

The Reduction of *o*-Quinols with Complex Hydrides

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2-Acetyl-*o*-quinols (I and II) have been reduced to 1,2-dihydroxy-2-(2-hydroxypropyl)-3,5-cyclohexadienes (III and IV) with LiAlH_4 or NaBH_4 . As a result of a reversed aldol reaction combined with reduction, a catechol (IX) was formed from I as a by-product in the reduction with NaBH_4 and as main-product on treatment with $\text{Zn}/\text{Na}_2\text{CO}_3$. The cyclohexadienes (III and IV) were dehydrated by acid to form phenols (V and VI).

cis- and *trans*-1,2-Dihydroxy-3,5-cyclohexadiene ("benzeneglycols") are key intermediates in the preparation of a great many cyclitols.¹ Nakajima and co-workers² successfully prepared these benzeneglycols from tetrachlorocyclohexene by oxidation followed by dechlorination. We now wish to report that reduction of the *o*-quinols I and II with complex hydrides leads to the substituted 1,2-dihydroxy-3,5-cyclohexadienes III and IV. In analogy with previously known benzeneglycols, III and IV were readily dehydrated by acid to give the phenols V and VI, respectively.

o-Quinols have been obtained by the oxidation of phenols with sodium periodate,³ by aldol condensation of *o*-quinones with acetone,⁴ and (as acetates) in the oxidation of phenols with lead tetraacetate.⁵ Upon treatment with zinc in acidic solution, *o*-quinols are reduced to phenols;³⁻⁶ the catalytic hydrogenation of *o*-quinols leads to cyclohexanones.⁷

Treatment of an aqueous solution of *o*-quinol I with NaBH_4 and subsequent extraction with ether gave about 60 % of a neutral oil which partially crystallized. Elemental analysis and ultraviolet absorption (λ_{max} 272 $\text{m}\mu$) of the crystalline product as well as its conversion to phenol V proved that it was one of the four possible diastereoisomeric 1,3-cyclohexadienes III. The remaining aqueous phase on acidification also yielded the phenol V (about 30 %).

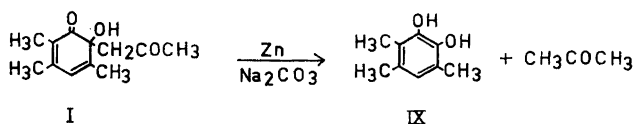
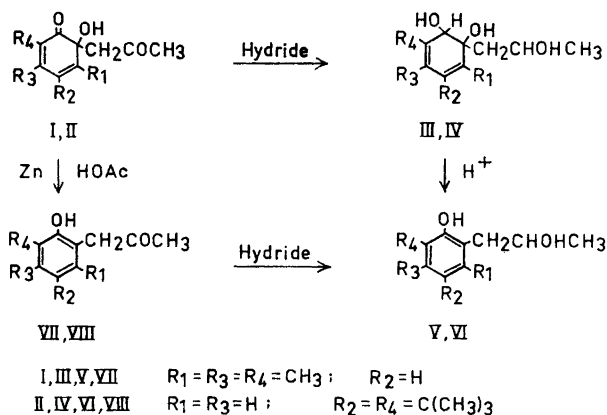
The ring carbonyl group in the 2-acetylquinol I was reduced with NaBH_4 more rapidly than the acetyl keto group. This conclusion results from the observation that during the reduction the formation of a colorless intermediate — probably 1,2-dihydroxy-2-acetyl-3,5,6-trimethylcyclohexadiene — could be demonstrated chromatographically. It disappeared upon further

reduction at the same time that the completely reduced cyclohexadiene (III) was produced.

3,4,6-Trimethylcatechol (IX) was found to be a by-product in the borohydride reduction of I. This catechol was the main product when the reduction was carried out with zinc and sodium carbonate. Obviously, the acetyl residue was removed by a base-catalyzed aldol cleavage.

Reduction of *o*-quinol II with LiAlH_4 gave the benzeneglycol IV in good yield; one of the possible diastereoisomers was obtained in a crystalline state. Treatment of IV with acid readily produced the phenol VI.

Phenols V and VI were also obtained by reduction of the acetylphenols VII and VIII, respectively, with NaBH_4 or LiAlH_4 .



EXPERIMENTAL

o-Quinols I and II were prepared according to Ref. 4. Reduction with Zn/HOAc to the 2-acetylphenols VII and VIII is described in Ref. 6. Analyses were done by Alfred Bernhardt, Mülheim, Germany.

Reduction of 2-acetyl-3,5,6-trimethyl-o-benzoquinol (I) with NaBH_4 . a) Solutions of quinol I (210 mg, 1 mmole) in water (10 ml) and of NaBH_4 (95 mg, 2.5 mmoles) in water (5 ml) were mixed. After 6 h, the mixture was extracted with ether (2×10 ml) (continued extraction gave no further material). The aqueous phase, called A, was treated as described below. The ethereal phase was washed with 1 N NaOH , dried with Na_2SO_4 and evaporated to dryness. The residue was a colorless oil (126 mg); probably a mixture of stereoisomeric cyclohexadienes III. The oil partially crystallized on scratching, and crystals were filtered off after the addition of ligroin. Recrystallization from the same solvent yielded one of the stereoisomeric 1,2-dihydroxy-2-(2-hydroxypropyl)-3,5,6-trimethyl-3,5-cyclohexadienes (III) as prisms, m.p. $113\text{--}120^\circ$. (Found: C 67.45; H 9.53. Calc. for $\text{C}_{15}\text{H}_{20}\text{O}_3$: C 67.89; H 9.50). λ_{max} (EtOH) $272\text{ m}\mu$, $\log \epsilon$: 3.71. The IR-spectrum showed no carbonyl absorption. The wide melting range was probably due to decom-

position; by thin-layer chromatography (see b below) a small amount of the phenol V was shown to be present in the cooled melt.

The alkaline aqueous phase (A) was acidified with 5 N HCl and extracted with ether. On evaporation, the extract yielded a residue of 2-(2-hydroxypropyl)-3,5,6-trimethylphenol (V, 71 mg) which, after recrystallization from hexane, was identified by m.p. and mixed m.p. with the product obtained by reduction of 2-acetyl-3,5,6-trimethylphenol (VII) as described below.

b) The following experiment is intended to demonstrate that the ring carbonyl group is reduced more readily than the acetyl group. During a reduction carried out in a manner similar to that described above under a), the yellow color of the solution disappeared within 30 min, at the same time that an absorption maximum at 269 μ appeared. The course of the reaction was followed by extracting portions of the solution with ether at different time intervals and then chromatographing the extracts on plates (SiO_2 ; benzene-ethyl acetate 1:1; development with iodine vapor). Two main components were shown to be present after 30 min; one of them had the same R_F -value (0.78) as 3,4,6-trimethylcatechol (IX), whereas the other (R_F : 0.20) was most likely 1,2-dihydroxy-2-acetyl-3,5,6-trimethyl-3,5-cyclohexadiene. The latter component disappeared successively in samples with longer reaction times at the same time that a product with the same R_F -value (0.30) as the completely reduced cyclohexadiene (III) was formed.

Reduction of 2-acetyl-4,6-di-tert-butyl-o-benzoquinol II with LiAlH_4 . A solution of quinol II (1.5 g) in ether (25 ml) was added to a suspension of LiAlH_4 (600 mg) in ether (25 ml). After 10 min excess LiAlH_4 was destroyed with wet ether. The mixture was filtered and the filtrate dried (Na_2SO_4) and evaporated to dryness. The residue (1.6 g), which was probably a mixture of stereoisomeric cyclohexadienes (IV), slowly crystallized in part. The crystals (600 mg) were filtered off after the addition of a small amount of hexane. Recrystallization from hexane yielded one of the possible stereoisomeric 1,2-dihydroxy-2-(2-hydroxypropyl)-4,6-di-tert-butyl-3,5-cyclohexadienes (IV) as narrow plates, m.p. 139–141°. (Found: C 72.58; H 10.51. Calc. for $\text{C}_{17}\text{H}_{26}\text{O}_3$: C 72.30; H 10.71). λ_{max} (EtOH) 263 μ , log ϵ : 3.73. The IR-spectrum showed no carbonyl absorption.

2-(2-Hydroxypropyl)-3,5,6-trimethylphenol (V). A. *From 1,2-dihydroxy-2-(2-hydroxypropyl)-3,5,6-trimethyl-3,5-cyclohexadiene (III).* A solution of the crystalline cyclohexadiene III (50 mg) in water (10 ml) was acidified with a drop of 5 N HCl and thereupon extracted with ether (5 ml). The extract was evaporated to dryness and the residue recrystallized from hexane. Phenol V was obtained as prisms grown together in the form of rosettes (30 mg), m.p. 83–84°. (Found: C 74.20; H 9.24. Calc. for $\text{C}_{12}\text{H}_{18}\text{O}_2$: C 74.19; H 9.34).

B. *From 2-acetyl-3,5,6-trimethylphenol (VII).* Acetylphenol VII (130 mg) was reduced with NaBH_4 in aqueous solution. After 3 h the reaction mixture was extracted with ether; and the extract was dried and evaporated to dryness. The residue, upon recrystallization from hexane, yielded phenol V (92 mg), identical by melting point and mixed melting point with the product obtained according to A.

2-(2-Hydroxypropyl)-4,6-di-tert-butylphenol (VI). A. *From 1,2-dihydroxy-2-(2-hydroxypropyl)-4,6-di-tert-butyl-3,5-cyclohexadiene (IV).* One drop of 5 N HCl was added to a solution of cyclohexadiene IV (94 mg) in ethanol (2 ml). The mixture was treated with ether and the ethereal solution was washed with water, dried and evaporated to dryness. The residue was recrystallized from hexane and phenol VI obtained as irregular prisms, m.p. 89–91°. (Found: C 77.18; H 10.56. Calc. for $\text{C}_{17}\text{H}_{26}\text{O}_2$: C 77.22; H 10.67).

B. *From 2-acetyl-4,6-di-tert-butylphenol (VIII).* Acetylphenol VIII (3.7 g) was reduced with LiAlH_4 in ether solution. After recrystallization from hexane, 2.1 g of VI, m.p. 89–91°, was obtained.

Treatment of 2-acetyl-3,5,6-trimethyl-o-benzoquinol (I) with $\text{Zn}/\text{Na}_2\text{CO}_3$. Powdered zinc (10 g) and 10 % Na_2CO_3 solution (25 ml) were added to a stirred solution of quinol I (0.50 g) in water (25 ml). After 30 min, the filtered solution was extracted with ether. The dried ether extract provided a crystalline product (0.34 g). Repeated sublimation gave 0.18 g of 3,4,6-trimethylcatechol (IX) identified by m.p. and mixed m.p. (112°, Kofler hot stage) with authentic material. The latter was obtained by reduction of 3,5,6-trimethyl-*o*-quinone according to Beer et al.,⁸ who, however, report melting point 118–120° for IX.

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