Electrochemical synthesis of chroman and euglobal skeletons *via* cycloaddition reaction of *o*-quinone methides and alkenes

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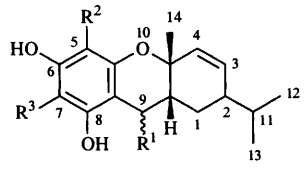
Euglobal skeletons were synthesized by the intermolecular cycloaddition reaction of terpenes and *o*-quinone methides generated *in situ* by electrochemical oxidation. In a two-phase reaction medium composed of hexane–lithium perchlorate/nitromethane, 2-[1-(propylsulfanyl)alkyl]phenols were selectively oxidized to give the corresponding unstable *o*-quinone methides. These intermediates were trapped *in situ* by unactivated alkenes or easily oxidizable terpenes to form varied chromans and spirochromans including euglobal skeletons. In particular, in the presence of β-pinene, the euglobal II_b skeleton, which possesses a β-phellandrene moiety, is formed by the cycloaddition *via* skeletal rearrangement of β-pinene.

Introduction

o-Quinone methides are important intermediates in organic synthesis, and have also received much attention as precursors to polycyclic aromatic natural products.[1] Although the generation and trapping of *o*-quinone methides are difficult in comparison with those of *p*-quinone methides, there are several syntheses already reported. Trimethylsilyl derivatives of *o*-hydroxybenzyl alcohols successively give chromans by an intramolecular cycloaddition reaction.[1] *o*-Hydroxybenzyl compounds are known to form cycloadducts *via* *o*-quinone methides in high temperature,[2] and *o*-[1-(phenylsulfanyl)-alkyl]phenols are converted into *o*-quinone methides to form cycloadducts with activated alkenes in the presence of Ag salts or Lewis acids.[3]

Natural euglobals and robustadials, isolated from Eucalyptus as inhibitors of Epstein-Barr virus activation or antimalarial compounds, are composed of terpenes and *o*-quinone methides **6** which are suggested to be derived from corresponding phloroglucinol derivatives.[4] For example, euglobal Ia_1 **1**, Ia_2 **2**, T1 **3** and IIc **4** possess an α-phellandrene moiety **7**, and euglobal II_b **5** has a β-phellandrene moiety **8** in the molecule. There are some synthetic approaches towards these unique chroman or spirochroman skeletons,[5] and robustadial dimethyl ethers and their precursors have already been synthesized.[6] It has been found, however, to be difficult to accomplish the intermolecular cycloaddition of *o*-quinone methides with unactivated alkenes such as terpenes, since most *o*-quinone methides are liable to decompose just after their generation, and unactivated alkenes, including terpenes, generally show poor reactivity with the desired *o*-quinone methides in the usual reaction media. Moreover, terpenes are also apt to decompose under Lewis acid-catalysed conditions in which some *o*-quinone methides can be generated.

The promotional effect of lithium perchlorate in diethyl ether on the rate of the Diels–Alder reaction is interesting,[7] and the role of lithium ion and perchlorates has been discussed extensively.[8] In addition to the role of accelerator, lithium perchlorate has been used as an electrolyte in electrochemical synthesis. In view of these characteristics, we accomplished Diels–Alder reaction of dienes and unstable quinones generated *in situ* by electrochemical oxidation in lithium perchlorate/nitromethane.[9] Furthermore, dimethoxy-2-[1-(phenylsulfanyl)-alkyl]phenols were also electrochemically converted into the corresponding *o*-quinone methides, which form cycloadducts with alkenes in lithium perchlorate/nitroalkane, and euglobal

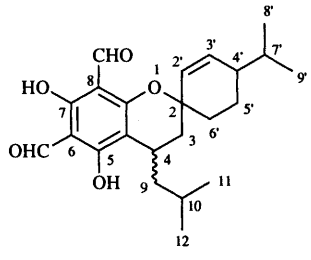


euglobal Ia_1 **1** : $R^1 = 9\beta\text{-}CH_2CH(CH_3)_2$, $R^2 = R^3 = CHO$

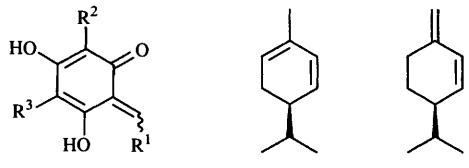
euglobal Ia_2 **2** : $R^1 = 9\alpha\text{-}CH_2CH(CH_3)_2$, $R^2 = R^3 = CHO$

euglobal T1 **3** : $R^1 = H$, $R^2 = COCH_2CH(CH_3)_2$, $R^3 = CHO$

euglobal II_c **4** : $R^1 = H$, $R^2 = CHO$, $R^3 = COCH_2CH(CH_3)_2$



euglobal II_b **5**



6 **7** **8**

Ia_1 and Ia_2 skeletons were synthesized.[10] Currently, *o*-quinone methides which possess varied substituents have been successfully generated by the selective oxidation of 2-[1-(propylsulfanyl)alkyl]phenols in the two-phase electrooxidation system, and diverse chromans and spirochromans including euglobal T1, II_c and II_b skeletons were synthesized in addition to euglobal Ia_1 and Ia_2 skeletons.

Results and discussion

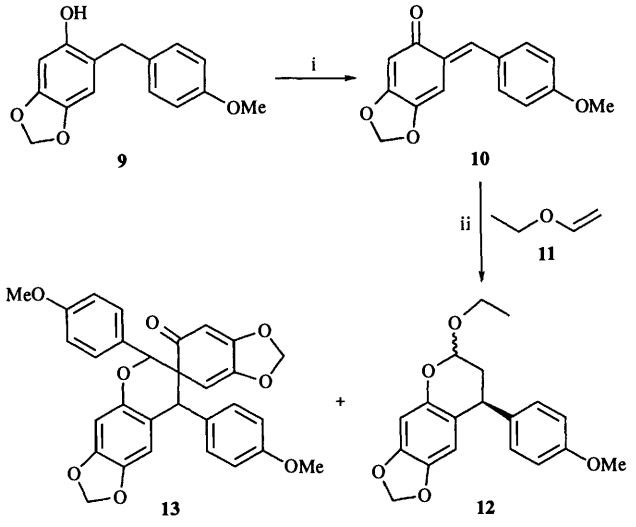
In a preliminary study, the effect of medium on the acceleration of the desired intermolecular cycloaddition of *o*-quinone methides and alkenes was examined. A stable *o*-quinone methide **10**, which can be prepared by Ag_2O oxidation of 2-(4-

Table 1 Medium effect on the cycloaddition of *o*-quinone methide **10**

Solvent	Yield (%)[a]		
	12	**13**	**10** (recovered)
Et_2O	54	29	17
CH_3CN	27	23	50
MeOH	—	—	—
CH_3NO_2	82	—	18
0.5 mol dm^{-3} $LiClO_4/CH_3NO_2$	100	—	—

[a] The reaction mixtures were stored at room temperature for 16 h. Yields were determined by NMR spectroscopy.

methoxybenzyl)-4,5-methylenedioxyphenol **9** is known to form cycloadduct **12** and a dimer **13** when it was stored in ethyl vinyl ether **11** (Scheme 1).[11] Table 1 shows the effect of medium on

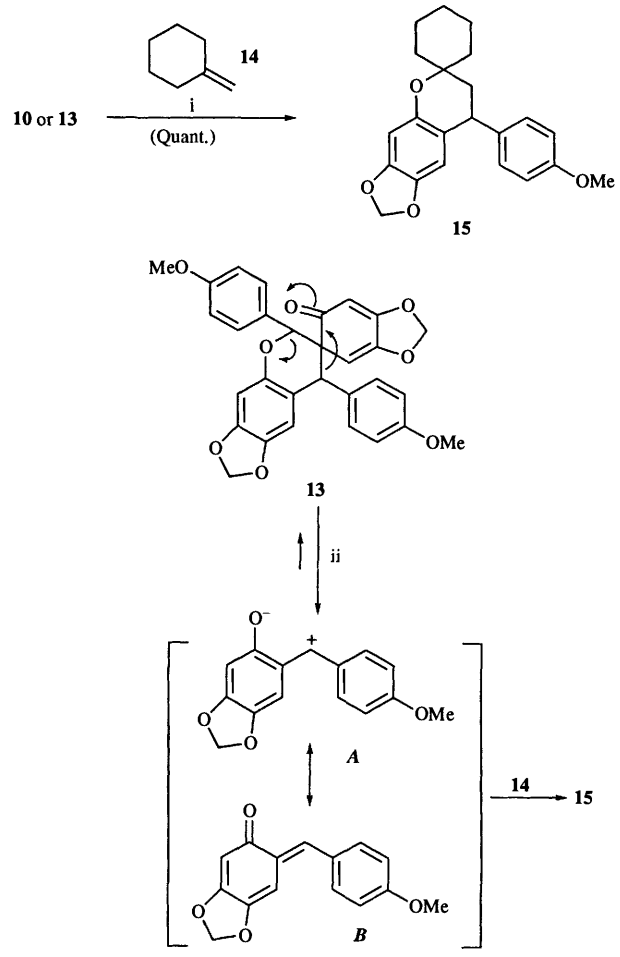


Scheme 1 *Reagents and conditions:* i, Ag_2O; ii, **11**, room temp., 16 h

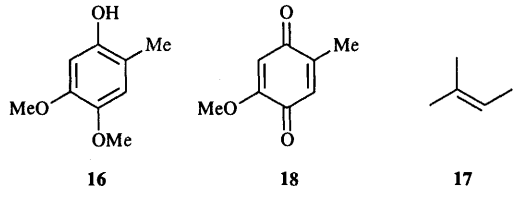
the product ratio by using compounds **10** and **11**. In nitromethane, cycloadduct **12** was predominantly obtained without formation of the dimer **13**, and in the presence of lithium perchlorate in nitromethane the desired reaction proceeded quantitatively. Furthermore, an unactivated alkene, methylenecyclohexane **14**, gave a spiro-compound **15** quantitatively with 1.0 mol equiv. of quinone methide **10** or 0.5 mol equiv. of dimer **13** after storage for 2 h at 60 °C in 0.5 mol dm^{-3} lithium perchlorate/nitromethane. These results show that the reaction medium stabilized the zwitterion intermediate ***A*** which is an equivalent of *o*-quinone methide ***B*** and promoted its cycloaddition with alkenes (Scheme 2).

In addition, in 2.0 mol dm^{-3} lithium perchlorate/nitromethane, compound **9** gave an oxidation peak at 700 mV [*vs.* saturated calomel electrode (SCE)] on cyclic voltammetry. Anodic oxidation of the phenol **9** was hence carried out in the same solvent system containing 5 mol equiv. of ethyl vinyl ether **11** at the peak potential by using a glassy carbon plate as anode and a platinum plate as cathode, respectively. After the oxidation was complete, the desired cycloadduct **12** was obtained in 54% yield. These results showed that the lithium perchlorate/nitromethane system is one of the promising reaction media for electrochemical generation and reaction of *o*-quinone methides.

Accordingly, the deliberate generation of unstable *o*-quinone methides followed by their cycloaddition with unactivated alkenes was extensively studied. First, electrochemical oxidation of 4,5-dimethoxy-2-methylphenol **16** in the presence of 2-methylbut-2-ene **17** was tried, but it did not give the desired product, only 2-methoxy-5-methyl-*p*-benzoquinone **18**. There-



Scheme 2 *Reagents:* i, 0.5 mol dm^{-3} $LiClO_4/CH_3NO_2$; ii, $LiClO_4/CH_3NO_2$



fore, 2-[1-(phenylsulfanyl)alkyl]phenol derivatives were chosen as a precursor of *o*-quinone methides. Thus, a 2-1-(hydroxyalkyl)-4,5-dimethoxyphenol was treated with thiophenol in the presence of ZnI_2 in CH_2Cl_2[12] to give 4,5-dimethoxy-2-(phenylsulfanylmethyl)phenol **19** whose oxidation potential was observed at 880 mV *vs.* SCE (1.0 mmol of **19** in 2.0 mol dm^{-3} $LiClO_4/CH_3NO_2$) (see Table 2). Anodic oxidation of compound **19** was performed in the presence of 4 mol equiv. of alkene **17** in 2.0 mol dm^{-3} lithium perchlorate/nitromethane at ambient temperature under Ar, and was complete at ~1.2 F mol^{-1} to afford the desired cycloadduct **29** in 74% yield (structure given in Table 3). In the absence of current, the cycloadduct was scarcely observed after 48 h storage under Ar, and compound **29** was obtained in 12% yield under air after 48 h storage. The above results suggested that the phenylsulfanyl group is eliminated by a one-electron oxidation to give the corresponding *o*-quinone methide, which was trapped by the alkene. On the other hand, when the reaction system was applied to the oxidation of 3,5-dimethoxy-2-[3-methyl-1-(phenylsulfanyl)butyl]phenol **21** in the presence of α-phellandrene **7** or β-pinene **39** at the peak potential of compound **21** (1080 mV *vs.* SCE) for the construction of the euglobal skeletons, the reaction medium became turbid just after the electric current had been applied and the current density soon

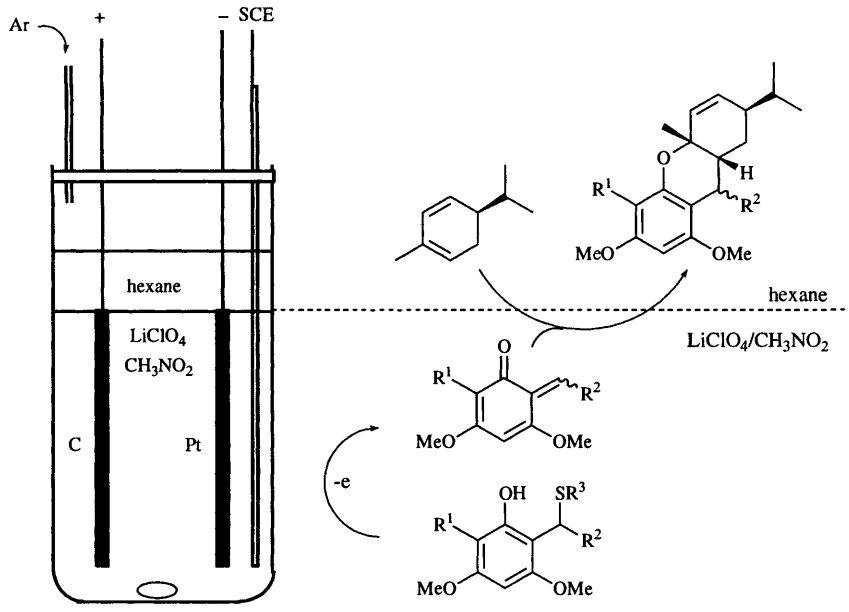
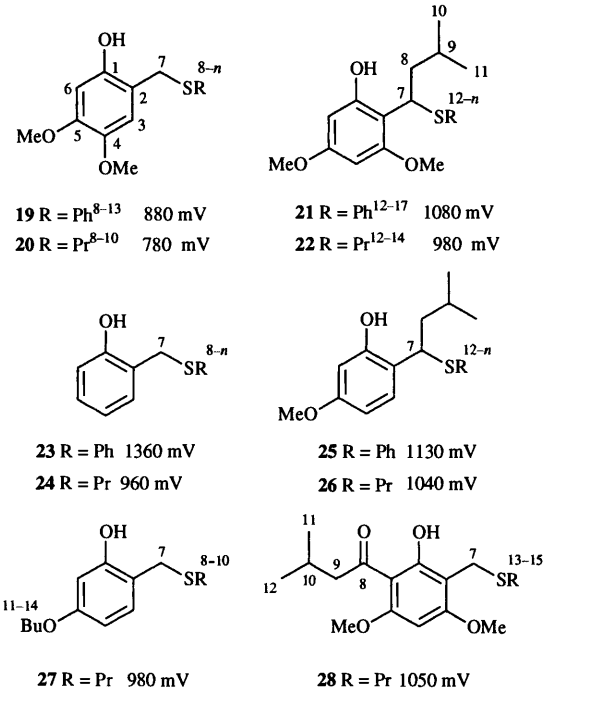


Fig. 1 Electrochemical reaction system for generation and cycloaddition reaction of *o*-quinone methides with terpenes

Table 2 Oxidation potentials of sulfides in 2.0 mol dm^{-3} $LiClO_4$/CH_3NO_2



19 R = Ph^{8-13} 880 mV
20 R = Pr^{8-10} 780 mV

21 R = Ph^{12-17} 1080 mV
22 R = Pr^{12-14} 980 mV

23 R = Ph 1360 mV
24 R = Pr 960 mV

25 R = Ph 1130 mV
26 R = Pr 1040 mV

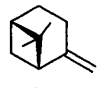
27 R = Pr 980 mV

28 R = Pr 1050 mV

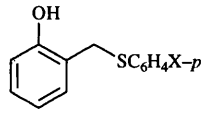
decreased. Although the oxidation potential of compound **17** was higher than 1600 mV (*vs.* SCE), those of compounds **7** and **39** were 1050 and 1300 mV (*vs.* SCE), respectively. After work-up and evaporation of the mixture, non-volatile alkenes were obtained from the reaction mixture. The results suggested that terpenes polymerized around their oxidation potentials to form insoluble materials in nitromethane, and that they also coated the surface of the electrodes.

For the selective oxidation of sulfides to generate *o*-quinone methides in the presence of terpenes, the effect of leaving groups on the peak potentials was studied. Oxidation potentials of *o*-(phenylsulfanylmethyl)phenol **23**, *o*-[(4-chlorophenylsulfanyl)methyl]phenol **40**, *o*-[(4-*tert*-butylphenylsulfanyl)methyl]phenol **41**, *o*-[(4-methylphenylsulfanyl)methyl]phenol **42** and *o*-(propylsulfanylmethyl)phenol **24** in 2.0 mol dm^{-3} lithium perchlorate/nitromethane were 1360, 1300, 1050 and 960 mV (*vs.* SCE), respectively. These results showed that electron-releasing groups lowered the oxidation potentials of sulfides, and the propylsulfanyl group was expected to be most favourable as the elimination group among those tested. Table 2 shows oxidation potentials of *o*-[1-(propylsulfanyl)alkyl]phenols and some of which were compared with those of *o*-[1-(phenylsulfanyl)alkyl]phenols. The peak potentials of phenols which possess a propylsulfanyl group were lower by about 90–400 mV in comparison with those having a phenylsulfanyl group. Moreover, the two-phase electrochemical oxidation system composed of hexane and 2.0 mol dm^{-3} lithium perchlorate/nitromethane allowed successful accomplishment of cycloaddition of phenol derivatives and alkenes (Fig. 1). In this reaction system, current density scarcely decreased during electrolysis and very small amounts of polymerized products were determined after the completion of the reaction.

Table 3 shows the results of cycloaddition of unactivated alkenes and *in situ* *o*-quinone methides. Electrochemical oxidation of *o*-[1-(propylsulfanyl)alkyl]phenols at their peak potentials gave varied cycloadducts *via* the corresponding *o*-quinone methides. In the reaction of phenols and 2-methylbut-2-ene **17**, compounds **20**, **22** and **27** gave cycloadducts **29**, **30** and



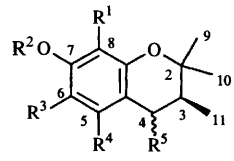
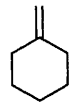
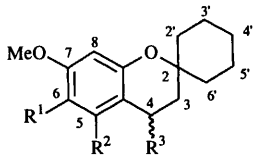
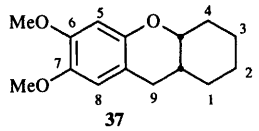
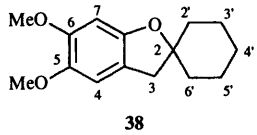
39



40 X = Cl
41 X = Bu^t
42 X = Me

32 respectively in moderate yields. The phenol **26**, however, gave the corresponding cycloadduct **31** in lower yield, and electrochemical oxidation of *o*-[1-(propylsulfanyl)methyl]-

Table 3 Cycloaddition of alkenes and *o*-quinone methides generated by electrochemical oxidation of phenols in hexane–2.0 mol dm^{-3} $LiClO_4/CH_3NO_2$

Phenols	Alkenes	Products	Yield (%)
20		 **29** R^1, R^4, R^5=H, R^2 = Me, R^3 = OMe	77
22		**30a** R^1, R^3 = H, R^2 = Me, R^4 = OMe, R^5 = α-$CH_2CH(CH_3)_2$ (12 13 14,15) + **30b** R^1, R^3 = H, R^3 = Me, R^4 = OMe, R^5 = β-$CH_2CH(CH_3)_2$	83 (**30a**:**30b** 2:1)
26	17	**31** R^1,R^3,R^4,R^5 = H, R^2 = Bu (12–15)	41
27		**32** R^1 = $COCH_2CH(CH_3)_2$ (12), R^2 = Me, R^3,R^5 = H, R^4 = OMe	78
20		 **33** R^1 = OMe, R^2,R^3 = H	66
22		**34** R^1 = H, R^2 = OMe, R^3 = $CH_2CH(CH_3)_2$ (9 10 11,12)	70
26	14	**35** R^1, R^2 = H, R^3 = $CH_2CH(CH_3)_2$ (9)	81
20		 + 	100 (**37**:**38** 2:1)
	36	**37** **38**	

phenol **24** in the presence of alkene **17** or **36** did not give the desired cycloadducts. This result suggested that the alkoxy group at C-5 was essential to the formation and/or cycloaddition of *o*-quinone methides, and highly electronegative aromatic carbon in a less hindered position (*e.g.*, **24**; C-4, C-6, **27**; C-4) was susceptible to electrophilic attack of the primary benzyl cation generated from sulfides. On the other hand, the acid-unstable methylenecyclohexane **14** gave the corresponding spirochroman **33–35** without migration to 1-methylcyclohexene. Cyclohexene **36** and the phenol **20** gave a rearranged cycloadduct **38** accompanied by the desired product **37**.

Electrochemical oxidation of 3,4-dimethoxy-2-(propylsulfanylmethyl)phenol **20** in the presence of 3 mol equiv. of alkene **7** or **39** gave cycloadduct **43** or **44a**,**b**, respectively. The stereochemistry of product **43** was established by nuclear Overhauser enhancement (NOE) between 9α-H and 2-H, 9β-H and 14-H_3; 9a-H and 14-H_3 and other isomers were not isolated. On the other hand, compounds **44** were obtained as a mixture of two diastereoisomers which correspond to the cycloadducts of *o*-quinone methide and β-phellandrene **8**. Although the stereochemistry of isomers **44a** and **44b** was not established, their planar structure was confirmed by NOE and chemical-shift correlation spectroscopy (COSY). 3,5-Dimethoxy-2-[3-methyl-1-(propylsulfanyl)butyl]phenol **22** was oxidized in the presence of 3 mol equiv. of alkene **7** at 50 °C to give compounds **45a** and **45b** (5:6) in 60% yield.† Compound **22** and 3 mol equiv. of the terpene **39** gave four diastereoisomers **46a**,**b**,**c** and **d** which could be separated by careful HPLC fractionation on ODS. Similarly, compound **28** was converted into **47** or **48** by cycloaddition with diene **7** or terpene **39**, respectively (structures and yields **43–48** are given in Table 4).

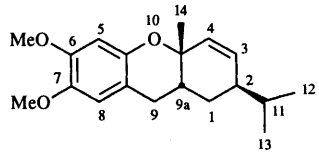
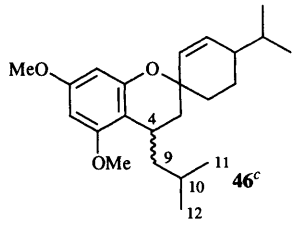
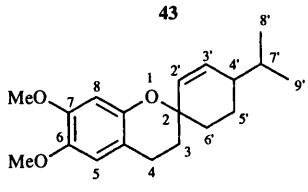
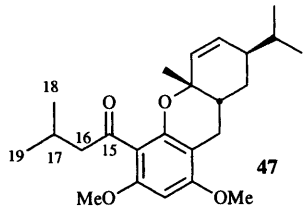
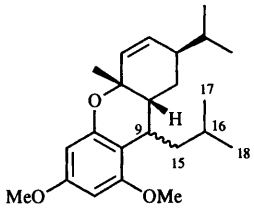
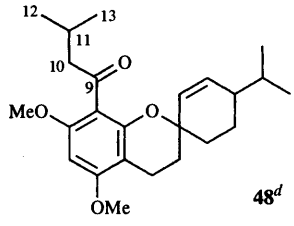
The present cycloaddition was highly regioselective except for the formation of compound **38**. In the reaction of compounds **20** and **36** (Table 3), the rearranged cycloadduct **38** should be obtained, first through bis-salt ***C***, and then *via* a carbocation intermediate ***D*** followed by hydride rearrangement to give a stabler carbocation ***E*** (Scheme 3). In the hexane–lithium perchlorate/nitromethane system (Fig. 1), most of the alkenes and cycloadducts dissolved in hexane phase did not prevent the electron transfer on the glassy carbon anode by oxidative decomposition and polymerization. On the other hand, when β-pinene **39** was just dissolved in hexane–lithium perchlorate/nitromethane in the absence of electric current, no rearranged isomer was obtained. Under electrolytic conditions, however, β-pinene **39** was partially converted into rearranged products. It can therefore be presumed that, for example, both unstable diene **8** and *o*-quinone methide ***G*** (through the cation-medical ***F***) were generated *in situ* in the electrochemical reaction medium to give euglobal II_b skeleton **46** regioselectively *via* the most stable allylic carbocation ***H***. The cycloadducts **45a**, **45b**, **46** and **47** have euglobal $1a_1$ **1**, $1a_2$ **2**, II_b **5** and T1 **3** skeletons, respectively, which suggests that biogenetic cycloaddition proceeds similarly. The products obtained here should be important synthetic intermediates of natural euglobals.

Experimental

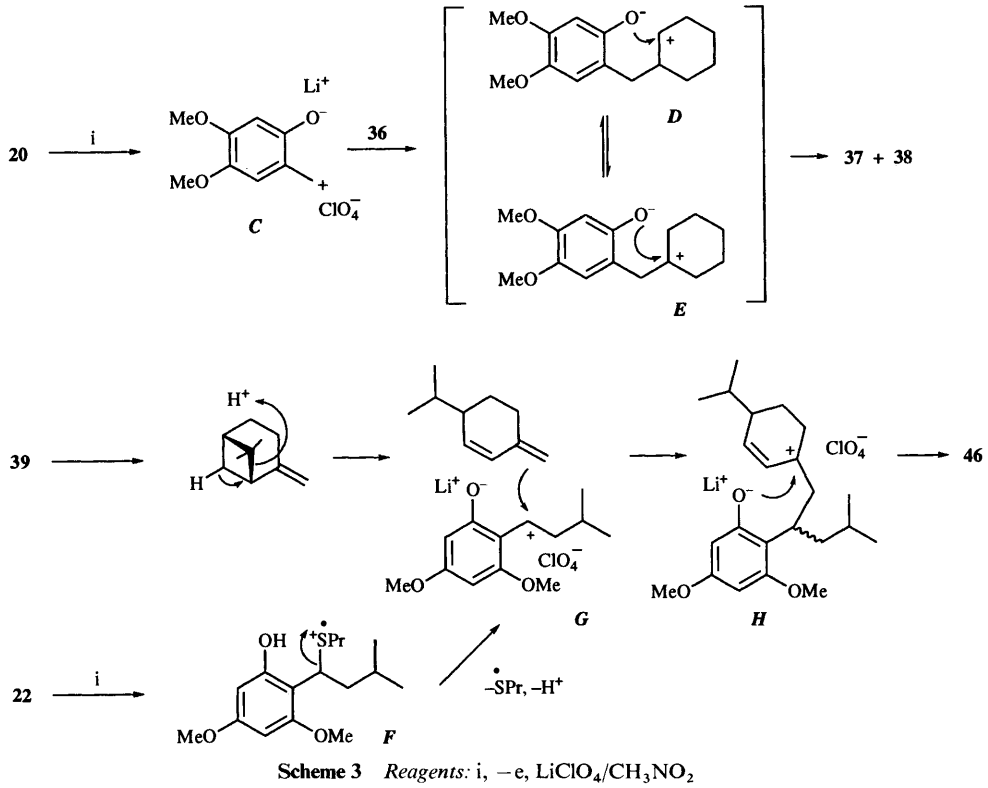
NMR spectra were measured on a JEOL LA-500 and an EX-270 spectrometer at 500 or 270 (^1H) and 125.7 or 67.9 MHz (^{13}C) for samples in $CDCl_3$ containing tetramethylsilane as internal standard; *J* values are given in Hz. IR and UV spectra were measured on a JASCO IR-810 IR spectrometer and a JASCO UVDEC-460 spectrophotometer, respectively. Mass spectra were recorded on a JEOL JMS-SX-102A spectrometer. Microanalyses were performed on a Perkin-Elmer 2400 II organic elemental microanalyser. TLC was carried out on Kieselgel GF_{254} (0.25 mm thickness). Wakogel C-200 was used for column chromatography with hexane–ethyl acetate (EtOAc). HPLC was performed on a JASCO BIP-1 instrument (UV detector) with a column of LiChroprep Si-60 (Merck) (hexane–EtOAc) or LiChrosphere RP-18 (5 μm; MeOH–water). Optical rotations were measured on a JASCO DIP-360 digital polarimeter, and $[\alpha]_D$-values are recorded in units of 10^{-1} deg cm^2 g^{-1}. Oxidation potentials were measured by cyclic voltammetry (Yanagimoto P-900 cyclic polarograph) by using a glassy carbon as anode and a Pt wire as cathode *vs.* SCE.

† Spectral data of xanthenes **45a** and **45b** were presented in the preliminary communication (ref. 10).

Table 4 Cycloaddition of *o*-quinone methides and terpenes[a]

Phenol	Terpene	Products		Phenol	Terpene	Products	
20	**7**	 **43**	75%	**22**	**39**	 **46**[c]	78%
20	**39**	 **44**[b]	68%	**28**	**7**	 **47**	41%
22	**7**	 **45a**(9α-H):**45b**(9β-H)	60% (5:6)	**28**	**39**	 **48**[d]	72%

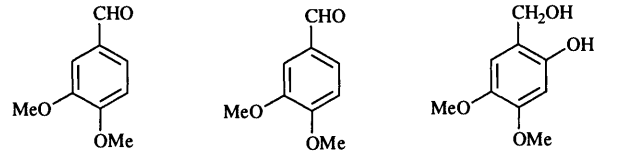
[a] Electrochemical oxidation was performed in 2.0 mol dm^{-3} $LiClO_4/CH_3NO_2$ at 50 °C. [b] Two diastereoisomers (**44a** and **44b** 2:1) were separated. [c] Four diastereoisomers (**46a**, **46b**, **46c** and **46d**, 4:4:1:1) were separated. [d] Two diastereoisomers (**48a** and **48b**, 2:1) were separated.



Scheme 3 *Reagents:* i, −e, $LiClO_4/CH_3NO_2$

Cycloaddition of 6-(4-methoxybenzylidene)-3,4-(methylenedioxy)cyclohexa-2,4-dienone 10

Compound **10** was prepared by Ag_2O oxidation of 2-(4-methoxybenzyl)-4,5-(methylenedioxy)phenol **9** followed by recrystallization. To a solution of quinone methide **10** (10 mg) in Et_2O, CH_3CN, MeOH, CH_3NO_2 or 0.5 mol dm^{-3} $LiClO_4/CH_3NO_2$ (20 cm^3 for any solvent), was added ethyl vinyl ether **11** (0.2 cm^3) and the mixture was stored for 16 h at ambient temperature. The reaction mixture was partitioned with AcOEt and water, and the AcOEt layer was dried over Na_2SO_4. After filtration and evaporation, the residue was separated by silica gel column chromatography (hexane–AcOEt). ^1H NMR spectra of quinone methide **10** and dimer **13** were identical with those previously reported.[11]



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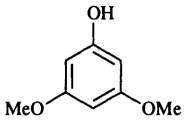
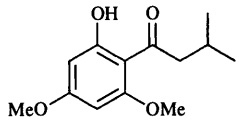
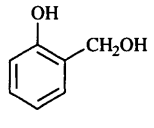


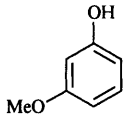
52



53



54



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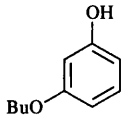

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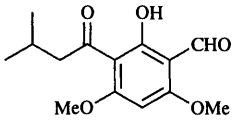

57

Synthesis of compound 12 by anodic oxidation of the phenol 9
A solution of compound **9** (40 mg) and ethyl vinyl ether **11** (56 mg) in 2.0 mol dm^{-3} $LiClO_4/CH_3NO_2$ was electrolysed at a constant potential (700 mV *vs.* SCE) and the reaction was quenched at 2.5 F mol^{-1}. After addition of brine, the solution was extracted with AcOEt. The extract was dried over anhydrous Na_2SO_4 and concentrated under reduced pressure. The residue was purified using hexane–AcOEt (20:1; silica gel) to afford cycloadduct **12** (51 mg, 54%).

4-(4-Methoxyphenyl)-6,7-(methylenedioxy)-3,4-dihydrospiro-[2*H*-1-benzopyran-2,1′-cyclohexane] 15
Compound **10** (25.8 mg) and methylenecyclohexane **14** (19 mg) were dissolved in 0.5 mol dm^{-3} $LiClO_4/CH_3NO_2$ (10 cm^3). The reaction mixture was heated at 60 °C for 2 h in a sealed glass tube. After cooling, the solution was poured into brine, and extracted with AcOEt. The organic layer was dried over $MgSO_4$, and evaporated to give spiro-compound **15** (35.4 mg, 100%). The reaction mixture of compound **13** (25.8 mg) and methylenecyclohexane **14** (19 mg) also gave title compound **15** (100%) by the same procedure. Compound **15** was an oil (Found: M^+, 352.3014. $C_{22}H_{24}O_4$ requires M, 352.2977); *m/z* 352 (M^+, 72%) and 257 (100); ν_{max}(neat)/cm^{-1} 1515, 1248, 1153 and 1040; δ_H 7.09 (2 H, d, *J* 8.9), 6.83 (2 H, d, *J* 8.9), 6.41 (1 H, s, 5-H), 6.18 (1 H, s, 8-H), 5.80 (1 H, d, *J* 1.3, OCH_2O), 5.77 (1 H, d, *J* 1.3, OCH_2O), 3.90 (1 H, dd, *J* 6.6 and 12.2, 4-H), 3.78 (3 H, s, OCH_3), 2.02 (1 H, dd, *J* 6.6 and 13.9, 3-H) and 1.2–1.95 (11 H, m, 2′–6′-H_2 and 3-H); δ_C 158.2, 148.3, 146.6, 141.0, 137.3, 129.4, 117.0, 113.9, 108.2, 100.6, 98.7, 75.1, 55.0, 42.7, 38.2, 31.8, 25.8 and 21.6.

Synthesis of 2-[1-(alkylsulfanyl)alkyl]phenols
3,4-Dimethoxybenzaldehyde **49** (520 mg) and *m*-chloroperbenzoic acid (MCPBA) (780 mg) were dissolved in CH_2Cl_2 (20 cm^3) and the solution was heated under reflux for 24 h. After the addition of AcOEt and 5% aq. $NaHCO_3$, the organic layer was separated, washed with brine and evaporated. The residue was dissolved in MeOH–5% aq. KOH (1:4) (30 cm^3) and the solution was stirred at ambient temperature for 3 h before being acidified with 1 mol dm^{-3} HCl and extracted with AcOEt. The organic layer was washed successively with 5% aq. $NaHCO_3$ and brine, and was dried over $MgSO_4$. After filtration and evaporation, 2-hydroxy-4,5-dimethoxybenzaldehyde **50** was obtained as a residue (450 mg). Reduction of aldehyde **50** (364 mg) with $NaBH_4$ (100 mg) in MeOH at 0 °C, followed by addition of brine and extraction with AcOEt, gave 2-hydroxy-4,5-dimethoxybenzyl alcohol **51** (338 mg, 92%). After the product was dissolved in CH_2Cl_2, 0.5 mol equiv. of ZnI_2 and 1.2 mol equiv. of thiophenol were added at −20 °C. The reaction mixture was kept for 4 h after which it was poured onto ice and was extracted with AcOEt. The extract was washed with 10% aq. $NaHCO_3$, dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel to give 4,5-*dimethoxy*-2-(*phenylsulfanylmethyl*)*phenol* **19** (43%), mp 39–41 °C (Found: M^+, 276.0880. $C_{15}H_{16}O_3S$ requires M, 276.0820); *m/z* 276 (M^+, 55%), 168 (53) and 167 (100); ν_{max}(neat)/cm^{-1} 3440, 1517 and 1200; δ_H 7.30–7.38 (2 H, m), 7.18–7.30 (3 H, m), 6.50 (1 H, s), 6.48 (1 H, s), 5.79 (1 H, br s, OH), 4.10 (2 H, s, 7-H_2), 3.82 (3 H, s, OCH_3) and 3.72 (3 H, s, OCH_3); δ_C 149.4, 148.6, 142.7, 134.7, 130.9, 128.9, 127.0, 113.7, 113.3, 101.7, 56.4, 55.8 and 35.3.

4,5-Dimethoxy-2-(propylsulfanylmethyl)phenol 20. 2-Hydroxy-4,5-dimethoxybenzyl alcohol **51** (368 mg) was dissolved in CH_2Cl_2, and ZnI_2 (0.5 mol equiv.) and propane-1-thiol (1.2 mol equiv.) were added at −20 °C. The reaction mixture was kept for 4 h and then was poured into crushed ice and extracted with AcOEt. The extract was washed with 10% aq. $NaHCO_3$, dried ($MgSO_4$) and evaporated. The residue was chromatographed on silica gel to give *title compound* **20** (58%) as an oil (Found: M^+, 242.0960. $C_{12}H_{18}O_3S$ requires M, 242.0977); *m/z* 242 (M^+, 30%) and 167 (100); ν_{max}(neat)/cm^{-1} 3420, 1612, 1511 and 1199; δ_H 6.63 (1 H, br s, OH), 6.58 (1 H, s), 6.48 (1 H, s), 3.78 (6 H, s, OMe), 3.71 (2 H, s, 7-H_2), 2.37 (2 H, t, *J* 7.0), 1.57 (2 H, sext, *J* 7.0) and 0.92 (3 H, t, *J* 7.0); δ_C 149.4, 149.3, 142.4, 113.8, 113.1, 101.9, 56.6, 55.8, 32.7, 32.4, 22.4 and 13.4.

3,5-Dimethoxy-2-[3-methyl-1-(phenylsulfanyl)butyl]phenol 21. 3,5-Dimethoxyphenol **52** (308 mg) and 3-methylbutyric acid (306 mg) were heated at 80 °C in $BF_3{\cdot}Et_2O$ (10 cm^3) for 2 h. After cooling, the reaction mixture was poured into 5% aq. AcOK and extracted with AcOEt. The organic layer was washed successively with 5% aq. $NaHCO_3$ and brine, and dried over $MgSO_4$. After filtration and evaporation, the residue was purified by silica gel column chromatography (hexane–AcOEt) to give 3,5-*dimethoxy*-2-(3-*methylbutyryl*)*phenol* **53** (466 mg, 98%), mp 32 °C; λ_{max}(EtOH)/nm 289 (log ε 4.70) (Found: M^+ 238.1198. $C_{13}H_{18}O_4$ requires M, 238.1206); *m/z* 238 (M^+, 26%), 223 (8) and 181 (100); ν_{max}(KBr)/cm^{-1} 1618, 1580, 1212, 1150 and 1112; δ_H 6.06 (1 H, d, *J* 2.3, ArH), 5.92 (1 H, d, *J* 2.3, ArH), 3.85 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.85 (2 H, d, *J* 6.6, $COCH_2$), 2.22 (1 H, oct, *J* 6.6, C*H*Me_2) and 0.96 (6 H, d, *J* 6.6, CH_3); δ_C 205.6, 167.8, 165.8, 162.6, 105.9, 93.6, 90.8, 55.5 (2 C), 53.1, 25.3 and 22.8 (2 C).

Compound **53** was reduced by $NaBH_4$ in MeOH, as described above, and the product was treated by thiophenol in CH_2Cl_2 at 0 °C for 1 h in the presence of ZnI_2 (0.05 mol equiv.) to give *title compound* **21** (81%) as an oil (Found: M^+, 332.1402. $C_{19}H_{24}O_3S$ requires M, 332.1446); *m/z* 332 (M^+, 2%), 223 (86), 207 (34) and 167 (100); ν_{max}(neat)/cm^{-1} 3300, 1620, 1202, 1141 and 1083; δ_H 7.60 (1 H, br s, OH), 7.30 (2 H, m), 7.14 (3 H, m), 6.03 (1 H, dd, *J* 2.6, 4-H), 5.93 (1 H, d, *J* 2.6, 6-H), 5.14 (1 H, dd, *J* 5.3 and 9.2, 7-H), 3.70 (3 H, s, OCH_3), 3.66 (3 H, s, OCH_3), 1.65–1.95 (2 H, m, 8-H_2), 1.57 (1 H, sep, *J* 6.6, 9-H), 0.94 (3 H, d, *J* 6.6, 10-H_3) and 0.90 (3 H, d, *J* 6.6, 11-H_3); δ_C 160.1, 158.7, 157.4, 133.5, 131.2, 128.6, 127.1, 107.2, 95.2, 91.4, 55.8, 55.1, 42.5, 41.5, 26.4, 22.7 and 22.2.

3,5-Dimethoxy-2-[3-methyl-1-(propylsulfanyl)butyl]phenol 22. Compound **53** was reduced with $NaBH_4$, and the corresponding alcohol was converted into title compound **22** with propane-1-thiol (1.0 mol equiv.) and ZnI_2 (0.05 mol equiv.) in CH_2Cl_2 as described above. Title compound **22** (92%) was obtained as an oil (Found: M^+, 298.1622. $C_{16}H_{26}O_3S$ requires M, 298.1603); *m/z* 298 (M^+, 11%), 223 (73) and 167 (100); ν_{max}(neat)/cm^{-1} 3210, 1615, 1582, 1203 and 1140; δ_H 8.17 (1 H, s, OH), 6.10 (1 H, d, *J* 2.3, 4-H), 6.05 (1 H, d, *J* 2.3, 6-H), 4.74 (1 H, dd, *J* 6.6 and 8.6, 7-H), 3.76 (3 H, s, OCH_3), 3.75 (3 H, s,

OCH_3), 2.32 (2 H, m, 12-H_2), 1.63 (5 H, m), 0.92 (6 H, m, 10- and 14-H_3) and 0.87 (3 H, d, *J* 6.6, 11-H_3); δ_C 160.1, 158.9, 106.5, 95.0, 91.1, 55.6, 55.2, 42.9, 37.3, 32.7, 26.2, 22.5, 22.3, 22.2 and 13.3.

2-(Phenylsulfanylmethyl)phenol 23. Salicyl alcohol **54** was converted into title compound **23** as described in the synthesis of compound **19**. Compound **23** (93%) was obtained as an oil, *m/z* 216 (M^+, 38%) and 107 (100); ν_{max}(neat)/cm^{-1} 3400, 3060, 1579 and 1235; δ_H 7.32 (2 H, br d, *J* 7.0), 7.0–7.4 (5 H, m), 6.79 (2 H, m), 6.22 (1 H, br s, OH) and 4.13 (2 H, s, 7-H_2); δ_C 154.4, 134.7, 130.6, 130.5, 129.0, 128.9, 126.9, 122.7, 120.7, 116.5 and 35.1.

2-(Propylsulfanylmethyl)phenol 24. Salicyl alcohol **54** was converted into title compound **24** as described in the synthesis of compound **20**. Compound **24** (95%) was obtained as an oil, *m/z* 182 (M^+, 32%) and 107 (100); ν_{max}(neat)/cm^{-1} 3380, 1584, 1450 and 1232; δ_H 7.10 (2 H, m, 4- and 5-H), 6.82 (2 H, m, 3- and 6-H), 3.78 (2 H, s, 7-H_2), 2.38 (2 H, t, *J* 7.2, 8-H_2), 1.60 (2 H, m, 9-H_2) and 0.93 (3 H, t, *J* 7.2, 10-H_3); δ_C 154.8, 130.3, 128.7, 122.9, 120.3, 116.6, 32.7, 31.9, 22.2 and 13.2.

5-Methoxy-2-[3-methyl-1-(phenylsulfanyl)butyl]phenol 25. Compound **25** was synthesized from 3-methoxyphenol **55** as described in the synthesis of compound **21**. Title product **25** (83% from substrate **55**) was obtained as an oil (Found: M^+, 302.1339. $C_{18}H_{22}O_2S$ requires M, 302.1341); *m/z* 302 (M^+, 2%), 193 (43), 177 (28) and 137 (100); ν_{max}(neat)/cm^{-1} 3400, 1612, 1505, 1198 and 1158; δ_H 7.30 (2 H, m), 7.20 (3 H, m), 6.90 (1 H, br s, OH), 6.88 (1 H, d, *J* 8.2, 3-H), 6.39 (1 H, d, *J* 2.3, 6-H), 6.31 (1 H, dd, *J* 8.2 and 2.3, 4-H), 4.44 (1 H, m, 7-H), 3.69 (3 H, s, OCH_3), 1.82 (2 H, m, 8-H_2), 1.62 (1 H, sep, *J* 6.6, 9-H), 0.90 (3 H, d, *J* 6.6, 10-H_3), and 0.88 (3 H, d, *J* 6.6, 11-H_3); δ_C 159.8, 155.4, 132.4, 129.9, 128.7 (4 C), 127.4, 118.9, 106.0, 102.8, 55.1, 43.3, 25.9, 22.7 and 22.0.

5-Methoxy-2-[3-methyl-1-(propylsulfanyl)butyl]phenol 26. Compound **26** was synthesized from 3-methoxyphenol **55** as described in the synthesis of compound **22**. Compound **26** (87% from substrate **55**) was obtained as an oil (Found: M^+, 268.1496. $C_{15}H_{24}O_2S$ requires M, 268.1450); *m/z* 268 (M^+, 13%), 193 (41) and 137 (100); ν_{max}(neat)/cm^{-1} 3600, 1615, 1500, 1191 and 1158; δ_H 7.53 (1 H, br s, OH), 6.81 (1 H, d, *J* 8.3, 3-H), 6.35 (1 H, d, *J* 2.7, 6-H), 6.29 (1 H, dd, *J* 2.7 and 8.3, 4-H), 3.91 (1 H, dd, *J* 8.6 and 6.9, 7-H), 3.64 (3 H, s, OCH_3), 2.18 (2 H, m, 12-H_2), 1.65 (1 H, m, 9-H), 1.40 (4 H, m, 8- and 13-H_2) and 0.82 (9 H, m, 10-, 11- and 14-H_3); δ_C 160.05, 156.35, 130.37, 118.07, 105.89, 103.05, 55.07, 45.46, 43.28, 32.55, 25.81, 22.45, 22.37, 22.08 and 13.33.

5-Butoxy-2-(propylsulfanylmethyl)phenol 27. Compound **27** was synthesized from 3-butoxyphenol **56** as described in the synthesis of compound **20**. *Title compound* **27** (43% from substrate **56**) was obtained as an oil (Found: M^+, 254.1325. $C_{14}H_{22}O_2S$ requires M, 254.1341); *m/z* 254 (M^+, 33%), 179 (100) and 123 (82); ν_{max}(neat)/cm^{-1} 3338, 1612, 1500, 1280 and 1163; δ_H 6.93 (1 H, d, *J* 8.3, 3-H), 6.92 (1 H, s, OH), 6.47 (1 H, d, *J* 2.6, 6-H), 6.40 (1 H, dd, *J* 8.3 and 2.6, 4-H), 3.91 (2 H, t, *J* 6.3, 11-H), 3.75 (2 H, s, 7-H_2), 2.37 (2 H, t, *J* 7.6, 9-H_2), 1.74 (2 H, m), 1.57 (2 H, m, 12-H_2), 1.47 (2 H, m), 0.96 (3 H, t, *J* 7.6) and 0.94 (3 H, t, *J* 7.6); δ_C 160.9, 156.46, 130.88, 114.13, 106.75, 103.33, 67.66, 32.49, 32.31, 31.24, 22.33, 19.20, 13.82 and 13.34.

1-[2-Hydroxy-4,6-dimethoxy-3-(propylsulfanylmethyl)-phenyl]-4-methylbutan-1-one 28. To a solution of compound **53** (738 mg) in CH_2Cl_2 (20 cm^3) were added $TiCl_4$ (2.1 cm^3) and dichloromethyl methyl ether (0.56 cm^3) were added at −10 °C.[13] The reaction mixture was stored at ambient temperature for 1 h and was poured into crushed ice. The product was extracted with AcOEt, and the extract was washed successively with 5% aq. $NaHCO_3$ and brine, dried over $MgSO_4$, filtered and evaporated to dryness to give 2-*hydroxy*-4,6-*dimethoxy*-3-(3-*methylbutyryl*)*benzaldehyde* **57** (98%), mp 62 °C; λ_{max}(EtOH)/nm 294 (log ε 4.68) and 267 (log ε 4.58) (Found: M^+, 266.1145. $C_{14}H_{18}O_5$ requires M, 266.1154); *m/z* 266 (M^+, 22%) and 209 (100); ν_{max}(neat)/cm^{-1} 1620, 1210 and 1120; δ_H 13.05 (1 H, br s, OH), 10.13 (1 H, s, CHO), 5.96 (1 H, s, ArH), 3.93 (3 H, s, OCH_3), 3.91 (3 H, s, OCH_3), 2.69 (2 H, d, *J* 7.0), 2.18 (1 H, oct, *J* 7.0) and 0.95 (6 H, d, *J* 7.0); δ_C 203.0, 191.1, 165.2, 165.1, 163.2, 110.7, 105.6, 85.8, 55.9, 55.8, 53.5, 24.7 and 22.5 (2 C).

Compound **57** (624 mg) was dissolved in MeOH (20 cm^3) and $NaBH_3CN$ (282 mg) was added. The reaction mixture was kept at ambient temperature for 3 h and was then poured into AcOEt–water (1 : 1; 100 cm^3). After the organic layer had been dried over $MgSO_4$ and evaporated, the residue was dissolved in CH_2Cl_2 (30 cm^3) with propane-1-thiol (1 mol equiv.) and ZnI_2 (0.5 mol equiv.). The reaction mixture was stored at ambient temperature for 16 h to give *title compound* **28** (88% from aldehyde **57**) as an oil, ν_{max}(EtOH)/nm 291 (log ε 4.21) and 236 (sh) (Found: M^+, 326.1522. $C_{17}H_{26}O_4S$ requires M, 326.1552); *m/z* 326 (M^+, 48%), 251 (100), 233 (47), 209 (72) and 195 (37); ν_{max}(neat)/cm^{-1} 1620 and 1218; δ_H 14.50 (1 H, s, OH), 5.95 (1 H, s, 4-H), 3.90 (6 H, s, OCH_3), 3.73 (2 H, s, 7-H_2), 2.60 (2 H, t, *J* 6.7, 9-H_2), 2.52 (2 H, t, *J* 7.3, 14-H_2), 2.18 (1 H, m, 10-H), 1.63 (2 H, sext, *J* 7.3, 14-H_2), 0.96 (6 H, d, *J* 6.6 11- and 12-H_3) and 0.95 (3 H, t, *J* 7.3, 15-H_3); δ_C 205.26, 163.80, 162.93, 162.01, 107.45, 105.59, 85.76, 55.42, 55.33, 55.27, 35.73, 34.19, 25.09, 23.02, 22.95, 22.62 and 13.43.

General method for the electrochemical generation and cycloaddition of *o*-quinone methides with dienes

A 2-[1-(propylsulfanyl)alkyl]phenol derivative (0.2–0.5 mmol) was dissolved in a solution composed of hexane (5 cm^3) and 2.0 mol dm^{-3} $LiClO_4/CH_3NO_2$ (15 cm^3). To this solution was added an alkene (3 mol equiv.) and electrolysed at peak potentials of the phenol derivative by using a glassy carbon anode (60 mm × 20 mm) and a Pt cathode (10 mm × 10 mm) at a constant potential under Ar. After the reaction was complete (~ 1.2 F mol^{-1}), the reaction mixture was poured into AcOEt and the AcOEt solution was washed successively with 5% aq. $NaHCO_3$ and brine. The organic layer was dried over anhydrous $MgSO_4$. After filtration, and evaporation under reduced pressure, the residue was purified by silica gel column chromatography (hexane–AcOEt) to give the corresponding cycloadduct. When the products were obtained as a mixture of diastereoisomers, they were further separated by HPLC (ODS; MeOH). (−)-Phellandrene and (−)-β-pinene (Tokyo Kasei Kogyo Co.) were used for the syntheses of compounds **43–48**.

6,7-Dimethoxy-2,2,3-trimethyl-3,4-dihydro-2*H*-1-benzopyran 29. This was obtained as an *oil* (Found: M^+, 236.1410. $C_{14}H_{20}O_3$ requires M, 236.1412); *m/z* 236 (M^+ 32%), 167 (100) and 129 (49); ν_{max}(neat)/cm^{-1} 1510, 1220 and 1190; δ_H 6.52 (1 H, s, 5-H), 6.37 (1 H, s, 8-H), 3.82 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.67 (1 H, dd, *J* 5.5 and 16.7, 4-H), 2.38 (1 H, dd, *J* 9.9 and 16.7, 4-H), 1.91 (1 H, m, 3-H), 1.36 (3 H, s, 9-H_3), 1.15 (3 H, s, 10-H_3) and 1.00 (3 H, d, *J* 6.9, 11-H_3); δ_C 148.3, 147.4, 142.8, 112.1, 111.9, 101.1, 77.4, 56.5, 55.8, 35.7, 30.8, 27.3, 20.0 and 16.6.

4-Isobutyl-5,7-dimethoxy-2,2,3-trimethyl-3,4-dihydro-2*H*-1-benzopyran 30a. This was obtained as an *oil* (Found: M^+, 292.2018. $C_{18}H_{28}O_3$ requires M, 292.2038); *m/z* 292 (M^+, 96%), 236 (83), 235 (100), 207 (63), 179 (67) and 167 (93); ν_{max}(neat)/cm^{-1} 1616, 1589, 1200 and 1144; δ_H 6.04 (1 H, d, *J* 2.3), 6.01 (1 H, d, *J* 2.3), 3.76 (3 H, s, OCH_3), 3.74 (3 H, s, OCH_3), 2.51 (1 H, m, 4-H), 1.83 (1 H, dq, *J* 12.7 and 6.9, 3-H), 1.54–1.71 (3 H, m, 12-H_2 and 13-H), 1.38 (3 H, s, 9-H_3), 1.14 (3 H, s, 10-H_3), 1.01 (3 H, d, *J* 6.9, 11-H_3), 0.92 (3 H, d, *J* 6.1, 14-H_3) and 0.79 (3 H, d, *J* 6.1, 15-H_3); δ_C 159.0, 158.9, 154.7, 108.7, 94.1, 91.7, 77.2, 55.2, 55.0, 43.5, 41.5, 35.8, 27.9, 26.4, 23.9, 22.9, 22.6 and 17.4.

4β-Isomer **30b** was obtained as an oil (Found: M^+, 292.2019); *m/z* 292 (M^+, 98%), 236 (83), 235 (100), 207 (62), 179 (66) and 167 (92); ν_{max}(neat)/cm^{-1} 1616, 1589, 1200 and 1145; δ_H 6.05 (1 H, d, *J* 2.6), 6.03 (1 H, d, *J* 2.6), 3.75 (3 H, s, OCH_3), 3.74 (3 H, s, OCH_3), 2.93 (1 H, ddd, *J* 1.9, 3.3 and 12.0, 4-H), 1.91 (1

H, dq, *J* 1.9 and 7.1, 3-H), 1.50–1.65 (2 H, m), 1.43 (1 H, m), 1.34 (3 H, s, 9-H_3), 1.28 (3 H, s, 10-H_3), 1.05 (3 H, d, *J* 7.1, 11-H_3), 0.94 (3 H, d, *J* 6.3, 14-H_3) and 0.88 (3 H, d, *J* 6.3, 15-H_3); δ_C 159.1, 158.2, 154.7, 111.4, 94.4, 91.4, 79.4, 55.2, 55.0, 40.7, 39.1, 32.6, 29.3, 26.6, 24.8, 23.4, 22.5 and 13.7.

7-Butoxy-2,2,3-trimethyl-3,4-dihydro-2*H*-1-benzopyran 31. This was obtained as an *oil* (Found: M^+, 248.1760. $C_{16}H_{24}O_2$ requires M, 248.1776); *m/z* 248 (M^+, 23%), 179 (62) and 123 (100); ν_{max}(neat)/cm^{-1} 1618, 1501 and 1150; δ_H 6.90 (1 H, d, *J* 8.2, 5-H), 6.41 (1 H, dd, *J* 8.2 and 2.6, 6-H), 6.34 (1 H, d, *J* 2.6, 8-H), 3.90 (2 H, t, *J* 6.8, 12-H_2), 2.67 (1 H, dd, *J* 16.2 and 5.6, 4-H), 2.38 (1 H, dd, *J* 16.2 and 10.3, 4-H), 1.91 (1 H, m, 3-H), 1.76 (2 H, quin, *J* 6.8, 13-H_2), 1.45 (2 H, m, 14-H_2), 1.37 (3 H, s, 9-H_3), 1.15 (3 H, s, 10-H_3), 0.99 (3 H, d, *J* 6.9, 11-H_3) and 0.95 (3 H, t, *J* 6.8, 15-H_3); δ_C 158.6, 154.3, 129.6, 113.4, 107.5, 102.1, 77.7, 67.6, 35.7, 31.3, 30.4, 27.4, 20.1, 19.3, 16.6 and 13.8.

1-(5,7-Dimethoxy-2,2,3-trimethyl-3,4-dihydro-2*H*-1-benzopyran-4-yl)methylbutan-1-one 32. This had mp 64–65 °C (Found: M^+, 320.1983. $C_{19}H_{28}O_4$ requires M, 320.1988); *m/z* 320 (M^+, 11%), 263 (57) and 193 (100); λ_{max}(EtOH)/nm 280 (log ε 3.44) and 225 (sh); ν_{max}(neat)/cm^{-1} 1700, 1603 and 1110; δ_H 6.02 (1 H, s, 6-H), 3.83 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 2.68 (1 H, dd, *J* 5.6 and 16.2, 4-H), 2.63 (2 H, d, *J* 6.9, 13-H_2), 2.21 (1 H, sep, *J* 6.6, 14-H_2), 2.15 (1 H, dd, *J* 16.2 and 10.6, 4-H), 1.83 (1 H, m, 3-H), 1.33 (3 H, s, 9-H), 1.11 (3 H, s, 10-H_3), 0.99 (3 H, d, *J* 6.6, 11-H_3) and 0.94 (6 H, d, *J* 6.6, 15- and 16-H_3); δ_C 204.9, 158.6, 155.9, 151.9, 113.4, 103.3, 87.1, 78.3, 55.9, 55.4, 34.8, 27.2, 25.3, 24.8, 22.8 (2 C), 19.7 and 16.7.

6,7-Dimethoxy-3,4-dihydrospiro[2*H*-1-benzopyran-2,1′-cyclohexane] 33. This was obtained as an *oil* (Found: M^+, 262.1576. $C_{16}H_{22}O_3$ requires M, 262.1569); *m/z* 262 (M^+, 37%) and 167 (100); ν_{max}(neat)/cm^{-1} 1511, 1220, 1190 and 1120; δ_H 6.54 (1 H, s, 5-H), 6.41 (1 H, s, 8-H), 3.83 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.67 (2 H, t, *J* 6.3, 4-H_2) and 1.20–1.80 (12 H, m, 2′–6′- and 3-H_2); δ_C 148.2, 147.5, 142.6, 112.3, 111.9, 101.3, 74.4, 56.5, 55.8, 35.0, 31.7, 26.0, 21.8 and 21.3.

4-Isobutyl-5,7-dimethoxy-3,4-dihydrospiro[2*H*-1-benzopyran-2,1′-cyclohexane] 34. This was obtained as an *oil* (Found: M^+, 318.2169. $C_{20}H_{30}O_3$ requires M, 318.2194); *m/z* 318 (M^+, 16%), 261 (100) and 167 (53); ν_{max}(neat)/cm^{-1} 1620, 1582, 1142 and 1108; δ_H 6.04 (2 H, s, 6- and 8-H), 3.79 (3 H, s, OCH_3), 3.75 (3 H, s, OCH_3), 2.85 (1 H, br q, *J* 6.6, 4-H), 1.98 (1 H, m, 3-H), 1.2–1.85 (14 H, m), 0.95 (3 H, d, *J* 6.6, 11-H_3) and 0.89 (3 H, d, *J* 6.6, 12-H_3); δ_C 159.0 (2 C), 154.9, 108.9, 94.4, 91.7, 75.4, 55.2, 55.1, 44.6, 39.3, 37.6, 33.3, 26.3, 25.9, 24.2, 22.0 and 21.4.

4-Isobutyl-7-methoxy-3,4-dihydrospiro[2*H*-1-benzopyran-2,1′-cyclohexane] 35. This was obtained as an *oil* (Found: M^+, 288.2061. $C_{19}H_{28}O_2$ requires M, 288.2089); *m/z* 288 (M^+, 60%), 231 (100), 193 (41), 151 (39) and 137 (57); ν_{max}(neat)/cm^{-1} 1615, 1500 and 1199; δ_H 7.11 (1 H, d, *J* 8.6, 5-H), 6.44 (1 H, dd, *J* 2.6 and 8.6, 6-H), 6.38 (1 H, d, *J* 2.6, 8-H), 3.76 (3 H, s, OCH_3), 2.81 (1 H, m, 4-H), 1.99 (1 H, dd, *J* 6.3 and 13.5, 3-H), 1.76 (5 H, m), 1.58 (4 H, m), 1.32 (5 H, m) and 0.95 (6 H, d, *J* 5.9, 11- and 12-H_3); δ_C 158.8, 154.3, 127.6, 118.9, 106.8, 101.9, 75.2, 55.2, 44.9, 38.6, 38.4, 32.5, 27.6, 26.0, 25.2, 24.3, 21.9 and 21.1.

***cis*-6,7-Dimethoxy-2,3,4,4a,9,9a-hexahydro-1*H*-xanthene 37**. This was obtained as an *oil* (Found: M^+, 248.1401. $C_{15}H_{20}O_3$ requires M, 248.1412); *m/z* 248 (M^+, 85%) and 167 (100); ν_{max}(neat)/cm^{-1} 1512, 1190 and 1121; δ_H 6.51 (1 H, s, 8-H), 6.40 (1 H, s, 5-H), 4.14 (1 H, m, 4a-H), 3.83 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.95 (1 H, dd, *J* 6.2 and 16.7, 9-H), 2.37 (1 H, dd, *J* 2.1 and 16.7, 9-H), 2.02 (2 H, m), and 1.22–1.81 (7 H, m); δ_C 148.1, 147.9, 142.8, 112.7, 110.9, 100.6, 73.4, 56.4, 55.8, 33.3, 30.9, 30.8, 26.6, 25.0 and 20.3.

5,6-Dimethoxy-2,3-dihydrospiro[benzofuran-2,1′-cyclohexane] 38. This was obtained as an *oil* (Found: M^+, 248.1401. $C_{15}H_{20}O_3$ requires M, 248.1412); *m/z* 248 (M^+, 100%) and 167 (87); ν_{max}(neat)/cm^{-1} 1500 and 1190; δ_H 6.71 (1 H, s, 4-H), 6.24 (1 H, s, 7-H), 3.82 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.91 (2 H, s, 3-H_2) and 1.22–1.89 (10 H, m, 2′–6′-H_2); δ_C 153.1, 149.3, 142.8, 116.4, 109.7, 95.1, 89.1, 57.0, 56.0, 41.3, 37.2, 25.2 and 23.0.

2-Isopropyl-6,7-dimethoxy-4a-methyl-2,4a,9,9a-tetrahydro-1*H*-xanthene 43. This was obtained as an *oil*, $[\alpha]_D^{20}$ −101 (*c* 2.4, $CHCl_3$) (Found: C, 75.3; H, 8.5%; M^+, 302.1880. $C_{19}H_{26}O_3$ requires C, 75.46; H, 8.67%; M, 302.1882); *m/z* 302 (M^+, 40%), 168 (62), 167 (100) and 153 (28); ν_{max}(neat)/cm^{-1} 1510, 1196 and 1120; δ_H 6.52 (1 H, s, 8-H), 6.40 (1 H, s, 5-H), 5.72 (2 H, s, 3- and 4-H), 3.81 (6 H, s, OCH_3), 2.76 (1 H, dd, *J* 6.1 and 16.7, 9β-H), 2.54 (1 H, dd, *J* 6.8 and 16.7, 9α-H), 2.05 (1 H, m, 2-H), 2.01 (1 H, m, 9a-H), 1.69 (3 H, m, 1-Hz and 11-H), 1.41 (3 H, s, 14-H_3), 0.95 (3 H, d, *J* 6.3, 12-H_3) and 0.93 (3 H, d, *J* 6.3, 13-H_3); δ_C 148.2, 146.7, 142.7, 132.4, 132.3, 112.0, 111.6, 100.9, 74.4, 56.4, 55.8, 39.1, 34.2, 31.9, 27.8, 27.4, 27.2, 20.2 and 20.0.

6′-Isopropyl-6,7-dimethoxy-3,4-dihydrospiro-[2*H*-1-benzopyran-2,3′-cyclohexene] 44. *Stereoisomer* **44a** was an oil, $[\alpha]_D^{20}$ −4.8 (*c* 0.15, $CHCl_3$) (Found: C, 75.4; H, 8.6%; M^+, 302.1889. $C_{19}H_{26}O_3$ requires C, 75.46; H, 8.67%; M, 302.1882); *m/z* 302 (M^+, 36%) and 167 (100); ν_{max}(neat)/cm^{-1} 1511 and 1195; δ_H 6.55 (1 H, s, 5-H), 6.41 (1 H, s, 8-H), 5.77 (1 H, dd, *J* 10.5 and 2.3, 2′-H), 5.73 (1 H, d, *J* 10.5, 1′-H), 3.82 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.70 (2 H, t, *J* 6.0, 4-H_2), 1.52–2.13 (7 H, m), 1.43 (1 H, m, 5′-H), 0.92 (3 H, d, *J* 6.6, 8′-H_3) and 0.89 (3 H, d, *J* 6.6, 9′-H_3); δ_C 148.4, 147.6, 142.7, 133.5, 129.9, 112.1, 111.7, 101.4, 74.7, 56.5, 55.8, 42.0, 33.1, 31.8, 31.7, 22.4, 21.7, 19.8 and 19.4.

Stereoisomer **44b** was an oil, $[\alpha]_D^{20}$ +3.0 (*c* 0.7, $CHCl_3$) (Found: C, 75.3; H, 8.7%; M^+, 302.1884); *m/z* 302 (M^+, 34%) and 167 (100); ν_{max}(neat)/cm^{-1} 1510 and 1192; δ_H 6.55 (1 H, s, 5-H), 6.41 (1 H, s, 8-H), 5.91 (1 H, dd, *J* 2.0 and 10.2, 2′-H), 5.70 (1 H, ddd, *J* 2.0, 2.0 and 10.2, 1′-H), 3.82 (3 H, s, OCH_3), 3.81 (3 H, s, OCH_3), 2.70 (2 H, m, 4-H_2), 2.06 (1 H, br d, *J* 13.5, 6′-H), 1.56–1.93 (6 H, m), 1.37 (1 H, m, 5′-H), 0.96 (3 H, d, *J* 6.3, 8′-H_3) and 0.94 (3 H, d, *J* 6.3, 9′-H_3); δ_C 148.4, 147.6, 142.7, 135.7, 130.2, 112.2, 111.4, 101.5, 72.3, 56.5, 55.8, 42.7, 32.8, 32.0, 31.9, 21.4, 21.3, 19.9 and 19.6.

4-Isobutyl-6′-isopropyl-5,7-dimethoxy-3,4-dihydrospiro[2*H*-1-benzopyran-2,3′-cyclohexene] 46a. This was obtained as an *oil*, $[\alpha]_D^{20}$ −6.0 (*c* 1.2, $CHCl_3$) (Found: C, 76.9; H, 9.7%; M^+, 358.2510. $C_{23}H_{34}O_3$ requires C, 77.05; H, 9.56%; M, 358.2508); *m/z* 358 (M^+, 18%), 301 (100) and 231 (33); ν_{max}(neat)/cm^{-1} 1604, 1581, 1140 and 1103; δ_H 6.05 (2 H, s, 6- and 8-H), 5.90 (1 H, dd, *J* 10.3 and 2.0, 2′-H), 5.70 (1 H, ddd, *J* 10.3, 2.8 and 1.6, 1′-H), 3.77 (3 H, s, OCH_3), 3.74 (3 H, s, OCH_3), 2.90 (1 H, br, q, *J* 3.0, 4-H), 2.04 (1 H, m, 6′-H), 2.00 (1 H, m, 9-H), 1.94 (1 H, dd, *J* 13.7 and 7.4, 3-H), 1.85 (1 H, m, 5′-H), 1.62–1.78 (3 H, m, 3-, 10- and 7′-H), 1.50 (1 H, m, 5′-H), 1.15–1.25 (2 H, m, 9- and 4′-H), 0.94 (6 H, d, *J* 6.6) and 0.90 (6 H, d, *J* 6.6) (4 × Me); δ_C 159.2, 159.1, 155.1, 135.2, 131.4, 108.6, 94.8, 91.9, 73.5, 55.2, 55.1, 44.6, 42.5, 40.7, 31.9, 31.0, 26.3, 25.8, 24.1, 21.5, 21.4, 19.9 and 19.6.

Isomer **46b** was obtained as an oil, $[\alpha]_D^{20}$ +6.5 (*c* 0.9, $CHCl_3$ (Found: C, 77.0; H, 9.5%; M^+, 358.2512); *m/z* 358 (M^+, 15%), 301 (100) and 231 (32); ν_{max}(neat)/cm^{-1} 1604, 1581, 1140 and 1103; δ_H 6.04 (1 H, d, *J* 2.5, 6-H), 6.00 (1 H, d, *J* 2.5, 8-H), 5.81 (1 H, d, *J* 10.3, 2′-H), 5.67 (1 H, ddd, *J* 10.3, 1.5 and 2.5, 1′-H), 3.77 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 2.98 (1 H, m, 4-H), 2.06 (1 H, br d, *J* 13.5, 6′-H), 1.98 (1 H, dd, *J* 14.2 and 7.8, 3-H), 1.88 (2 H, m, 9- and 5′-H), 1.74 (1 H, dd, *J* 14.2 and 5.9, 3-H), 1.71 (1 H, m), 1.6–1.7 (3 H, m), 1.52 (1 H, dt, *J* 13.5 and 3.4, 5′-H), 1.33 (1 H, ddd, *J* 3.4, 10.0 and 13.5, 9-H), 0.96 (3 H, d, *J* 6.9), 0.93 (3 H, d, *J* 6.9), 0.91 (3 H, d, *J* 6.9) and 0.90 (3 H, d, *J* 6.9) (4 × Me); δ_C 159.1, 159.0, 155.0, 135.6, 129.7, 108.3, 94.3, 91.7, 72.7, 55.22, 55.15, 44.3, 42.5, 38.7, 35.0, 31.8, 26.6, 25.9, 24.1, 21.5, 21.3, 19.8 and 19.4.

Isomer **46c** was obtained as an oil, $[\alpha]_D^{20}$ −8.5 (*c* 1.1, $CHCl_3$) (Found: C, 76.8; H, 9.7%; M^+, 358.2503); *m/z* 358 (M^+, 18%), 301 (100) and 231 (30); ν_{max}(neat)/cm^{-1} 1604, 1581, 1140 and 1103; δ_H 6.05 (2 H, s, 6- and 8-H), 5.77 (1 H, dd, *J* 1.5 and 10.3,

2′-H), 5.68 (1 H, dd, *J* 2.0 and 10.3, 1′-H), 3.77 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 2.89 (1 H, m, 4-H), 1.85–2.1 (3 H, m, 3-, 9- and 6′-H), 1.55–1.83 (4 H, m, 3-, 10-, 5′- and 7′-H), 1.2–1.5 (4 H, m, 9- and 5′-H and 4′-H_2), 0.98 (3 H, d, *J* 6.9), 0.96 (3 H, d, *J* 6.9), 0.88 (3 H, d, *J* 6.9) and 0.87 (3 H, d, *J* 6.9) (4 × Me); δ_C 159.2, 158.9, 154.7, 132.1, 131.8, 108.6, 94.2, 91.8, 75.4, 55.2, 55.1, 44.1, 41.9, 37.5, 33.6, 31.8, 26.7, 25.8, 24.1, 22.4, 21.4, 19.5 and 19.2.

Isomer **46d** was obtained as an oil, $[\alpha]_D^{20}$ less than ± 1 (*c* 1.2, $CHCl_3$) (Found: C, 76.9; H, 9.7%; M^+, 358.2504); *m*/*z* 358 (M^+, 16%), 301 (100) and 231 (20); ν_{max}(neat)/cm^{-1} 1604, 1581, 1142 and 1103; δ_H 6.05 (1 H, d, *J* 2.6), 6.04 (1 H, d, *J* 2.6), 5.67 (2 H, s, 1′- and 2′-H), 3.74 (3 H, s, OCH_3), 3.73 (3 H, s, OCH_3), 2.90 (1 H, m, 4-H), 2.14 (1 H, dd, *J* 14.3 and 7.3, 3-H), 2.03 (1 H, m, 6′-H), 1.95 (1 H, m, 9-H), 1.85 (1 H, m, 5′-H), 1.64–1.69 (3 H, m, 3-, 10- and 7′-H), 1.48 (2 H, m, 5′- and 4′-H), 1.15–1.35 (2 H, m, 9-and 5′-H), 0.94 (3 H, d, *J* 6.9), 0.91 (3 H, d, *J* 6.9) and 0.90 (3 H, d, *J* 6.9) (4 × Me); δ_C 159.3, 159.0, 155.1, 133.1, 129.8, 108.9, 94.4, 92.0, 75.4, 55.2, 55.1, 44.4, 41.9, 39.4, 34.8, 31.8, 26.8, 26.0 24.1, 22.4, 21.5, 19.8 and 19.4.

2-Isopropyl-6,8-dimethoxy-4a-methyl-5-(3-methylbutyryl)-2,4a,9,9a-tetrahydro-1*H*-xanthene 47. This was obtained as an *oil*, $[\alpha]_D^{20}$ −71.2 (*c* 0.9, $CHCl_3$) (Found: C, 74.3; H, 9.0%; M^+, 386.2444. $C_{24}H_{34}O_4$ requires C, 74.57; H, 8.87%; M, 386.2457); *m*/*z* 386 (M^+, 42%), 329 (42), 251 (100) and 193 (62); λ_{max}(EtOH)/nm 277 (log ε 3.74) and 222 (sh); ν_{max}(neat)/cm^{-1} 1700, 1603 and 1111; δ_H 6.01 (1 H, s, 7-H), 5.62 (2 H, s, 3- and 4-H), 3.82 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 2.67 (2 H, d, *J* 6.6, 16-H_2), 2.63 (1 H, dd, *J* 16.8 and 6.6, 9-H), 2.38 (1 H, dd, *J* 16.8 and 8.6, 9-H), 2.20 (1 H, sep, *J* 6.6, 17-H), 2.12 (1 H, m, 9a-H), 2.03 (1 H, m, 2-H), 1.68 (3 H, m, 1-H_2 and 11-H), 1.39 (3 H, s, 14-H_3), 0.95 (6 H, d, *J* 6.6), 0.92 (3 H, d, *J* 6.6) and 0.90 (3 H, d, *J*, 6.6) (4 × Me); δ_C 204.8, 158.6, 155.8, 151.5, 132.0, 131.9, 113.2, 103.2, 87.2, 75.9, 56.0, 55.4, 54.2, 38.5, 33.8, 31.9, 27.8, 27.7, 24.9, 22.8 (2 C), 21.4, 20.0 and 19.7.

6′-Isopropyl-5,7-dimethoxy-8-(3-methylbutyryl)-3,4-dihydrospiro[2*H*-1-benzopyran-2,3′-cyclohexene] 48a. This was obtained as an *oil*, $[\alpha]_D^{20}$ less than ± 1 (*c* 0.8, $CHCl_3$) (Found: C, 74.3; H, 8.9%; M^+, 386.2485. $C_{24}H_{34}O_4$ requires C, 74.57; H, 8.87%; M, 386.2457); *m*/*z* 386 M^+, 32%), 343 (33), 329 (26), 251 (100) and 193 (44); λ_{max}(EtOH)/nm 277 (log ε 3.58) and 226 (sh); ν_{max}(neat)/cm^{-1} 1690, 1603, 1580 and 1100; δ_H 6.03 (1 H, s, 6-H), 5.85 (1 H, dd, *J* 9.9 and 1.8, 2′-H), 5.67 (1 H, ddd, *J* 9.9, 1.6 and 1.2, 1′-H), 3.83 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 2.62 (2 H, d, *J* 7.0, 10-H_2), 2.61 (2 H, m, 4-H_2), 2.22 (1 H, sep, *J* 7.0, 11-H), 2.04 (1 H, m, 7′-H), 1.40–1.95 (7 H, m), 0.92 (9 H, d, *J* 7.0) and 0.90 (3 H, d, *J* 7.0) (2 × Me); δ_C 204.9, 158.7, 156.0, 152.1, 135.7, 133.3, 129.2, 102.8, 87.2, 73.0, 56.0, 55.5, 54.0, 42.5, 32.9, 31.82, 31.77, 24.7, 22.8 (2 C), 21.1, 19.7, 19.4 and 16.0.

Isomer **48b** was obtained as an oil, $[\alpha]_D^{20}$ less than ± 1 (*c* 0.2, $CHCl_3$) (Found: C, 74.5; H, 8.7%; M^+, 386.2485); *m*/*z* 386 (M^+, 33%), 343 (35), 329 (33), 251 (100) and 193 (45); λ_{max}(EtOH)/nm 277 (log ε 3.48) and 226 (sh); ν_{max}(neat)/cm^{-1} 1690, 1603, 1580 and 1100; δ_H 6.03 (1 H, s, 6-H), 5.69 (2 H, s, 1′- and 2′-H), 3.83 (3 H, s, OCH_3), 3.77 (3 H, s, OCH_3), 2.61 (2 H, d, *J* 7.0, 10-H_2), 2.57 (2 H, t, *J* 7.0, 4-H_2), 2.22 (1 H, sep, *J* 7.0, 11-H), 2.03 (1 H, m, 7′-H), 1.60–1.95 (7 H, m), 0.92 (6 H, d, *J* 7.0), 0.91 (3 H, d, *J* 7.0) and 0.88 (3 H, d, *J* 7.0) (4 × Me); δ_C 204.9, 158.7, 156.0, 151.3, 133.3, 129.5, 113.6, 103.1, 87.2, 75.3, 55.9, 55.4, 54.1, 41.9, 32.9, 31.8, 30.7, 24.8, 22.8 (2 C), 22.3, 19.8, 19.4 and 16.2.

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