

action with furoic acid.<sup>2</sup> Oxidation of the crude mixture from the latter reaction to yield anthraquinone has already been presented as evidence for the formation of an acid with an anthracene nucleus.<sup>2</sup> This observation has now been substantiated by degradation of the crude reaction mixture to anthracene by subjecting it to soda-lime distillation. Crystallization from benzene of the oily distillate so obtained yielded anthracene in 10% yield, m. p. 208–210°. Its identity was checked by a mixed melting point determination.

Thus, although the pure acid has yet to be isolated, analogy with the methyl furoate reaction supports the suggestion that the anthroic acid present in the mixture of acids formed from benzene and furoic acid is 9-ethyl-9,10-dihydro-9-anthroic acid (II).

The oily residue left after crystallization of anthracene from the soda-lime distillate was dehydrogenated with sulfur to yield 1,4-diphenyl-naphthalene, previously obtained as a degradation product of the acid mixture. It is believed to be derived from 1,4-diphenyl-1,2,3,4-tetrahydro-1-naphthoic acid.<sup>2</sup>

Soda-lime distillation of the crude acid mixture obtained by reaction of toluene and furoic acid yielded 2,7-dimethylantracene, m. p. 238–239°, which showed no depression in melting point when mixed with an authentic sample. Isolation of this hydrocarbon indicates that this reaction also gives rise to an anthroic acid. Again, the pure acid has yet to be isolated, but analogy with the product from benzene, as well as consideration of the simplest product of the reaction, 6-methyl-1-naphthoic acid, suggests that the anthracenic component of the toluene-furoic acid reaction may be 3,6-dimethyl-9-ethyl-9,10-dihydro-9-anthroic acid (III).

Repeated efforts to isolate a substance from the crude toluene product, corresponding to the 1,4-diphenyl-naphthalene obtained from the benzene product, have failed. Attempted decarboxylation of the toluene product by heating with copper chromite in quinoline, successful for the benzene product, yielded a black, intractable tar from the toluene product. Evidently the tar was formed by oxidation, since the black powdery copper chromite catalyst was transformed to a mixture of green chromium oxide powder and small bright balls of metallic copper. Treatment with sulfur

or selenium of the pale yellow oil from the mother liquor of the soda-lime distillate led to copious evolution of hydrogen sulfide or selenide, but no crystalline product could be isolated.

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### A Color Test for Citrinin and a Method for its Preparation

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The following is a color test for citrinin and a method for the preparation of the anti-bacterial substance.

**The Color Test.**—One mg. of citrinin (prepared as given below) is dissolved in 0.5 cc. of 95% alcohol and 0.3 cc. of 3% hydrogen peroxide is added. The mixture is agitated for one minute. The intense yellow solution becomes first colorless, then light brown. Hereafter, 0.3 cc. of 0.2 *N* sodium hydroxide is added. A deep wine-red color forms at once. On the addition of 0.3 cc. of 0.2 *N* sulfuric acid the wine-red color turns orange-yellow and on the addition of a further 0.3 cc. of 0.2 *N* sodium hydroxide the wine-red color reappears again. In a control tube in which water is substituted for hydrogen peroxide an orange-yellow color develops. This color reaction with sodium hydroxide from intense yellow to orange-yellow was also noted by A. C. Hetherington and H. Raistrick [*Trans. Roy. Soc., London*, **B220**, 279 (1931)] who stated that "Citrinin is readily soluble in aqueous NaOH giving rise to an orange-yellow solution which on standing changes color to orange-red." This is indeed the case when a fairly concentrated sodium hydroxide solution is added to a citrinin solution. We found, however, that when 0.25 to 0.5 cc. of 0.02 *N* sodium hydroxide is added to 1 mg. of citrinin in 0.5 cc. of ethyl alcohol, a very light pink color forms which does not change in intensity on further addition of the alkali or on standing. H. W. Hirschy and Ruff [THIS JOURNAL, **64**, 1490 (1942)] have recently observed that above pH 9.9 the color of a citrinin solution changed from orange-pink to cherry-red.

Continued exposure of citrinin to dioxane results in a hydrogen peroxide-like reaction. On long exposure to air alcoholic citrinin solutions undergo certain changes which do not appear to be identical with hydrogen peroxide-oxidation.

The hydrogen peroxide-sodium hydroxide color reaction is also given by the original cultures, by the acid precipitated crude citrinin, and after it had been recrystallized from 95% alcohol. Citrinin solutions that have been treated with sodium hydroxide and readjusted to the original pH do not give the hydrogen peroxide-sodium hydroxide reaction.

Penicillin obtained from *P. notatum* (A. T. C. C.) gives a lemon-yellow color with this test.

**Preparation of Citrinin.**—1500 cc. of the filtrate of a fourteen-day old culture of *P. citrinum* prepared according to H. Raistrick and G. Smith [*Chemistry and Industry*, **60**, 828 (1941)] is adjusted to pH 3.0 to 2.5 with *N* hydro-

(2) Price, Chapin, Goldman, Krebs and Shafer, THIS JOURNAL, **63**, 1857 (1941).

chloric acid. After about five minutes the crystals of crude citrinin are centrifuged off, dissolved in 30 cc. of dioxane at room temperature, and the solution is centrifuged. A small amount of insoluble material is discarded, and to the clear supernatant fluid one volume of distilled water is added. Citrinin crystallizes out immediately in long microscopic needles or plates. If the citrinin concentration is low, it is necessary to add more water in order to effect crystallization. The citrinin is centrifuged off and dried in vacuum at room temperature (yield, 1.5 g.). The melting point is at 163 to 166°. We were able to confirm fully the action of citrinin on *Streptococcus aureus* as reported by Raistrick and associates.

*P. citrinum* (P25 and ad95) was very kindly sent by Dr. H. Raistrick and forwarded to us through the courtesy of Dr. C. Thom of U. S. Department of Agriculture.

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### Acidic and Basic Catalysis in Urethan Formation

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Urethans, because of their favorable characteristics, are frequently used to identify alcohols and phenols. They are usually prepared by heating an alcohol or phenol in the absence of a catalyst.<sup>1</sup> However, scattered statements indicate that this formation of urethans, particularly from phenols, is catalyzed not only by bases<sup>2</sup> but by aluminum chloride<sup>3</sup> and hydrogen chloride.<sup>4</sup> A general survey of the effect of acidic and basic catalysts on urethan formation has therefore been undertaken, but, as this work has been interrupted, the present brief report is now submitted.

Experiments in which equivalent amounts of *o*-cresol and phenyl isocyanate were heated without solvent but with catalyst at 100° and the urethan which had formed after varying times isolated, showed that the following substances have a catalytic effect: sodium carbonate, sodium acetate, pyridine, acetic acid, trichloroacetic acid, zinc chloride and hydrogen chloride. Without a catalyst a yield of less than 50% was obtained after nine hours of heating. The addition of 2% of either zinc chloride or pyridine gave a 100% yield in less than fifteen minutes.

Similar experiments with other phenols varying greatly in acid character, from *p*-nitrophenol to *p*-triphenylmethylphenol, gave in fifteen minutes without a catalyst zero, with the same catalysts, practically 100% yields of urethan. On the other hand, 2,4-dinitrophenol, 2,6-di-

nitro-4-chlorophenol and picric acid did not form urethans under any conditions tried.

More exact experiments using purified *o*-cresol and  $\alpha$ -naphthyl isocyanate were made as follows: solutions of 9.2 mmol. of each reagent and a small amount of a catalyst in 3.00 cc. of purified ligroin (b. p. 60–65°) in stoppered test-tubes, were heated in the vapors of refluxing methanol (65°) and after a definite time cooled in ice and filtered. The resultant crystals were washed twice with 2-cc. portions of cold ligroin in which they are practically insoluble, dried and weighed.

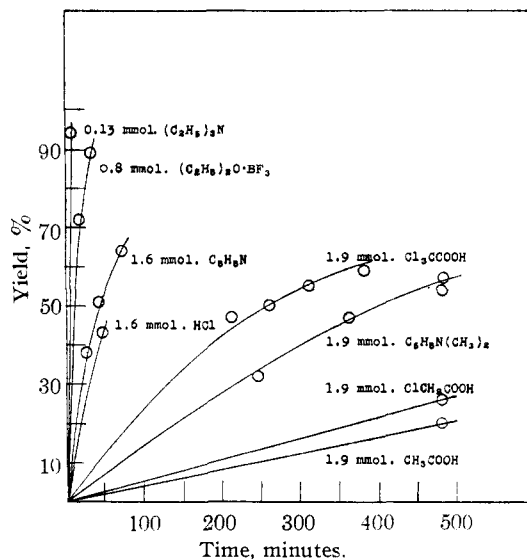


Fig. 1.

The results are shown as curves in Fig. 1, and from them it can be seen that triethylamine is by far the most effective catalyst tried. It is probably significant that it is a much stronger base than the less effective catalysts pyridine and dimethylaniline.<sup>5</sup> Boron fluoride etherate is the most active acid tested, and the catalytic activity of the other acids tested is roughly in the order of their acid strengths in water. When no catalyst was used, only an 11% yield was obtained after nine days, a result which could not be shown on the graph.

An 80% yield of the urethan (m. p. 141–142.5°)<sup>6</sup> was obtained by mixing the above quantities of *o*-cresol and  $\alpha$ -naphthyl isocyanate in 30 cc. of ligroin with two drops of triethylamine, and letting the mixture stand for two and one-half hours at room temperature. From this it appears that an excellent and rapid procedure for preparing urethans from phenols in general would be to use the above quantities of materials, reflux the solution a few minutes and cool slowly to allow crystallization.

**Phenylurethans of Tertiary Alcohols.**—These compounds were prepared by heating a mixture of 2 or 3 g. of the *t*-alcohol with an equivalent quantity of phenyl isocyanate and 0.1 g. of anhydrous sodium acetate for four to five hours on a steam-bath. In each case the reaction product was contaminated with some diphenylurea and unreacted phenyl isocyanate. If the oily product failed to crystal-

(1) Shriner and Fuson, "Identification of Pure Organic Compounds," 2nd Edition, John Wiley and Sons, Inc., New York, N. Y., 1940, p. 136.

(2) Dieckmann, Hoppe and Stein, *Ber.*, **37**, 4627 (1904); Michael and Cobb, *Ann.*, **363**, 64 (1908); Vallee, *Ann. chim. phys.*, (7) **15**, 331 (1908); Claisen, *Ann.*, **418**, 82 (1919); French and Wirtel, *This Journal*, **48**, 1736 (1926).

(3) Leuckart, *Ber.*, **18**, 873 (1885); Farinholt, Harden and Twiss, *This Journal*, **55**, 3383 (1933).

(4) Tarbell and Kincaid, *ibid.*, **62**, 728 (1940).

(5) Hall, *ibid.*, **52**, 5115 (1930).

(6) French and Wirtel, ref. 2, give 141–142°.