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.

The assistance afforded by two grants from the Penrose Fund of the American Philosophical Society is gratefully acknowledged.

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).