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Synthons for Biologically Active Compounds on the Basis of Naphthalene Ozonolysis Products

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Abstract—Ozonolysis of naphthalene in aqueous methanol, followed by the reduction of peroxy compounds thus formed with potassium iodide in the presence of acetic acid, gave 3-methoxy-2-benzofuran-1(3*H*)-one. In the absence of water, the product was methyl *o*-formylbenzoate. The latter was used as a synthon for the preparation of aromatic analogs of (2*E*)-2,6-dimethyloct-2-ene-1,8-diol ethers which are effective juvenoids.

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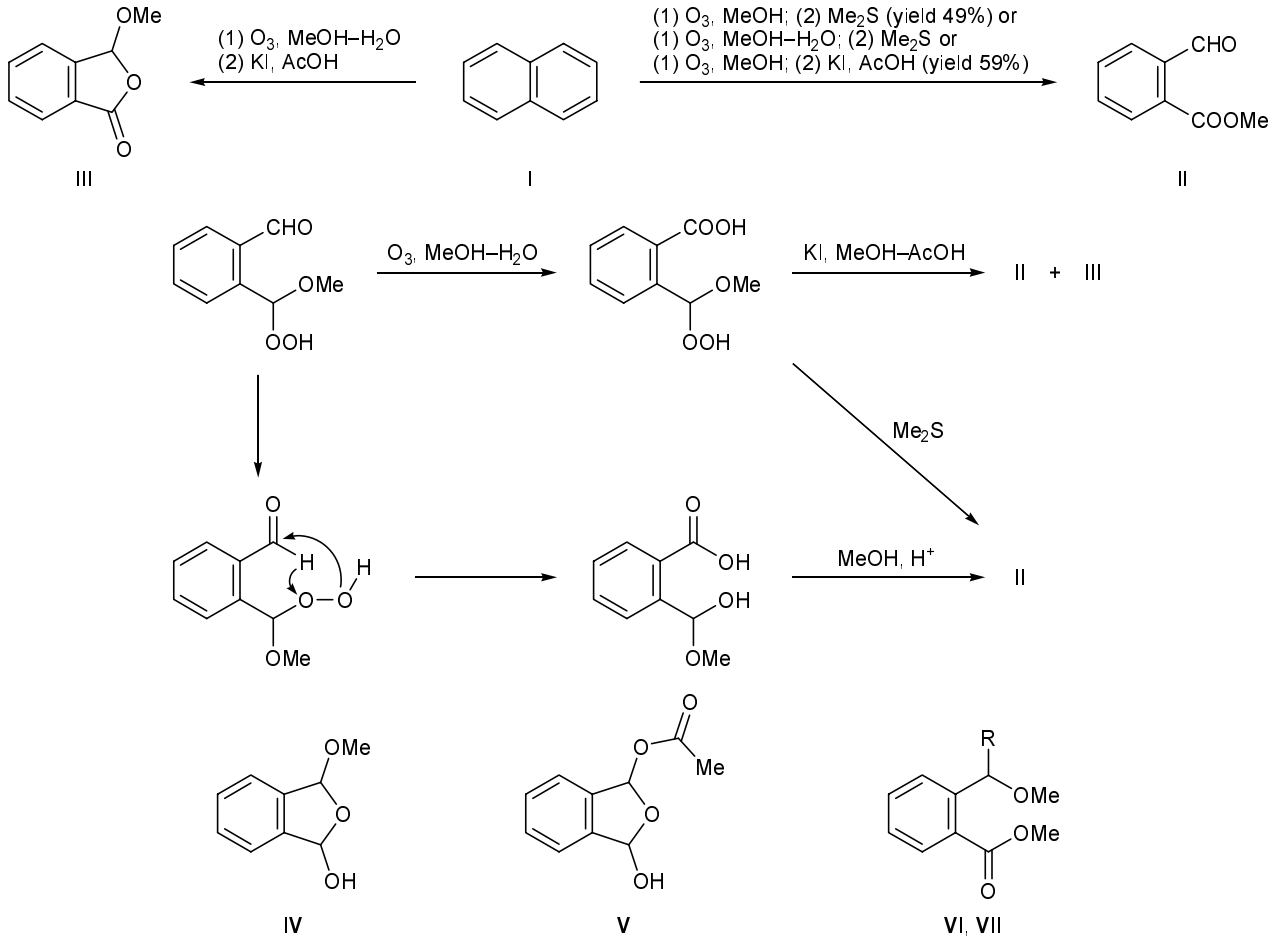
Juvenoids are efficient agents regulating growth and development of insects by influencing their hormone system. Diethers derived from (2*E*)-2,6-dimethyloct-2-ene-1,8-diol exhibited a high species-specific juvenoid activity in *Culex* mosquitoes [1], as well as in other mosquitoes and red cotton moth [2]. The presence of an aromatic ring enhances the juvenoid activity, as was shown with aryl alkenyl ethers [3] and aromatic acid derivatives [4] as examples. However, there are almost no published data on the activity of related systems in which an aromatic ring is incorporated into the principal hydrocarbon chain. Such structures can readily be synthesized starting from *ortho*-disubstituted benzene derivatives where the substituents possess different reactivities. We believed it promising to approach such synthons via selective cleavage of one aromatic ring in naphthalene by the action of ozone.

While studying the reaction of naphthalene with ozone, we have found that complete cleavage of the substrate requires 3 equiv of ozone. In the reaction with an equimolar amount of O_3, the conversion of naphthalene does not exceed 12%. The product structure depends on the conditions of ozonolysis and subsequent decomposition of peroxy compounds thus formed. Contrary to published data [5], the major product of ozonolysis of naphthalene (**I**) in aqueous methanol, followed by reduction of peroxide products with potassium iodide in the presence of acetic acid, was 3-methoxy-2-benzofuran-1(3*H*)-one (**III**, 67%) rather than methyl *o*-formylbenzoate (**II**) (Scheme 1). Compound **III** was isolated from the reaction mixture by chromatography, and its structure was proved by spectral data. The IR spectrum of **III** contained absorption bands at 1490, 1610, and 3080 cm^{-1}, which are typical of aromatic ring, and a strong band at 1785 cm^{-1}, which is characteristic of five-membered lactones. In the ^1H NMR spectrum of **III** we observed signals from the methoxy group (δ 3.63 ppm, s) and proton neighboring to two oxygen atoms (δ 6.30 ppm, s), as well as two doublets and a multiplet at δ 7.89, 7.74, and 7.60 ppm, respectively, from protons in the aromatic ring.

Reduction of the ozonolysis products with dimethyl sulfide afforded 44% of ester **II**, while only a small amount of methoxy lactone **III** was formed under these conditions. It should be noted the ozonolysis of naphthalene (**I**) in anhydrous methanol led to formation of ester **II**, regardless of the reducing agent used in the second step (KI or Me_2S); the yield of **II** was 59% (reduction with KI) and 49% (Me_2S). Oxidation of the formyl group to carboxy may be effected by excess ozone; in addition, intramolecular oxidation of the formyl group with peroxy group is possible as shown in (Scheme 1).

Apart from methoxy lactone **III** and a small amount of ester **II**, the ozonolysis of naphthalene (**I**) in aqueous methanol, followed by reduction of peroxy compounds with KI in AcOH, gave 9% of a mixture of isobenzofurans **IV** and **V**. These compounds were

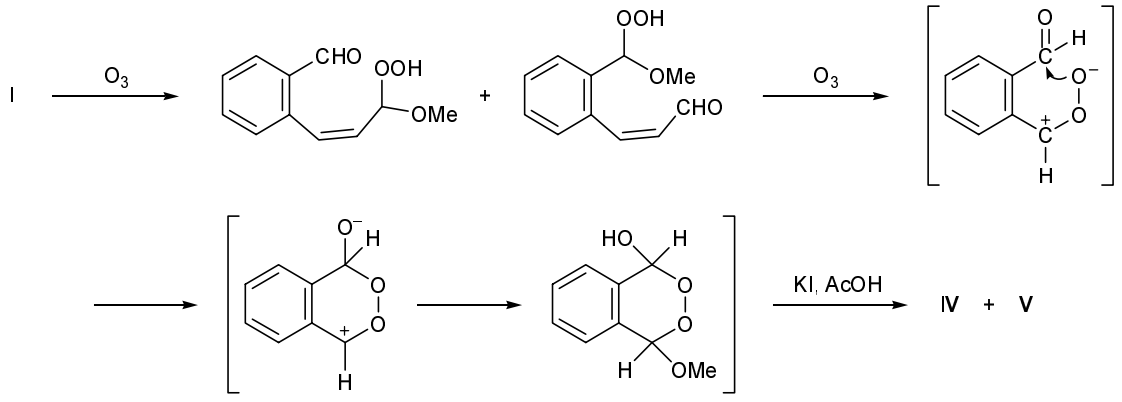
Scheme 1.



VI, R = HO; **VII**, R = MeO.

identified by the ^{1}H NMR spectrum of the reaction mixture, which contained signals from methoxy protons (δ 3.46 ppm) and acetate moiety (δ 2.01 ppm), and four signals at δ 6.09, 6.13, 6.33, and 6.34 ppm. Among the latter, the first two signals belong to the OC**H**OMe or OC**H**OCOMe proton, and the second pair of signals was assigned to the OC**H**OH fragment in **IV** and **V**. The experimental OC**H**O chemical shifts were consistent with the calculation data. The spectra also contained a broadened singlet at δ 7.43 ppm from the aromatic protons. Furthermore, the formation of compounds **IV** and **V** is readily rationalized in terms

Scheme 2.



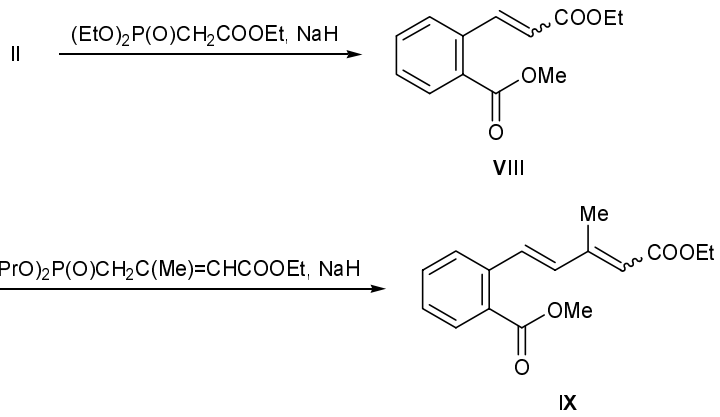
of generally accepted views on the mechanism of ozonolysis (Scheme 2). No isobenzofurans **IV** and **V** were detected when the ozonolysis products of naphthalene (in both aqueous and anhydrous methanol) were reduced with dimethyl sulfide. In the second case, we isolated small amounts of semiacetal **VI** and methyl *o*-(dimethoxymethyl)benzoate (**VII**).

We examined a synthetic approach to arylterpenoids on the basis of olefination of aldehyde **II**. The reactions of **II** with ethyl (diethoxyphosphoryl)acetate and ethyl 4-(diisopropoxyphosphoryl)-3-methylbut-2-enoate led to formation of ethyl 2-methoxycarbonylcinnamate (**VIII**) and ethyl (4*E*)-5-(2-methoxycarbonylphenyl)-3-methylpenta-2,4-dienoate (**IX**) in 64 and 53% yield, respectively (Scheme 3). In the IR spectrum of **VIII** we observed two absorption bands from stretching vibrations of the ester carbonyl groups at 1735 (isolated) and 1695 cm^{-1} (conjugated with the aromatic ring). A medium-intensity band typical of α,β-unsaturated esters was also present at 1660 cm^{-1}. The ^1H NMR spectrum of **VIII** contained two doublets at δ 7.44 (*J* = 16.5 Hz) and 6.83 ppm (*J* = 12.0 Hz), which were assigned to the 3-H proton in the 2*E* and 2*Z* isomers; the isomer ratio was estimated at 65:35 on the basis of the GLC and ^1H NMR data (the signal at δ 7.44 ppm was more intense). Protons at the α-carbon atom gave rise to a multiplet at δ 6.12–6.22 ppm; in addition, signals from the methoxy, ethoxy, and aromatic protons were present.

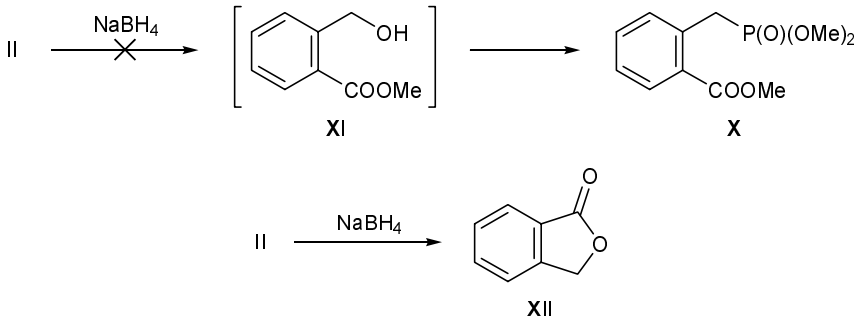
Dienoate **IX** showed in the ^1H NMR spectrum signals from the COOEt and COOMe groups, aromatic ring (see Experimental), and protons at the double bonds at δ 5.70 (d, 2-H, *J* = 0.9 Hz), 6.50 (d, 5-H, *J* = 16.5 Hz), 6.82 (d, 4-H, *J* 16.5 Hz, 2*E*), and 8.11 ppm (d, 4-H, *J* = 16.0 Hz, 2*Z*). According to the GLC data, the ratio of the *E* and *Z* isomers with respect to the $C^2=C^3$ bond is 75:25. The *E* configuration of the $C^4=C^5$ bond in **IX** was assigned on the basis of published data on the Horner–Emmons olefination [6]; in addition, the absence of an additional downfield signal from methyl group in the ^{13}C NMR spectrum of **IX** was taken into account.

Another approach to the introduction of an isoprenoid fragment into aromatic ring implies olefination of unsaturated aldehydes with phosphonates like **X**. The latter could be prepared from methyl *o*-bromomethylbenzoate. However, we failed to obtain this compound from compound **II** by successive reduction of the aldehyde group and transformation of benzyl alcohol **XI** into the corresponding benzyl bromide. The

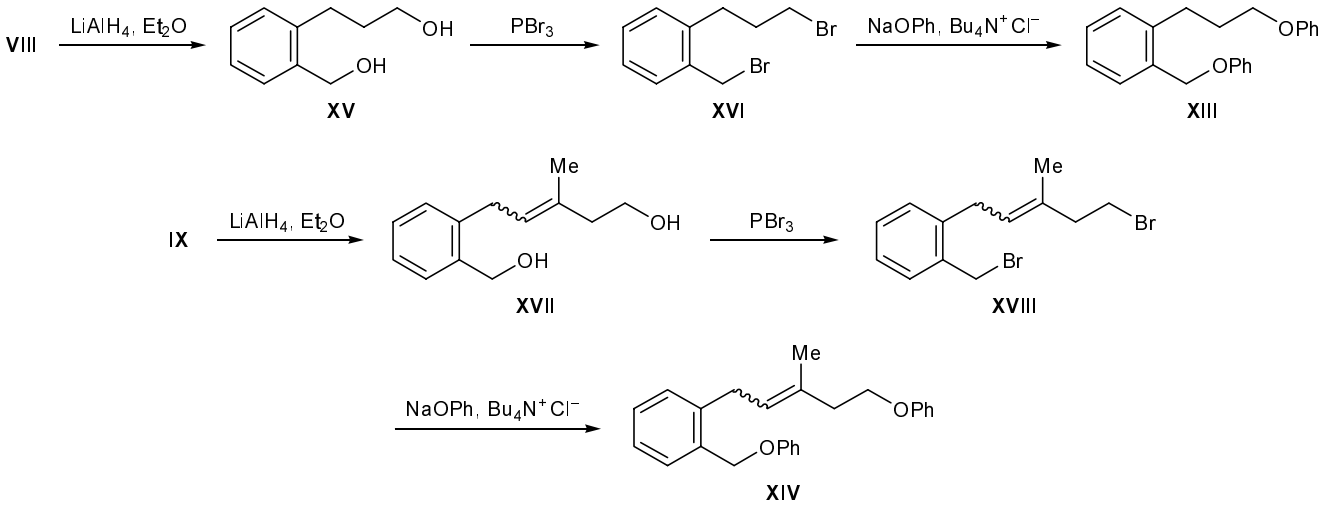
Scheme 3.



Scheme 4.



Scheme 5.



product obtained by reaction of **II** with sodium tetrahydridoborate showed in the IR spectrum no hydroxy group absorption, while the presence of a band at 1775 cm^{-1} led us to presume that intermediate alcohol **XI** underwent intramolecular cyclization to give five-membered lactone **XII** (Scheme 4). The NMR data confirmed the structure of **XII**. Compound **XII** may be interesting as a latent form of hydroxy acid.

Unsaturated esters **VIII** and **IX** were used as initial compounds for the synthesis of bis-phenyl ethers **XIII** and **XIV** which are aromatic analogs of (2*E*)-2,6-dimethyloct-2-ene-1,8-diol diethers. For this purpose, ester **VIII** was reduced with $LiAlH_4$, and 3-[2-(hydroxymethyl)phenyl]propanol (**XV**) thus formed was treated with phosphorus(III) bromide to obtain 3-[2-(bromomethyl)phenyl]propyl bromide (**XVI**). The reaction of **XVI** with sodium phenoxide in the presence of tetrabutylammonium bromide as phase-transfer catalyst gave 1-(phenoxymethyl)-2-(3-phenoxypropyl)-benzene (**XIII**) whose spectral parameters were consistent with the assumed structure (Scheme 5).

The reduction of diene **IX** with lithium tetrahydridoaluminate afforded unsaturated 5-[2-(hydroxymethyl)phenyl]-3-methylpent-3-en-1-ol (**XVII**) which was converted into 1-(3-methyl-5-phenoxypent-2-en-1-yl)-2-(phenoxymethyl)benzene (**XIV**) through dibromide **XVIII** (Scheme 5).

The formation of diol (**XVII**) followed from the spectral data. The IR spectrum of **XVII** contained absorption bands due to stretching vibrations of the hydroxy groups (3250–3460 cm^{-1}) and aromatic ring (1505, 1600 cm^{-1}) and a weak absorption in the region typical of double C=C bonds (1640 cm^{-1}). In the ^1H NMR spectrum, signals from protons of the methyl group at the double bond (δ 1.72 ppm), OCH_2 group (δ 3.64 and 4.64 ppm), and aromatic ring were present. The proton at the double bond appeared as a triplet at δ 5.06 ppm, indicating that hydrogenation of the conjugated diene system occurred at the 1,4-position; otherwise, its signal should be located in a weaker field. In addition, the spectrum contained a doublet at δ 3.74 ppm, which was assigned to the methylene protons between the double bond and aromatic ring.

EXPERIMENTAL

The IR spectra were recorded on UR-20 and Specord M-80 spectrometers from samples prepared as thin films or dispersed in mineral oil. The ^1H and ^{13}C NMR spectra were measured from solutions in $CDCl_3$ on a Bruker AM-300 instrument operating at 300 and 75.25 MHz, respectively; tetramethylsilane was used as internal reference. Gas chromatographic analysis was performed on a Chrom-5 chromatograph (1.2-m column packed with SE-30 on Chromaton N-FW-DMCS, 0.16–0.20 mm; carrier gas helium; oven temperature programming from 50 to 300°C at a rate of 12 deg/min). Silufol UV 366 plates were used for thin-layer chromatography. The mass spectra (electron impact, 80 eV) were obtained on an MKh-1303 mass spectrometer (ion source temperature 200°C).

Methyl *o*-formylbenzoate (II) and 3-methoxy-2-benzofuran-1(3*H*)-one (III). *a*. An ozone–oxygen mixture (5.5 wt % of O_3) was passed at 0–5°C through a solution of 2.00 g (15.60 mmol) of naphthalene (**I**) in a mixture of 84.0 ml of MeOH and 18.0 ml of H_2O until naphthalene disappeared completely (TLC, silica

gel, hexane–ethyl acetate, 4:1); 2.25 g (46.8 mmol) of ozone was consumed. The mixture was purged with argon, 5.20 g (31.32 mmol) of potassium iodide and 2.0 ml of glacial acetic acid were added, the mixture was stirred for 1.5 h, and the liberated iodine was titrated with a 10% solution of $Na_2S_2O_3$. The solvent was distilled off, the residue was dissolved in ethyl acetate, and the solution was washed in succession with saturated solutions of NaCl, $NaHCO_3$, and again NaCl, dried over $MgSO_4$, and evaporated. The residue, 2.34 g, was subjected to column chromatography on silica gel using hexane–ethyl acetate (4:1) as eluent to isolate 1.72 g (67%) of methoxy lactone **III** and 0.24 g (9%) of a mixture of compound **II**, 3-methoxy-1,3-dihydro-2-benzofuran-1-ol (**IV**), and 3-hydroxy-1,3-dihydro-2-benzofuran-1-yl acetate (**V**).

b. The ozonolysis was performed as described above in *a* using 2.00 g (15.60 mmol) of naphthalene (**I**) in 84.0 ml of anhydrous methanol. The mixture was then treated with 5.20 g (31.32 mmol) of potassium iodide and 2.0 ml of glacial acetic acid. By column chromatography we isolated 1.51 g (59%) of ester **II** and 0.11 g (4%) of compound **III**.

c. Likewise, 2.00 g (15.60 mmol) of naphthalene in a mixture of 84.0 ml of methanol and 18.0 ml of water was subjected to ozonolysis at 0–5°C. Dimethyl sulfide, 2.3 ml, was added to the ozonolysis products, and the mixture was stirred until peroxy compounds disappeared (2 h; test with an acidified aqueous solution of KI). The solvent was distilled off, the residue was dissolved in chloroform, and the solution was washed with a saturated solution of NaCl, dried over $MgSO_4$, and evaporated. Chromatographic separation of the residue (1.96 g) on silica gel (hexane–ethyl acetate, 4:1) gave 1.14 g (44%) of ester **II** and 0.18 g (7%) of methoxy lactone **III**.

d. Following a similar procedure, the ozonolysis of 2.00 g (15.60 mmol) of naphthalene in 84.0 ml of anhydrous methanol, followed by treatment with 2.3 ml of dimethyl sulfide, gave 2.41 g of a mixture of products which were separated by column chromatography to isolate 1.25 g (49%) of ester **II** and 0.08 g (3%) of lactone **III**.

Compound II. IR spectrum, ν, cm^{-1}: 785 s, 1110 s, 1510 m, 1620 m, 1705 s, 1725 s, 2785 w. ^1H NMR spectrum, δ, ppm: 3.42 s (3H, OCH_3), 7.65 m and 7.90 m (4H, H_{arom}), 10.62 s (1H, CHO). ^{13}C NMR spectrum, δ_C, ppm: 52.26 (OCH_3), 127.88 d (C^2), 129.95 s (C^1), 131.54 d (C^5), 131.98 (C^3), 132.56 (C^4), 136.63 s (C^6), 166.21 s (COO), 191.60 d (CHO). Mass spectrum, *m*/*z*: 164 $[M]^+$, 149 $[M - CH_3]^+$, 136 $[M - CO]^+$, 133 $[M - CH_3O]^+$, 132 $[M - CH_3OH]^+$.

Compound III. IR spectrum, ν, cm^{-1}: 880 m, 1235 m, 1490 m, 1610 m, 1785 s, 3080 m. ^1H NMR spectrum, δ, ppm: 3.63 s (3H, OCH_3), 6.30 s (1H, OCHO), 7.60 m (2H, 5-H, 6-H), 7.74 d (1H, 4-H, J = 8.0 Hz), 7.89 d (1H, 7-H, J = 8.0 Hz). Found, %: C 61.70; H 4.30. $C_9H_8O_3$. Calculated, %: C 65.80; H 4.87.

Ethyl 2-(methoxycarbonyl)cinnamate (VIII). Sodium hydride, 0.10 g (3.97 mmol), was added to a solution of 0.89 g (3.97 mmol) of ethyl (diethoxyphosphoryl)acetate in 15.0 ml of anhydrous THF under stirring at 15°C. The mixture was stirred for 30 min at that temperature and cooled to 5°C, and a solution of 0.50 g (3.05 mmol) of ester **II** in 10.5 ml of anhydrous THF was added dropwise. The mixture was stirred until compound **II** disappeared (TLC, silica gel, hexane–ethyl acetate, 4:1), washed in succession with saturated solutions of NH_4Cl and NaCl, and dried over $MgSO_4$. The solvent was removed, and the residue (0.62 g) was subjected to column chromatography on silica gel using hexane–ethyl acetate (4:1) as eluent to isolate 0.46 g (64%) of compound **VIII**. IR spectrum, ν, cm^{-1}: 780 m, 1080 m, 1250 s, 1360 s, 1480 s, 1600 m, 1660 s, 1695 s, 1735 s. ^1H NMR spectrum, δ, ppm: 1.22 t (3H, CH_3, J = 7.0 Hz), 3.53 s (3H, OCH_3), 3.94 q (2H, OCH_2, J = 7.0 Hz), 6.12–6.22 m (1H, 2-H), 6.83 d and 7.44 d (1H, 3-H, J = 12.0, 16.5 Hz), 7.52 m (2H, 5'-H, 4'-H), 7.64 d (1H, 6'-H, J = 8.0 Hz), 7.74 d (1H, 3'-H, J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.43 q (CH_3), 51.02 t (OCH_2), 60.30 q (OCH_3), 110.13 d (C^2, 2*E*), 120.34 d (C^2, 2*Z*), 125.84 s and 125.89 s ($C^{2'}$), 126.05 d ($C^{6'}$), 130.71 d ($C^{3'}$), 133.18 d ($C^{5'}$), 136.13 s and 137.01 s ($C^{1'}$), 143.01 d and 143.94 d (C^3), 162.54 s (**C**$OOCH_3$), 166.48 s (C^1), 167.04 s ($C^{4'}$). Found, %: C 66.25; H 5.47. $C_{13}H_{14}O_4$. Calculated, %: C 66.67; H 5.98.

Ethyl (4*E*)-5-[2-(methoxycarbonyl)phenyl]-3-methylpenta-2,4-dienoate (IX). A solution of 0.68 g (4.14 mmol) of compound **II** in 10.5 ml of anhydrous THF was added under stirring at 5°C to the anion generated by the action of 0.13 g (5.38 mmol) of sodium hydride on 1.57 g (5.38 mmol) of ethyl 4-(diisopropoxyphosphoryl)-3-methylbut-2-enoate in 25.0 ml of anhydrous THF. The mixture was stirred until the initial compound disappeared, and the product was isolated as described above for compound **VIII**. The crude product, 0.92 g, was purified by column chromatography on silica gel using hexane–ethyl

acetate (4:1) as eluent. Yield 0.60 g (53%). IR spectrum, ν, cm^{-1}: 780 m, 840 m, 1090 s, 1200 s, 1600 m, 1620 m, 1670 m, 1710 s, 1735 s, 3080 w. ^1H NMR spectrum, δ, ppm: 1.26 t (3H, CH_3, J = 7.0 Hz), 2.03 d (*Z*) and 2.28 d (*E*) (3H, CH_3C=C, J = 0.9 Hz), 3.64 s (3H, OCH_3), 3.94 q (2H, OCH_2, J = 7.0 Hz), 5.70 d (1H, 2-H, J = 0.9 Hz), 6.50 d (1H, 5-H, J = 16.5 Hz), 6.82 d (2*E*) and 8.11 d (2*Z*) (1H, 4-H, J = 16.5, 16.0 Hz), 7.52 m (2H, 4'-H, 5'-H), 7.64 d (1H, 6'-H, J = 8.0 Hz), 7.69 d (1H, 3'-H, J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 14.35 q (**C**H_3CH_2), 18.50 q (CH_3, 2*E*), 20.43 q (CH_3, 2*Z*), 51.02 q (OCH_3), 59.74 t (OCH_2), 119.11 d and 120.70 d (C^{2}), 125.11 s ($C^{2'}$), 123.59 s (C^{3}, 2*E*), 126.03 s (C^{3}, 2*Z*), 126.53 d and 126.71 d ($C^{4'}$, $C^{6'}$), 129.13 d ($C^{3'}$), 133.41 d and 133.96 d ($C^{5'}$, C^{5}), 136.48 d (C^{4}, 2*E*), 138.91 (C^{4}, 2*Z*), 137.16 s ($C^{1'}$), 162.94 s and 167.18 s (C=O). Found, %: C 70.14; H 6.32. $C_{16}H_{18}O_4$. Calculated, %: C 70.07; H 6.57.

2-Benzofuran-1(3*H*)-one (XII). *a*. Sodium tetrahydridoborate, 0.23 g (6.05 mmol), was added in small portions to a solution of 0.50 g (3.05 mmol) of compound **II** in 20.0 ml of anhydrous methanol under stirring at 0–5°C in a stream of argon. The suspension was stirred for 3 h and acidified with 2.2 ml of aqueous acetic acid (0.2 ml of acetic acid in 2.0 ml of water), and the mixture was stirred for 1 h at 0–5°C and was left overnight in a refrigerator. The solvent was distilled off, the residue was dissolved in ethyl acetate, the solution was washed in succession with saturated solutions of NaCl, $NaHCO_3$, and NaCl, dried over $MgSO_4$, and evaporated. The residue, 0.42 g, was subjected to column chromatography on silica gel using hexane–ethyl acetate (4:1) as eluent to isolate 0.28 g (68%) of lactone **XII**, mp 73–74°C. IR spectrum, ν, cm^{-1}: 844 w, 1628 m, 1775 s. ^1H NMR spectrum, δ, ppm: 5.19 s (2H, OCH_2), 7.40 m (2H, 4-H, 6-H), 7.57 t (1H, 5-H, J = 8.0, 8.5 Hz), 7.72 d (1H, 3-H, J = 8.5 Hz). ^{13}C NMR spectrum, δ_C, ppm: 69.45 t (OCH_2), 122.01 d (C^{3}), 125.16 s (C^{1}), 128.63 d and 128.94 d (C^{5}, C^{6}), 133.74 d (C^{4}), 146.34 s (C^{2}), 170.82 s (C=O). Mass spectrum, *m/z*: 134 $[M]^+$, 120 $[M - CH_2]^+$, 105 $[M - CH - O]^+$. Found, %: C 71.63; H 4.73. $C_8H_6O_2$. Calculated, %: C 71.64; H 4.48.

b. An ozone–oxygen mixture (46.80 mmol of O_3) was passed at 0°C through a solution of 2.00 g (15.60 mmol) of naphthalene (**I**) in 40.0 ml of anhydrous methanol. The mixture was purged with argon, 1.19 g (31.32 mmol) of sodium tetrahydridoborate was added, and the mixture was stirred for 0.5 h at 0°C, allowed to warm up to 20°C, and left to stand for 12 h. Aqueous acetic acid, 8.0 ml (0.7 ml of AcOH and 7.3 ml of H_2O), was then added, the mixture was stirred for 3 h, the solvent was distilled off, and the residue was treated as described above in *a*. From 2.14 g of the crude product we isolated by column chromatography 0.34 g (16%) of lactone **XII**.

1-(Phenoxymethyl)-2-(3-phenoxypropyl)benzene (XIII). Phenol, 0.21 (2.3 mmol), was added to a solution of 0.62 g (4.52 mmol) of K_2CO_3 in 8.0 ml of H_2O, and the mixture was stirred until phenol disappeared completely (TLC, silica gel, pentane–diethyl ether, 3:2). Tetrabutylammonium bromide, 0.56 g, was added to the resulting solution of sodium phenoxide, and a solution of 0.57 g (1.94 mmol) of dibromide **XVI** in 18.0 ml of benzene was then added. The mixture was stirred for 2–2.5 h at 60–65°C, and the benzene layer was separated, washed with a 2 N solution of sodium hydroxide and a saturated solution of sodium chloride, and dried over $MgSO_4$. The solvent was distilled off to obtain crude diether **XIII** as an oily substance. The product was purified by chromatography on silica gel using petroleum ether–ethyl acetate (9.5:0.5) as eluent. Yield 0.44 g (71%). IR spectrum, ν, cm^{-1}: 1100 s, 1505 m, 1600 m, 1645 m. ^1H NMR spectrum, δ, ppm: 1.54 m (2H, CH_2), 2.43 t (2H, C**H**$_2$Ph, J = 6.0 Hz), 4.08 t (2H, C**H**$_2$Ph, J = 7 Hz), 4.96 s (2H, C_6H_4C**H**$_2$-OPh), 6.7–7.6 m (14H, H_{arom}). Found, %: C 83.09; H 6.84. $C_{22}H_{22}O_2$. Calculated, %: C 83.02; H 6.92.

1-(3-Methyl-5-phenoxypent-2-en-1-yl)-2-(phenoxymethyl)benzene (XIV). Compound **XVII**, 0.6 g (2.9 mmol), was converted into dibromooctene **XVIII** by treatment with 1.2 g (3.6 mmol) of CBr_4 in CH_2Cl_2 in the presence of 0.94 g of triphenylphosphine. Compound **XVIII** was isolated as described below for dibromide **XVI**; yield 1.13 g (3.4 mmol, 94%). It was added to a solution of 0.53 g (4.03 mmol) of potassium phenoxide in 17 ml of water containing 1.0 g of tetrabutylammonium bromide as catalyst. Compound **XIV** was isolated as described above for diether **XIII**. Yield 0.33 g (62%). IR spectrum, ν, cm^{-1}: 1500 m, 1605 m, 1640 w. ^1H NMR spectrum, δ, ppm: 1.70 d (3H, Me, J = 0.9 Hz), 2.39 br.t (2H, CH_2C=C), 3.69 d (2H, C**H**$_2C_6H_4$, J = 6.0 Hz), 4.26 t (2H, C**H**$_2$OPh, J = 7.5 Hz), 4.87 s (2H, C_6H_4C**H**$_2$OPh), 5.08 t (1H, HC=C, J = 6.0 Hz), 6.5–7.8 m (14H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 16.58 q (Me), 31.24 t (C^{5}), 40.21 t (C^{2}), 63.14 t (C^{1}), 67.17 t (C^{8}), 114.24 d and 115.19 d (C^{o} in OC_6H_5), 120.94 and 121.02 (C^{p} in OC_6H_5), 124.32 d (C^{4}), 124.72 d ($C^{4'}$), 127.39 d ($C^{3'}$), 128.41 d ($C^{2'}$), 128.94 d and 129.36 d (C^{m} in OC_6H_5), 130.76 s ($C^{1'}$),

134.66 s (C^6), 135.19 s (C^7), 138.71 s (C^3), 158.14 s and 159.26 s (C^i in OC_6H_5). Found, %: C 83.72; H 7.31. $C_{25}H_{26}O_2$. Calculated, %: C 83.80; H 7.26.

3-[2-(Hydroxymethyl)phenyl]propan-1-ol (XV). Lithium tetrahydridoaluminate, 0.9 g (23.7 mmol), was added in portions at 5–10°C to a solution of 1.5 g (6.4 mmol) of diester **VIII** in 20 ml of anhydrous diethyl ether. The mixture was allowed to warm up to room temperature, 0.15 ml of water was carefully added, and the solution was separated from the precipitate by decanting. A new portion of diethyl ether, 20 ml, was added to the precipitate, the mixture was thoroughly stirred, and the liquid phase was separated by decanting. The ether solutions were combined, washed with a small amount of a saturated solution of NaCl, dried over $MgSO_4$, filtered, and evaporated. The residue was subjected to chromatography on silica gel using hexane–ethyl acetate (3:2) as eluent to isolate 0.61 g (58%) of diol **XV**. IR spectrum, ν, cm^{-1}: 1500 m, 1600 m, 3450 br.s. ^{1}H NMR spectrum, δ, ppm: 1.58 m (2H, CH_2), 2.42 t (2H, C**H**$_2$C$_6$H$_4$, J = 6.5 Hz), 3.8 t (2H, OCH_2, J = 7.0 Hz), 4.18 br.s (2H, OH), 4.56 s (2H, OC**H**$_2$C$_6$H$_4$), 7.32 m (4H, H_{arom}). Found, %: C 72.49; H 8.31. $C_{10}H_{14}O_2$. Calculated, %: C 72.29; H 8.43.

1-(Bromomethyl)-2-(3-bromopropyl)benzene (XVI). Carbon tetrabromide, 4.98 g (14.94 mmol), was added in one portion under stirring to a mixture of 2.0 g (12.0 mmol) of diol **XV** and 3.93 g of triphenylphosphine in 25 ml of anhydrous methylene chloride. The mixture was stirred for 2 h and filtered through a thin layer of silica gel. The product was then isolated by chromatography on silica gel using petroleum ether as eluent. Yield 3.33 g (98%). IR spectrum, ν, cm^{-1}: 680 m, 1505 w, 1595 w, 3080 w. ^{1}H NMR spectrum, δ, ppm: 1.48 m (2H, CH_2), 2.43 t (2H, C**H**$_2$C$_6$H$_4$, J = 6.0 Hz), 3.18 t (2H, CH_2Br, J = 7.0 Hz), 4.8 s (2H, C$_6$H$_4$C**H**$_2$Br), 7.34 m (4H, H_{arom}). Found, %: C 41.04; H 4.18; Br 55.01. $C_{10}H_{12}Br_2$. Calculated, %: C 41.10; H 4.11; Br 54.79.

5-[2-(Hydroxymethyl)phenyl]-3-methylpent-3-en-1-ol (XVII) was synthesized by reduction of 2.0 g (7.3 mmol) of diester **VIII** with 1.03 g (27.0 mmol) of $LiAlH_4$. The product was isolated and purified by chromatography (silica gel, hexan–ethyl acetate, 2:3). Yield 0.92 g (61%). IR spectrum, ν, cm^{-1}: 1505 m, 1600 m, 1640 w, 3250–3460 br.s. ^{1}H NMR spectrum, δ, ppm: 1.72 d (3H, CH_3, J = 0.9 Hz), 2.06 t (2H, $CH_2C{=}C$, J = 7.0 Hz), 3.64 bt.t (2H, CH_2O, J = 7.0 Hz), 3.74 d (2H, C$_6$H$_4$C**H**$_2$C=C, J = 6.0 Hz), 4.56 br.s (2H, OH), 4.64 s (2H, C$_6$H$_4$C**H**$_2$O), 5.06 t (1H, HC=C, J = 6.0 Hz), 6.8–7.6 m (4H, H_{arom}). ^{13}C NMR spectrum, δ_C, ppm: 16.04 q (CH_3); 36.75 t (C^5); 45.18 t (C^2); 57.94 t (C^8); 59.69 t (C^1); 124.18 d (C^4); 125.04 d, 127.40 d, 128.54 d, and 130.6 (CH_{arom}); 134.22 s (C^6); 135.41 s (C^7); 139.56 s (C^3). Found, %: C 75.63; H 8.82. $C_{13}H_{18}O_2$. Calculated, %: C 75.73; H 8.74.

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