Total Synthesis of *dl*-Ascofuranone and Related Compounds

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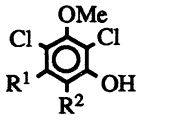
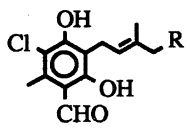
Convergent synthesis of an antitumor protective agent, ascofuranone, was accomplished by (1) preparation of the terpenoid side chain having a furanone moiety, (2) coupling the side chain with a protected phenol derivative, and (3) deprotection to regenerate the hydroxyl groups. This strategy was successfully applied to the synthesis of oxidized and cyclized analogs of ascofuranone. Some of the ascofuranone derivatives were found to inhibit the growth of P388 leukemia cells.

Recently phenolic compounds[1] such as differanisole A (**1**),[2] DIF-1 (**2**),[3] colletochlorin B (**3**),[4] and ascofuranone (**4**)[5] have received much attention in connection with their differentiation inducing activity. Among them, ascofuranone (**4**) having both benzaldehyde and furanone moieties was first isolated[6] and synthesized[7] as antitumor protective[8] and hypolipidemic agents[9] (Chart 1). For the convergent synthesis of **4**, it should be disconnected into the corresponding arene **5** and the furanone type side chain **6** (Scheme 1). As terpenoid side chains have not been efficiently introduced to unprotected resorcinols,[10] we planned to employ a protected aromatic segment leading to protected ascofuranone **7**. This strategy has, however, not been used due to the difficulty in deprotection of the hydroxyl groups, because the protecting group should be not only easily removed from the highly functionalized coupling product **7** but also so stable as to tolerate the coupling conditions. Development of new approaches for cleaving substituted and unsubstituted methyl ethers[11,12]



1 $R^1 = n\text{-}C_3H_7$, $R^2 = COOH$

2 $R^1 = OH$, $R^2 = n\text{-}C_5H_{11}C(=O)$



3 $R = CH_2CH{=}CMe_2$

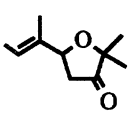
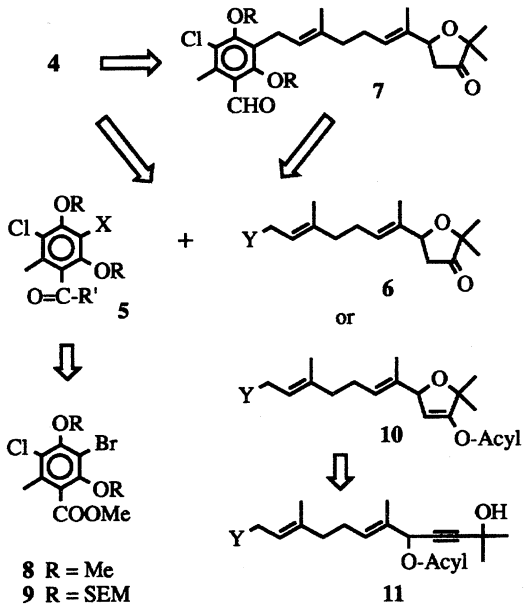
4 $R = CH_2$ 

Chart 1.



SEM = $CH_2OCH_2CH_2SiMe_3$

Scheme 1.

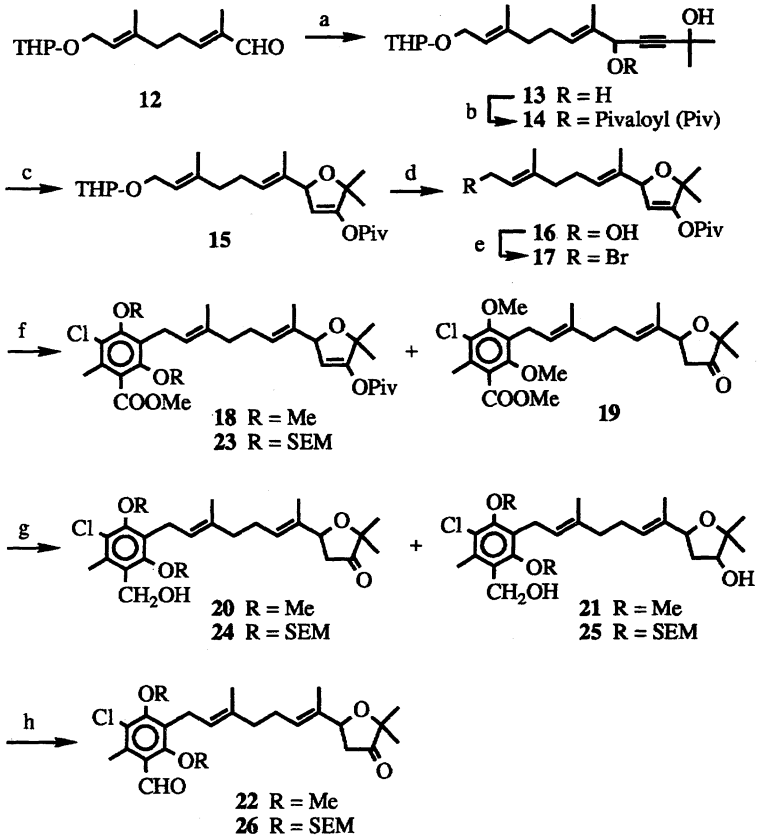
prompted us to apply the methods to the synthesis of ascofuranone and its analogs. Based on the model study for the synthesis of colletochlorins,[13] we employed resorcinol derivatives **8** and **9** as an aryl group precursor, whose hydroxyl groups were protected by methyl or 2-(trimethylsilyl)ethoxymethyl (SEM) group, respectively. Concerning construction of the furanone moiety in the side chain, transformation of 2-butyne-1,4-diol derivatives **11** into 2,5-dihydrofurans **10** would provide

a convenient pathway.[14] Hence we employed enol ester form **10** instead of keto form **6** as a side chain segment. Herein we report the total synthesis of **4** and its derivatives as well as their antitumor activities. The synthetic process involves preparation of the side chain precursor **10** and the coupling with aromatic segments followed by deprotection to regenerate the hydroxyl groups.

Synthesis of the Terpenoid Side Chain Having a Furanone Moiety and Coupling Reaction with Aromatic Precursors. As shown in Scheme 2, aldehyde **12**[15] obtained from geraniol (4 steps, 49%) seems to be a suitable starting material because it has oxygen functions at the both ends of geranyl chain. Addition reaction of 2-methyl-3-butyn-2-ol with **12** afforded diol **13**, which was transformed selectively into monopivalate **14**. Treatment of **14** with a catalytic amount of $AgBF_4$ in benzene afforded **15**, whose THP protecting group was selectively removed to give **16** (48% yield from **12**). In a preliminary study, the primary alcohol in **14** was protected as 1-ethoxyethyl ether, but the 1-ethoxyethyl group proved to be partially cleaved during the rearrangement and cyclization to yield dihydrofurans in low yields. Bromination of **16** with $CBr_4/(n\text{-}C_8H_{17})_3P$ afforded the desired side chain precursor **17** (92%), while treatment with CBr_4/Ph_3P or PBr_3/pyridine resulted in low yields.

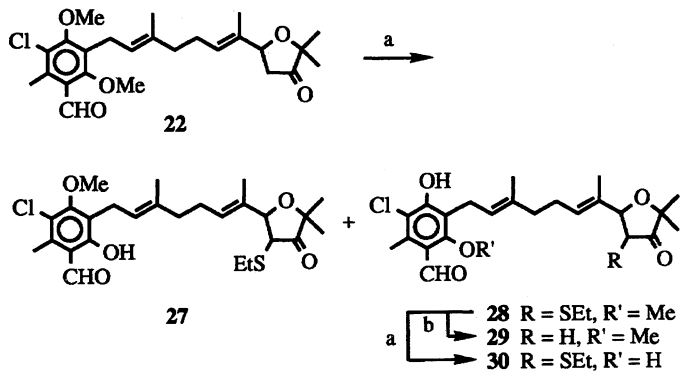
The aromatic segment **8**,[13] prepared from dimethyl malonate and pent-3-en-2-one in 41% overall yield, was treated with butyllithium at −78 °C to give the corresponding substituted phenyllithium, which was converted into a mixed cuprate[16] and was coupled with the bromide **17** to yield **18** (61%) along with a furanone type product **19** (10%).[17] The enol ester form **18** and keto form **19** were useful for the following reduction with $LiAlH_4$ and oxidation with pyridinium chlorochromate (PCC). In the case of **18**, both deprotection of the carbonyl group in the furanone moiety and transformation of the ester function attached to the aromatic ring into the formyl group were accomplished to afford ascofuranone dimethyl ether **22** (96%). Although reduction of **18** afforded a separable mixture of keto alcohol **20** and diol **21**, subsequent oxidation of the crude mixture gave **22** in better yields. Similarly, **19** was transformed into **22** quantitatively.

The SEM ether **9**,[13] prepared from dimethyl malonate and pent-3-en-2-one in 42% overall yield, under-



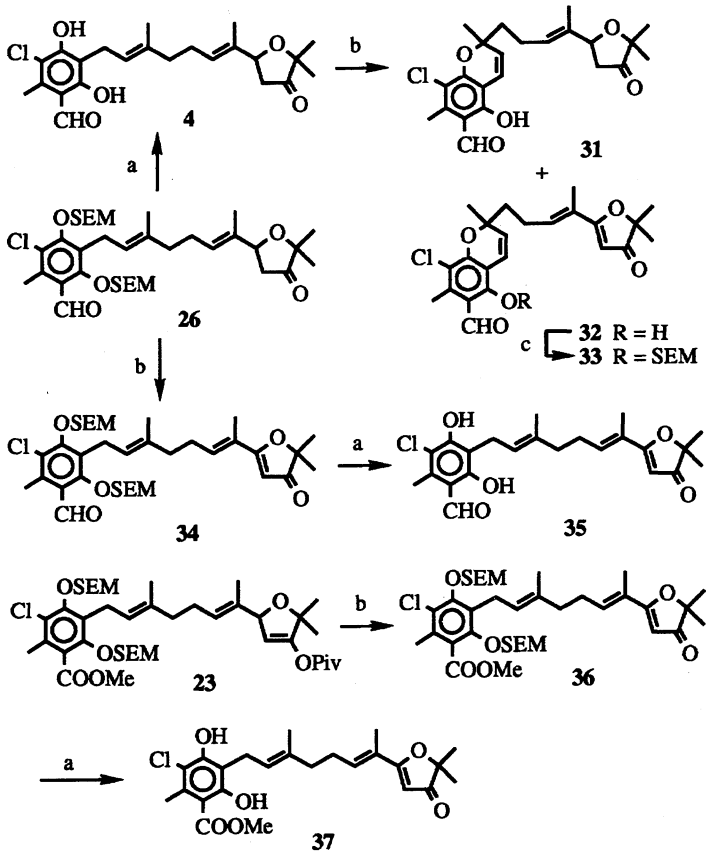
a: $HC{\equiv}CC(OH)Me_2$, *n*-BuLi, THF; b: *t*-BuCOCl, 4-$(Me_2N)C_5H_4N$, Py; c: 7-10 mol% $AgBF_4$, C_6H_6; d: PyHOTs, EtOH; e: CBr_4, $(n\text{-}C_8H_{17})_3P$, Et_2O; f: **8** or **9**, *n*-BuLi, $CuC{\equiv}CC(OMe)Me_2$, THF, HMPA; g: $LiAlH_4$, Et_2O; h: $PyHClCrO_3$, CH_2Cl_2.

Scheme 2.



a: EtSNa, HMPA; b: 1. Raney-Ni, EtOH; 2. PCC, CH_2Cl_2.

Scheme 3.



a: P_2I_4, CH_2Cl_2; b: DDQ, C_6H_6; c: SEMCl, *i*-Pr_2NEt, CH_2Cl_2.

Scheme 4.

went the analogous coupling reaction with **17** to give **23**, which was reduced with $LiAlH_4$ and then oxidized with PCC to afford **26** (69% yield from **17**). Also in this case, the reduction-oxidation without isolation of intermediates **24** and **25** resulted in better yield of **26**.

Synthesis of *dl*-Ascofuranone. Although EtSNa/HMPA was effective on the deprotection of dimethyl ether of colletochlorin B (**3**),[13] this reagent could cleave only one of the methyl ether bonds in **22** as shown in Scheme 3. Treatment of **22** with EtSNa in HMPA at 100 °C gave ethylthio derivatives **27** and **28** along with ascofuranone monomethyl ether **29**. Further reaction of **28** with EtSNa carried out at 120 °C afforded an ethylthio derivative of ascofuranone **30** in a low yield, whereas similar reaction of **29** failed to give ascofuranone (**4**). The sulfide **28** was transformed to **29** by the reduction with Raney-Ni followed by oxidation with PCC. Treatment of **29** or the diol **21** with the thiolate reagents such as EtSLi, EtSNa, MeSLi,[18] MeSNa, or EtSMgBr[13] at high temperatures yielded a

complex mixture. These results mean that the thiolate reagents are not applicable to cleavage of the methyl ether bond in highly functionalized compounds like **21** and **22**.

On the other hand, removal of the SEM group in **26** with diphosphorus tetraiodide in CH_2Cl_2 at 0 °C proceeded efficiently as was the case of the SEM ether of the colletochlorin B precursor,[13] and *dl*-ascofuranone (**4**) was obtained in 62% yield. Consequently, overall yields of **4** from geraniol and from dimethyl malonate/pent-3-en-2-one were 9.2% and 15.8%, respectively. In contrast, the well-known procedure for the elimination of various SEM ethers using tetrabutylammonium fluoride (TBAF) in HMPA or THF[19] failed to transform the SEM ethers **25** and **26** into the corresponding resorcinol derivatives. All attempts using tris(diethylamino)-sulfonium difluorotrimethylsilicate, BBr_3, BBr_3·NEt_3, BBr_3·$HN(SiMe_3)_2$, or EtSNa failed to regenerate the phenolic hydroxyl groups. Hence the deprotection procedure with P_2I_4[11] serves as an effective tool to cleave alkoxymethyl aryl ethers of complex molecules under the mild conditions.

Synthesis of Ascofuranone Analogs and Their biological Activities. As shown in Scheme 4, our strategy enabled us to synthesize various ascofuranone analogs. Oxidative cyclization of **4** occurred upon treatment with 2,3-dichloro-5,6-dicyano-1,4-benzoquinone (DDQ) in benzene to give chromenes **31** and **32**.[20] The hydroxyl group at the *p*-position of the formyl moiety of **4** was selectively incorporated into this chromene formation, because the one at the *o*-position was deactivated by an intramolecular hydrogen bonding with the carbonyl oxygen of the aldehyde function. Treatment of **32** with SEMCl/*i*-Pr_2NEt afforded SEM ether **33**. When the ascofuranone precursor **26** was first oxidized with DDQ and then deprotected with P_2I_4, dehydroascofuranone **35**, 3(2*H*)-furanone analog of **4**, was synthesized via **34**. In order to obtain ester analogs of aldehydes **34** and **35**, the one-pot procedure to transform enol esters to enones[21] was applied to the preparation of **36** from enol pivalate **23**. Removal of the SEM ether in **36** was accomplished by the P_2I_4 method to yield **37**.

The synthetic ascofuranone analogs were subjected to in vitro test for the growth inhibition of P388 leukemia cells.[22,23] Although dehydro analogs **32**, **33**, and **35** exhibited IC_{50} ($\mu mol\,cm^{-3}$) 1.3—4.0×10^{-3}, comparable to the cytotoxicity of prostaglandin A2 (2.8×10^{-3}), most of ascofuranone analogs synthesized in this study showed weak cytotoxicity. The weak cytotoxicity is particularly advantageous in the study on differentiation inducing factor.[4,5]

Experimental

All the reactions were carried out under an argon atmosphere. All mps and bps were uncorrected. Microscale distillation was performed with Kugelrohr (Buchi). ^{1}H NMR spectra in $CDCl_3$ were recorded on a Hitachi R-90H or Varian XL-100A spectrometer, and IR spectra (neat liquid film samples unless otherwise noted) on a JASCO A 202 spectrometer. Mass spectra were obtained on a Hitachi RMU-6MG or Hitachi M-80A spectrometer. Preparative TLC plates were prepared using Kieselgel 60 PF_{254} (Merck). Column chromatography was performed using Kieselgel 60 (Merck) or Wakogel C-200 unless otherwise noted. The known aldehyde **12**[15] was prepared from geraniol via 3,7-dimethyl-8-oxoocta-2,6-dienyl acetate.[24]

(*E*,*E*)-2,6,10-Trimethyl-12-(tetrahydropyran-2-yloxy)dodeca-6,10-dien-3-yne-2,5-diol (13) and (*E*,*E*)-2,6,10-Trimethyl-5-pivaloyloxy-12-(tetrahydropyran-2-yloxy)dodeca-6,10-dien-3-yn-2-ol (14). Butyllithium (1.71 $mol\,dm^{-3}$ in hexane, 44 ml, 76 mmol) was added to a THF (200 ml) solution of 2-methylbut-3-yn-2-ol (3.2 g, 30 mmol) at −20 °C. After 2 h, a THF (100 ml) solution of **12** (6.5 g, 26 mmol) was added to the reaction mixture at −50 °C, and the whole was stirred for 7 h and warmed to 0 °C. Extractive workup gave crude **13** (8.9 g). The crude product was once purified by column chromatography (hexane–ethyl acetate 1:1) to afford **13** (88% yield). Bp 243—246 °C (bath temp)/0.41 Torr (1 Torr=133.322 Pa); IR 3420, 2260, 1163, 1137, 1118, and 1023 cm^{-1}; ^{1}H NMR δ=1.45—1.95 (m+s(δ=1.50)+s(δ=1.66)+s(δ=1.71), 18H), 2.03—2.18 (m, 4H), 3.05 (br s, 2H), 3.46—3.57 (m, 1H), 3.83—3.94 (m, 1H), 4.03 (dd, *J*=8.7, 12.0 Hz, 1H), 4.23 (dd, *J*=6.2, 12.0 Hz, 1H), 4.62—4.67 (m, 1H), 4.72 (s, 1H), 5.35 (t, *J*=6.8 Hz, 1H), 5.56 (t, *J*=6.4 Hz, 1H); MS *m/z* (%) 336 (M^+; 4), 318 (M^+-H_2O; 8), 85 (100).

The crude product (8.9 g) was dissolved in diethyl ether (5 ml) and treated with 2,2-dimethylpropionyl chloride (5.6 g, 47 mmol), pyridine (5 ml), and 4-dimethylaminopyridine (0.63 g, 5.2 mmol) at 0 °C. After 50 min diethyl ether (500 ml) and saturated aq NaCl (50 ml) were added. The organic phase was separated, dried over Na_2SO_4, and concentrated. Purification by flash chromatography (hexane–ethyl acetate 10:1—8:1) gave **14** (8.8 g, 81% yield from **12**), which showed IR 3420, 1730, 1140, 1110, and 1020 cm^{-1}; ^{1}H NMR δ=1.21 (s, 9H), 1.4—1.8 (m+s(δ=1.51)+s(δ=1.68), 18H), 2.0—2.3 (m, 4H), 3.46—3.58 (m, 1H), 3.84—3.94 (m, 1H), 4.04 (dd, *J*=7.6, 12.0 Hz, 1H), 4.23 (dd, *J*=6.1, 12.0 Hz, 1H), 4.64 (t, *J*=3.4 Hz, 1H), 5.36 (t, *J*=6.4 Hz, 1H), 5.64 (t, *J*=6.8 Hz, 1H), 5.76 (s, 1H); MS *m/z* (%) 403 (M^+-OH; 1), 135 (32), 85 (100). Anal. ($C_{25}H_{40}O_5$) C, H.

5-[(*E*,*E*)-1,5-Dimethyl-7-(tetrahydropyran-2-yloxy)hepta-1,5-dienyl]-2,2-dimethyl-3-pivaloyloxy-2,5-dihydrofuran (15). A benzene (26 ml) solution of **14** (1.10 g, 2.61 mmol) was treated with $AgBF_4$ (33 mg, 0.17 mmol) at 80 °C for 2.5 h in the dark. The reaction mixture was diluted with dichloromethane (50 ml) and washed with 10% aq ammonia (30 ml) and saturated aq NaCl (30 ml). The organic phase was dried over Na_2SO_4 and concentrated. Purification by flash chromatography (hexane–ethyl acetate 10:1) gave **15** (0.71 g, 65%). IR 1765, 1660, 1273, 1148, 1111, 1079, and 1024 cm^{-1}; ^{1}H NMR δ=1.28 (s, 9H), 1.34 (s, 3H), 1.37 (s, 3H), 1.4—1.9 (m+s(δ=1.60)+s(δ=1.68), 12H), 2.0—2.3 (m, 4H), 3.49 (dt, *J*=11.7, 3.0 Hz, 1H), 3.89 (dt, *J*=11.7, 5.3 Hz, 1H), 3.99 (dd, *J*=7.5, 11.9 Hz, 1H), 4.22 (dd, *J*=5.0, 11.9 Hz, 1H), 4.5—4.7 (m, 1H), 5.13 (br s, 1H), 5.2—5.6 (m+dd(δ=5.36, *J*=5.0, 7.5 Hz)+d(δ=5.56, *J*=1.7 Hz), 3H); MS *m/z* (%) 336 (M^+-DHP; 2), 251 (10), 85 (68),

57 (100). Anal. ($C_{25}H_{40}O_5$) C, H.

5-[(*E*,*E*)-7-Hydroxy-1,5-dimethylhepta-1,5-dienyl]-2,2-dimethyl-3-pivaloyloxy-2,5-dihydrofuran (16). A mixture of **15** (0.83 g, 2.0 mmol) and pyridinium *p*-toluenesulfonate (50 mg, 0.20 mmol) in ethanol (16 ml) was stirred at 50 °C for 4 h. Extractive workup followed by preparative TLC (hexane–ethyl acetate 2:1) gave **16** (0.61 g, 92%), which showed bp 177—181 °C (bath temp)/0.42 Torr; IR 3430, 1767, 1659, 1273, 1147, 1110, 1026, and 1005 cm^{-1}; ^1H NMR δ=1.29 (s, 9H), 1.34 (s, 3H), 1.37 (s, 3H), 1.60 (s, 3H), 1.68 (s, 3H), 2.0—2.3 (m, 4H), 4.14 (d, J=7.1 Hz, 2H), 5.1—5.2 (m, 1H), 5.3—5.6 (m+t(δ=5.40, J=7.1 Hz)+d(δ=5.58, J=1.5 Hz), 3H); MS m/z (%) 336 (M^+; 3), 321 (3), 167 (67), 85 (70), 57 (100). Anal. ($C_{20}H_{32}O_4$) C, H.

5-[(*E*,*E*)-7-Bromo-1,5-dimethylhepta-1,5-dienyl]-2,2-dimethyl-3-pivaloyloxy-2,5-dihydrofuran (17). Trioctylphosphine[25] (0.33 g, 0.88 mmol) was added to a diethyl ether (3 ml) solution of **16** (0.15 g, 0.45 mmol) and carbon tetrabromide (0.29 g, 0.88 mmol) at 0 °C. After stirring for 10 min, carbon tetrabromide (51 mg, 0.15 mmol) and trioctylphosphine (57 mg, 0.15 mmol) were added. The whole was stirred at 0 °C for 3 min and concentrated. Purification by column chromatography (neutral alumina, benzene) afforded **17** (0.16 g, 92%), which was characterized spectrometrically and immediately used for the next transformation. IR 1765, 1657, 1273, 1150, 1109, and 1028 cm^{-1}; ^1H NMR δ=1.28 (s, 9H), 1.33 (s, 3H), 1.36 (s, 3H), 1.59 (s, 3H), 1.72 (s, 3H), 2.0—2.3 (m, 4H), 3.99 (d, J=8.7 Hz, 2H), 5.12 (br s, 1H), 5.3—5.7 (m+d(δ=5.57, J=1.4 Hz), 3H); MS m/z (%) 319 (M^+−Br; 6), 235 (12), 167 (13), 85 (20), 57 (100).

Coupling of Bromobenzenes with Allylic Bromides. Methyl 3-Chloro-5-[(*E*,*E*)-7-(2,5-dihydro-5,5-dimethyl-4-pivaloyloxyfuran-2-yl)-3-methylocta-2,6-dienyl]-4,6-dimethoxy-2-methylbenzoate (18) and Methyl 3-Chloro-4,6-dimethoxy-2-methyl-5-[(*E*,*E*)-3-methyl-7-(tetrahydro-5,5-dimethyl-4-oxofuran-2-yl)octa-2,6-dienyl]benzoate (19). Butyllithium (1.79 mol dm^{-3} in hexane, 1.40 ml, 2.51 mmol) was added to a THF (10 ml) solution of methyl 5-bromo-3-chloro-4,5-dimethoxy-2-methylbenzoate (**8**) (0.55 g, 1.71 mmol) at −78 °C in 20 min. Consumption of **8** was confirmed by TLC analysis. After further 10 min-stirring, a solution of 3-methoxy-3-methylbut-1-ynylcopper[16] (1.88 mmol) in THF (3.8 ml)–HMPA (0.40 ml)–hexane (1.05 ml) was added to the reaction mixture over a period of 15 min, and the resulting yellowish orange solution was stirred for 30 min at −78 °C. To this mixture was added a THF (8 ml) solution of **17** (0.53 g, 1.33 mmol) over a period of 10 min. The whole was stirred for 5 h and warmed to room temperature. Diethyl ether (150 ml) and saturated aq NaCl (15 ml) was added and the organic layer was separated. The aqueous phase was extracted with diethyl ether. Combined organic phase was dried over Na_2SO_4 and concentrated. Purification by column chromatography (hexane–ethyl acetate 15:1—1:1) gave **18** (0.46 g, 61% yield from **17**) and **19** (63 mg, 10% yield from **17**) along with methyl 3-chloro-4,6-dimethoxy-2-methylbenzoate[13] (87 mg, 21% yield from **8**). The coupling product **18** showed IR 1765, 1735, 1658, 1586, 1459, 1322, 1267, 1158, and 1096 cm^{-1}; ^1H NMR δ=1.26 (s, 9H), 1.31 (s, 3H), 1.33 (s, 3H), 1.55 (s, 3H), 1.75 (s, 3H), 1.9—2.2 (m, 4H), 2.28 (s, 3H), 3.36 (d, J=7.1 Hz, 2H), 3.72 (s, 3H), 3.77 (s, 3H), 3.88 (s, 3H), 5.0—5.2 (m+t(δ=5.15, J=7.1 Hz), 2H), 5.3—5.6 (m+d(δ=5.52, J=1.7 Hz), 2H); MS m/z (%) 564 (M^++2; 2), 562 (M^+; 5), 463 (M^++2−t−BuCOO; 5), 461 (M^+−t−BuCOO; 10), 257 (38), 167 (36), 85 (37), 57 (100). Found: m/z 562.2686. Calcd for $C_{31}H_{43}ClO_7$: M, 562.2694. **19**: IR 1755, 1735, 1266, 1159, and 996 cm^{-1}; ^1H NMR δ=1.22 (s, 3H), 1.28 (s, 3H), 1.62 (s, 3H), 1.77 (s, 3H), 1.9—2.3 (m, 4H), 2.2—2.5 (m+s(δ=2.28), 5H), 3.36 (d, J=6.6 Hz, 2H), 3.75 (s, 3H), 3.80 (s, 3H), 3.91 (s, 3H), 4.49 (dd, J=7.5, 9.2 Hz, 1H), 5.16 (t, J=7.1 Hz, 1H), 5.4—5.6 (m, 1H); MS m/z (%) 480 (M^++2; 3), 478 (M^+; 7), 446 (7), 281 (37), 279 (100), 135 (32). Found: m/z 478.2144. Calcd for $C_{26}H_{35}ClO_6$: M, 478.2120.

Methyl 3-Chloro-5-[(*E*,*E*)-7-(2,5-dihydro-5,5-dimethyl-4-pivaloyloxyfuran-2-yl)-3-methylocta-2,6-dienyl]-2-methyl-4,6-bis[2-(trimethylsilyl)ethoxymethoxy]benzoate (23). Butyllithium (1.71 mol dm^{-3} in hexane, 1.24 ml, 2.1 mmol) was added to a THF (11 ml) solution of bis[2-(trimethylsilyl)ethoxymethoxy]benzoate **9** (0.93 g, 1.68 mmol) at −78 °C. Consumption of **9** was confirmed by TLC analysis. After 30 min, a solution of 3-methoxy-3-methylbut-1-ynylcopper[16] (1.49 mmol) in THF (3 ml)–HMPA (0.47 ml)–hexane (1.2 ml) was added to the reaction mixture over a period of 5 min, and the whole was stirred for 30 min at −78 °C before addition of a THF (10 ml) solution of **17** (0.60 g, 1.49 mmol). The mixture was stirred for 3 h and warmed to −40 °C. After addition of wet diethyl ether (100 ml), the reaction mixture was washed with water, dried over Na_2SO_4, and concentrated. Purification by preparative TLC (dichloromethane) gave **23** (0.83 g, 70% yield from **17**, 62% yield from **9**, R_f 0.29—0.37) along with methyl 3-chloro-2-methyl-4,6-bis[2-(trimethylsilyl)ethoxymethoxy]benzoate[13] (0.20 g, 25% yield from **9**, R_f 0.46—0.51). The coupling product **23** showed IR 1766, 1737, 1659, 1150, 1109, 860 and 837 cm^{-1}; ^1H NMR δ=0.03 (s, 18H), 0.9—1.1 (m, 4H), 1.27 (s, 9H), 1.32 (s, 3H), 1.34 (s, 3H), 1.56 (s, 3N), 1.73 (s, 3H), 1.9—2.2 (m, 4H), 2.27 (s, 3H), 3.45 (d, J=6.3 Hz, 2H), 3.7—4.0 (m+s(δ=3.84), 7H), 4.9—5.6 (m+s(δ=4.97)+s(δ=5.09)+d(δ=5.54, J=1.5 Hz), 8H); MS m/z (%) 796 (M^++2; trace), 794 (M^+; trace), 665 (M^++2−SEM; 1), 663 (M^+−SEM; 2), 250 (22), 167 (40), 103 (60), 85 (67), 73 (100), 57 (100). Anal. ($C_{41}H_{67}ClO_7Si_2$) C, H, Cl.

3-Chloro-2-methyl-5-[(*E*,*E*)-3-methyl-7-(tetrahydro-5,5-dimethyl-4-oxofuran-2-yl)octa-2,6-dienyl]-4,6-bis[2-(trimethylsilyl)ethoxymethoxy]benzaldehyde (26). A solution of **23** (48 mg, 0.060 mmol) in diethyl ether (3 ml) was added to $LiAlH_4$ (7 mg, 0.181 mmol) suspended in diethyl ether (1 ml) at 0 °C. After 10 min, additional diethyl ether (10 ml) and saturated aq Na_2SO_4 were added to the reaction mixture. The resulting supernatant and precipitates were separated. The precipitates were dissolved in aq HCl (1 mol dm^{-3}, 1 ml) and extracted with ether. Combined ethereal extracts were dried and concentrated to give crude products (41 mg), which were treated with PCC (65 mg, 0.30 mmol) and AcONa (25 mg, 0.30 mmol) in dichloromethane (4 ml) at room temperature for 1 h. Additional PCC (100 mg, 0.46 mmol) was added, and the reaction mixture was stirred for 1h, diluted with diethyl ether (20 ml), and filtered through Celite. The filtrate was concentrated and purified by column chromatography (di-

ethyl ether) to give **26** (40 mg, 98%). IR 1756, 1695, 1110, 1059, 937, 909, 857 and 834 cm^{-1}; ^1H NMR δ=0.02 (s, 9H), 0.03 (s, 9H), 0.94—1.02 (m, 4H), 1.21 (s, 3H), 1.28 (s, 3H), 1.63 (s, 3H), 1.77 (s, 3H), 2.00—2.06 (m, 2H), 2.10—2.16 (m, 2H), 2.40 (dd, J=9.9, 18.2 Hz, 1H), 2.44 (dd, J=6.4, 18.2 Hz, 1H), 2.63 (s, 3H), 3.46 (d, J=6.4 Hz, 2H), 3.76—3.82 (m, 2H), 3.86—3.92 (m, 2H), 4.52 (dd, J=6.4, 9.9 Hz, 1H), 5.02 (s, 2H), 5.16 (s, 2H), 5.23 (t, J=6.4 Hz, 1H), 5.52 (t, J=6.8 Hz, 1H), 10.36 (s, 1H); MS m/z (%) 566 (M^++2−Me_3SiCH_2CHO; 1), 564 (M^+−Me_3SiCH_2CHO; 3), 551 (M^++2−SEM; 3), 549 (M^+−SEM; 7), 397 (28), 103 (32), 73 (100). Anal. ($C_{35}H_{57}ClO_7Si_2$) C, H, Cl.

This reduction–oxidation procedure applies to the transformation of **18** and **19** into **22**. Isolation of **20/21** and **24/25** was performed according to the reduction part of this procedure.

3- Chloro- 4, 6- dimethoxy- 2- methyl- 5- [(*E*,*E*)- 3- methyl-7-(tetrahydro-5,5-dimethyl-4-oxofuran-2-yl)- octa-2,6-dienyl]benzaldehyde (22). Quantitative yield from **19** and 96% yield from **18**. IR 1755, 1695, 1378, 1310, 1228, and 1098 cm^{-1}; ^1H NMR δ=1.23 (s, 3H), 1.29 (s, 3H), 1.64 (s, 3H), 1.81 (s, 3H), 2.0—2.2 (m, 4H), 2.3—2.6 (m, 2H), 2.65 (s, 3H), 3.42 (d, J=6.6 Hz, 2H), 3.85 (s, 3H), 3.91 (s, 3H), 4.54 (dd, J=7.2, 9.3 Hz, 1H), 5.20 (t, J=6.6 Hz, 1H), 5.55 (t, J=6.2 Hz, 1H), 10.46 (s, 1H); MS m/z (%) 450 (M^++2; 6), 448 (M^+; 13), 281 (54), 227 (100), 135 (82), 81 (71). Found: m/z 448.1995. Calcd for $C_{25}H_{33}ClO_5$: M, 448.2013.

5-[(*E*,*E*)-7-(3-Chloro-5-hydroxymethyl-2,6-dimethoxy-4-methylphenyl)-1,5-dimethylhepta-1,5-dienyl]-4,5-dihydro-2,2-dimethyl-3(2*H*)-furanone (20) and 5-[(*E*,*E*)-7-(3-Chloro-5-hydroxymethyl-2,6-dimethoxy-4-methylphenyl)-1,5-dimethylhepta-1,5-dienyl]-tetrahydro-2,2-dimethylfuran-3-ol (21). Reduction of **18** followed by preparative TLC (hexane–ethyl acetate 3 : 2) gave **20** (13%, R_f 0.61—0.66) and **21** (60%, R_f 0.18—0.28). Furanone **20** showed IR 3450, 1755, 1454, 1173, 1097, 1026, and 990 cm^{-1}; ^1H NMR δ=1.22 (s, 3H), 1.28 (s, 3H), 1.63 (s, 3H), 1.80 (s, 3H), 2.0—2.2 (m, 4H), 2.28 (dd, J=9.3, 18.2 Hz, 1H), 2.45 (dd, J=7.1, 18.2 Hz, 1H), 2.46 (s, 3H), 3.35 (s, 1H), 3.39 (d, J=6.5 Hz, 2H), 3.80 (s, 3H), 3.82 (s, 3H), 4.2—4.6 (m, 1H), 4.78 (s, 2H), 5.20 (t, J=6.5 Hz, 1H), 5.4—5.6 (m, 1H); MS m/z (%) 452 (M^++2; 0.7), 450 (M^+; 1.2), 267 (30), 265 (81), 71 (60), 55 (100). Found m/z 450.2130. Calcd for $C_{25}H_{35}ClO_5$: M, 450.2171.

21: IR 3390, 1450, 1227, 1096, 1020, and 984 cm^{-1}; ^1H NMR δ=1.19 (s, 3H), 1.22 (s, 3H), 1.57 (s, 3H), 1.77 (s, 3H), 1.9—2.3 (m, 4H), 2.3—2.6 (m+s(δ=2.45), 5H), 3.38 (d, J=6.7 Hz, 2H), 3.78 (s, 3H), 3.82 (s, 3H), 3.91 (dd, J=4.9, 6.0 Hz, 1H), 4.2—4.5 (m, 1H), 4.76 (s, 2H), 5.19 (t, J=6.7 Hz, 1H), 5.3—5.5 (m, 1H); MS m/z (%) 454 (M^++2; 2), 452 (M^+; 5), 213 (31), 81 (46), 71 (100), 55 (98). Found: m/z 452.2338. Calcd for $C_{25}H_{37}ClO_5$: M, 452.2327.

5- [(*E*,*E*)- 7- {3- Chloro- 5- hydroxymethyl- 4- methyl-2,6-bis[2-(trimethylsilyl)ethoxymethoxy]phenyl}- 1,5- dimethylhepta- 1,5- dienyl]- 4,5- dihydro- 2,2- dimethyl-3(2*H*)-furanone (24) and 5-[(*E*,*E*)-7-{3-Chloro-5-hydroxymethyl-4-methyl-2,6-bis[2-(trimethylsilyl)ethoxymethoxy]phenyl}-1,5-dimethylhepta-1,5-dienyl]tetrahydro-2,2-dimethylfuran-3-ol (25). Reduction of **23** followed by preparative TLC (hexane–ethyl acetate 2 : 1) gave **24** (33%, R_f 0.67—0.72) and **25** (60%, R_f 0.28—0.39). Furanone **24** showed IR 3500, 1755, 1375, 1247, 1059, 858, 836, and 733 cm^{-1}; ^1H NMR δ=0.02 (s, 9H), 0.04 (s, 9H), 0.9—1.2 (m, 4H), 1.21 (s, 3H), 1.27 (s, 3H), 1.62 (s, 3H), 1.75 (s, 3H), 1.9—2.2 (m, 4H), 2.2—2.5 (m+s(δ=2.48), 5H), 3.39 (d, J=6.4 Hz, 2H), 3.7—4.0 (m, 4H), 4.4—4.7 (m, 3H), 4.95 (s, 2H), 5.09 (s, 2H), 5.20 (t, J=6.4 Hz, 1H), 5.3—5.6 (m, 1H); MS m/z (%) 390 (17), 309 (22), 257 (30), 131 (SEM; 36), 103 (50), 101 (40), 73 (100). Anal. ($C_{35}H_{59}ClO_7Si_2$) C, H, Cl.

25: IR 3450, 1252, 1062, 860, 838, and 735 cm^{-1}; ^1H NMR δ=0.02 (s, 9H), 0.04 (s, 9H), 0.85—1.15 (m, 4H), 1.17 (s, 3H), 1.21 (s, 3H), 1.56 (s, 3H), 1.74 (s, 3H), 1.9—2.5 (m+s(δ=2.46), 9H), 3.37 (d, J=6.4 Hz, 2H), 3.7—4.0 (m, 4H), 4.1—4.7 (m+s(δ=4.61), 4H), 4.93 (s, 2H), 5.08 (s, 2H), 5.17 (t, J=6.4 Hz, 1H), 5.3—5.6 (m, 1H); MS m/z (%) 535 (M^+−SEM−H_2O; 2), 381 (5), 329 (10), 309 (20), 257 (32), 150 (30), 131 (SEM; 31), 103 (49), 101 (42), 73 (100). Anal. ($C_{35}H_{61}ClO_7Si_2$) C, H, Cl.

3-Chloro-5-{(*E*,*E*)-7-[3-(ethylthio)tetrahydro-5,5-dimethyl-4-oxofuran-2-yl]-3-methylocta-2,6-dienyl}-6-hydroxy-4-methoxy-2-methylbenzaldehyde (27), 3-Chloro-5-{(*E*,*E*)-7-[3-(ethylthio)tetrahydro-5,5-dimethyl-4-oxofuran-2-yl]-3-methylocta-2,6-dienyl}-4-hydroxy-6-methoxy-2-methylbenzaldehyde (28), 3-Chloro-4-hydroxy-6-methoxy-2-methyl-5-[(*E*,*E*)-3-methyl-7-(tetrahydro-5,5-dimethyl-4-oxofuran-2-yl)octa-2,6-dienyl]benzaldehyde (29), and 3-Chloro-5-{(*E*,*E*)-7-[3-(ethylthio)tetrahydro-5,5-dimethyl-4-oxofuran-2-yl]-3-methylocta-2,6-dienyl}-4,6-dihydroxy-2-methylbenzaldehyde (30). An HMPA (0.66 ml) solution of NaSEt (0.66 mmol)[13] was added to an HMPA (0.05 ml) solution of **22** (29 mg, 0.066 mmol). The resulting mixture was stirred at 100 °C for 17 min and then cooled to 0 °C. Extractive workup with diethyl ether (20 ml) and aq HCl (1 mol dm^{-3}, 1 ml) followed by purification by preparative TLC (hexane–ethyl acetate 3 : 1) gave **27** (2 mg, 7 %, R_f 0.61—0.66), **28** (17 mg, 52%, R_f 0.50—0.56), and **29** (3 mg, 11%, R_f 0.44—0.50). Unstable products **27** and **28** were characterized only by spectrometric data.

27: ^1H NMR δ=1.22 (s, 3H), 1.23 (t, J=7.3 Hz, 3H), 1.32 (s, 3H), 1.68 (s, 3H), 1.80 (s, 3H), 2.0—2.2 (m, 4H), 2.63 (s, 3H), 2.68 (q, J=7.3 Hz, 2H), 3.25 (d, J=9.7 Hz, 1H), 3.40 (d, J=7.0 Hz, 2H), 3.88 (s, 3H), 4.23 (d, J=9.7 Hz, 1H), 5.23 (t, J=7.0 Hz, 1H), 5.5—5.7 (m, 1H), 10.28 (s, 1H), 12.53 (s, 1H).

28: IR 3405, 1755, 1680, 1592, 1583, 1310, 1230, and 1096 cm^{-1}; ^1H NMR δ=1.24 (t, J=7.4 Hz, 3H), 1.28 (s, 3H), 1.33 (s, 3H), 1.68 (s, 3H), 1.81 (s, 3H), 1.9—2.4 (m, 4H), 2.67 (s, 3H), 2.69 (q, J=7.4 Hz, 2H), 3.29 (d, J=9.6 Hz, 1H), 3.43 (d, J=7.0 Hz, 2H), 3.84 (s, 3H), 4.24 (d, J=9.6 Hz, 1H), 5.26 (t, J=7.0 Hz, 1H), 5.5—5.7 (m, 1H), 6.40 (s, 1H), 10.36 (s, 1H); MS m/z (%) 496 (M^++2; 2), 494 (M^+; 5), 213 (21), 144 (66), 116 (100), 115 (46) 79 (23).

29: IR (CH_2Cl_2) 3400, 1754, 1680, 1629, 1582, 1562, 1230, 1169, and 1097 cm^{-1}; ^1H NMR δ=1.23 (s, 3H), 1.29 (s, 3H), 1.63 (s, 3H), 1.79 (s, 3H), 2.0—2.3 (m, 4H), 2.4—2.6 (m, 2H), 2.65 (s, 3H), 3.14 (d, J=6.9 Hz, 2H), 3.81 (s, 3H), 4.51 (dd, J=6.9, 9.0 Hz, 1H), 5.39 (t, J=6.9 Hz, 1H), 5.4—5.6 (m, 1H), 6.36 (br s, 1H), 10.37 (s, 1H); MS m/z (%) 436 (M^++2; 3), 434 (M^+; 9), 269 (15), 267 (41), 215 (19), 213 (62), 135 (75), 81 (63), 55 (89), 41 (100). Found:

m/z 434.1870. Calcd for $C_{24}H_{31}ClO_5$: M, 434.1858.

Similarly, **28** (17.3 mg, 0.035 mmol) was treated with Et-SNa (10 equiv) in HMPA at 100 °C for 30 min and then at 120 °C for 1.2 h. Extractive workup and preparative TLC (hexane–ethyl acetate 3:1) gave **30** (2.1 mg, 12%, R_f 0.55—0.62) as a mixture of diastereomers, which were characterized only spectrometrically. IR 3330, 1753, 1626, 1286, 1248, and 741 cm^{-1}; ^1H NMR δ=1.18 (t, J=7.4 Hz, 3H), 1.21 (s, 3H), 1.28 (s, 3H), 1.65 (s, 3H), 1.78 (s, 3H), 1.9—2.3 (m, 4H), 2.5—3.1 (m+s(δ=2.58)+q(δ=2.60, J=7.4 Hz), 6H), 3.39 (d, J=7.3 Hz, 2H), 4.20 (d, J=10.0 Hz, 0.5H), 4.63 (d, J=10.0 Hz, 0.5H), 5.23 (t, J=7.3 Hz, 1H), 5.4—5.7 (m, 1H), 6.40 (br s, 1H), 10.14 (s, 1H), 12.67 (s, 1H).

Removal of the Ethylthio Group of Furanone Derivative 28. An ethanol (0.5 ml) suspension of Raney-Ni (W-2, 0.06 g) was added to an ethanol (0.05 ml) solution of **28** (4.6 mg, 9.3 μmol), and the mixture was stirred at 50 °C for 30 min and then at 70 °C for 15 min. Filtration of the reaction mixture through Celite followed by concentration of the filtrate gave a crude mixture (5 mg), which was treated with PCC (6 mg, 0.028 mg) and AcONa (3.8 mg, 0.047 mmol) in dichloromethane (0.5 ml) at room temperature for 30 min. Workup and purification by column chromatography (diethyl ether) afforded **29** (3.3 mg, 82%).

Removal of SEM groups with P_2I_4. Synthesis of Ascofuranone (4) (A Typical Procedure). The precursor **26** (14 mg, 0.020 mmol) was treated with P_2I_4 (9.3 mg, 0.016 mmol) at 0 °C for 25 min. The reaction mixture was filtered through silica gel (Wakogel C-100, 2.5 g, eluted with diethyl ether at 0 °C) and concentrated to give crude products (9 mg). Purification by preparative TLC (hexane–ethyl acetate 3:1) afforded **4** (5.3 mg, 62%). Mp 90—92 °C (acetone–hexane); IR (CH_2Cl_2) 3410, 1754, 1625, 1418, 1284, 1249, and 1111 cm^{-1}; ^1H NMR δ=1.22 (s, 3H), 1.28 (s 3H), 1.68 (s, 3H), 1.79 (s, 3H), 2.0—2.1 (m, 2H), 2.1—2.2 (m, 2H), 2.35 (dd, J=9.9, 18.2 Hz, 1H), 2.42 (dd, J=6.4, 18.2 Hz, 1H), 2.61 (s, 3H), 3.39 (d, J=7.2 Hz, 2H), 4.52 (dd, J=6.4, 9.9 Hz, 1H), 5.21 (t, J=7.2 Hz, 1H), 5.51 (t, J=7.0 Hz, 1H), 6.44 (s, 1H), 10.15 (s, 1H), 12.70 (s, 1H); MS m/z (%) 422 (M^++2; 5), 420 (M^+; 15), 253 (76), 252 (53), 199 (100), 149 (94), 73 (86), 57 (66). Found: m/z 420.1686. Calcd for $C_{23}H_{29}ClO_5$: M, 420.1701. When **26** was treated similarly at 0 °C for 10 min and then 20 °C for 10 min, **4** was obtained in a lower yield (40%).

In a similar manner, **35** and **37** were obtained.

3-Chloro-5-[(*E*,*E*)-7-(4,5-dihydro-5,5-dimethyl-4-oxofuran-2-yl)-3-methylocta-2,6-dienyl]-4,6-dihydroxy-2-methylbenzaldehyde (35). Purified by column chromatography (diethyl ether); 89% yield; IR (CH_2Cl_2) 2600—3700, 1696, 1679, 1630, 1555, 1384, 1247, and 804 cm^{-1}; ^1H NMR δ=1.36 (s, 6H), 1.82 (s, 3H), 1.84 (s, 3H), 2.1—2.2 (m, 2H), 2.3—2.4 (m, 2H), 2.61 (s, 3H), 3.40 (d, J=7.2 Hz, 2H), 5.24 (t, J=7.2 Hz, 1H), 5.39 (s, 1H), 6.37 (s, 1H), 6.52 (t, J=7.4 Hz, 1H), 10.14 (s, 1H), 12.71 (s, 1H); MS m/z (%) 420 (M^++2; 3), 418 (M^+; 9), 166 (100), 149 (31), 57 (33). Found: m/z 418.1536. Calcd for $C_{23}H_{27}ClO_5$: M, 418.1545.

Methyl 3-Chloro-5-[(*E*,*E*)-7-(4,5-dihydro-5,5-dimethyl-4-oxofuran-2-yl)-methylocta-2,6-dienyl]-4,6-dihydroxy-2-methylbenzoate (37). Purified by column chromatography (diethyl ether); 95% yield; mp 116—119 °C; IR (CH_2Cl_2) 2500—3700, 1695, 1658, 1634, 1556, 1382, 1293, 1267, and 1166 cm^{-1}; ^1H NMR δ=1.35 (s, 6H), 1.82 (s, 3H), 1.84 (s, 3H), 2.1—2.2 (m, 2H), 2.3—2.4 (m, 2H), 2.59 (s, 3H), 3.42 (d, J=7.1 Hz, 2H), 3.94 (s, 3H), 5.26 (t, J=7.1 Hz, 1H), 5.41 (s, 1H), 6.18 (s, 1H), 6.53 (t, J=7.5 Hz, 1H), 11.71 (s, 1H); MS m/z (%) 450 (M^++2; 3), 448 (M^+; 7), 253 (11), 251 (29), 197 (15), 166 (100). Found: m/z 448.1658. Calcd for $C_{24}H_{29}ClO_6$: M, 448.1651.

8-Chloro-2-[(*E*)-4-(4,5-dihydro-5,5-dimethyl-4-oxofuran-2-yl)pent-3-enyl]-2,7-dimethyl-5-[2-(trimethylsilyl)ethoxymethoxy]-2*H*-1-benzopyran-6-carbaldehyde (33). *N*-Ethyldiisopropylamine (1.9 mg, 0.014 mmol) was added to a dichloromethane (0.1 ml) solution of **32** (1.2 mg, 2.9 μmol) and 2-(trimethylsilyl)ethoxymethyl chloride (1.6 mg, 9.6 μmol). Stirring at 20 °C for 8 h, extractive workup, followed by preparative TLC (hexane–ethyl acetate 2:1), gave **33** (0.8 mg, 51%). IR 1692, 1637, 1554, 1380, 1367, 1176, and 1107 cm^{-1}; ^1H NMR δ=0.03 (s, 9H), 0.9—1.0 (m, 2H), 1.38 (s, 6H), 1.51 (s, 3H), 1.8—2.0 (m+s(δ=1.85), 5H), 2.4—2.5 (m, 2H), 2.66 (s, 3H), 3.8—3.9 (m, 2H), 5.07 (s, 2H), 5.46 (s, 1H), 5.66 (d, J=10.0 Hz, 1H), 5.69 (t, J=7.4 Hz, 1H), 6.65 (d, J=10.0 Hz, 1H), 10.34 (s, 1H); MS m/z (%) 548 (M^++2; 1), 546 (M^+; 2), 488 (22), 311 (17), 309 (42), 239 (18), 237 (51), 73 (100), 57 (34). Found: m/z 546.2184. Calcd for $C_{23}H_{27}ClO_5$: M, 546.2201.

Oxidation with DDQ. 8-Chloro-5-hydroxy-2,7-dimethyl-2-[(*E*)-4-(tetrahydro-5,5-dimethyl-4-oxofuran-2-yl)pent-3-enyl]-2*H*-1-benzopyran-6-carbaldehyde (31) and 8-Chloro-2-[(*E*)-4-(4,5-dihydro-5,5-dimethyl-4-oxofuran-2-yl)pent-3-enyl]-5-hydroxy-2,7-dimethyl-2*H*-1-benzopyran-6-carbaldehyde (32) (A Typical Procedure). DDQ (4.1 mg, 0.018 mmol) was added to a benzene (0.5 ml) solution of **4** (3.8 mg, 9.0 μmol). After stirring at 80 °C for 50 min, the reaction mixture was poured onto a silica gel column and eluted with hexane–ethyl acetate (2:1) to give **31** (0.7 mg, 18%) and **32** (0.9 mg, 24%). Diastereomers of **31** showed IR (CH_2Cl_2) 2600—3700, 1752, 1633, 1619, 1382, 1370, 1250, and 1166 cm^{-1}; ^1H NMR δ=1.22 (s, 3H), 1.289 (s, 1.5H), 1.293 (s, 1.5H), 1.48 (s, 3H), 1.63 (s, 3H), 1.7—1.9 (m, 2H), 2.2—2.3 (m, 2H), 2.40 (dd, J=10.2, 18.2 Hz, 1H), 2.47 (dd, J=6.2, 18.2 Hz, 0.5H), 2.49 (dd, J=6.1, 18.2 Hz, 0.5H), 2.60 (s, 3H), 4.527 (dd, J=6.2, 10.2 Hz, 0.5H), 4.534 (dd, J=6.1, 10.2 Hz, 0.5H), 5.55 (d, J=10.1 Hz, 1H), 5.58 (t, J=7.2 Hz, 1H), 6.72 (d, J=10.1 Hz, 0.5H), 6.73 (d, J=10.1 Hz, 0.5H), 10.13 (s, 1H), 12.70 (s, 1H); MS m/z (%) 420 (M^++2; 3), 418 (M^+; 7), 239 (33), 238 (15), 237 (100), 149 (79), 69 (36), 55 (55). Found: m/z 418.1568. Calcd for $C_{23}H_{27}ClO_5$: M, 418.1545.

32: IR (CH_2Cl_2) 2600—3700, 1697, 1635, 1556, 1374, 1251, and 1174 cm^{-1}; ^1H NMR δ=1.376 (s, 3H), 1.382 (s, 3H), 1.51 (s, 3H), 1.8—2.0 (m+s(δ=1.84), 5H), 2.4—2.5 (m, 2H), 2.59 (s, 3H), 5.45 (s, 1H), 5.55 (d, J=10.1 Hz, 1H), 6.60 (t, J=7.5 Hz, 1H), 6.76 (d, J=10.1 Hz, 1H), 10.13 (s, 1H), 12.71 (s, 1H); MS m/z (%) 418 (M^++2; 12), 416 (M^+; 31), 401 (12), 239 (33), 238 (15), 237 (100), 69 (31), 55 (30). Found: m/z 416.1392. Calcd for $C_{23}H_{25}ClO_5$: M, 416.1389.

This procedure applies to the transformation of **26** and **23** into **34** and **36**, respectively.

3-Chloro-5-[(*E*,*E*)-7-(4,5-dihydro-5,5-dimethyl-4-oxofuran-2-yl)-3-methylocta-2,6-dienyl]-2-methyl-4,6-bis[2-(trimethylsilyl)ethoxymethoxy]benzaldehyde (34). Purified by column chromatography (hex-

ane–ethyl acetate 4:1); 58% yield; IR 1694, 1637, 1560, 1252, 1176, 1067, 858, and 837 cm^{-1}; ^1H NMR δ=0.02 (s, 9H), 0.03 (s, 9H), 0.94—1.03 (m, 4H), 1.36 (s, 6H), 1.80 (s, 3H), 1.86 (s, 3H), 2.09—2.16 (m, 2H), 2.27—2.35 (m, 2H), 2.63 (s, 3H), 3.48 (d, J=6.5 Hz, 2H), 3.76—3.83 (m, 2H), 3.86—3.92 (m, 2H), 5.02 (s, 2H), 5.16 (s, 2H), 5.28 (t, J=6.5 Hz, 1H), 5.45 (s, 1H), 6.53 (t, J=7.4 Hz, 1H), 10.36 (s, 1H); MS m/z (%) 665 (M^++2−Me; trace), 663 (M^+−Me; trace), 549 (M^++2−SEM; 0.5), 547 (M^+−SEM; 1), 238 (66), 75 (12), 73 (100). Found: m/z 547.2282. Calcd for $C_{29}H_{40}ClO_6Si$: M−SEM, 547.2280.

Methyl 3-Chloro-5-[(*E*,*E*)-7-(4,5-dihydro-5,5-dimethyl-4-oxofuran-2-yl)-3-methylocta-2,6-dienyl]-2-methyl-4,6-bis[2-(trimethylsilyl)ethoxymethoxy]-benzaldehyde (36). Purified by column chromatography (hexane–ethyl acetate 3:1); 50% yield; IR 1735, 1700, 1637, 1561, 1263, 1252, 941, 859, and 838 cm^{-1}; ^1H NMR δ=0.02 (s, 9H), 0.03 (s, 9H), 0.95—1.02 (m, 4H), 1.36 (s, 6H), 1.77 (s, 3H), 1.85 (s, 3H), 2.08—2.14 (m, 2H), 2.26—2.34 (m+s(δ=2.29), 5H), 3.48 (d, J=6.7 Hz, 2H), 3.73—3.79 (m, 2H), 3.85—3.92 (m+s(δ=3.90), 5H), 4.98 (s, 2H), 5.09 (s, 2H), 5.27 (t, J=6.7 Hz, 1H), 5.45 (s, 1H), 6.52 (t, J=7.4 Hz, 1H); MS m/z (%) 695 (M^++2−Me; 0.4), 693 (M^+−Me; 0.7), 549 (M^++2−SEM; 0.2), 547 (M^+−SEM; 0.5), 296 (6), 239 (21), 238 (100), 73 (83). Found: m/z 708.3297. Calcd for $C_{36}H_{57}ClO_8Si_2$: M, 708.3277.

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