Direct Synthesis of *trans*-1,4-Diacetoxycyclohexa-2,5-diene by Electrochemical Reduction of *r*-1,*t*-4-Diacetoxy-*t*-2,*c*-3-dibromocyclohex-5-ene†

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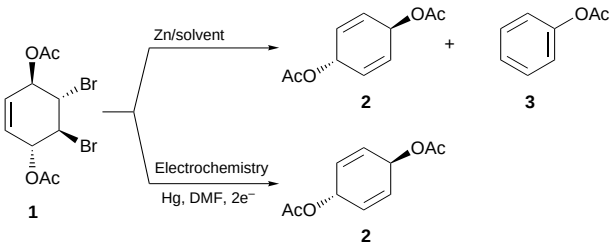
Electrochemical reduction of *r*-1,*t*-4-diacetoxy-*t*-2,*c*-3-dibromocyclohex-5-ene **1** gives only *trans*-1,4-diacetoxycyclohexa-2,5-diene **2** in good yield while the commonly used Zn reduction gives a product mixture containing **2** and acetoxybenzene **3** derived from acetoxy elimination.

Cyclohexadienediols have been identified as intermediates in the biological breakdown of arene oxides by Burice *et al.*[1] These compounds are also useful intermediates for the preparation of natural aromatic compounds, quinone derivatives,[2] conduritols[3] and cyclitols.[4] The direct and easy electrochemical synthesis of *trans*-1,4-diacetoxycyclohexa-2,5-diene **2** leading to conduritol and inositols will facilitate the investigation of biological activities of this compound acting as an inhibitor of D-glycosidases and exhibiting an inhibitory effect on the growth of tumour cells.[5]

For the synthesis of cyclohexadienediols, a method based on 1,2-nucleophilic addition of various alkyl metal reagents such as RMgX,[6] RLi[7] and R_3Al[8] to *p*-benzoquinones has been used. These type of reactions result in poor yields and diastereoisomeric mixtures.[9] Another method would be the direct reduction of *p*-benzoquinone with metal hydrides (*e.g.*, $LiAlH_4$, $NaBH_4$); however, these reagents give mainly hydroquinone and a small amount of 1,4-dihydroxycyclohexadiene either with little or no stereoselectivity.[10] Therefore, in order to block the formation of hydroquinone one of the double bonds must be protected by bromination before reducing with metal hydrides. Then, there are two possible ways to eliminate the bromines: (*a*) dehalogenation with conventional reducing reagents, or (*b*) electrochemical reduction. The dehalogenation of vicinal dehalides with zinc[11] has been performed for the synthesis of new double bonds which can be reduced to yield the conduritols having the desired conformation.[12] In addition to zinc, magnesium, iodine and electrochemical reduction can be used.[13] Electroreduction of 1,2-dibromides as a preparative method offers an attractive alternative to chemical procedures due to the potential mildness of the reaction conditions. Consequently, there has been a need for a simple, efficient, and a stereospecific procedure for the preparation of cyclohexadienediols and compounds of related structure.

In this study, we report the ready synthesis of *trans*-1,4-diacetoxycyclohexa-2,5-diene **2**, which we first synthesized by the electroreduction of *r*-1,*t*-4-diacetoxy-*t*-2,*c*-3-dibromocyclohex-5-ene **1**[12] and to make comparisons between the Zn and electrochemical reductions.

Reductions performed with Zn in different solvents gave mixtures of two compounds, acetoxybenzene **3** and the desired diene product **2**, depending on the reaction conditions. The ratio of **2** to **3** in the reaction mixture was found to be dependent on the nature of the solvent used and the temperature. While compound **3** was the only product in DMSO at 90 °C, a mixture containing compounds **2** and **3** was obtained in diethyl ether and $MeCO_2H$ solutions at 45 °C for the reductions with Zn. In the latter reaction conditions, compound **2** was the predominant product (**2**:**3** = 3:1).



Scheme

Cyclic voltammetry was performed on **1** using a mercury electrode in order to determine the reduction potential of **1**. Only a broad and irreversible peak was observed at about −1.5 V (SCE) at room temperature at sweep rates up to 100 mV s^{-1}. Cyclic voltammograms showed the same peak shape and cathodic peak potential as in the literature.[14] The reductions were carried out in a divided cell on a stirred mercury electrode using DMF as solvent and 0.1 mol dm^{-3} $LiClO_4$ as supporting electrolyte. A constant potential electrolysis (cpe) at −1.7 V of **1** gave exclusively compound **2** in high yields.

It has been reported that *β*-haloethers and esters on treatment with Zn undergo alkoxy-halo-elimination reaction[11,15] or acetoxy elimination resulting from removal of one acetoxy group by Lewis acid ($ZnBr_2$) formed in the reduction stage after formation of **2** by debromination. In the case of acetoxy-halo-elimination, benzene or 1-acetoxy-2-bromocyclohexa-3,5-diene would be obtained, but these compounds were never observed. The formation of compound **3** can be explained by removal of one acetoxy group by $ZnBr_2$ yielding a cation and then an aromatization process.[16]

In contrast to Zn reductions, we obtained quantitatively only compound **2** by the electrochemical reduction of **1** on Hg electrodes in DMF. Similar results have been reported for the electrochemical reduction of vicinal dibromides.[14,17,18] Two possible mechanisms are proposed for this reduction in these studies: first carbanion formation followed either by proton abstraction resulting in a monobromo compound or elimination of the second bromide giving compound **2**. The second mechanism is the concerted elimination yielding only compound **2**. In both aprotic and protic conditions, since we never observed either a monobromo compound or an aromatic compound, the mechanism of electrochemical debromination can therefore be considered as concerted.

In conclusion, a short and practical synthesis of **2** has been described. We have shown that electrochemical reduction of **1** for the synthesis of **2** has some advantages over Zn reduction. These are selectivity, mild conditions of the reaction, simplicity of the procedure, and good yields of the product.

Experimental

Cyclic voltammetric determinations were performed using a Potentioscan Wenking POS 73 potentiostat, YEW 3022 A4 X-Y recorder. NMR spectra were recorded on a Varian-Gemini 2000 spectrometer at 200 MHz for ^{1}H NMR and 50 MHz for ^{13}C NMR. The IR spectra were recorded on a Mattson 1000 FTIR spectro-

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meter. In all cases reaction mixtures were separated by column chromatography.

Zn Reduction of **1**.—(*i*) To a solution of **1** (200 mg, 0.561 mmol) in DMSO (5 ml) was added 73 mg (1.1 mmol) of zinc dust and 20 mg of iodine. The mixture was magnetically stirred at 95 °C for 12 h. After cooling to room temperature, water (25 ml) and diethyl ether (25 ml) were added. The aqueous phase was extracted with diethyl ether (2×25 ml), and the combined organic extracts were dried (Na_2SO_4). Evaporation of the solvent gave acetoxybenzene **3**. (*ii*) To a solution of **1** (200 mg, 0.561 mmol) in diethyl ether (10 ml) and $MeCO_2H$ (2.5 ml) was added zinc dust (325 mg, 5 mmol). The mixture was magnetically stirred at 40–50 °C for 2 h and then enough water was added dropwise to dissolve any solid and give a clear solution. The aqueous phase was extracted with diethyl ether (2×25 ml) and the combined organic extracts were dried (Na_2SO_4). Evaporation of the solvent gave acetoxybenzene **3** plus **2** in a ratio of 1:3 (combined yield: 78%).

Cathodic Reduction of **1**.—Cathodic reduction of **1** (300 mg, 0.842 mmol) was carried out at room temperature in a divided three-compartment-cell separated by a porous glass diaphragm. A platinum electrode and saturated calomel electrode (SCE) served as a counter electrode and reference electrode, respectively. The solvent was 50 ml of DMF containing $LiClO_4$ (0.1 mol dm^{-3}). Electrolysis was carried out at constant potential (−1.7 V) until the current became zero. Work-up as described above with diethyl ether and removal of the solvent under reduced pressure at room temperature gave **2** (96%): δ_H ($CDCl_3$) 6.46 (m, 4 H), 5.70 (m, 2 H), 2.07 (s, 6 H); δ_C ($CDCl_3$) 172.32, 130.75, 66.03, 22.96; ν_{max} (KBr)/cm^{-1} 2927, 1753, 1446, 1395 and 1242; mp 89–90 °C (recrystallized from hexane–CCl_4).

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