An Improved Method for the Preparation of *dl*-Hydrobenzoin

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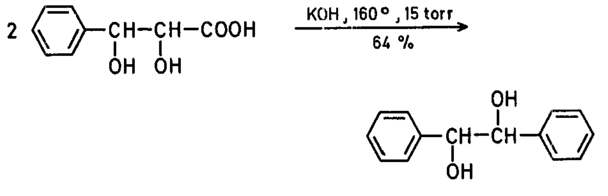
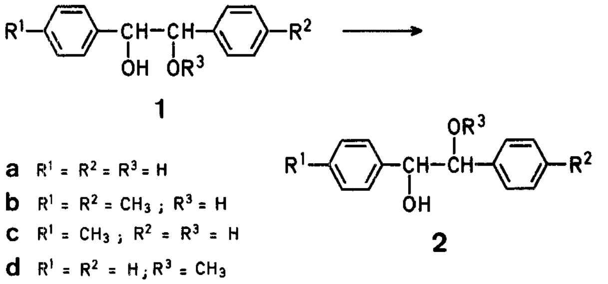
The usual methods for the preparation of hydrobenzoins, i.e. hydrogenation of benzoins[1] or reductive C—C coupling of benzaldehydes[2,3], lead to the formation of the *meso* (or *erythro*) isomers or of mixtures of the two isomers (which are generally difficult to separate). The *dl*- (or *threo*-) hydrobenzoins are less readily obtained: the reaction of phenylmagnesium bromide with glyoxal sulfate (poor yield)[4], treatment of *meso*-stilbene dibromide with wet silver acetate[5], and *cis* ring opening of stilbene oxide[6] are possible routes to these compounds. Our attempts[7] to epimerize *meso*-hydrobenzoin into *dl*-hydrobenzoin following the method of Schlosser[11] afforded only a mixture of the two isomers.

We describe here a simple and efficient method for the preparation of *dl*-hydrobenzoin from the readily available *meso* isomer. It has been reported[8] that heating of *threo*-3-phenylglyceric acid with potassium hydroxide under reduced pressure leads to the formation of *dl*-hydrobenzoin.



We reinvestigated this reaction and found that *dl*-hydrobenzoin is obtained starting from both *erythro*- and *threo*-3-phenylglyceric acid. This result indicates that under the above reaction conditions *dl*-hydrobenzoin (possibly as the alkoxide) is the thermodynamically more stable isomer. In accordance with this fact, we found that treatment of *meso*-hydrobenzoin (**1a**) with potassium hydroxide at 160° under reduced pressure affords pure *dl*-hydrobenzoin (**2a**) in 90% yield within a few minutes. The procedure can also be applied to the epimerization of certain substituted *meso*- and *erythro*-hydrobenzoins to the corresponding *dl* and *threo* isomers, respectively.



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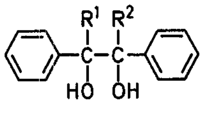
a $R^1 = R^2 = R^3 = H$
b $R^1 = R^2 = CH_3$; $R^3 = H$
c $R^1 = CH_3$; $R^2 = R^3 = H$
d $R^1 = R^2 = H$; $R^3 = CH_3$

2

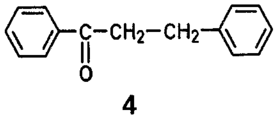
meso-4,4′-Dimethylhydrobenzion (**1b**, *meso*) is completely converted into the *dl* isomer (**2b**). The analogous epimerization of *erythro*-4-methylhydrobenzoin (**1c**, *erythro*) gives rise to a mixture of the *threo* isomer **2c** and the *dl* compounds **2a** and **2b**, the product ratio depending upon the reaction time; when heating is limited to 10 min, compounds **2a** and **2b** are formed only in minor amounts and **2c** (*threo*) can be isolated by crystallization. The monomethyl ethers **1d** (*erythro*) and **2d** (*threo*) remain unaffected under the above reaction conditions.

Complete epimerization of *meso*-hydrobenzoin (**1a**) into the *dl* isomer (**2a**) (70% yield) may also be achieved by heating **1a** in boiling xylene in the presence of an equimolar amount of potassium for 6 hr. However, this procedure is preparatively less useful since benzyl alcohol and minor amounts of deoxybenzoin are obtained as by-products.

Treatment of the *erythro*-α,α′-dialkylhydrobenzoins **3** with potassium hydroxide as described above does not lead to the formation of the expected *threo* isomers. Instead, the reaction of *erythro*-**3a** affords 1,3-diphenyl-1-oxopropane [**4**; m.p. 72° (Ref.[9], m.p. 72–73°)] in 78% yield, *erythro*-**3b** undergoes fragmentation to acetophenone and 1-phenylethanol, and *erythro*-**3c** is cleaved to give benzoic acid and 1-phenylpropanol.



erythro-**3a** $R^1 = H$; $R^2 = CH_3$
erythro-**3b** $R^1 = R^2 = CH_3$
erythro-**3c** $R^1 = C_2H_5$; $R^2 = H$



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Attempts to epimerize *meso*-hydrobenzoin (**1a**) using sodium hydroxide were unsuccessful, a mixture of **1a** (*meso*) and **2a** (*dl*) being obtained in very low yield.

Analysis of the Reaction Products:

The reaction mixtures were extracted with ether, the ethereal extracts dried, and the ether evaporated. The residue was analyzed either by ^{1}H-N.M.R. in $CDCl_3$ (Perkin Elmer R12 and Varian HA 100) or by G.L.C. (crude or *O*-acetylated products; 2m column, SE30 1%, 175°).

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Epimerization of *meso*-Hydrobenzoin (1a) to *dl*-Hydrobenzoin (2a):
A finely powdered mixture of *meso*-hydrobenzoin (6 g) and potassium hydroxide (50 g) is placed in a Claisen flask and moistened with methanol (~10–15 ml). The flask is connected to a water pump and fitted with a thermometer immersing into the mixture. The mixture is rapidly heated in an oil bath. As soon as the temperature of the mixture has reached 100–110° the pressure is gradually reduced to 15–20 torr. After complete evaporation of methanol from the mixture, the temperature of the oil bath is raised to 180–190° (internal temperature: 160–170°) and this temperature is maintained for 15 min (gentle effervescence occurs). The mixture is then cooled under vacuum and the vacuum removed. Water is added, the mixture extracted with ether, and the organic extract washed with dilute acid and dried. Evaporation of ether affords *dl*-hydrobenzoin; yield: 5.4 g (90%); m.p. 118–119°. The product may be purified by recrystallization from methanol/water (1:2) or ethyl acetate/cyclohexane (1:2); m.p. 121°.

meso-4,4′-Dimethylhydrobenzoin (**1b**) is analogously epimerized to *dl*-4,4′-dimethylhydrobenzoin (**2b**); m.p. 163° (Ref.[3], m.p. 163°).

Epimerization of *erythro*-4-Methylhydrobenzoin (1c) to *threo*-4-Methylhydrobenzoin (2c):
A mixture of 4-methylhydrobenzoin (*erythro*:*threo* = 8:2; 2.5 g), potassium hydroxide (20 g), and methanol (8 ml) is heated as described above (10 min, 160–170°/15 torr); total yield of products: 1.9 g (80%). The product mixture consists of *threo*-4-methylhydrobenzoin (**2c**; 82%), *dl*-hydrobenzoin (**2a**; 9%), and *dl*-4,4′-dimethylhydrobenzoin (**2b**; 9%), as evidenced by G.L.C. of the *O,O*-diacetylated mixture. Pure *threo*-4-methylhydrobenzoin (**2c**) may be obtained by two recrystallizations of the epimerization product mixture from ethyl acetate/cyclohexane (1:2); m.p. 128° (Ref.[10], m.p. 128–129°).

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