Synthesis of $\alpha$-tocopherol (vitamin E), vitamin $K_1$-chromanol, and their analogs in the presence of aluminosilicate catalysts Tseokar-10 and Pentasil

Victor N. Odinokov, Anna Yu. Spivak, Gulnara A. Emelyanova, Marina I. Mallyabaeva, Oksana V. Nazarova, and Usein M. Dzhemilev

Institute of Petrochemistry and Catalysis, Bashkortostan Republic Academy of Sciences and the Ufa Scientific Centre of the Russian Academy of Sciences, 141 prosp. Oktyabrya, Ufa, 450075, Russian Federation
E-mail: ink@anrb.ru

Dedicated to Professor Boris A. Trofimov on his 65th birthday
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Abstract
The highly effective heterogeneous catalysts, the aluminosilicates Tseokar-10 and Pentasil, were found to condense hydroquinones with tertiary isoprenoid allylic alcohols. Using these catalysts $d,l\alpha$-tocopherol, $(2RS, 4'R, 8'R)-\alpha$-tocopherol, and vitamin $K_1$-chromanol with chiral homogeneous side chains were synthesized in high yields. The analogs of $\alpha$-tocopherol – chromanols and chromenols with the terminal isopropylidene group in the side chain – were synthesized, whose selective ozonolysis resulted in the corresponding chromanes with $\omega$-formyl- or $\omega$-hydroxyl groups in the side chain.

Keywords: $\alpha$-Tocopherol, vitamin $K_1$-chromanol, $\Delta^3$-chromenes, condensation, aluminosilicate catalysts

Introduction

$\alpha$-Tocopherol is the most significant representative of the tocopherol group (vitamin E); it is a natural inhibitor of the peroxidation of lipids in vivo, and helps to retain intact the structure and functional activity of cells’ membranes.$^1$

The chemistry of tocopherol has been extensively studied over sixty years, but now this compound is of interest as a treatment- and prophylactic agent, and as a nutritional additive. At present, intensive searches are being carried out for new methods of synthesis of racemic and optically active $\alpha$-tocopherol using new catalysts, reagents and synthons.$^2$

The method based on the acid-catalyzed condensation of 2,3,5-trimethylhydroquinone (TMHQ) with phytol and isophytol to obtain racemic $\alpha$-tocopherol (a mixture of all possible stereoisomers), and $(2RS, 4'R, 8'R)-\alpha$-tocopherol is of great importance. Brønsted and Lewis
acids e.g., HCO₂H, MeCO₂H, BF₃·OEt₂, ZnCl₂, are used as catalysts. Recently, data were published concerning the use of heterogeneous catalysts, whose main merits are the simple separation of a solid catalyst from the reaction mass, the absence of washing water containing the dead catalyst, and a higher purity (96–97%) of α-tocopherol. The aluminosilicates are most preferred heterogeneous catalysts, owing to their accessibility and capacity. The AShNTs and Tseokar-2 aluminosilicates have been used for TMHQ condensation with isophytol and dihydrolinalool.

**Synthesis of all-rac.-α-tocopherol, 2-ambo-α-tocopherol and vitamin K₁-chromanol**

We have studied the new aluminosilicate catalyst Tseokar-10 (which contains the high module zeolite Y as the active component (10 wt. %) and is used for cracking of petroleum fractions manufactured at the Salavatnefteorgsintez plant) to condense TMHQ with isophytol. It was found that reaction in boiling hydrocarbon solvents (n-heptane, n-nonane) gave all-rac.-α-tocopherol (3) in nearly quantitative yield (≥ 98%) (Scheme 1).

![Scheme 1](image)

Scheme 1. TMHQ, Tseokar-10, n-C₉H₂₀.

Tseokar-10 was also effective in the synthesis of (2RS, 4'R, 8'R)-α-tocopherol (7) (equimolar mixture of 2R- and 2S- epimers, called 2-ambo-α-tocopherol). This compound was obtained by the condensation of TMHQ with (2E,7R,11R)-phytol, whose syntheses are complicated and have many steps. The treatment of the acetone extract of chlorophyll of green plants with alkali also leads to this compound, but this pathway requires pre-purification of the chlorophyll from lipids. In addition, the alkaline hydrolysis of chlorophyll in acetone solution gives the products of acetone self-condensation, and salts of fatty and chlorophyll-based acids hampers the isolation of pure phytol.

In the condensation reaction with TMHQ (3RS,7R,11R)-isophytol (6) was used, which was obtained by the vinylation of (6R,10R)-6,10,14-trimethylpentadecane-2-one (R,R-phytone) (5). To synthesize the latter an effective method was developed of ozonolysis of the acetone extract of chlorophyll (4) (a mixture of chlorophyll a and b, R = Me or CHO, respectively) from the great nettle (Urtica dioica L.) without its pre-purification from accompanying lipids (Scheme 2). Ozonolysis in the presence of Ba(OH)₂ (the so-called “non-peroxide ozonolysis”) led to phytone (5) in ~90% yield (with respect to chlorophyll 4 in the acetone extract, determined using electronic spectroscopy in the range λ 640–665 nm). The pure phytone 5 was isolated most easily, and in high yield, from the ozonization product when 9 mol. equiv. of ozone, with respect to the content of chlorophyll in the extract, was used, whereas decreasing the excess of ozone hinders the isolation of the pure target product. Apparently, ozone is needed not only to cleave the double
bonds in the vinyl group at C(3) and the phytol propionate residue at C(17) in chlorophyll 4, but also to ozonize the corresponding unsaturated compounds in the acetone extract (carotenoids and xanthophylls). The condensation of isophytol 6 with TMHQ in the presence of the Tseokar-10 catalyst (nonane, boiling, 5 h) led to the target 2-ambo-α-tocopherol 7 in high yield.

![Chemical Structure](image)

**Scheme 2.** (a) O₃, Me₂CO, Ba(OH)₂; (b) CH₂=CHMgBr, THF; (c) TMHQ, Tseokar–10, n-C₉H₂₀; (d) Tseokar –10, PhMe; (e) LiAlH₄, Et₂O.

The same approach was used to synthesize 2,5-dimethyl-2-(4,8,12-trimethyltridecan-1-yl)-6-hydroxybenzo[h]chroman, a cyclic form of vitamin K₁, also called vitamin K₁-chromanol, or naphthotocopherol, 9. The effect of vitamin K₁ on a number of biochemical processes (blood coagulation, conjugate oxidation, phosphorylation) is known to be caused by naphthotocopherolidentified in the product of the enzymic reduction of vitamin K₁.
Spectrophotometric studies of antioxidants in the phenol series confirmed the highest activity of naphthotocopherol, whose antioxidant activity was 6.9 times as great as that of α-tocopherol.\textsuperscript{12}

First, we have synthesized optically active naphthotocopherol with the chiral homogeneous side phytol chain of (\(R,R\))-configuration, 9, based on the condensation of 1-\(O\)-acetyl-2-methyl-1,4-naphthohydroquinone (menadiol acetate) 10 with (3RS,7R,11R)-isophytol 6 in the presence of the Tseokar-10 catalyst. The condensation product 8 was further deacetylated with lithium aluminum hydride in diethyl ether. The yield of the target naphthotocopherol 9 was equal to 68\% with respect to isophytol 6.

**Synthesis of analogs of α-tocopherol and naphthotocopherol with a shortened side chain**

In recent years, considerable attention has been given to the synthesis of analogs of α-tocopherol with a shortened side chain. The resulting compounds, based on linalool and dihydrolinalool, were found to exhibit high biological activity. These analogs are named \(C_6\)-anals of α-tocopherol, from the number of carbon atoms in the side chain.\textsuperscript{4}

The condensation of (3RS,4S)-3,4,8-trimethyl-1-nonene-3-ol 11, obtained from the accessible enantiomerically enriched (\(ee\sim\)50\%) (\(S\)-(+) -dihydromyrcene\textsuperscript{13,14} with TMHQ\textsuperscript{14} and menadiol acetate, 10, catalyzed by Tseokar-10, resulted in new optically active analogs of α-tocopherol 12 and naphthotocopherol 14, and converted then into the acetate 13 and the alcohol 15, respectively (Scheme 3). The \(C_8\)-chromans 12, 13 and \(C_8\)-benzochromans 14, 15 were synthesized in equimolar mixtures of (2\(R\),1\(S\))-\textit{erythro}- and (2\(S\),1\(S\))-\textit{threo}- diastereomers. Since the starting 11 is characterized by an \(ee\) of \(\sim\)50\%, it is evident that the \textit{erythro}- and \textit{threo}-diastereomers of the chromans 12 and 15 are enriched to the same extent with the epimers with the \(S\)- configuration at the C(1\(′\))-atom.

![Scheme 3](image.png)

\textbf{Scheme 3.} (a) TMHQ, Tseokar-10, \(n\)-C\(_9\)H\(_{20}\); (b) 10, Tseokar-10, PhMe; (c) Ac\(_2\)O; (d) LiAlH\(_4\), Et\(_2\)O.

The usual catalysts are known to be unsuitable for reactions of tertiary vinyl carbinols with unsaturated isoprenoid radicals because the reaction is complicated by side cyclization resulting in tricyclic compounds.\textsuperscript{15} At the same time, analogs of α-tocopherol with an unsaturated side chain are of interest as precursors of the corresponding chromans with an \(\omega\)-functionalized side chain, which are of interest in biological studies and as building blocks for the synthesis of other vitamin E analogs.
We report the capacity of the aluminosilicate catalyst Tseokar-10 in the synthesis of chromanols with the terminal isopropylidene group in the isoprenoid side chain. In this, (3RS,4S)-3,4,8-trimethyl-1,7-nonadien-3-ol 16 (a 1:1 mixture of (3R,4S)-erythro- and (3S,4S)-threo- diastereomers, ee ~50%, obtained according to refs 13 and 14) and linalool 19 served as the allyl isoprenoid alcohols for the condensation with TMHQ.

It was found that the reaction of TMHQ with 16 in boiling heptane in the presence of the Tseokar-10 aluminosilicate gives a mixture of diastereomeric optically active chromanols 17 (erythro- /threo- ~ 1:1, GLC data, ee ~50%). Under the same conditions, the condensation of TMHQ with 19 is less selective, resulting in the formation of a considerable amount of the tricyclic isomer 22 besides the target chromanol 20. Compounds 20 and 22 were separated and characterized as the corresponding acetates 21 and 23 (Scheme 4).

Oxidative cleavage of the chromanyl acetates 18 and 21 by ozonolysis in aqueous acetone in the presence of Ba(OH)$_2$, gave aldehydes 24 and 25 in 52% and 80%, respectively, in one step. The hydride reduction of 24 and 25 yielded the corresponding alcohols 26 and 27 (Scheme 4).

In contrast to TMHQ, the reaction of menadiol acetate 10 with linalool 19 in the presence of the Tseokar-10 leads mainly to the cyclic compound 28 (70%, GLC).

**Synthesis of chromenes with isoprenoid side chains**

Chromenes with isoprenoid side chains are frequently encountered in nature, being structural analogs of prenylated coumarins, chalcones, and cannabinoids, this accounts for the increased interest in their synthesis. Two approaches have been developed most thoroughly, (1) using the pyridine-catalyzed reaction of α,β-unsaturated aldehydes with phenols, and (2) a two-step route comprising the reaction of trimethylhydroquinone (TMHQ) with tertiary allylic alcohols to give prenylated 1,4-benzoquinones, and subsequent cyclization of these compounds induced by pyridine. Alkylation of TMHQ with allylic alcohols catalyzed by Lewis acids (usually ZnCl$_2$ or BF$_3$-OEt$_2$) is the key step in the latter method.

We synthesized prenylated 1,4-benzoquinones using a heterogeneous zeolite of the Pentasil type in the H-form.
Scheme 4. (a) TMHQ, Tseokar-10, n-C7H16; (b) Ac2O, pyridine; (c) 10, Tseokar-10, PhMe; (d) O3, Me2CO, Ba(OH)2; (e) NaBH4, MeOH.

The reactions of TMHQ with the vinyl carbinal 16 (a 1:1 mixture of (3R,4S)-erythro- and (3S,4S)-threo- diastereomers (ee ~50%)) and linalool 19 in the presence of Pentasil were found to afford the 1,4-benzoquinones 29 and 30, respectively. Pyridine-induced cyclization of these products proceeded smoothly to give chromenes 31 and 32, respectively (Scheme 5). As in the case of the vinyl carbinals 16 and 19, the use of isophytol 2 resulted in the syntheses of the quinone 35 and chromene 36.
Ozonolysis of chromenes 33 and 34 at the side-chain double bond opens the way to ω-functionalized chromenes, which can be further converted into more complex chromene derivatives. However, under the ozonolysis conditions described previously, the chromenes gave only benzaldehydes and benzoic acids with the corresponding substituents. We found that in the ozonolysis of chromenyl acetates 33 and 34 with an equimolar amount of ozone it is possible to cleave selectively the double bond in the side chain and obtain the required aldehydes 37 and 38. Thus, using a zeolite catalyst of the Pentasil type, chromenes were synthesized with the
isoprenoid side chain containing the double bond, and whose partial ozonolysis yielded chromenes with the aldehyde group in the side chain.

**Conclusions**

For the condensation of trimethylhydroquinone and 2-methyl-1,4-naphthohydroquinone with allylic isoprenoid alcohols, the new catalysts Tseokar-10 aluminosilicate and zeolite Pentasil were used. Using these catalysts, \(d,l-\alpha\)-tocopherol, \((2RS,4'R,8'R)-\alpha\)-tocopherol, vitamin \(K_1\)-chromanol and their analogs with the shortened side chain were synthesized in high yields. The possibility of preparing the analogs of \(\alpha\)-tocopherol-chromanols and chromenols with the double bond in the side chain is a particular quality of the new catalysts compared to those usually used in this type of reaction. The selective ozonolysis of these compounds resulted in analogs of \(\alpha\)-tocopherol with an \(\omega\)-functionalized side chain serving as synthons for \(\alpha\)-tocopherol and its analogs.

**Experimental Section**

**General Procedures.** IR spectra were recorded on a Specord 75-IR spectrometer (in thin film); UV spectra using a Specord M-40 instrument. \(^1\)H- and \(^{13}\)C- NMR spectra were run on a Bruker AM-300 spectrometer (300.13 and 75 MHz for \(^1\)H and \(^{13}\)C, respectively) in CDC\(_3\). Chemical shifts are on the \(\delta\) scale, relative to internal Me\(_4\)Si. GLC analysis used a Chrom-5 chromatograph with 2400 x 4 mm columns with the Chromaton N-AW-DMCS and SE-30 (5%) stationary phase at a temperature of 50–300°C (8 K min\(^{-1}\)) using helium as carrier gas. The preparative separation of acetates 21 and 23 was carried out using a Carlo Erba chromatograph (6000 x 6 mm column) with SE-30 stationary phase, at 300 °C, with helium as carrier gas. HPLC used an LKB liquid chromatograph (Sweden) equipped with UV detector (\(\lambda = 249\) nm) and a column with Separon-C18 as adsorbent (125 x 4 mm, 5 \(\mu\)m); 87:13 MeOH–H\(_2\)O was used as eluent (0.3 mL·min\(^{-1}\), 20°C). Optical rotation was measured using a Perkin–Elmer-141 polarimeter. Mass spectra at 70 eV, using the electron impact mode, were measured on a Finnigan MAT 8200 instrument.

\((6R,10R)-6,10,14\)-Trimethylpentadecane-2-one (phytone) (5). Finely crushed air-dried leaves of great nettle (\(Urtica dioica\) \(L\)) (100 g) were extracted with acetone (1 L) until the extract became slightly green. The latter was extracted to give the pasty dark-green residue containing chlorophyll 4 (0.38 g, 0.42 mmol) (determined from the solution’s optical density according to Ref. 23). The residue was dissolved in 30 mL of acetone, then Ba(OH)\(_2\) (8.6 g, 50 mmol) and H\(_2\)O (2 mL) were added, an ozone–oxygen mixture (ozonizer productivity 11 mmol·h\(^{-1}\)) was passed at 30 L·h\(^{-1}\) for 20 min (~9 mol O\(_3\) /mol of chlorophyll 4) at room temperature. The precipitate was filtered, washed with acetone (~30 mL), and the combined filtrates evaporated in vacuo. The residue (0.8 g) was separated on a column (SiO\(_2\), 20 g), eluting with petroleum (bp 40–60 °C) to give the fraction of colorless non-polar substances (\(R_f = 0.71\)), then a fraction of \(R_f\)
= 0.49. The latter was evaporated to give 5 (0.1 g, 89%), $n_D^{20} 1.4482$, $[\alpha]_D^{20} +1.1^\circ$ (c 1.78, CHCl$_3$); [lit.$^{24}$ $n_D^{23} 1.4430$, $[\alpha]_D^{24} +0.78^\circ$]; IR ν 1720 cm$^{-1}$; $^1$H-NMR δ 0.85 (12 H, m, CH$_3$), 1.25 (16 H, m, CH$_2$), 1.43–1.62 (3H, m, CH), 2.10 (3 H, s, CH$_3$CCO), 2.38 (2 H, t, CH$_3$CCO), $J = 7.4$ Hz); $^{13}$C-NMR δ 19.46 and 19.63 (6-CH$_3$, 10-CH$_3$), 22.50 and 22.50 (14-CH$_3$, 15-C), 24.34 and 24.72 (8-C, 12-C), 27.89 (14-C), 29.63 (4-C), 31.51 (1-C), 32.60 and 32.71 (6-C, 10-C), 37.17, 37.22, 37.34 and 37.57 (5-C, 7-C, 9-C, 11-C), 39.31 (13-C), 43.96 (3-C), 208.75 (2-C).

**$^{3RS,7R,11R}$-Isophytol (6).** A solution of 5 (0.5 g, 1.87 mmol) in THF (0.6 mL) (Ar, ~25 °C) was added to a solution of Normant reagent prepared from Mg chips (0.2 g, 8.45 mmol) and vinyl bromide (0.9 g, 8.6 mmol) in THF (4 mL). The reaction mixture was stirred for 3 h, then treated with saturated NH$_4$Cl solution (5 mL). The organic layer was separated, and the aqueous one extracted with Et$_2$O. The combined organic layers were washed with NaCl, dried (MgSO$_4$), and evaporated in vacuo to give isophytol 6 (0.44 g, 80%) (the content of the basic compound is 97%, from GLC), $n_D^{23} 1.4582$; $[\alpha]_D^{20} +1.1^\circ$ (c 2.8, CHCl$_3$) [lit.$^{25}$ $n_D^{20} 1.4570$]; $^1$H-NMR δ 0.85 (12 H, m, CH$_3$), 1.0–1.6 (24 H, m, 3-CH$_3$, CH$_2$, CH), 5.0 (1 H, d, C=C$_{trans}$ $Trans$ $J = 10.7$ Hz), 5.18 (1 H, d, C=C$_{cis}$ $cis$ $J = 17.3$ Hz), 5.89 (1 H, dd, HCC$=C$, $J = 10.7$ Hz and 17.3 Hz); $^{13}$C-NMR δ 19.68 and 19.63 (7-CH$_3$, 11-CH$_3$), 22.56 and 22.66 (3-CH$_3$, 15-CH$_3$, 16-C), 24.42 and 24.74 (9-C, 13-C), 27.90 (15-C), 29.66 (5-C), 32.73 (7-C, 11-C), 32.73 and 37.38 (6-C, 8-C, 10-C, 12-C), 42.66 (4-C), 73.95 (3-C), 111.42 (1-C), 145.18 (2-C).

**2RS,4'R,8'R)-$\alpha$-Tocopherol (2-ambo-$\alpha$-tocopherol) (7).** Compound 6 (0.78 g, 2.64 mmol) was added to a boiling suspension of TMHQ (0.2 g, 1.32 mmol) and finely crushed Tseokar-10 catalyst (0.45 g) in 6 mL of dried n-nonane at boiling (under Ar). The mixture was boiled for 5 h, cooled to room temperature, the catalyst was filtered off, and the filtrate was evaporated. The residue (0.85 g) was chromatographed on a SiO$_2$ column (20 g), eluting with n-hexane to isolate the fraction (R$_f$ = 0.87) of non-polar substances, then with 10:1 n-hexane–Et$_2$O to give a fraction of R$_f$ = 0.35, which was evaporated to give 7 (0.55 g, 97%). $[\alpha]_D^{20} +0.31^\circ$ (c 0.26, CHCl$_3$) [lit.$^{21}$ $[\alpha]_D^{25} +0.38^\circ$ (C$_2$H$_5$OH)]; UV (C$_2$H$_5$OH) $\lambda_{max}$/nm (ε) 295 (3800); $^1$H-NMR δ 0.90 (12 H, m, CH$_3$), 1.0–1.9 (26 H, m, CH$_3$-2, CH$_2$, CH), 2.10 and 2.17 (9 H, both s CH$_3$-Ar), 2.61 (2 H, t, 4-H, $J = 6.7$ Hz), 4.3 (1 H, s OH); $^{13}$C-NMR δ 11.26, 11.75 and 12.19 (CH$_3$-Ar), 19.67 and 19.75 (4'-CH$_3$, 8'-CH$_3$), 20.79 and 20.81 (4-C, 8'-CH, 12'-CH$_3$), 22.62 and 22.70 (12'-CH$_3$, 13'-C), 24.46 and 24.81 (2'-C, 6'-C, 10'-C), 27.99 (12'-C), 31.60 (3-C), 32.75 and 32.83 (4'-C, 8'-C), 37.32 and 37.48 (3'-C, 5'-C, 7'-C, 9'-C), 39.42 (11'-C), 39.91 and 39.97 (11'-C), 74.55 (2-C), 116.38 (5-C), 118.51 (10-C), 121.05 (8-C), 122.64 (7-C), 144.57 (9-C), 145.63 (6-C).

**2,5-Dimethyl-2RS-(4R,8R,12-trimethyldecan-1-yl)-6-acetoxy-benzoh[hl]chroman (8).** Compound 6 (0.4 g, 1.35 mmol) was slowly added to a boiling suspension of menadion monoacetate 10 (0.56 g, 2.6 mmol) and finely crushed Tseokar-10 catalyst (1.1 g) in 8.4 mL of abs. toluene at boiling, under Ar. The mixture was boiled for 4 h, cooled to room temperature, the catalyst filtered off, and the filtrate evaporated. The residue was chromatographed on a SiO$_2$ column (20 g) using n-hexane to give the fraction (R$_f$ = 0.7) of non-polar substances, then the fraction of R$_f$ = 0.4 was eluted with a mixture (10:1) n-hexane–Et$_2$O, and evaporated to give 8 (0.56 g, 85%); the content of the basic compound was ≥97% (GLC data). $[\alpha]_D^{20} +1.1^\circ$ (c 1.34, CHCl$_3$); IR ν 1760 (C=O), 1210, 1080 and 1060 (C=O) cm$^{-1}$; UV (C$_2$H$_5$OH) $\lambda_{max}$/nm (ε) 244 (39830), 305 (5330), 328 (3900); $^1$H-NMR δ 0.95 (12 H, m, CH$_3$), 1.0–1.8 (21 H, m, CH$_2$CH), 1.35 and 1.40 (3H, both s,
2-CH3), 1.97 (2 H, m, 3-H), 2.28 (3 H, s, 5-CH3), 2.51 (3 H, s, CH3CO), 2.76 (2 H, t, 4-H, J = 6.4 Hz), 7.50 (2 H, m, 8-H, 9-H), 7.70, 8.30 (2 H, both d, 7-H, 10-H, J = 8.1 Hz); 13C-NMR δ 12.56 (5-CH3), 19.63, 19.69 (4′-CH3, 8′-CH3), 20.50 (CH3CO), 20.59 and 21.00 (4-C), 22.58, 22.68 (12′-CH3, 13′-C), 23.65 (2-CH3), 24.38, 24.75 (2′-C, 6′-C, 10′-C), 27.90 (12′-C), 30.95 (3-C), 32.61, 32.70 (4′-C, 8′-C), 37.23, 37.33, 37.50 (3′-C, 5′-C, 7′-C, 9′-C), 39.31 (11′-C), 39.99 and 40.06 (1′-C), 75.67 (2-C), 113.95 (5-C); 120.21, 121.90, 124.46, 126.0 (7-C, 8-C, 9-C, 10-C); 124.78, 125.72, 126.12 (3a-C, 6a-C, 10a-C); 136.79 (10b-C); 146.63 (6-C); 169.54 (CH3CO); Mass-spectra (70 eV), m/z (%): 494 [M]+ (34), 452 [M-COCH2]+ (100), 229 (9), 187 (37), 186(49), 158 (3), 129 (2), 105 (6), 83 (2), 71 (6), 57 (14), 43 [COCH3]+ (31). Exact mass Calcd: 494.37597 for C33H50O3. Found: m/z 494.37600 [M]+.

2,5-Dimethyl-2RS-(4R,8R,12-trimethyltridecan-1-yl)-6-hydroxy-benzol[α]chroman (9). A solution of 8 (0.28 g, 0.56 mmol) and lithium aluminumhydride (0.02 g) in 22.7 mL of abs. diethyl ether was boiled for 1 h (Ar) with stirring. The mixture was cooled to 0 °C then 2 mL of moist ether and 0.5 mL of 3 M HCl were added. After shaking, the ether layer was separated, washed with water to neutral, dried MgSO4, evaporated in vacuo, to give 9 (0.2 g, 80%) as a dark yellow viscous oil, [α]D 18 +0.89° (c 6.0, CHCl3). IR ν 1080, 1060, (C–O), 3400 (OH) cm−1; UV (CHCl3) λmax/nm (ε) 253 (17310), 303 (1960), 322 (2360), 341 (2490); 1H-NMR δ 0.95 (12 H, m, CH3), 1.0–1.85 (21 H, m, CH2, CH), 1.34 and 1.40 (3 H, both s, 2-CH3), 1.98 (2 H, m, 3-H), 2.30 (3 H, s, 5-CH3), 2.75 (2 H, t, 4-H, J = 6.5 Hz), 5.25 (1H, s, OH), 7.50 (2 H, m, 8-H, 9-H), 7.70 8.30 (2 H, both d, 7-H, 10-H, J = 8.1 Hz); 13C-NMR δ 15.27 (5-CH3), 19.78, 19.86 (4′-CH3, 8′-CH3), 21.01 and 21.18 (4-C), 22.75, 22.85 (12′-CH3, 13′-C), 23.60 (2-CH3), 24.56, 24.93 (2′-C, 6′-C, 10′-C), 28.07 (12′-C), 31.52 (3-C), 32.78, 32.87 (4′-C, 8′-C), 37.39, 37.49, 37.69 (3′-C, 5′-C, 7′-C, 9′-C), 39.47 (11′-C), 39.91 and 39.96 (1′-C), 75.12 (2-C), 114.48 (5-C), 117.50, 124.44, 124.57 (4a-C, 6a-C, 10a-C), 120.63, 121.66, 124.44, 125.08 (7-C, 8-C, 9-C, 10-C), 141.08 (10b-C), 142.88 (6-C).

2RS,5,7,8-Tetramethyl-2-(1S,5-dimethylhexyl)-6-hydroxychromans (12). A mixture of the alcohols 11 (0.7 g, 3.8 mmol) was added dropwise (Ar, 150 °C) to a suspension of TMHQ (0.24 g, 1.59 mmol) and the powdered catalyst Tseokar-10 (0.52 g) in anhydrous n-nonane (7 mL). The reaction mixture was heated at reflux for 4 h, cooled to ~20 °C, and filtered. The filtrate was concentrated and the residue was chromatographed on SiO2. Elution first with n-hexane and then with an n-hexane–Et2O mixture (10:1) gave 0.47 g (93%) of the chromans 12. According to the HPLC data, these compounds existed as a mixture (1:1) of the erythro- and threo- diastereomers (t = 25.2 and 28.8 min respectively), [α]D 12 -1.67° (c 2.0, CHCl3). Anal. Calcd. for C21H34O2 (318.5): C, 79.19; H, 10.76. Found: C, 79.35; H, 10.88. UV (CHCl3) λmax/nm (ε) 295 (3900); 1H-NMR δ 0.80–0.88 (6 H, m, 6′-H, 5′-CH3), 0.90 (1.5 H, d, 1′-CH3, J = 6.7 Hz), 0.95 (1.5 H, d, 1′-CH3, J = 6.8 Hz), 1.11 (3 H, s, 2-CH3), 1.2–1.19 (10 H, m, 3-H, 1′-H, 2′-H–4′H, 5′-H), 2.10 s (6 H, ArCH3), 2.15 s (3 H, ArCH3), 2.57 t (2 H, 4-H2C, J = 6.7 Hz), 4.25 s (1 H, OH); 13C-NMR δ 11.35 (5-CH3), 11.86, 12.28 (8-CH3), 13.47, 14.39 (7′-CH3), 19.45, 19.94 (1′-CH3), 20.52, 20.60 (4-C), 22.62 (6′-C), 22.80, 22.86 (2-CH3), 25.89, 25.97 (3′-C), 27.84, 27.97 (5′-C), 29.24, 29.67 (3-C), 30.69, 31.66 (2′-C), 39.29 (4′-C), 39.90 (1′-C), 77.15, 77.21 (2-C), 117.63 (5-C), 118.45, 118.55 (10-C), 121.04, 121.05 (8-C), 122.65 (7-C), 144.49 (9-C), 145.35 (6-C).
2RS,5,7,8-Tetramethyl-2-(1S,5-dimethylhexyl)-6-acetoxychromans (13). A solution of a mixture of chromans 12 (0.15 g, 10.47 mmol) in Ac₂O (0.15 mL) was heated at reflux for 3 h, cooled, poured into iced water (10 mL), and extracted with Et₂O. The extract was successively washed with saturated solutions of NaHCO₃ and NaCl, dried with MgSO₄, concentrated, and chromatographed (SiO₂, hexane). A 1:1 mixture of the erthro- and threo-diastereomers of 13 (GLC data) was obtained in a yield of 0.13 g (77%), [α]D¹⁴ –4.75° (c 1.8, CHCl₃). Anal. Calcd. for C₂₃H₃₆O₃ (360.5): C, 76.62; H, 10.07. Found: C, 76.91; H, 10.20%. IR ν 1740 (C=O) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 277 (1760), 286 (3100). ¹H-NMR δ 0.83–0.92 (6 H, t, 6'-H, 5'-CH₃), 0.95 (1.5 H, d, 1'-CH₃, J = 6.8 Hz), 1.05 (1.5 H, d, 1'-CH₃, J = 6.7 Hz), 1.18 (3 H, s, 2-CH₃), 1.30–1.90 (10 H, m, 3-H, 1’-H, 2’-H–4’-H, 5’-H), 2.02, 2.09, 2.18 (9 H, all s, ArCH₃), 2.39 (3 H, s, O=CCH₃), 2.60 (2 H, t, 4-H, J = 6.6 Hz); ¹³C-NMR δ 11.85, 12.09 (8-CH₃), 12.94 (5-CH₃), 13.55, 14.15 (7-CH₃), 20.33, 20.41 (4-C), 20.56 (1’-CH₃, O=CCH₃), 22.55 (6'-C), 22.78 (2-CH₃), 25.85, 25.90 (3’-C), 27.83, 27.92 (5’-C), 30.73, 31.55 (2’-C), 31.91 (3-C), 39.25 (1’-C, 4’-C), 77.67 (2-C), 117.60 (10-C), 124.80, 124.86 (8-C), 123.06 (5-C), 126.63 (7-C), 140.48 (9-C), 149.20 (6-C), 169.75 (C=O).

2,5-Dimethyl-2RS-(1S,5-dimethylhexyl)-6-acetoxybenzo[h]chroman (14). The alcohols 11 (0.21 g, 1.2 mmol) were slowly added to a boiling suspension of 10 (0.50 g, 2.3 mmol) and finely crushed Tsekar-10 catalyst (1.0 g) in 7.0 mL of abs. toluene at boiling (Ar). The reaction mixture was boiled for 10 h, cooled to room temperature, the catalyst filtered off, and the filtrate evaporated. The residue was chromatographed on a SiO₂ column (20 g) eluted with n-hexane to give the fraction (Rf = 0.7) of non-polar substances, then the fraction (Rf = 0.4) was eluted using a mixture (10:1) of n-hexane–Et₂O, evaporated to give a 1:1 mixture of erthro- and threo-diastereomers of 14 (0.21 g, 49%), the content of the basic compound was ≥97% (GLC data). [α]D¹⁸ = 1.0° (c 2.0, CHCl₃). Anal. Calcd. for C₂₃H₃₄O₃ (382.5): C, 78.43; H, 8.89. Found: C, 78.71; H, 8.91%. IR ν 1760 (C=O), 1210, 1080 and 1060 (C-O) cm⁻¹. UV (CHCl₃) λ_max/nm (ε) 245 (80200), 309 (4080), 330 (3560); ¹H-NMR δ 0.92 (6 H, m, 6'-H, 5'-CH₃), 1.04 (1.5 H, d, 1’-CH₃, J = 6.7 Hz), 1.15 (1.5 H, d, 1’-CH₃, J = 6.8 Hz), 1.32 (3 H, s, 2-CH₃), 1.20–2.10 (10 H, m, 3-H, 1’-H, 2’-H–4’-H, 5’-H), 2.25 (3 H, s, ArCH₃), 2.54 (3 H, s, CH₂C=O), 2.75 (2 H, t, 4-H, J = 6.7 Hz), 7.48 (2 H, m, 8-H, 9-H), 7.70, 8.28 (2 H, both d, 7-H, 10-H, J = 8.7 Hz); ¹³C-NMR δ 12.56 (5-CH₃), 20.30, 20.38 (4-C), 20.56 (CH₃C=O, 1’-CH₃), 22.43 (6’-C), 22.64 (2-CH₃), 25.76, 25.81 (3’-C), 27.75, 27.84 (5’-C, 1’-C), 30.77 (2’-C), 31.38 (4’-C), 39.13 (4’-C), 78.33 (2-C), 114.28 (5-C), 120.19, 121.86, 124.47, 126.02 (7-C, 8-C, 9-C, 10-C), 124.79, 125.72 (4a-C, 6a-C, 10a-C), 136.67 (10b-C), 146.48 (6-C), 169.64 (CH₂C=O).

2,5-Dimethyl-2RS-(1S,5-dimethylhexyl)-6-hydroxybenzo[h]chroman (15). A solution of 14 (0.12 g, 0.32 mmol) and lithium aluminumhydride (0.01 g) in 10.0 mL of abs. diethyl ether was boiled for 1 h with stirring (Ar). The reaction mixture was cooled to 0 °C then 2 ml of moist ether and 0.5 mL of 3 M HCl added. The ether layer was separated, washed with water to neutral, dried over MgSO₄, and evaporated in vacuo, to give 15 (0.085 g, 78%) as dark yellow viscous oil, [α]D¹⁸ = 0.70° (c 5.8, CHCl₃). Anal. Calcd. for C₂₃H₃₂O₂ (340.5): C, 81.06; H, 9.40. Found: C, 81.21; H, 9.37%. IR ν 1080, 1060, (C=O), 3400 (OH) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 251 (15400), 325 (3070), 340 (3050); ¹H-NMR δ 0.95 (6 H, m, 6’-H, 5’-CH₃), 1.10 (1.5 H, d, 1’-CH₃,
J = 6.5 Hz), 1.18 (1.5 H, d, 1′-CH3, J = 6.5 Hz), 1.25 (1.5 H, s, 2-CH3), 1.32 (1.5 H, s, 2-CH3), 1.40–2.10 (10 H, m, 3-H, 1′-H, 2′-H, 4′-H, 5′-H), 2.30 (3 H, br. s, ArCH3), 2.70 (2 H, m, 4-H), 7.45 (2 H, m, 8-H, 9-H), 8.00, 8.20 (2 H, m, 7-H, 10-H).

2RS,5,7,8-Tetramethyl-2-(1S,5-dimethyl-4-hexen-1-yl)-6-hydroxychromans (17). A mixture of alcohols 16 (2.5 g, 13.74 mmol) prepared by a known procedure14 was added dropwise (Ar, 98 °C) to a suspension of TMHQ (1.04 g, 6.87 mmol) and the powdered Tseokar-10 catalyst (2.4 g) in 30 mL of dry n-heptane. The reaction mixture was refluxed for 5 h, cooled to ~20 °C, and filtered. The filtrate was concentrated and the residue chromatographed on SiO2. Elution, first with n-hexane and then with an n-hexane–Et2O mixture (10:1) gave 1.16 g (54%) of chromans 17; according to GLC, this was a 1:1 mixture of erythro- and threo-diastereomers; [α]D14 -2.0° (c 3.0, CHCl3). Anal. Calcd. for C21H32O2 (316.5): C, 79.70; H, 10.19. Found: C, 79.52, H, 10.02%. UV (CHCl3) λmax/nm (ε) 296 (3780); 1H-NMR δ 1.02 (1.5 H, d, 1′-CH3, J = 6.7 Hz), 1.08 (1.5 H, d, 1′-CH3, J = 6.8 Hz), 1.22 (3 H, s, 2-CH3), 1.6–2.1 (7 H, m, 3-H, 1′-H, 2′-H, 1′-H), 1.66, 1.70, 1.72, 1.80 (6 H, all s, 5′-CH3, 6′-H), 2.18, 2.22, 2.24 (9 H, all s, ArCH3), 2.68 (2 H, t, 4-H, J = 6.6 Hz), 4.50 (1 H, s, OH), 5.13 (0.5 H, t, 4′-H, J = 7.5 Hz), 5.26 (0.5 H, t, 4′-H, J = 7.5 Hz).

2RS,5,7,8-Tetramethyl-2-(1S,5-dimethyl-4-hexen-1-yl)-6-acetoxychromans (18). A solution of the mixture of chromans 17 (0.5 g, 1.58 mmol) in 4 mL of Ac2O and 5 mL of anhydrous pyridine was added with stirring. The mixture was kept for 0.5 h at ~20 °C, and dried with MgSO4, then poured into 20 mL of ice water and extracted with EtOAc. The extract was washed with 3–5 mL of dry MIBK and the powdered Tseokar-10 catalyst (1.8 g) in 24 mL of boiling anhydrous pyridine was added dropwise (Ar, 98 °C) to a suspension of TMHQ (0.8 g, 5.28 mmol) and powdered Tseokar-10 catalyst (1.04 g, 6.87 mmol) was added dropwise to a suspension of TMHQ (0.8 g, 5.28 mmol) and powdered Tseokar-10 catalyst (1.8 g) in 24 mL of boiling anhydrous pyridine and 5 mL of anhydrous HCl, aq. NaHCO3, then H2O, dried with MgSO4, and concentrated to give 0.5 g (88.3%) of a mixture of erythro- and threo-diastereomers of 18: [α]D20 -5.7° (c 0.34, CHCl3). Anal. Calcd. for C23H34O3 (358.5): C, 77.10; H, 9.50. Found: C, 77.27; H, 9.63%. IR ν 1740 (C=O) cm⁻¹; UV (EtOH) λmax/nm (ε) 285 (2400). 1H-NMR δ 0.97, 1.03 (3H, d of d, 1′-CH3, J = 7.0 Hz), 1.99 (3 H, s, 2-CH3), 1.6–2.0 (7 H, m, 3-H, 1′-H – 3′-H), 1.62, 1.75 (6 H, both s, 5′-CH3, 6′-H), 2.02, 2.06, 2.18 (9 H, all s, ArCH3), 2.38 (3 H, s, CH3-O), 2.60 (2 H, t, 4-H), 5.17 t (1 H, 4′-H, J = 6.7 Hz).

2RS,5,7,8-Tetramethyl-2-(4-methylpent-3-en-1-yl)-6-acetoxychroman (21) and 7-acetoxy-1,1,4a,5,6,8-hexamethyldibenzo[a]chirano[12,3,4,a]hexasubanethene (23). Alcohol 19 (1.63 g, 10.56 mmol) was added dropwise to a suspension of TMHQ (0.8 g, 5.28 mmol) and powdered Tseokar-10 catalyst (1.8 g) in 24 mL of boiling anhydrous n-heptane (under Ar). The mixture was heated at reflux for 6 h, cooled to ~20 °C, and filtered. The filtrate was concentrated and the residue chromatographed on SiO2 as described above for 17, to give a mixture of chromanols 20 and 22 (1.12 g) (2:1, GLC retention times 20.89 and 22.02 min, respectively). The mixture of 20 and 22 was dissolved in 11 mL of anhydrous pyridine and 8.5 mL of Ac2O added with stirring. The mixture was kept for 0.5 h at ~20 °C and poured into 25 mL of ice water, the products extracted with EtOAc, then washed with 3 M HCl, aq. NaHCO3, and H2O, and dried with MgSO4 to give 1.20 g (68.9%) of a mixture of acetates 21 and 23 (2:1, GLC retention times 21.45 and 22.76 min, respectively). The mixture was separated by preparative GLC.

Acetate 21. IR ν 1740 (C=O) cm⁻¹; UV (EtOH) λmax/nm (ε) 285 (1900). 1H-NMR δ 1.30 (3 H, s, 2-CH3), 1.65, 1.73 (6 H, both s, 4′-CH3, 5′-H), 1.70–1.95 (6 H, m, 3-H, 1′-H, 2′-H), 2.02, 2.08,
2.15 (9 H, all s, ArCH3), 2.38 (3 H, s, CH3CO), 2.68 t (2 H, 4-H, J = 6.7 Hz), 5.19 t (1 H, 3'-H, J = 7.0 Hz).

**Acetate 23.** mp 138–9 °C; IR v 1740 (C=O) cm⁻¹; UV (EtOH) λ_max/nm (ε) 285 (1700). ¹H-NMR δ 0.95, 1.03 (6 H, both s, 1-CH3). 1.19 (3 H, s, 4a-CH3), 1.30–1.80 (6 H, m, 2-H–4-H), 2.10 (1 H, m, 9a-H), 2.01, 2.03, 2.10 (9 H, all s, ArCH3). 2.38 (3 H, s, CH3C=O), 2.61 (2 H, dd, 9-H, J = 5.1 and J = 16.0 Hz).

**2RS,5,7,8-tetramethyl-2-(1S-methyl-4-oxobut-1-yl)-6-acetoxychroman (24).** An ozone–oxygen mixture was passed for 8 min through a mixture of acetates 18 (0.5 g, 1.4 mmol), Ba(OH)2 (0.48 g, 2.8 mmol), H2O (0.12 mL), and acetone (5 mL) at ~20 °C, at a flow of 30 L·h⁻¹ (1.45 mmol of O₃). After the reaction was completed, the precipitate was filtered off and the filtrate concentrated in vacuo. The residue was dissolved in 10 mL of Et₂O, dried with MgSO₄, and concentrated. The residue was chromatographed on SiO₂ using an n-hexane–Et₂O mixture (10:1) as eluent to give 0.24 g (52%) of aldehyde 24, [α]D ²⁰ = 5.9° (c 0.54, CHCl₃). Anal. Calcd. for C₂₀H₂₈O₄ (332.4): C, 72.26; H, 8.49. Found: C, 72.47; H, 8.50%. IR v 1710 and 1740 (C=O) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 280 (1400), 288 (1600); ¹H-NMR δ 0.92, 0.98 (3 H, both d, 1'-CH3, J = 6.9 Hz, J = 6.7 Hz), 1.15 (3 H, s, 2-CH₃), 1.6–2.0 (5 H, m, 3-H, 1'-H, 2'-H), 1.98, 2.00, 2.10 (9 H, all s, ArCH₃), 2.30 (3 H, s, CH₃CO), 2.58 (4 H, m, 4-H, 3'-H), 9.80 (1 H, s, 4'-H).

**2RS,5,7,8-Tetramethyl-2-(3-oxoprop-1-yl)-6-acetoxychroman (25).** An ozone–oxygen mixture was passed for 15 min through a mixture of acetates 21 and 23 (0.8 g) (containing 0.48 g [1.45 mmol] of 21), Ba(OH)₂ (0.87 g, 5.04 mmol), H₂O (0.2 mL), and acetone (8 mL) at ~20 °C at a velocity of 30 L·h⁻¹ (2.05 mmol of O₃). The mixture was worked-up as described in the previous experiment to give 0.35 g (80%) of aldehyde 25 and 0.25 g of compound 23.

**Aldehyde 25.** IR v 1710 and 1740 (C=O) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 278 (1600), 287 (1800). ¹H-NMR δ 1.20 (3 H, s, 2-CH₃), 1.75 (4 H, m, 3-H, 1'-H), 1.95, 2.00, 2.03 (9 H, all s, ArCH₃), 2.10 (3 H, s, CH₃CO), 2.58 (4 H, m, 4-H, 2'-H), 9.75 (1 H, s, 3'-H).

**2RS,5,7,8-Tetramethyl-2-(1S-methyl-4-hydroxybut-1-yl)-6-acetoxychroman (26).** NaBH₄ (0.017 g, 0.42 mmol) was added in one portion to a solution of aldehyde 24 (0.14 g, 0.4 mmol) in 2 mL of MeOH. The mixture was stirred for 12 h, then the solvent was removed in vacuo. The residue was dissolved in EtOAc, washed with 3 M HCl, saturated aq. NaHCO₃, then brine, and dried with MgSO₄. The solution was concentrated and the residue was chromatographed on SiO₂ using a 10:1 hexane–EtOAc mixture as eluent to give 0.08 g (58%) of alcohol 26, [α]D ²⁰ = 5.8° (c 0.37, CHCl₃). Anal. Calcd. for C₂₀H₂₈O₄ (334.5): C, 71.82; H, 8.90. Found: C, 71.97; H, 8.90. IR v 3400 (OH), 1740 (C=O) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 280 (2100), 288 (2500); ¹H-NMR δ 0.94, 1.00 (3 H, both d, 1'-CH₃, J = 6.5 Hz), 1.15 (3 H, s, 2-CH₃), 1.61–2.02 (7 H, m, 3-H, 1'-H – 3'-H), 2.00, 2.07, 2.13 (9 H, all s, ArCH₃), 2.34 (3 H, s, CH₃CO), 2.58 (2 H, t, 4-H, J = 6.6 Hz), 3.60, 3.65 (2 H, both t, 4'-H, J = 6.1 Hz).

**2RS,5,7,8-Tetramethyl-2-(3-hydroxyprop-1-yl)-6-acetoxychroman (27).** The reaction of aldehyde 25 (0.32 g, 1.04 mmol) and NaBH₄ (0.04 g, 1.04 mmol) in 3 mL of MeOH, carried out as above gave 0.18 g (58%) of alcohol 27. IR ν 3400 (OH), 1740 (CH₃CO) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 280 (1500), 287 (1700); ¹H-NMR δ 1.25 (3 H, s, CH₃-2), 1.65 (4 H, m, 1'-H, 2'-H),
1.78 (2 H, m, 3-H), 1.98, 2.02, 2.10 (9 H, all s, ArCH3), 2.32 (3 H, s, CH3CO), 2.59 (2 H, t, 4-H, J = 6.6 Hz), 3.60 (3 H, m, 3′-H, OH).

**9-Acetoxyl-1,1,4a,10-tetramethyl-1,2,3,4,4a,11a-hexahydro-benzo[fl]xanthene (28).** Alcohol 19 (0.21 g, 1.4 mmol) was added slowly to a boiling suspension of 10 (0.60 g, 2.8 mmol) and finely crushed Tseokar-10 catalyst (1.0 g) in 9.0 mL of boiling abs. toluene at (Ar). The mixture was boiled for 5 h, cooled to room temperature, the catalyst filtered off, and the filtrate evaporated. The residue was chromatographed on a SiO2 column (20 g) eluting with n-hexane to give the fraction (Rf = 0.7) of non-polar substances, then the fraction (Rf = 0.5) was eluted using n-hexane–Et2O (10:1), and evaporated to give 28 (0.307 g, 62%), mp 191–3°C. Anal. Calcd. for C23H28O3 (352.5): C, 78.30; H, 7.94. Found: C, 78.16; H, 7.81%. IR v 1760 (C=O), 1210, 1080 and 1060 (C-O) cm\(^{-1}\); UV (CHCl3) \(\lambda_{max}/\text{nm (e)}\) 245 (34650), 308 (6410), 343 (5410); \(^1\)H-NMR \(\delta\) 1.00, 1.10 (6 H, both s, 1-CH3), 1.30 (3 H, s, 4a-CH3), 1.40–1.90 (6 H, m, 2-H–4-H), 2.15 (1 H, m, 11a-H), 2.28 (3 H, s, 10-CH3), 2.50 (3 H, s, CH3–C=O), 2.80 (2 H, dd, 11-H, J = 5.2 Hz and J = 16.1 Hz), 7.48 (2 H, m, 6-H, 7-H), 7.70, 8.28 (2 H, both d, 8-H, 5-H, J = 8.0 Hz); \(^13\)C-NMR \(\delta\) 12.60 (10-CH3), 20.55 (1-CH3, CH3–C=O), 21.69 (1-C), 32.03 (4a-CH3), 33.33 (3-C, 11-C), 39.71 (2-C), 41.50 (4-C), 47.92 (11a-C), 75.41 (4a-C), 114.00 (10a-C), 120.04, 120.15, 121.97, 124.43, 124.62, 125.91, 125.99 (10-C, 8a-C, 8-C, 7-C, 6-C, 5-C, 4-C), 136.86 (4b-C), 146.01 (9-C), 169.66 (CH3–C=O).

**2,3,5-Trimethyl-6-(3,7-dimethylocta-2,6-dien-1-yl)-1,4-benzoquinone(geranyltrimethylbenzoquinone) (30).** The allylic alcohol 19 (0.4 g, 2.6 mmol) was slowly added in a flow of Ar to a vigorously stirred suspension of TMHQ (0.2 g, 1.3 mmol) and finely crushed ZSM-5/11 catalyst (0.45 g) in 9 mL of anhydrous nonane. The mixture was heated at reflux for 5 h and cooled to ~20 °C, the catalyst filtered off, and the filtrate evaporated. The fraction (Rf = 0.7) of non-polar substances, then the fraction (Rf = 0.5) was eluted using n-hexane–Et2O (10:1), and evaporated to give 28 (0.307 g, 62%), mp 191–3°C. Anal. Calcd. for C23H28O3 (352.5): C, 78.30; H, 7.94. Found: C, 78.16; H, 7.81%. IR v 1760 (C=O), 1210, 1080 and 1060 (C-O) cm\(^{-1}\); UV (CHCl3) \(\lambda_{max}/\text{nm (e)}\) 245 (34650), 308 (6410), 343 (5410); \(^1\)H-NMR \(\delta\) 1.00, 1.10 (6 H, both s, 1-CH3), 1.30 (3 H, s, 4a-CH3), 1.40–1.90 (6 H, m, 2-H–4-H), 2.15 (1 H, m, 11a-H), 2.28 (3 H, s, 10-CH3), 2.50 (3 H, s, CH3–C=O), 2.80 (2 H, dd, 11-H, J = 5.2 Hz and J = 16.1 Hz), 7.48 (2 H, m, 6-H, 7-H), 7.70, 8.28 (2 H, both d, 8-H, 5-H, J = 8.0 Hz); \(^13\)C-NMR \(\delta\) 12.60 (10-CH3), 20.55 (1-CH3, CH3–C=O), 21.69 (1-C), 32.03 (4a-CH3), 33.33 (3-C, 11-C), 39.71 (2-C), 41.50 (4-C), 47.92 (11a-C), 75.41 (4a-C), 114.00 (10a-C), 120.04, 120.15, 121.97, 124.43, 124.62, 125.91, 125.99 (10-C, 8a-C, 8-C, 7-C, 6-C, 5-C, 4-C), 136.86 (4b-C), 146.01 (9-C), 169.66 (CH3–C=O).

\* Preparation of the ZSM-5/11 catalyst. A Pentasil zeolite prepared by a previously described procedure (except that mono-ethanolamine was used as the template) was converted into the H-form on treatment with a 1 M solution of NH4NO3, at 60 °C, followed by heating at 540 °C for 4 h in an air flow.
9.48%. IR ν 1630 (C=O) cm⁻¹; UV (CHCl₃) λₘₐₓ/ₙₘ (ε) 257 (16117), 265 (16476). ¹H-NMR δ 0.87 (3 H, d, 4'-CH₃, J = 6.8 Hz), 1.10–1.30 (2 H, m, 5'-H), 1.42, 1.57, 1.59 (each 3 H, all s, 3'-CH₃, 8'-CH₃, 9'-CH₃), 1.60–1.80 m (2 H, 6'-H₂), 1.90 m (9 H, 2-CH₃, 3-CH₃, 5-CH₃), 3.12 d (2 H, 1-H₂C, J = 6.8 Hz), 4.85 t (1 H, 2'-HC, J = 6.9 Hz), 4.95 t (1 H, 7'-HC, J = 7.1 Hz); ¹³C-NMR δ 11.9, 12.1 (2-CH₃, 3-CH₃, 5-CH₃), 17.3 (3'-CH₃, 8'-CH₃), 19.5 (4'-CH₃), 25.1 (6'-C), 25.6 (9'-C), 25.9 (1'–C), 34.7 (5'-C), 42.3 (4'–C), 118.9 (2'–C), 124.5 (7'–C), 130.8 (8'–C), 140.7 (3'–C), 139.9, 140.0, 140.2 (2-C, 3-C, 5-C), 143.0 (6-C), 186.6, 187.5 (1-C, 4-C).

2,3,5-Trimethyl-6-(3RS,11RS,15-tetramethylhexadec-2E-en-1-yl)-1,4-benzoquinones (phytrol-trimethylbenzoquinones) (35). Heating under reflux of TMHQ (0.1 g, 0.66 mmol), isophytol 2 (0.39 g, 1.32 mmol), and ZSM-5/11 (0.1 g) in 4 mL of anhydrous nonane for 3 h, as described above, gave 0.16 g (57%) of quinones 35, nD²⁰ 1.4942; IR ν 1630 (C=O) cm⁻¹; UV (CHCl₃) λₘₐₓ/ₙₘ (ε) 257 (16120), 265 (16711); ¹H-NMR δ 0.85 (12 H, d, 7'-CH₃, 11'-CH₃, 15'-CH₃, 16'–H, J = 6.1 Hz), 1.00–2.10 (21 H, m, 4'-H–15'H), 2.00 (9 H, m, 2-CH₃, 3-CH₃, 5-CH₃), 3.10 (2 H, d, 1'-H, J = 6.9 Hz), 4.95 (1 H, t, 2'-H, J = 6.9 Hz); ¹³C-NMR δ 11.9, 12.2, 13.0 (2-CH₃, 3-CH₃, 5-CH₃), 16.2 (3'-CH₃), 19.7 (7'-CH₃, 11'-CH₃), 22.7 (15'-CH₃, 16'-C), 24.8 (9'-C), 25.3 (5'-C), 25.6 (1'–C), 28.0 (15'-C), 32.7 (11'-C), 32.8 (7'-C), 36.7 (6'-C), 37.4 (8'-C, 10'-C, 12'-C), 39.5 (14'-C), 40.1 (4'–C), 119.3 (2'–C), 137.2 (3'–C), 137.4, 140.3, 143.2 (2-C, 3-C, 5-C, 6-C), 186.8, 187.7 (1-C, 4-C).

2RS,5,7,8-Tetramethyl-2-(4-methylpent-3-en-1-yl)-6-hydroxy-3-chromene (32). A solution of the quinone 30 (0.59 g, 1.22 mmol) in 9 mL of anhydrous pyridine was heated at reflux for 16 h, cooled to ~20 °C, diluted with brine, and extracted with hexane. The extract was washed with H₂O and dried with MgSO₄. The residue after solvent evaporation in vacuo was chromatographed on SiO₂, the product being eluted with a 10:1 n-hexane–Et₂O mixture to give 0.39 g (66%) of chromone 32, nD²⁰ 1.5448; UV (CHCl₃) λₘₐₓ/ₙₘ (ε) 276 (8528), 286 (8210), 334 (3113). ¹H-NMR δ 1.45 (3 H, s, 2-CH₃), 1.68 and 1.75 (6 H, both s, 4'-CH₃, 5'-H), 1.75 (2 H, m, 1'-H), 2.20 (11 H, m, 2'-H, ArCH₃), 4.65 (1 H, s, OH), 5.18 (1 H, t, 3'-H, J = 7.1 Hz), 5.68 (1 H, d, 3-H, J = 10.0 Hz), 6.60 (1 H, d, 4-H, J = 10.0 Hz); ¹³C-NMR δ 10.8, 11.5, 12.3 (5-CH₃, 7-CH₃, 8-CH₃), 17.4 (4'-CH₃), 22.6 (2'–C), 25.2 (2-CH₃), 25.6 (5'-C), 40.2 (1'–C), 76.4 (2-C), 120.1 (3'-C), 116.5 (10-C), 117.6 (5-C), 122.1 (8-C), 123.2 (7-C), 124.3 (3-C), 129.6 (4-C), 131.3 (4'-C), 144.5 (9-C), 145.2 (6-C).

2RS,5,7,8-Tetramethyl-2-(1S,5-dimethylhex-4-en-1-yl)-6-hydroxy-3-chromenes (31). Heating of quinone 29 (0.21 g, 0.69 mmol) at reflux in 3 mL of anhydrous pyridine, as described above, gave 0.13 g (59%) of a mixture of (2R,1'S)-erythro- and (2S,1'S)-threo- chromones 31, [α]D²⁰ –7.0° (c 0.47, CHCl₃). Anal. Calcd. for C₃₂H₃₅O₂ (314.5): C, 80.21, H, 9.62. Found: C, 80.13, H, 9.50%. UV (CHCl₃) λₘₐₓ/ₙₘ (ε) 273 (7828), 284 (7617), 334 (3513); ¹H-NMR δ 1.00 (3 H, m, 1'-CH₃), 1.30 (3 H, s, 2-CH₃), 1.59, 1.61, 1.67, 1.70 (6 H, all s, 5'-CH₃, 6'-H), 1.50–1.90 (5 H, m, 1'-H – 3'-H), 2.15 (9 H, m, ArCH₃), 4.48 (1 H, br, s, OH), 5.10 (1 H, m, 4'-H), 5.68 (1 H, m, 3-H), 6.53 (1 H, d, 4-H, J = 10.0 Hz); ¹³C-NMR δ 10.9, 11.6, 12.5 (5-CH₃, 7-CH₃, 8-CH₃), 13.9, 14.0 (1'–CH₃), 17.7 (5'-CH₃), 21.9, 22.7 (2-CH₃), 25.7 (6'-C), 26.2, 26.5 (3'-C), 31.3, 31.6 (2'–C), 40.5, 40.7 (1'–C), 79.2, 79.3 (2-C), 120.1 (4'–C), 116.2 (10-C), 118.0 (5-C), 122.2 (8-C), 123.2 (7-C), 124.8 (3-C), 129.2, 129.6 (4-C), 131.4 (5'-C), 144.5 (9-C), 145.3 (6-C).
The quinones 35 (0.44 g, 1.02 mmol) were heated at reflux in 4.4 mL of anhydrous pyridine, as described above, gave 0.29 g (66%) of a mixture of chromenes 36, \( n_D^{24} 1.5096; \) UV (CHCl₃) \( \lambda_{max}/nm (\epsilon) \) 272 (9200), 283 (8200), 333 (4100); \(^1\)H-NMR \( \delta \) 0.92 (12 H, m, 4'-CH₃, 8'-CH₃, 12'-CH₃, 13'-H), 1.05–1.72 (21 H, m, 1'-H − 12'-H), 1.38 (3 H, s, 2-CH₃), 2.20 (9 H, m, ArCH₃), 4.48 (1 H, br. s, OH), 5.65 (1 H, d, 3-H, J = 10.0 Hz), 6.57 (1 H, d, 4-H, J = 10.0 Hz); \(^1^3\)C-NMR \( \delta \) 10.8, 11.5, 12.4 (5-CH₃, 7-CH₃, 8-CH₃), 19.6, 19.7 (4'-CH₃, 8'-CH₃), 22.6, 22.7 (12'-CH₃, 13'-C), 24.4 (6'-C), 24.8 (2'-C, 10'-C), 28.0 (12'-C), 32.8, 32.9 (4'-C, 8'-C), 37.2, 37.3, 37.4 (3'-C, 5'-C, 7'-C, 9'-C), 39.4 (11'-C), 40.0 (1'-C'), 76.6 (2-C), 116.2 (5-C), 118.5 (10-C), 120.1 (3-C), 122.2 (8-C), 123.1 (7-C), 129.9 (4-C), 144.9 (9-C), 145.3 (6-C).

A solution of the chromene 32 (0.42 g, 1.48 mmol) in 4 mL of Ac₂O and 5.3 mL of anhydrous pyridine was kept at ~20 °C for 3 h, poured on ice, extracted with Et₂O, washed with 3 M HCl, then a saturated solution of NaHCO₃, and H₂O, and dried with MgSO₄ to give 0.42 g (87%) of a mixture of the chromenes 34. Anal. Calcd. for C₃₂H₃₃O₃ (328.5): C, 76.79; H, 8.59. Found: C, 76.53; H, 8.45%. IR ν 1740 (C=O) cm⁻¹; UV (CHCl₃) \( \lambda_{max}/nm (\epsilon) \) 272 (8600), 283 (6900), 320 (2600); \(^1\)H-NMR \( \delta \) 1.38 (3 H, s, 2-CH₃), 1.60, 1.70 (6 H, both s, 5'-H, 4'-CH₃), 1.70 (2 H, m, 1'-H); 2.04, 2.08, 2.15 (9 H, all s, ArCH₃), 2.15 (2 H, m, 2'-H), 2.33 (3 H, s, CH₃C=O), 5.12 (1 H, t, 3'-H, J = 6.9 Hz), 5.60 (1 H, d, 3-H, J = 10.0 Hz). 6.52 (1 H, d, 4-H, J = 10.0 Hz); \(^1^3\)C-NMR \( \delta \) 11.4, 11.8, 13.0 (5-CH₃, 7-CH₃, 8-CH₃), 17.5 (4'-CH₃), 20.2 (CH₃CO), 22.6 (2'-C), 25.5 (2-CH₃), 25.7 (5'-C), 40.6 (1'-C), 77.1 (2-C), 117.4 (10-C), 119.8 (3'-C), 122.2 (8-C), 122.4 (5-C), 124.1 (3-C), 129.2 (7-C), 129.3 (4-C), 131.3 (4'-C), 145.0 (9-C), 148.3 (6-C), 169.3 (C=O).

A solution of a mixture of chromenes 31 (0.63 g, 2.01 mmol) in 5.5 mL of Ac₂O and 7 mL of anhydrous pyridine was kept at ~20 °C for 3 h, poured on ice, extracted with Et₂O, washed with 3 M HCl, then a saturated solution of NaHCO₃, and H₂O, and dried with MgSO₄ to give 0.63 g (88%) of a mixture of (2R,1'S)-erythro- and (2S,1'S)-threo-diastereomers 33, [\( \alpha \)]D\textsubscript{20} = 5.5° (c 0.74, CHCl₃). Anal. Calcd. for C₃₂H₃₃O₃ (356.5): C, 77.49; H, 9.05. Found: C, 77.31; H, 8.96%. IR ν 1740 (C=O) cm⁻¹; UV (CHCl₃) \( \lambda_{max}/nm (\epsilon) \) 273 (5700), 283 (5000), 321 (1950). \(^1\)H-NMR \( \delta \) 0.98 (3 H, d, 1'-CH₃, J=6.8 Hz), 1.32 (3 H, s, 2-CH₃), 1.58, 1.60, 1.68, 1.70 (6 H, all s, 5'-CH₃, 6'-H), 1.50–2.00 (5 H, m, 1'-H − 3'-H), 2.00, 2.08, 2.10 (9 H, all s, ArCH₃), 2.33 (3 H, s, CH₃C=O), 5.10 (1 H, m, 4'-H), 5.15 (1 H, m, 3-H), 6.50 (1 H, d, 4-H, J=10.2 Hz); \(^1^3\)C-NMR \( \delta \) 11.3, 11.4, 13.0 (5-CH₃, 7-CH₃, 8-CH₃), 13.7, 13.8 (1'-CH₃), 17.8 (5'-CH₃), 20.3 (CH₃CO), 22.4 (2'-CH₃), 25.5 (6'-C), 26.0, 26.2 (3'-C), 31.2, 31.3 (2'-C), 40.9, 41.0 (1'-C), 79.8 (2-C), 117.5 (10-C), 119.6 (4'-C), 122.2 (8-C), 122.3 (5-C), 124.6 (3-C), 128.6 (7-C), 128.8, 129.0 (4-C), 131.2 (5'-C), 141.1 (9-C), 148.2 (6-C), 169.4 (C=O).

An ozone–oxygen mixture (ozonizer productivity 15 mmol·h\textsuperscript{-1}) at a flow rate of 30 L·h\textsuperscript{-1} was passed for 5 min (1.28 mmol O₃) at ~20 °C through a mixture of the acetate 34 (0.42 g, 1.28 mmol), Ba(OH)\textsubscript{2} (0.44 g, 2.57 mmol), 0.1 mL of H₂O, and 4 mL of acetone at ~20 °C. After completion of the reaction, the precipitate was filtered off and the filtrate was concentrated in vacuo. The residue was dissolved in 10 mL of EtOAc, dried with MgSO₄ and the solvent evaporated. The residue
was chromatographed on SiO₂ using a 10:1 n-hexane–Et₂O mixture as eluent to give 0.123 g (41%) of aldehyde 38. Anal. Calcd. for C₁₈H₂₂O₄ (302.4): C, 71.50; H, 7.33. Found: C, 71.29; H, 7.20%. IR ν 1710 and 1740 (C=O) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 272 (9300), 282.5 (7500), 318 (2900); ¹H-NMR δ 1.35 (3 H, s, 2-CH₃), 2.02, 2.05, 2.08 (9 H, all s, ArCH₃), 2.15 (2 H, m, 1’-H), 2.32 (3 H, s, CH₂C=O), 2.60 (2 H, m, 2’-H), 5.53 (1 H, d, 3-H, J = 10.1 Hz), 6.55 (1 H, d, 4-H, J = 10.1 Hz), 9.78 (1 H, t, 3’-H, J = 1.1 Hz); ¹³C-NMR δ 11.5, 13.1 (5-CH₃, 7-CH₃, 8-CH₃), 20.4 (CH₃CO), 26.1 (2-CH₃), 39.1 (1’-C), 65.8 (2’-C), 76.8 (2-C), 117.2 (10-C), 120.9 (3-C), 122.6 (8-C), 122.7 (5-C), 128.1 (4-C), 129.4 (7-C), 141.6 (9-C), 148.0 (6-C), 169.4 (CH₃CO), 202.1 (C=O).

2RS,5,7,8-Tetramethyl-2-(1S-methyl-4-oxobut-1-yl)-6-acetoxy-3-chromenes (37). An ozone–oxygen mixture was passed for 4 min (0.98 mmol O₃) at a flow rate of 30 L·h⁻¹ at ~20 °C through a mixture of acetates 33 (0.35 g, 0.95 mmol), Ba(OH)₂ (0.34 g, 1.99 mmol), 0.08 mL of H₂O, and 3 mL of acetone. The mixture was worked up as described in the previous experiment to give 0.2 g (62.5%) of a mixture of (2R,1’S)-erythro- and (2S,1’S)-threo-aldehydes 37, [α]D²⁰ -4.5 (c 0.3, CHCl₃). Anal. Calcd. for C₂₈H₃₀O₄ (330.4): C, 72.70; H, 7.93. Found: C, 72.56; H, 7.81%. IR ν 1710 and 1740 (C=O) cm⁻¹; UV (CHCl₃) λ_max/nm (ε) 273 (7500), 283 (6600), 319 (2400); ¹H-NMR δ 0.87, 0.98 (3 H, both d, 1’-CH₃, J = 5.9 Hz), 1.32 (3 H, s, 2-CH₃), 2.02, 2.05, 2.10 (9 H, all s, ArCH₃), 2.33 (3 H, s, CH₂C=O), 1.40–2.00 (3 H, m, 2’-H, 1’-H), 2.53 (2 H, m, 3’-H), 5.65 (1 H, m, 3-H), 6.50 (1 H, m, 4-H), 9.80 (1 H, t, 4’-H, J = 1.1 Hz); ¹³C-NMR δ 11.4, 13.0 (5-CH₃, 7-CH₃, 8-CH₃), 17.3, 17.4 (1’-CH₃), 20.3 (CH₃CO), 20.6 (2-CH₃), 31.3, 31.5 (2’-C), 40.9, 41.1 (1’-C), 65.7 (3’-C), 79.7 (2-C), 117.6 (10-C), 120.2 (3-C), 122.2 (8-C), 122.4 (5-C), 128.8 (4-C), 128.9, 129.0 (7-C), 141.1, 141.2 (9-C), 148.1 (6-C), 169.4 (CH₃CO), 202.7 (C=O).

References


