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β-Hydroxyalkylation of Sterically Hindered Phenols with Epoxides in Acid Medium

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Abstract—Reactions of 2,6-dialkylphenols with ethylene oxide, propylene oxide and epichlorohydrin in the presence of $SnCl_4$ at the temperature from –5 to +5°C leads to the formation of respective phenols containing a hydroxy group in the β-position of the aliphatic chain of the *para*-substituent. The conditions for maximum selectivity of the reaction of 2,6-di-*tert*-butylphenol with ethylene oxide were determined. By HPLC–MS method the directions of the side reactions were explored. The method has been successfully tested in a pilot installation. With 2,6-dimethylphenol instead of 2,6-di-*tert*-butylphenol a sharp increase occurs in the content of ethers in the reaction product. With epichlorohydrin, 2,6-di-*tert*-butylphenol affords a product, which is easily converted into an epoxide containing a sterically hindered phenol in its structure.

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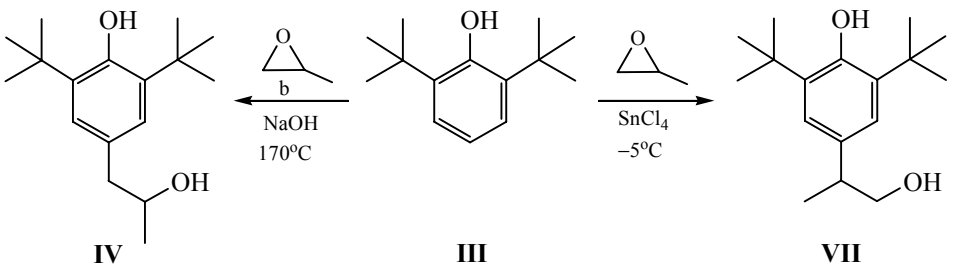
Interest in the properties and the preparation methods of 4-(2-hydroxyethyl)phenol **I** and its deriatives is connected with the public health prophylaxis: reducing the impact of adverse social and environmental factors and stresses of various etiology [1]. In this regard we have described earlier in the survey [2] various ways of synthesis of compounds **I**, its natural origin, and biological properties. It was notes that the most promising method of the synthesis of compound **I** and its *tert*-butyl derivative **II** is the reaction of phenols with ethylene oxide. To reduce the process of side formation of ethers, the phenol hydroxy group is blocked by bulky alkyl substituents located in the aromatic ring adjacent to the hydroxy group [3]. In the case of phenol, another method is used: the access of alkylating agents to the hydroxy group is prevented by creating near the latter a complex multilevel protection using organometallic compounds [4].

As has been noted, the most technologically acceptable method of producing compound **I** is based on the reaction of ethylene oxide (a) with a dilithium derivative prepared preliminary from 4-bromophenol [5]. But this approach only emphasizes the problems of developing a technologically convenient methods of compound **I** production. We have suggested a route for producing it without the use of organometallic compounds, based on the de-*tert*-butylation of compound **II** [6]. But the problem of the availability of parent compound **II** remains. This work is directed at solving the problem in a general way: it aims at the developing a one-step methods for producing spatially hindered phenols containing hydroxyethyl group in the *para*-position. We believe that the synthesis of a series of compounds with such structure by one-step method would make available a systematic set of intermediates and a number of biologically active substances of new generation based on them. These compounds were hardly accessible previously, and were obtained by a multistage method [7].

In the alkaline medium the reaction of compound **III** with ethylene oxide proceeds with predominant formation of a complex mixture of ethers. In the reaction of propylene oxide (b) with the compound **III** at 140°C a mixture is formed which is difficult to separate containing up to 50% of compound **IV** [8]. The reaction of 2,6-dimethylphenol **V** with ethylene oxide and alkali at 50°C leads to the formation of ether **VI** in a good yield [9]. Alkaline catalysis proved to be unsuitable for products of C-alkylation of phenols by epoxides, so we started to investigate the course of this reaction in an acid medium.



But even in the acid medium, according to [10], sterically hindered phenols react with ethylene oxide exclusively with the formation of ethers, while the products of their C-alkylation were not revealed. Patent [11] indicated that among the acid catalysts of the reaction of compound **III** with propylene oxide (b) the most convenient was the anhydrous $SnCl_4$: at a temperature from 0 to +15°C the yield of the C-alkylation product **VII** is 11–16%. We decided to examine in more detail the conditions of action of $SnCl_4$ as a catalyst in the C-alkylation of sterically hindered phenols.

We found that the yield of the final product and the selectivity of the reaction of phenols with epoxides can be substantially raised mainly by reducing the contact time of the reaction mixture with the catalyst and applying a specific mode of the epoxide feeding in the course of the reaction, trying not to allow its excess [12]. Compared with the patent [11], in this work we succeeded to increase the yield of the reaction product **VII** from 11 to 43%.

The difference in the structures of the final product **IV** obtained with alkaline catalysis and the product **VII** obtained with acid catalysis can be ascribed to the difference in the activation of the substituted epoxide in alkaline and acid environments. In the second case, propylene oxide reacts with $SnCl_4$ to form a carbocation stabilized by the methyl group, which leads to preferential formation of compound **VII** with branching at the α-atom of the aliphatic chain in the *para*-substituent. According to [12], in alkaline medium in the first stage the propylene oxide is activated by cleavage of the hydride ion from the primary carbon atom that leads to compound **IV**.

We showed that the reaction of an excess of ethylene oxide (a) with compound **III** in the presence of $SnCl_4$ at a temperature from –5 to +2°C led to 4-(2-hydroxyethyl)-2,6-di-*tert*-butylphenol **II** in 75% yield. The ethylene oxide excess in the course of reaction is converted into diethylene glycol. The latter was identified as a sole organic substance in water extract of the reaction products by ^{1}H NMR spectroscopy. As the solvent we examined chlorobenzene, chloroform, and trichlorethylene, the latter was proved as the most convenient one.

By the distillation of the reaction mixture along with compound **II** we isolated 2,4,6-tri-*tert*-butylphenol **VIII** in 4% yield and 4-(2-hydroxyethyl)-2-*tert*-butylphenol **IX**. The still bottoms after distillation were analyzed by HPLC–MS. The most probable structures of all components found are listed below.

Compound **X** and dienone **XI** were isolated from the still bottoms in the individual form. The presence in the reaction mixture of a large number of by-products **VIII–XVI** indicates the occurrence of the acid-catalyzed processes. This leads to the formation of ethers and de-*tert*-butylated compounds. The acid catalyzes also the process of their subsequent hydroxyethylation.

The scaled production of compound **II** was performed in the technological equipment of the Institute, which enabled the reduction of the negative effect of the heat evolved in this reaction, and the regulation of the rate and the order of feeding using pumps.

The experiments showed that we should not try to achieve a complete transformation of the parent compound **III** in this reaction. The process selectivity and economical efficiency increase when the reaction mixture still contains 30–40% of compound **III** [12]. The high yield of the products can be achieved by controlling the medium acidity and preventing excess of ethylene oxide. Essentially, $SnCl_4$ is an initiator, because after the reaction with the final product **II**, diethylene glycol and other alcohols formed in the process it looses its catalytic activity.

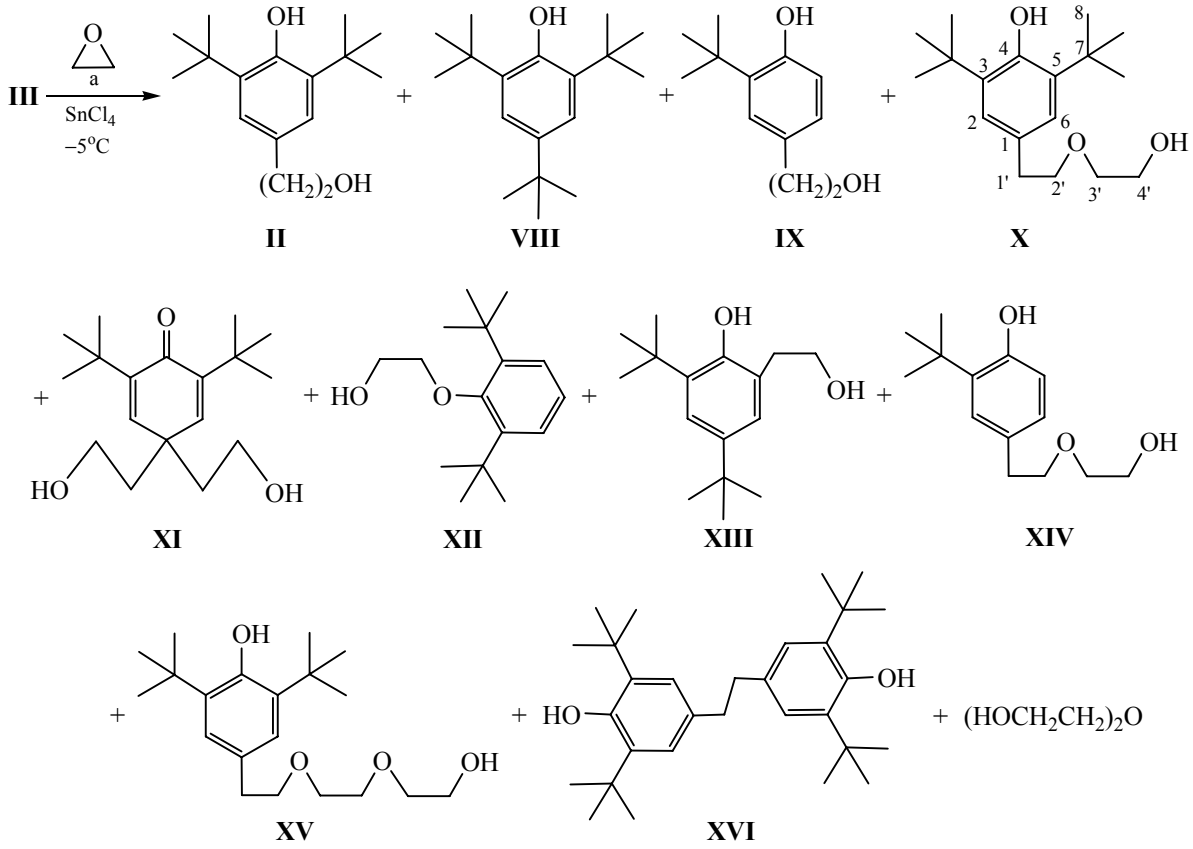
It should be noted that the reaction of phenol with ethylene oxide under the chosen conditions does not afford an appreciable amounts of compound **I**.

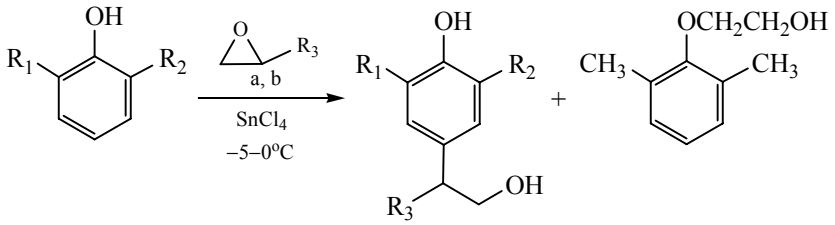
The HPLC–MS data of analysis of the still bottoms in the process of hydroxyethylation of 2,6-di-*tert*-butylphenol

Retention time, min	Phenoxide anion $[M - H]^+$, *m/z*	Positive ions, *m/z*	UV spectrum maximum, nm	Compound (formula)
17.6	237.152	261.148	278	**XIV** ($C_{14}H_{22}O_3$)
18.7	–	295.227 317.211	248	**XI** ($C_{18}H_{30}O_3$)
19.8	249.187	273.183	276	**II** ($C_{16}H_{26}O_2$)
20.0	293.214	317.211	276	**X** ($C_{18}H_{30}O_3$)
20.1	337.240	361.237	277	**XV** ($C_{20}H_{34}O_4$)
21.3	249.188	273.184	278	**XIII** ($C_{16}H_{26}O_2$)

We found that the catalysis of the reaction of compound **V** with ethylene oxide by $SnCl_4$ leads to the formation of a mixture of ether **VI** and phenol **XVIII** in a 4:1 ratio. Alkaline treatment of the mixture allows effective separation of these compounds. Although the yield of product **XVIII** obtained by this method is low (9%), this process is much more economical than the well-known multistage approach [7].

Reaction of 2-methyl-6-*tert*-butylphenol **XVII** with ethylene oxide (a) in the presence of $SnCl_4$ occurs at a temperature of about 0°C and leads to product **XIX**.



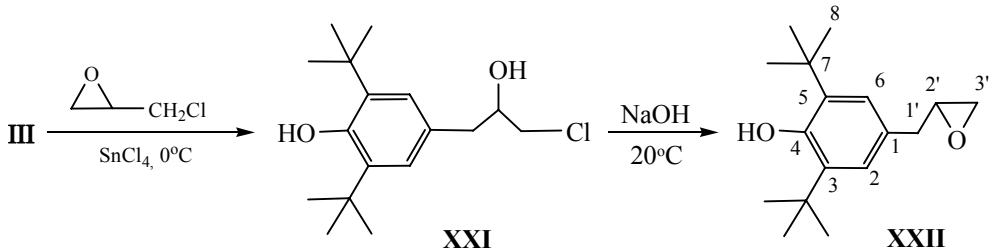


V, XVII **XVIII–XX** **VI**

V, $R_1 = R_2 = CH_3$; **XVII,** $R_1 = CH_3$, $R_2 = C_4H_9$-*t*; **XVIII**, $R_1 = R_2 = CH_3$, $R_3 = H$; **XIX**, $R_1 = CH_3$, $R_2 = C_4H_9$-*t*, $R_3 = H$; **XX**, $R_1 = CH_3$, $R_2 = C_4H_9$-*t*, $R_3 = CH_3$; a, $R_3 = H$; b, $R_3 = CH_3$.

Under the same conditions compound **XVII** reacts with an excess of propylene oxide affording compound **XX**.

The reaction of 2,6-di-*tert*-butylphenol with epichlorohydrin is a new opportunity for one-step producing phenol **XXI** containing both hydroxy group and halogen atom in the aliphatic chain of the *para*-substituent at a sufficient distance from the aromatic ring. Note that the propylene oxide and epichlorohydrin react with phenol **III** differently: in the latter case a β-hydroxyalkylphenol derivative of a new type is formed, which has no additional substituent in the benzyl position. This structural feature is proved also by the quantitative conversion of compound **IX** into epoxide **XXII** in alkaline medium.



XXI **XXII**

Some analogs of compounds **XXII**, the glycide ethers based on epichlorohydrine and sterically hindered hydroquinones, are of practical interest for the stabilization of polymers and food [3, 14].

EXPERIMENTAL

Melting points were determined on a Mettler Toledo instrument, the thermal system FP 900 with the measuring cell FP 81. The ^1H and ^{13}C NMR spectra were recorded on a Bruker DRX500 NMR instrument. The components ratio in the mixtures was determined by GLC on a Tsvet chromatograph (Russia). The elemental composition and molecular weight of individual compounds were obtained by processing the data of the high resolution mass spectra taken on a Finnigan MAT 8200 mass spectrometer at 200°C.

The system for HPLC–MS analysis consisted of a liquid chromatograph Agilent 1200 (with diode-matrix detector) and a hybrid quadrupole-TOF mass spectrometer micrOTOF-Q (Bruker). Column: Zorbax XDB-C8, 2.1×150 mm, particle size of 3.5 μm. Eluent: 2% HCOOH–MeOH, linear gradient from 30 to 90% of methanol since 5th to 15th min. Flow rate: 0.2 ml min^{-1}. UV detection was carried out at three wavelengths: 240/8, 280/16, and 320/32 nm. Besides, every second UV spectrum available in the system (150 spectra per minute) in the range 230–450 nm was saved. The operating parameters of the mass detection: ionization method electrostatic spraying at atmospheric pressure (API-ES). Scanning of negative ions in the range m/z = 200–1300. The flow of gas-dryer (nitrogen): 8 l min^{-1}, temperature: 230°C, the pressure in the sprayer: 1.6 bar.

Hydroxyethylation of 2,6-di-*tert*-butylphenol II. In a reactor of a capacity 0.3 l with a stirrer, dropping funnel, and thermometer was loaded 72.5 g (0.35 mol) of 2,6-di-*tert*-butylphenol, it was dissolved in 75 ml of trichlorethylene and cooled to –10ºC. To the reactor was added 16 ml (0.137 mol) of $SnCl_4$, and within

45 min, a solution of 16 ml (0.32 mol) of ethylene oxide in 20 ml of trichlorethylene was dosed at the temperature in the reactor 0ºC or below. Then to the reactor was added a new 16 ml portion of $SnCl_4$ and within 45 minutes a portion of solution of 16 ml $SnCl_4$ in 20 ml of trichlorethylene at the temperature 2°C or below. Again was introduced a 16 ml portion of the solution of $SnCl_4$ and next portion of solution of 16 ml of ethylene oxide in 20 ml of trichlorethylene was dosed within 30 minutes at +5ºC. Totally 48 ml (0.41 mole) of $SnCl_4$ solution and 48 ml (0.96 mol) of ethylene oxide solution was added to the reaction mixture. The mixture was stirred at 5–10ºC for 20 min and then 70 ml of water was added. The stirring was continued for 20 min, then the lower acid layer was separated and the organic layer was washed with water (3×150 ml) to neutral reaction. Then the reaction mixture was evaporated to half volume in a vacuum rotary evaporator. The concentrated solution was left for 24 h at –10ºC. The precipitate formed was filtered off and washed with 100 ml of petroleum ether. 63.5 g (0.253 mol, yield 73.8%) of 4-(2-hydroxyethyl)-2,6-di-*tert*-butylphenol **II** was obtained, mp 99–101°C, containing according to GLC at least 98% of the main substance. The filtrates were evaporated to remove the solvent, and the residue (20 g) was distilled in a vacuum collecting 10.8 g of liquid fraction with bp 90–125°C at 2–3 mm Hg, containing, according to GLC, compounds **III** and **VIII** in a ratio of 5:1, from which by repeated distillation individual compound **VIII** was isolated. This volatile fraction was returned to the next operation. Besides, at the distillation 5 g was obtained of the fraction with bp 140–160°C at 2 mm Hg, which was crystallized from petroleum ether giving an additional 2.5 g of compound **II**.

The composition of the components of still bottoms (9 g, yield 10%) is given in the table. The residue was distilled and 1.5 g of viscous oil was obtained with bp 205–210°C at 2 mm Hg, which solidified at storage. After its crystallization from *n*-heptane 1.0 g of ethylene glycol 2-(3,5-di-*tert*-butyl-4-hydroxyphenyl) - ethyl ether **X** was obtained, mp 85.6°C. According to [15], mp 84–85°C. Found: M^+ 294.2191 (mass spectrometry). Calculated: M^+ 294.2195; $C_{18}H_{30}O_3$. ^{1}H NMR spectrum in CCl_4, δ, ppm: 1.39 s (18 H, C_4H_9-*tert*), 2.3 s (1H, CH_2OH); 2.71 t (J = 7.5, 2H, $ArCH_2$), 3.4–3.7 m (4H,OCH_2CH_2O), 3.55 t (J = 7.5, 2H, $ArCH_2CH_2O$); 4.95 s (OH), 6.86 s (2H, Ar*H*). ^{13}C NMR spectrum in CCl_4, δ_C, ppm: C^8 30.17, C^7 33.93, $C^{1'}$ 35.94, $C^{4'}$ 60.97, $C^{2'}$ and $C^{3'}$ 71.73 and 72.25; C^3 and C^5 124.78; C^1 128.92; C^2 and C^6 135.34; C^4 151.72.

2,6-Di-*tert*-butyl-4,4-bis(2-hydroxyethyl)cyclohexyl-2,5-dien-1-one XI was isolated from the still bottoms by column chromatography at a gradient elution with a mixture of hexane–methanol. Oil, hardening at prolonged storage. Found: M^+ 294.223 (mass spectrometry). $C_{18}H_{30}O_3$. Calculated: M^+ 294.220. The ^{1}H NMR spectrum (CCl_4), δ, ppm: 1.21 s (18H, C_4H_9-*tert*), 1.88 t (4H, J = 7.0, PCH_2), 2.77 s (2H, OH), 3.37 t (4H, J = 7.0, $HOCH_2$), 6.44 s (2H, *H*C=CC_4H_9-*tert*). IR spectrum (KBr): 1635 and 1660 cm^{-1} (C=C and C=O). UV spectrum in alcohol: λ_{max} 248 nm, log ε 4.06.

This method of synthesis of compound **II** was reproduced in a pilot installation of the Institute of Organic Chemistry at 42-fold scaling in an enameled reactor with a capacity of 20 l equipped with an anchor stirrer and two dozing devices, which fed into the reactor simultaneously the solutions of ethylene oxide and catalyst $SnCl_4$ in trichloroethylene. The reactor jacket was cooled with a brine with the temperature of –15°C. To the reactor was loaded 3.2 kg of 2,6-di-*tert*-butylphenol. Under these conditions of experiment in a series of operations was obtained on the average 2.7 kg of product **II**, purity 97%. Yield 66.4%.

2-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)propanol VII. To a solution of 20.6 g (0.1 mol) of compound **III** in 50 ml of chlorobenzene cooled to 0°C was added 9.7 ml (0.083 mol) of $SnCl_4$. Then to the reactor at stirring was added dropwise within 50 min a solution of 12.4 ml (0.184 mol) of propylene oxide (b) in 10 ml of chlorobenzene maintaining the temperature at 5°C or below. The reaction mixture was kept at this temperature for 1 h, heated to room temperature, and stirred for 1 h, then quenched by adding 50 ml of cold water. The layers were separated, the organic layer was washed with water, and the solvent was distilled off by steam-distillation. An oil was obtained, 26.5 g, containing according to GLC 63% of compound **VII** and 32% of the parent compound **III**. By distillation of this mixture in a vacuum 6.0 g of the fraction containing compound **III** was separated. The residue (16.3 g) was dissolved in 30 ml of hexane and left overnight in a refrigerator. The precipitate was filtered off and dried in air. We obtained 11.24 g (43%) of product **VII**, mp 93–95°C (published [16] mp 93.2–94.5°C). ^{1}H NMR spectrum (CCl_4), δ, ppm: 1.24 d (3H, J = 7.5, CH_3), 1.44 s (18H, C_4H_9-*tert*) 1.60–1.80 m (1H, OH), 2.60–3.00 m (1H, ArCH), 3.6–3.7 d.d (2H, CH_2OH), 5.12 s (1H, ArOH), 7.01 s (2H, ArH).

2-(2,6-Dimethylphenoxy)ethanol VI and 4-(2-hydroxyethyl)-2,6-dimethylphenol XVIII. To the cooled to –5°C solution of 24.4 g (0.2 mol) of 2,6-dimethylphenol **V** in 150 ml of chlorobenzene was added with stirring 23 ml (0.2 mol) of $SnCl_4$ and then for 4 h to the reactor, through the layer of the reaction mixture, was passed 10 ml (0.2 mol) of ethylene oxide with a flow of nitrogen. The reaction mixture was maintained for 1 h at room temperature and at stirring to it was added 100 ml of cold water. The layers were separated. The organic layer was washed with water, and chlorobenzene was distilled off by steam-distillation. The residue, 16.9 g, was dissolved in ether and shaken for 5 minutes with a solution of 12.9 g of NaOH in 90 ml of water to obtain alkaline aqueous solution (A) and the ether solution (B) which were treated separately.

The alkaline solution (A) was acidified with hydrochloric acid to pH = 5, extracted with ether, the ether was evaporated, and the residue was distilled in a vacuum. A faction with bp 63–75°C at 5 mm Hg (2 g) contained 2,6-dimethylphenol, and the fraction with bp130–145°C at 5 mm Hg (3.1 g, 9.0%) hardened. According to GLC, it contained 97% of 4-(2-hydroxyethyl)-2,6-dimethylphenol **XVIII**, mp 63–64°C, that corresponds to the data [7]. ^{1}H NMR spectrum (CCl_4), δ, ppm: 2.16 s (6H, $ArCH_3$), 2.67 t (2H, J = 7.5, $ArCH_2$), 3.73 t (2H, J = 7.5, CH_2OH); 5.43 s (1H, ArOH), 6.75 s (2H, ArH). The ether layer (B) was washed with water, dried over anhydrous Na_2SO_4, and evaporated. The residue (11.0 g), containing, according to GLC, 87% of ether **VI**, was distilled in a vacuum. Faction with bp 120–125°C at 5 mm Hg (3.8 g) was crystallized from heptane. We obtained 2-(2,6-dimethylphenoxy)ethanol **VI** with mp 71.0–72.0°C (published [9] mp 70–71°C). ^{1}H NMR spectrum (CCl_4), δ, ppm: 2.29 s (6H, $ArCH_3$), 2.58 s (1H, OH), 3.8–4.0 m (4H, OCH_2CH_2OH), 6.9–7.0 m (3H, ArH).

4-(2-Hydroxyethyl)-6-*tert*-butyl-2-methylphenol XIX. To a solution of 1.72 g (0.01 mol) of compound **XVIII** in 10 ml of chlorobenzene at –5°C was added with stirring 5.22 g (0.02 mol) of $SnCl_4$. Through 2.50 g (0.05 mol) of ethylene oxide was passed nitrogen and the vapor obtained was bubbled for 1 h through a layer of the reaction mixture cooled to 0°C. During this time the ethylene oxide sample fully evaporated. The reaction mixture was stirred then for 1 h, and then diluted with cold water. The organic layer was separated, washed with water, and the solvent was distilled off by steam-distillation. 2.08 g of crystals with oil was obtained, from which by crystallization from a mixture of hexane and ether (5:1) was isolated 0.83 g (33%) of compound **XIX**, mp 69–70°C (published [7] mp 75–76°C). ^{1}H NMR spectrum (CCl_4), δ, ppm: 1.40 s (9H, C_4H_9-*tert*) 1.60–1.80 m (1H, OH), 2.21 s (3H, CH_3), 2.74 t (2H, J = 7.5, $ArCH_2$), 3.79 t (2H, J = 7.5, CH_2OH), 4.85 s (ArOH), 6.87 d (1H, J = 2, ArN), 6.99 d (1H, J = 2, ArH).

4-(1-Methyl-2-hydroxyethyl)-6-*tert*-butyl-2-methylphenol XX. To the cooled to 5°C solution of 5.2 g (0.032 mol) of 6-*tert*-butyl-2-methylphenol **XVIII** in 40 ml of dry chlorobenzene was added with stirring 3.5 ml (0.03 mol) of freshly distilled $SnCl_4$. To the reaction mixture through a pipe reaching the bottom was bulbled for 1 h a vapor mixture containing 3.1 g (0.05 mol) of propylene oxide and nitrogen at the rate 60 ml/min at a temperature of the reaction mixture no higher than 5°C. The reaction mixture was stirred for 1 h at room temperature and then diluted with an equal amount of cold water. The organic layer was washed with water to pH 6–7 and chlorobenzene removed by steam-distillation. According to GLC, the residue contained 36% of the parent compound **XVIII** and 54% of the product **XX**. The residue was distilled in a vacuum, and 2.2 g of starting compound **XVIII** was isolated with bp 60–75°C at 2 mm Hg and 3.3 g of **XX** with bp 140–160°C at 2 mm Hg. After crystallization from hexane 2.2 g (yield 30%) of compound **XX** was obtained with mp 103–105°C. ^{1}H NMR spectrum (CCl_4), δ, ppm: 1.23 d (3H, J = 7.5, CH_3), 1.42 s (9NH, C_4H_9-*tert*) 1.60–1.80 m (1H, OH), 2.22 s (3H , CH_3), 2.60–3.00 m (1H, ArCH), 3.65 d (2H, J = 7.5, CH_2OH), 4.99 s (ArO*H*), 6.87 d (1H, J = 2, ArH), 6.99 d (1H, J = 2.0, ArH).

3-(3,5-Di-*tert*-butyl-4-hydroxyphenyl)-2-hydroxy-1-chloropropane XXI. In a glass flask with a stirrer and dropping funnel was placed a solution of 20 g (0.097 mol) of 2,6-di-*tert*-butylphenol in 20 ml of trichlorethylene. At cooling the solution to –3°C, 4 ml of distilled $SnCl_4$ was added and at this temperature for 30 min at stirring into the reactor was dosed 6 ml of epichlorohydrin. To the reactor was added another portion of 4 ml of $SnCl_4$ and at the temperature of 0–3°C within 30 min was dosed a solution of 5 ml of epichlorohydrin in 4 ml of trichlorethylene maintaining the temperature in the reactor at 5–7°C or below. To the reactor was added a new 4 ml portion of $SnCl_4$ and within 40 min a solution was dosed of 5 ml of epichlorohydrin in 4 ml of trichlorethylene at a temperature no higher than 5°C. In total to the reaction

mixture was introduced 12 ml (0.103 mol) of $SnCl_4$ and 18 ml (0.23 mol) of epichlorohydrin. The mixture was stirred at a temperature of 10–15°C for 20 min. To the reactor was added 20 ml of cold water in small portions maintaining room temperature of the reaction mixture. The organic layer was separated, washed with water to neutral reaction, and the solvent was evaporated. The obtained oil was distilled in a vacuum, and 4.6 g (0.022 mol) of 2,6-di-*tert*-butyl-phenol was isolated. The oily residue, 20 g, was dissolved in 10 ml of petroleum ether and the resulting solution was left overnight at –15°C. The precipitate was filtered off and washed with 10 ml of cold petroleum ether. 13.9 g of 3-(3,5-di-*tert*-butyl-4-hyd-roxyphenyl)-2-hydroxy-1-chloropropane **XXI** was obtained. Combined filtrates were evaporated and distilled in a vacuum, 3.7 g fraction with bp 160°C at 1 mm Hg was isolated. It was crystallized from an equal amount of hexane, and thus an additional 2.1 g portion of compound **XXI** was obtained, mp 97–98°C. The total yield of compound **XXI** 16 g (53%). Found, %: C 68. 56; H 9.34, Cl 11.90. $C_{17}H_{27}ClO_2$. Calculated, %: C 68.32, H 9.10, Cl 11.86. ^{1}H NMR spectrum (in $CDCl_3$), δ, ppm: 1.45 s (18 H, C_4H_9-*tert*) 2.31 s (1H, CHO*H*), 2.81 d (2H, *J* = 7.0, PhCH_2), 3.5–3.7 m (2H, CH_2C1), 4.02 m (1H, C*H*OHCH_2C1), 5.16 s (1H, ArO*H*); 7.03 s (2H, ArH).

2-(3,5-Di-*tert*-butyl-4-hydroxybenzyl)oxirane XXII. To a solution of 2 g (0.0066 mol) of compound **IX** in 2 ml of DMF was added a solution of 0.4 g (0.01 mol) of NaOH in 0.5 ml of water. The reaction mixture was stirred for 2 h in a nitrogen atmosphere at room temperature. A solution of compound **X** in DMF was thus obtained, containing according to GLC no more than 3% of the initial compound **IX**. For isolation of pure compound **XXII** this solution was poured on the snow to obtain an oil, which solidified at introducing a seed. The solid product was filtered off, washed with water, dried, the obtained oxirane **XXII** (1.64 g) was distilled in a vacuum, bp 160–165°C at 2 mm Hg, mp 83.2°C. Found: M^+ 262.19330 (mass spectrometry). Calculated: M^+ 262.19327; $C_{17}H_{26}O_2$. ^{1}H NMR spectrum in CCl_4, δ, ppm: 1.41 s (18H, C_4H_9-*tert*), two groups of proton signals from $C^{1'}H_2$: 2.48–2.51 d.d (1H, *J* = 0.55, 2.490 and 2,497) and 2.71–2.74 d.d (1H, *J* = 0.55, 2.725 and 2.732), two groups of proton signals $C^{3'}H_2$: 2.62–2.67 d.d (1H, *J* = 0.55, 2.630 and 2.660) and 2.75–2.80 d.d (1H, *J* = 0.55, 2.63 and 2.66), 3.04–3.08 m (1H, $C^{2'}$H), 5.02 s (1H, OH), 6.96 s (2H, ArH). The ^{13}C NMR spectrum (CCl_4), δ_C, ppm: C^8, 30.37; C^7, 34.27, $C^{1'}$, 38.83; $C^{3'}$, 46.69; $C^{2'}$, 52.65; C^2 and C^6, 125.33; C^1, 127.83; C^3 and C^5, 135.80; C^4, 152.43.

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