Pergamon

PII: S0031-9422(97)00118-0

Phytochemistry, Vol. 45, No. 6, pp. 1235–1247, 1997

0031-9422/97 $17.00+0.00

BIBENZYL DERIVATIVES FROM *PELLIA EPIPHYLLA**

FRANK CULLMANN, HANS BECKER,† ENRIQUE PANDOLFI,‡ ECKARD ROECKNER§ and THEOPHIL EICHER§

Fachrichtung 12.3 Pharmakognosie und Analytische Phytochemie der Universität des Saarlandes, Postfach 151150, D-66041 Saarbrücken, Germany; ‡Catedra de Quimica Organica, Facultad de Quimica, Universidad de la Republica, Montevideo, Uruquay; §Fachrichtung 11.2 Organische Chemie der Universität des Saarlandes, D-66041 Saarbrücken, Germany

(*Received* 11 *November* 1996)

Key Word Index—*Pellia epiphylla*; Hepaticae; bibenzyls; pellepiphyllin; perrottetin-type bisbibenzyls; perrottetin-type bisbibenzyl dimer; synthesis; structure revision.

Abstract—Reinvestigation of the phenolic constituents from a diethyl ether extract of gametophytes of *Pellia epiphylla* yielded pellepiphyllin, 7-hydroxypellepiphyllin, perrottetin E, perrottetin E-11-methyl ether, 14′-hydroxyperrottetin E, 10′-hydroxyperrottetin E, 10′-hydroxyperrottetin E-11-methyl ether, 10,10′-dihydroxyperrottetin E and 13′,13‴-bis(10′-hydroxyperrottetin E). The structures of three bisbibenzyls published earlier are revised. The new structures have been elucidated by two-dimensional NMR-techniques and chemical synthesis. In contrast to previous publications, pellepiphyllin has been found as a constituent of *P. epiphylla*.

INTRODUCTION

In earlier publications [1, 2], we reported the isolation of perrottetin-type bisbibenzyls and lignans from a methanolic extract of *Pellia epiphylla*, a common liverwort in Central Europe. Studies on the synthesis of these bisbibenzyls revealed that the substitution pattern of two perrottetins has to be revised. A reinvestigation of the lipophilic extract of this plant yielded greater amounts of these substances together with new compounds. Application of two-dimensional NMR-techniques allowed the determination of the new structures unambiguously together with the first assignment of ^{13}C NMR data for perrottetins. The final proof of the new structural types was achieved by independent synthesis of five of the compounds presented in this paper.

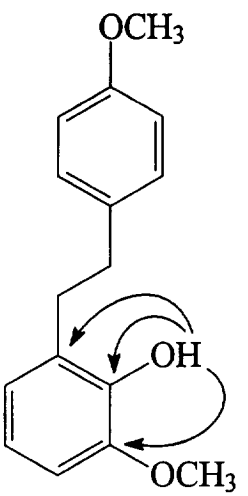


Fig. 1. Important HMBC correlations of compound **1**.

RESULTS AND DISCUSSION

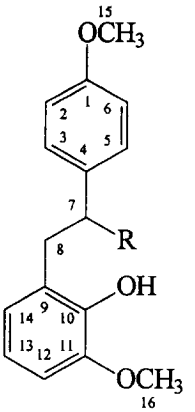
From the diethyl ether extract of *P. epiphylla*, obtained as previously reported [1], two bibenzyls, six bisbibenzyls and one dimeric bisbibenzyl were obtained. Compound **1** has the molecular formula $C_{16}H_{18}O_3$ ([M]$^+$ *m/z* 258). The ^{13}C NMR spectra revealed the existence of a bibenzyl derivative with two benzylic methylenes (δ_C 35.1, *t*; 32.2, *t*), 12 benzene ring carbon atoms and two methyl ethers (δ_C 55.2, *q*; 56.0, *q*). The ^1H NMR showed the AA′BB′ spin system of a *para*-substituted benzene ring (δ_H 7.13 and 6.81 2H, *d*, $J = 8.6$ Hz each) and three signals of higher-order spin systems, allowing no decision to be made on the substitution pattern of the second benzene ring. This problem could be solved by the observation of a cross-peak for the phenolic proton in the HMBC spectrum (Fig. 1). Correlations were detected with the quaternary carbon atom C-9 (δ_C 127.8, *s*), the atom bearing the phenolic group (C-10, δ_C 143.6, *s*) and another hydroxylated aromatic carbon atom (C-11,

* Part 108 in the series of 'Arbeitskreis Chemie und Biologie der Moose'. For part 107, see ref. [19].

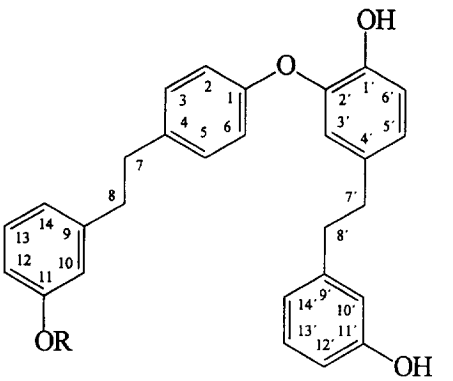
† Author to whom correspondence should be addressed.

δ_C 146.4, *s*). Thus, in compound **1**, the two oxygen functions of the second ring have to be at C-10 and C-11, with the methyl ethers at C-1 and C-11, suggesting the structure of pellepiphyllin. Since no new, reliable NMR data were available and no conclusive information could be drawn from the proton NMR, pellepiphyllin was synthesised by a route providing an unambiguous structural proof, namely by catalytic hydrogenation of the stilbene derivative **12** obtained from Wittig reaction of 2-benzyloxy-3-methoxybenzaldehyde (**10**) and the (*p*-methoxybenzyl)-phosphonium salt **11** (Scheme 1). Pellepiphyllin is described as a substance, which should occur only in *P. neesiana* but not in *P. epiphylla* [3, 4]. The plant material investigated had been identified unequivocally as *P. epiphylla* in the fertile state, so the statement of Benešová and Herout no longer holds true. As Huneck and Schreiber reported the occurrence of the corresponding unmethylated compound from *P. endiviifolia* [5], this substitution pattern is characteristic for the whole genus.

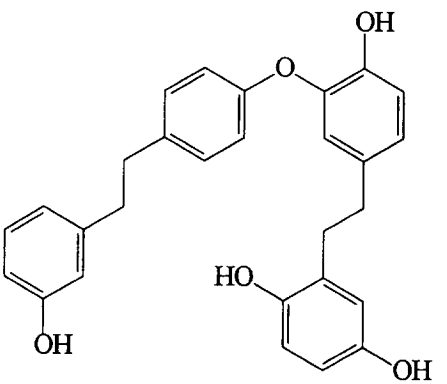
The ^{1}H NMR spectrum of compound **2**, negative CI spectrum $[M-H]^-$ *m/z* 273 ($C_{16}H_{18}O_4$), showed a close similarity to pellepiphyllin. The chemical shifts



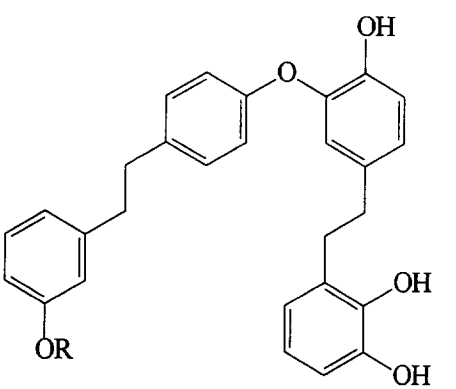
1 R = H
2 R = OH



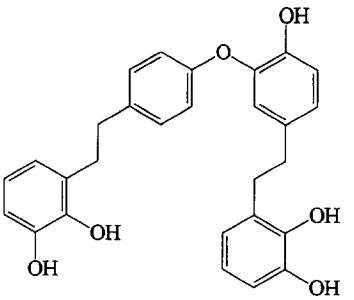
3 R = H
4 R = Me



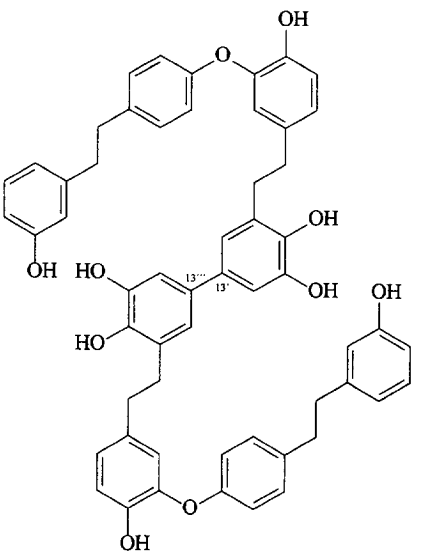
5



6 R = H
7 R = Me



8



9

and the spin systems of the aromatic protons were nearly identical but instead of the usual signal of the aliphatic bridge, two signals were detected at δ 4.96 ppm (1H, *t*, J = 6.3 Hz, H-7) and δ 3.03 (2H, *d*, J = 6.3 Hz, H-8) indicating hydroxylation of this bridge. The highfield shift of H-3/5 compared with pellepiphyllin suggested the structure 7-hydroxypellepiphyllin, which was confirmed by the NOESY correlations

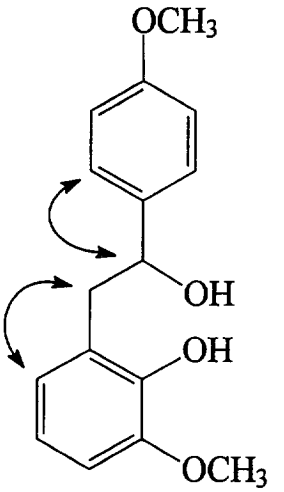
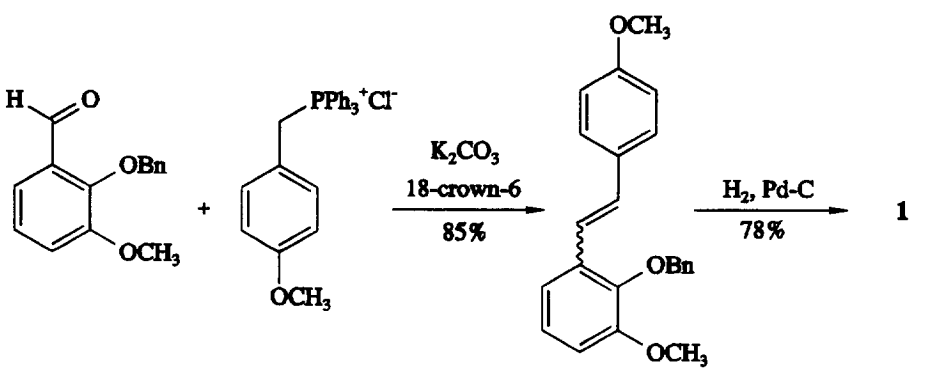


Fig. 2. Important NOE interactions of compound **2**.

from H-7 to H-3/5 and H-8 to H-14 (Fig. 2). 7-Hydroxypellepiphyllin has not been reported so far. Although compound **2** contains an asymetrically substituted carbon atom, no optical rotation can be given. This is due to the small amount isolated (1.8 mg), together with an apparently small value of rotation. Optical rotation at 436 and 365 nm suggested the existence of the laevorotatory enantiomer.

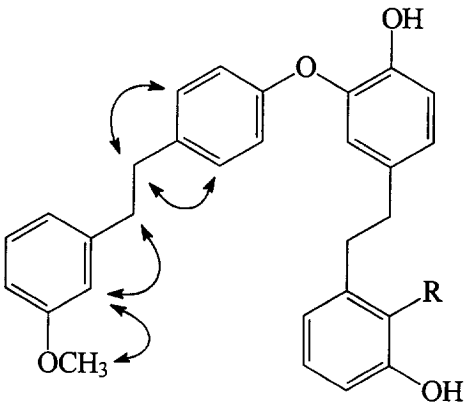
Compound **3**, $C_{28}H_{26}O_4$ ($[M]^+$ *m/z* 426.1834) could be identified from its ^{1}H NMR spectrum as perrottetin E [1, 6]. With 2.36 g isolated, perrottetin E is the major compound in *P. epiphylla*.

Compound **4**, $C_{29}H_{28}O_4$ ($[M]^+$ *m/z* 440), was a methyl ether of perrottetin E according to its molecular formula and its NMR spectra (δ_H 3.78, 3H, *s*, H-15; δ_C 55.1, *q*, C-15). The position of the ether could be easily detected by a NOESY spectrum (Fig. 3). A correlation was detected between the AA′BB′ system of the *para*-substituted ring (δ_H 7.11, H-3/5) and the signal of the left bridge (δ_H 2.89, H-7/8). The latter signal showed a cross-peak with a doublet of doublets (δ_H 6.72, J = 1.5 and 1.5 Hz), which must be H-10. H-10 finally showed a correlation with the signal of the methyl ether, resulting in the structure of a perrottetin E-11-methyl ether. This substance is a new



10 **11** **12**

Scheme 1. Synthesis of compound **1**.



4 R = H

7 R = OH

Fig. 3. Important NOE interactions of compounds **4** and **7**.

natural product; Hashimoto *et al.* reported the isomeric perrottetin E-11′-methyl ether from *P. endiviifolia* [7]. The remaining NOESY correlations allowed the assignment of all ^{1}H NMR signals (Table 2).

Compound **5**, $C_{28}H_{26}O_5$ ([M]$^+$ *m/z* 442.1778), was one of the bisbibenzyls reported earlier, whose structure had been elucidated as 14-hydroxyperrottetin E due to the similarities to 14-hydroxyperrottetin E-11-methyl ether, isolated from *P. endiviifolia* [7]. However, studies on the synthesis of **5** [8] revealed that the substitution pattern of a 2-substituted hydroquinone moiety was erroneously attributed to the 'left one' of the terminal benzene rings. Thus, the revised structure of 14′-hydroxyperrottetin E has to be attributed to compound **5** and was proven by independent synthesis [8].

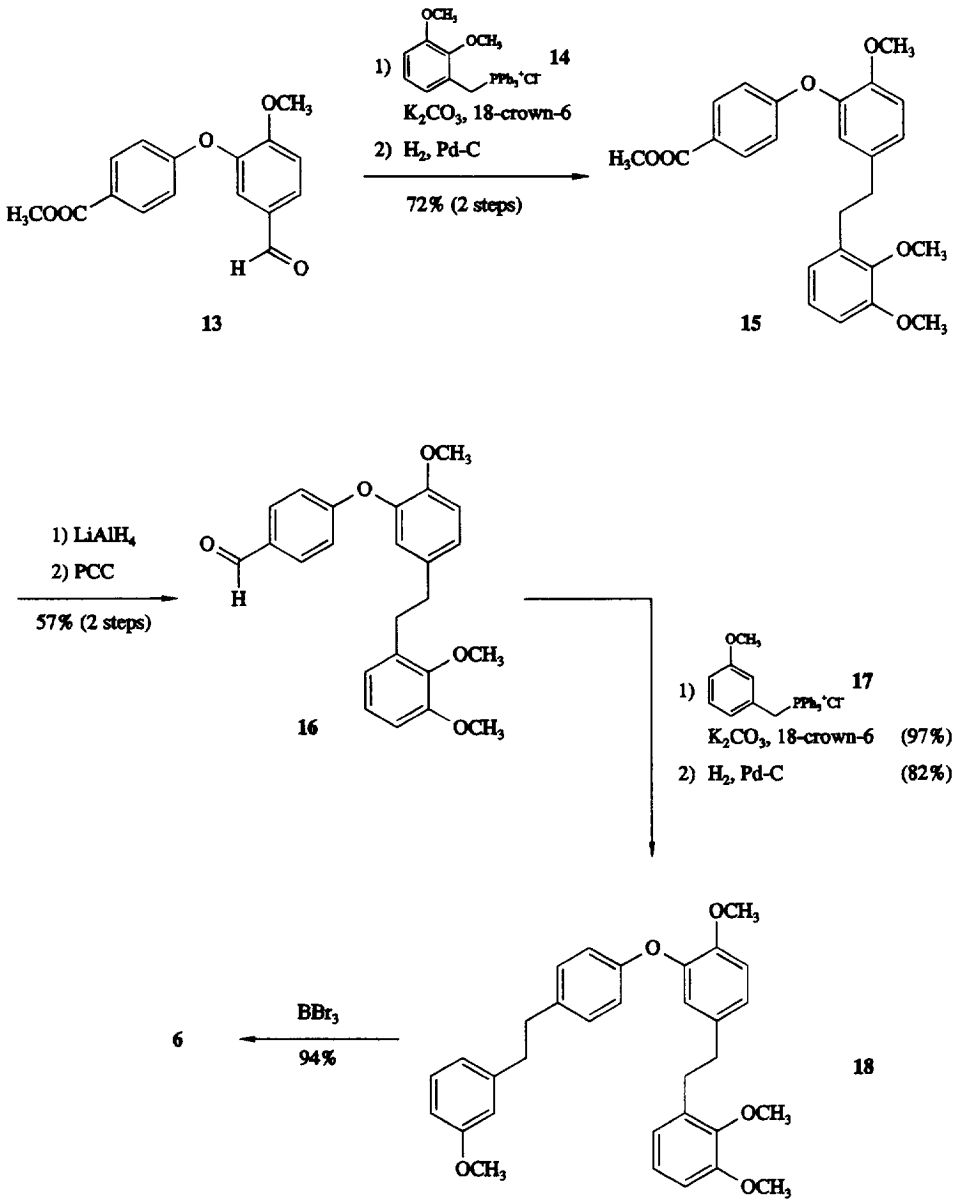
Compound **6**, $C_{28}H_{26}O_5$ ([M]$^+$ *m/z* 442.1777) reported earlier as 14′-hydroxyperrottetin E is the second bisbibenzyl, whose structure has to be revised, since the 14- and 14′-hydroxyperottetins E obtained by chemical synthesis showed a substitution pattern of the aromatic protons in the ^{1}H NMR different from the natural product **6** [8]. The original structure had been proposed on the basis of the NOE-effects between the bridge and only one aromatic ring proton and the lack of the triplet signal of H-13′. However, in the course of the structure elucidation of pellepiphyllin **1**, we learned that even in the case of an *ortho*-substitution, this signal may appear as a singlet due to the effect of higher order spin systems. Thus, for compound **6** the structure of a 10′-hydroxyperrottetin E had to be taken into consideration; this was confirmed by synthesis [9] according to the protocol shown in Scheme 2. The diphenyl ether aldehydoester (**13**) [10] was subjected to a Wittig reaction with the (2,3-dimethoxybenzyl)phosphonium salt (**14**) in the presence of K_2CO_3-18-crown-6 and the stilbene intermediate formed by carbonyl olefination was hydrogenated (H_2, Pd-C) to give the bibenzyl ester (**15**), which was then reduced with $LiAlH_4$ to the primary alcohol and re-oxidized with PCC to yield the aldehyde (**16**). In **16**, the second bibenzyl moiety was introduced as before by Wittig reaction with the (*m*-methoxybenzyl)phosphonium salt (**17**) in the presence of K_2CO_3 18-crown-6 followed by catalytic hydrogenation (H_2 Pd-C) giving rise to the tetramethoxyperrottetin (**18**), whose demethylation by means of BBr_3 led to 10′-hydroxyperrottetin E (**6**). being identical in all spectroscopic data with the natural product.

Compound **7**, $C_{29}H_{28}O_5$ ([M]$^+$ *m/z* 456), according to ^{1}H and ^{13}C NMR spectra, had to be a methyl ether derivative of compound **6** (δ_H 3.78, *s*, 3H, H-15; δ_C 55.2, *q*, C-15). Again the NOESY spectrum (Fig. 3) showed the presence of a methoxyl group at C-11. Correlations were seen between the methyl group to H-10 (δ_H 6.71, *dd*, *J* = 1.9 and 1.9 Hz) and from this signal to the bridge (δ_H 2.89, 4H, *s*, H-7/8). The remaining correlations, together with H,H-COSY, HSQC and HMBC allowed the assignment of all ^{1}H and ^{13}C NMR signals (Tables 2 and 3).

Compound **8**, $C_{28}H_{26}O_6$ ([M]$^+$ *m/z* 458.1731) was the third of the reported structures, which have to be revised. The structure was given as 14,14′-dihydroxyperrottetin E from the ^{13}C NMR data, which showed the substitution pattern of compound **6** in both of the terminal phenyl rings. As a consequence, the structure of **8** has to be revised to be 10,10′-dihydroxyperrottetin E and was proven unambiguously by synthesis according to the protocol shown in Scheme 3.

Two-fold Wittig reaction of the diphenyl ether dialdehyde **21** [easily accessible by S_NAr reaction of *p*-fluorobenzaldehyde (**19**) and isovanilline (**20**)] with the (2,3-dimethoxybenzyl)-phosphonium salt (**14**) in the presence of K_2CO_3 18-crown-6 gave rise to the bisstilbene (**23**) as a mixture of *E*/*Z*-stereoisomers, which was hydrogenated (H_2/Pd-C) to the pentamethoxyperrottetin (**22**). Demethylation with BBr_3 yielded 10,10′-dihydroxyperrottetin E **8**, being identical in all spectroscopic data to the natural product.

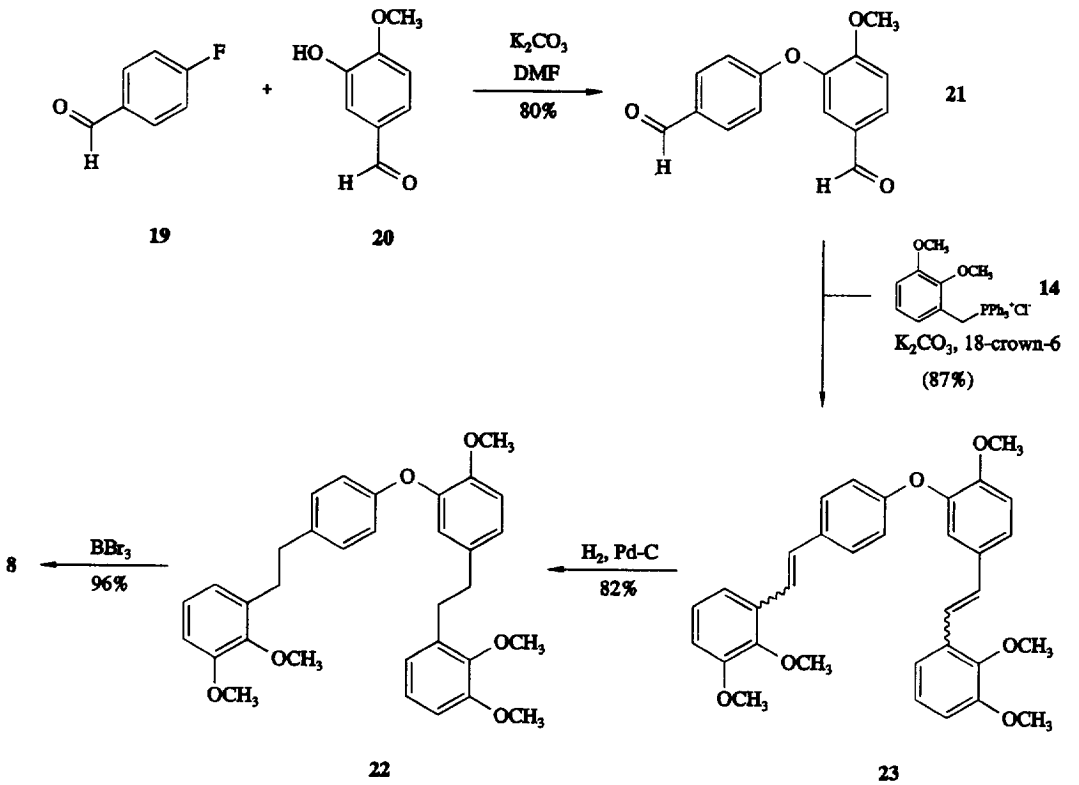
^{1}H and ^{13}C NMR data of compound **9**, $C_{56}H_{50}O_{10}$ ([M]$^+$ *m/z* 882), showed the signals of a bisbibenzyl, but according to its mass spectrum results from the oxidative combination of two perrottetin units. Assignment of the ^{1}H and ^{13}C NMR signals for rings A, B, and C could be easily achieved by comparison with data of the perrottetins discussed above. Comparison between the ^{13}C NMR data of ring D with those of 10′-hydroxyperrottetin E showed a downfield shift of C-13′ by 13 ppm (δ_C 132.9, *s*), suggesting substitution at this centre; ^{1}H NMR data confirmed this assumption. Only two doublets with *meta*-coupling were observed (δ_H 6.65, *d*, *J* = 1.9 Hz, H-12′ and 6.47, *d*, *J* = 1.9 Hz, H-14′). Thus, for compound **9**, the symmetrical structure of a 13′,13‴-bis(10′-hydroxyperrottetin E) seemed to be reasonable and was proven by chemical synthesis as shown in Scheme 4. Firstly, the tetramethoxysubstituted biphenyl-3,3′-dialdehyde (**27**) was prepared by the Pd(0)-assisted



Scheme 2. Synthesis of compound **6**.

Suzuki biphenyl coupling from the formylboronic acid (**28**) and 5-bromo-2,3-dimethoxy benzaldehyde (**25**) obtained from 2,3-dimethoxy benzaldehyde (**24**) via **25**/**26**. Secondly, the diphenyl ether (**29**) bearing an appropriate benzylic phosphonium salt moiety was obtained by reaction of the precursor **30** (for which an expedient synthesis was elaborated starting from isovanilline [10]) with $SOCl_2$ followed by triphenyl phosphine. Finally, the two building blocks **27** and **29** were combined in a two-fold Wittig reaction. The bisstilbene (**31**) obtained as an *E*/*Z*-mixture was hydrogenated to the octamethoxybisperrottetin (**32**), which was demethylated by means of BBr_3 to the bisperrottetin (**9**) identical in all spectroscopic respects with the natural product. Compound **9** is the fifth representative of the hitherto small group of dimeric bisbibenzyls, previously isolated from *Blasia pusilla* [11] and *Ricciocarpos natans* [12]. Another dimeric bisbibenzyl, cruciatin, connected by two oxygen bridges was reported recently by Hashimoto and Asakawa [13] from *Lunularia cruciata*.

The bisbibenzyls reported in this paper showed close relationship to those from *P. endiviifolia* [7] but with significant differences. The former have substitution in ring D and are methylated in ring B, while in the latter, the hydrochinon moiety is in ring B and the methyl ether in ring D. It would be worthwhile checking the third species of this genus, *P. neesiana*, for the substitution pattern of its bisbibenzyls. If these are, as in the case of pellepiphyllin, identical to *P. epiphylla*, it would provide further evidence for the close relationship between these species, as proposed



Scheme 3. Synthesis of compound **8**.

by Asakawa, based on the sesquiterpenoid pattern [14] and the systematic evidence of Schuster [15] and Grolle [16].

EXPERIMENTAL

Solvents used for spectral measurements: $CDCl_3$ for NMR; ^1H NMR: 400 MHz; ^{13}C NMR: 100 MHz for 1D, 500 and 125 MHz for 2D techniques, respectively. Chemical shifts are given in δ values from TMS.

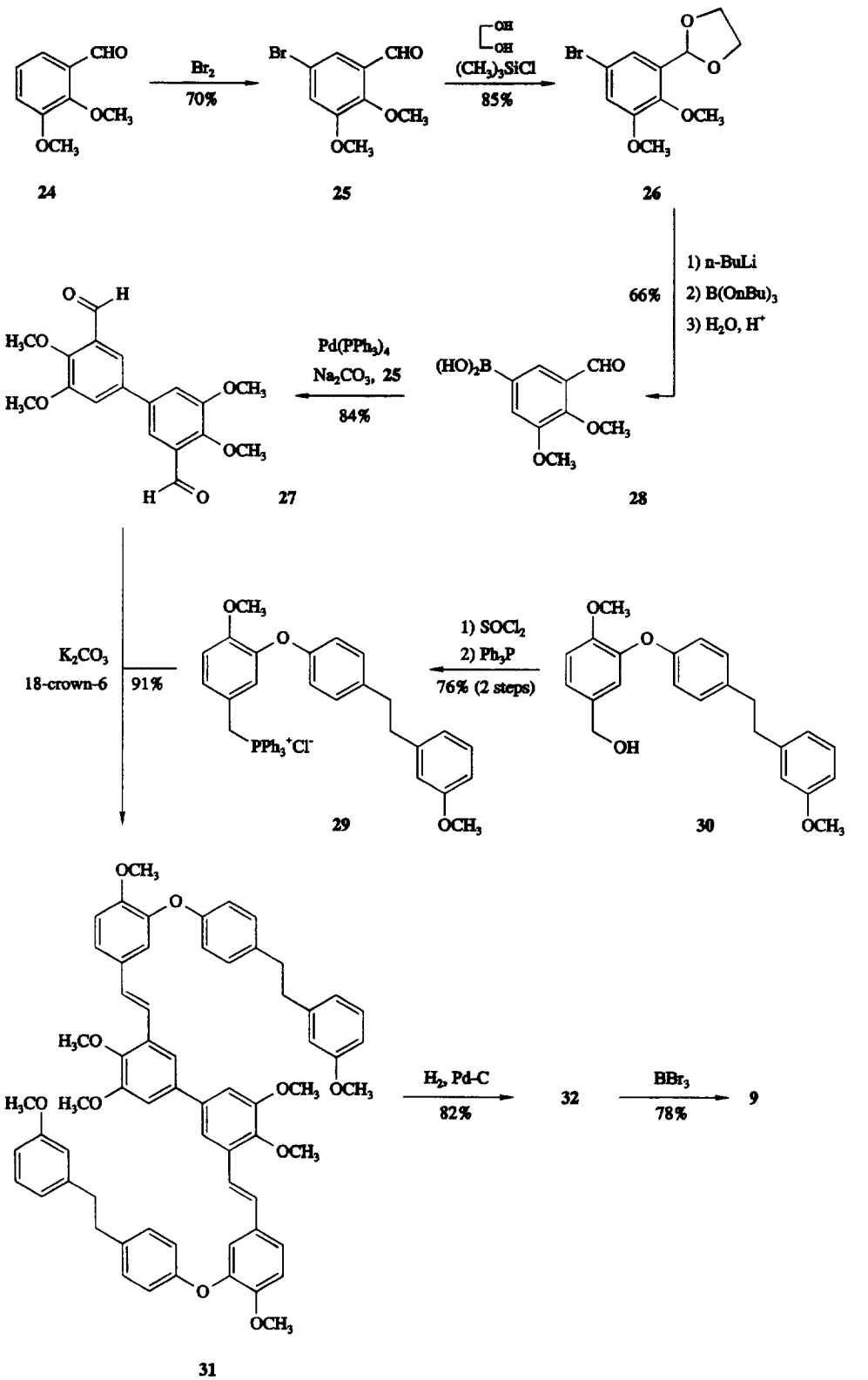
Plant material. Pellia epiphylla was collected in Hassel, Saarland, Germany in June 1992 and identified by F.C. Fertile gametophytes were collected from the same place in March 1995 and identified by Prof. Mues, Fachrichtung Botanik, Universität des Saarlandes. Voucher specimen are deposited in the Herbarium of the Fachrichtung 12.3, Pharmakognosie und Analytische Phytochemie, Universität des Saarlandes.

Extraction and isolation. Freeze-dried, powdered gametophytes (750 g) were extracted with Et_2O. The extract was evapd *in vacuo* and chromatographed on Sephadex LH-20 using MeOH–CH_2Cl_2 (1:1) as eluent to yield four main frs. Fr. 1 was chromatographed on silica gel via VLC using a hexane–EtOAc gradient. Perrottetin E-11-methyl ether (**4**) (204 mg) was obtained as a pure compound. Further purification of other frs by HPLC afforded pellepiphyllin (**1**) (51 mg) (silica gel, hexane–TBME, 19:1) and 7-hydroxypellepiphyllin (**2**) (1.8 mg) (diol-modified silica gel, hexane–EtOAc, 3:1). Fr. 2 was also chromatographed on diol-modified silica gel. Two of the three VLC-frs were pure compounds: perrottetin E (**3**) (1.39 g) and 10′-hydroxyperrottetin E (**6**) (49.8 mg). The remaining fr. was separated by HPLC (hexane–EtOAc, 7:3) to yield 10′-hydroxyperrottetin E-11-methylether (**7**) (85.4 mg), another 15.8 mg of compound **4** and another 33 mg of perrottetin E (**3**). VLC of fr. 3 on diol-modified silica gel yielded two frs. Further purification of the first fr. by MPLC (hexane–EtOAc, 3:2) yielded 996 mg of 10′-hydroxyperrottetin E (**6**), and another fr. from which 215 mg of perrottetin E was obtained by HPLC (hexane–EtOAc, 7:3). Purification of the latter fr. by reverse-phase chromatography (RP18, MeOH–H_2O, 13:7) afforded 14′-hydroxyperrottetin E (**5**) (131 mg). The last main fr. yielded, after VLC on diol-modified silica gel using a hexane–EtOAc gradient, 10,10′-dihydroxyperrottetin E (**8**) (613 mg) and another fr., from which 13′,13‴-bis(10′-hydroxyperrottetin E) (**9**) (15.3 mg) was obtained by HPLC (RP18, MeOH–H_2O, 3:7).

Compound **1**. IR ν cm^{-1}: 3505, 2990, 2930, 2830, 1615, 1595, 1510, 1480, 1445, 1360, 1300, 1275, 1245, 1220, 1180, 1080, 1035, 915, 825, 775, 730, 700. ^1H and ^{13}C NMR: Table 1. EIMS *m/z* (rel. int.): 258 $[M]^+$ (9), 137 (7), 121 (100).

Compound **2**. IR ν cm^{-1}: 3400, 2920, 2850, 1610, 1510, 1480, 1270, 1240, 1170, 1130, 1030, 820; ^1H and ^{13}C NMR: Table 1. CIMS $[M-H]^-$ *m/z* 273.

Compound **4**. IR ν cm^{-1}: 3400, 3040, 2920, 2860, 1590, 1510, 1450, 1270, 1210, 1160, 1040, 780, 690. ^1H NMR: Table 2. ^{13}C NMR; Table 3. EIMS *m/z* (rel.



Scheme 4. Synthesis of compound **9**.

int.): 440 $[M]^+$ (4), 319 (33), 211 (17), 107 (18), 85 (39), 83 (60), 43 (100).

Compound **5**. IR ν cm^{-1}: 3400, 2940, 2860, 1590, 1510, 1400, 1280, 1220, 1170, 1110, 1020; ^1H NMR: Table 2. ^{13}C NMR: Table 3. HRMS: found $[M]^+$ m/z 442.1778; $C_{28}H_{26}O_5$ requires: 442.1780. EIMS m/z (rel. int.): 442 (100), 335 (59), 320 (90), 319 (93), 199 (21), 107 (28).

Table 1. NMR spectral data of compounds **1** and **2**

H	1	2	C	1	C	1
H-2/6	6.81 *d* (8.6)	6.86 *d* (8.8)	C-1	157.8 *s*	C-9	127.8 *s*
H-3/5	7.13 *d* (8.6)	7.31 *d* (8.8)	C-2	113.7 *d*	C-10	143.6 *s*
H-7	2.85 *m*	4.96 *t* (6.3)	C-3	129.3 *d*	C-11	146.4 *s*
H-8	2.89 *m*	3.03 *d* (6.3)	C-4	134.5 *s*	C-12	108.5 *d*
H-12	6.72 *h.o.*	6.76 *h.o.*	C-5	129.3 *d*	C-13	119.2 *d*
H-13	6.74 *h.o.*	6.77 *h.o.*	C-6	113.7 *d*	C-14	122.4 *d*
H-14	6.69 *h.o.*	6.66 *h.o.*	C-7	35.1 *t*	C-15	55.2 *q*
H-15	3.77 *s*	3.79 *s*	C-8	32.2 *t*	C-16	56.0 *q*
H-16	3.87 *s*	3.88 *s*				
OH	5.68 *s*					

h.o.: higher order spin system.

Compound **6**. IR ν cm^{-1}: 3400, 3040, 2920, 2860, 1600, 1500, 1480, 1460, 1440, 1360, 1280, 1220, 1170, 1100, 1070. ^1H NMR: Table 2. ^{13}C NMR: Table 3. HRMS: found $[M]^+$ *m/z* 442.1778; $C_{28}H_{26}O_5$ requires 442.1780. EIMS *m/z* (rel. int.): 442 (40), 335 (57), 320 (24), 319 (100), 211 (22), 199 (26), 107 (38).

Compound **7**. IR ν cm^{-1}: 3400, 3040, 2920, 2860, 1590, 1500, 1270, 1220, 1160, 1100, 1090, 960, 820, 980. ^1H NMR: Table 2. ^{13}C NMR: Table 3. EIMS *m/z* (rel. int.): 456 $[M]^+$ (14), 335 (40), 333 (24), 227 (14), 211 (24), 199 (30), 135 (24), 123 (52), 121 (51), 107 (69) 91 (42), 57 (48), 55 (55), 43 (100).

Compound **8**. IR ν cm^{-1}: 3400, 3040, 2920, 2860, 1620, 1600, 1505, 1480, 1440, 1350, 1280, 1220, 1170, 1110, 1070. ^1H NMR: Table 2. ^{13}C NMR: Table 3. HRMS: found $[M]^+$ *m/z* 458.1731; $C_{28}H_{26}O_6$ requires 458.1729. EIMS *m/z* (rel. int.): 458 (62), 336 (27), 335 (100), 199 (31), 123 (18), 107 (21).

Compound **9**. IR ν cm^{-1}: 3400, 3040, 2920, 2840, 1590, 1500, 1450, 1270, 1210, 1160, 1100, 820. ^1H NMR: Table 2. ^{13}C NMR: Table 3. EIMS *m/z* (rel. int.): 882 $[M]^+$ (2), 458 (14), 335 (34), 199 (11), 107 (41), 28 (100).

General synthetic procedures. (A) *Wittig reaction.* The aryl aldehyde (10 mM) and the benzyl phosphonium salt (12 mM) were dissolved in dry Cl_2Cl_2 (150 mM). K_2CO_3 (1.66 g, 12 mM) and a catalytic amount of 18-crown-6 (*ca* 10 mg) was added and the reaction mixt. heated under reflux for 12 hr. Excess of K_2CO_3 was filtered off and the solvent removed *in vacuo*. The crude product thus obtained was purified by CC on silica with the eluent noted. (B) *Catalytic hydrogenation.* The stilbene derivative (10 mM) was dissolved in freshly distilled EtOAc (100 ml), the catalyst (5% Pd on charcoal, 0.50 g) added and hydrogenation performed (5 bar H_2 pres., 16 hr). Catalyst was filtered off, the solvent removed *in vacuo* and the residue purified as noted by chromatography and/or recrystallization. (C) *Demethylation with boron tribromide.* A soln of the Me ether component (1 mM) in dry CH_2Cl_2 (50 ml) was cooled to $-78°C$ and a 1 M soln of BBr_3 in CH_2Cl_2 (2 mM BBr_3 per OCH_3 group) was added dropwise; the temp. should not exceed $-60°$. When addition was complete, the reaction mixt. was allowed to rise to room temp. (12 hr). After careful addition of H_2O (40 ml), the organic phase was sepd, the aq. phase extracted twice with Et_2O (50 ml), the combined organic phases washed twice with H_2O (30 ml) and dried ($MgSO_4$). Solvents were removed *in vacuo* and the crude product purified as noted.

Synthesis of pellepiphyllin (**1**). (a) Benzaldehyde (**10**) [17] (1 g, 4.1 mM), phosphonium salt (**11**) [10] (2.07 g, 4.95 mM) and K_2CO_3 (0.68 g, 4.95 mM) were reacted according to procedure **A** in CH_2Cl_2 (80 ml). Purification by chromatography (silica gel, eluent CH_2Cl_2). Yield: 1.21 g (85%) **12**, colourless oil. ^1H NMR ($CDCl_3$): δ 7.50–6.71 (12.6H, *m*), 6.60 (0.7H, *d*, J = 12.2 Hz), 6.53 (0.7H, *d*, J = 12.2 Hz), 5.25 (1.4H, *s*), 5.00 (0.6H, *s*), 3.87 (1.0H, *s*), 3.86 (2.0H, *s*), 3.76 (1.0H, *s*), 3.75 (2.0H, *s*). ^{13}C NMR ($CDCl_3$): δ 158.7, 153.3, 153.1, 146.1, 137.9, 132.6, 132.2, 130.6, 130.3, 130.2, 129.7, 129.3, 128.5, 128.4, 128.3, 128.0, 127.8, 124.4, 124.2, 123.6, 122.2, 121.4, 117.8, 114.1, 113.5, 111.5, 111.2, 75.5, 74.9, 55.9, 55.3, 55.2. CI-MS (120 eV), *m/z* (rel. int.): 347 $[M+1]^+$ (19), 346 $[M]^+$ (83), 256 (30), 255 (100), 254 (23), 240 (8.4), 228 (17), 227 (66), 212 (8.9), 210 (8.3), 197 (12), 196 (8.6), 121 (37), 92 (8.4), 91 (36), 57 (11). (b) The silbene derivative (**12**) (1.12 g, 3.2 mM) was hydrogenated according to procedure **B** in EtOAc (100 ml). After work-up, the product was obtained directly in a pure form. Yield: 0.65 g (78%) **1**, colourless crystals, mp 71°. IR (KBr): ν cm^{-1}: 3505. ^1H NMR ($CDCl_3$): δ 7.14 (2H, *d*, J = 8.7 Hz), 6.82 (2H, *d*, J = 8.7 Hz), 6.75–6.69 (3H, *m*), 5.73 (1H, *s*), 3.86 (3H, *s*), 3.77 (3H, *s*), 2.91–2.89 (2H, *m*), 2.87–2.85 (2H, *m*). ^{13}C NMR ($CDCl_3$): δ 157.8, 146.4, 143.7, 134.6, 129.4, 127.9, 122.5, 119.2, 113.8, 108.6, 56.0, 55.3, 35.1, 32.2. EI-MS (70 eV), *m/z* (rel. int.): 259 $[M+1]^+$ (3.7), 258 $[M]^+$ (23), 137 (25), 122 (34), 121 (100), 94 (10), 91 (22), 81 (11), 79 (11), 78 (28), 77 (32), 65 (13), 63 (11), 57 (11), 51 (16), 43 (23), 41 (16), 39 (19).

Synthesis of compound **6**. (a) The diphenylether aldehyde (**13**) [10] (2 g, 7.0 mM) and the phosphonium salt (**14**) [10] (3.76 g, 8.4 mM) were reacted according to procedure A. The crude product was purified by chromatography (silica gel, eluent CH_2Cl_2) and recrys-

Table 2. ^{1}H NMR spectral data of compounds **4–9**

H	**4**	**5**	**6**	**7**	**8**	**9**
H-2/6	6.85 *d* (8.6)	6.78 *d* (8.5)	6.81 *d* (8.5)	6.84 *d* (8.6)	6.82 *d* (8.6)	6.73 *d* (8.5)
H-3/5	7.11 *d* (8.6)	7.01 *d* (8.5)	7.05 *d* (8.5)	7.10 *d* (8.6)	7.09 *d* (8.6)	6.93 *d* (8.5)
H-7/8	2.89 *s*	2.81 *s*	2.84 *s*	2.89 *s*	2.89 *br s*	2.80 *s*
H-10	6.72 *dd* (1.5, 1.5)	6.52 *br s*	6.58 n.r.	6.71 *dd* (1.9, 1.9)	—	6.50 *dd* (1.7, 1.7)
H-12	6.74 *br dd* (8.4, 2.1)	6.61 *br d* (7.8)	6.74 *br d* (8.3)	6.75 *br dd* (8.3, 2.6)	6.69 n.r.	6.66 *br dd* (8.1, 2.0)
H-13	7.20 *t* (7.7)	7.06 *t* (7.8)	7.13 *t* (7.8)	7.20 *t* (7.8)	6.70 n.r.	7.07 *t* (7.8)
H-14	6.68 *br d* (7.6)	6.66 *br d* (7.8)	6.64 *br dd* (7.8, 2.1)	6.78 *br d* (7.6)	6.62 n.r.	6.61 *br dd* (8.1, 2.0)
H-3′	6.61 *d* (2.0)	6.60 *d* (1.9)	6.60 n.r.	6.62 *d* (1.9)	6.63 n.r.	6.56 *d* (1.8)
H-5′	6.82 *dd* (8.2, 2.0)	6.77 n.r.	6.85 *dd* (8.2, 1.9)	6.86 *dd* (8.5, 1.9)	6.83 *dd* (8.5, 1.9)	6.81 *dd* (8.2, 1.8)
H-6′	6.93 *d* (8.1)	6.85 *d* (8.2)	6.94 *d* (8.2)	6.95 *d* (8.5)	6.94 *d* (8.5)	6.88 *d* (8.2)
H-7′	2.76 *s*	2.78 *s*	2.77 *m*	2.77 *m*	2.78 *m*	2.80 *m*
H-8′	2.76 *s*	2.78 *s*	2.77 *m*	2.84 *m*	2.83 *m*	2.80 *m*
H-10′	6.56 *dd* (1.7, 1.7)	6.43 *d* (2.1)	—	—	—	—
H-12′	6.62 *br dd* (8.3, 2.0)	6.45 *dd* (8.3, 2.1)	6.66 h.o.	6.66 h.o.	6.69 n.r.	6.65 *d* (1.9)
H-13′	7.09 *t* (7.8)	6.53 *d* (8.3)	6.67 h.o.	6.67 h.o.	6.70 n.r.	—
H-14′	6.66 *br d* (7.6)	—	6.57 n.r.	6.58 h.o.	6.58 h.o.	6.47 *d* (1.9)
H-15	3.78 *s*	—	—	3.78 *s*		—

h.o., higher order spin system; n.r., peaks not resolved.

Table 3. ^{13}C NMR spectral data of compounds **4–9**

C	4	5	6	7	8	9
C-1	155.0 *s*	155.2 *s*	155.0[a] *s*	154.9 *s*	154.7 *s*	155.2 *s*
C-2	117.7 *d*	117.7 *d*	117.4 *d*	117.8 *d*	117.8 *d*	117.4 *d*
C-3	129.6 *d*	129.8 *d*	129.6 *d*	129.7 *d*	129.7 *d*	129.6 *d*
C-4	136.7 *s*	136.6 *s*	136.4 *s*	136.6 *s*	137.1 *s*	136.4 *s*
C-5	129.6 *d*	129.8 *d*	129.6 *d*	129.7 *d*	129.7 *d*	129.6 *d*
C-6	117.7 *d*	117.7 *d*	117.4 *d*	117.8 *d*	117.8 *d*	117.4 *d*
C-7	36.8[a] *t*	36.8 *t*	36.6 *t*	36.6 *t*	35.2 *t*	36.7 *t*
C-8	37.8[b] *t*	37.8 *t*	37.6 *t*	37.9 *t*	32.0 *t*	37.6 *t*
C-9	143.3[c] *s*	143.4[a] *s*	143.2 *s*	143.2 *s*	128.5 *s*	143.2 *s*
C-10	114.4 *d*	115.8 *d*	115.5 *d*	114.4 *d*	142.2 *s*	115.4 *d*
C-11	159.5 *s*	156.3 *s*	155.8[a] *s*	159.5 *s*	143.2 *s*	156.3 *s*
C-12	111.3 *d*	113.0 *d*	112.8 *d*	111.3 *d*	113.3 *d*	112.7 *d*
C-13	129.3 *d*	129.2[b] *d*	129.3 *d*	129.3 *d*	120.1 *d*	129.2 *d*
C-14	120.9 *d*	120.4 *d*	120.4 *d*	121.0 *d*	122.1 *d*	120.0 *d*
C-1′	145.4 *s*	145.6 *s*	145.3 *s*	145.5 *s*	145.1 *s*	145.4 *s*
C-2′	143.2[c] *s*	143.5[a] *s*	143.5[b] *s*	143.4 *s*	143.2 *s*	143.7 *s*
C-3′	118.8 *d*	119.3 *d*	119.2 *d*	118.9 *d*	118.9 *d*	119.5 *d*
C-4′	134.1 *s*	134.6 *s*	134.7 *s*	134.5 *s*	134.6 *s*	134.7 *s*
C-5′	124.3 *d*	124.5 *d*	124.4 *d*	124.3 *d*	124.3 *d*	124.5 *d*
C-6′	115.9 *d*	116.2 *d*	116.0 *d*	116.0 *d*	116.0 *d*	116.1 *d*
C-7′	36.7[a] *t*	35.3 *t*	35.1 *t*	35.4 *t*	35.2 *t*	35.1 *t*
C-8′	37.7[b] *t*	32.6 *t*	32.1 *t*	32.2 *t*	31.9 *t*	32.3 *t*
C-9′	143.1[c] *s*	129.4[b] *s*	128.2 *s*	128.3 *s*	128.3 *s*	128.0 *s*
C-10′	115.4 *d*	116.2 *d*	142.3 *s*	142.0 *s*	142.1 *s*	141.5 *s*
C-11′	155.8 *s*	149.6 *s*	143.3[b] *s*	143.4 *s*	143.4 *s*	143.3 *s*
C-12′	112.9 *d*	113.5 *d*	112.9 *d*	113.1 *d*	113.2 *d*	111.3 *d*
C-13′	129.3 *d*	117.1 *d*	119.7 *d*	120.2 *d*	120.1 *d*	132.9 *s*
C-14′	120.5 *d*	147.5 *s*	121.7 *d*	122.1 *d*	122.0 *d*	120.0 *d*
C-15	55.1 *q*	—	—	55.2 *q*	—	—

[a,b,c] Assignments can be interchanged in vertical columns.

tallization (EtOH). Yield: 2.50 g (85%) of the stilbene derivative corresponding to **15**, mp 124° (mixt. of *E*/*Z*-stereoisomers, ratio 3:2). For spectroscopic data see ref. [10]. (b) The stilbene derivative from (a) (0.79 g, 1.9 mM) was hydrogenated according to procedure B and purified by chromatography (silica gel, eluent Et_2O). Yield: 0.67 g (84%) **15**, colourless crystals, mp 118°. IR ν (film) cm^{-1}: 1715. ^1H NMR ($CDCl_3$): δ 7.95 (2H, *d*, $J = 8.6$ Hz), 7.02 (1H, *d*, $J = 7.6$ Hz), 6.95–6.91 (2H, *m*), 6.87 (1H, *s*), 6.86 (2H, *d*, $J = 8.6$ Hz), 6.77 (1H, *d*, $J = 8.2$ Hz), 6.68 (1H, *d*, $J = 7.6$ Hz), 3.88 (3H, *s*), 3.84 (3H, *s*), 3.79 (3H, *s*), 3.75 (3H, *s*), 2.89–2.88 (2H, *m*), 2.85–2.83 (2H, *m*). ^{13}C NMR ($CDCl_3$): δ 166.7, 162.4, 152.8, 149.8, 147.3, 143.2, 135.6, 135.2, 131.5, 125.8, 123.8, 123.7, 122.5, 122.1, 115.8, 113.2, 110.6, 60.6, 56.1, 55.7, 51.9, 36.0, 32.1. EI-MS (70 eV), *m/z* (rel. int.): 422 $[M]^+$ (1.4), 302 (10), 152 (56), 151 (84), 137 (28), 135 (17), 109 (43), 107 (19), 91 (42), 81 (20), 79 (30), 78 (18), 77 (37), 66 (24), 65 (36), 61 (19), 51 (25), 45 (67), 43 (100), 42 (27), 41 (21), 39 (45), 31 (16). (c) A soln of the bibenzyl ester (**15**) (1.15 g, 2.7 mM) in anhydrous THF (50 ml) was added dropwise to a well-stirred suspension of $LiAlH_4$ (0.26 g, 6.8 mM) in THF (50 ml) at such a rate, that the reaction mixt. gently refluxed. When addition was complete, the mixt. was refluxed for 2 hr. After 12 hr at 20°, H_2O was added carefully at 0° until gas evolution ceased. The ppt. (Al-hydroxide) was filtered, washed with Et_2O and the combined organic phases dried ($MgSO_4$). Solvent was removed *in vacuo* and the residue purified by chromatography (silica gel, eluent Et_2O). Yield: 0.90 g (84%) of the corresponding benzyl alcohol, colourless oil; for spectroscopic data see ref. [10]. (d) The benzyl alcohol from (c) (0.83 g, 2.1 mM) was stirred for 2 hr at 20° in CH_2Cl_2 (50 ml) with PCC/Al_2O_3 [18]. Excess oxidant was filtered off and washed with CH_2Cl_2. Solvent was removed from the filtrate, the residue dissolved in Et_2O and purified by chromatography (silica gel, eluent Et_2O). Yield: 0.56 g (68%) **16**, colourless oil. IR (film): ν cm^{-1}: 1695. ^1H NMR ($CDCl_3$): δ 9.90 (1H, *s*), 7.80 (2H, *d*, $J = 8.7$ Hz), 7.05 (1H, *dd*, $K_1 = 8.3$ Hz, $J_2 = 1.8$ Hz), 6.95–6.89 (5H, *m*), 6.77 (1H, *d*, $J = 8.3$ Hz), 6.68 (1H, *d*, $J = 7.7$ Hz), 3.84 (3H, *s*), 3.79 (3H, *s*), 3.75 (3H, *s*), 2.93–2.89 (2H, *m*), 2.87–2.82 (2H, *m*). ^{13}C NMR ($CDCl_3$): δ 190.7, 163.7, 152.9, 149.9, 147.4, 142.8, 135.7, 135.2, 131.8, 131.0, 126.2, 123.7, 122.7, 122.1, 116.3, 113.3, 110.7, 60.6, 56.1, 55.8, 36.0, 32.1. CI-MS (120 eV), *m/z* (rel. int.): 393 $[M+1]^+$ (20), 392 $[M]^+$ (45), 302 (11), 257 (13), 256 (23), 242 (20), 241 (100), 197 (13), 151 (51), 136 (38), 135 (10), 106 (10), 105 (13), 91 (32), 78 (11), 77 (26), 65 (22), 51 (19). (e) The aldehyde (**16**) (0.54 g, 1.4 mM) and the phosphonium salt (**17**) (0.69 g, 1.65 mM) were reacted according to

procedure A and purified by chromatography (silica gel, eluent CH_2Cl_2). Yield: 0.66 g (97%) of the stilbene derivative corresponding to **18** (mixt. of *E*/*Z*-stereoisomers, ratio 1:1); for spectroscopic data see ref. [10]. (f) The stilbene derivative from (e) (0.63 g, 1.3 mM) was hydrogenated according to procedure B and purified by chromatography (silica gel, eluent CH_2Cl_2). Yield: 0.52 g (82%) **18**, colourless oil. ^{1}H NMR ($CDCl_3$): δ 7.18 (1H, *dd*, $J_1 = J_2 = 7.6$ Hz), 7.08 (2H, *d*, $J = 8.4$ Hz), 6.94–6.88 (3H, *m*), 6.84 (2H, *d*, $J = 8.4$ Hz), 6.80 (1H, *d*, $J = 1.8$ Hz), 6.78–6.76 (2H, *m*), 6.75–6.74 (1H, *m*), 6.72 (1H, *s*), 6.69 (1H, *dd*, $J_1 = 7.6$ Hz, $J_2 = 1.3$ Hz), 3.84 (3H, *s*), 3.80 (3H, *s*), 3.77 (6H, *s*), 2.88 (4H, *s*), 2.88–2.85 (2H, *m*), 2.81–2.77 (2H, *m*). ^{13}C NMR ($CDCl_3$): δ 159.7, 156.2, 152.8, 149.6, 147.3, 145.2, 143.5, 135.7, 135.4, 129.4, 129.3, 124.3, 123.7, 122.1, 121.1, 120.9, 117.2, 114.3, 113.1, 111.3, 110.6, 60.6, 56.3, 55.8, 55.2, 38.1, 37.0, 36.1, 32.2. CI-MS (120 eV), *m*/*z* (rel. int.): 500 $[M+2]^+$ (7.3%), 499 $[M+1]^+$ (41), 498 $[M]^+$ (100), 378 (21), 377 (75), 347 (42), 241 (18), 227 (27), 213 (37), 211 (36), 209 (35), 151 (54), 149 (17), 136 (55), 135 (29), 122 (17), 121 (81), 107 (27), 105 (19), 91 (60), 90 (16), 78 (29), 77 (26), 65 (18). (g) The tetramethoxy perrottetin (**18**) (0.42 g, 0.85 mM) was demethylated with BBr_3 according to procedure C and purified by chromatography (silica gel, eluent Et_2O). Yield: 0.35 g (94%) **6**, colourless oil. IR (film): ν cm^{-1}: 3385. ^{1}H NMR ($CDCl_3$): δ 7.13 (1H, *t*, $J = 7.8$ Hz), 7.06 (2H, *d*, $J = 8.6$ Hz), 6.95 (1H, *d*, $J = 8.2$ Hz), 6.86 (1H, *dd*, $J_1 = 8.2$ Hz, $J_2 = 2.0$ Hz), 6.82 (2H, *d*, $J = 8.6$ Hz), 6.75 (1H, *d*, $J = 7.6$ Hz), 6.69–6.64 (3H, *m*), 6.61–6.57 (3H, *m*), 2.85 (4H, *s*), 2.84–2.75 (4H, *m*). ^{13}C NMR ($CDCl_3$): δ 155.5, 154.9, 145.6, 143.5, 142.0, 136.9, 134.4, 129.9, 129.6, 128.4, 124.3, 122.3, 121.1, 120.4, 118.8, 117.9, 116.1, 115.6, 113.2, 113.0, 37.7, 36.8, 35.5, 32.3. CI-MS (120 eV), *m*/*z* (rel. int.): 443 $[M+1]^+$ (33), 442 $[M]^+$ (100), 335 (48), 320 (23), 319 (66), 227 (29), 214 (27), 213 (35), 199 (29), 167 (30), 149 (54), 123 (44), 121 (23), 107 (90), 91 (23), 77 (34), 70 (23), 57 (21), 55 (25).

Synthesis of compound **8**. (a) 4-Fluorobenzaldehyde (8.16 g, 65.7 mM) and *iso*vanillin (10.0 g, 65.7 mM) were dissolved in anhydrous DMF, dry K_2CO_3 (10 g, 72.5 mM) added and the resulting suspension heated under flux for 4 hr. The reaction mixt. was cooled to 20°, H_2O (200 mL) and Et_2O (200 ml) added, the organic phase sepd and dried ($MgSO_4$), and the solvent removed *in vacuo*. The resulting yellow oil recrystallized on treatment with petrol (40–60°). Yield: 13.5 g (80%) **21**, colourless crystals, mp 126°. IR ν^{KBr} cm^{-1}: 1685. ^{1}H NMR ($CDCl_3$): δ 9.92 (1H, *s*), 9.88 (1H, *s*), 7.84 (2H, *d*, $J = 8.6$ Hz), 7.78 (1H, *dd*, $J_1 = 8.4$ Hz, $J_2 = 2.0$ Hz), 7.63 (1H, *d*, $J = 2.0$ Hz), 7.17 (1H, *d*, $J = 8.4$ Hz), 7.01 (2H, *d*, $J = 8.6$ Hz), 3.90 (3H, *s*). ^{13}C NMR ($CDCl_3$): δ 190.6, 190.0, 162.8, 156.9, 143.9, 131.9, 131.6, 130.6, 129.5, 122.3, 116.7, 112.7, 56.3. CI-MS (120 eV), *m*/*z* (rel. int.): 257 $[M+1]^+$ (9.6), 256 $[M]^+$ (68), 255 (21), 167 (12), 166 (100), 165 (25), 151 (8.8), 149 (26), 148 (14), 123 (7.7), 95 (12), 79 (5.4), 77 (9.0), 51 (6.0). (b) The dialdehyde (**21**) (2 g, 7.8 mM) and the phosphonium salt (**14**) [10] (7.71 g, 17.2 mM) were reacted according to procedure A and purified by chromatography (silica gel, $CHCl_3$). Yield: 3.58 g (87%) **23**, colourless oil (mixture of *E*/*Z*-stereoisomers). ^{1}H NMR ($CDCl_3$): δ 7.60–7.22 (6H, *m*), 7.17–7.01 (4H, *m*), 6.91–6.79 (5H, *m*), 6.73–6.55 (2H, *m*), 3.96–3.79 (13H, *m*), 3.78–3.74 (2H, *m*). ^{13}C NMR ($CDCl_3$): δ 157.8, 153.2, 152.9, 151.3, 147.0, 144.9, 131.8, 131.6, 131.4, 130.5, 130.3, 130.2, 129.8, 129.3, 128.9, 127.9, 127.8, 125.5, 125.4, 125.1, 124.7, 124.1, 123.6, 122.1, 122.0, 121.8, 121.1, 119.5, 117.9, 117.9, 117.1, 116.9, 116.4, 113.1, 112.5, 111.5, 61.0, 60.6, 56.1, 56.0, 55.9, 55.8. CI-MS (120 eV), *m*/*z* (rel. int.): 524 $[M]^+$ (1.7), 390 (7.1), 303 (9.9), 302 (47), 301 (21), 300 (100), 288 (6.1), 286 (19), 285 (5.2), 269 (5.3), 196 (6.3), 168 (5.4), 166 (17), 165 (7.4), 152 (10), 151 (32), 149 (12), 136 (12), 109 (5.7), 91 (6.4), 85 (16), 83 (29). (c) The bisstilbene (**23**) (1.19 g, 2.3 mM) was hydrogenated according to procedure B and purified by chromatography (silica gel, eluent Et_2O). Yield: 0.98 g (82%) **22**, colourless oil. ^{1}H NMR ($CDCl_3$): δ 7.11 (2H, *d*, $J = 8.5$ Hz), 6.97–6.88 (4H, *m*), 6.83 (2H, *d*, $J = 8.5$ Hz), 6.79–6.74 (4H, *m*), 6.69 (1H, *dd*, $J_1 = 7.6$ Hz, $J_2 = 1.2$ Hz), 3.85 (3H, *s*), 3.83 (3H, *s*), 3.80 (3H, *s*), 3.79 (3H, *s*), 3.77 (3H, *s*), 2.92–2.78 (8H, *m*). ^{13}C NMR ($CDCl_3$): δ 156.2, 152.9, 149.6, 147.4, 145.3, 136.2, 135.7, 135.4, 129.4, 124.2, 123.7, 122.1, 121.1, 117.2, 113.1, 110.7, 60.6, 56.3, 55.8, 36.4, 36.2, 32.2, 32.2. CI-MS (120 eV), *m*/*z* (rel. int.): 530 $[M+2]^+$ (7.4), 529 $[M+1]^+$ (37), 528 $[M]^+$ (100), 514 (6.7), 378 (16), 377 (57), 151 (6.1). (d) The pentamethyl perrottetin (**22**) (0.60 g, 1.15 mM) was demethylated with BBr_3 according to procedure C and purified by chromatography (silica gel, eluent Et_2O). Yield: 0.50 g (96%), colourless oil. IR ν^{film} cm^{-1}: 3490–3370. ^{1}H NMR ($CDCl_3$): δ 7.10 (2H, *d*, $J = 8.4$ Hz), 6.93 (1H, *d*, $J = 8.1$ Hz), 6.84 (1H, *dd*, $J_1 = 8.3$ Hz, $J_2 = 1.6$ Hz), 6.82 (2H, *d*, $J = 8.4$ Hz), 6.70–6.62 (5H, *m*), 6.59 (1H, *s*), 6.56 (1H, *d*, $J = 7.0$ Hz), 6.00 (2H, *bs*), 5.61 (1H, *bs*), 5.36 (1H, *bs*), 5.23 (1H, *bs*), 2.90 (4H, *s*), 2.85–2.81 (2H, *m*), 2.79–2.75 (2H, *m*). ^{13}C NMR ($CDCl_3$): δ 154.9, 145.5, 143.6, 143.5, 143.4, 142.4, 142.2, 137.3, 134.5, 129.8, 128.5, 128.3, 124.3,122.2, 122.1, 120.2, 118.8, 118.1, 116.0, 113.2, 113.2, 35.4, 32.3, 32.1. CI-MS (120 eV), *m*/*z* (rel. int.): 458 $[M]^+$ (3.5), 336 (3246), (33), 213 (54), 182 (35), 124 (19), 123 (71), 107 (17), 106 (11), 105 (100), 91 (7814), (14), 77 (64), 65 (21), 57 (14), 55 (17), 51 (44), 50 (11), 44 (10), 43 (20), 41 (19).

Synthesis of compound **9**. (a) 5-Bromo-2,3-dimethoxy benzaldehyde (**25**) [10] (4 g, 16.3 mM), ethylene glycol (2.23 g, 39.5 mM, 2 ml) and trimethyl chlorosilane (7.80 g, 71.8 mM, 9.1 ml) were dissolved in dry CH_2Cl_2 (50 ml) and heated at reflux for 48 hr. When reaction was complete, a aq. soln of $NaHCO_3$ (5%, 50 ml) was added, the organic phase sepd and the aq. phase extracted twice with Cl_2Cl_2 (20 ml). The organic phases were combined, washed with satd NaCl soln (50 ml) and dried ($MgSO_4$). After filtration, solvent

was removed *in vacuo* and the product obtained of purity sufficient for the next reaction step. Yield: 3.99 g (85%) **26**, yellow oil. ^{1}H NMR ($CDCl_3$): δ 7.25 (1H, *d*, J = 2.3 Hz), 7.03 (1H, *d*, J = 2.3 Hz), 6.07 (1H, *s*), 4.14–4.10 (2H, *m*), 4.04–4.00 (2H, *m*), 3.86 (3H, *s*), 3.84 (3H, *s*). ^{13}C NMR ($CDCl_3$): δ 153.5, 147.3, 133.4, 121.6, 116.8, 116.4, 99.0, 65.4, 61.5, 56.2. CI-MS (120 eV), *m/z* (rel. int.): 291 [M + 1 (^{81}Br)]$^+$ (14), 290 [M (^{81}Br)]$^+$ (48), 289 [M + 1 (^{79}Br)]$^+$ (24), 288 [M (^{79}Br)]$^+$ (45), 275 (18), 273 (18), 257 (11), 216 (12), 211 (34), 210 (100), 209 (25), 195 (31), 177 (18), 166 (13), 165 (20), 151 (11), 149 (14), 138 (28), 73 (81), 45 (22). (b) The bromoaldehyde (**26**) (1 g, 3.45 mM) was dissolved in anhydrous Et_2O (50 ml) and cooled to −65° and *n*-butyl lithium (1.52 ml of a 2.5 M soln in *n*-hexane), added at a rate, such that the temp. did not exceed −60°. When addition was complete, the reaction mixt. was stirred at −60° for 3.5 hr. Tri-*n*-butyl borate (1 g, 4.3 mM, 1.15 ml) was then added in one portion and the reaction mixt. stirred for 4 hr at −65°. The mixt. was allowed to reach 20° (12 hr) and then hydrolysed by addition of 2 M HCl (100 ml). The organic phase was sepd and extracted twice with 2 M aq. NaOH (50 ml). The alkaline soln was cooled to 0° and conc. HCl added dropwise until the boronic acid separated. For purification, the crude product was dissolved in hot H_2O and ppted on cooling by addition of $CHCl_3$. Yield: 0.48 g (66%) **28**, colourless crystals, mp 218°. IR ν^{KBr} cm^{-1}: 3385, 1680. ^{1}H NMR (DMSO): δ 10.33 (1H, *s*), 8.22 (2H, *bs*), 7.80 (2H, *s*), 3.93 (3H, *s*), 3.90 (3H, *s*). ^{13}C NMR (DMSO): δ 190.2, 153.4, 151.8, 128.4, 125.2, 124.0, 61.7, 55.9. (c) Tetrakis (triphenylphosphane) Pd (0.08 g, 0.07 mM), a 2 M aq. soln of Na_2CO_3 and the formyl boronic acid (**28**) (0.50 g, 2.4 mM) were added under a N_2 atmosphere to a soln of the bromoacetal (**25**) (0.53 g, 2.2 mM) in toluene (50 ml). The reaction mixt. was refluxed for 6 hr. After cooling to 20°, the phases were sepd and the aq. phase extracted × 3 with CH_2Cl_2 (50 ml). The combined organic phases were washed with satd NaCl soln (50 ml) and dried ($MgSO_4$). After filtration, solvents were removed *in vacuo*, the crude product re-dissolved in CH_2Cl_2 and purified by chromatography (silica gel, eluent CH_2Cl_2). Yield: 0.60 g (84%) **27**, yellowish crystals, mp 156°. IR ν^{KBr} cm^{-1}: 1685 (C=O). ^{1}H NMR ($CDCl_3$): δ 10.46 (2H, *s*), 7.58 (2H, *d*, J = 2.2 Hz), 7.33 (2H, *d*, J = 2.2 Hz), 4.03 (6H, *s*), 3.98 (6H, *s*). ^{13}C NMR ($CDCl_6$): δ 189.9, 153.5, 152.6, 136.2, 129.9, 117.5, 117.1, 62.4, 56.5. CI-MS (120 eV), *m/z* (rel. int.): 332 [M + 2]$^+$ (6.7), 331 [M + 1]$^+$ (30), 330 [M]$^+$ (100), 316 (6.2), 315 (21), 272 (5.6), 262 (18), 183 (9.6), 57 (5.8), 49 (5.5). (d) The benzyl alcohol (**30**) [10] (2.41 g, 6.6 mM) was dissolved in anhydrous Et_2O (30 ml) together with some drops of pyridine. $SOCl_2$ (1.57 g, 13.2 mM, 1 ml) in Et_2O (30 ml) was then added dropwise. After stirring for 1 hr at 20°, a white solid separated which was dissolved by addition of Cl_2Cl_2 (30 ml). The soln was washed twice with H_2O (40 ml), dried ($MgSO_4$) and the solvent removed *in vacuo*. Since the resulting benzyl chloride corresponding to **30** is unstable, the crude product was used for the next step. IR ν cm^{-1}: 2995, 2930, 2830, 1610, 1590, 1510, 1455, 1445, 1430, 1315, 1275, 1230, 1170, 1155, 1130, 1050, 1030, 975, 875, 825, 780, 695. (e) The crude benzyl chloride from (d) was dissolved in dry toluene (10 ml) and triphenyl phosphine (1.74 g, 6.6 mM) added. The resulting soln was refluxed for 24 hr and, after cooling to 20°, petrol (40–60°, 40 ml) was added. After stirring for 10 min, the ppt. was filtered off, washed several times with petrol (40–60°, 20 ml) and dried over P_4O_{10}. Yield: 3.26 g (76% over two steps) **29**, colourless crystals, mp 141°. ^{1}H NMR ($CDCl_3$): δ 7.74–7.69 (9H, *m*), 7.60–7.54 (6H, *m*), 7.32–7.12 (2H, *m*), 7.00 (2H, *d*, J = 8.4 Hz), 6.78–6.71 (4H, *m*), 6.60 (2H, *d*, J = 8.4 Hz), 6.33 (1H, *d*, J = 1.8 Hz), 5.37 (2H, *d*, J = 13.9 Hz), 3.76 (3H, *s*), 3.75 (3H, *s*), 2.88 (4H, *s*). ^{13}C NMR ($CDCl_3$): δ 159.6, 155.1, 151.2, 145.5, 143.2, 136.2, 134.8, 134.3, 134.2, 130.2, 130.1, 129.5, 129.3, 129.0, 128.3, 128.2, 125.3, 122.3, 120.9, 119.5, 118.4, 117.5, 114.4, 113.1, 111.2, 56.1, 55.2, 38.0, 36.9, 30.2 (*d*, J = 184.4 Hz). CI-MS (120 eV), *m/z* (rel. int.): 610 [M$^+$–Cl] (5.3), 609 (12), 526 (20), 525 (67), 524 (100), 490 (23), 489 (56), 448 (35), 447 (69), 446 (52), 445 (94), 370 (47), 369 (51), 353 (20), 264 (67), 263 (100), 262 (98), 261 (21), 183 (43). (f) The biphenyl dialdehyde (**27**) (0.25 g, 0.76 mM), the phosphonium salt **29** (1.17 g, 1.8 mM) and K_2CO_3 (0.25 g, 1.8 mM) were reacted according to procedure A. The crude product was purified by chromatography (silica gel, eluent CH_2Cl_2). Yield: 0.68 g (91%) **31**, yellowish oil (mixture of *E*/*Z*-stereoisomers with 80% of the *cis,cis*-bisstilbene according to ^{1}H NMR). ^{1}H NMR ($CDCl_3$): δ 7.23–6.68 (25.2H, *m*), 6.63 (1.6H, *d*, J = 12.0 Hz), 6.59 (1.6H, *s*), 6.55 (1.6H, *d*, J = 12.0 Hz), 3.92–3.71 (24H, *m*), 2.87–2.81 (8H, *m*). ^{13}C NMR ($CDCl_3$): δ 159.9, 155.6, 153.0, 150.3, 146.9, 145.8, 143.5, 136.4, 136.2, 131.6, 130.8, 130.3, 129.4, 129.4, 125.2, 124.9, 121.0, 120.7, 117.9, 117.2, 114.5, 112.8, 111.5, 110.5, 60.8, 56.1, 56.0, 55.2, 38.0, 37.0. CI-MS (120 eV), *m/z* (rel. int.): 991 [M]$^+$ (8.5), 990 (12), 497 (4.2), 364 (44), 362 (49), 348 (57), 243 (84), 241 (97), 228 (54), 227 (100), 121 (54), 107 (78), 105 (33), 91 (40), 81 (46), 57 (25), 55 (26). (g) The bisstilbene (**31**) (0.61 g, 0.6 mM) was hydrogenated according to procedure B; the crude product obtained was analytically pure. Yield: 0.50 g (82%) **32**, yellowish oil. ^{1}H NMR ($CDCl_3$): δ 7.19 (2H, *t*, J = 7.7 Hz), 7.06 (4H, *d*, J = 8.5 Hz), 6.95 (2H, *dd*, K_1 = 8.3 Hz, J_2 = 1.8 Hz), 6.91 (2H, *d*, J = 8.3 Hz), 6.86–6.72 (16H, *m*), 3.91 (6H, *s*), 3.82 (6H, *s*), 3.80 (6H, *s*), 3.78 (6H, *s*), 2.94–2.82 (16H, *m*). ^{13}C NMR ($CDCl_3$): δ 159.8, 156.4, 152.8, 149.8, 146.9, 143.5, 137.0, 135.7, 135.4, 129.4, 129.3, 124.4, 121.3, 120.9, 117.1, 114.4, 113.4, 111.4, 110.0, 60.7, 56.4, 56.1, 55.2, 38.0, 36.9, 36.2, 32.4. CI-MS (120 eV), *m/z* (rel. int.): 995 [M]$^+$ (2.4), 994 (4.0), 449 (14), 348 (36), 243 (48), 241 (53), 227 (75), 151 (68), 121 (39), 107 (33), 97 (38), 91 (53), 85 (30), 83 (51), 81 (43), 77 (42), 71 (49), 69 (59), 67 (35), 57 (93), 56 (41), 55 (100). (h) The octamethyl perrottetin (**32**) (0.44 g, 0.4 mM) was demethylated

with BBr_3 according to procedure C and the crude product purified by chromatography (silica gel, eluent Et_2O). Yield: 0.31 g (78%) **9**, colourless oil. IR ν^{KBr} cm^{-1}: 3395 (OH). ^1H NMR ($CDCl_3$/MeOH-d_4): δ 7.07 (2H, *t*, $J = 7.7$ Hz), 6.96 (4H, *d*, $J = 8.4$ Hz), 6.88 (2H, *d*, $J = 7.9$ Hz), 6.82 (2H, *dd*, $J_1 = 7.9$ Hz, $J_2 = 1.2$ Hz), 6.75 (4H, *d*, $J = 8.4$ Hz), 6.69–6.60 (8H, *m*), 6.54 (2H, *s*), 6.51 (2H, *d*, $J = 1.6$ Hz), 2.83–2.77 (8H, *m*), 2.79 (8H, *s*). ^{13}C NMR ($CDCl_3$/MeOH-d_4): δ 157.4, 156.5, 146.7, 145.0, 144.3, 144.0, 142.5, 136.7, 135.3, 133.7, 130.0, 129.7, 129.0, 125.1, 120.9, 120.5, 120.3, 117.8, 117.1, 115.9, 113.4, 112.0, 38.4, 37.4, 35.7, 32.9. EI-MS (70 eV), *m/z* (rel. int.): 882 [M^+] (5), 458 (30), 442 (5), 214 (23), 199 (26), 335 (55), 199 (24), 107 (100).

Acknowledgements—We thank Dr J. Zapp for the NMR measurements and Mr W. Rubik and Dr R. Graf for running MS.

REFERENCES

1. Cullmann, F., Adam, K.-P. and Becker, H., *Phytochemistry*, 1993, **34**, 831.
2. Cullmann, F., Adam, K.-P., Zapp, J. and Becker, H., *Phytochemistry*, 1996, **41**, 611.
3. Benešová, V. and Herout, V., *Collections of Czechoslovakian Chemical Communications*, 1970, **35**, 1926.
4. Benešová, V. and Herout, V., *Collections of Czechoslovakian Chemical Communications*, 1972, **37**, 1764.
5. Huneck, S. and Schreiber, K., *Journal of the Hattori Botany Laboratory*, 1975, **39**, 215.
6. Toyota, M., Tori, M., Takikawa, K., Shiobara, Y., Kodama, M. and Asakwa, Y., *Tetrahedron Letters*, 1985, **26**, 6097.
7. Hashimoto, T., Suzuki, H., Tori, M. and Asakawa, Y., *Phytochemistry*, 1991, **30**, 1523.
8. Seoane, G., Pandolfi, E., Gamenara, D. and Eicher, Th., *Journal of the Brazilian Chemistry Society*, 1996, **7**, 307.
9. Eicher, Th. and Walter, M., *Synthesis*, 1991, 469.
10. Roeckner, E., Synthese von Inhaltsstoffen des Lebermooses *Pellia epiphylla* (L.) Corda Ph.D. thesis, Saarbrücken, 1996.
11. Hashimoto, T., Yoshida, T., Kan, Y., Takaoka, S., Tori, M. and Asakawa, Y., *Tetrahedron Letters*, 1994, **35**, 909.
12. Kunz, S. and Becker, H., *Phytochemistry*, 1994, **36**, 675.
13. Hashimoto, T., Asakwa, Y., Nakashima, K. and Tori, M., *Journal of the Hattori Botany Laboratory*, 1993, **74**, 121.
14. Asakawa, Y., Suire, C., Toyota, M., Tokunaga, N., Takemoto, T., Hattori, S. and Mizutani, M., *Journal of the Hattori Botany Laboratory*, 1980, **48**, 285.
15. Schuster, R. M., *The Hepaticae and Anthoceratae of North America*, Vol. V. Field Museum of Natural History, Chicago, 1992.
16. Grolle, R., *Journal of Bryology*, 1983, **12**, 403.
17. Huneck, S., *Tetrahedron*, 1976, **32**, 109.
18. Tietze, L. F. and Eicher, Th., *Reaktionen und Synthesen im organisch-chemischen Praktikum*, 2. Auflage, 1991, S.100.
19. Kraut, L., Klaus, Th., Mues, R., Eicher, Th. and Zinsmeister, H. D., *Phytochemistry*, in press.