"sparing action" on the product of the blocked reaction. Previous evidence[3] involving pantothenate in the oxidation of pyruvate can also be explained on the basis of pantothenate mediating *cis*-aconitate synthesis.

That the above effect directly involves pantothenic acid was demonstrated by the reversing effect of both pantothenic and α-ketoglutaric acids on a pantothenic acid antagonist, N-α,γ-dihydroxy - β,β - dimethylvaleryl - β - aminobutyric acid, for *E. coli*. Further, the pantothenic acid requirement of *Proteus morganii* in a medium of inorganic salts, glucose, nicotinamide and cystine was appreciably decreased by α-ketoglutaric acid.

With *Lactobacillus arabinosus*, an oleic acid source ("Tween 80") or sodium glycocholate increased the antibacterial index from approximately 3,000 to 30,000 for the competitive inhibition of N-pantoyl-*n*-butylamine[4] of pantothenic acid functioning. Both substances added simultaneously did not enhance the effect. Since this organism presumably requires acetate for synthesis of sterols and fatty acids, this inhibitor appears to prevent the conversion of acetate to an intermediate common to both sterol and oleic acid synthesis.

The reported involvement of pantothenic acid in the conversion of glycine to threonine,[5] the demonstration by Lipmann, *et al.*,[6] of the presence of pantothenic acid in the coenzyme for acetylation of sulfanilamide and choline, and the results of the above *inhibition analyses* tend to indicate that many of the enzymatic reactions in which pantothenic acid functions involve the hypothetical "active" acetyl radical.

(3) Dorkman, *et al.*, *J. Biol. Chem.*, **144**, 393 (1942).
(4) Snell and Shive, *ibid.*, **160**, 287 (1945).
(5) Rossi and Cennamo, *Chem. Abstr.*, **40**, 6543 (1946).
(6) Lipmann, *et al.*, *J. Biol. Chem.*, **167**, 869 (1947).

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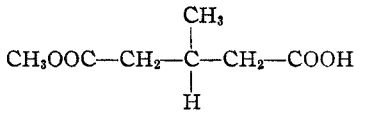
REARRANGEMENT IN THE PREPARATION OF ESTER ACID CHLORIDES

Sir:

Cason[1] has recently drawn attention to the fact that during the preparation of the ester acid chlorides of the isomeric half esters of dibasic acids such as α-ethyl-α-butylglutaric acid by means of thionyl chloride rearrangement may occur, the derivatives obtained from the ester acid chlorides being mixtures derived from both isomers.

The writer has studied the conditions under which this type of rearrangement occurs when preparing the ester acid chlorides of the two enantiomorphs[2] of methyl hydrogen β-methylglutarate (I)



(I)

Rearrangement leads in this case to racemization and can be detected simply by pouring the ester acid chloride into water and measuring the rotation of the recovered half ester. In this way it has been found that no rearrangement takes place when the ester acid chloride is prepared by the action of oxalyl chloride in benzene solution. In case of thionyl chloride the occurrence and extent of rearrangement depend on the purity of the reagent and on the reaction temperature. If pure thionyl chloride (Kahlbaum "reinst, wasserhell") is used no rearrangement occurs if the reaction takes place at 30° and excess reagent is removed under reduced pressure on a water-bath kept at 50°. Use of less pure thionyl chloride (Kahlbaum, "purum") leads under the conditions just described to rearrangement, the extent of which increases if the reaction temperature is raised. (The ester acid chlorides have not been distilled.)

It is well known that anhydrides may be formed during the action of thionyl chlorides on acids and that the yield of acid chloride is lower if impure thionyl chloride is used or if the reaction temperature is too high.[3] With dibasic acids of the succinic and glutaric acid series thionyl chloride gives the cyclic anhydrides only. It appears likely that the rearrangement observed in the preparation of the ester acid chlorides occurs via the anhydrides.

That rearrangement may be avoided during the preparation of the ester acid chloride of (I) is evident from the fact that lengthening of the chain of the dextrorotatory enantiomorph of (I) by the Arndt–Eistert synthesis has given (+)-β-methyladipic acid identical with that derived from natural products.[2] Furthermore, the two enantiomorphs of (I) have been used as starting material for the synthesis of $d(+)$- and $l(-)$-3-methyltetracosanoic acids. The intermediate ester acid chloride was in case of one enantiomorph prepared by means of oxalyl chloride and in case of the other by means of pure thionyl chloride. The enantiomorphic long chain β-methyl substituted acids both melted sharply at 65.5° (cor.), and showed numerically equal optical rotations, $[M]^{25}D$ 13.2° (chloroform, *c*, 5.78). Mixed in equal proportions the acids gave a racemic compound melting sharply at 68.6° (cor.).

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(1) J. Cason, THIS JOURNAL, **69**, 1548 (1947).
(2) S. Ställberg-Stenhagen, *Arkiv Kemi, Min., Geol.*, **25A**, No. 10 (1947).
(3) "Organic Syntheses," Coll. Vol. I, 2nd ed., p. 147.