β-Naphthyl Mesitoate.—This ester was prepared in 96% yield from mesitoyl chloride and β-naphthol. It crystallized from alcohol in colorless needles; m. p. 112–113° (cor.).

Anal. Calcd. for $C_{20}H_{18}O_2$: C, 82.73; H, 6.25. Found: C, 82.42; H, 6.37.

DEPARTMENT OF CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS
REYNOLD C. FUSON
STANLEY B. SPECK

RECEIVED NOVEMBER 27, 1944

The Inner Carbonate of 2,3-Butanediol

Hammond[1] and Mitchell[2] have patented methods for the preparation of the alkyl carbonates and chlorocarbonates by the interaction of the aliphatic monohydric alcohols and phosgene. These procedures have been applied by the present authors to the interaction of 2,3-butanediol and phosgene.

Procedure.—A vertical glass tube, 46 mm. by 450 mm. in dimensions, was filled with glass beads and electrically heated so that a thermometer imbedded in the glass beads was maintained at 150°. Liquid 2,3-butanediol was dropped into the top of the tube at the rate of 44 g. per hour while phosgene gas was introduced into the bottom of the tube at the rate of 200 ml. per minute. The products boiling above 150° were collected at the bottom of the tube. The resulting material was heated, on a boiling water-bath under a reflux condenser, for two hours to complete the reaction. During the heating period copious evolution of hydrogen chloride took place. The resulting product was distilled at reduced pressure, a large fraction distilling at 96° at 8 mm. pressure; yield, 75%.

Anal. Calcd. for $C_5H_8O_3$: C, 51.7; H, 7.0. Found: C, 51.5; H, 7.1.

Properties.—The molecular weight in phenanthrene was 116; n^{26}_D 1.4226, d^{26}_4 1.129, b. p. 240° (740 mm.). The compound is colorless and insoluble in water. It is an excellent solvent for cellulose nitrate and cellulose acetate.

CHEMISTRY DEPARTMENT
IOWA STATE COLLEGE
AMES, IOWA
J. J. KOLFENBACH
E. I. FULMER
L. A. UNDERKOFLER

RECEIVED DECEMBER 18, 1944

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[1] J. A. Hammond, U. S. Patents 1,603,689 (October 19, 1926); 1,618,824 (February 22, 1927).

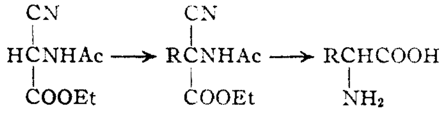
[2] H. G. Mitchell, U. S. Patents 1,603,703 (October 19, 1926); 1,638,014 (August 9, 1927).

COMMUNICATIONS TO THE EDITOR

THE SYNTHESIS OF AMINO ACIDS FROM ACETAMIDOCYANOACETIC ESTER

Sir:

Recently considerable interest has been shown in the preparation of amino acids from acetamidomalonic ester. We have found that ethyl acetamidocyanoacetate (I)[1] possesses even greater advantages as a general reagent. Alkylation is effected under the same conditions employed for acetamidomalonic ester.[2] Direct hydrolysis of the condensation product proceeds in either acid or basic media to yield the amino acid.



$$\begin{array}{c} \mathrm{CN} \\ | \\ \mathrm{HCNHAc} \\ | \\ \mathrm{COOEt} \end{array} \longrightarrow \begin{array}{c} \mathrm{CN} \\ | \\ \mathrm{RCNHAc} \\ | \\ \mathrm{COOEt} \end{array} \longrightarrow \begin{array}{c} \mathrm{RCHCOOH} \\ | \\ \mathrm{NH_2} \end{array}$$

I II

Alkylation of I with gramine gave 98% of ethyl α-acetamido-α-cyano-β-(3-indolyl)-propionate (II, R = skatyl), m. p. 196–198° (calcd. N, 14.02. Found: N, 13.78). Alkaline hydrolysis gave *dl*-tryptophan, m. p. 288–290° (cor.). A 71% yield of pure amino acid was obtained from crude indole.

When 4-chloromethylimidazole hydrochloride was condensed with I, a 66% yield of ethyl α-acetamido-α-cyano-β-imidazolepropionate (II, R = 4-imidazolemethyl), m. p. 100–103° anhydrous or 111° as monohydrate, was obtained (calcd. anhydrous: N, 22.39. Found: N, 21.98. Calcd. monohydrate: C, 49.25; H, 6.01. Found: C, 49.40; H, 5.89). Hydrolysis with sulfuric acid gave a 61% yield of *dl*-histidine, m. p. 285°. The dihydrochloride melted at 232°.[3] The overall yield of *dl*-histidine from cane sugar was 18%.

Methylation of monothioethylene glycol with dimethyl sulfate gave 80% of β-methylthiolethanol. Chlorination with thionyl chloride and condensation with I without isolation of the methylthiolethyl chloride or chlorination with hydrogen chloride followed by condensation with I gave 60% of the theoretical amount of ethyl α-acetamido-α-cyano-γ-methylthiolbutyrate (II, R = methylthiolethyl), m. p. 118° (calcd. N, 11.47. Found: N, 11.62). Basic hydrolysis gave 80% of recrystallized *dl*-methionine. The N-benzoyl derivative melted at 150°.

Alkylation of I with isopropyl bromide gave 66% of ethyl α-acetamido-α-cyano-β-methylbutyrate (II, R = isopropyl), m. p. 149° (calcd.: N, 13.20. Found: N, 13.52). Alkaline hydrolysis gave 65% of pure *dl*-valine, m. p. 289–290°. Acid hydrolysis gave an 80% yield, but the melting point was lower. The N-acetyl derivative melted at 147° and the N-benzoyl derivative at 131°.

Condensation of benzyl chloride with I gave 83% of ethyl α-acetamido-α-cyano-β-phenylpropionate (II, R = benzyl); m. p. 134° (calcd. N, 10.75. Found: N, 10.57). Hydrolysis with sodium hydroxide gave a 75% yield of *dl*-phenylalanine, m. p. 275–277°.

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[1] Cerchez and Colesiu, *Compt. rend.*, **194**, 1954 (1932).

[2] (a) Albertson, Archer and Suter, THIS JOURNAL, **67**, 36 (1945); (b) Albertson and Archer, *ibid.*, **67**, 308 (1945).

[3] Pyman, *J. Chem. Soc.*, **99**, 1395 (1911).

Isobutylation of I with isobutyl bromide gave 65% of ethyl α-carbethoxy-α-cyano-γ-methylpentanoate (II, R = isobutyl), m. p. 120° (calcd. N, 12.38. Found: N, 11.97). Hydrolysis with hydrochloric acid gave 79% of *dl*-leucine, m. p. 278°.

WINTHROP CHEMICAL COMPANY NOEL F. ALBERTSON
RENSSELAER, NEW YORK B. F. TULLAR

RECEIVED FEBRUARY 19, 1945

B-STRAIN AND BASE STRENGTH

Sir:

The peculiar behavior of the methylamines—an increase in base strength from ammonia to methylamine, a further increase to dimethylamine, followed by a marked decrease to trimethylamine—has been ascribed to B-strain.[1]

In the trimethylamine molecule B-strain results from the steric requirements of the three methyl groups crowded about the small nitrogen atom. It is postulated that these requirements are met by a spreading of the C–N–C bond angle to a value greater than the tetrahedral angle. The molecule therefore resists the addition of the acid to the free electron pair which would tend to reduce the bond angle to the tetrahedral value. Trimethylamine thus behaves as a much weaker base than it otherwise would.

Electron diffraction data reveal that the C–P–C bond angle in trimethylphosphine[2] is 100 ± 4°. B-strain must therefore be absent. Consequently, the strength of the phosphine bases should increase regularly with the number of methyl groups: $PH_3 < CH_3PH_2 < (CH_3)_2PH < (CH_3)_3P$.

It is possible to estimate from published data the relative strengths of the phosphine bases. Phosphine does not react with hydrochloric acid. Methylphosphine is absorbed by concentrated hydrochloric acid, but dilution decomposes the salt and liberates the free base. Neither dimethylphosphine nor trimethylphosphine may be liberated from its salts in this way—addition of alkali is necessary.[3] It is thus evident that methylphosphine is a stronger base than phosphine itself, and that both dimethyl- and trimethylphosphine are stronger than the monomethyl derivative. However, no decision can be reached on the critical point—the relative strength of dimethyl- and trimethylphosphine. Accordingly, the hydrochlorides of these two bases were prepared and their relative strength determined.

Dimethylphosphonium chloride is a white crystalline solid of moderate volatility, exhibiting saturation pressures of 1.3 mm. and 46 mm. at 25 and 75° respectively. Trimethylphosphonium chloride is much less volatile. Its saturation pressure is but 0.4 mm. at 75° and 14 mm. at 120°. (Methylphosphonium chloride is an unstable compound of high volatility at room temperature.[3]) The conclusion drawn from these data, that trimethylphosphine is a considerably stronger base than dimethylphosphine, was verified by a competition experiment. Thus, a mixture of 14.0 cc. of each of the two phosphines and of hydrogen chloride yielded 13.9 cc. of uncombined phosphine which analyzed for 95% dimethylphosphine.

Although supplementary data involving other reference acids are desirable and are being procured, it is evident from these data that the strength of the phosphine bases (measured with hydrogen chloride) increases regularly with the number of methyl groups. This verification of prediction is strong support for the B-strain hypothesis. Certainly, no other simple explanation for the markedly different behavior of the methylamines and the methylphosphines is now available.

There is good reason to believe that B-strain is also an important factor in the carbon compounds and can account for many of the peculiar reactions of tertiary butyl and related highly branched derivatives. This point will be developed in subsequent publications.

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DEPARTMENT OF CHEMISTRY
WAYNE UNIVERSITY
DETROIT 1, MICHIGAN HERBERT C. BROWN

RECEIVED FEBRUARY 1, 1945

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[1] Brown, Bartholomay and Taylor, THIS JOURNAL, **66**, 435 (1944).

[2] Springall and Brockway, *ibid.*, **60**, 996 (1938).

[3] Hofmann, *Ber.*, **4**, 604 (1871).

ON THE BIOGENESIS OF NORNICOTINE AND ANABASINE[1]

Sir:

The localization of the nicotine synthetic mechanism in the root of the tobacco plant (*Nicotiana tabacum*) has been established earlier by the use of reciprocal grafts and of sterile excised root cultures.[2] Similar experiments recently performed in this Laboratory have shown that nornicotine in *Nicotiana glutinosa* and in *N. glauca* is formed only in the leaves and at the expense of nicotine translocated from the roots.

Specifically, it has been found that *N. glutinosa* leaves do not carry out total alkaloid synthesis, for these leaves contain none of the three major tobacco alkaloids when grown on tomato roots. Conversely, *N. glutinosa* roots produce not nornicotine but nicotine, for only nicotine is present in tomato shoots grown on *N. glutinosa* roots. In this respect the root systems of *N. tabacum* and *N. glutinosa* are equivalent and have been experimentally interchanged without resulting marked changes in the alkaloid composition of the leaves. It is concluded, therefore, that the leaves of *N. glutinosa* contain a mechanism capable of convert-

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[1] This work was supported in part by the Rockefeller Foundation.

[2] Dawson, *Am. J. Botany*, **29**, 66 (1942); **29**, 813 (1942).