The angles between the lithium and boron vary from 97 to 116°. A tetrahedral arrangement of the hydrogens about the boron leads to an arrangement in which each lithium is surrounded by four hydrogen atoms which are arranged about it in the form of a distorted tetrahedron, each of the hydrogens being from a different borohydride group. The over-all structure of lithium borohydride may be described as that of strings of borohydride tetrahedra stacked edge on edge in the b direction of the crystal.

Lithium borohydride does not appear to be isomorphous with lithium aluminum hydride, lithium perchlorate, lithium fluoborate, or with the sulfates of magnesium and beryllium.

More complete details will be presented shortly.

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RECEIVED APRIL 18, 1947

THE COMPETITIVE INHIBITION OF THE METABOLISM OF α-AMINO ACIDS BY THEIR HALOGENATED ANALOGS

Sir:

A wild type strain of *Neurospora crassa* 8815-3a, has been used for testing a number of halogenated phenylalanines and tyrosines in respect to their capacities as growth inhibitors. Relative activities of the individual compounds were determined from the quantities of substance required to reduce the growth rate of the mold in growth tubes[1] to one-half of the normal value. The tubes contained 10 ml. of minimal medium[2] solidified with one per cent. agar and a small amount of the natural amino acid corresponding to the derivative being tested. Some of the results obtained are given in Table I.

INHIBITION OF GROWTH OF *Neurospora crassa* BY SOME HALOGENATED α-AMINO ACIDS

Compound	Mg./ml. for 50% inhibition[a]	moles inhibitor / moles amino acid
3-Fluoro-DL-phenylalanine	0.04	1.2
3-Fluoro-DL-tyrosine	.23	10.5
3-Fluoro-L-tyrosine	.15	6.8
3-Fluoro-D-tyrosine	.41	18.5

[a] Tubes for testing phenylalanine derivatives contained 0.03 mg./ml. of DL-phenylalanine; for tyrosine derivatives 0.02 mg./ml. of L-tyrosine.

It also has been shown that the inhibitory quotients for 2-chloro-, 3-chloro-, 4-chloro-, 3-bromo-, 3-iodo-DL-phenylalanine and for 3,5-difluoro-DL-tyrosine are greater than 150 and that the inhibitory action observed for all compounds is competitive in nature. Further it has been noted that effective inhibitors exhibit a high degree of specificity.

In respect to the inhibitory action of 3-fluoro-D-tyrosine and 3-fluoro-L-tyrosine the L-isomer is the more active of the two but in the presence of the D-isomer the mold produces considerable quantities of a dark brown pigment, an effect which is not observed with either the L-isomer or the racemic mixture. It is evident that the above actions must be interpreted in terms of at least two different systems concerned with the metabolism of tyrosine.

The most effective of the inhibitors described have not been tested on pure cultures of organisms other than *Neurospora*. However, it has been demonstrated that 3-fluoro-DL-phenylalanine is far more effective than sulfathiazole for inhibition of growth of those micellaneous airborne yeasts, molds and bacteria that can be obtained on exposed plates containing a yeast extract–agar medium.

The outstanding effectiveness of the monofluoro-phenylalanines and tyrosines as competitive inhibitors for their parent amino acids, and as antimetabolites, may be interpretable on simple steric grounds associated with the small size of the fluorine atom. In this connection it may be significant to consider the *p*-aminobenzoic acid reversal of the inhibition of growth of *E. coli* by 3-fluoro-*p*-aminobenzoic acid,[3] the apparent replacement of *p*-aminobenzoic acid by 2-fluoro-*p*-aminobenzoic acid[3] and the inhibition of acetate metabolism by fluoroacetate.[4]

Studies are now in progress on the effectiveness of the various isomeric monofluoro-tyrosines and phenylalanines as growth inhibitors in *Neurospora* and other biological systems and in extending the principles disclosed in the case of the above two α-amino acids to other α-amino acids.

(1) F. J. Ryan, G. W. Beadle, and E. L. Tatum, *Am. J. Bot.*, **30**, 784 (1943).

(2) G. W. Beadle and E. L. Tatum, *ibid.*, **32**, 678 (1945).

(3) (a) F. C. Schmelkes and M. Rubin, THIS JOURNAL, **66**, 1631 (1944); (b) O. Wyss, M. Rubin and F. B. Strandskov, *Proc. Soc. Exptl. Biol. Med.*, **52**, 155 (1943).

(4) (a) E. S. Guzman-Barron, G. R. Bartlett and G. Kalnitsky, *Proc. Fed. Am. Soc. Expll. Biol.*, **5**, 121 (1946); (b) E. S. Guzman-Barron and G. Kalnitsky, *Biol. Bull.*, **91**, 238 (1946).

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RECEIVED APRIL 5, 1947

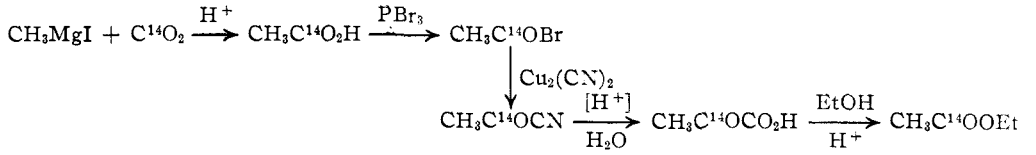
THE DECARBONYLATION OF ETHYL PYRUVATE[1]

Sir:

The decarbonylation of α-keto-esters has importance in synthetic chemistry,[2] and related reactions are widely postulated in biochemical mechanisms. We have investigated one aspect of the mechanism of the thermal decarbonylation of ethyl pyruvate with the aid of C^{14}. Pyruvic ester labelled in the α carbon atom was synthesized by the following sequence of reactions:

(1) This paper is based on work performed under Contract #W-7405-Eng-48 with the Atomic Energy Commission in connection with the Radiation Laboratory, and the Department of Chemistry, University of California, Berkeley, California.

(2) "Org. Synth.," Coll. Vol. II, p. 531.



The ester, after purification by distillation, was subjected to thermal decomposition between 110 and 130°. Traces of carbon dioxide were removed from the carbon monoxide formed, and the carbon monoxide was burned to carbon dioxide, absorbed in 1 *N* sodium hydroxide, and precipitated as barium carbonate. The radioactivity of the α-carbon atom in the pyruvate was 3180 counts/min./mg. C (12.9 disintegrations per count). There was no detectable activity in the carbon monoxide formed in 90% yield, or in the trace of carbon dioxide formed. It is found in the acid obtained by hydrolysis of the pyrolytic residue. Without further kinetic studies, it is difficult to suggest a detailed mechanism, but it is clear that the evolved carbon monxide comes from the carboxyl group of the α-keto-ester.

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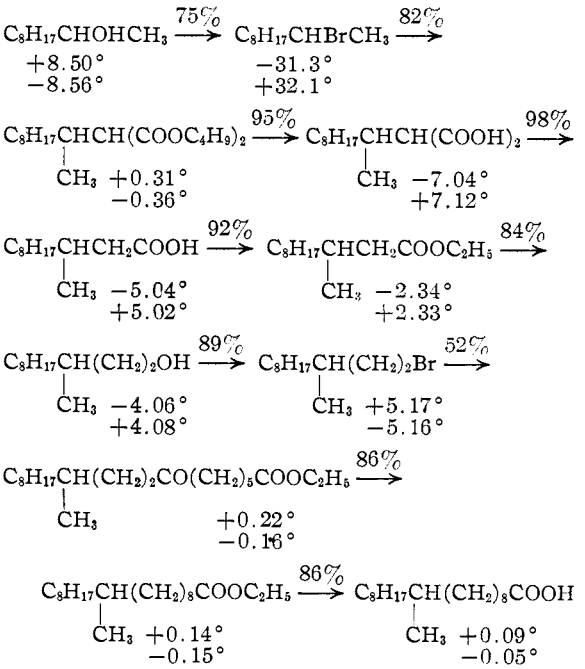
THE SYNTHESIS OF TUBERCULOSTEARIC ACID

Sir:

Tuberculostearic acid is one of the branched-chain acids isolated by Anderson[1] and co-workers from acid-fast bacteria. From oxidation experiments Spielman[2] concluded that the acid was 10-methyloctadecanoic acid and prepared the *dl*-form of this acid for comparison. The synthetic acid melted at 20–21°; the natural acid at 10–11°. The amides and tribromoanilides of the two acids had closely similar melting points. The natural acid was reported as optically inactive, but Spielman suggested that it might nevertheless be an active form having a faint rotation and a lower melting point than the corresponding *dl*-form.

In order to test this suggestion we have again synthesized *dl*-10-methyloctadecanoic acid by another method and have also synthesized pure *d*- and *l*-10-methyloctadecanoic acids. These acids were purified by repeated crystallization: *dl*-form, m. p. 25.4–26.1°; *d*- and *l*-forms, m. p. 13.0–13.5°, $[\alpha]_D$ *ca.* 0.05°. These data strongly indicate that tuberculostearic acid is one of the active isomers of 10-methyloctadecanoic acid. This conclusion was tested further by means of mixture melting point experiments using our active acids and their derivatives and samples of tuberculostearic acid and its derivatives kindly furnished by Dr. Anderson. The mixture of once-crystallized tuberculostearic acid (m. p. 10.3–11.7°) with approximately an equal amount of the synthetic *l*-acid melted at 11.0–12.4°, while a similar mixture with the *d*-acid melted at 19.4–20.1°. A mixture of the two synthetic acids melted at 21.0–25.8°. Melting points were determined also for the amides and the tribromoanilides of our *l*-acid and tuberculostearic acid, singly and as mixtures. The respective values were 75.1–76.3°, 71.5–75.6° and 72.5–76.3° for the amides, and 94.0–95.3°, 94.5–95.4° and 93.9–95.5° for the tribromoanilides. It thus appears to be established that tuberculostearic acid is the levorotatory isomer of 10-methyloctadecanoic acid.



The scheme of synthesis is outlined in the accompanying chart. The first rotation value, $[\alpha]_D$, in each instance refers to the isomer derived from (+)-2-decanol. Configurational inversion and slight racemization occurred in the formation of the 2-bromodecanes and the dibutyl 2-decylmalonates. Rigorous purification by fractional crystallization of the less soluble active 2-decylmalonic acids, however, assured the antipodal purity of all succeeding compounds in both series.

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(1) Anderson and Chargaff, *J. Biol. Chem.*, **85**, 77, (1929).
(2) Spielman, *ibid.*, **106**, 87 (1934).