The value in the table for the heat of combustion of lanthanum metal as used must be corrected for the impurities present. If it is assumed that the oxygen is present as La_2O_3, that the nitrogen is present as LaN which burns to $N_2O_5(s)$ and La_2O_3, that the carbon exists as free graphite which burns to CO_2, and that the other impurities are negligible, the corrected value for the heat of combustion of lanthanum is found to be 6439.2 joules/g. Actually the carbon probably exists as lanthanum carbide, but the heat of formation of this compound is not available. Essentially we are taking its heat of formation as zero. For the small amount of carbon present this does not introduce an error of any consequence.

The uncertainty to be attached to this value must include the uncertainty in the energy equivalent. When this is included the value becomes 6439.2 ± 2.9 joules/g. There are small additional unknown uncertainties due to the corrections for the impurities.

Composition of the Lanthanum Oxide.—The La_2O_3 formed was tan in color. A Debye X-ray pattern showed only lines of hexagonal La_2O_3. Analysis by the "active oxygen" method of Barthauer and Pearce[8] gave a formula of $La_2O_{3.001}$. This analysis was made on run No. 2 in which the combustion was assumed to be complete.

Heat of Formation of La_2O_3.—The heat of combustion reported above gives, for the reaction in the bomb, a value of $\Delta E_{24.6}° = -1789.1 \pm 0.8$ kjoules/mole. The correction of this value to 25° is less than the uncertainty in the result. To obtain the heat of formation it is necessary to correct for the deviation of oxygen from the perfect gas law and to convert from ΔE to ΔH. Using Rossini and Frandsen's[9] value of $(\partial\Delta E/\partial P)_{301°K} = -6.51$ joules/atm./mole for oxygen and taking $\Delta H = \Delta E + \Delta(PV)$, we have for the heat of formation of La_2O_3, $\Delta H_{25}° = -1793.1 \pm 0.8$ kjoules/mole. In defined calories this is -428.57 ± 0.19 kcal./mole. This value differs by about 6.4% from the value of −458 kcal./mole selected by the National Bureau of Standards.[10]

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(8) G. L. Barthauer and D. W. Pearce, *Ind. Eng. Chem.*, **18**, 479 (1946).

(9) F. D. Rossini and M. Frandsen, *J. Research Natl. Bur. Standards*, **9**, 733 (1932).

(10) Selected Values of Chemical Thermodynamic Properties, N. B. S. Circular 500, 1952, p. 351.

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The Isolation of Desacetylneoprotoveratrine from *Veratrum Viride* Ait.

BY M. W. KLOHS, M. D. DRAPER, F. KELLER, W. MALESH AND F. J. PETRACEK

RECEIVED MARCH 13, 1953

A further investigation of the more hydrophilic ester alkaloids of *Veratrum viride* Ait. has resulted in the isolation of a new hypotensively active triester, desacetylneoprotoveratrine; m.p. 182–183°, $[\alpha]^{24}D$ −9.6 ± 2 (*c* 1.0 in py.). Mild alkaline hydrolysis afforded protoverine, acetic acid, (levo) α-methylbutyric acid and α-methyl-α,β-dihydroxybutyric acid. On the basis of the hydrolysis products and analytical data, the empirical formula $C_{39}H_{61}O_{14}N$ was established.

Except for the absence of an acetyl group, it seemed probable that the new ester was structurally identical with neoprotoveratrine.[1] A similar relationship has been demonstrated in the germine ester series (germitrine → germerine,[2] neogermitrine → germidine,[3] germanitrine → germanidine[4]) where in each case a labile acetyl group is lost upon subjecting the triester to methanolysis. For this reason, neoprotoveratrine was treated with methanol and a compound was obtained which proved to be identical with the triester, desacetylneoprotoveratrine, isolated directly. The ease with which the acetyl group was removed from neoprotoveratrine suggests the possibility that desacetylneoprotoveratrine may be of secondary rather than primary origin.

Pharmacology.[5]—The hypotensive activity of desacetylneoprotoveratrine was found to be 1.0 μg. [0.72 – 1.64].[6]

Experimental[8]

Countercurrent Separation of the "Amorphous Bases" of *Veratrum Viride* Ait.—The amorphous bases (30 g.) remaining after the removal of protoveratrine and neoprotoveratrine as described in our previous publication[4] were subjected to an 8-plate Craig countercurrent distribution using benzene–2 *M* acetate buffer *p*H 5.5 (1500 ml. per phase, lower phase moving). The material recovered from tube 8 (6.4 g.) was then distributed on a 24-plate countercurrent machine using benzene–2 *M* acetate buffer *p*H 6.9 (450 ml. per phase, lower phase moving).

Desacetylneoprotoveratrine.—The material recovered from tubes 22–24 (2.25 g.) was dissolved in benzene with heating. On standing, desacetylneoprotoveratrine separated as clusters of needles (0.7 g.); m.p. 182–183° (vac.), $[\alpha]^{24}D$ −9.6 ± 2 (*c* 1.0 in py.), +9.8 ± 2 (*c* 0.89 in $CHCl_3$). For analysis the sample was dried at 120° (2 mm.) to constant weight.

Anal. Calcd. for $C_{39}H_{61}O_{14}N$: C, 61.00; H, 8.01; N, 1.83; equiv. wt., 767.89. Found: C, 60.47; H, 8.40; N, 1.76; equiv. wt., 777.

In a volatile acid determination 8.185 mg. required 2.01 ml. of 0.01 *N* $Na_2S_2O_3$ or 1.87 equivalents.[9]

Hydrolytic Cleavage of Desacetylneoprotoveratrine to Protoverine, Acetic Acid, (levo)α-Methylbutyric Acid[10] and α-Methyl-α,β-dihydroxybutyric Acid.—Desacetylneoprotoveratrine (0.48 g.) was hydrolyzed in the same manner as that reported for neoprotoveratrine,[4] yielding protoverine,[11] m.p. 193°; $[\alpha]^{25}D$ −16.2 ± 2 (*c* 1.03 py.). On admixture with an authentic sample of protoverine, no melting point depression was observed.

The acid fraction when treated in the same manner as re-

(1) M. W. Klohs, R. Arons, M. D. Draper, F. Keller, S. Koster, W. Malesh and F. J. Petracek, THIS JOURNAL, **74**, 5107 (1952).

(2) Josef Fried, Howard L. White and O. Wintersteiner, *ibid.*, **72**, 4621 (1950).

(3) J. Fried, P. Numerof and N. H. Coy, *ibid.*, **74**, 3041 (1952).

(4) M. W. Klohs, M. D. Draper, F. Keller, S. Koster, W. Malesh and F. J. Petracek, *ibid.*, **74**, 4473 (1952).

(5) The pharmacological tests were carried out under the supervision of Dr. R. O. Bauer of the Riker pharmacology section.

(6) Expressed as micrograms per kilogram of anesthetized dog per minute required for a 10-minute intravenous infusion to lower the mean arterial blood pressure 30% when administered according to a previously described assay procedure.[7] The bracketed numbers express the 95% confidence limits.

(7) George L. Maison and J. W. Stutzman, *Arch. Intern. pharmacodynamie*, **85**, 357 (1951).

(8) All melting points are corrected. We are indebted to Dr. Adalbert Elek for the micro analyses and to C. H. Stimmel for equivalent weight determinations.

(9) It has previously been shown[4] that α-methyl-α,β-dihydroxybutyric acid is non-volatile under the conditions of the volatile acid determination.

(10) The specific rotation of the volatile acids from desacetylneoprotoveratrine indicated the presence of one mole of (levo) α-methylbutyric acid.

(11) By hydrolyzing for longer periods of time, isoprotoverine rather than protoverine was obtained.

ported for neoprotoveratrine,[4] yielded *p*-phenylphenacyl acetate, m.p. 110–111°, *p*-phenylphenacyl α-methylbutyrate, m.p. 69–70°, and α-methyl-α,β-dihydroxybutyric acid, m.p. 97–98.5°. The above compounds were further identified by mixed melting points with authentic samples and by their infrared spectra.

Conversion of Neoprotoveratrine to Desacetylneoprotoveratrine by Methanolysis.—Neoprotoveratrine (0.78 g.) was allowed to stand for 15 hours in methanol (100 ml.). At the end of this time, the methanol was evaporated to dryness *in vacuo* and the residue was subjected to a 24-plate countercurrent distribution using the same solvent system employed in the isolation of desacetylneoprotoveratrine. The material recovered from tubes 22–24 (0.262 g.) was crystallized from benzene, yielding clusters of needles (0.12 g.), m.p. 182–183.5°, $[\alpha]^{24}D$ −9.6 ± 2 (*c* 0.99 in py.). A mixed melting point with desacetylneoprotoveratrine isolated directly gave no depression. The infrared spectra of the two compounds were identical. For analysis the sample was dried at 120° (2 mm.) to constant weight.

Anal. Calcd. for $C_{39}H_{61}O_{14}N$: C, 61.00; H, 8.01. Found: C, 60.99; H, 8.02.

In a volatile acid determination 16.31 mg. required 3.654 ml. of 0.01 *N* $Na_2S_2O_3$ or 1.72 equivalents.

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Preparation of 7,8-Benzocoumarin and 1-Methoxynaphthalene-2-propionic Acid[1]

BY C. F. KOELSCH AND P. T. MASLEY

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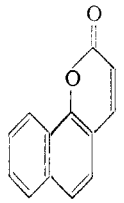
α-Naphthol reacts with malic acid in presence of sulfuric acid to form 7,8-benzocoumarin (I)[2] but



I

the best yields so far reported[3] were only 25–30%. Through systematic experiments it has now been found that nearly double the previous yield can be obtained by using acetic acid as a diluent for the reaction mixture and by using an excess of malic acid.

Experimental

A well ground mixture of 170 g. of technical α-naphthol and 226 g. of technical malic acid was added in portions during 20 minutes to a hot solution of 360 ml. of concd. sulfuric acid in 240 ml. of acetic acid. Gas evolution and some refluxing took place. During the addition and for 90 minutes afterwards, the mixture was stirred and kept at 135–141°. The solution was then stirred into one liter of crushed ice. The resulting mixture was boiled and then cooled while it was being stirred. The crude tarry product was separated, suspended in one liter of boiling water, and treated with enough sodium carbonate to cause the aqueous liquor to turn from dark brown to a reddish color. The mixture was cooled, and the solid was removed and washed with water. The product could be crystallized from acetic acid at this point, but it was usually easier to obtain a colorless product if it was distilled first, b.p. 235–240° at 6 mm., m.p. 141–142°, yield 110–127 g., 45–55%.

Anal. Calcd. for $C_{13}H_8O_2$: C, 79.6; H, 4.1. Found: C, 79.9; H, 4.1.

Reduction of 35 g. of the coumarin dissolved in 200 ml. of 10% sodium hydroxide by treatment with 360 g. of 3% sodium amalgam gave a little dimeric product and mainly **3,4-dihydro-7,8-benzocoumarin.** The product was precipitated with hydrochloric acid, distilled (b.p. 210–220° at 15 mm.) and then crystallized from alcohol, yielding 29 g. of needles, m.p. 76–77°.

Anal. Calcd. for $C_{13}H_{10}O_2$: C, 78.7; H, 5.6. Found: C, 78.7; H, 5.1.

The dihydrocoumarin reacted rapidly with phenylhydrazine in alcohol, forming **1-hydroxynaphthalene-2-propiophenylhydrazide**, colorless crystals from alcohol, m.p. 176–178° dec.

Anal. Calcd. for $C_{19}H_{18}N_2O_2$: C, 74.5; H, 5.9. Found: C, 74.9, 74.2; H, 5.7, 5.9.

The dihydrocoumarin (40 g.) was methylated with aqueous sodium hydroxide and methyl sulfate, giving 80–90% of **1-methoxynaphthalene-2-propionic acid**, colorless needles from ligroin containing 5% of chloroform, m.p. 94–96°, b.p. *ca.* 240° at 20 mm.

Anal. Calcd. for $C_{14}H_{14}O_3$: C, 73.1; H, 6.1. Found: C, 72.8, 73.2; H, 6.1, 5.7.

1-Methoxynaphthalene-2-propionamide, colorless needles from dilute alcohol, m.p. 103–105°, was obtained from the acid with thionyl chloride and ammonium hydroxide.

Anal. Calcd. for $C_{14}H_{15}NO_2$: C, 73.3; H, 6.0. Found: C, 73.5; H, 6.3.

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(1) From the M.S. Thesis of Paul Thomas Masley, July, 1942.
(2) V. Pechmann, *Ber.*, **17**, 1651 (1884).
(3) K. Bartsch, *ibid.*, **36**, 1966 (1903).

Direct Halogenation of Some Aromatic Amines

BY GENNADY M. KOSOLAPOFF

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The complexes between dioxane and halogens which were noted by Favorskii some years ago[1] afford an interesting method for mild direct halogenation of sensitive aromatic compounds. We have examined the bromination of several amines by means of the dioxane–bromine complex and found that monohalogenation can be carried out with moderately good yields without resorting to the customary blocking procedure.

Experimental Part

The complex, an orange-yellow solid, m.p. 64°, is readily prepared in quantity by mixing equimolar amounts of the components and quenching the hot product in ice-water. However, if the material is to be used in solution, it is merely necessary to add the desired amount of bromine to a cooled and stirred mass of dioxane. The bromination of amines can be carried out either by direct addition of the finely powdered complex to a solution of the amine, preferably in dioxane, or by addition of a dioxane solution of the complex to a cooled and stirred solution of the amine in dioxane in the presence of the requisite amount of concentration aqueous alkali. The latter procedure appears to be more economical of the amine.

Aniline.—The complex (25 g.) was added over 15 minutes in its original crystalline state (crystals 1–2 mm. diameter) to 9.3 g. of aniline in 20 g. of dioxane at 5–10° with stirring, in a beaker. The resulting precipitate was filtered off, washed with a little water and dilute sodium hydroxide, and again with water. The product (7 g.) was then dissolved in 75 ml. of hot ethanol and cooled, yielding 1.75 g. of 2,4,6-tribromoaniline. The solution was diluted with two volumes of water and on cooling yielded 4.5 g. (26%) of *p*-bromoaniline, m.p. 66.0–66.5°, characterized by mixed melting point with an authentic specimen and further by conversion to the acetyl derivative, which melted at 165°.

When the above experiment was repeated with finely ground complex which permitted more rapid solution and better distribution of the halogenating agent in the mixture, yields up to 50–57% were obtained and the amount of tribromoaniline declined to a small fraction of a gram.

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