have not been found in known carbonium ion type polymerizations. The good third-order rate constants obtained by Moore, Burk and Lankelma are evidence that their technique of flushing with nitrogen was effective in suppressing the effect of air in their experiments.

A puzzling observation, which at first seems difficult to reconcile with the idea that the polymerization of styrene in phenolic solvents is a radical type reaction, is that *m*-cresol, and presumably other phenols, inhibit the benzoyl peroxide catalyzed polymerization of styrene at 60 and 100° (Table IV). The answer, however, is apparently found in the rate of disappearance of benzoyl peroxide. In a number of inert solvents the half life of benzoyl peroxide is fifty-five to seventy-five hours at 60° and thirty-five to forty-five minutes at 100°.[28] In 3.68 molar styrene in cresol at 60°, however, the peroxide can no longer be detected after six hours, while at 100° it is approximately 95% consumed in ten minutes. Whether the cresol liberates the radicals of the peroxide so rapidly that they are consumed by mutual interaction, or destroys the peroxide by another mechanism, is not known; but in either case the catalyst is effectively prevented from promoting the polymerization.

(28) Values obtained by extrapolation of the data of Kamenskaya and Medvedev, *Acta Physicochim. U. R. S. S.*, **13**, 565 (1940).

Acknowledgment.—The author extends his thanks to Dr. Frank R. Mayo of this Laboratory for much helpful discussion and advice.

Summary

1. The rate of polymerization of styrene at 131° has been measured in a number of phenolic solvents.

2. The rate is affected by air and by benzoquinone and bears no simple relation to the acid strengths of the phenols as measured in water, and the polymer is of low molecular weight.

3. In thymol the rate is third order in respect to styrene and inversely proportional to the concentration of thymol. In *m*-cresol the rate lies between second and third order.

4. These results are interpreted on the basis that the polymerization is of the uncatalyzed, free radical type, somewhat inhibited by the phenolic solvent; and that this inhibition takes place through a chain transfer reaction yielding relatively unreactive solvent radicals. No evidence is found that the polymerization involves a carbonium ion.

5. Cresol has been found to destroy benzoyl peroxide. This observation has been used to explain the inhibition of the benzoyl peroxide catalyzed polymerization of styrene by this solvent.

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NOTES

Abnormalities in the Willgerodt Reaction

BY RICHARD T. ARNOLD, EVERETT SCHULTZ AND HAROLD KLUG

Very few irregularities have been observed during the course of the Willgerodt reaction. At an early date, Willgerodt[1] showed that with insufficient sulfur *p*-tolyl methyl ketone is converted into 2,5-di-*p*-tolylthiophene and more recently Fieser and Kilmer[2] reported the reduction of 3-acetoacenaphthene under the conditions employed in the Willgerodt synthesis.

In this Laboratory the Schwenk and Bloch[3] modification of the Willgerodt reaction has been used successfully with numerous ketones. When applied to 6-tetralyl ethyl ketone, however, there was obtained not only the normal acid, β-6-tetralylpropionic acid, but a certain amount (about 6%) of 5,6,7,8-tetrahydro-2-naphthoic acid; m. p. 150–152° (uncor.).[4]

The substance which undergoes oxidative degradation to give rise to this unexpected acid may or may not be an intermediate in the normal Willgerodt reaction.

(1) Willgerodt, *J. prakt. Chem.*, **80**, 192 (1909).
(2) Fieser and Kilmer, THIS JOURNAL, **62**, 1354 (1940).
(3) Schwenk and Bloch, *ibid.*, **64**, 305 (1942).
(4) Newman and Zahm, *ibid.*, **65**, 1097 (1943).

Experimental

A mixture containing 46.9 g. of 6-tetralyl ethyl ketone, 8.0 g. of sulfur, and 24.0 g. of morpholine was heated at a temperature of 120–125° for eleven hours in a 200-cc. round-bottomed flask equipped with a condenser.

The hot mixture was poured onto 300 g. of ice and, after the melting was completed, the water layer was decanted. The semi-solid residue was washed with warm water to remove water soluble impurities, and the water was again separated. The remaining solid was just covered with ethanol and the whole was warmed for several minutes during which time the ethanol boiled gently. After removing the source of heat, the alcoholic solution was decanted from the crystalline precipitate and discarded. When recrystallized twice from ethanol, the solid yielded 25.2 g. of pure thiomorpholide; m. p. 133–135°.

Anal. Calcd. for $C_{17}H_{23}ONS$: C, 70.6; H, 8.0. Found: C, 71.0; H, 7.8.

Saponification of this thiomorpholide gave a quantitative yield of β-6-tetralylpropionic acid.

The mother liquor from the first recrystallization of the above thiomorpholide was evaporated to dryness, and the resulting dark oil was hydrolyzed with boiling 10% potassium hydroxide, cooled and filtered. This alkaline solution was treated with norite, filtered, ether extracted and

finally acidified with concentrated hydrochloric acid. The crude acid was collected on a filter and recrystallized first from 50% acetic acid and finally from benzene–petroleum ether (b. p. 90–100°). A product resulted which weighed 2.8 g. and melted at 150–152° (uncor.).

That this product is actually 5,6,7,8-tetrahydro-2-naphthoic acid was established by analysis, m. p. and mixed m. p., and by a comparison of the X-ray powder diffraction patterns of the authentic and unknown samples.

The above experiment has been repeated several times with consistent results.

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3-Amidinopyridine (Nicotinamidine)

BY H. J. BARBER AND R. SLACK

The failure of Bernthsen[1] to obtain 3-amidinopyridine by the interaction of nicotinonitrile and ammonium chloride, as cited by Krewson and Couch,[2] makes it desirable to publish details of the preparation of this amidine, accomplished some time ago in these laboratories.

Trypanocidal activity is developed in monoamidines on introduction of a second amidine group,[3] and the function of this may be merely to provide a second basic center. Though some of the monoamidines described by Easson and Pyman[4] fall into this class, the second basic group in these is a weak one. It was thought that a compound such as nicotinamidine would possess a second strongly basic center but in fact it titrated as a monoacid base, so that it gave no evidence on the point at issue.

In addition, the work of Fildes[5] has shown that the antibacterial action of the sulfanilyl drugs is probably due to competition with an enzymic metabolic process. Hence the synthesis of compounds with a close spatial resemblance to substances vital to, or associated with, bacterial growth, is of particular interest. The relationship between nicotinamide and nicotinamidine is sufficiently close to suggest that the latter might have possessed some anti-bacterial properties.

On treating nicotinonitrile[6] in excess ethyl alcohol with dry hydrogen chloride, a vigorous exothermic reaction occurred, the main reaction product being the hydrochloride of ethyl nicotinate. It was decided, therefore, to use an amount of alcohol only slightly in excess of that required by theory for the production of the corresponding iminoether hydrochloride. Following this procedure, the iminoether base was isolated as an oil which decomposed on attempted distillation at 8 mm. pressure. No further efforts were made to purify this compound, which reacted readily with ammonium chloride to give nicotinamidine hydrochloride. The amidine (1 in 4000 aqueous solution) was not active against *Staphylococcus aureus;* it was also found to be inactive against *T. equiperdum* infection in mice.

(1) Bernthsen, *Ann.*, **184**, 321-370 (1876).
(2) Krewson and Couch, THIS JOURNAL, **65**, 2256 (1943).
(3) Ashley, *et al.*, *J. Chem. Soc.*, 103 (1942).
(4) Easson and Pyman, *ibid.*, 2091 (1931).
(5) P. Fildes, *Lancet*, **1**, 855 (1940).
(6) La Forge, THIS JOURNAL, **50**, 2477 (1928).

Experimental

3-Amidinopyridine.—3-Cyanopyridine (6.0 g.) was dissolved in dry chloroform (50 cc.) to which absolute ethyl alcohol (3.0 g.) had been added. This mixture was saturated at 0° with dry hydrogen chloride and allowed to stand at 0° for sixteen to eighteen hours. The viscous bottom layer which rapidly separated had by this time solidified. The whole was poured into ice-cold 50% sodium hydroxide solution (excess, final reaction alkaline to phenolphthalein), shaken vigorously, and the chloroform extract separated. This was then washed neutral with water, dried (potassium carbonate) and the solvent distilled to leave the crude iminoether base. This was dissolved in 75% ethyl alcohol (20 cc.) containing ammonium chloride (1.2 g.) and heated at 70° for four hours. After filtration (charcoal) a little ammonium chloride was removed after dilution of the liquors with acetone (2–3 vol.). The residual liquors were again diluted with acetone to cloudiness, when they were left to stand at 0° for several hours. 3-Amidinopyridine monohydrochloride separated in long slender colorless needles, m. p. 190°; yield 4 g.

Anal. Calcd. for $C_6H_7N_3 \cdot HCl$: N, 26.9; Cl, 21.97. Found: N, 26.1; Cl, 21.6.

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CHEMICAL RESEARCH DEPARTMENT
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A Medium for Obtaining Maximal Growth Response in Microbiological Assays of Amino Acids

BY W. BAUMGARTEN, J. C. GAREY, MARY JEAN OLSEN, L. STONE AND C. S. BORUFF

In microbiological assays of amino acids the data given in support of the proposed media[1–6] demonstrate that practically no growth was observed when any one of the amino acids essential for the nutrition of the organisms was omitted. When an attempt was made to repeat the work of the above investigators, it was found that substitution of acid-hydrolyzed casein supplemented with cystine and tryptophan produced a greater growth response than when the casein hydrolyzate was replaced by a mixture of eighteen amino acids. The above results indicated that some stimulatory material was absent from the amino acid medium that was necessary for obtaining maximal growth.

The purpose of this paper is to show that maximal growth response with *L. casei* or *L. arabinosus 17-5* can be obtained when certain stimulatory nutrilites are added to a synthetic

(1) S. Shankman, *J Biol. Chem.*, **150**, 305 (1943).
(2) S. Shankman, Max S. Dunn and Louis B. Rubin, *ibid.*, **150**, 477 (1943).
(3) K. A. Kuiken, W. H. Norman, C. M. Lyman, F. Hale and L. Blotter, *ibid.*, **151**, 615 (1943).
(4) D. M. Hegsted, *ibid.*, **152**, 193 (1944).
(5) B. L. Hutchings and W. H. Peterson, *Proc. Soc. Exptl. Biol. Med.*, **52**, 36 (1943).
(6) S. Shankman, Max S. Dunn and Louis B. Rubin, *J. Biol. Chem.*, **151**, 511 (1943).