An Improved Synthesis of *cis*-Δ^4-Tetrahydrophthalic Anhydride and *cis*-Hexahydrophthalic Acid

BY EDWARD F. JENKINS AND EDWARD J. COSTELLO

In the course of a synthetic problem it became necessary to prepare some *cis*-hexahydrophthalic acid.

The syntheses of this acid described in the literature are those of Baeyer,[1] Willstätter and Jaquet,[2] and Diels and Alder.[3] Because of slow reaction speeds and repeated recrystallizations these procedures are time-consuming and laborious.

By modifying the method of Diels and Alder it was found possible to prepare *cis*-hexahydrophthalic acid very easily and in excellent yield. All the repeated recrystallizations, as well as the vacuum concentration of the final product, were eliminated. In addition to this, the time required for the reaction of the maleic anhydride and butadiene was greatly reduced, as was also the time needed for the reduction of the *cis*-Δ^4-tetrahydrophthalic anhydride.

Experimental

Preparation of *cis*-Δ^4-Tetrahydrophthalic Anhydride.—Ninety-eight grams (1 mole) of finely ground maleic anhydride was partly dissolved and partly suspended in 150 ml. of benzene. After this suspension had been cooled to 5°, 54 g. (1 mole) of liquid butadiene was added. The mixture was then heated in an autoclave to 115°. At this temperature heating was discontinued, but within fifteen minutes the temperature had spontaneously risen to 145° and the pressure to 11 atmospheres. The reaction mixture was left to stand overnight in the autoclave.

The crude product was freed from benzene and was then extracted with ether by use of a Soxhlet extractor. A white crystalline mass of pure *cis*-Δ^4-tetrahydrophthalic anhydride formed in the ether during the extraction, and more precipitated upon cooling to room temperature. The unreacted maleic anhydride remained in the ether solution but could be recovered by cooling the solution to 0°. The product melted at 103–104°. The yield was 137 g., or 90.3% of the theoretical amount.

Preparation of *cis*-Hexahydrophthalic Acid.—Instead of following the procedure of Diels and Alder and preparing the tetrahydrophthalic acid before hydrogenation, the anhydride itself was hydrogenated. The *cis*-Δ^4-tetrahydrophthalic anhydride was ground up, suspended in glacial acetic acid, and hydrogenated at room temperature and a total pressure of 4.5 atmospheres of hydrogen. Adams platinic oxide catalyst was used, 100 mg. of the catalyst for every 15.2 g. (0.1 mole) of the anhydride.

30.4 g. (0.2 mole) of the anhydride was suspended in 150 ml. of glacial acetic acid; hydrogenation took place smoothly and quickly, and the theoretical amount of hydrogen was absorbed in one-half hour. In another experiment 60.8 g. (0.4 mole) of the anhydride was suspended in the same quantity of acetic acid and hydrogenation was complete in about the same time. In the resultant solution the reduction product was entirely dissolved in the solvent.

After separating the catalyst by filtration, the solution of *cis*-hexahydrophthalic anhydride was poured into 450 ml. of water. This solution was then cooled to 0° and allowed to stand at that temperature for about an hour. The crude anhydride, along with some *cis*-hexahydrophthalic acid, precipitated out as a white crystalline mass. In filtering this product in warm weather the filter should be cooled and the operation must be completed quickly, because the anhydride melts at 32°.

The acid was then prepared from the mixture by dissolving it in boiling water to which a little activated charcoal was added for purpose of purification. The mixture was boiled for fifteen minutes and filtered hot. On cooling, the *cis*-hexahydrophthalic acid crystallized out. This was purified by one recrystallization from water. The product melted at 190–191°. The yield was about 90% of the theoretical.

All the melting points obtained agreed with those recorded in the literature. Anschütz thermometers calibrated by the Bureau of Standards were used in taking the melting points.

DEPARTMENT OF CHEMISTRY
VILLANOVA COLLEGE
VILLANOVA, PA.

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[1] Bayer, *Ann.*, **258**, 219 (1890).

[2] Willstätter and Jaquet, *Ber.*, **51**, 776 (1918).

[3] Diels and Alder, *Ann.*, **460**, 98–122 (1928).

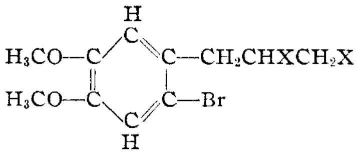
Halogenated Derivatives of Methyleugenol. II. 6-Bromomethyleugenol Glycol and 6-Bromohomoveratraldehyde

BY ST. KAUFMANN, G. ROSENKRANZ[1] AND JOSEFINA LÓPEZ

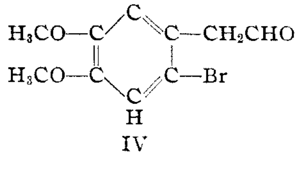
Recently it was proved by G. Rosenkranz and Mercedes Pérez[2] in these Laboratories that the position of the nuclear bromine atom in bromomethyleugenol dibromide (I) is the position 6 of the benzene ring. On the basis of this knowledge we have synthesized, starting from 6-bromomethyleugenol dibromide, a number of new compounds which may serve as intermediates for further syntheses.

The reaction of 6-bromomethyleugenol dibromide with silver acetate in glacial acetic acid leads to the formation of the hitherto unknown diacetate of 6-bromomethyleugenol glycol (II). This diacetate constitutes a viscous yellow oil which is saponified by means of alcoholic potassium hydroxide to the corresponding glycol (III) without previous purification.

This glycol with an equimolecular quantity of lead tetraacetate in chloroform solution is cleaved



I. X = Br
II. X = OOCCH$_3$
III. X = OH



IV

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[1] Present address: Laboratorios "SYNTEX" S. A., Mexico City.

[2] Number I in this series: G. Rosenkranz and Mercedes Pérez, *Ciencia*, **6**, pp. 364–368 (1946).

into formaldehyde and hitherto unknown 6-bromohomoveratraldehyde (IV).

The oxime and the semicarbazone are easily prepared from the aldehyde by the usual methods.

Experimental

6-Bromo-methyleugenol Dibromide.—To 100 g. of methyleugenol dissolved in 200 cc. of ether, 60 cc. of bromine is slowly added with mechanical stirring and external cooling. The reaction is over when the escape of hydrogen bromide ceases. The product separates as a crystalline sludge. It is filtered at the pump, washed with sodium carbonate solution and water and, after drying, recrystallized from ether–petroleum ether. An additional quantity of the product may be recovered from the ethereal mother liquors; yield, 137 g.; white crystals of m. p. 77–78°.

Diacetate of 6-Bromo-methyleugenol Glycol.—Sixty-five grams of 6-bromomethyleugenol dibromide dissolved in 325 cc. of glacial acetic acid is refluxed for two hours with 62.5 g. of silver acetate. The solution is filtered to remove the precipitate of silver bromide and excess silver acetate and the filtrate is concentrated *in vacuo*. Water is added to the residue and the oil which separates is extracted with ether. After washing with sodium carbonate solution and water and drying over sodium sulfate, the ether is distilled. The crude 6-bromomethyleugenol glycol diacetate is obtained as an amber-colored viscous oil; yield 46.6 g.

6-Bromo-methyleugenol Glycol.—46.6 grams of the crude diacetate is refluxed for two hours with 373 cc. of an approximately normal alcoholic solution of potassium hydroxide. Most of the alcohol is then removed by distillation, and the residue diluted with water. The glycol separates and is extracted with chloroform. The chloroform solution is washed once with a small quantity of water, dried, and the solvent is distilled. The impure glycol is recrystallized twice from acetone–petroleum ether; yield 27.7 g.; white, silky needles of m. p. 114–116°.

Anal.[3] Calcd. for $C_{11}H_{14}O_4Br$: C, 45.38; H, 5.20; Br, 27.47. Found: C, 45.42; H, 5.17; Br, 27.54.

6-Bromo-homoveratraldehyde.—To 31.6 g. of 6-bromomethyleugenol glycol dissolved in 200 cc. of absolute chloroform, a solution of 50 g. of lead tetraacetate in 300 cc. of chloroform is slowly added with stirring and external cooling. The temperature is not allowed to rise above 25°. After all the tetraacetate has been added, stirring is continued for thirty minutes at room temperature and the solution is left to stand another three hours. It is then washed thoroughly, first with water, then with sodium bicarbonate solution, and again with water. After drying with sodium sulfate, the chloroform is distilled. The product is purified by distillation in a high vacuum; b. p. 140–145° (0.2 mm.). The distillate crystallizes almost instantaneously. It forms white crystals of m. p. 64–65°; yield 13.3 g. For analysis the product is redistilled in high vacuum. The melting point remains unchanged.

Anal. Calcd. for $C_{10}H_{11}O_3Br$: C, 46.33; H, 4.24. Found: C, 46.33; H, 4.27.

The **oxime** gave white, glittering leaflets; m. p. 115–116°.

Anal. Calcd. for $C_{10}H_{12}O_3NBr$: C, 43.80; H, 4.41. Found: C, 43.89; H, 4.52.

The **semicarbazone** is white, glittering leaflets; m. p. 200–202°.

Anal. Calcd. for $C_{11}H_{14}O_3N_3Br$: C, 41.78; H, 4.46. Found: C, 41.66; H, 4.33.

RESEARCH LABORATORY
LABORATORIES VIETA PLASENCIA S. A.
HAVANA, CUBA

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[3] Microanalysis by Huffman Microanalytical Laboratories, Denver, Colorado.

A Synthesis of Thiophene-2-glyoxal

BY FRANK KIPNIS AND JOHN ORNFELT

During work on the synthesis of polycarbonyl compounds, it was found desirable to prepare thiophene-2-glyoxal. Two methods have been reported in the literature. That of Fujise[1] proceeds rather deviously from 2-acetylthiophene to the nitroso-ketone, hydrolysis to the glyoxal bisulfite, and, finally, hydrolysis to the glyoxal hydrate. The method of Kröhnke and Börner[2] involves the interaction of 2-bromoacetylthiophene with pyridine to the pyridinium bromide, followed by treatment with *p*-nitrosodimethylaniline to give the N-*p*-dimethylaminophenylnitrone of thiophene glyoxal and, ultimately, acid hydrolysis to the glyoxal hydrate.

It has been found possible to go directly from 2-acetylthiophene to anhydrous thiophene-2-glyoxal by oxidation with selenium dioxide, according to the method indicated for the preparation of phenylglyoxal[3] from acetophenone.

Experimental

To a 500-ml., 3-necked interjoint flask fitted with sealed Hershberg stirrer, reflux condenser and thermometer and heated by a "Glas-Col" mantle, was added 320 ml. of dioxane, 11 ml. of water and 55.5 g. (0.5 mole) of powdered selenium dioxide. Stirring and heating at 55° was continued until solution was complete. Sixty-three grams (0.5 mole) of 2-acetylthiophene[4] was added all at once and the mixture maintained at reflux with stirring for four hours. It was filtered hot through a layer of Hyflo Super-cel and the dioxane and other volatiles stripped under a short column at atmospheric pressure, removing final traces of solvent at water pump vacuum. The residue was fractionated through a 20-cm. Vigreux column at 92–93° (11 mm.) to give 30 g. (43%) of a yellow oil with a rather piercing odor.

The glyoxal gave a violet coloration with concentrated sulfuric acid, rapidly formed a solid derivative with saturated aqueous sodium bisulfite and gave a solid hydrate on warming with twice its volume of water and allowing to stand for two hours. The hydrate was washed with pentane and recrystallized from benzene to give a product melting at 93°[5] (Fujise,[1] 94°). The monosemicarbazone, prepared from the hydrate in the usual manner, melted at 222° (dec.).[5]

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[1] Fujise, *Biochem. Z.*, **236**, 241 (1931).

[2] Kröhnke and Börner, *Ber.*, **69**, 2006 (1936).

[3] Riley and Gray, "Organic Syntheses," Coll. Vol. II, John Wiley and Sons, Inc., 1943, p. 509.

[4] Supplies through the courtesy of Socony-Vacuum Oil Company.

[5] All melting points were taken with a Fisher–Johns apparatus.

RESEARCH LABORATORY
AMERICAN HOME FOODS, INC.
G. WASHINGTON DIVISION
MORRIS PLAINS, NEW JERSEY

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Traces of Oxygen in Hydrogen or Nitrogen

BY HERMAN A. LIEBHAFSKY AND EARL H. WINSLOW

During the war, oxygen determinations on "oxygen-free" gases were required in the Research Laboratory. A method sensitive to 0.0001% oxygen by volume was developed to