pacity and with the necessary operating equipment. The reaction temperature during addition was 30–40° and 50–60° for half an hour after completing the addition. Total reaction period one and quarter hours. The excess thionyl chloride, solvent and volatile gases were immediately removed and the crude chlorinated product distilled under vacuum in an atmosphere of carbon dioxide. The yield of once-distilled product obtained under the above conditions was 80%. Employing ether as a solvent, and distillation of the product in an atmosphere of carbon dioxide, but without eliminating vapor phase reaction, the yield was 53%. Eliminating both the solvent and distillation of the product in an atmosphere of carbon dioxide the yield was 41%. The significant condition appears to be the elimination of vapor phase chlorination by introducing the hydroxy compound beneath the surface of the thionyl chloride–ether mixture. For material of purity of 99% see Table I.

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The Vapor Phase Rearrangement of Pinacols

BY WILLIAM S. EMERSON

Our success in converting styrene glycol to phenylacetaldehyde[1] in the vapor phase suggested the possibility of applying this technique to the pinacol rearrangement. We have found that pinacol is converted to pinacolone in 94% yield by passing its vapors together with steam over silica gel impregnated with phosphoric acid. This compares favorably with the 65–72% yield obtained in the liquid phase with sulfuric acid.[2] Under similar conditions, using a catalyst of silica gel impregnated with sodium bisulfate, 2,3-diphenyl-2,3-butanediol yielded 98% of material boiling in the proper range for 3,3-diphenylbutanone, from which 63% of crude product was isolated.

Experimental

Pinacolone.—A quartz tube[1] was packed with silica gel impregnated with phosphoric acid (10 cc. of 85% acid poured on 90 cc. of silica). While steam (about five volumes) was continuously passed over the catalyst, a solution of 50 g. of pinacol in 50 cc. of dioxane was introduced over a one-hour period. The tube was held at 275–300° and evacuated to 170 mm. After the pinacol was added, the tube was steamed out for an additional fifteen minutes before cooling. The layers in the receiver were separated and the aqueous portion twice extracted with ether. The combined extracts and organic layer were dried over Drierite. Distillation yielded 35 g. of pinacolone, b. p. 95–105° (103–106°),[3] n^{25}D 1.4019. By redistilling the ether an additional 4.5 g. was obtained, b. p. 98–105°, n^{25}D 1.4020 to give a total yield of 39.5 g. (94%).

The 2,4-dinitrophenylhydrazone of the main fraction melted at 122–124° (125°).[3]

3,3-Diphenylbutanone.—The tube was packed with silica gel impregnated with sodium bisulfate (5 g. in 15 cc. of water poured on 110 cc. of silica) and held at 275–300° and 80–100 mm. While steam was continuously passed over the catalyst, a solution of 32.5 g. of 2,3-diphenyl-2,3-butanediol in 50 cc. of dioxane and 65 cc. of toluene was introduced over an eighty-minute period. Some difficulty was encountered in keeping the tube from clogging. The steam introduction was continued for fifteen minutes more before cooling the tube. The layers in the receiver were separated and the aqueous phase was twice extracted with benzene. Distillation yielded 23 g. of crude 3,3-diphenylbutanone, b. p. 175–185° (15 mm.) (180° (18 mm.)),[4] n^{25}D 1.5870. The tube was washed out with 25 cc. of dioxane and then with 50 cc. of benzene. These washings were similarly worked up to obtain an additional 6.5 g., b. p. 178–188° (15 mm.), n^{25}D 1.5890. The total yield of crude ketone was 29.5 g. (98%). By cooling and recrystallizing from hexane there was isolated from the combined fractions 10 g. of product, m. p. 36–38° (41.0–41.5°),[5] 2 g., m. p. 31–33°; and 7 g., m. p. $> 26° < 35°$ (oily). The total yield of solid material was 19 g. (63%).

The oxime of the first fraction melted at 147–149° (151°)[6] after two crystallizations from alcohol. The residual oil after the isolation of all the solid ketone fractions yielded 49% of very impure oxime, m. p. 104–109° after one crystallization from alcohol.

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[1] Emerson and Agnew, THIS JOURNAL, **67**, 518 (1945).

[2] Hill and Flosdorf, "Organic Syntheses," Coll. Vol. I, p. 462.

[3] Heilbron, "Dictionary of Organic Compounds," Oxford University Press, New York, N. Y., 1938, Vol. III, p. 493.

[4] Parry, *J. Chem. Soc.*, **107**, 108 (1915).

[5] Thorner and Zincke, *Ber.*, **11**, 1988 (1878).

[6] Tiffeneau and Levy, *Bull. soc. chim.*, [4] **41**, 1351 (1927).

CENTRAL RESEARCH DEPARTMENT
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Further Evidence for the Configuration of Methionine

BY GUNTHER S. FONKEN AND RALPH MOZINGO

Hydrogenolysis of *d*(+)-methionine[1] (non-proteogenous) by Raney nickel catalyst has been found to give *d*(−)-α-aminobutyric acid. This is further evidence[2] that the levorotatory methionine found in proteins belongs to the same absolute configurational series as the other "*l*" α-amino acids.

It has been shown[3] that benzoyl-*l*(−)-cystine is converted into benzoyl-*l*(+)-alanine by Raney nickel catalyst. Using this procedure, *l*(−)-cystine has now been converted into *l*(+)-alanine, with no apparent racemization. Treatment of dextrorotatory methionine with excess Raney nickel catalyst gave an α-aminobutyric acid whose hydrochloride was levorotatory. Since the α-aminobutyric acids and their hydrochlorides have the same sign of rotation,[4] the amino acid is also levorotatory. Benzoylation of the α-aminobutyric acid gave levorotatory benzoyl-α-aminobutyric acid. From correlation of α-aminobutyric acid with alanine and the other amino acids,[5] it follows that levorotatory α-aminobutyric acid belongs to the "*d*" series. Dextrorotatory methionine then must belong also to the "*d*" series.

On the basis of the results reported here, levorotatory methionine and dextrorotatory α-aminobu-

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[1] Kindly supplied by Drs. William C. Rose and Madelyn Womack, University of Illinois; $[\alpha]^{28}$D +8.12°. *Anal.* Calcd. for $C_5H_{11}O_2SN$: N, 9.39. Found: N, 9.37.

[2] Windus and Marvel, THIS JOURNAL, **53**, 3490 (1931).

[3] Mozingo, Wolf, Harris and Folkers, *ibid.*, **65**, 1013 (1943).

[4] Fischer and Mouneyrat, *Ber.*, **33**, 2390 (1900).

[5] Clough, *J. Chem. Soc.*, **113**, 526 (1918).

tyric acid are configurationally identical and, by the previous correlation[5] of this latter compound into the natural amino acid series, the methionine derived from proteins is *l*(–)-methionine.

Experimental

Hydrogenolysis of *d*(+)-Methionine.—A solution of 150 mg. of *d*(+)-methionine[1] in 15 ml. of water was heated with about 1.5 g. of Raney nickel catalyst[3] at 90–95° for one-half hour. The nickel was removed by filtration and was washed on the filter with 350 ml. of hot water, the washings being added to the filtrate. The aqueous solution was concentrated *in vacuo* to a 1-ml. volume. Addition of absolute alcohol precipitated the amino acid, which was recovered by filtration. Recrystallization from dilute alcohol gave 16.9 mg. of *d*(–)-α-aminobutyric acid, m. p. 275° (dec.) (macro-block); $[\alpha]^{23}\mathrm{D}$ $-17.1°$ (*c*, 1.1 in *N* hydrochloric acid). The recorded[4] melting point for this compound is 303° (cor.). The recorded[4] rotation for the hydrochloride is $[\alpha]^{20}\mathrm{D}$ $-14.34°$; if the above be recalculated on the basis of the hydrochloride, the value becomes $[\alpha]^{23}\mathrm{D}$ $-13.1°$.

***d*(–)-α-Benzoylaminobutyric Acid.**—The α-aminobutyric acid used to determine the rotation was recovered by neutralization of the solution, followed by concentration and precipitation with alcohol. It was combined with the aminobutyric acid recovered from the recrystallization filtrates and used to prepare the benzoyl derivative.

The *d*(–)-α-aminobutyric acid was dissolved in 10 ml. of *N* sodium hydroxide. To the cooled solution was added 0.5 ml. of benzoyl chloride. The mixture was stirred for four hours at 0°. At the end of this time some insoluble material was removed by filtration. The filtrate was slightly acidified by addition of *N* hydrochloric acid, and was extracted continuously with chloroform for fifteen hours to remove the greater part of the benzoic acid. This extract was evaporated to dryness and the residue was extracted with hot petroleum ether (b. p. 90–100°); the residue was entirely soluble and was discarded.

The aqueous solution in the extractor was made acid to congo red by addition of concentrated hydrochloric acid, and was again extracted continuously with chloroform for sixteen hours. Evaporation of the chloroform extract gave a crystalline material which, after being extracted twice with boiling petroleum ether (b. p. 90–100°), weighed 55.9 mg.; m. p. 108–110°. This was recrystallized from ethyl acetate-petroleum ether to constant melting point, 110–111°; $[\alpha]^{24}\mathrm{D}$ $-31.4°$ (*c*, 1.2 in 0.07 *N* sodium hydroxide). The literature values are m. p. 120–121° (cor.),[4] 110–111°,[6] 111–112°[7] and 113–114°[7]; $[\alpha]^{20}\mathrm{D}$ $-31.8°$ (in sodium hydroxide solution).

Anal. Calcd. for $C_{11}H_{13}O_3N$: C, 63.76; H, 6.32; N, 6.76. Found: C, 63.46; H, 6.60; N, 6.51.

Hydrogenolysis of *l*(–)-Cystine.—To a solution of 9.6 g. of *l*(–)-cystine in 300 ml. of water was added about 60 g. of Raney nickel catalyst. The mixture was shaken vigorously for a few minutes, and then was heated at about 45° for one-half hour. At the end of this time the nickel was removed and was washed on the filter with 600 ml. of water, these washings being added to the filtrate. Concentration *in vacuo* of this aqueous solution to a sirup, followed by the addition of absolute alcohol, gave white crystals of *l*(+)-alanine. This product was recrystallized from dilute alcohol; $[\alpha]^{21}\mathrm{D}$ $+13.5°$ (*c*, 6.29 in 1.07 *N* hydrochloric acid). Recalculation of the specific rotation based upon the concentration of alanine hydrochloride in the solution gives $[\alpha]^{21}\mathrm{D}$ $+9.6°$; the recorded value[8] is $[\alpha]^{20}\mathrm{D}$ $+10.4°$ for *l*(+)-alanine hydrochloride in water.

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[6] Smorodinzew, *Z. physiol. Chem.*, **124**, 123 (1923).

[7] Abderhalden and Bahn, *ibid.*, **245**, 246 (1937).

[8] Fischer, *Ber.*, **39**, 453 (1906).

The Basic Dissociation Constants of Some Aliphatic Hydroxyamines[1]

BY SAMUEL GLASSTONE AND ALFRED F. SCHRAM

The aliphatic hydroxyamines form a group of compounds of considerable interest. A comprehensive study of their electrochemical properties had been planned, but the work was interrupted by the war emergency; as its continuation is uncertain, the results so far obtained, on the basic dissociation constants in aqueous solution of four mono- two di-, and one tri-hydroxyamines, are reported here.

With the exception of 2-amino-1-propanol, which was obtained from the Eastman Kodak Company, the hydroxyamines were supplied by the Commerical Solvents Corporation. The liquids were in general purified by fractional distillation under reduced pressure, and the solids by crystallization from absolute alcohol. Since 2-amino-1,3-propanediol is very viscous, it could not be distilled satisfactorily. It was therefore purified by dissolving in chloroform and adding ether until about half of the original material had separated. This procedure was repeated until a clear, colorless liquid was obtained.

The dissociation constants were calculated from *p*H measurements, made with a glass electrode, of aqueous solutions of the hydroxyamines to which had been added various known amounts of hydrochloric acid. It can be readily shown[2] that in such solutions

$$a_{\mathrm{OH^-}} = K_b \frac{b - B}{B} \cdot \frac{\gamma_{\mathrm{B}}}{\gamma_{\mathrm{BH^+}}} \qquad (1)$$

where $a_{\mathrm{OH^-}}$ is the activity of the hydroxyl ions, K_b is the true (or thermodynamic) dissociation constant of the base, γ_{B} and $\gamma_{\mathrm{BH^+}}$ are the activity coefficients of the undissociated base (RNH_2) and of the corresponding ammonium ion (RNH_3^+), respectively, b is the initial concentration of the base in moles per liter, and B is defined by

$$B = a + c_{\mathrm{OH^-}} - c_{\mathrm{H^+}}$$

where a is the concentration of the added acid in the solution, and $c_{\mathrm{OH^-}}$ and $c_{\mathrm{H^+}}$ represent the concentrations of the hydroxyl and hydrogen ions, respectively. In virtually all the cases studied $c_{\mathrm{H^+}}$ was negligible, and $c_{\mathrm{OH^-}}$ was taken as $K_w/a_{\mathrm{H^+}}$, with $a_{\mathrm{H^+}}$ derived from the measured *p*H value. Upon taking logarithms of eq. (1) and utilizing the fact that $p\mathrm{H} + p\mathrm{OH} = pK_w$, it is seen that

$$pK_w - p\mathrm{H} = pK_b + \log \frac{B}{b - B} + \log \frac{\gamma_{\mathrm{BH^+}}}{\gamma_{\mathrm{B}}} \qquad (2)$$

According to the Debye–Hückel–Brønsted equation, $\log \gamma_{\mathrm{BH^+}}/\gamma_{\mathrm{B}}$ may be replaced by $-A\sqrt{\mu} + C\mu$, where μ is the ionic strength of the solution, and the Debye–Hückel constant A is 0.509 at 25°.

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[1] From the Master's Thesis of Alfred Francis Schram, University of Oklahoma, 1943.

[2] *Cf.* S. Glasstone, "An Introduction to Electrochemistry," D. Van Nostrand Co. Inc., New York, N. Y., 1942, p. 394.