

of 1 m/kg of xanthopterin by the technique previously described (4).

The above experiments explain much of the confusion and conflicting results that have been obtained in the study of the extrinsic and intrinsic factors of Castle. Apparently the extrinsic factor may not be a single substance, but xanthopterin, folic acid, teropterin, and possibly other pteroyl derivatives may serve as the extrinsic factor. Enzyme systems which were present and which were very strong in the gastric mucosa extract and present in the milk xanthine oxidase preparation and the liver homogenate, served as the intrinsic factor. Vitamin B₁₄ and the products produced by the action of the oxidase systems on xanthopterin and folic acid appeared to be

not identical compounds, although they had similar activity when measured by the techniques used. The end-products of the action of milk, liver, and gastric mucosa enzymes on a single substrate may be different. The active material from xanthopterin is not leucopterin. The chemistry of the various materials is under investigation.

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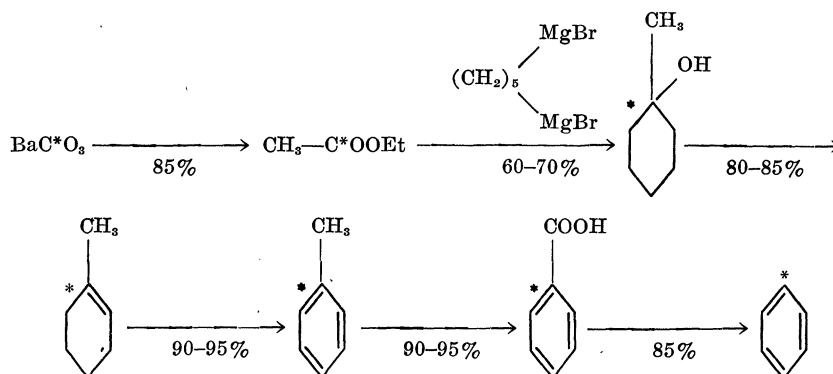
A Synthesis of Benzene, Toluene, and Benzoic Acid Labeled in the Ring With Isotopic Carbon

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The development of an efficient procedure for the synthesis of benzene, toluene, and benzoic acid labeled in the ring with carbon 13 or carbon 14 is of considerable interest because of the utility of these aromatic compounds in the preparation of numerous substances of importance in organic chemistry, medicine, and biology.

the procedure of Sakami, Evans, and Gurin (4). Preparation of 1-methylcyclohexanol-1 labeled on carbon 1 was achieved by reaction of carboxyl-labeled ethyl acetate with the Grignard reagent from pentamethylene dibromide according to the procedure of Grignard and Vignon (1). Dehydration of the carbinol with iodine as described by Mosher (3) afforded 1-methylcyclohexene, which was converted to toluene by vapor-phase dehydrogenation over platinized asbestos (6). The benzoic acid, prepared by oxidation of toluene with potassium permanganate (5), underwent smooth decarboxylation on treatment with copper oxide and quinoline. The overall yields from barium carbonate varied from 35 to 50% for toluene, from 3% to 40% for benzoic acid, and from 25 to 40% for benzene.



While the synthesis of C¹⁴-labeled mesitylene (2) affords an intermediate for the preparation of tagged benzene, this procedure suffers from the disadvantages that half of the radioactivity is converted to barium carbonate in an early step of the synthesis and the over-all yield is quite low.

We have found a satisfactory route to toluene and benzoic acid labeled on carbon 1 of the ring and to tagged benzene in the sequence of reactions illustrated above.

The synthesis of carboxyl-labeled ethyl acetate was accomplished by carbonation of methyl magnesium iodide with isotopic carbon dioxide, followed by reaction of the sodium acetate with diethyl sulfate in a modification of

A particularly attractive feature of this synthesis is the production of toluene and benzoic acid singly labeled on a specific position of the ring. Complete details of the work will be published elsewhere.

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