SYNTHESIS OF 3,4-bis-(p-HYDROXYPHENYL)-HEXANE-3,4-DIOL BY CATHODIC HYDRODIMERIZATION OF p-HYDROXYPROPIOPHENONE

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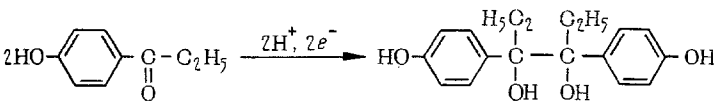
One of the stages in the preparation of the estrogen hormones, diethylstilbestrol and phosphestrol [1], is the reduction of p-hydroxypropiophenone to 3,4-bis-(p-hydroxyphenyl)-hexane-3,4-diol:



The reduction can be carried out with the aid of alloys of alkali metals with lead or with amalgams, or electrochemically [2, 3]. Despite the significantly high yield of the reduction, it is undesirable to use compounds of lead in mercury in industrial processes.

The synthesis of 3,4-bis-(p-hydroxyphenyl)-hexane-3,4-diol using a tin cathode is described below, and a comparison is shown of the results obtained with those obtained using the same process with a mercury cathode.

The reduction was carried out in an electrolytic cell with a ceramic diaphragm. The anode space was filled with a 20% solution of sodium sulfate; the anode was lead. The catholyte was usually a 10% solution of NaOH containing p-hydroxypropiophenone. The cathodes were either a layer of mercury, being poured onto the bottom of the vessel, or a copper cylinder electrolytically coated with tin [4]; the thickness of the coating was 10 microns (before each experiment a fresh coating was laid down). The 3,4-bis-(p-hydroxyphenyl)-hexane-3,4-diol was isolated by the known method [3]. The product obtained had mp 200-205°C; after recrystallization from acetone the mp was 226°, the elementary composition was: calculated, %: C 71.52; H 7.29; found, %: C 71.34; H 7.37.

For the electrolysis aqueous and aqueous-alcoholic alkali solutions were used; also, aqueous and aqueous-alcoholic acid solutions. The experimental results, given in Table 1, show that the maximum yields of the pinacone of p-hydroxypropiophenone were achieved in aqueous alkali solutions with the tin and with the mercury cathodes.

p-Hydroxypropiophenone had poor solubility in the aqueous and aqueous-alcoholic acid media, and the reduction proceeded with little effect; the presence of alcohol in the alkaline medium decreased the yield of product. Under these conditions most of the current was expended in discharging hydrogen, and the unreduced p-hydroxypropiophenone remaining in the solution was isolated with the final product. Hence, the most favorable medium for the electro-reduction, both with the tin and with the mercury cathode, was 10% NaOH solution.

The effect of concentration of the initial product on the yield of 3,4-bis-(p-hydroxyphenyl)-hexane-3,4-diol was studied over the concentration range 0.065-1.32 mole/liter. With the tin cathode, a decreased yield of the pinacone, based either on the starting material or on the current, was observed below a p-hydroxypropiophenone concentration of 0.22 mole/liter. In line with this decreased yield based on the current, the yield of hydrogen increased. For electrolysis with the mercury cathode, the yield of pinacone increased from 64-91% based on materials and from 34-48% based on current when the concentration of p-hydroxypropiophenone was increased from 0.065-0.88 mole/liter.

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TABLE 1. Effect of Solution Composition on the Yield of 3,4-bis-(p-hydroxyphenyl)-hexane-3,4-diol (concentration of p-hydroxypropiophenone, 0.22 mole/liter; temperature, 20°), Calculated on the Hydroxypropiophenone Charged (h.c.), on the Hydroxypropiophenone Reacting (h.r.), and on the Current

Medium	Conc. of C_2H_5OH (in % by vol.)	Tin cathode					Mercury cathode				
		D_c (in A/dm²)	Q_{prop} (in A/h)	Yield (in %)			D_c (in A/dm²)	Q_{prop} (in A/h)	Yield (in %)		
				on h.c.	on h.r.	on the current			on h.c.	on h.r.	on the current
NaOH concentration (in %)											
2,5	0	5,0	4,0	0	0	0	18,0	1,5	48,0	—	25,0
5	0	5,0	4,0	78,1	78,1	17,4	18,0	1,5	76,0	—	41,0
10	0	5,0	4,0	87,0	87,0	19,4	18,0	1,5	80,0	80,0	43,5
15	0	5,0	4,0	63,2	83,5	14,1	18,0	1,5	73,5	—	39,4
10	50,0	5,0	4,0	62,5	90,5	14,0	18,0	1,5	Considerable amount of unreacted propiophenone remaining		
10	50,0	5,0	6,0	67,4	85,0	15,0	18,0	3,0	50,0	73,0	15,6
10	50,0	10,0	4,0	8,3	26,7	1,9	—	—	—	—	—
H_2SO_4 concentration (in %)											
3	0	10,0	4,0	0	0	0	18,0	4,5	0	0	0
3	50,0	5	4,0	24,4	29,6	5,5	18,0	4,5	19,4	29,0	3,8

Note: D_c — cathodic current density; Q_{prop} — quantity of electricity consumed.

The cathodic current density was shown to have a significant effect on the electro-reduction of p-hydroxypropiophenone; the maximum yield of product was obtained with a current density of 2 A/dm². With the mercury cathode, a current density range of 7-18 A/dm² can be recommended, the optimal being 18 A/dm².

Carrying out the reduction at temperatures above 40° caused a decrease in the yield of the pinacone while agitation increased the yield of product, both with the tin and with the mercury cathode.

The work carried out elucidated the optimum conditions for the preparation of 3,4-bis-(p-hydroxyphenyl)-hexane-3,4-diol using a tin cathode, with yield of 90% based on materials and 20% based on current; and using a mercury cathode, with yield of 90% based on materials and 48% on current.

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