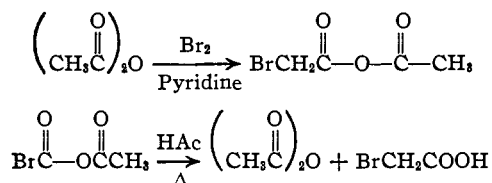


hydride itself is readily brominated in the presence of pyridine. If glacial acetic acid is added subsequently and the reaction mixture is boiled, acetic anhydride is regenerated, liberating bromoacetic acid. The two products can then be separated by distillation. These observations would indicate that the reaction probably proceeds as follows:



Experimental

Bromoacetic Acid Ester.—The reaction is carried out in a hood. An all-glass outfit is advisable. If not available, one-hole asbestos stoppers may be made by soaking strips of asbestos in water, wrapping them around pieces of glass tubing of slightly less than the desired diameter, to the desired outer diameter, and allowing them to dry at 110°. A mixture of 1000 cc. of glacial acetic acid, 200 cc. of acetic anhydride and 1 cc. of pyridine is added to a 5-liter three-necked flask fitted with reflux condenser, drying tube and dropping funnel. The mixture is heated to boiling, the flame is removed and 1100 g. of bromine is dropped in at a rate designed to keep the mixture just refluxing. At the beginning there is a lag (ten minutes) before the reaction starts. The mixture clears up and decolorizes the bromine as rapidly as it is added. Toward the end the reaction slows up and the solution remains colored. Heat is then applied and the reaction mixture is refluxed until decolorized (one hour). The excess acetic anhydride and glacial acetic acid are now removed under slight vacuum (about 300 cc. recovered), 2 liters of 95% ethyl alcohol and 200 cc. of concentrated sulfuric acid (less may be used if absolute alcohol is used) is added to the residue. The mixture is refluxed for two hours and then poured into four liters of water. The bromoacetic ester is separated, dried over sodium sulfate and distilled: b. p. 159°; yield 785 g. of product boiling within 0.5°.

Reformatsky Reaction.—A mixture of 800 cc. of benzene and 700 cc. of toluene is made with 334 g. (2 moles) of bromoacetic ester and (2 moles) of the required ketone. Three hundred cc. of this mixture is added to a five-liter three-necked flask fitted with mechanical stirrer, condenser with drying tube and dropping funnel; 130 g. (2 moles) of zinc foil which has been scraped with sandpaper is cut up in strips and added to the flask. A few crystals of iodine are added and the stirrer is started. The mixture is heated by means of a boiling water-bath. A vigorous reaction sets in. The remainder of the reaction mixture is now added through the dropping funnel at a rate designed to keep the mixture refluxing but not too vigorously. After the addition is complete, stirring is continued for two hours more. Practically all the zinc dissolves. The mixture is cooled. The condensation product is decomposed with dilute sulfuric acid (sufficient to dissolve

all the zinc hydroxide). The benzene-toluene layer is separated, dried over sodium sulfate and vacuum distilled on a water-bath to remove the benzene and toluene. Through the residue heated on a boiling water-bath is passed dry hydrogen chloride for two hours. The material is vacuum distilled. The water which has split out comes over first and then the unsaturated ester; yield 60-70%. For tetrahydrophenylethyl acetate the yield is 238 g. (about 71%).

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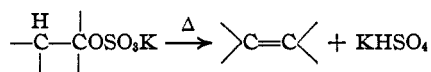
BROOKLYN, NEW YORK

RECEIVED JANUARY 21, 1939

Dehydration of Hydroxy Compounds by Pyrolysis of their Potassium Sulfate Esters; Cholesterilene and Camphene

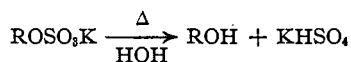
BY SAMUEL NATELSON AND SIDNEY P. GOTTFRIED

While carrying out investigations on methods for the isolation of sterols from natural occurring sources,¹ it was observed that if anhydrous potassium cholesteryl sulfate is heated at 100° for an hour in a sealed tube or autoclave, complete decomposition takes place with the separation of a colorless oil which crystallizes on cooling. The crystals were readily identified as cholesterilene (3,5-cholestadiene), the yield being excellent. Potassium acid sulfate was split out yielding the unsaturated compound.



Since a method for preparing potassium cholesteryl sulfate in quantitative yields is described herein, this is by far the best method for preparing large amounts of cholesterilene.²

If water is present, the reaction takes another route, cholesterol being regenerated. This hydrolysis is catalyzed by small amounts of hydrogen ion.



The ease with which the unsaturated compound is formed, encouraged us in the hope that this method might be applied as a general method for the dehydration of compounds where there existed danger of rearrangement. Potassium bornyl sulfate was therefore chosen as a test compound. It is well known that dehydration of bornyl yields a variety of dehydration products and

(1) Natelson and Sobel, *J. Biol. Chem.*, **109**, 687 (1935); Natelson, Sobel and Kramer, *ibid.*, **105**, 763 (1934).

(2) Haltori, *THIS JOURNAL*, **60**, 3082 (1938); Bergmann, *J. Org. Chem.*, **1**, 567 (1937).

only the method of Tchugaev will give fair yields of bornylene.³

Anhydrous potassium bornyl sulfate is much more stable than potassium cholesteryl sulfate and only after heating to relatively high temperatures (200°) can decomposition be induced. Rearrangement does occur and the main product of the reaction is camphene in about 60% yield. If water is present borneol is regenerated readily before decomposition can set in.

Experimental

Potassium Cholesteryl Sulfate.—The procedure described herein is adapted from a method previously reported⁴ for estimating small amounts of cholesterol as pyridine cholesteryl sulfate.

Pyridine sulfur trioxide is prepared by adding 100 g. (1 mole) of sulfur trioxide to 200 g. (excess) of pyridine dissolved in 300 cc. of chloroform, in an ice-bath. The almost quantitative yield of pyridine sulfur trioxide is filtered off under anhydrous conditions, washed with chloroform and dried in a sulfuric acid desiccator.

Twenty-five grams of cholesterol is added to 100 cc. of anhydrous benzene with mechanical stirring and cooling using an ice-bath. A mixture of 25 cc. of acetic anhydride and 25 cc. of pyridine is added, followed by 25 g. of pyridine sulfur trioxide (excess), with vigorous stirring. The pyridine cholesteryl sulfate separates almost immediately. The reaction mixture is heated to 50° for thirty minutes with continual stirring. The mixture is cooled, an equal volume of petroleum ether is added and the mixture filtered. The residue which consists of pyridine cholesteryl sulfate mixed with some excess pyridine sulfur trioxide is transferred to an Erlenmeyer flask and treated with 8 g. of potassium hydroxide in 80 cc. of water, shaking vigorously for about fifteen minutes. The insoluble potassium cholesteryl sulfate separates at the top and is filtered off, washed with water and then with several portions of boiling anhydrous methyl alcohol. The residue is now transferred to a vacuum desiccator where the last traces of solvent are removed: yield 30 g.; m. p. 212° (dec.). A small portion was crystallized from 70% methyl alcohol. *Anal.* Calcd. for C₂₇H₄₈OSO₃K: K, 7.74; S, 6.35. Found: K, 7.88; S, 6.56.

Potassium Bornyl Sulfate.—Prepared as for potassium cholesteryl sulfate. Potassium bornyl sulfate should be precipitated in and washed with a limited volume of water for it is very water soluble; m. p. 220° (dec.). *Anal.* Calcd. for C₁₀H₁₇OSO₃K: K, 14.34; S, 11.76. Found: K, 14.31; S, 11.80.

Cholesterilene.—Twenty-five grams of anhydrous potassium cholesteryl sulfate is placed in a sealed tube from which the air has been evacuated. The tube is placed in an oven at 100° for one hour. A colorless liquid separates from the potassium acid sulfate. The tube is allowed to cool and the crystallized cholesterylene is recrystallized

from alcohol: yield 14 g.; m. p. 79°. *Anal.* Calcd. for C₂₇H₄₄: C, 88.04; H, 11.96. Found: C, 87.74; H, 12.20.

Camphene.—Anhydrous potassium bornyl sulfate (100 g.) is placed in a distilling flask heated by means of an oil-bath. The temperature is raised to 200°. The salt decomposes and material begins to distill over. When no more distillate is obtained the distillate is fractionated. The main fraction distills from 158–162°, and crystallizes on cooling, m. p. 50°. *Anal.* Calcd. for C₁₀H₁₆: C, 88.23; H, 11.76. Found: C, 87.99; H, 11.90.

Cholesterol from Potassium Cholesteryl Sulfate.—Twenty-five grams of potassium cholesteryl sulfate is suspended in 100 cc. of water to which 1 drop of concd. sulfuric acid is added. The mixture is heated at 100° in a sealed tube or autoclave for one hour. The mixture is cooled, filtered and the residue is recrystallized from alcohol: yield 15 g.; m. p. 145°.

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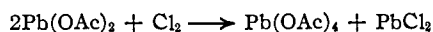
The Preparation of Lead Tetraacetate

BY RALPH E. OESPER AND CLARA L. DEASY

Lead tetraacetate is usually prepared by warming red lead with acetic acid containing acetic anhydride sufficient to combine with the water formed¹

$$\text{Pb}_3\text{O}_4 + 8\text{SHOAc} \longrightarrow \text{Pb}(\text{OAc})_4 + 2\text{Pb}(\text{OAc})_2 + 4\text{H}_2\text{O}$$

Colson¹ (p. 891) found that a precipitate containing some tetraacetate is formed when chlorine is passed into a cold glacial acetic acid solution of lead diacetate



We have made a systematic study of these procedures, varying the temperature, time of reaction and proportions of the reactants, and have found that improved yields result when these procedures are combined. Purification of the acetic acid by distillation over permanganate and then over phosphorus pentoxide raises the yield, but not enough to make this extra precaution profitable. The acetic anhydride content must not be unduly increased, nor may the total volume of the acetic acid-anhydride mixture be too drastically diminished.

Procedure.—The reaction is best carried out in a three-necked flask fitted with a gas-inlet tube, a thermometer and a mechanically driven stirrer (seal unnecessary). A mixture of 600 ml. of glacial acetic acid and 150 ml. of acetic anhydride is heated to 65°, the stirrer is started and a not

(3) Tchugaev, *J. Russ. Phys.-Chem. Soc.*, **36**, 1039; *Chem. Centr.*, **76**, 1, 94 (1905).

(4) Sobel, Drecker and Natelson, *J. Biol. Chem.*, **115**, 381 (1936); Drecker, Sobel and Natelson, *ibid.*, **115**, 391 (1936).

(1) Hutchinson and Pollard, *J. Chem. Soc.*, **63**, 1136 (1893); **69**, 212 (1896); Dimroth, Friedemann and Kämmerer, *Ber.*, **53**, 451 (1920); Dimroth and Schweizer, *Ber.*, **56**, 1375 (1923); Ruff, "Die Chemie des Fluors," Verlag von Julius Springer, Berlin, 1920, p. 41; Colson, *Compt. rend.*, **136**, 675 (1903); Hellmuth, Dissertation, Würzburg, 1930.