

ing this period a thin slush formed. The temperature was then raised to 63–66° and maintained for ten minutes. The pale pink slurry was then chilled to 20–25°, 77 cc.<sup>5</sup> of 3 *N* hydrochloric acid added *cautiously* from a dropping funnel (ice-water cooling as required), resulting in a pale slightly cloudy solution.

The charge then was steam-distilled (about 90 cc. distillate) to remove the solvent, digested while hot with 0.3 g. of Norit and 0.2 g. of Filter-Cel and filtered with suction. The colorless filtrate was cooled to 0–5°, 10 cc. of concentrated hydrochloric acid added, then titrated at this temperature with molar sodium nitrite solution to a strong blue streak (ten minutes end-point) on starch-iodide paper. Almost the theoretical amount was required. During the titration pale yellow nitrosamine needles separated. The crystals were filtered with suction, washed with water and dried at 55°; yield 2.66 g., m. p. 134–135°. The filtrate, on extraction with ether, yielded an additional 0.12 g.; total yield 92%.

On recrystallizing the combined crops from 10% ethanol, in the presence of a little Norit, the m. p. was raised to 135.5°, identical with purified *N*-nitroso-*N*-methyl-*p*-aminophenol prepared from photographic Metol as shown by mixed m. p.

(5) The first 20 cc. of 3 *N* hydrochloric acid must be fed very slowly, dropwise. During this period the main heat effect is evident and the bulk of the hydrogen gas evolved (by decomposition of the excess lithium aluminum hydride). Thereafter the balance may be added faster. Prior to the acid addition the calcium chloride tube is removed (*versus* any back pressure) and the flask vented to the hood.

CONTRIBUTION FROM THE  
EHRlich LABORATORY

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### The Constitution of Citrinin

By T. S. GORE, T. B. PANSE AND K. VENKATARAMAN

The structures originally assigned<sup>1</sup> to citrinin (I) and its degradation products (II) and (III) are untenable in the light of their behavior towards diazonium salts.<sup>2</sup> Cram<sup>3</sup> has now shown by synthesis and direct comparison that (III) is 4-methyl-5-ethylresorcinol, a conclusion at which we had arrived by circumstantial evidence. The 2,4 and 4,6-compounds were ruled out by the ability of (III) to form disazo dyes. Comparison of the absorption spectra and the color reactions of the bis-benzeneazo derivative of (III) with those of 2,4- and 4,6-bis-benzeneazoresorcinol and a series of analogous dyes showed that (III) is 5-methyl-4-ethylresorcinol (IV) or 4-methyl-5-ethylresorcinol (V). The absorption curves for 2,4-bis-benzeneazoresorcinol, 2,6-bis-benzeneazo-5-methyl-4-ethyl resorcinol and the bis-benzeneazo derivative of (III) had a well-defined, high intensity band in the visible region ( $\lambda_{\max.} \sim 415 \mu\mu$ ;  $\epsilon_{\max.} \sim 60,000$ ). 4,6-bis-Benzeneazoresorcinol and 4,6-bis-benzeneazo-2-ethylresorcinol exhibited a band of relatively low intensity in the visible region ( $\lambda_{\max.} \sim 415 \mu\mu$ ;  $\epsilon_{\max.} \sim 20,000$ ) and absorption maxima in the near ultraviolet ( $\lambda_{\max.} \sim 340 \mu\mu$ ;  $\epsilon_{\max.} 36,000$ ).

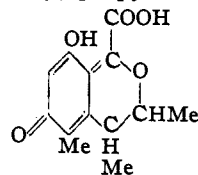
(1) Raistrick, Robinson, *et al.*, *Phil. Trans. Roy. Soc.*, **B220**, 269, 297 (1931).

(2) Gore, *et al.*, *Nature*, **167**, 333 (1946).

(3) Cram, *THIS JOURNAL*, **70**, 440 (1948).

Shah and Robinson's synthesis<sup>4</sup> of (IV) was repeated, and it was found to melt at 79–82° (Shah and Robinson, m. p. 75–80°), while (III) as a monohydrate melts at 68–69°, and after dehydration at 98–99°; the m. p. of (III) was considerably depressed by admixture with (IV). Cram<sup>3</sup> has quoted us erroneously as reporting a m. p. of 65–70° for (III). The bis-benzeneazo derivatives of (III) and (IV) melted, respectively, at 171° and 188°, and the mixed m. p. was lower. It followed therefore that (III) is 4-methyl-5-ethylresorcinol. However, this is in conflict with the observation of Hetherington and Raistrick<sup>1</sup> that neither of the acids obtained by oxidation of the dimethyl ether of (III) gave the anthrachryson reaction. We prepared 3,5-dimethoxy-2-methylbenzoic acid (VII) by the methylation of the corresponding  $\alpha$ -resorcylic acid,<sup>5</sup> and found that it readily gave a Bordeaux-red color on warming with sulfuric acid (the anthrachryson reaction); Cram has recorded that the acid (VI) synthesized by him corresponds in its properties to one of Hetherington and Raistrick's acids. The m. p. (157–158°) reported for (VI) by Cram is in agreement with ours, while Hetherington and Raistrick's two acids melted at 142–146° and 98–99°.

From the formulation of (III) as 4-methyl-5-ethylresorcinol, the properties of (II), including the formation of (III) from (II) by alkali fusion, are fully explained by the structure 4-methyl-5-(1-methyl-2-hydroxy)-propyl-resorcinol, proposed



by Cram. The experimental results of Hetherington and Raistrick<sup>1</sup> and the behaviour of citrinin towards diazonium salts<sup>2</sup> would then agree with the above constitution for citrinin.

(4) Shah and Robinson, *J. Chem. Soc.*, 1491 (1934).

(5) Woodward and Reed, *THIS JOURNAL*, **65**, 1569 (1943).

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### The Employment of Sodium Hydride as a Condensing Agent

By NATHAN GREEN AND F. B. LAForge

Sodium hydride is now being produced on a large scale, and its advantages as a catalyst in various organic reactions have been indicated by Hansley and Carlisle.<sup>1</sup> Its use in this Laboratory in the preparation of ethyl  $\beta$ -oxocaprylate, ethyl  $\beta$ -carbethoxy- $\alpha$ -oxo-enanthate, and 5-carbethoxy-dihydrocinerone has been described in previous articles.<sup>2,3</sup> We have since employed this reagent in

(1) Hansley and Carlisle, *Chem. Eng. News*, **23**, 1332 (1945).

(2) Soloway and LaForge, *THIS JOURNAL*, **69**, 2677 (1947).

(3) LaForge and Soloway, *ibid.*, **69**, 2932 (1947).

the preparation of carbethoxy derivatives of other ketones, and of their substitution products, for Claisen condensations of alkyl esters with ketones, and for cyclizations of the Dieckman type. It probably could be used with advantage for many reactions where powdered sodium or sodium ethylate is usually employed. We are therefore presenting some observations which we have made in the use of this catalyst in these reactions.

The reaction of ketones with ethyl carbonate starts promptly when the finely ground catalyst is employed, but with the coarser material there is a considerable lag, or occasionally the reaction may not start at all. Since at present sodium hydride is supplied only in the coarser size, which is easier and less hazardous to handle but less reactive, it is generally necessary to reduce the particle size by some means of grinding.

A laboratory apparatus for this purpose has been designed by V. L. Hansley<sup>4</sup> in which reactions are carried out in a revolving closed cylinder containing steel balls. Since this rather expensive equipment will not be generally available, we have employed the same principle in connection with the usual glass apparatus. When several ceramic spheres about 13 mm. in diameter are placed in the reaction flask with the solvent and the ethyl carbonate, and rolled slowly over the catalyst with a glass paddle stirrer for about thirty minutes, the particle size of the sodium hydride is reduced sufficiently so that the reaction starts soon on addition of a small quantity of the ketone. Care should be taken not to add very much of the ketone until the reaction, which is observed by the evolution of hydrogen, has definitely started. When the experiment is performed in this manner, the yield in the case of ethyl  $\beta$ -oxocaprylate is usually 80 to 85% of the theoretical.

In the preparation of sodium derivatives of  $\beta$ -keto esters the reaction starts at once regardless of the physical state of the sodium hydride, and the addition of the ester is regulated according to the rate of evolution of hydrogen. The solvent is generally anhydrous ether. Dioxane, in which most sodium enolates are soluble, is sometimes used.

Alcohol-free sodium alcoholates are conveniently prepared by dropping a slight excess of the alcohol on sodium hydride covered with benzene and, after refluxing, distilling off the solvent until it is alcohol-free, as shown by measurement of the refractive index. Sodium hydride dissolves more readily than sodium lumps or wire.

The following examples illustrate the employment of sodium hydride in reactions referred to above.<sup>5</sup>

Ethyl 3-oxo-6-octenoate<sup>6</sup> was prepared from 58 g. (2.4 moles) of sodium hydride covered with 300 ml. of

(4) Private communication from V. L. Hansley of E. I. du Pont de Nemours and Co., Niagara Falls, N. Y.

(5) We wish to express our appreciation to the E. I. du Pont de Nemours and Co. for donating the sodium hydride we employed in this and previous work.

(6) Prepared in collaboration with S. B. Soloway.

dry ether and 283 g. (2.4 moles) of ethyl carbonate in a nitrogen atmosphere by dropping 136 g. (1.2 moles) of 5-heptene-2-one into the stirred suspension over a period of five hours. More ether was added as the contents of the flask thickened. Acetic acid was added in quantity equivalent to the sodium hydride diluted with ice and water, and the reaction product was isolated from the ethereal solution by removing first the ether and then the excess ethyl carbonate in vacuum: b. p. 110–120° (10 mm.),  $n_D^{20}$  1.4460, yield 188 g. (85%).

Anal. Calcd. for  $C_{10}H_{16}O_3$ : C, 65.19; H, 8.76. Found: C, 64.67; H, 8.80.

**2,4-Nonanedione.**—A mixture of 28.8 g. (0.2 mole) of ethyl caproate and 12.7 g. (0.22 mole) of dry acetone was added to 4.8 g. (0.2 mole) of sodium hydride covered with 10 ml. of dry ether. The evolution of hydrogen started after refluxing for several minutes, and more ether was added as solid material separated. Refluxing was continued for one hour. Ice and water containing a suitable quantity of sulfuric acid were added, and the reaction product was isolated from the ethereal solution and distilled from a modified Claisen flask: b. p. 94–98° (11 mm.),  $n_D^{20}$  1.4222, yield 16.8 g. (54%).

**2,5-Dioxo-1,4-cyclohexandicarboxylic Acid Diethyl Ester.**—The Dieckman cyclization between two molecules of ethyl succinate occurs smoothly on addition of the ester to two equivalents of sodium hydride covered with a small quantity of ether and refluxing until the evolution of hydrogen has ceased. Upon addition of dilute acid the reaction product separates in crystalline form on removal of the ether and it can be recrystallized from ethanol (m. p. 130–131°).

**Ethyl  $\beta$ -Carbethoxy- $\gamma$ -oxo-pelargonate.**—To 4.8 g. (0.2 mole) of sodium hydride covered with 100 ml. of ether, 37.2 g. (0.2 mole) of ethyl  $\beta$ -oxocaprylate was slowly added with stirring, more ether being added as the contents of the flask thickened. It was refluxed for thirty minutes, after which 37 g. (0.22 mole) of ethyl bromoacetate was added dropwise at a rate to cause gentle refluxing of the ether. The reaction was completed by further refluxing for thirty minutes, after which the separated sodium bromide was dissolved by addition of water containing 5% of sulfuric acid. The ethereal layer was washed and dried and the solvent removed. The residue was distilled on a modified Claisen flask: b. p. 133–136° (0.4 mm.),  $n_D^{20}$  1.4388. The yield was 46 g. (84.5%).

Anal. Calcd. for  $C_{14}H_{24}O_5$ :  $C_2H_5O$ , 32.4. Found:  $C_2H_5O$ , 33.0.

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### The Action of Copper Sulfate on the Phenylsazones of the Sugars. VI.<sup>1</sup> Gentiobiose Phenylsotriazole<sup>2</sup>

BY W. T. HASKINS, RAYMOND M. HANN AND C. S. HUDSON

In continuation of the investigation of the conversion of the sugar phenylsazones to the corresponding phenylsotriazoles through the action of copper sulfate, we have prepared the phenylsotriazole of gentiobiose. This phenylsotriazole differs from those described in the previous articles in that its crystals contain one molecular equivalent of ethanol which is tenaciously retained at ordinary temperatures even in moderately high

<sup>1</sup> (1) Number V was published in THIS JOURNAL, 69, 1461 (1947).

(2) Presented in part before the Division of Sugar Chemistry and Technology at the Chicago meeting of the American Chemical Society, April 19–23, 1948.