[CONTRIBUTION FROM THE BIOCHEMICAL LABORATORY, STATE UNIVERSITY OF IOWA]

Monoacetates of Hydroquinone and Catechol

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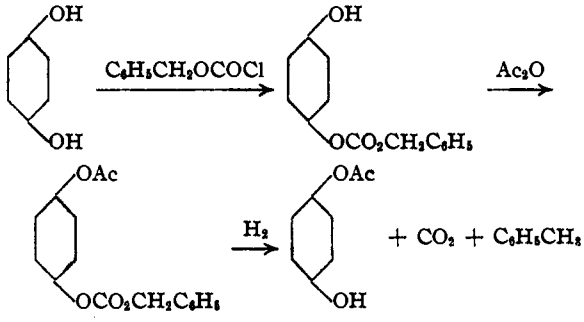
In the course of studies on antioxidants in fats[1] we wished to investigate, among other phenolic compounds, hydroquinone and catechol monoacetates, and could find no references to their preparation or properties. Preliminary attempts at synthesis with limited quantities of an acetylating reagent yielded appreciable amounts of the diacetates. The successful use of benzyl chloroformate by Bergmann and Zervas[2] in the synthesis of peptides suggested that this reagent might also be useful in the preparation of the compounds mentioned above. Carbobenzoxy esters, prepared by means of benzyl chloroformate, can be split by hydrogen in the presence of a platinum or palladium catalyst, thus avoiding the hydrolyzing action of acids or bases.

The monoacetate of hydroquinone or catechol was prepared easily by a series of reactions involving the preparation of the monocarbobenzoxy derivative, acetylation of the remaining hydroxyl, and removal of the carbobenzoxy group by hydrogenation.



It was later found possible, and much more practicable, to obtain the monoacetates in fair yields by careful acetylation of the dihydroxy compounds in aqueous solution. However, the methods used in the first syntheses are described inasmuch as they may prove useful in more complicated synthetic procedures.

Experimental

The benzyl chloroformate[3] was prepared as directed by Bergmann and Zervas.

Monocarbobenzoxyhydroquinone.—A mixture of 2 g. of hydroquinone and 1 g. of sodium carbonate was dissolved in 30 cc. of water in a 200 cc. rubber-stoppered bottle kept filled with nitrogen. To this solution was added 3.5 g. of benzyl chloroformate in several portions. Between the additions the bottle was shaken in a mechanical shaker. When the reaction was complete, as indicated by the disappearance of the odor of benzyl chloroformate, the solid product was filtered, washed with water, dissolved in alcohol, boneblacked and crystallized from 50% alcohol. The white, irregular flat prisms melted at 120–120.5°[4]; yield, approximately 50%.

Anal. Calcd. for $C_{14}H_{12}O_4$: C, 68.8; H, 5.0. Found: C, 68.8; H, 5.5.

Dicarbobenzoxyhydroquinone.—This compound was prepared by a similar procedure except that double the quantities of sodium carbonate and benzyl chloroformate were used. The insoluble reaction product crystallized from hot alcohol in the form of fine white needles, m. p. 142–143°.

Anal. Calcd. for $C_{22}H_{18}O_6$: C, 69.8; H, 4.8. Found: C, 69.6; H, 5.2.

Dicarbobenzoxyhydroquinone in alcohol was hydrogenated in the presence of a platinum catalyst.[5] The catalyst was removed and the alcohol evaporated to dryness. The residue was identified as hydroquinone, by the m. p. of the impure product, 163°, and of the sublimed crystals, 169°.

Monocarbobenzoxyhydroquinone Monobenzoate.—Monocarbobenzoxyhydroquinone was dissolved in five parts of pyridine to which was added one part of benzoyl chloride. The mixture was allowed to stand overnight and then poured into an excess of water. The precipitate was filtered, washed and recrystallized from alcohol. The fine white platelets melted at 97–98°.

On hydrogenation, monocarbobenzoxyhydroquinone benzoate yielded hydroquinone monobenzoate which, after crystallization from 70% alcohol, melted at 160°. A mixture with a specimen synthesized by the method of Robertson and Waters[6] melted at 160–161°.

Monocarbobenzoxyhydroquinone Monoacetate.—Monocarbobenzoxyhydroquinone (1 part) was quantitatively acetylated with acetic anhydride (1 part) in pyridine (5 parts) by standing at room temperature for twelve hours. The precipitate which formed when the mixture was poured into water was filtered, washed and recrystallized from small amounts of alcohol in which it tended to form supersaturated solutions. The minute colorless crystals melted at 75–76°.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.1; H, 5.0. Found: C, 67.2; H, 5.2.

Hydroquinone Monoacetate. Method 1.—Monocarbobenzoxyhydroquinone monoacetate was hydrogenated in

(1) Olcott, THIS JOURNAL, **56**, 2492 (1934).
(2) Bergmann and Zervas, *Ber.*, **65**, 1192 (1932).
(3) Dr. R. M. Conrad kindly supplied this reagent.
(4) All melting points are corrected.
(5) "Organic Syntheses," Coll. Vol. I, John Wiley and Sons, Inc., New York, 1932, p. 452.
(6) Robertson and Waters, *J. Chem. Soc.*, 2729 (1930).

alcohol with a platinum catalyst. Palladium[6] and Raney nickel[7] were also effective but hydrogen was absorbed more slowly. When absorption had ceased, the catalyst was filtered and washed with alcohol, and the filtrate was evaporated to dryness. The residue was crystallized from large amounts of petroleum ether (b. p. 60–70°).

Method 2.—Hydroquinone was acetylated with the equivalent of one mole of acetic anhydride following the directions of Chattaway[8] for the preparation of acetates except that sodium carbonate was substituted for sodium hydroxide. Stirring was continued for an hour after the addition of the last of the acetic anhydride and the mixture was then allowed to stand at room temperature overnight. The hydroquinone diacetate, amounting approximately to 30% of the original hydroquinone, was filtered off. The filtrate was extracted with ether, and the ether layer was washed, dried with anhydrous sodium sulfate and evaporated to dryness. The residue was extracted repeatedly with boiling petroleum ether, from which, on cooling, hydroquinone monoacetate crystallized in colorless irregular prisms, m. p. 62–63°.

Hydroquinone monoacetate is very soluble in water, alcohol and ether. The aqueous solution gives no color with ferric chloride.

Anal. Calcd. for $C_8H_8O_3$: C, 63.1; H, 5.3. Found: C, 63.1; H, 5.6.

On further acetylation, hydroquinone monoacetate yields the diacetate, m. p. 120.5–121°; mixed m. p. with a product obtained from hydroquinone and an excess of acetic anhydride, 121°.

Monocarbobenzoxycatechol.—This compound, prepared by procedures similar to those used for the analogous hydroquinone derivative, crystallized from petroleum ether (b. p. 60–70°) in rosets of colorless needles, m. p. 88.5–89°.

Anal. Calcd. for $C_{14}H_{12}O_4$: C, 68.8; H, 5.0. Found: C, 69.1; H, 5.1.

Monocarbobenzoxycatechol Monoacetate.—On pouring the mixture used to acetylate monocarbobenzoxycatechol into water, a colorless oil separated. This was extracted with ether. The ether layer was washed, dried and evaporated to dryness and the residue distilled in high vacuum (0.1 mm.). Only 2 cc. was distilled and a satisfactory distilling temperature was not recorded; most of the material distilled between 100–150°.

Anal. Calcd. for $C_{16}H_{14}O_5$: C, 67.1; H, 5.0. Found: C, 67.2; H, 5.0.

Catechol Monoacetate.—Prepared by both methods outlined under hydroquinone monoacetate, catechol monoacetate was obtained as a colorless oil which did not crystallize at low temperatures. Traces of catechol were removed by crystallization from petroleum ether in which the monoacetate is more soluble. The monoacetate distilled approximately at 130–140° (0.1 mm.).

Anal. Calcd. for $C_8H_8O_3$: C, 63.1; H, 5.3. Found: C, 62.9; H, 5.5.

Catechol monoacetate possesses a slight phenolic odor and is soluble in water, alcohol, ether and petroleum ether. Dilute aqueous solutions give a green color with ferric chloride. On acetylation, the diacetate of m. p. 60° is obtained.

Antioxidant Properties.—All of the compounds described were assayed for their antioxygenic properties by determining the effect of adding small amounts to lard. The method used for measuring the length of the induction period has been described previously.[1,9] Only the monoacetates showed any protective effect (Table I). The monoacetate of catechol was more effective than that of hydroquinone, in contrast to the results with the monomethyl esters of these two phenols.[1,10] Other monoesters of hydroquinone are ineffective.[1] Neither monoacetate approaches the effectiveness of the original dihydroxy compounds. In view of the fact that catechol monoacetate could not be purified by crystallization, its antioxygenic effect might have been due to traces of catechol.

TABLE I

ANTIOXIDANT PROPERTIES OF THE MONOACETATES OF HYDROQUINONE AND CATECHOL IN LARD

Amount of added substance, %		Induction period (75°), hrs. With inhibitor	Induction period (75°), hrs. Without inhibitor
0.02		19	18
.02	Hydroquinone	25	22
.02	monoacetate	15	11
.10		52	11
.02	Catechol	52	18
.02	monoacetate	62	22
.01	Hydroquinone[9]	410	14
.01	Catechol[11]	408	9

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Summary

Hydroquinone and catechol monoacetates have been prepared by careful acetylation of the diphenols and also with the use of carbobenzoxy derivatives. Catechol monoacetate is more effective as an antioxidant than hydroquinone monoacetate but much less effective than either catechol or hydroquinone.

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(7) Covert and Adkins, THIS JOURNAL, **54**, 4116 (1932).

(8) Chattaway, *J. Chem. Soc.*, 2495 (1931).

(9) French, Olcott and Mattill, *Ind. Eng. Chem.*, **27**, 724 (1935).

(10) Mattill, *J. Biol. Chem.*, **90**, 141 (1931).

(11) These results are representative. Duplicate runs would be subject to the variations previously described [Olcott and Mattill, THIS JOURNAL, **58**, 1627 (1936)].