

devoid of optical activity in chloroform solution; it melted at 131–132° (cor.), which is much higher than the melting point of its components, from which fact it is evident that the crystalline substance is a true racemate.

Summary

D-Sorbitol, in solution with 4 *N* hydrochloric acid and one molecular equivalent of benzaldehyde, condenses to yield principally a cryptocrystalline dibenzylidene-D-sorbitol melting at 219–221°. The latter substance, upon oxidation with lead tetraacetate in glacial acetic acid, produces formaldehyde and aldehydo-2,3,4,5-dibenzylidene-L-xylose, which is conveniently isolated as a crys-

talline methyl hemiacetal. This hemiacetal is converted by acid hydrolysis to L-xylose, which was isolated as the crystalline sugar and further characterized by preparation of L-xylose phenylosazone; the latter compound combines with D-xylose phenylosazone to yield the long known racemic xylose phenylosazone. Also, L-xylose phenylosazone triacetate forms a true racemate with D-xylose phenylosazone triacetate.

The work constitutes a definitive proof that the structure of dibenzylidene-D-sorbitol is that of 1,2,3,4-dibenzylidene-D-sorbitol.

BETHESDA, Md.

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[CONTRIBUTION FROM THE CHEMICAL LABORATORY, UNIVERSITY OF MISSOURI]

The Action of Alkali on Cyclohexenecarbonals¹

BY H. E. FRENCH AND D. M. GALLAGHER

Although the cyclohexenecarbonals possess alpha hydrogens, one might reasonably expect reactions like those of the aromatic series toward alkaline reagents, because of the steric effect of the large radical attached to the alpha carbon. In order to test this supposition, we have investigated the reactions with several 3-cyclohexenecarbonals, particularly the 3,4,6-trimethyl derivative. Concentrated aqueous solutions of sodium or potassium hydroxide acted on this aldehyde forming a tripolymer. Similar tripolymers of cyclohexanecarbal and of 3-cyclohexenecarbal had previously been prepared by the action of mineral acids.² Saturated aqueous solutions of barium hydroxide gave very small yields of the polymer, most of the aldehyde being recovered. A cold 10% solution of potassium hydroxide in methyl alcohol was also without action on the aldehyde. At 70°, using a methyl alcohol–water solution, reaction took place with the formation of the corresponding acid and the alcohol. The acid had previously been prepared from ethyl crotonate and 2,3-dimethylbutadiene.³ The structure of the alcohol was shown by its synthesis from the aldehyde using aluminum isopropoxide, and by carbon and hydrogen analyses of the naphthyl urethan.

Under similar conditions, 3,4-dimethyl-6-phenyl-3-cyclohexenecarbal, 6-methyl-3-cyclohexenecarbal, and 3-cyclohexenecarbal were found to give the Cannizzaro reaction. In all cases the acids formed were known compounds⁴ but the alcohols had not previously been reported. These were identified by their syntheses from the aldehydes using aluminum isopropoxide, and analyses of their phenyl or naphthyl urethans. Yields of the pure acids were of the order of 80%. Varying amounts of polymerization products were obtained if the temperature of reaction was much in excess of 70°.

Freshly distilled 6-methyl-3-cyclohexenecarbal gave but a trace of reaction in the usual reaction time, while aldehyde used after long standing, or through which air had been bubbled, readily entered into the reaction. This is in accord with the observation that peroxide is a catalyst for the Cannizzaro reaction.⁵

Each of the aldehydes was dissolved in aqueous methyl alcohol and heated to approximately 70° with potassium hydroxide and formalin solution. Diols, in yields of from 50 to 60% of the pure redistilled or recrystallized compounds, were obtained in all cases. The formation of these compounds presumably follows the course indicated by the equation

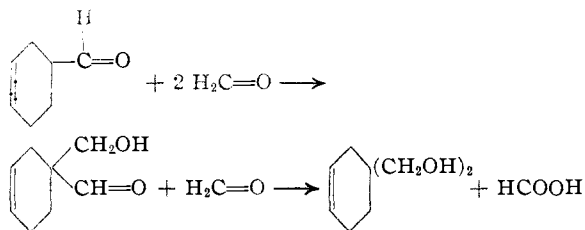
(1) This work is part of the thesis material to be submitted by Mr. Gallagher to the graduate faculty of the University of Missouri.

(2) Wallach, *Ann.*, **347**, 336 (1906); Zelinsky and Gutt, *Ber.*, **40**, 3051 (1907); Chayanov, *J. Gen. Chem.* (U. S. S. R.), **8**, 460 (1938).

(3) Farmer and Pitkethly, *J. Chem. Soc.*, 11 (1938).

(4) Fujisi, Horiuchi, and Takahashi, *Ber.*, **69**, 2102 (1936); Chayanov and Grishiu, *Colloid J.* (U. S. S. R.), **3**, 461 (1937); Perkin, *J. Chem. Soc.*, **85**, 416 (1904).

(5) Kharasch and Foy, *THIS JOURNAL*, **57**, 1510 (1935).



The molecular weight of 3,4,6-trimethyl-3-cyclohexene-1,1-dicarbonyl in camphor and in dioxane was found to be 184 and 183.5, respectively, and in the Grignard machine was found to possess two active hydrogens. Each of the diols combined with two molecules of phenyl isocyanate to yield crystalline urethans. The ring unsaturation of the 3-cyclohexene-1,1-dicarbonyl was reduced, and on oxidation the known cyclohexane-1,1-dioic acid was obtained.⁶

Experimental

The cyclohexenecarbonyls were prepared by the Diels-Alder condensation, and their properties corresponded to those given in the literature for the pure compounds.

3,4,6-Trimethyl-3-cyclohexenecarbonyl with Alkali.—Twelve and one-half grams of the aldehyde was allowed to stand for twenty-four hours at room temperature with a solution of 20 g. of potassium hydroxide in 12.5 cc. of water. An insoluble oil was then separated from the aqueous layer and washed with water. In the course of a month this oily material partly solidified. The pasty mass was filtered with suction and was washed with ethyl alcohol. The white solid thus obtained was found to be soluble in benzene and in acetone, and insoluble in ethyl alcohol and in ether; white, powdery material from acetone; m. p. 132–134°; molecular weight in benzene, 482; molecular weight of the original aldehyde, 152; yield of polymer, 2 g.

A solution containing 20 g. of the aldehyde in 20 cc. of ether was shaken for forty-eight hours at room temperature with 20 cc. of a saturated solution of barium hydroxide in water. Practically all of the aldehyde was recovered from the ether solution as the bisulfite compound, together with a trace of an oily material, presumably a polymer of the aldehyde.

A solution of 10 g. of the aldehyde in 20 cc. of methyl alcohol was shaken for three days at room temperature with 10 cc. of a 10% solution of potassium hydroxide in methyl alcohol. Eight and a half grams of the aldehyde was recovered.

The Cannizzaro Reaction.—The following procedure is typical for the Cannizzaro reactions using the various aldehydes. A solution of 9 g. of potassium hydroxide in 5.5 cc. of water was added rapidly to 8.5 g. of the aldehyde in 11 cc. of methyl alcohol, with mechanical stirring at 65–75° for two hours. At temperatures much in excess of 75°, considerable polymerization occurred. Addition of an equal volume of water caused the separation of a second layer, which was extracted with ether. After drying, the

ether and methyl alcohol were removed on the water-bath. Vacuum distillation of the residue gave the carbinols as colorless liquids which readily formed urethans with α naphthyl isocyanate. In each case the identity of the carbinol was demonstrated by its synthesis from the aldehyde with aluminum isopropoxide and a comparison of the urethans. The acids were obtained from the alkaline solutions remaining after the ether extraction, in yields which were generally of the order of 78%. Melting points of the acids were found to correspond to those given in the literature for those compounds.

3,4-Dimethyl-6-phenyl-3-cyclohexenecarbonyl.—Naphthyl urethan; white crystals from petroleum ether; m. p. 110–111°.

Anal. Calcd. for $C_{26}H_{27}O_2N$: C, 81.03; H, 7.01. Found: C, 80.84; H, 7.32.

6-Methyl-3-cyclohexenecarbonyl.—Phenyl urethan; white crystals; m. p. 83°. *Anal.* Calcd. for $C_{15}H_{19}O_2N$: N, 5.71. Found: N, 5.86.

3-Cyclohexenecarbonyl.—Naphthyl urethan; white crystals from petroleum ether; m. p. 106°.

Anal. Calcd. for $C_{18}H_{19}O_2N$: C, 76.86; H, 6.76. Found: C, 76.92; H, 6.94.

3,4,6-Trimethyl-3-cyclohexenecarbonyl.—Naphthyl urethan; white crystals from petroleum ether; m. p. 112°.

Anal. Calcd. for $C_{21}H_{25}O_2N$: C, 78.01; H, 7.74. Found: C, 78.35; H, 8.05.

The Cross Cannizzaro Reaction.—The following represents a typical reaction for these aldehydes. A mixture of 8 g. of the aldehyde, 10 cc. of methyl alcohol, and 5 cc. of formalin in a 3-neck flask equipped with dropping funnel, motor stirrer, and reflux condenser was heated to 70°, and maintained at that temperature while a solution of 8.4 g. of potassium hydroxide in 6 cc. of water was added. The mixture was heated at 70° for forty minutes, then refluxed for one hour. The reaction mixture was cooled, diluted with an equal volume of water, and extracted with ether. From this ether solution the diol was obtained. The unsubstituted and the monomethyl substituted compounds were obtained as oils which solidified after vacuum distillation and standing for several hours in an ice chest. The others were obtained as crystalline compounds, and were recrystallized from petroleum ether. The diols were obtained in yields of 50–60% of the pure compounds. In each case the diol combined with two molecules of phenyl isocyanate, yielding crystalline urethans which were recrystallized from dilute alcohol.

3,4,6-Trimethyl-3-cyclohexene-1,1-dicarbonyl.—White crystals; m. p. 86.5°; molecular weight in camphor, 184; in dioxane, 183.5; calcd. for $C_{11}H_{20}O_2$, 184; active hydrogens, 1.91; urethan, m. p. 121.5–123°.

Anal. Calcd. for $C_{25}H_{30}O_4N_2$: C, 71.09; H, 7.10. Found: C, 71.01; H, 7.34.

3,4-Dimethyl-6-phenyl-3-cyclohexene-1,1-dicarbonyl.—White crystals; m. p. 131.5°; phenyl urethan, m. p. 166°.

Anal. Calcd. for $C_{30}H_{32}O_4N_2$: C, 74.36; H, 6.61. Found: C, 74.22; H, 6.85.

6-Methyl-3-cyclohexene-1,1-dicarbonyl.—White crystals; m. p. 45°; phenyl urethan, m. p. 150°.

Anal. Calcd. for $C_{23}H_{26}O_4N_2$: C, 70.05; H, 6.59; N, 7.10. Found: C, 70.28; H, 6.53; N, 7.06.

(6) Wightman, *J. Chem. Soc.*, 2541 (1926).

3-Cyclohexene-1,1-dicarbonol.—White crystals; m. p. 92.5°; phenyl urethan, m. p. 118.5°.

Anal. Calcd. for $C_{22}H_{24}O_4N_2$: C, 69.45; H, 6.36. Found: C, 69.29; H, 6.57. Active hydrogens in the diol, 1.81.

Hydrogenation of 3,4,6-Trimethyl-3-cyclohexene-1,1-dicarbonol.—The compound was reduced at 2500 lb. pressure at 150°, using Raney nickel, to the known cyclohexane-1,1-dicarbonol, m. p. 95–96°.⁷

Oxidation of Cyclohexane-1,1-dicarbonol.—Oxidation with potassium permanganate in neutral and in alkaline solutions, using water and water-acetone solvents, gave only uncrystallizable oils. Nitric acid oxidation gave a small yield of a solid acid which was not identified.

1.7 g. of the diol was dissolved in 10 cc. of pyridine. A solution of 5.5 g. of potassium permanganate in 110 cc. of

(7) Franke and Sigmund, *Monatsh.*, **46**, 61 (1925).

water was added with stirring, at a temperature of 0°. The mixture was stirred for eight hours at that temperature and allowed to warm slowly to room temperature. The excess permanganate was discharged with 1 cc. of ethyl alcohol. After filtering, the solution was concentrated on a water-bath to 10 cc. using vacuum. Hydrochloric acid was added and the solution placed in the ice chest. A yield of 0.8 g. of the known cyclohexane-1,1-dioic acid was obtained.

Summary

1. The action of alkaline solutions on certain cyclohexenecarbonals has been studied.

2. These aldehydes were found to undergo the Cannizzaro reaction, and to react with formaldehyde to yield cyclohexene-1,1-dicarbonols.

COLUMBIA, MISSOURI

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Sulfanilamido Derivatives of Nitrogen Bases from California Petroleum¹

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Bobranski³ and Winterbottom⁴ have reported syntheses in the sulfanilamidoquinoline series; however, no alkylation in the quinoline nucleus higher than methyl was included. Since detailed pharmacological tests of their compounds have not been published, it was considered of interest to prepare sulfanilamido derivatives of a series of alkylated quinoline homologs encountered in nitrogen bases extracted from California petroleum. Since quinolines substituted in positions 2, 3 and 8 occur in appreciable quantity among the complex petroleum base fractions, this series was selected for investigation. The compounds prepared in this work are sulfanilamido and acetylated sulfanilamido derivatives of 5-amino-2,3,8-trimethylquinoline, and of the hitherto unreported 5-amino-8-ethyl-2,3-dimethylquinoline and 5-amino-2,3-dimethyl-8-*n*-propylquinoline.

Through the courtesy and cooperation of Parke, Davis and Company, the 2,3,8-trimethyl and 2,3-dimethyl-8-*n*-propylquinoline sulfanilamido derivatives have received preliminary testing for possible pharmacological activity. No activity was found in mice infected with experimental

Type I pneumococcus, *Staph. aureus* or *Strep. viridans*. The slight activity toward hemolytic streptococci indicates that the activity of sulfanilamide is lowered by substitution of the quinoline heterocycle at the N¹ position. Certainly the compounds here reported do not have the desirable properties obtained with other heterocycles such as pyridine, thiazole and pyrimidine.

Two of the new compounds reported herein have received preliminary testing for antimalarial activity (through the courtesy of Parke, Davis and Company). It is of interest to note the activity against avian malaria of 5-sulfanilamido-2,3,8-trimethylquinoline in the *blood*, whereas larger doses of this material are inactive in the tissue.

	Stage tested	Dose, mg.	Result
5-Sulfanilamido-2,3,8-trimethylquinoline	Blood	50	Active
	Tissue	100	Inactive
5-(N ⁴ -Acetylsulfanilamido)-2,3-dimethyl-8- <i>n</i> -propylquinoline	Blood	50	Inactive

Experimental

2,3,8-Trimethyl-5-nitroquinoline.—Fourteen grams of 2,3,8-trimethylquinoline,⁵ isolated from petroleum nitrogen bases, was converted to 2,3,8-trimethyl-5-nitroquinoline in accordance with Burger and Modlin.⁶ There was obtained 13 g. of purified product, crystallizing from petroleum ether as pale yellow needles melting at 124° (cor.).

(5) Poth, Schultze, King, Thompson, Slagle, Floyd and Bailey, *ibid.*, **52**, 1239 (1930).

(6) Burger and Modlin, *ibid.*, **62**, 1079 (1940).

(1) Constructed from a portion of a thesis presented to the Graduate Faculty of the University of Texas by Leslie M. Schenck in partial fulfillment of the requirements for the degree of Doctor of Philosophy, June, 1942.

(2) Parke, Davis Fellow, 1941–1942; present address, General Aniline and Film Corporation, Grasselli, N. J.

(3) Bobranski, *Arch. Pharm.*, **277**, 75 (1939).

(4) Winterbottom, *This Journal*, **62**, 160 (1940).