other sources. Oligo-1,6-glucosidase differs from R-enzyme (plants) in that the latter does not hydrolyze the terminal α-1,6-linked glucose residues of isomaltose or panose (except possibly when acting with α-amylase).[2] A limit dextrinase from *Aspergillus oryzae* culture filtrate has been described[17] which would seem to have an activity similar to oligo-1,6-glucosidase on "branched" oligosaccharides.

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DIVISION OF BIOCHEMISTRY
NOYES LABORATORY OF CHEMISTRY
UNIVERSITY OF ILLINOIS
URBANA, ILLINOIS
JOSEPH LARNER
C. M. MCNICKLE

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THE SYNTHESIS OF (+)-α-LIPOIC ACID AND ITS OPTICAL ANTIPODE

Sir:

The racemic form of a compound active as a coenzyme in the oxidative decarboxylation of pyruvate has been synthesized.[1,2] This racemate has been designated DL-α-lipoic acid[1] and 6-thioctic acid.[2] The synthesis of the naturally occurring biologically active isomer, (+)-α-lipoic acid, has not been reported. We wish to report a new synthesis which has made possible the preparation of (+)-, (−)- and DL-α-lipoic acid.

The addition of thioacetic acid to 7-carboethoxy-2-heptenoic acid (I)[3] yielded 7-carboethoxy-3-acetylthioheptanoic acid (II) which was converted to 7-carboethoxy-3-acetylthioheptanoyl chloride (III). The reduction of III with sodium borohydride yielded a mixture of ethyl 6-acetylthio-8-hydroxyoctanoate (IV) and ethyl 6-thiol-8-hydroxyoctanoate (V). The mixture was converted by alkaline hydrolysis to 6-thiol-8-hydroxyoctanoic acid (VI), $n^{23.5}$D 1.4989. Iodine oxidation of VI produced bis-[3-(1-hydroxy-7-carboxyheptyl)] disulfide (VII). The introduction of the thiol group into the 8-position of both VI and VII was carried out by refluxing with thiourea in aqueous hydrobromic acid followed by alkaline hydrolysis. Following the introduction of sulfur into VII, the product was reduced with sodium borohydride and reoxidized to yield DL-α-lipoic acid (VIII), m.p. 59.5–61.0° (micro-block); $\lambda_{max}^{CH_3OH}$ 333 mμ (ϵ 150); *anal.* Calcd. for $C_8H_{14}O_2S_2$ (206.2): C, 46.60; H, 6.84; S, 31.05. Found: C, 46.90; H, 6.91; S, 31.34; mol. wt. (ebull.), 212 ± 7; neut. equiv., 206.

For the preparation of (+)- and (−)-α-lipoic acid, DL-7-carboethoxy-3-acetylthioheptanoic acid (II) was resolved. Treatment of II with *l*-ephedrine yielded the crystalline salt of the levorotatory form, m.p. 130.0–134.5°. The dextrorotatory isomer was isolated from the residue by precipitation in the form of its benzhydrylamine salt, m.p. 92–96°.

(+)-7-Carboethoxy-3-acetylthioheptanoic acid, $[\alpha]^{24}$D + 7.1° (*c*, 6.93; CH_3OH), when used in the above sequence yielded (+)-α-lipoic acid, m.p. 46.0–48.0° (micro-block); $[\alpha]^{23}$D +104° (*c*, 0.88; C_6H_6), $\lambda_{max}^{CH_3OH}$ 333 mμ (ϵ 150). *Anal.* Calcd. for $C_8H_{14}O_2S_2$ (206.2): C, 46.60; H, 6.84; S, 31.05. Found: C, 46.95; H, 6.85; S, 31.00; mol. wt. (ebull.), 194 ± 2; neut. equiv., 208. In a similar manner (−)-7-carboethoxy-3-acetylthioheptanoic acid, $[\alpha]^{24}$D −7.2 (*c*, 6.91; CH_3OH), yielded (−)-α-lipoic acid, m.p. 45.5–47.5° (micro-block); $[\alpha]^{23}$D −113° (*c*, 1.88; C_6H_6); $\lambda_{max}^{CH_3OH}$ 333 mμ (ϵ 140). Found: C, 46.65; H, 6.66; S, 31.32; mol. wt. (ebull.), 212 ± 3; neut. equiv. 208. When equal amounts of (+)- and (−)-α-lipoic acid were mixed and recrystallized from cyclohexane, the racemic compound, DL-α-lipoic acid, m.p. 60–61° (micro-block), was obtained.

In the enzymatic POF assay,[4] the activity of synthetic (+)-α-lipoic acid was double that of DL-α-lipoic acid. The activity of (−)-α-lipoic acid was essentially zero, *ca.* 1% that of DL-α-lipoic acid. The properties listed above substantiate the identity of our synthetic (+)-α-lipoic acid and the natural α-lipoic acid.[5,6,7] This lends additional support to the structural conclusions advanced[5,6] previously.

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RESEARCH LABORATORIES
CHEMICAL DIVISION
MERCK & CO., INC.
RAHWAY, NEW JERSEY
EDWARD WALTON
ARTHUR F. WAGNER
LOUIS H. PETERSON
FREDERICK W. HOLLY
KARL FOLKERS

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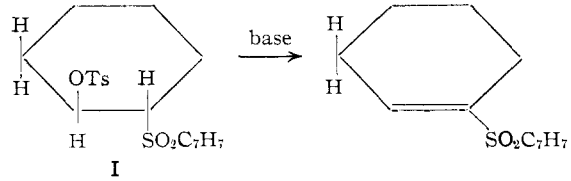
E2 ELIMINATION REACTIONS IN THE CYCLOHEXANE AND CYCLOPENTANE SERIES[1]

Sir:

A study of base-catalyzed E2 elimination reactions of *trans*-2-(*p*-tolylsulfonyl)-cyclohexyl *p*-toluenesulfonate (I), its *cis* isomer (II), the corresponding *trans* and *cis* isomers (III and IV) in the cyclopentane series, and an open-chain analog, 1-(*p*-tolylsulfonyl)-2-propyl *p*-toluenesulfonate, $C_7H_7SO_2CH_2CH(OTs)CH_3$ (V), with trimethylamine, triethylamine and hydroxide ion has revealed the information reported below.



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(1) Each of these reactions gives an α,β-unsaturated sulfone. For I and III this corresponds to elimination of a hydrogen *cis* to the tosylate group in preference to a hydrogen *trans* to the tosylate

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