CYCLIZATION OF ACETYLENE-d_2 TO BENZENE-d_6

Sir:

Benzene-d_6 may be prepared directly from acetylene-d_2 at room temperature by use of a modified silica–alumina catalyst. Previously described methods of preparation of benzene-d_6 required either high-temperature (650°) pyrolysis[1] of acetylene-d_2 or the exchange[2] of benzene with D_2SO_4. Both of these methods are inherently wasteful of deuterium in that the pyrolysis reaction results in a number of undesirable deuterium-containing products while the exchange reaction requires a number of exchanges. Also, the subsequent separation and purification procedures are laborious and time-consuming. On the other hand, the preparation described here is relatively easy and efficient. No products other than benzene-d_6 are formed in the reaction.

The deuterium content of the benzene-d_6 depends only on the purity of the deuterium oxide[3] used to form acetylene-d_2 from calcium carbide. Prior to reaction with deuterium oxide, the calcium carbide is heated to 600° to remove all traces of hydrogen or acetylene from the solid. By this means acetylene-d_2, analyzed mass spectrometrically to contain 99.5% D, is prepared.

The modified catalyst is prepared by repeatedly exposing Houdry Type M-46 silica–alumina cracking catalyst (previously dried at 275°) to diborane.[4] The drying temperature is not critical but does determine the amount of bound water[5] retained by the catalyst and, consequently, the amount of diborane that will react with the hydroxyl groups on the surface.[6]

In a typical preparation approximately 300 cc. of acetylene-d_2 was circulated through a 3-cm.-thick bed of the modified catalyst (10 g.) in a closed system whose total capacity was 600 cc. As it was formed, the product was collected in a trap cooled by Dry Ice. After circulation for forty-five minutes the Dry Ice was replaced by liquid nitrogen to condense the unused acetylene-d_2. The catalyst was then heated to 150° *in vacuo* to recover any adsorbed benzene-d_6. The benzene-d_6 was separated from the acetylene-d_2 by high-vacuum fractionation. Under these conditions approximately 50% of the acetylene-d_2 had been converted to benzene-d_6. By mass spectral analysis the benzene-d_6 was found to contain 2.7% of the C_6D_5H species (equivalent to 0.45%H). The mass spectrum of the product compared favorably with that of the API[7]; however, the product prepared here had a slightly higher deuterium content.

When the acetylene-d_2 was first exposed to the catalyst bed, an appreciable amount of heat was evolved; consequently, for larger scale preparations it may be advisable to cool the catalyst.

Significantly, there was no exchange of deuterium or hydrogen between the modified catalyst and the acetylene or benzene. It was possible to prepare, alternately, benzene and benzene-d_6 on the same catalyst bed without forming partially-deuterated products. However, when a mixture of acetylene and acetylene-d_2 was passed through the modified catalyst, the product consisted of both even and odd numbered deuteriated benzenes with deuterium and hydrogen statistically distributed among these species. A detailed study of the cyclization reaction, directed toward shedding light both on the mechanism of cyclization of acetylene and the catalytic nature of silica–alumina gels, is being carried out and will be reported later.

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RESOLUTION OF DL-MEVALONIC ACID AND THE SYNTHESIS AND BIOLOGICAL ACTIVITIES OF DL-3-HYDROXY-3-METHYLGLUTARALDEHYDIC ACID

Sir:

The discovery of mevalonic acid, a new acetate-replacing and growth factor for lactobacilli, was reported recently,[1,2] and its structure was proven to be 3,5-dihydroxy-3-methylpentanoic acid (I).[3,4] The synthesis of DL-mevalonic acid has been reported,[3,4,5] and it was found to have one-half the microbiological activity of the natural compound.[3,4]

Fractional crystallization of the amides obtained by reaction of DL-mevalonic acid lactone with (+)-α-phenyl-1-naphthalenemethylamine yielded an amide melting at 151–152° (*Anal.* Calcd. for $C_{23}H_{25}NO_3$: C, 76.00; H, 6.93; N, 3.85. Found: C, 76.28; H, 6.90; N, 3.81) $[\alpha]^{25}D$ + 29° (*c*, 1.1 in chloroform). Alkaline hydrolysis of this amide yielded mevalonic acid (isolated as the crystalline N,N′-dibenzylethylenediammonium salt, m.p. 125–126°; *Anal.* Calcd. for $C_{28}H_{44}N_2O_8$: C, 62.66; H, 8.26. Found: C, 62.60; H, 8.28) which had microbiological activity for *Lactobacillus acidophilus*, ATCC 4963,[1] equal to that of the natural isomer.

When it became known[6] that mevalonic acid is a precursor in the formation of cholesterol, consideration of alternative biosynthetic reactions led to an evident interest in the closely related aldehyde, 3-hydroxy-3-methylglutaraldehydic acid (mevaldic acid, II). This new aldehyde has now been synthesized for study in "isoprenoid" biosynthetic systems.

A Reformatsky reaction involving the dimethylacetal of acetoacetaldehyde and ethyl bromoacetate

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