Reactions of 4-acylresorcinol derivatives with 3,5-di-*tert*-butyl-4-hydroxybenzyl acetate

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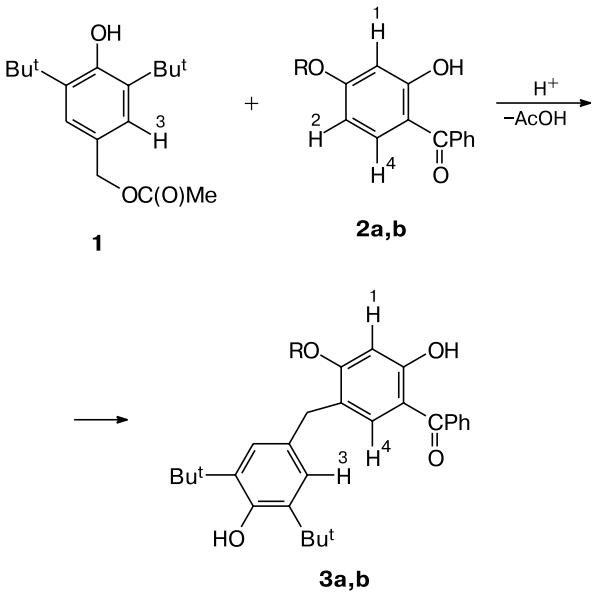
Reactions of hydroxyphenylcarbonyl derivatives with 3,5-di-*tert*-butyl-4-hydroxybenzyl acetate under mild conditions gave novel functionalized diarylmethanes.

Key words: C-benzylation, diarylmethanes, resorcinols, arenes, carbonyl compounds, X-ray diffraction analysis.

Researchers are giving much attention to problems of the synthesis, structures, and properties of phenol stabilizers of polymeric materials. Relevant data, including those on their efficiencies and stabilization mechanism, have been reported in some monographs.[1—7] 2-Hydroxyphenylcarbonyl compounds belong to a commonly used class of light stabilizers of polymers.[8] Introduction of sterically hindered phenolic fragments (*e.g.*, 3,5-di-*tert*-butyl-4-hydroxybenzyl group) affords polyfunctional stabilizers that function as both UV absorbers and scavengers for peroxide radicals.[9] However, a search for efficient benzylating agents for selective introduction of 3,5-di-*tert*-butyl-4-hydroxybenzyl fragments with the aim of obtaining novel sterically hindered phenol derivatives remains of topical interest. Recently, we have developed a simple and feasible method for the synthesis of 3,5-di-*tert*-butyl-4-hydroxybenzyl acetate (**1**) and showed some of its synthetic potentialities.[10]

Here we studied acetate **1** as a possible reagent for the benzylation of 2-hydroxy-4-methoxybenzophenone (**2a**) and 2-hydroxy-4-octyloxybenzophenone (**2b**) (Scheme 1). Reactions catalyzed by acetic, formic, or perchloric acid under mild conditions (1.5 h, 40 or 50 °C) gave 5-benzylated benzophenones **3a,b** in high yields.

Scheme 1



R = Me (**2a, 3a**), C_8H_{17} (**2b, 3b**)

The ^{1}H NMR spectra of products **3a,b** show no signal for the H(2) proton, which is present in the spectra of the starting compounds **2a,b**. The signal for the OH proton at δ 12.9 is retained, while the signals for the H(1) and H(4) protons appear as singlets. The ^{1}H NMR data unambiguously confirm our conclusion about the structures of the final products. Analogous reactions of benzyl acetate **1** with 2,4-dihydroxybenzophenone (**4a**) and 2,4-dihydroxybenzaldehyde (**4b**) gave 3,5-dibenzylated products (Scheme 2). Earlier,[11] it has been assumed that such reactions involve simultaneous benzylation of position 5 of the aromatic ring and of the OH group at the C(4) atom.

It should be noted that dibenzylation products **5a,b** were detected in the reaction mixture even when the reagents had been used in an equimolar ratio. Their structures were proven by ^{1}H and ^{13}C NMR spectroscopy. The

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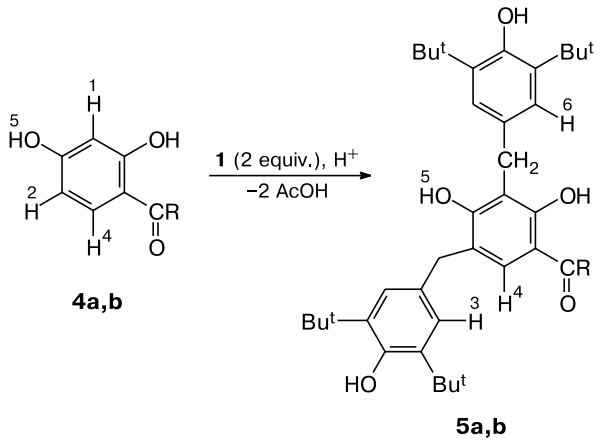
Scheme 2



R = Ph (**4a, 5a**), H (**4b, 5b**)

crystal structure of compound **5b** was determined by X-ray diffraction analysis (Fig. 1, Table 1).

The asymmetric part of the unit cell contains a molecule of compound **5b** and a molecule of formic acid. The aromatic fragments have standard geometries. The angles between the plane of the central aromatic fragment C(1)—C(6) and the terminal aromatic fragments C(8)—C(13) and C(24)—C(29) are 121.0(3)° and 103.3(3)°, respectively. The angle between the C(8)—C(13) and C(24)—C(29) planes is 17.8(4)°.

In the crystal of complex **5b** · HCO_2H, intermolecular OH...O hydrogen bonds unite molecules of compound **5b** and solvate molecules of formic acid into an infinite zigzag chain aligned with the axis 0*x* (Fig. 2). The hydrogen bonds parameters for the fragment O(1)—H(1)...O(43′) (*x*, 1 − *y*, 1/2 + *z*) are O(1)—H(1) 0.82 Å, H(1)...O(43) 2.06 Å, O(1)...O(43) 2.78(1) Å, and O(1)—H(1)...O(43) 148° and for the fragment O(41)—H(41)...O(15) are O(41)—H(41) 0.82 Å, O(41)...H(41) 2.02 Å, O(41)...O(15) 2.83(2) Å, and O(41)—H(41)...O(15) 175°.

A reaction of benzylic acetate **1** with 2,4-dihydroxybenzophenone (**4a**) in the presence of triethylamine gave 3-(3,5-di-*tert*-butyl-4-hydroxybenzyl)-2,4-dihydroxybenzophenone (**6**) (Scheme 3). Here triethylamine acts as a base with respect to both benzophenone **4a** and benzylic acetate **1**, thus providing the formation of 2,6-di-*tert*-butyl-*p*-quinone methide (**7**) from the latter.[12] Compound **6** is an adduct of anion **8** and *p*-quinone methide **7**.

Structure **6** was confirmed by ^1H and ^{13}C NMR spectroscopy and X-ray diffraction analysis (Fig. 3, Table 1).

The asymmetric part of the crystal of compound **6** contains two independent molecules **A** and **B**. It should be noted that the geometrical parameters of molecules **A**

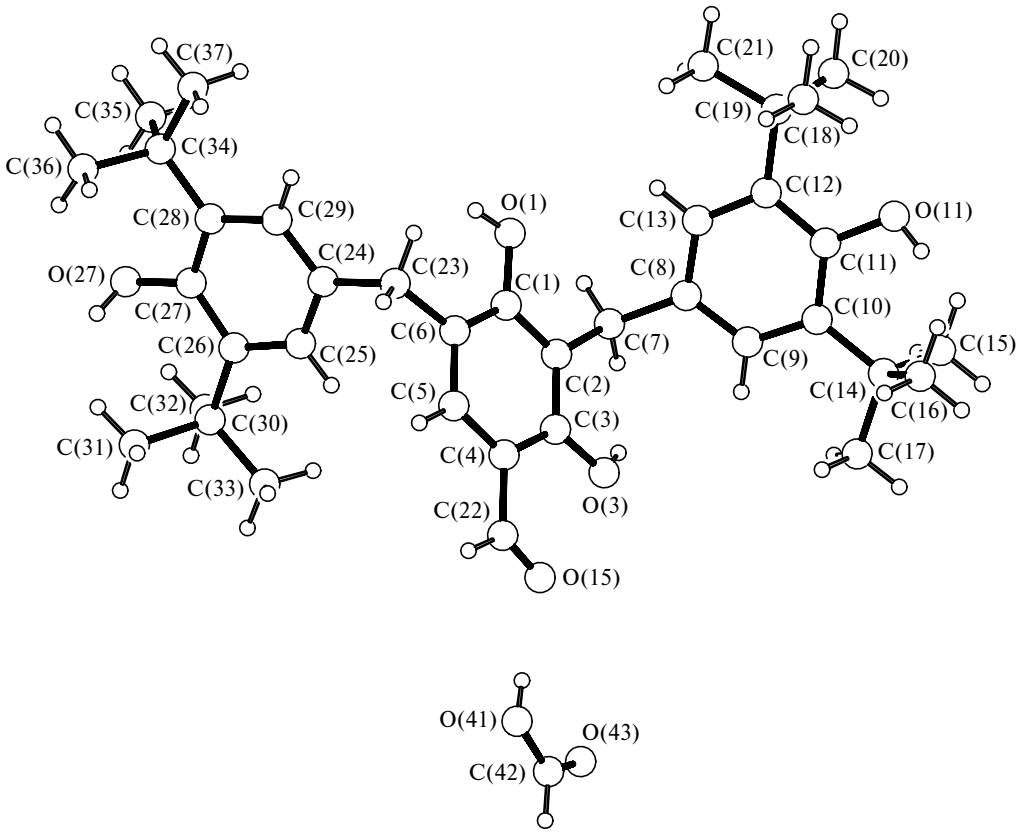


Fig. 1. Crystal geometry for the complex of compound **5b** with formic acid.

Table 1. Crystallographic parameters of compounds **5b** and **6** and a summary of data collection

Parameter	**5b**	**6**
Color, habitus	Colorless prismatic	
Molecular formula	$C_{37}H_{50}O_5 \cdot CO_2H_2$	$C_{28}H_{32}O_4$
Crystal system	Orthorhombic	Monoclinic
Space group	*Pbcn*	$P2_1/n$
Unit cell parameters:[2]		
a/Å	32.748(10)	8.473(2)
b/Å	11.33(2)	15.54(6)
c/Å	19.171(10)	38.03(10)
β/deg	—	95.2(4)
V/Å^3	7115(13)	4986(24)
Z	8	8
Molecular mass	620.80	432.54
ρ_{calc}/g cm^{-3}	1.159	1.152
Absorption coefficient, μCu/cm^{-1}	6.27	6.02
F(000)	2688	1856
Radiation	CuKα	
λ/Å	1.54184	
θ range	$2.7 \le \theta \le 55.06$	$4.67 \le \theta \le 59.95$
Scan mode	ω-Scan mode	
Ranges of *hkl* indices	$0 \le h \le 34$, $-12 \le k \le 12$, $-163 \le l \le 20$	$0 \le h \le 6$, $17 \le k \le 17$, $-42 \le l \le 42$
Number of measured reflections	10234	5940
Number of observed reflections with $I > 2\sigma(I)$	1357	877
Final residuals		
R	0.064	0.088
R_w	0.171	0.161
GOOF	0.939	1.522
Δ/σ	0.04	0
Number of reflections used in the refinement	4459	5940
Number of parameters refined	400	298

Note. Standard (two orientation checking and three intensity control) reflections were measured after every 200 reflections. Absorption correction was not applied.

and **B** are equal to within the experimental error. The aromatic fragments have standard bond lengths and angles, as in the crystal of compound **5b**. In molecule **A**, the angles between the plane of the central aromatic fragment C(16A)—C(21A) and the terminal aromatic fragments C(2A)—C(7A) and C(22A)—C(28A) are 101.3(5)° and 125.5(5)°, respectively. The angle between the C(2A)—C(7A) and C(22A)—C(28A) planes is 53.8(5)°. In molecule **B**, the angles between the plane of the central aromatic fragment C(16B)—C(21B) and the terminal aromatic fragments C(2B)—C(7B) and C(22B)—C(28B) are 100.8(5)° and 124.2(5)°, respectively. The angle between the C(2B)—C(7B) and C(22B)—C(28B) planes is 54.1(5)°.

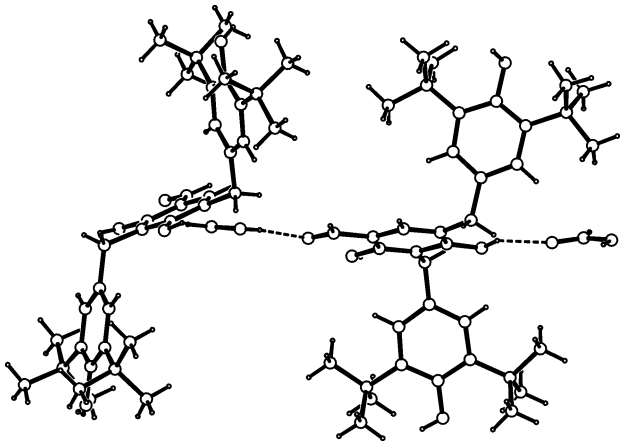
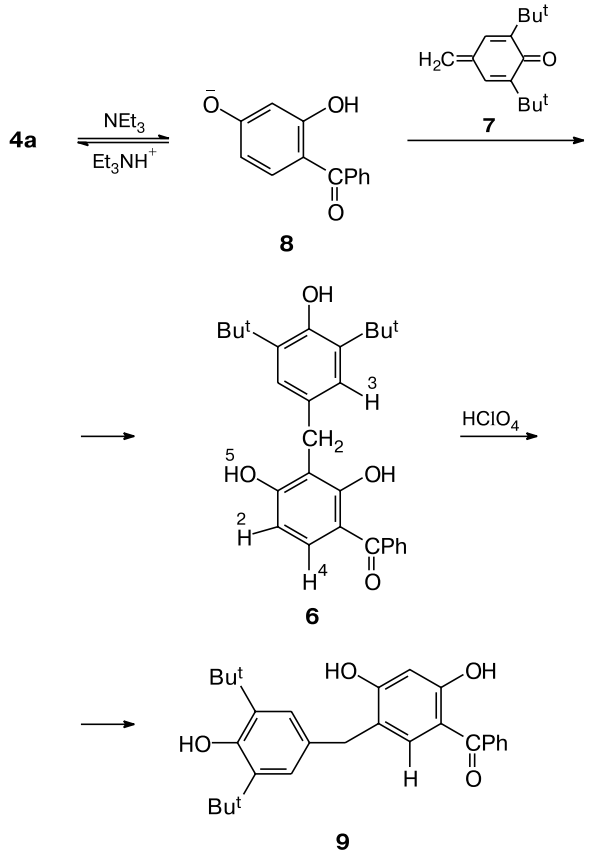


Fig. 2. Hydrogen bonds in the crystal of complex **5b** · HCO_2H.

Scheme 3



Intra- and intermolecular OH...O hydrogen bonds were detected in the crystal of compound **6** (Fig. 4). The intramolecular hydrogen bond O(17A)—H(17A)...O(22A) (O(17A)—H(17A) 0.82 Å, H(17A)...O(22A) 1.80 Å, O(17A)...O(22A) 2.53(2) Å, O(17A)—H(17A)...O(22A) 145°) closes a six-membered ring. The parameters of the intermolecular hydrogen bonds are as follows: O(21A)—H(21A) 0.82 Å, H(21A)...O(22A)

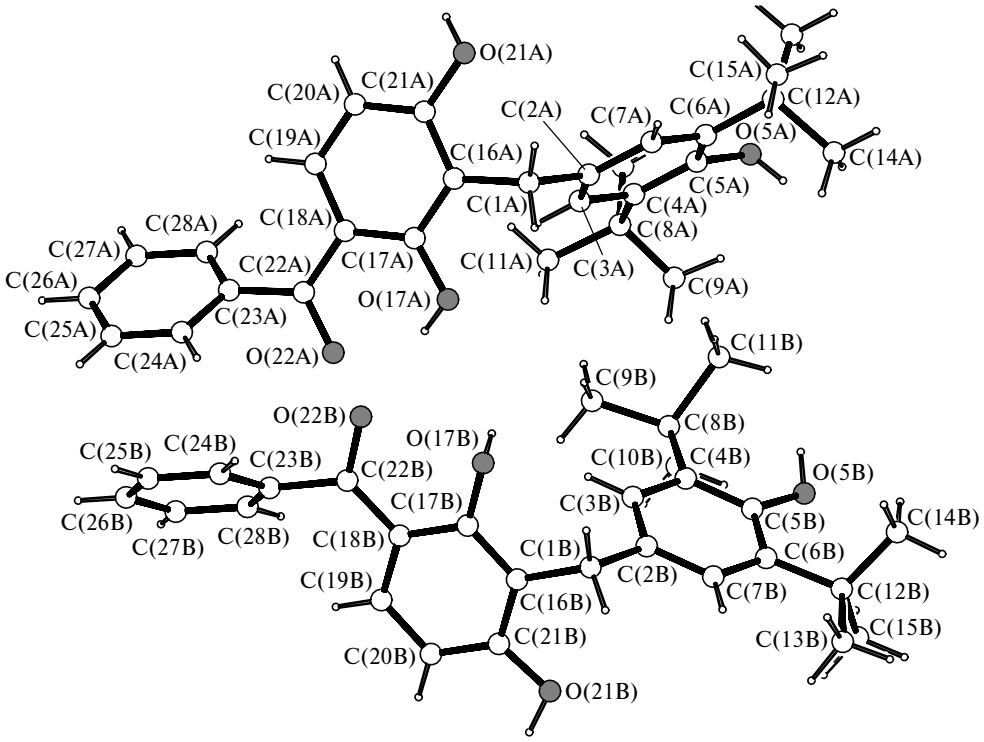


Fig. 3. Geometry of the independent molecules in the crystal of compound **6**.

2.04 Å, O(21A)...O(22A) 2.79(2) Å, and O(21A)—H(21A)...O(22A) 151° in the fragment O(21A)—H(21A)...O(22A) $(1/2 - x, 1/2 + y, 1/2 - z)$ and O(21B)—H(21B) 0.96 Å, H(21B)...O(22B) 1.84 Å, O(21B)...O(22B) 2.71(2) Å, and O(21B)—H(21B)...O(22B) 150° in the fragment O(21B)—H(21B)...O(22B) $(1/2 - x, -1/2 + y, 1/2 - z)$. The resulting parallel infinite zigzag chains are aligned with the axis 0*b* and linked by the π...π-interactions of the aromatic rings. Interestingly, the chains consist of molecules of one type (**A** or **B**).

The π...π-interactions give rise to molecular stacks in the crystal, which are parallel to the axis 0*a* (Fig. 5). The parameters of the interaction are as follows: distance between the C(16A)—C(21A) and C(16B)—C(21B) planes $(3/2 - x, 1/2 + y, 1/2 - z)$ is 3.550 Å and the angle between the planes is 1°.

To elucidate the causes of the regioselectivity of this reaction, additional investigation is required.

The acid-catalyzed benzylation of 2,4-dihydroxyphenylcarbonyl compounds is a reversible process. This is evident from a structural change in compound **6** upon its heating in acetone in the presence of perchloric acid (see Scheme 3). The ^{1}H NMR spectrum of the reaction mixture contains a signal for the methylene protons at δ 3.76 characteristic of a 3,5-di-*tert*-butyl-4-hydroxybenzyl sub-

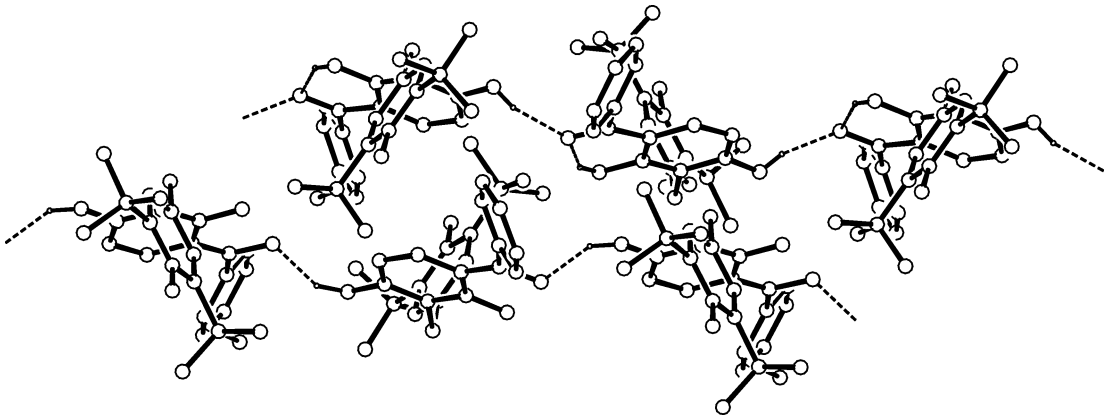


Fig. 4. Hydrogen bonds in the crystal of compound **6** (hydrogen atoms are omitted).

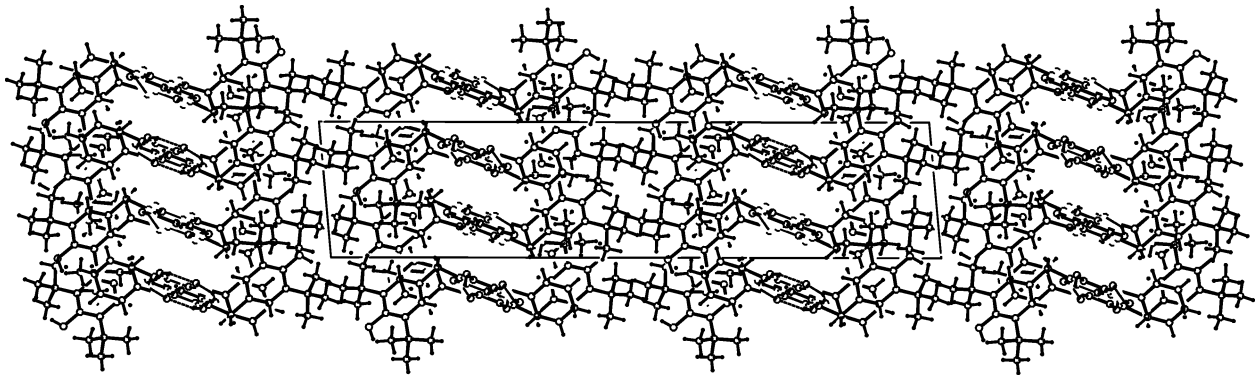


Fig. 5. Crystal packing of compound **6**.

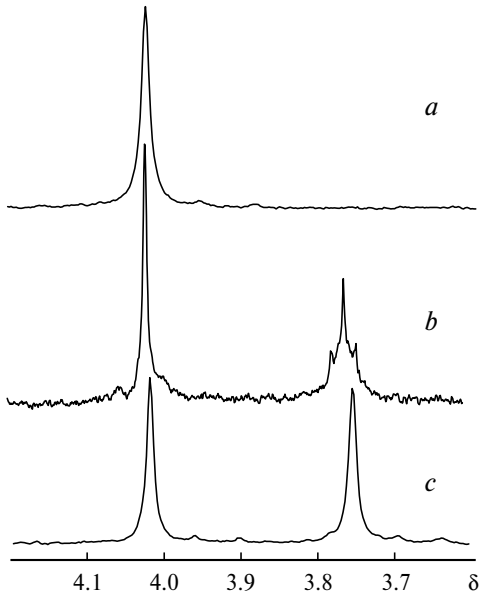


Fig. 6. Fragments of the ^{1}H NMR spectra ($CDCl_3$) of compound **6** prior to (*a*) and after the treatment with perchloric acid (*b*) and the ^{1}H NMR spectrum of compound **5a** (*c*).

stituent at the C(5) atom of the 2,4-dihydroxybenzophenone system (Fig. 6, *b*). The data obtained suggest easy *ipso*-substitution in resorcinol derivatives, which seems to lead, in our case, to compound **9**. This circumstance may be responsible for earlier reported[13] easy decomposition of a calix[4]resorcinol system under the action of benzyl acetate **1** in the presence of acids.

Experimental

^{1}H and ^{13}C NMR spectra were recorded on a Bruker WM-250 instrument (250 (^{1}H) and 62.9 MHz (^{13}C)) in $CDCl_3$ at 20 °C. Chemical shifts were measured with reference to signals for residual protons (^{1}H) and for a deuterated solvent (^{13}C).

5-(3,5-Di-*tert*-butyl-4-hydroxybenzyl)-2-hydroxy-4-methoxybenzophenone (3a). Two to three drops of 72% $HClO_4$ were added to a solution of 2-hydroxy-4-methoxybenzophenone (**2a**) (2.28 g, 0.01 mol) and 3,5-di-*tert*-butyl-4-hydroxybenzyl acetate (**1**)[10] (2.78 g, 0.01 mol) in AcOH (20 mL). The reaction mixture was kept at 50 °C for 90 min and poured into water. The precipitate that formed was filtered off, washed with water, dried, and crystallized from hexane. The yield of compound **3a** was 3.17 g (71%), m.p. 136 °C. Found (%): C, 78.26; H, 7.70. $C_{29}H_{34}O_4$. Calculated (%): C, 78.00; H, 7.67. ^{1}H NMR, δ: 1.38 (s, 18 H, CMe_3); 3.71 (s, 2 H, CH_2); 3.90 (s, 3 H, MeO); 5.04 (s, 1 H, OH); 6.50 (s, 1 H, H(1)); 6.94 (s, 2 H, H(3)); 7.21 (s, 1 H, H(4)); 7.35—7.55 (m, 5 H, ArH); 12.68 (s, 1 H, OH...O). ^{13}C NMR ($CDCl_3$, 20 °C), δ: 30.3 ($C\underline{Me}_3$); 34.2 ($\underline{C}Me_3$); 34.8 ($Ar\underline{C}H_2Ar$); 55.7 (MeO); 199.8 (C=O); 99.2; 112.3; 122.3; 125.3; 128.1; 128.7; 130.7; 131.3; 134.6; 135.7; 138.3; 151.9; 164.0; 165.1 (C_{arom}).

5-(3,5-Di-*tert*-butyl-4-hydroxybenzyl)-2-hydroxy-4-octyloxybenzophenone (3b). Two to three drops of 72% $HClO_4$ were added to a solution of 2-hydroxy-4-octyloxybenzophenone (**2b**) (3.26 g, 0.01 mol) and ester **1** (2.78 g, 0.01 mol) in AcOH (20 mL). The reaction mixture was kept at 40 °C for 1.5 h and poured into water. The resulting oil was extracted with diethyl ether, the extract was concentrated, and the residue was washed with hexane. The yield of compound **3b** was 3.81 g (70%), m.p. 103—104 °C. Found (%): C, 79.81; H, 8.36. $C_{36}H_{48}O_4$. Calculated (%): C, 79.37; H, 8.88. ^{1}H NMR, δ: 0.89 (t, 3 H, CH_3); 1.10—1.65 (m, 10 H, CH_2); 1.39 (s, 18 H, CMe_3); 1.74—1.95 (m, 2 H, CH_2); 3.71 (s, 2 H, $ArCH_2Ar$); 4.03 (t, 2 H, CH_2O; J = 6.5 Hz); 5.03 (s, 1 H, OH); 6.47 (s, 1 H, H(1)); 6.95 (s, 2 H, H(3)); 7.24 (s, 1 H, H(4)); 7.35—7.65 (m, 5 H, ArH); 12.69 (s, 1 H, OH...O).

3,5-Bis(3,5-di-*tert*-butyl-4-hydroxybenzyl)-2,4-dihydroxybenzophenone (5a). Two to three drops of 72% $HClO_4$ were added to a solution of 2,4-dihydroxybenzophenone (**4a**) (2.14 g, 0.01 mol) and ester **1** (5.56 g, 0.02 mol) in AcOH (40 mL). The reaction mixture was kept at 50 °C for 1.5 h. The precipitate that formed was filtered off, washed successively with AcOH and water, and recrystallized from EtOH. The yield of compound **5a** was 5.26 g (81%), m.p. 166—167 °C. Found (%): C, 79.53; H, 8.80. $C_{43}H_{54}O_5$. Calculated (%): C, 79.35; H, 8.36. ^{1}H NMR, δ: 1.37, 1.39 (both s, 18 H each, CMe_3); 3.74, 4.00 (both s, 2 H each, CH_2); 5.08, 5.10 (both s, 1 H each, OH); 5.66 (s, 1 H, OH(5)); 7.00 (s, 2 H, H(3)); 7.18 (s, 2 H, H(6)); 7.22 (s, 1 H, H(4)); 7.35—7.67 (m, 5 H, Ph); 12.90 (s, 1 H, OH...O).

3,5-Bis(3,5-di-*tert*-butyl-4-hydroxybenzyl)-2,4-dihydroxybenzaldehyde (5b). Ester **1** (2.64 g) was added to a solution of 2,4-dihydroxybenzaldehyde (**4b**) (0.59 g) in acetone (9 mL) and HCO_2H (26 mL). The reaction mixture was heated with stirring

at 45 °C for 2 h. The crystals that formed were filtered off and washed with pentane and water. The yield of compound **5b** was 1.96 g (80% in respect to **4b**), m.p. 92—94 °C. Found (%): C, 77.52; H, 8.93. $C_{37}H_{50}O_5$ Calculated (%): C, 77.36; H, 8.72. ^{1}H NMR, δ: 1.36, 1.39 (both s, 18 H each, CMe_3); 3.84, 4.02 (both s, 2 H each, CH_2); 5.14 (s, 2 H, OH); 6.98 (s, 2 H(3)); 7.12 (s, 2 H, H(6)); 7.17 (s, 1 H, H(4)); 9.68 (s, 1 H, CH(O)); 11.65 (s, 1 H, OH...O).

3-(3,5-Di-*tert*-butyl-4-hydroxybenzyl)-2,4-dihydroxybenzophenone (6). A solution of ester **1** (2.78 g, 0.01 mol) in acetone (30 mL) was added dropwise to a solution of 2,4-dihydroxybenzophenone (**4a**) (2.14 g, 0.01 mol) and triethylamine (2.8 mL, 0.02 mol) in acetone (10 mL). The reaction mixture was kept at room temperature for a day, diluted with water, and neutralized with AcOH. The precipitate that formed was washed with water and recrystallized from ethanol. The yield of compound **6** was 2.16 g (50%), m.p. 223—225 °C. Found (%): C, 77.65; H, 7.30. $C_{28}H_{32}O_4$. Calculated (%): C, 77.78; H, 7.41. ^{1}H NMR, δ: 1.42 (s, 18 H, CMe_3); 4.02 (s, 2 H, CH_2); 5.11 (s, 1 H, OH); 5.55 (s, 1 H, H(5)); 6.31 (d, 1 H, H(2), J = 8.5 Hz); 7.21 (s, 2 H, H(3)); 7.39 (d, 1 H, H(4), J = 8.5 Hz); 7.42—7.84 (m, 5 H, Ph). ^{13}C NMR, δ: 28.2 (CH_2); 30.4 ($C\underline{Me}_3$); 34.3 ($\underline{C}Me_3$); 103.8, 107.6, 107.8, 113.4, 115.5, 125.3, 128.2, 128.9, 129.8, 131.3, 133.6, 136.0, 136.4, 138.6, 152.4, 161.3, 164.0, 166.3 (C_{arom}), 200.5 (C=O).

Transformation of 3-(3,5-di-*tert*-butyl-4-hydroxybenzyl)-2,4-dihydroxybenzophenone (6) in an acidic medium. A drop of $HClO_4$ was added to a solution of compound **6** (0.1 g, $2.3 \cdot 10^{-4}$ mol) in AcOH (5 mL) and acetone (2 mL). The mixture was heated at 50 °C for 2 h and poured into water. The precipitate was filtered off, washed with water, and dried. The composition of the reaction mixture was monitored by ^{1}H NMR spectroscopy.

X-ray diffraction analyses of compounds **5b** and **6** (Table 1) were performed on an Enraf-Nonius CAD-4 automatic four-circle diffractometer (λ(Cu-Kα), graphite monochromator, ω-scan mode, $\theta \leq 74°$). Three intensity control reflections showed no decrease in intensity during the experiments. The structures were solved by the direct method with the SIR program[14] and refined first isotropically and then anisotropically with the SHELX-97 program.[15] The coordinates of the hydrogen atoms were calculated from stereochemical criteria and refined in the riding model. All calculations were performed with the MoLEN[16] and WinGX programs.[17] Figures were drawn and the hydrogen bonds were analyzed with the PLATON program.[18]

Structural data have been deposited with the Cambridge Crystallographic Data Center.

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