-pentanones in nearly equal amounts by the sulfuric acid method.[5]

Since there had been previously described[6] a simple catalytic method for triple bond hydrations in high yield, it was decided to apply this procedure to 2-heptyne. A mixture of the two ketones, 2-heptanone and 3-heptanone, was easily

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(1) Paper LV on substituted acetylenes; previous paper, THIS JOURNAL, **72**, 3542 (1950).

(2) Rev. Conrad J. Pillar, O.S.B., St. Benedict's College, Atchison, Kansas.

(3) Robinson and Robinson, *J. Chem. Soc.*, 2204 (1926).

(4) Sherrill and Smith, *ibid.*, 1501 (1937).

(5) Mowat and Smith, *ibid.*, 19 (1938).

(6) Thomas, Campbell and Hennion, THIS JOURNAL, **60**, 718 (1938).

obtained. Analysis of the product was achieved by gravimetric determination of the iodoform produced by treatment with iodine and potassium hydroxide.

Hydration of one-third mole (32 g.) of 2-heptyne in 80% methanol at 65° gave 26 g. of distilled ketones, b. p. 70–70.5° (50 mm.), $n^{25}\text{D}$ 1.4067, d^{25} 0.8128. Six analyses showed a 2-heptanone content of 47 ± 2%. A similar experiment with 70% acetic acid yielded 24 g. of ketones, $n^{25}\text{D}$ 1.4067, d^{25} 0.8123, containing 48% 2-heptanone.

It is well known that terminal acetylenes, $R-C\equiv CH$, produce methyl ketones, $R-CO-CH_3$, *exclusively*. Hence the formation of the two possible products (from both 2-pentyne[5] and 2-heptyne) *in substantially equal amounts* is noteworthy. This implies that the direction of electromeric polarization of the triple bond in alkyl- and dialkylacetylenes is not seriously affected by hyperconjugation or other factors ascribable to simple alkyl groups.

Experimental

Preparation of 2-Heptyne.—Acetylene was converted to the acetylide with 69 g. of sodium in 2.5 l. of liquid ammonia and the solution treated, in turn, with 3 moles of butyl bromide, 3 moles of sodamide[7] and an excess (200 ml.) of liquid methyl bromide. The product was recovered in the usual way[8]; yield 140 g. (48%), b. p. 110.5–111°, $n^{25}\text{D}$ 1.4192 (lit.[9] b. p. 111.8°, $n^{20}\text{D}$ 1.4237).

Hydrations.—2-Heptyne (0.33 mole) was converted to the heptanones in 100 ml. of 80% methanol at 65° and in 50 ml. of 70% acetic acid at 105°, as previously described.[6] The catalyst in each case consisted of 1 g. of mercuric oxide and 1 ml. of concentrated sulfuric acid.

Analytical Method.—Carefully purified 2-heptanone and 3-heptanone, separately and together, were weighed into a 100-ml. volumetric flask so that the total sample was about 2 g. and diluted to the mark with reagent grade methanol. After thorough mixing, 2.0 ml. of the solution was transferred to a 125 ml. glass-stoppered erlenmeyer flask. Ten ml. of methanol, 10 ml. of 2 *N* potassium hydroxide and 5 ml. of 2 *N* iodine solution were then admitted, the mixture shaken for thirty seconds, and an additional 2 ml. of potassium hydroxide added. Ten ml. of 1 *N* sodium thiosulfate was then added, the iodoform extracted with 10 ml. of ether and the ether extract in turn washed with 10 ml. of water. The ethereal solution was evaporated to dryness on a 10-cm. weighed watch glass. The iodoform was carefully washed with 5 ml. of distilled water, the washings removed with a fine capillary pipet. The iodoform, now in the form of clean yellow crystals, was air-dried and weighed. Blank determinations were run and corrections made in the usual way. Typical results are given in Table I. While the yields of iodoform did not correspond to the theoretical amounts, a plot of yield *vs.* composition (columns 1 and 4) yielded a straight line. This empirical relationship was employed for the analytical work, following the procedure described.

TABLE I

YIELDS OF IODOFORM FROM MIXTURES OF 2- AND 3-HEPTANONES

2-Heptanone content, %	Sample, mg.[a]	Iodoform, mg.[b]	Ratio, iodof./sample
0	42.5	10.3	0.24
20.6	43.1	26.2	0.61
37.6	42.9	42.9	1.00
41.6	73.1	83.2	1.14
48.2	43.5	52.5	1.21
50.9	42.1	53.7	1.28
60.8	44.9	67.3	1.50
77.3	46.5	83.9	1.80
87.0	41.0	81.7	1.99
100.0	41.9	93.2	2.22

[a] Two ml. of methanol solution containing about 2 g. per 100 ml. [b] Average of two or three determinations.

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[7] Vaughn, Vogt and Nieuwland, THIS JOURNAL, **56**, 2120 (1934).

[8] Bried and Hennion, *ibid.*, **59**, 1310 (1937).

[9] Egloff, "Physical Constants of Hydrocarbons," Reinhold Publishing Co., New York, N. Y., 1939, Vol. I, p. 369.

Thermal Properties of the Compound BPO_4

BY F. A. HUMMEL AND T. A. KUPINSKI

The purpose of this note is to report some data on the thermal stability and expansion of the compound boron phosphate. The binary compound is unusual since it is far more refractory than either B_2O_3 or P_2O_5, it is related to the high cristobalite form of silica crystallographically, and it shows reluctance to form a glass although its components comprise two of the most common glass-forming oxides known to ceramists.

G. E. R. Schulze[1] reported the X-ray structure analysis and some of the optical properties of boron phosphate. He apparently was the first to recognize the structure as a distorted high cristobalite type, and observed the crystal in the form of tetragonal bipyramids with indices 1.595 and 1.601. Both P^{+5} and B^{+3} were shown tetrahedrally coördinated with oxygen and the density calculated from X-ray data was 2.802.

The boron phosphate was obtained from the Victor Chemical Works and contained 31.0% B_2O_3, 64.4% P_2O_5, and 3.0% ignition loss; the ignited product was then 32.5% B_2O_3 and 67.5% P_2O_5. An X-ray pattern of the material as received showed it to be the compound boron phosphate.

Batches of 0.2–0.5 g. of the material were heated in platinum envelopes by the conventional quench technique to determine thermal stability. The quenching procedure, which has been described in detail elsewhere,[2] consists of enclosing small charges of material to be studied in a thin platinum envelope, inserting these charges in the hot zone of a platinum-wound furnace, holding for a desired length of time at a particular temperature to attain equilibrium in the charge, and then quickly dropping the envelope and charge into a quenching medium such as carbon tetrachloride or mercury in order to freeze in the high temperature equilibrium state. The accuracy of temperature measurement during the experiments was ±4°.

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[1] G. E. R. Schulze, *Z. physik. Chem.*, **B24**, 215 (1934).

[2] G. W. Morey, *J. Soc. Glass Technol.*, **20** [80], 245 (1936); *Cer. Abs.*, **17** [1], 30 (1938).