Interaction of functionally-substituted 4-alkyl-2,6-di-*tert*-butylphenols with hydrohalic acids*

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Reactions of 4-alkyl-2,6-di-*tert*-butylphenols containing OH, SH, COOH, and COOMe groups in their *para* substituents with hydrogen chloride and hydrohalic acids were studied. One-step transformations of 2,6-di-*tert*-butyl-4-(ω-hydroxyalkyl)phenols to the corresponding 4-(ω-halogenoalkyl)phenols, as well as of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionic acid and its esters to phloretic acid were proposed. 4-(3-Mercaptopropyl)phenol upon heating with conc. HBr undergoes condensation to 3-(4-hydroxyphenyl)propyl 4-(3-mercaptopropyl)phenyl sulfide as the main product.

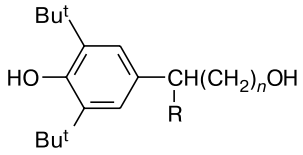
Key words: 2,6-di-*tert*-butylphenols, hydrobromic acid, *para*-dihydrocoumaric alcohol, phloretic acid, dealkylation, substitution of aromatic OH group.

Among biologically active phenolic compounds, functionally-substituted *p*-alkylphenols, such as 4-(β-hydroxyethyl)phenol (tyrosol),[1] 4-(γ-hydroxypropyl)phenol (*p*-dihydrocoumaric alcohol), β-(4-hydroxyphenyl)propionic (phloretic) acid, 4-(β-aminoethyl)phenol (tyramine),[2] *etc.*, are ranked particularly. Hitherto, these compounds have not readily been available, since the suggested methods for their synthesis, based as a rule on the use of natural raw materials,[3,4] were multi-step and laborious.[5,6]

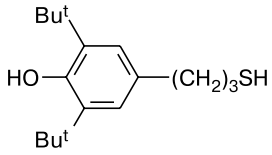
Earlier, the synthesis of 4-alkylphenols with chloro, hydroxy, carboxy, or ester groups in the alkyl substituent based on the thermal dealkylation[7] of the corresponding derivatives of 2,6-di-*tert*-butylphenol or dealkylation in the presence of protic acids, such as heteropolyacids[8] and conc. H_2SO_4,[9] was described. In the present work, a possibility for the synthesis of functionally-substituted *p*-alkylphenols by the reactions of sterically hindered phenols **1**—**3** with hydrohalic acids was investigated.

Specifically, we studied transformations of alcohol **1b** upon its heating with hydrogen chloride, hydrochloric, hydrobromic, and hydroiodic acids.

The reactions of nucleophilic substitution of the alcoholic OH group and mono-de-*tert*-butylation began already at 80 °C on passage of hydrogen chloride through a melt of alcohol **1b**, which was indicated by appearance of chloride **4** and alcohol **5** in the reaction mixture. An increase in the temperature of the melt up to 100 °C and further up to 140 °C accelerated both processes and promoted elimination of the second *tert*-butyl group. No products of the other possible reactions (isomerization and *O*-alkylation) under given conditions were observed, which enabled us to make the following suggestion about



1a—d



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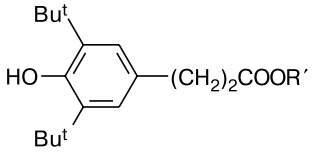


3a,**b**

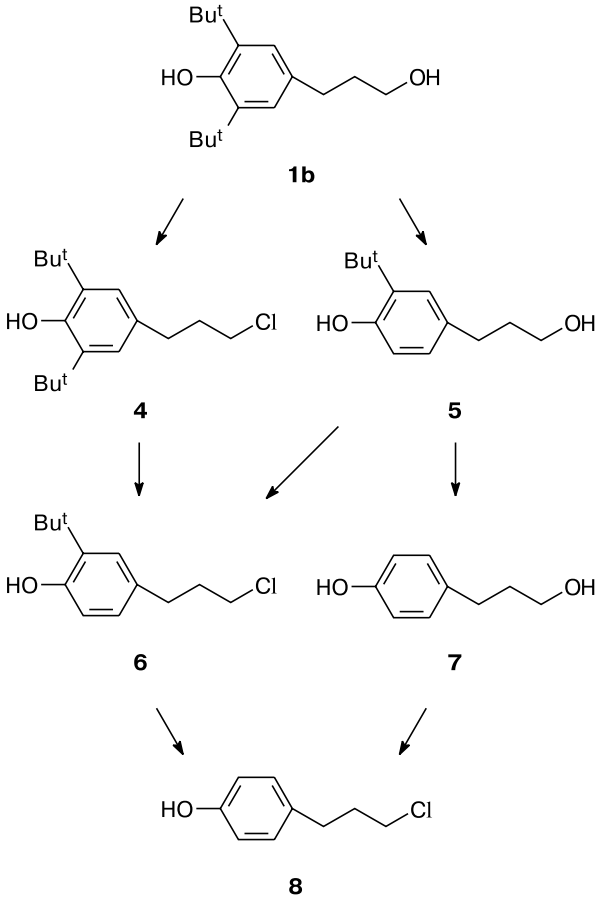
R = H, *n* = 1 (**1a**), 2 (**1b**), 3 (**1c**); R = Me, n = 2 (**1d**);
R′ = H (**3a**), Me (**3b**)

* Dedicated to the memory of Academician N. N. Vorozhtsov on the 100th anniversary of his birth.

Published in Russian in *Izvestiya Akademii Nauk. Seriya Khimicheskaya,* No. 6, pp. 1078—1083, June, 2007.
1066-5285/07/5606-1119 © 2007 Springer Science+Business Media, Inc.

transformations of alcohol **1b** under action of hydrogen chloride (Scheme 1).

Scheme 1



The intermediate products **4**—**7** were identified by GC/MS with the use of the authentic compounds obtained by alternative syntheses: chlorides **4** and **6**, by reaction of alcohol **1b** with PCl_3 in the presence of DMF[10] or with hydrochloric acid; alcohols **5** and **7**, by thermal dealkylation of alcohol **1b**. In contrast to the described procedure[7], dealkylation of the latter was carried out with bubbling of an inert gas, which enabled us to reduce the reaction time and to increase the yields of the target products (in particular of alcohol **7**) up to 76%.

The study of the dynamics of changes of the composition of the reaction mixture during heating of alcohol **1b** in the flow of HCl (140 °C) revealed the initial accumulation of alcohol **5**, indicating the higher rate of elimination of the first *tert*-butyl group in comparison to the second one. Apparently, the replacement of the alcoholic OH group by chlorine is a limiting step of the process: after 10 h, the total amount of mono-*ortho*-substituted alcohol **5** and chloride **6** in the reaction mixture was 9.3%, while for alcohols **5** and **7** it was 21.6%. After 14 h, the content of the final product, *viz.*, chloride **8**, in the reaction mixture was as high as 93%.

Similarly, the corresponding 4-(ω-chloroalkyl)phenols were obtained by reactions of alcohols **1a**,**d** with HCl.

The reaction of alcohol **1b** with conc. hydrochloric acid was carried out either under atmospheric (reflux) or under high (in a sealed tube, 110—180 °C) pressure. The transformations of compound **1b** occurred also according to Scheme 1.

The formation of the target product **8** under atmospheric pressure occurred with a remarkably lower rate than with the use of hydrogen chloride. Thus after reflux for 20 h, the content of chloride **8** in the reaction mixture did not exceed 50%.

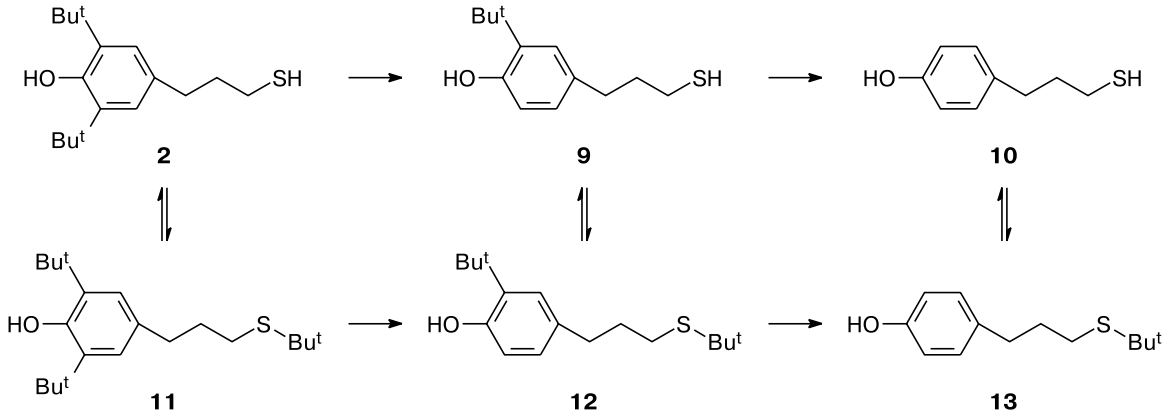
The conversion of alcohol **1b** to the target product **8** upon its heating with hydrochloric acid in a sealed tube was also incomplete: the content of chloride **6** in the mixture of compounds **6** and **8** obtained varied from 55 to 81%, depending on the temperature and heating time. Obviously, this result can be explained by accumulation of *tert*-butyl chloride in the reaction mixture and, consequently, by reversible transformation of product **8** to chloride **6**.

The reaction of alcohols **1** with hydrochloric acid under high pressure can be used for the preparative purposes, taking into account the easiness of separation of compounds **6** and **8** due to their different solubility in aqueous alkalis. Earlier, in this way we synthesized 4-(2-chloroethyl)- and 4-(4-chlorobutyl)-2-*tert*-butylphenols.[11]

Concentrated hydrobromic and hydroiodic acids were found to be more efficient. Obviously, this is due to the fact that HBr and HI, in contrast to hydrogen chloride, form azeotropic mixtures with water with considerably higher percentage of hydrogen halide and with higher boiling points. Thus after reflux of alcohol **1b** in conc. HBr for 3 h with azeotropic distillation of the resulting *tert*-butyl bromide, the content of the target 4-(3-bromopropyl)phenol in the organic phase of the reaction mixture reached 60%, and after 8 h, it increased to 91%. In addition, alcohols **5** and **7**, as well as 4-(3-bromopropyl)-2-*tert*-butyl- and -2,6-di-*tert*-butylphenols, were identified in the reaction mixture by GC/MS. This allows us to consider that HBr brings about transformations of alcohol **1b** similar to those effected by HCl (see Scheme 1).

Thiol **2**, in contrast to alcohol **1b**, does not undergo de-*tert*-butylation neither upon passage of hydrogen chloride through its melt nor under reflux with hydrochloric acid. At the same time, complete conversion of thiol **2** to the mono- and di-dealkylation products **9** and **10**, as well as to (*tert*-butylthio)propylphenols **11**—**13**, takes place on heating with conc. hydrochloric acid for 4.5 h at 160 °C. Compounds **9**—**13** were identified by GC/MS with the use of the authentic compounds obtained by alternative

Scheme 2



syntheses. The synthesis of sulfide **11** has been described earlier.[12]

The de-*tert*-butylation of thiol **2** on treatment with HBr actively proceeded even under atmospheric pressure: after 2.5 h of reflux with conc. HBr, its conversion to products **9**—**13** was as high as 94%, and after 3.5 h, complete conversion occurred to give only products **9** and **10**.

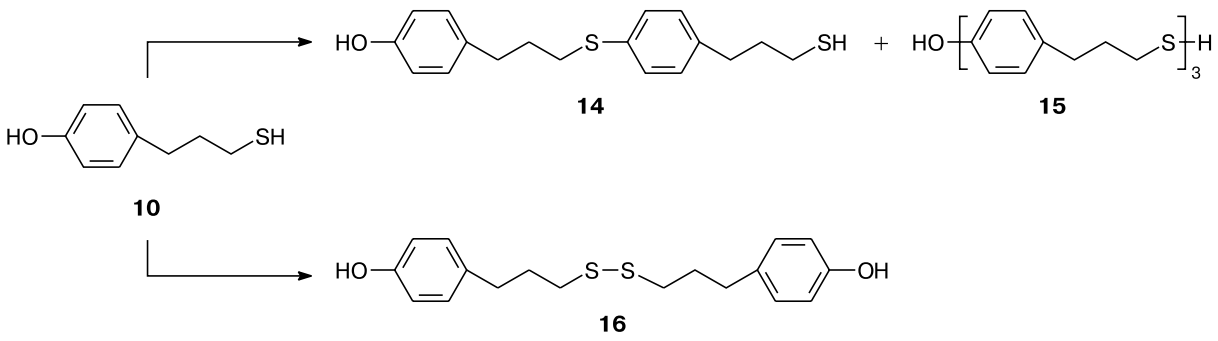
Thus, thiol **2** upon treatment with HHal, apparently, undergoes the following transformations (Scheme 2).

After heating of thiol **2** with HBr for 6 h, mercaptopropylphenol **10** was the main product of the reaction with its content in organic phase of the reaction mixture being 60%. In addition, the condensation products **14** and **15** (30 and 8%, respectively), as well as disulfide **16** (~2%) were also observed (Scheme 3). The presence of compounds **14** and **16** in the reaction mixture was confirmed with the use of the authentic samples obtained by alternative syntheses (see Experimental). Compound **15** was not isolated in pure form. However, data from mass spectrometry (the presence of the molecular ion peak with *m/z* 468 and the correspondence of the correlation of the isotope lines to that of the expected formula $C_{27}H_{32}OS_3$) allow us to suggest the structure shown in Scheme 3.

Sulfide **14** as the reaction product of thiol **2** with HBr was isolated in a crystalline form, its structure and composition were confirmed by elemental analysis, mass spectrometric and spectroscopic data. Thus the correlation of the isotope lines M, M + 1, M + 2 and M + 3 in the mass spectrum of product **14** corresponds to that expected for a compound with the molecular formula $C_{18}H_{22}OS_2$. In the ^{1}H NMR spectrum of this compound, a triplet of the proton of the SH group (δ 1.39), a singlet of phenolic proton (δ 5.50), and four doublets of aromatic hydrogen atoms with relative intensities of 1 : 1 : 2 : 2 : 2 : 2 were present. The chemical shifts of signals of two aromatic protons (δ 6.75 and 7.02) correspond to those in the spectrum of thiol **10**, and chemical shifts of another two protons are shifted downfield (δ 7.09 and 7.25).

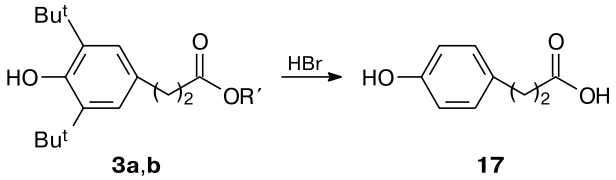
The identification of compounds **14** and **15** among the reaction products of thiol **2** with HBr is of particular interest, since the substitution reaction of a sulfide function for the phenolic OH group is virtually not documented. Thus in the STN International database, we found the only work[13] close to the described transformations, in which it was shown that the heating of phenol with thiols and conc. hydrochloric acid for 48—119 h at 180 °C gave the corresponding sulfides in 22—43% yield.

Scheme 3



Concentrated HBr was found to be also an efficient catalyst of de-*tert*-butylation of acid **3a** and its methyl ester **3b**: reflux of this compounds with HBr (≥30 wt.%) for 1.5—2 h afforded phloretic acid (**17**) in 91—92% yield (Scheme 4).

Scheme 4



3a,**b** **17**

R′ = H (**a**), Me (**b**)

This method for the synthesis of phloretic acid has undeniable advantages over that covered by a patent,[9] which is based on de-*tert*-butylation of acid **3a** and its esters upon treatment with H_2SO_4: our method differs in higher yield of the target product and does not require the use of additional solvents.

In conclusion, in the present work it was shown that on heating of 2,6-di-*tert*-butyl-4-(ω-hydroxyalkyl)phenols **1** with hydrohalic acids, the parallel processes of de-*tert*-butylation and substitution of halogen atom for the aliphatic OH group took place. This allows one to convert phenols **1** to the corresponding 4-(ω-haloalkyl)phenols, valuable intermediates in the synthesis of biologically active compounds, in one step and in good yields.

It was found that 4-(3-mercaptopropyl)phenol (**10**), obtained upon heating of 2,6-di-*tert*-butyl-4-(3-mercaptopropyl)phenol (**2**) with conc. HBr undergoes condensation under the reaction conditions to form 3-(4-hydroxyphenyl)propyl[4-(3-mercaptopropyl)phenyl] sulfide (**14**) as the main product.

A method for the synthesis of phloretic acid by de-*tert*-butylation of 3-(3,5-di-*tert*-butyl-4-hydroxyphenyl)propionic acid and its methyl ester upon treatment with conc. HBr was proposed.

Experimental

Alcohols **1a**—**d** [14,15] and thiol **2** [16] were obtained according to the described procedures. Acid **3a** is a commercial product from NIIKhIMPOLIMER. Ester **3b** was synthesized by esterification of acid **3a** with methyl alcohol.

NMR spectra were recorded on a Bruker DRX500 spectrometer with the working frequency of 500.13 MHz, for acid **17**, in D_2O ($SiMe_4$ as the standard), for other compounds, in $CDCl_3$ ($CHCl_3$ as the standard). Mass spectral analysis was performed on a Finnigan MAT 8200 mass spectrometer.

Chromato-mass spectrometry was performed on a Hewlett Packard G1801A spectrometer, which included HP 5890 gas chromatograph of the II series and HP 5971 mass-selective detector (EI, 70 eV). Column, HP-5MS 30 m × 0.25 mm × 0.25 μm; carrier gas, helium, 1 mL min^{-1}. Temperature conditions of the columns: 2 min at 50 °C, heating with the rate of 10 °C min^{-1}, 5 min at 280 °C. Temperature of injector, 280 °C, of the ion source, 173 °C. The data were collected with the rate of 1.2 scan s^{-1} in the mass region 30—650 a.u.m.

Chromatographic analysis was performed on an LKhM-80MD chromatograph (model 5) with the thermal conductivity detector. Column 3 m × 3 mm, phase 3% OV-17 on N-Super Chromaton (0.16—0.20 mm); carrier gas, helium, 30 mL min^{-1}. Temperature of injector, 280 °C, of detector, 290 °C. Temperature conditions of the columns: 220 °C (isothermic) or from 150 to 220 °C (in programming conditions).

4-(3-Chloropropyl)phenol (8). Hydrogen chloride was passed through a melt of alcohol **1b** (13.2 g, 50 mmol) for 14 h at 140 °C with the rate of 100—150 mL min^{-1}. The resulting mixture was distilled *in vacuo*, and a fraction with b.p. 120—125 °C (1—2 Torr) was collected. Product **8** (7 g, 82%) was obtained, m.p. 36—37 °C (from pentane). Found (%): C, 62.23; H, 6.53; Cl, 20.79. $C_9H_{11}ClO$. Calculated (%): C, 63.35; H, 6.50; Cl, 20.78. ^{1}H NMR, δ: 1.70—2.15 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.63 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.37 (t, 2 H, CH_2Cl, J = 6.5 Hz); 5.00 (s, 1 H, OH); 6.80, 7.14 (both d, 2 H each, Ar, J = 8.5 Hz).

4-(2-Chloroethyl)phenol was obtained similarly from alcohol **1a**, the yield was 61%, m.p. 56—57 °C (from hexane). Found (%): C, 61.29; H, 5.94; Cl, 22.83. C_8H_9ClO. Calculated (%): C, 61.35; H, 5.79; Cl, 22.64. ^{1}H NMR, δ: 2.98 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.66 (t, 2 H, CH_2Cl, J = 6.5 Hz); 5.02 (s, 1 H, OH); 6.68, 6.95 (both d, 2 H each, Ar, J = 8.5 Hz).

4-(3-Chloro-1-methylpropyl)phenol was obtained similarly from alcohol **1d**, the yield was 79%, b.p. 137—138 °C (5 Torr). Found (%): C, 65.05; H, 6.95; Cl, 19.08. $C_{10}H_{13}ClO$. Calculated (%): C, 65.04; H, 7.10; Cl, 19.20. ^{1}H NMR, δ: 1.22 (d, 3 H, Me, J = 7 Hz); 1.93—2.99 (m, 2 H, $CHC\underline{H}_2CH_2$); 2.88—2.90 (m, 1 H, $ArC\underline{H}$); 3.27—3.33, 3.39—3.45 (both m, 1 H each, CH_2Cl); 6.23 (s, 1 H, OH); 6.78, 7.04 (both d, 2 H each, Ar, J = 8.5 Hz).

Reaction of alcohol 1b with hydrochloric acid. Alcohol **1b** (5 g, 19 mmol) and hydrochloric acid (15 mL, 0.17 mol of HCl) were placed in a 80-mL tube made of thermostable glass, the tube was sealed and kept in a thermostat equipped with a shaking device for 2 h at 180 °C. After cooling and opening of the tube, the content was treated with benzene. The extract was washed with water, treated with aq. NaOH, and the benzene and aq. alkaline layers were separated. The benzene extract was treated with hydrochloric acid, washed with water, dried with Na_2SO_4, and the solvent was evaporated. 2-*tert*-Butyl-4-(3-chloropropyl)phenol (**6**) (1.90 g, 44%) was obtained. Found (%): C, 68.84; H, 8.39; Cl, 15.57. $C_{13}H_{19}ClO$. Calculated (%): C, 68.86; H, 8.45; Cl, 15.64. ^{1}H NMR, δ: 1.40 (s, 9 H, Bu^t); 2.00—2.06 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.68 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.52 (t, 2 H, CH_2Cl, J = 6.5 Hz); 4.85 (s, 1 H, OH); 6.56 (d, 1 H, Ar, J = 8 Hz); 6.87 (dd, 1 H, Ar, J = 8 Hz, J = 2 Hz); 7.07 (d, 1 H, Ar, J = 2 Hz). The aq. alkaline layer was neutralized with hydrochloric acid and treated with toluene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. Chloropropylphenol **8** (1.46 g, 45%) was obtained.

2-*tert*-Butyl-4-(3-hydroxypropyl)phenol (5). Argon was bubbled through a melt of alcohol **1b** (25 g, 94 mmol) for 80 min

at 315 °C, then the reaction mixture was cooled and dissolved in toluene. The solution was sequentially treated with 5% and 10% aq. NaOH, the latter extract was neutralized with hydrochloric acid and treated with toluene. The toluene extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was distilled *in vacuo* and the target alcohol **5** (14.8 g, 75%) was obtained, b.p. 139—140.5 °C (1 Torr), m.p. 47—49 °C (from hexane). Found (%): C, 75.16; H, 9.88. $C_{13}H_{20}O_2$. Calculated (%): C, 74.96; H. 9.68. ^{1}H NMR, δ: 1.39 (s, 9 H, Bu^t), 1.57 (br.s, 1 H, $CH_2O\underline{H}$); 1.84—1.88 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.61 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.69 (t, 2 H, $C\underline{H}_2OH$, J = 6.5 Hz); 5.28 (s, 1 H, OH); 6.57 (d, 1 H, Ar, J = 8 Hz); 6.86 (dd, 1 H, Ar, J = 8 Hz, J = 2 Hz); 7.06 (d, 1 H, Ar, J = 2 Hz).

4-(3-Hydroxypropyl)phenol (7) was obtained similarly to alcohol **5** upon heating of alcohol **1b** for 11 h at 324 °C. The yield was 76%, m.p. 55 °C (from $CHCl_3$). Found (%): C, 71.17; H, 8.08. $C_9H_{12}O_2$. Calculated (%): C, 71.03; H. 7.95. ^{1}H NMR, δ: 1.85 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.62 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.40 (s, 1 H, $CH_2O\underline{H}$); 3.63 (t, 2 H, $C\underline{H}_2OH$, J = 6.5 Hz); 6.73, 7.02 (both d, 2 H each, Ar, J = 8 Hz); 7.86 (s, 1 H, OH).

4-(3-Bromopropyl)phenol. Alcohol **1b** (120 g, 0.45 mol) and 41% aq. hydrobromic acid (384 mL, 2.67 mol of HBr) were refluxed for 12 h with azeotropic distillation of an $HBr—H_2O$ mixture. Then the reaction mixture was cooled and treated with toluene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was distilled *in vacuo* and the target bromopropylphenol (87.9 g, 91%) was obtained, b.p. 121—124 °C (1 Torr), m.p. 38—40 °C (from pentane). Found (%): C, 50.33; H, 5.21; Br, 36.97. $C_9H_{11}BrO$. Calculated (%): C, 50.26; H, 5.15; Br, 37.15. ^{1}H NMR, δ: 2.08—2.14 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.70 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.37 (t, 2 H, CH_2Br, J = 7 Hz); 5.00 (s, 1 H, OH); 6.76, 7.14 (both d, 2 H each, Ar, J = 8 Hz).

4-(2-Bromoethyl)phenol was obtained similarly from alcohol **1a**, the yield was 79%, b.p. 108—110 °C (1—2 Torr), m.p. 85—87 °C (from hexane). Found (%): C, 47.95; H, 4.48; Br, 40.00. C_8H_9BrO. Calculated (%): C, 47.79; H, 4.51; Br, 39.74. ^{1}H NMR, δ: 3.00 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.48 (t, 2 H, CH_2Br, J = 7.5 Hz); 5.03 (s, 1 H, OH); 6.71, 6.99 (both d, 2 H each, Ar, J = 8.5 Hz).

4-(4-Bromobutyl)phenol was obtained similarly from alcohol **1c**, the yield was 91%, b.p. 146—148 °C (3 Torr). Found (%): C, 52.56; H, 5.96; Br, 34.73. $C_{10}H_{13}BrO$. Calculated (%): C, 52.42; H, 5.72; Br, 34.87. ^{1}H NMR, δ: 2.10—2.13 (m, 4 H, $ArCH_2(C\underline{H}_2)_2$); 2.62 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.33 (t, 2 H, CH_2Br, J = 7 Hz); 5.02 (s, 1 H, OH); 6.75, 7.10 (both d, 2 H each, Ar, J = 8 Hz).

4-(3-Iodopropyl)phenol. Alcohol **1b** (20 g, 76 mmol) and 45% aq. hydroiodic acid (57.6 mL, 0.3 mol of HI) were stirred for 36 h at 120—130 °C. Then the reaction mixture was cooled and treated with toluene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was distilled *in vacuo* and the target iodopropylphenol (6.5 g, 36%) was obtained, b.p. 150—152 °C (2 Torr), m.p. 32 °C (from pentane). Found (%): C, 41.18; H, 4.35; I, 48.32. $C_9H_{11}IO$. Calculated (%): C, 41.25; H, 4.23; I, 48.42. ^{1}H NMR, δ: 1.75—2.25 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.57 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 3.04 (t, 2 H, CH_2I, J = 7 Hz); 6.09 (s, 1 H, OH); 6.63, 6.95 (both d, 2H each, Ar, J = 8 Hz).

2-*tert*-Butyl-4-(3-mercaptopropyl)phenol (9). Chloride **6** (10.2 g, 45 mmol), 25% aq. NH_4HS (10.7 mL, 67.4 mmol), and ethanol (25 mL) were placed in a 80-mL tube made of thermostable glass, the tube was sealed and kept in a thermostat equipped with a shaking device for 4 h at 120 °C. After cooling and opening of the tube, the content was treated with benzene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was distilled *in vacuo* to obtain the target thiol **9** (8.52 g, 81%), b.p. 142—146 °C (3 Torr). Found (%): C, 69.43; H, 9.07; S, 14.01. $C_{13}H_{20}OS$. Calculated (%): C, 69.59; H, 8.98; S, 14.29. ^{1}H NMR, δ: 1.13 (t, 1 H, SH, J = 8 Hz); 1.40 (s, 9 H, Bu^t); 1.82 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.58 (m, 4 H, $C\underline{H}_2CH_2C\underline{H}_2$); 4.68 (s, 1 H, OH); 6.54 (d, 1 H, Ar, J = 8 Hz); 6.86 (dd, 1 H, Ar, J = 8 Hz, J = 2 Hz); 7.04 (d, 1 H, Ar, J = 2 Hz).

***tert*-Butyl 3-(3-*tert*-butyl-4-hydroxyphenyl)propyl sulfide (12).** Thiol **2** (5 g, 17.8 mmol) and *tert*-butylbromide (30 mL, 0.27 mol) were placed in a 80-mL tube made of thermostable glass, the tube was sealed and kept in a thermostat equipped with a shaking device for 8 h at 150 °C. After cooling and opening of the tube, the content was treated with benzene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was chromatographed on silica gel with hexane as the eluent. Sulfide **12** (1.8 g, 36%) was obtained. Found (%): C, 72.98; H, 10.19; S, 11.64. $C_{17}H_{28}OS$. Calculated (%): C, 72.80; H, 10.06; S, 11.43. ^{1}H NMR, δ: 1.31 (s, 9 H, SBu^t); 1.39 (s, 9 H, Bu^t); 1.98 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.55 (t, 2 H, CH_2S, J = 8 Hz); 2.64 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 5.06 (s, 1 H, OH); 6.59 (d, 1 H, Ar, J = 8 Hz); 6.78 (dd, 1 H, Ar, J = 8 Hz, J = 2 Hz); 7.07 (d, 1 H, Ar, J = 2 Hz).

***tert*-Butyl 3-(4-hydroxyphenyl)propyl sulfide (13)** was obtained similarly from thiol **10**. The yield was 47%. Found (%): C, 69.60; H, 9.04; S, 14.15. $C_{13}H_{20}OS$. Calculated (%): C, 69.59; H, 8.98; S, 14.29. ^{1}H NMR, δ: 1.31 (s, 9 H, Bu^t); 1.87 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.57 (t, 2 H, CH_2S, J = 8 Hz); 2.66 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 4.80 (s, 1 H, OH); 6.74, 7.04 (both d, 2 H each, Ar, J = 8.5 Hz).

Reaction of thiol 2 with hydrochloric acid. Thiol **2** (5 g, 17.8 mmol) and hydrochloric acid (23 mL, 0.21 mol of HCl) were placed in a 80-mL tube made of thermostable glass, the tube was sealed and kept in a thermostat equipped with a shaking device for 4.5 h at 160 °C. After cooling and opening of the tube, the content was treated with benzene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. According to GC/MS data, the obtained product contained thiol **9** (42%), thiol **10** (10%), sulfide **12** (46%) and sulfide **13** (2%).

Reaction of thiol 2 with hydrobromic acid. A mixture of thiol **2** (20 g, 71.3 mmol) and hydrobromic acid (125 mL, 0.87 mol of HBr) was refluxed for 6 h with azeotropic distillation of an $HBr—H_2O$ mixture under flow of argon, then the reaction mixture was cooled and treated with toluene. The extract was washed with brine, dried with Na_2SO_4, and the solvent was evaporated. The residue was distilled *in vacuo* to yield 4-(3-mercaptopropyl)phenol (**10**) (6.72 g, 56%), b.p. 117—118 °C (1 Torr). Found (%): C, 63.18; H, 7.29; S, 19.17. $C_9H_{12}OS$. Calculated (%): C, 64.25; H, 7.19; S, 19.06. ^{1}H NMR, δ: 1.37 (t, 1 H, SH, J = 8 Hz); 1.85—1.89 (m, 2 H, $CH_2C\underline{H}_2CH_2$); 2.47—2.52 (m, 2 H, CH_2S); 2.63 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 4.95 (br.s, 1 H, OH); 6.75, 7.02 (both d, 2 H each, Ar, J = 8 Hz).

The residue in the distillation flask was sequentially recrystallized from toluene and hexane to give 3-(4-hydroxyphenyl)propyl[4-(3-mercaptopropyl)phenyl] sulfide (**14**) (2.84 g, 25%), m.p. 54—56 °C. Found (%): C, 67.77; H, 7.00; S, 20.34. $C_{18}H_{22}OS_2$. Calculated (%): C, 67.88; H, 6.96; S, 20.13. ^{1}H NMR, δ: 1.39 (t, 1 H, SH, J = 8 Hz); 1.89—1.92 (m, 4 H, $CH_2C\underline{H}_2CH_2$); 2.50—2.54 (m, 2 H, $C\underline{H}_2SH$); 2.67—2.69 (m, 4 H, $ArC\underline{H}_2$); 2.88 (t, 2 H, $C\underline{H}_2SAr$, J = 7.5 Hz); 5.50 (br.s, 1 H, OH); 6.75, 7.02, 7.09, 7.25 (all d, 2 H each, Ar, J = 8 Hz). MS (EI, 70 eV), m/z (I_{rel} (%)): 318 $[M]^+$ (33), 257 $[M - HSCH_2CH_2]^+$ (2), 211 $[M - HOC_6H_4CH_2]^+$ (2), 184 $[HSC_6H_4(CH_2)_3SH]^+$ (2), 149 $[CH_2{=}CHSC_6H_4CH_2]^+$ (9), 134 $[HOC_6H_4CH_2CH{=}CH_2]^+$ (100), 123 $[HSC_6H_4CH_2]^+$ (7), 107 $[HOC_6H_4CH_2]^+$ (37), 91 $[C_7H_7]^+$ (8), 77 $[C_6H_5]^+$ (9).

3-(4-Hydroxyphenyl)propyl 4-(3-mercaptopropyl)phenyl sulfide (14). A mixture of thiol **10** (4.26 g, 25 mmol) and hydrobromic acid (30.5 mL, 0.24 mol of HBr) was kept for 16 h at 120—122 °C in an atmosphere of argon, then the reaction mixture was cooled and treated with toluene. The extract was washed with water, dried with Na_2SO_4, and the solvent was evaporated. The residue was distilled *in vacuo*. The residue in the distillation flask was sequentially recrystallized from toluene and hexane. The title compound **14** (2.6 g, 33%) was obtained, m.p. 55—56 °C.

Bis[3-(4-hydroxyphenyl)propyl] disulfide (16). Sodium hydroxide (0.8 g, 20 mmol) was dissolved in water (40 mL), then thiol **10** (3 g, 17.9 mmol) was added under argon, and after its dissolution, 30% aq. H_2O_2 (2 mL, 19.5 mmol of H_2O_2) was added. The solution was stirred for 1 h at 20 °C, neutralized with HCl, and treated with Et_2O. The extract was washed with brine, dried with Na_2SO_4, and the solvent was evaporated. Disulfide **16** (1.45 g, 84%) was obtained, m.p. 76—77 °C (from hexane). Found (%): C, 64.71; H, 6.77; S, 19.08. $C_{18}H_{22}O_2S_2$. Calculated (%): C, 64.63; H, 6.63; S, 19.17. ^{1}H NMR, δ: 1.92 (m, 4 H, $CH_2C\underline{H}_2CH_2$); 2.60 (m, 8 H, $C\underline{H}_2CH_2C\underline{H}_2$); 4.48 (s, 2 H, OH); 6.65, 6.97 (both d, 4 H each, Ar, J = 8 Hz).

3-(4-Hydroxyphenyl)propionic acid (17). A mixture of acid **3a** (8 g, 28.7 mmol) and 41% aq. hydrobromic acid (24.5 mL, 0.17 mol of HBr) was refluxed for 2 h, then the reaction mixture was cooled, the formed crystals were filtered off. The yield of acid **17** was 4.4 g (92%), m.p. 132 °C (from toluene). Acid **17** was similarly obtained from ester **3b**, the yield was 91%. Found (%): C, 64.93; H, 6.15. $C_9H_{10}O_3$. Calculated (%): C, 65.05; H, 6.07. ^{1}H NMR, δ: 2.60 (t, 2 H, $C\underline{H}_2COOH$, J = 7.5 Hz); 3.86 (t, 2 H, $ArC\underline{H}_2$, J = 7.5 Hz); 6.67, 7.01 (both d, 2 H each, Ar, J = 8.5 Hz).

This work was financially supported by the Russian Foundation for Basic Research (Project No. 00-03-32721); access to the STN International database was made through the Novosibirsk STN Center in NIOKh SB RAS.

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Received February 9, 2007;
in revised form May 15, 2007