

SYNTHESIS AND REACTIONS OF 6-HYDROXY-2,4-DIMETHYL-1,3-BENZODIOXANE

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The reaction of hydroquinone and acetaldehyde in a mixture of acetic and hydrochloric acids (3:1) at 0-5°C gives 6-hydroxy-2,4-dimethyl-1,3-benzodioxane, which forms ethers and esters at the hydroxy group, undergoes diazo coupling, and, under the influence of acids, undergoes polycondensation with opening of the 1,3-dioxane ring.

Although the reaction of phenols with aldehydes in acidic media is regarded as a general method for the synthesis of 1,3-benzodioxanes (the Borsche-Berkout method) [1, 2], this reaction actually may lead to compounds with different structures, particularly in the case of polyhydric phenols; for example, it can lead to porphyrinlike compounds [3], 1,3,5-benzo-trioxepines [4], and 3,3',6,6'-tetrahydroxydiphenylmethane [5]. In addition, in the presence of acidic catalysts hydroquinone may react with formaldehyde and other aldehydes to give polycondensation products [6]. From the data presented thus far it is apparent that the usefulness of the Borsche-Berkout method for the synthesis of 1,3-benzodioxane compounds from polyhydric phenols requires confirmation, despite the previously described [7] example of the preparation of a 1,3-benzodioxane derivative from 2,6-dichlorohydroquinone and chloral.

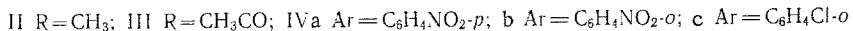
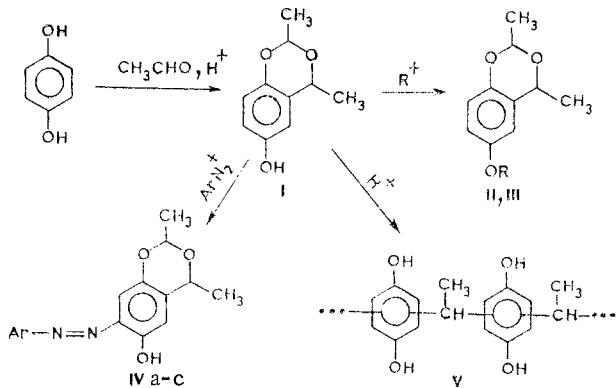
In order to develop a method for the preparation of 1,3-benzodioxane derivatives on the basis of hydroquinone we investigated the reaction of this dihydric phenol with acetoaldehyde. We found that hydroquinone does not undergo perceptible changes when it is treated with acetaldehyde in ether or benzene containing hydrochloric acid; this is in direct contrast to phenol, which reacts under similar conditions to give 2,4-dimethyl-1,3-benzodioxane [8]. We obtained the desired product, viz., 6-hydroxy-2,4-dimethyl-1,3-benzodioxane (I), by the reaction of hydroquinone with acetaldehyde (1:2) in a mixture of acetic and concentrated hydrochloric acids (3:1) at 0-5°C; paraldehyde can also be used in place of acetaldehyde.

When benzodioxane I is treated with dimethyl sulfate and alkali, it is converted to the methyl ether (II), and treatment with acetic anhydride gives the corresponding acetate (III). We found that benzodioxane I is capable of undergoing diazo coupling only with sufficiently active diazo components such as nitro- and chlorobenzene diazonium salts to give azo compounds IV. No reaction occurs with diazotized aniline, p-toluidine, and p-anisidine. The method that we developed for the synthesis of arylazo derivatives of 1,3-benzodioxane with electron-acceptor substituents in the azoaryl group may serve as a good supplement to the known method [9] for the preparation of azo compounds of the 1,3-benzodioxane series with electron-donor substituents in the azoaryl group, which is based on diazo coupling of diazotized 6-amino-1,3-benzodioxane with phenols.

In conformity with the literature data [1] benzodioxane I is relatively stable in alkaline media but is sensitive to the action of acids. When it is dissolved in dilute alkali, it withstands heating to the boiling point of the solution, whereas under the influence of hydrochloric acid it is easily decomposed with opening of the 1,3-dioxane ring. The decomposition product is a solid that does not melt upon heating to 300°C; on the basis of analytical and spectral data we assigned a polymer structure of the novolac type (V) to this product.

The molecular mass of polymer V formed during brief reaction (0.5 h at 20°C) of benzodioxane I in a mixture of hydrochloric and acetic acids (1:5) is ~1300. A polymer with a higher molecular mass is formed when the reaction time is increased. The hydroquinone

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residues in polymer V are linked with one another through ethylidene $[\text{CH}(\text{CH}_3)]$ groups. In addition to these, the macromolecule evidently contains one or several $\text{CH}(\text{CH}_3)-\text{O}-\text{CH}(\text{CH}_3)$ groups (judging from the results of elementary analysis and the IR spectrum). Polymer V is insoluble in water but is soluble in aqueous alkali, acetone, alcohol, dioxane, and pyridine. This polymer reacts with acetic anhydride through the hydroxy group to give the corresponding acetate. It should be noted that polymer V is formed as a side product in the synthesis of benzodioxane I; an increase in the temperature promotes the formation of the polymer.

EXPERIMENTAL

The IR spectra were recorded with a UR-20 spectrometer. The UV spectra were recorded with a Specord UV-Vis spectrophotometer. The PMR spectra were recorded with a Tesla BS-487 C spectrometer (80 MHz) with hexamethyldisiloxane as the internal standard.

6-Hydroxy-2,4-dimethyl-1,3-benzodioxane (I). A 5-ml sample of concentrated hydrochloric acid dropwise (with cooling of the reaction flask with ice) to a solution of 9 g (0.2 mole) of acetaldehyde or 13 g (0.1 mole) of paraldehyde in 15 ml of acetic acid, 11 g (0.1 mole) of hydroquinone was added, and the mixture was stirred at 0-5°C until all of the hydroquinone had dissolved (6-8 h). The resulting light-brown solution was maintained at 0-5°C for another 3 h, after which it was diluted with 100 ml of water, and the aqueous mixture was extracted with chloroform (five 50-ml portions). The extract was washed with water and dried over calcined magnesium sulfate. The chloroform was removed by distillation, and the residue was distilled *in vacuo* to give 13 g (72%) of a viscous colorless oil with bp 142-143°C (4 hPa). UV spectrum (in heptane), λ_{max} (log ϵ): 220 (3.65), 227 (3.60), and 295 nm (3.47). IR spectrum (in CCl_4): 3620 (free O-H); 3430 broad (associated O-H); 2945, 2885, and 2800 cm^{-1} (CHCH_3). PMR spectrum (in CCl_4): 1.34 (3H, d, $J = 6$ Hz, 4- CH_3), 1.40 (3H, d, $J = 5$ Hz, 2- CH_3), 4.90 (1H, q, $J = 6$ Hz, 4-H), 5.03 (1H, q, $J = 5$ Hz, 2-H), 6.42-6.58 (3H, m, C_6H_3), and 7.16 ppm (1H, broad, O-H). Found: C 66.60; H 6.9%; M⁺ 180. $\text{C}_{10}\text{H}_{12}\text{O}_3$. Calculated: C 66.6; H 6.7%; M 180 (also see [10]).

6-Methoxy-2,4-dimethyl-1,3-benzodioxane (II). A 53-g (0.42 mole) sample of dimethyl sulfate was added at 28-32°C in the course of 4 h to a solution of 20 g (0.11 mole) of benzodioxane I in a mixture of 200 ml of acetone and 400 ml of 10% sodium hydroxide solution, after which the mixture was stirred for 2 h. It was then poured into 500 ml of water, and the aqueous mixture was extracted with chloroform (four 150-ml portions). The extract was washed with water and dried over calcined magnesium sulfate. The chloroform was removed by distillation, and the residue was distilled *in vacuo* to give 18.4 g (85%) of methyl ether II as a colorless oil with bp 110°C (6 hPa). PMR spectrum (in CCl_4): 1.42 (3H, d, $J = 5$ Hz, 2- CH_3), 1.44 (3H, d, $J = 6.5$ Hz, 4- CH_3), 3.65 (3H, s, CH_3O), 4.96 (1H, q, $J = 6.5$ Hz, 4-H), 5.04 (1H, q, $J = 5$ Hz, 2-H), and 6.42-6.62 ppm (3H, m, C_6H_3). Found: C 68.0; H 7.4%. $\text{C}_{11}\text{H}_{14}\text{O}_3$. Calculated: C 68.0; H 7.2%.

6-Acetoxy-2,4-dimethyl-1,3-benzodioxane (III). A mixture of 20 g (0.11 mole) of benzodioxane I and 40 g (0.4 mole) of acetic anhydride in 40 ml of acetic acid was maintained at room temperature for 24 h, after which it was refluxed for 6 h. It was then cooled and poured over 200 g of ice, and the aqueous mixture was extracted with chloroform (four 100-ml portions). The extract was washed successively with water, 2% sodium carbonate solution, and water, and the chloroform was removed by distillation. The residue was distilled *in*

vacuo to give 22 g (90%) of acetate III as a colorless oil with bp 168°C (13 hPa). IR spectrum (in CCl_4): 1765 cm^{-1} (C=O). Found: C 64.6; H 6.3%. $\text{C}_{12}\text{H}_{14}\text{O}_4$. Calculated: C 64.9; H 6.3%.

Diazo Coupling of Benzodioxane I. A) A diazonium solution obtained by diazotization of 3.83 g (28 mmole) of *p*-nitroaniline by the method in [11] was added in the course of 1.5 h to a solution of 5 g (28 mmole) of benzodioxane I in 500 ml of 4% sodium hydroxide solution while maintaining the temperature of the mixture at 0-5°C, after which the mixture was stirred until the diazonium compound disappeared. The mixture was then acidified to pH 4, and the precipitated azo compound was removed by filtration, washed with water, and dried to give 6.1 g (67%) of 7-(*p*-nitrophenylazo)-6-hydroxy-2,4-dimethyl-1,3-benzodioxane (IVa) in the form of red needles with mp 201-201.5°C [from benzene-ethanol (1:2)]. UV spectrum (in alcohol), λ_{max} (log ϵ): 271 (3.79), 355 (4.34), and 494 nm (3.92). PMR spectrum (d_6 -DMSO): 1.46 (3H, d, J = 5 Hz, 4- CH_3), 1.55 (3H, d, J = 6 Hz, 2- CH_3), 5.15 (1H, q, J = 5 Hz, 4-H), 5.59 (1H, q, J = 6 Hz, 2-H), 6.80-7.00 (2H, m, C_6H_2), 8.13 (2H, d, J = 9 Hz, $\text{C}_6\text{H}_4\text{NO}_2$), and 8.35 ppm (2H, J = 9 Hz, $\text{C}_6\text{H}_4\text{NO}_2$). Found: C 58.4; H 4.7; N 12.4%; M⁺ 329. $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_5$. Calculated: C 58.3; H 4.7; N 12.7%; M 329.

B) Diazo coupling of benzodioxane I with diazotized *o*-nitroaniline by a procedure similar to that in the preceding experiment gave 7-(*o*-nitrophenylazo)-6-hydroxy-2,4-dimethyl-1,3-benzodioxane (IVb) (61%) in the form of violet crystals with mp 179-5-180.5°C [from benzene-ethanol (1:2)]. UV spectrum (in alcohol), λ_{max} (log ϵ): 264 (3.98), 356 (4.14), and 517 nm (3.85). Found: C 58.4; H 4.6; N 12.8%; M 329. $\text{C}_{16}\text{H}_{15}\text{N}_3\text{O}_5$. Calculated: C 58.3; H 4.7; N 12.7%; M 329.

C) Diazo coupling of benzodioxane I with diazotized *o*-chloroaniline gave 7-(*o*-chlorophenylazo)-6-hydroxy-2,4-dimethyl-1,3-benzodioxane (IVc) (97%) in the form of orange needles with mp 175-175.5°C (from alcohol). UV spectrum (in alcohol), λ_{max} (log ϵ): 362 (4.23) and 458 nm (3.71). PMR spectrum (CDCl_3): 1.55 (3H, d, J = 5 Hz, 4- CH_3), 1.66 (3H, d, J = 6 Hz, 2- CH_3), 5.08 (1H, q, J = 5 Hz, 4-H), 5.65 (1H, q, J = 6 Hz, 2-H), 6.90-7.85 (6H, m, Ar), and 13.39 ppm (1H, s, OH). Found: C 60.3; H 4.8; Cl 11.0%; M 332 (by isothermal distillation). $\text{C}_{16}\text{H}_{15}\text{ClN}_2\text{O}_3$. Calculated: C 60.3; H 4.7; Cl 11.1%; M 318.5.

Acidic Cleavage of Benzodioxane I. A) A 1-ml sample of hydrochloric acid (sp. gr. 1.18) was added to a solution of 0.5 g (3 mmole) of benzodioxane I in 5 ml of acetic acid, and the mixture was maintained at 20°C for 30 min. It was then poured into 40 ml of water, and the resulting precipitate was removed by filtration, washed with water, and dried to give 0.29 g of polymer V. Reprecipitation of the product from a solution in acetone-benzene (1:1) by means of hexane gave a light-brown powder, which did not melt when it was heated to 300°C. IR spectrum (in KBr): 3400 broad (O-H); 3040 (aromatic C-H); 2980, 2940, and 2880 (CHCH_3); 1630 and 1505 (C=C); 1430 (CHCH_3); 1070 (C-O-C); 830 cm^{-1} (C_6H_2). PMR spectrum (d_6 -acetone): 1.10-1.60 (3H, m, CH_3), 3.45 (1H, s, OH), 4.25-4.75 (1H, m, CH), 6.25-6.85 (2H, m, Ar), and 7.78 ppm (1H, s OH). Found: C 68.9; H 5.8%; M 1283; 1290 (by ebullioscopy).

B) A 2-ml sample of concentrated hydrochloric acid was added to a solution of 0.5 g (3 mmole) of benzodioxane I in 10 ml of acetic acid, and the mixture was maintained at 20°C for 5 h. It was then diluted with water, and the precipitate was separated and dried to give 0.41 g of polymer V in the form of a light-brown powder with mp > 300°C (after reprecipitation from solution in acetone by the addition of benzene). According to the IR spectrum, the compound obtained was identical to the sample described above. Found: M 2960 (by ebullioscopy).

Treatment of polymer V with acetic anhydride in pyridine at 25°C for 3 h gave an aqueous alkali-insoluble acetate, which indicates esterification of the hydroxy groups. The product was a light-gray powder that decomposed when it was heated above 160°C (after reprecipitation from solution in benzene by means of hexane). IR spectrum (in KBr): 1765 cm^{-1} (C=O). Found: C 64.7; H 5.5%.

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SYNTHESIS OF VINYL AND ETHYL ETHERS OF 4- β -HYDROXYETHYL-1,4-PERHYDRO-THIAZINE 1,1-DIOXIDE

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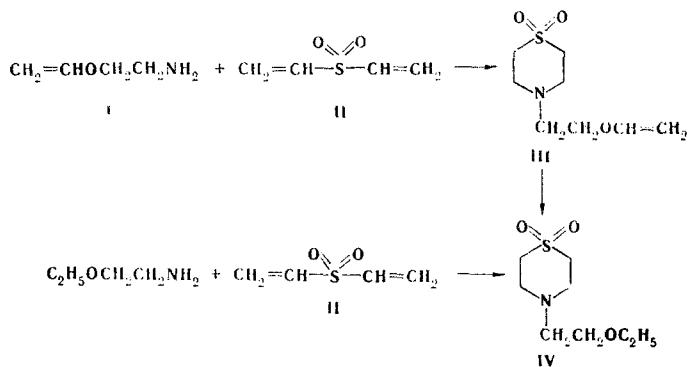
UDC 547.869.2'371'435.1.27.544.07:543.422

Derivatives of 1,4-perhydrothiazine 1,1-dioxide that contain an ether group were synthesized by the reaction of vinyl and ethyl ethers of monoethanolamine with divinyl sulfone in methanol.

It is known that one of the methods for the synthesis of derivatives of 1,4-thiazine 1-oxide and 1,4-thiazine 1,1-dioxide is the reaction of primary amines with divinyl sulfoxide and divinyl sulfone [1-4]. A 1,4-thiazine 1,1-dioxide with an ester group was obtained by the reaction of glycine ethyl ester with divinyl sulfone [5]. N-Vinyloxy(alkoxy)alkyl-substituted 1,4-thiazine 1,1-dioxides have not yet been described in the literature.

In order to synthesize a 1,4-perhydrothiazine 1,1-dioxide derivative that contains a vinyl ether fragment we studied the reaction of monoethanolamine vinyl ether (I) with di-vinyl sulfone (II).

Vinyl ether I was subjected to reaction with an equimolar amount of sulfone II in methanol (with cooling) with subsequent brief refluxing of the reaction mixture. Heterocyclization occurs under these conditions, and 4- β -hydroxyethyl-1,4-perhydrothiazine 1,1-dioxide vinyl ether (III) is formed in 82% yield. The corresponding 4- β -hydroxyethyl-1,4-perhydrothiazine 1,1-dioxide ethyl ether (IV) was obtained by the reaction of monoethanolamine ethyl ether with sulfone II.



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