The Process of 4-Hydroxybiphenyl Synthesis from 4-Isopropylbiphenyl

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ABSTRACT: The kinetics of the oxidation of 4-isopropylbiphenyl (**1**) in the liquid phase by oxygen to 1-(1,1′-biphenyl-4-yl)-1-methylethyl hydroperoxide (**2**) was investigated. The oxidizability of **1** in the temperature range from 60°C to 120°C and the overall energy activation of oxidation were determined. Long-term oxidation of **1** to **2** in the temperature range of 80–120°C was investigated, and the yield and selectivity of the process were determined. Pure **2** was obtained, and its properties were defined. 4-Hydroxybiphenyl was obtained as a result of the acidic decomposition of **2**. © 2008 Wiley Periodicals, Inc. Int J Chem Kinet 40: 527–532, 2008

INTRODUCTION

The presented investigations concern a perspective method of synthesis of 4-hydroxybiphenyl (**3**) from 4-isopropylbiphenyl (**1**) (Scheme 1) by means of a procedure similar to the process of phenol synthesis from cumene by applying Hock and Lang's method.

Compound **3** is an important raw material in the pharmaceutical industry and in the production of plant pesticides, emulsifiers, and anisotropic polymers with higher thermal and mechanical resistance [1,2].

The fundamental method for producing **3**, applied on the industrial scale, nowadays is sulfonation. This process is run in two stages: sulfonation of biphenyl and the fusion of the obtained (1,1′-biphenyl)-4-sulfonic acid with sodium hydroxide to **3** [3]. This way of producing **3** is characterized by high consumption of energy and environmental pollution due to the accumulation of wastes. A highly aggressive environment of reaction causes fast corrosion of apparatus.

The solution suggested in the present paper has not been quoted so far in the literature. Only a Japanese patent describes the synthesis of 3- and 4-hydroxybiphenyls, applying a mixture of 3- and 4-isopropylbiphenyls in a ratio of 98.6:1.2 as raw material. The oxidation was accomplished in a double-phase system in an alkaline aqueous emulsion in the presence of Bu_4NBr. The resulting product contained 38.9% hydroperoxides and 36.5% alcohols. The reaction product was refluxed with H_2SO_4 and aq. H_2O_2 in MeOH, yielding 88.6% 3- and 4-hydroxybiphenyls [4].

In the suggested method, the key stage for producing **3** is the oxidation of **1** to 1-(l,1′-biphenyl-4-yl)-1-methylethyl hydroperoxide (**2**). The oxidation of hydrocarbons in the liquid phase with oxygen to

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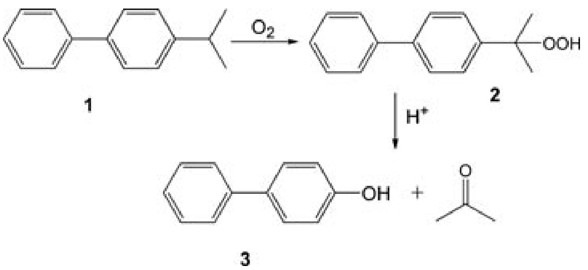


Scheme 1 Method of 4-hydroxybiphenyl synthesis.

hydroperoxides is a free-radical, chain process [5–7]:

$$
\begin{array}{ll}
\text{Initiation} & \text{initiator} \rightarrow \text{radicals} \\
\text{Propagation} & R^\bullet + O_2 \xrightarrow{k_o} RO_2^\bullet \\
 & RO_2^\bullet + RH \xrightarrow{k_p} ROOH + R^\bullet \\
\text{Termination} & 2RO_2^\bullet \xrightarrow{k_t} \text{stable products}
\end{array}
$$

For liquid-phase oxidation, under $p_{O_2} \approx 0.1$–1 atm (then the concentration of dissolved dioxygen in hydrocarbons is higher than 10^{-4} mol L^{-1}), the reaction of alkyl radical with oxygen is very fast and alkyl radicals are rapidly converted into peroxyl radicals. Because of this, the concentration of alkyl radicals is much lower than that of peroxyl radicals, and chains are terminated only by the reaction between two peroxyl radicals, while propagation is limited by the reaction of peroxyl radicals with hydrocarbons [8,9].

Assuming that the reaction runs in compliance with the presented diagram and assuming a stationary state for the rate of oxidation, the following expression will result:

$$r_{ox} = r_i^{1/2} \frac{k_p}{k_t^{1/2}} C_{RH} \qquad (1)$$

where r_{ox} is the rate of oxidation, r_i is the rate of initiation reaction, k_p is the constant rate of the propagation reaction, k_t is the constant rate of the termination reaction, and C_{RH} is hydrocarbon concentration.

The value of $k_p/k_t^{1/2}$, called oxidizability, is a measure of reactivity of hydrocarbons in the free-radical, chain oxidation. The combination with the Arrhenius equation allows transformation of Eq. (1) into the following form:

$$r_{ox} = r_i^{0.5} \frac{k_{p\infty}}{\sqrt{k_{t\infty}}} e^{\frac{E_p - 0.5E_t}{RT}} C_{RH} \qquad (2)$$

where $k_{p\infty}$, $k_{t\infty}$ are preexponential factors and E_p is energy of activation of the propagation reaction, E_t is energy of activation of the termination reaction, and $E_p - 0.5E_t$ is the overall energy of activation of oxidation.

The literature provides neither any kinetic data concerning the oxidation of **1** to **2** nor information about the properties of **2**. The range of investigations comprised the kinetics of oxidizing **1** to **2** as well as the determination of the oxidizability ($k_p/k_t^{1/2}$) of **1** and the overall energy activation of the oxidation of **1** ($E_p - 0.5E_t$). Also the long-term oxidation of **1** with oxygen in a bubbling reactor to **2** was investigated, and the yield and selectivity of such a reaction were determined. The acid decomposition of **2**, contained in the oxidate, gave product **3**.

EXPERIMENTAL

Compound **1** was supplied by Rütgers Kureha Solvents GmbH (Duisburg, Germany), with a purity of 99%, b.p. 293–303°C (lit. 291°C [10]), n_D^{20} 1.5800 (lit. 1.5831 [11]), $d^{15} = 0.9880$.

The oxidation reactions were carried out in a gasometric apparatus after applying the procedure described in the literature [12]. The oxidation was carried out in a thermostated, 4-cm^3 quartz flask, vigorously mixed by shaking and connected with a thermostated burette. Oxygen was supplied into the flask from a burette, in which the pressure was kept constant and amounted to 1 atm. The reaction was monitored by measuring the oxygen uptake.

Long-term oxidations of **1** were carried out in a bubbling reactor (oxygen was divided into small bubbles on entry into the reactor).

Analyses of 2-(1,1′-biphenyl-4-yl)propane-2-ol (**4**) and 1-(biphenyl-4-yl)ethane-1-on (**5**) were performed using an Alliance Waters 2690 high-performance liquid chromatograph, equipped with an autosampler and a UV detector (Waters 996 photodiode array). The Nova-Pak Silica column 60 Å 4 μm (150 mm × 3.9 mm; Waters) was applied. The mobile phase was a mixture of *n*-hexane and 2-propanol (99:1) [13]. The concentration of **2** in the product was determined by iodometry [14].

Qualitatively, the oxidate was analyzed by TLC (Kieselgel 60 F_{254} plates, gel layer 0.2 mm thick; CH_2Cl_2:$(CH_3)_2CO$ (9:1 v/v) as the developing liquid for products). Spots of the products were observed in 254 nm light. Elementary analyses were carried out on a Perkin-Elmer 2400 series II instrument. The ^{1}H NMR and ^{13}C NMR analyses of **2** were run on a Varian Unity Inowa 300 spectrometer.

1-(l,1′-Biphenyl-4-yl)-1-methylethyl hydroperoxide (**2**) was separated from the oxidate by its sodium salt. Thirty grams of the oxidate containing 34.5% of **2** (10.35 g, 45.3 mmol **2**) was dissolved in 120 cm^3 of toluene. The mixture was cooled to 5°C. Then 11.1 cm^3

of 20% aqueous solution of NaOH (67.7 mmol NaOH) was dropped into the stirred mixture for 0.5 h. The precipitate of sodium salt of **2** was filtered off and was washed with water (5 × 5 cm^3) and hexane (5 × 5 cm^3). Next, the precipitate of sodium salt of **2** was stirred in 60 cm^3 of water and neutralized with 5% aqueous HCl solution (until pH 7). Afterward, **2** was filtered and washed with water (3 × 5 cm^3) to give 7.18 g of **2** (yield 66%), 94% pure (as determined by iodometry). The **2** was purified twice by precipitation of the sodium salt and then neutralization. **2** was obtained with a purity exceeding 97%, m.p. 83.5–85°C. Elemental analysis: calculated for $C_{15}H_{16}O_2$, 78.92%C, 7.06%H; found, 78.93%C, 6.95%H; O_{active}: calculated 7.01; found, 6.80%. ^{1}H NMR ($CDCl_3$/TMS) $\delta = 7.26$–7.65 (m, 9H$_{arom}$, and 1H$_{OOH}$), 1.67 (s, 6H, C($\underline{C}\underline{H}_3$)$_2$OOH). ^{13}C NMR 143.6, 140.7, 140.4 (C-ar $_{1',1,4}$), 128.8, 127.3, 127.1, 125.9 (C-ar $_{2',2,3',3,5',5,6',6}$), 127.3 (C-ar $_{4'}$), 83.9 ($\underline{C}$(CH$_3$)$_2$OOH), 26.1 (C($\underline{C}$H$_3$)$_2$OOH).

The hydroperoxide **2** was relatively unstable and partially decomposed to **3** in the presence of traces of impurities.

4-Hydroxybiphenyl (**3**) was obtained from the acid decomposition of **2**. 13.62 g of the oxidate containing 34.5% of **2** (20.58 mmol **2**) with 2.5 cm^3 of acetone was dropped into a solution of 0.06 g of concentrated H_2SO_4 (0.58 mmol H_2SO_4) in 12 cm^3 of acetone at 56°C for 5 min. The heat of the decomposition reaction was removed by partial vaporization of the acetone. Since oxidate was added, the whole **2** decomposed to **3** during 5 min (the reaction was controlled by TLC analysis). Then the mixture was neutralized by adding 0.45 g of Na_2CO_3 (4.24 mmol). Next the precipitate of Na_2CO_3–Na_2SO_4 was filtered and acetone was evaporated. The remaining solid was diluted in 13 cm^3 of *t*-BuPh. Product **3** was isolated from the mixture by extraction with 2% aqueous solution of NaOH (60 cm^3, 30.6 mmmol) (to separate fractions a centrifuge was used). Then, the aqueous phase (at the bottom) was neutralized by adding 5% aq. HCl (23 cm^3) and the precipitate of **3** was filtered off. 2.93 g (17.22 mmol, yield = 84%) of chromatographic pure **3** was obtained, m.p. 165–167°C (lit. 166–167°C [15]).

RESULTS AND DISCUSSION

To determine the oxidizability of **1**, the initial rates of oxidation of **1** (r_{ox}) were measured in the presence of azo-initiators, the initiating properties of which (r_i) were known. The amount of initiator was adjusted to get similar initiation rate at different temperatures. By using Eq. (1), the oxidizability of **1** was calculated.

The kinetic data concerning the oxidation of **1** within a temperature range of 60–110°C are shown in Table I. For comparison, the kinetic data of the oxidation of cumene are quoted too. This table indicates that the susceptibility to oxidation of **1** is about 20%–30% lower that that of cumene.

Figure 1 illustrates the dependence of $-\ln(k_p/k_t^{1/2})$ on the reciprocal of temperature. Based on the presented data and employing Eq. (2), the overall energy of activation ($E_p - E_t/2$) could be calculated.

The overall energy of activation ($E_z = E_p - E_t/2$) of the free-radical chain process of the oxidation of **1** amounts to 25.8 ± 0.8 kJ/mol, and in the case of cumene amounts to 29.1 ± 0.8 kJ/mol.

To check the progress of the process at higher conversion of **1**, it was tested in the bubble reactor. As initiator 1,1′-azobis(cyanocyclohexane) was used. The oxidation was run within the temperature range of 80–120°C. The concentration of **2** in the reaction

Table I Kinetic Data of the Oxidation of 1 with Molecular Oxygen, $p = 1$ atm

T (°C)	Concentration of Initiator × 10^3 (mol/dm^3)	$r_i \times 10^{7c}$ (mol/dm^3·s)^c	Concentration of **1** (mol/dm^3)	$r_{ox} \times 10^5$ (mol/dm^3·s)	λ^d	$k_p/k_t^{1/2} \times 10^2$ (dm^3/(mol·s)$^{1/2}$)	$k_p/k_t^{1/2} \times 10^{2e}$ for Cumene (dm^3/(mol·s)$^{1/2}$)
60	15.09^a	1.72	4.91	0.69	39	0.34	0.42
70	3.89^a	1.76	4.87	1.07	60	0.48	0.57
80	1.08^a	1.76	4.83	1.12	63	0.55	0.77
90	5.80^b	1.76	4.79	1.43	81	0.71	0.98
100	1.60^b	1.81	4.76	1.81	99	0.94	1.36
110	0.40^b	1.57	4.72	2.04	130	1.17	1.72
120	0.10^b	1.29	4.68	2.55	198	1.47	2.08

[a] 2,2-Azo-bis-isobutyronitrile as initiator ($k_d = 1.6 \times 10^{15}e^{-30800/RT}$ [16]).

[b] 1,1′-Azobis(cyanocyclohexane) as initiator ($k_d = 5.24 \times 10^{16}e^{-35400/RT}$ [17]).

[c] r_i is calculated from the following equation: $r_i = 2ek_dC_i$, where e is efficiency of initiation (with 0.6 taken for oxidation in the presence of azo-initiators); k_d is the constant rate of the initiator decomposition; C_i is the initiator concentration [18].

[d] $\lambda = r_{ox}/r_i$ is the length of the kinetic chain.

[e] Data for cumene [19].

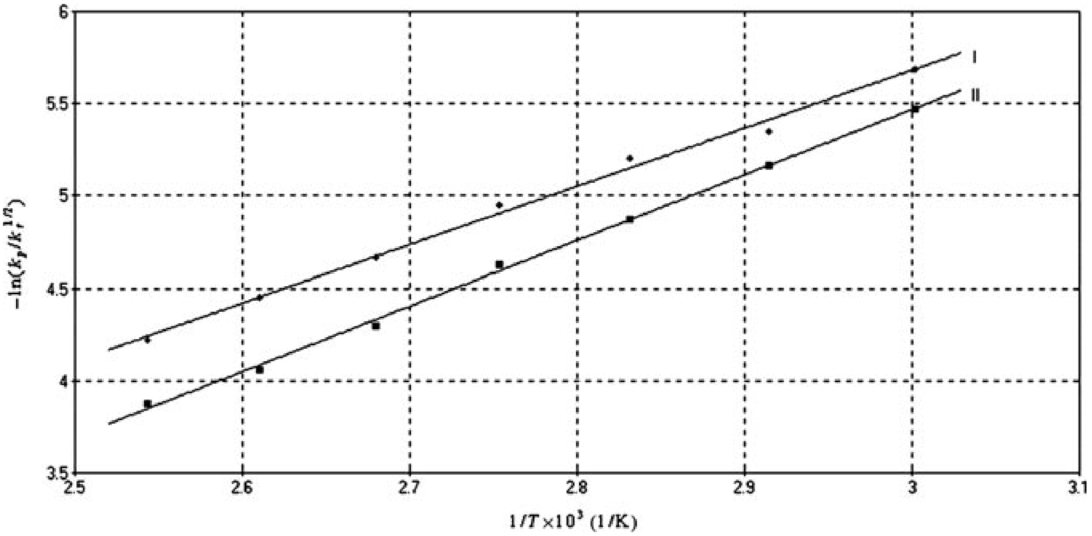


Figure 1 $-\ln(k_p/k_t^{1/2})$ of **1** (I) and cumene (II) versus reciprocal absolute temperature.

mixture was determined iodometrically. The kinetic curves indicating the accumulation of **2** are shown in Fig. 2.

The investigations have proved that **1** was oxidized quickly to **2**, and the reaction of oxidation did not need to be carried out in a double-phase system in an alkaline aqueous emulsion. Oxidation of **1** for 4 h at a temperature of 100°C and 110°C gave a product containing 37.4% and 32.0% of **2**, respectively. Later, the rate of oxidation was decreased due to the formation of by-products inhibiting the free-radical chain process.

When the reaction was run at 90°C, no inhibition was observed (after 7 h the reaction product contained 39.6% of **2**). Probably, the hydroperoxide did not decompose to inhibitors at this temperature. At 80°C the reaction rate was slower (after 7 h the reaction product contained 19.5% of **2**).

The by-products of the oxidation of **1** to **2** are alcohol **4** and ketone **5**, which are formed in small amounts as a result of the transformation of the respective alkoxy radical (Scheme 2).

The concentrations of **2**, **4**, and **5** in the mixture after the oxidation of **1** at 90°C, 100°C, and 110°C are presented in Table II.

The amount of **4** in the mixture after the oxidation is about 15 to 20 times less than **2**. A considerable increase in the content of **4** was observed when the oxidation took place at 110°C and the concentration of **2** decreased. The content of **5** was about three to four times less that the content of **4**.

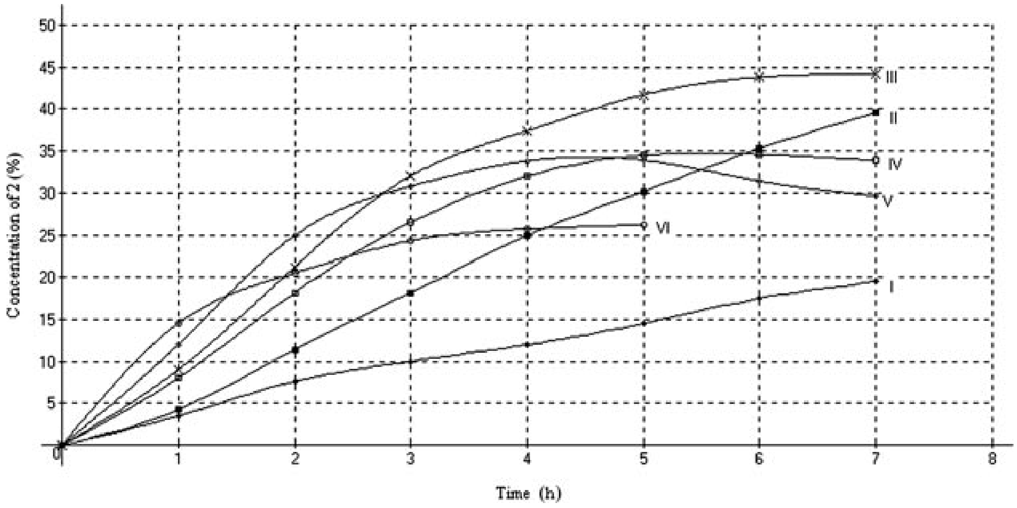
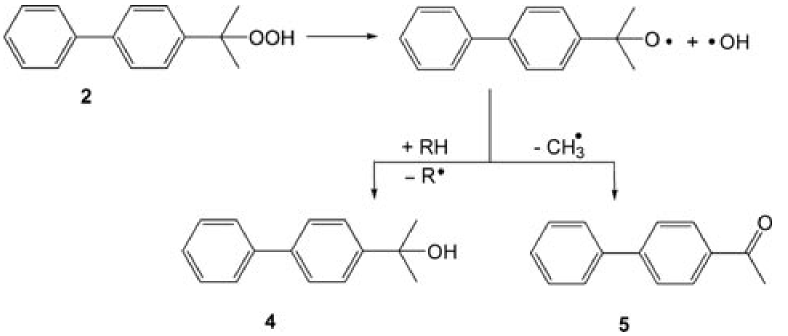


Figure 2 Oxidation of **1** (10 cm^3) with oxygen at 80°C (I), 90°C (II), 100°C (III), 105°C (IV), 110°C (V), and 120°C (VI). Initiator: 1,1′-azobis(cyanocyclohexane) 0.1706 g (I), 0.915 g (II), 0.0470 g (III), 0.0470 g (IV), 0.0224 g (V), and 0.0104 g (VI).



Scheme 2 Products of the thermal decomposition of **2**.

Table II Oxidation of **1** with Oxygen in the Bubble Reactor

Temperature (°C)	Time (h)	Concentration of **2** (%)	Concentration of **4** (%)	Concentration of **5** (%)	α(%)	S (%)
90°C	2	11.4	0.50	0.23	10.7	94
	3	18.2	0.86	0.29	16.8	94
	4	24.9	1.22	0.31	23.7	94
	5	30.2	1.51	0.45	29.1	94
	6	35.3	1.67	0.47	34.1	94
	7	39.6	2.06	0.44	38.9	94
100°C	2	21.2	1.11	0.37	20.2	93
	3	32.0	1.64	0.43	30.9	93
	4	37.4	2.12	0.44	37.2	93
	5	41.7	2.46	0.55	41.2	93
	6	43.8	2.68	0.70	43.6	92
	7	44.2	2.97	0.69	44.3	92
110°C	2	24.9	1.13	0.43	23.7	94
	3	30.8	1.58	0.48	29.7	93
	4	33.8	2.10	0.64	33.3	92
	5	33.9	2.70	0.83	34.2	90
	6	32.2	4.00	1.24	34.3	85
	7	30.9	4.97	1.54	34.3	81

The selectivity of the oxidation of **1** to **2** at 90°C was high and amounted to 94%. At 110°C it amounted, in the initial phase, to 94%–92%, after which it dropped to 81% due to the decrease in the concentration of **2**.

The product of oxidation run at 100°C, containing 34.5% of **2** was subjected to acid decomposition in the presence of H_2SO_4. Because of the high selectivity of oxidation (the low content of alcohol), H_2O_2 did not have to be applied, as stated in the patent [4]. The product **3** was selected by extraction with an aqueous NaOH solution. In result pure **3** was obtained with a yield of 84%.

CONCLUSIONS

The investigations showed that **3** can be obtained from **1** by applying a process similar to Hock-Lang's method of phenol production from cumene.

Compound **1** oxidizes quickly with a high selectivity to **2** in a single-phase system (without adding alkaline aqueous emulsion) and without any catalyst. The oxidizability of **1** is comparable with that of cumene. In the course of the oxidation of **1** with oxygen at 90–100°C after 5–7 h, a product, containing about 40% of **2**, was obtained. In these conditions **2** was formed with a selectivity of about 93%–94%.

Compound **2**, which was contained in the oxidate, can be immediately subjected to acid decomposition to **3** in the presence of H_2SO_4. Because of the low content of **4**, H_2O_2 need not be applied, so that the safety of work as well as the economical indices of the process is improved.

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