HYDROXYQUINONES

XIII. Synthesis of Dialkyldihydroxyquinones

SHICHIRO AKIYA

The Institute for Infectious Diseases

HIDEO TAKAHASHI, MASAYUKI KURIYAMA and

YOSHIKO KAGAWA

National Institute of Health

Previously, the late Mitizo Asano and his coworkers¹⁾ carried out the present investigation in order to find out the properties of dialkyldihydroxybenzoquinones. The present authors took up this study in order to find out the properties and anthelmintic action of dialkyldihydroxybenzoquinones. Fichter and Weise²⁾ obtained dialkyldihydroxyquinones in one step by the condensation of one mole each of the esters of fatty acid and oxalic acid with two moles of sodium. Assuming the formation of the ester of $\alpha\beta$ -diketonic acid as an intermediate, they explained the reaction mechanism as follows:

Later, Fichter, Jetzer, and Leepin³⁾ prepared dialkyldihydroxyquinones possessing $(\text{CH}_3)_2\text{CH}\cdot\text{CH}_2^-$, $\text{CH}_3(\text{CH}_2)_4^-$, $\text{CH}_3(\text{CH}_2)_5^-$, $\text{CH}_3(\text{CH}_2)_6^-$ and $\text{CH}_3(\text{CH}_2)_7^-$ and found that with the increase of the alkyl chain the reaction became so slow that the reaction was limited to capric acid ethyl ester, no product being obtained in reactions with lauric or palmitic esters. The present authors followed the above method and obtained dialkyldihydroxyquinones with the esters of isooctanthic, pelargonic and lauric acids as the original material to obtain alkyl groups of isoamyl, heptyl and decyl. In the present series of experiments dialkyldihydroxyquinones possessing dodecyl, tetradecyl and pentadecyl group were prepared from the esters of myristic, palmitic and margaric acids. However, yields of the products were so small that the method cannot be said to be suitable as a method of manufacture. The anthelmintic actions of these quinones will be reported later.

The constants of the dialkyldihydroxyquinones obtained are as follows:

Alkyl	Dialkyldihydroxy- quinones. m.p.	Benzoate m.p.	Leuco-tetra- acetate. m.p.
$\text{CH}_3(\text{CH}_2)_{11}-$	127-128°	79°	114.5°
$\text{CH}_3(\text{CH}_2)_{13}-$	124°	71°	117°
$\text{CH}_3(\text{CH}_2)_{14}-$	121°	67°	119°

EXPERIMENTAL

2,5-Didodecyl-3,6-dihydroxyquinone—In 80 g of dry ether, 3.2 g of wire-form metallic sodium is added, and to this are poured 11.2 g of ethyl oxalate and 18.4 g of ethyl myristate by which the reaction takes place gradually and the mixture begins to become turbid. The mixture becomes warm, turns from pale yellow and red to dark reddish brown. After standing overnight, water is added, aqueous layer is separated, and the ethereal layer is washed with sodium carbonate solution. This aqueous solution is collected, acidified with sulfuric acid and taken up in ether. Ethereal layer is washed with water, dried and ether is evaporated by which orange red powder is obtained. Yield, 0.2 g. By repeated recrystallization from glacial acetic acid, orange red lustrous scaly crystals of m.p. 127-128° are obtained. This substance dissolves in diluted sodium carbonate giving violet solution and its alcoholic solution colors dark purplish brown by ferric chloride.

Analysis: 3.160 mg of the substance gave 8.618 mg CO_2 , 3.123 mg H_2O .

Calcd. for $\text{C}_{30}\text{H}_{52}\text{O}_4$: C, 75.63; H, 10.92.

Found: C, 75.42; H, 11.06.

Dibenzoate of 2.5-Didodecyl-3.6-dihydroxyquinone—To a solution of 50 mg of the above didodecyl-dihydroxyquinone in 0.5 cc pyridine, 0.1 g of benzoyl chloride is added and the product is extracted with ether. The ether layer is washed consecutively with diluted hydrochloric acid, diluted sodium carbonate and cold water, and dried. The ethereal residue of 25 mg is recrystallized from alcohol to pale yellow needles of m.p. 79° .

Analysis: 1.292 mg of the sample gave 3.669 mg CO_2 , 1.000 mg H_2O

Calcd. for $\text{C}_{44}\text{H}_{60}\text{O}_6$: C, 77.19; H, 8.77.

Found: C, 77.45; H, 8.60.

2.5-Didodecyl-3.6-dihydroxyquinone leuco-tetraacetate—To a solution of 56 mg of didodecyl-dihydroxyquinone in 1.4 cc of acetic anhydride, obtained by slight warming, 350 mg of zinc dust and one drop of water are added and warmed by which the solution becomes discolored and a small amount of white precipitate begins to separate out. After 15 minutes, the mixture is cooled and three drops of concentrated sulfuric acid are added by which a slight heat is generated. After cooling, the reaction product is diluted with 20 cc of water, extracted with ether and the excessive zinc dust is removed by filtration. The ethereal layer is first washed with diluted sodium carbonated solution, then with cold water, dried and the ether distilled off. Yield of the residue, 32 mg. This is recrystallized from alcohol to colorless needles of silky lustre, m.p. 114.5° .

Analysis: 6.250 mg of the sample gave 16.180 mg CO_2 , 5.500 mg H_2O .

Calcd. for $\text{C}_{28}\text{H}_{62}\text{O}_8$: C, 70.59; H, 9.60.

Found: C, 70.60; H, 9.78.

2.5-Ditetradecyl-3.6-dihydroxyquinone—In 100 g of dry ether containing 4 g of wire-form metallic sodium 1.2 g of ethyl oxalate and 2.4 g of ethyl palmitate are added and condensed as in the former by which 0.2 g of the reaction product is obtained. Recrystallization from glacial acetic acid gives orange red lustrous scaly crystals of m.p. 124° which dissolves in diluted sodium carbonate giving a violet colored solution and its alcoholic solution colors dark purplish brown with ferric chloride.

Analysis: 4.355 mg of the sample gave 12.165 mg CO₂, 4.600 mg H₂O.

Calcd. for C₃₄H₆₀O₄ : C, 76.69; H, 11.28.

Found: C, 76.18; H, 11.74.

Dibenzoate of 2.5-Ditetradecyl-3.6-dihydroxyquinone—Obtained by the same method as for didodecyldihydroxyquinone. Recrystallized from alcohol to pale yellow needles of m.p. 71°.

Analysis: 5.203 mg of the sample gave 14.845 mg CO₂, 4.500 mg H₂O.

Calcd. for C₄₈H₆₈O₆ : C, 77.84; H, 9.19.

Found: C, 77.81; H, 9.61.

2.5-Ditetradecyl-3.6-dihydroxyquinone leucotetraacetate—Obtained in the same manner as for didodecyldihydroxyquinone. Colorless needles with silky lustre, m.p. 117°.

Analysis: 1.413 mg of the sample gave 3.716 mg CO₂, 1.300 mg H₂O.

Calcd. for C₄₂H₇₀O₈ : C, 71.79; H, 9.97.

Found: C, 71.72; H, 10.22.

2.5-Dipentadecyl-3.6-dihydroxyquinone—To 100 g of dry ether containing 4 g of wire-form metallic sodium, 12 g of ethyl oxalate and 24 g of ethyl margarate are added and treated in the same manner as for didodecyldihydroxyquinone. Yield, 0.2 g. Recrystallized from glacial acetic acid to orange yellow lustrous scaly crystals of m.p. 121° which dissolved in diluted sodium carbonate giving violet colored solution and its alcoholic solution colors dark purplish brown with ferric chloride.

Analysis: 1.293 mg of the sample gave 3.670 mg CO₂, 1.392 mg H₂O.

Calcd. for C₃₆H₆₄O₄ : C, 77.14; H, 11.43.

Found: C, 77.45; H, 11.97.

Dibenzoate of 2.5-Dipentadecyl-3.6-dihydroxyquinone—Obtained in the same manner as for the dibenzoate of didodecyldihydroxyquinone. Recrystallized from alcohol to pale yellow needles, m.p. 67°.

Analysis: 5.915 mg of the sample gave 17.040 mg CO₂, 5.000 mg H₂O.

Calcd. for C₅₀H₇₂O₆ : C, 78.13; H, 9.38.

Found: C, 78.57; H, 9.39.

2.5-Dipentadecyl-3.6-dihydroxyquinone Leuco-tetracetate—Obtained in the same manner as for didodecyldihydroxyquinone leucotetraacetate. Recrystallized from alcohol to colorless needles with silky lustre, m.p. 119°. Analysis: 1.980 mg of the sample gave 5.273 mg CO₂, 1.800 mg H₂O.

Calcd. for C₄₄H₇₄O₈ : C, 72.33; H, 10.14.

Found: C, 72.63; H, 10.10.

REFERENCES

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