carbon catalyst were heated at 240–245° (inside temperature) for one hour. The product was stirred mechanically. The product was allowed to cool until it solidified, and 100 cc. of alcohol was then added. The reaction mass was heated on the steam-bath until the catalyst was completely in suspension. It was then filtered hot, and the catalyst washed with 25 cc. of hot alcohol. The hot filtrate was diluted with 50 cc. of warm water. Crystallization took place at once, and the mass set to a paste. The cooled mass was filtered with suction, washed with 50 cc. of 50% alcohol, and dried at 80° in vacuum to constant weight. The yield was 23 g. or 92%. This crude product melted at 169–170°. For further purification, it was recrystallized from alcohol or ligroin (b. p. 60–90°). The recrystallized product[10] melted at 171–172°; $[\alpha]^{20}_{D}$ +55° in absolute alcohol.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.41; H, 10.01. Found: C, 80.00, 80.09; H, 9.61, 9.62.

Speed of Isomerization with Palladium–Carbon.—Twenty-five grams of *l*-abietic acid and 0.5 g. of palladium–carbon catalyst were heated in a 200-cc. three-necked distilling flask equipped with mechanical stirrer, in a bath brought to 250 ± 5°. Samples were then withdrawn at intervals, the isomerized acids extracted in each case with alkali from the ether solution of the reaction products as previously described, and rotations and melting points taken. The point of highest rotation is reached after a heating period of thirty-six minutes from the time the charge attained a temperature of 250°. Within the six minutes required to reach the bath temperature, a very substantial part of the isomerization had already taken place. The reaction was found to be exothermic.

Data from this experiment are shown graphically in Fig. 1 [graph (b)], and some indication of the relative speed of isomerization obtainable with this catalyst, as compared with the usual long heating period without catalyst, may be had from the comparative graphs (a) and (b) of Fig. 1. Graph (b) was plotted from experimental data given in the publication by Dupont and Dubourg.[5]

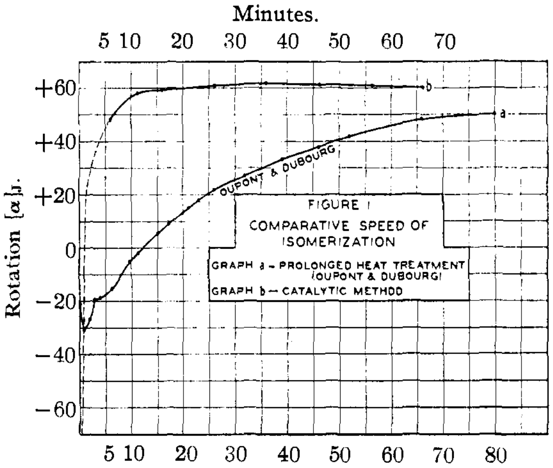

Fig. 1.

In view of the great difference in time factor, graph (a) is shown in terms of hours and graph (b) in terms of minutes.

Summary

A rapid method for the isomerization of resin and rosin acids by catalytic means has been described. Palladium–carbon, platinum–carbon, and certain brands of charcoal have been found effective catalysts, the palladium–carbon, however, being by far the best.

The catalytic method of isomerization has been found to be selective, α-(or dextro-)-pyroabietic acid being formed from the several resin acids and rosins from different sources used.

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[10] Combustion data kindly furnished by W. G. Rose of the Division of Insecticide Investigations, Bureau of Entomology and Plant Quarantine, Department of Agriculture.

[CONTRIBUTION FROM THE SCHOOL OF CHEMISTRY AND PHYSICS OF THE PENNSYLVANIA STATE COLLEGE, AND THE PARKE DAVIS & CO., RESEARCH LABORATORIES]

Sterols. XVIII. Preparation of *epi-allo*-Pregnanolone from *allo*-Pregnandiol

BY RUSSELL E. MARKER, OLIVER KAMM AND DAVID M. JONES

Recently we reported the isolation of *epi-allo*-pregnanolone,[1] an androgenic principle from human pregnancy urine, and later its preparation from chloro-*allo*-cholanic acid.[2] We have now prepared this product from *allo*-pregnandiol, obtaining it in good yields. Upon partial acetylation by refluxing a solution of *allo*-pregnandiol in acetic acid with one equivalent of acetic anhydride, the OH group in the 3-position is acetylated, leaving the OH group in the 20-position free. The OH group in the 20-position is then oxidized to a ketone, giving the acetate of *epi-allo*-pregnanolone, which is separated and purified by means of Girard's reagent, its half succinic ester and its semicarbazone.

In the course of this work some other unrelated derivatives of pregnandiol were prepared for biological assays, including the diacetate of preg-

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(1) Marker, Kamm and McGrew, THIS JOURNAL, **59**, 616 (1937).

(2) Marker, Kamm, Jones, Wittle, Oakwood and Crooks, *ibid.*, **59**, 768 (1937).

nanone-3-diol-4,20, isopregnandiol, in which both —OH groups are of opposite configuration to those occurring naturally, and pyro-*allo*-pregnandione.

Experimental

A solution of 10 g. of *allo*-pregnandiol in 100 cc. of acetic acid and 4 cc. of acetic anhydride was refluxed for three hours. The solution was cooled and 2 g. of chromic oxide in 10 cc. of 90% acetic acid was added. The product was let stand overnight and then the solvent was evaporated under reduced pressure. The residue was extracted with ether. The ether solution was washed with sodium carbonate, and then the ether was evaporated. The residue was dissolved in 50 cc. of alcohol and 5 g. of Girard's reagent was added. This solution was refluxed for thirty minutes, then poured on ice and extracted with ether. The ether extract contained some *allo*-pregnandiol diacetate. The aqueous layer was acidified with hydrochloric acid, warmed on a steam-bath, then extracted with ether. The ether was removed and the residue was refluxed for fifteen minutes with a slight excess of alcoholic potassium hydroxide solution. Water was added and the solid material was filtered. This product was dried; then it was warmed on a steam-bath with 5 cc. of pyridine and 3 g. of succinic anhydride. Ether was added and the pyridine was removed by washing with hydrochloric acid. The ethereal solution was washed with sodium carbonate solution. To this aqueous solution was added 5 g. of sodium hydroxide and the solution was heated for fifteen minutes. The product was extracted with ether, then crystallized from 60% alcohol; m. p. 176°. Mixed with natural *epi-allo*-pregnanolone of m. p. 176° it gave no depression in melting point.

Anal. Calcd. for $C_{21}H_{34}O_2$: C, 79.2; H, 10.8. Found: C, 79.4; H, 10.9.

This was converted into its semicarbazone which melted at 248°. Mixed with the semicarbazone of natural *epi-allo*-pregnanolone this gave no depression in melting point.

Anal. Calcd. for $C_{22}H_{37}N_3O_2$: C, 70.3; H, 9.9. Found: C, 69.7; H, 10.1.

Diacetate of Pregnanone-3-diol-4,20.—To a solution of 3 g. of 4-bromopregnanone-3-*ol*-20 acetate in 20 cc. of glacial acetic acid was added 4 g. of anhydrous potassium acetate. The mixture was refluxed for three hours. The solvent was removed under reduced pressure and the residue was crystallized from alcohol, m. p. 247°.

Anal. Calcd. for $C_{25}H_{38}O_5$: C, 71.7; H, 9.2. Found: C, 71.9; H, 9.4.

Isopregnandiol (both —OH Groups of Opposite Configuration to the Natural).—To a solution of 4 g. of pregnandione, m. p. 120°, in 100 cc. of acetic acid was added 2 g. of platinum oxide. The mixture was shaken with hydrogen under a pressure of 45 pounds (3 atm.) for three hours. The platinum was filtered and the acetic acid was evaporated under reduced pressure. The residue was crystallized from ethyl acetate–petrolic ether mixture to a constant melting point of 174°.

Anal. Calcd. for $C_{21}H_{36}O_2$: C, 78.8; H, 11.3. Found: C, 78.3; H, 11.4.

This was converted into its diacetate by refluxing with an excess of acetic anhydride. The product was crystallized from alcohol, m. p. 111°.

Anal. Calcd. for $C_{25}H_{40}O_4$: C, 74.4; H, 10.0. Found: C, 74.5; H, 10.4.

Pyro-*allo*-pregnandione.—To a solution of 5 g. of *allo*-pregnandione in 200 cc. of glacial acetic acid was added 5 g. of chromic anhydride. A temperature of 50° was maintained for five hours. Water was added and the product was filtered. This was purified by dissolving in sodium carbonate solution, from which the non-acidic material was extracted with ether. The alkaline layer was acidified and the organic acid was crystallized from 80% acetic acid, m. p. 218°.

To 2.5 g. of *allo*-pregnanone dicarboxylic acid was added 30 cc. of acetic anhydride in a retort. The solvent was distilled over slowly during one hour. The residue was heated for thirty minutes at 200–280°. The product was then distilled at 2 mm. pressure. The distillate was crystallized from alcohol, m. p. 180°.

Anal. Calcd. for $C_{20}H_{30}O_2$: C, 79.4; H, 10.1. Found: C, 79.4; H, 10.1.

Summary

epi-allo-Pregnanolone was prepared from *allo*-pregnandiol by partially acetylating, then oxidizing the unacetylated OH group in the 20-position.

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