A New Dimeric Stilbenoid with a Five-Membered Lactone Ring from *Shorea hemsleyana*

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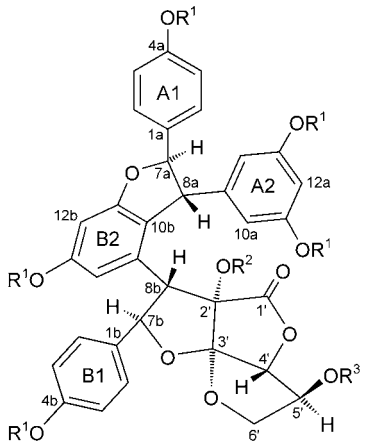
From the stem bark of *Shorea hemsleyana*, a new dimeric stilbenoid with a five-membered lactone ring, shorealactone (**1**) was isolated. The absolute configuration was determined by means of 2D NMR techniques and X-ray crystal-structure analysis of its 4-bromobenzoyl derivative **1e** by means of anomalous scattering of the Br-atom.

Introduction. – In our previous papers, we reported the structure elucidation of the stilbenoid derivatives hemsleyanols A – E and hemsleyanosides A – D, isolated from the stem bark of *Shorea hemsleyana* [1 – 3]. The structures of these isolates were composed of resveratrol (3,5,4′-trihydroxystilbene = 5-[(1*E*)-2-(4-hydroxyphenyl)-ethenyl]benzene-1,3-diol) unit(s) formally derived by homogeneous oligomerization; these structures ranged from monomeric to tetrameric derivatives. Further examination of the acetone extract of the stem bark resulted in the isolation of a new resveratrol dimer, called shorealactone (**1**), which is fused to a C_6 unit, thus forming a unique five-membered lactone ring and two tetrahydrofuran moieties. This report deals with the structure elucidation of shorealactone (**1**), including its absolute configuration.



1 $R^1 = R^2 = R^3 = H$
1a $R^1 = R^2 = R^3 = Ac$
1b $R^1 = Me$, $R^2 = R^3 = H$
1c $R^1 = R^2 = Me$, $R^3 = H$
1d $R^1 = R^2 = R^3 = Me$
1e $R^1 = R^2 = Me$, $R^3 = p$-bromobenzoyl

Results and Discussion. – Shorealactone (**1**), obtained as a pale yellow amorphous powder, showed a positive reaction with the *Gibbs* and the $FeCl_3$ reagent. The composition of **1** was deduced to be $C_{34}H_{28}O_{12}$ from the pseudo-molecular ion peak $[M-H]^-$ at *m/z* 627.1510 in the HR-FAB-MS (negative-ion mode). An absorption band (1788 cm^{-1}) in the IR spectrum and a signal in the ^{13}C-NMR spectrum (δ(C) 172.0) showed the presence of a carbonyl group (C(1′)) in the molecule. The ^1H- and ^{13}C-NMR spectra (*Tables 1* and *2*), $^1H,^1H$-COSY, HMQC, HMBC, and NOESY experiments, as well as the transformations to heptaacetate **1a** and methyl ethers **1b**–**d**, established the proposed structure and relative configuration of **1**.

Table 1. *^1H-NMR Data* (500 MHz, (D_6)Acetone) *of* **1**[1]). δ in ppm, *J* in Hz.

H–C(2a, 6a)	6.76 (*s*)	H–C(8b)	3.28 (*d*, *J* = 10.7)
H–C(3a, 5a)	6.76 (*s*)	H–C(12b)	6.18 (*d*, *J* = 2.0)
H–C(7a)	5.04 (*d*, *J* = 7.3)	H–C(14b)	7.16 (br. *s*)
H–C(8a)	3.26 (br. *s*)	H–C(4′)	4.43 (br. *s*)
H–C(10a, 14a)	5.92 (br. *d*, *J* = 2.0)	H–C(5′)	4.23 (*m*)
H–C(12a)	6.16 (*t*, *J* = 2.0)	H–C(6′)	3.97 (*dd*, *J* = 9.8, 4.4), 4.07 (*dd*, *J* = 9.8, 2.4)
H–C(2b, 6b)	6.97 (*d*, *J* = 8.3)	OH–C(2′)	5.24 (br. *s*)
H–C(3b, 5b)	6.77 (*d*, *J* = 8.3)	OH–C(5′)	4.79 (br. *s*)
H–C(7b)	5.28 (*d*, *J* = 10.7)		

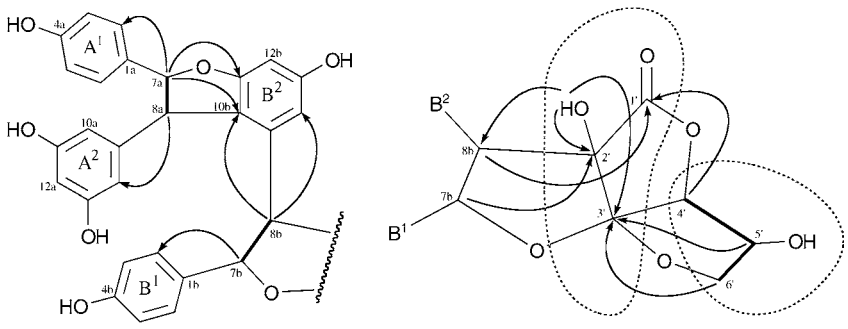
Table 2. *^{13}C-NMR Data* (125 MHz, (D_6)Acetone) *of* **1**. δ in ppm.

C(1a)	132.4	C(7b)	90.1
C(2a,6a)	129.2	C(8b)	56.5
C(3a,5a)	116.0	C(9b)	131.9
C(4a)	158.3	C(10b)	122.9
C(7a)	94.3	C(11b)	161.2
C(8a)	56.2	C(12b)	97.0
C(9a)	145.9	C(13b)	159.0
C(10a,14a)	107.2	C(14b)	110.7
C(11a,13a)	159.8	C(1′)	172.0
C(12a)	102.4	C(2′)	81.1
C(1b)	130.0	C(3′)	118.7
C(2b,6b)	128.2	C(4′)	89.1
C(3b,5b)	115.7	C(5′)	74.7
C(4b)	158.6	C(6′)	75.7

The ^1H-NMR spectrum of **1** exhibited the signals attributed to two resveratrol units and five phenolic OH H-atoms, *i.e.*, two 4-hydroxyphenyl groups (rings A1 and B1), a 3,5-dihydroxyphenyl group (ring A2), a 2,3-disubstituted 5-hydroxyphenyl group (ring B2), and two sets of mutually coupled aliphatic H-atoms (H–C(7a)/H–C(8a) and H–C(7b)/H–C(8b))[1]). The ^1H-NMR and the $^1H,^1H$-COSY plot (*Fig. 1*) also showed a sequence of two aliphatic methine H-atoms and a methylene H-atom coupled successively in this order (H–C(4′)/H–C(5′)/2 H–C(6′)). In the ^{13}C-NMR spectrum all signals attributed to six CH, one CH_2, and 24 aromatic C-atoms were assigned by analysis of the HMQC and HMBC spectra. Two broad signals in the ^1H-NMR spectrum at δ 5.24 (br. *s*) and 4.79 (br. *s*) disappeared upon usual acetylation of **1** ($\rightarrow$ **1a** see *Exper. Part*). Methylation of **1** with MeI and K_2CO_3 in acetone yielded the three methyl ethers **1b**–**d** (see *Exper. Part*), *i.e.*, a penta-, hexa-, and heptamethyl ether, respectively. Among them, **1b** showed two alcoholic OH groups (δ 5.43 (br. *s*) and 4.82 (br. *d*)) in the ^1H-NMR spectrum, suggesting that the two broad signals of **1** (δ 5.24 and 4.79) arose from two

[1]) Arbitrary numbering; for the systematic name, see *Exper. Part*.

alcoholic OH groups. In the ^{13}C-NMR and DEPT spectra, signals attributed to two aliphatic quaternary C-atoms binding to an O-atom were observed (δ(C) 81.1 (C(2′)) and 118.7 (C(3′))). These data implied that **1** was composed of two resveratrol units ($C_{28}H_{22}O_6$) and an aliphatic moiety ($C_6H_6O_6$) carrying carbonyl and two OH groups.



1A **1A** **1B** **1C**

Fig. 1. *^{1}H,^{1}H COSY* (–) *and selected correlations in the HMBC spectrum* (→)

Significant ^3J long-range correlations were observed for H–C(7a)/C(2a,6a), H–C(8a)/C(10a,14a), H–C(7b)/C(2b,6b), H–C(8b)/C(10b), and H–C(8b)/C(14b) in the HMBC spectrum (*Fig. 1*), indicating that two resveratrol units were composed of four rings (rings A1, A2, B1, and B2) and four CH units (H–C(7a), H–C(8a), H–C(7b), and H–C(8b)). Long-range correlations observed between the aliphatic H–C(7a) and the quaternary C(10b) and C(11b) of ring B2 indicated the presence of a dihydrobenzofuran moiety (C(7a)–C(8a)–C(10b)–C(11b)–O), leading to a plausible partial structure **1A**. On the other hand, ^3J long-range correlations observed for H–C(7b)/C(2′) and H–C(8b)/C(1′) suggested that C(8b), C(2′), and C(1′) were connected in this order. In addition, one of the alcoholic OH groups (δ 5.24) was correlated with the quarternary C(2′) and C(3′) and a CH group (C(8b)). Then the quarternary C(3′) was attached to C(2′), and the alcoholic OH group (δ 5.24) was located at C(2′). These results confirmed that **1** has further a C_3 unit, *i.e.*, C(1′), C(2′), and C(3′), which is connected to **1A** and carries a chelated OH group, corresponding to partial structure **1B** (*Fig. 1*). The correlations between H–C(5′) and the other alcoholic OH group (δ 4.79) in the ^{1}H,^{1}H COSY plot supported the partial structure **1C**. Considering the molecular formula ($C_{34}H_{28}O_{12}$), **1** had three other ether linkages in the molecule. The long range correlations (^3J) H–C(4′)/C(1′), H–C(5′)/C(3′), and H–C(6′)/C(3′) indicated that the tetrahydrofran ring C(3′)–C(4′)–C(5′)–C(6′)–O belongs to the partial structures **1B** and **1C** and is fused to the five-membered lactone ring C(1′)–C(2′)–C(3′)–C(4′)–O. Thus the remaining ether linkage was located between C(7b) and C(3′).

In the NOESY plot of **1** (*Fig. 2*), significant NOEs were observed between H–C(2a,6a)/H–C(8a), H–C(10a,14a)/H–C(7a), H–C(2b,6b)/H–C(8b), and H–C(14b)/H–C(7b), suggesting that the orientation of the two sets of methine H-atoms (H–C(7a)/H–C(8a), H–C(7b)/H–C(8b)) were both *trans*. H–C(8b) and the aromatic H–C(2b,6b) further displayed an NOE with H–C(4′), which can be observed only when H–C(8b), ring B1 and H–C(4′) are situated on the same side of the difurofuran moiety. In the DIFNOE study of **1d** (*Fig. 2*), an NOE was observed between MeO–C(2′) and H–C(7b), suggesting that OH–C(2′) of **1** was situated on the same side of the difurofuran moiety as H–C(7b). The orientation of H–C(5′) was opposite to that of H–C(4′), as shown by the NOEs H–C(4′)/MeO–C(5′), H–C(4′)/MeO–C(11a,13a), and MeO–C(5′)/MeO–C(11a,13a). Thus, the relative configuration of **1** was deduced as shown in *Fig. 2*.

The absolute configuration of **1** was established by X-ray crystallography. A crystalline 5′-(4-bromobenzoate) **1e** was obtained by bromobenzoylation of **1c**. The position of the 4-bromobenzoyl group in **1e** was ascertained to be at C(5′) by analysis of the NMR spectra. Details of the X-ray crystal-structure determination of **1e** are

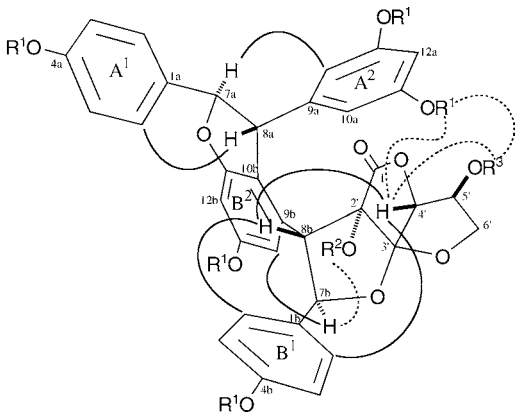


Fig. 2. *NOESY in* **1** (R1 = R2 = R3 = H) (—) *and DIFNOE in* **1d** (R1 = R2 = R3 = Me) (- - - -)

described in *Table 3*, and the absolute configuration (2′*S*,3′*R*,4′*R*,5′*S*,7a*R*,7b*R*,8a*R*,8b*S*) was established by using anomalous scattering of the Br-atom (*Fig. 3*)[2]).

Table 3. *Crystal Data of* **1e**

Formula	$C_{47}H_{43}O_{13}Br$	Space group	$P2_12_12_1$
M_r	895.75	Z value	4
Crystal system	orthorhombic	D_{calc}	1.425 g/cm^3
Cell data: a	15.0075(8) Å	μ (CuK_α)	19.20 cm^{-1}
b	21.083(1) Å		
c	13.1935(6) Å		
V	4174.5(3)) Å^3		

Although a number of stilbenoids have been isolated from nature, most of them are generally noncrystalline compounds, and usually only their relative configuration was determined by NMR analysis. (−)-Hopeaphenol, a resveratrol tetramer, is the only example among the stilbenoids of which the absolute structure was established by X-ray crystal-structure analysis [4].

The skeleton of shorealactone (**1**) consists of two resveratrol units (resveratrols A and B; $C_{28}H_{22}O_6$) and an aliphatic moiety ($C_6H_6O_6$). This aliphatic unit forms a novel framework composed of a five-membered lactone moiety (C(1′)−C(2′)−C(3′)−C(4′)−O) and a fused tetrahydrofuran ring (C(3′)−C(4′)−C(5′)−C(6′)−O). The lactone ring is further linked to the two methine atoms C(7b) and C(8b) of the resveratrol B *via* a C−C bond (C(8b)−C(2′)) and an ether linkage (C(7b)−O−C(3′)) giving rise to an additional tetrahydrofuran ring. As far as we know, this unique framework is unprecedented among naturally occurring phenols. Shorealactone (**1**) is considered to be a new kind of a complex stilbenoid. Its stilbene unit has been shown to

[2]) Crystallographic data (excluding structure factors) for the structure(s) reported in this paper have been deposited with the *Cambridge Crystallographic Data Centre* as deposition No. CCDC-211273. Copies of the data can be obtained, free of charge, on application to the CCDC, 12 Union Road, Cambridge CB2 1EZ UK (fax: +44(1223)336033; e-mail: deposit@ccdc.cam.ac.uk).

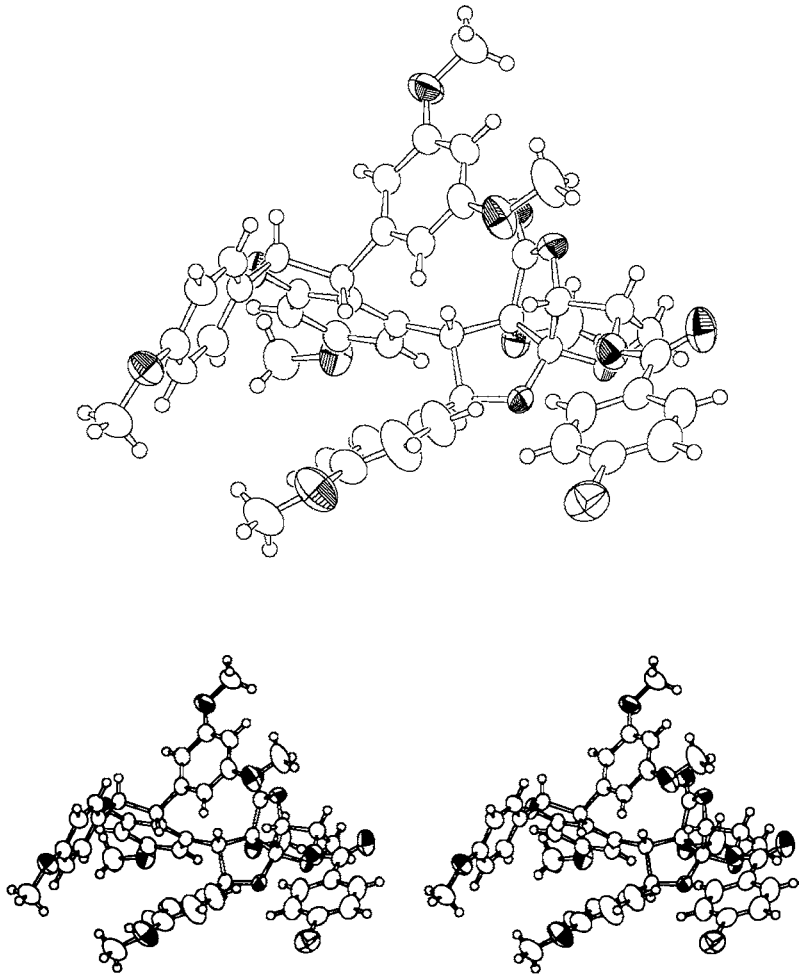


Fig. 3. *X-Ray crystal structure of 4-bromobenzoate derivative* **1e**

be connected to other skleletons such as in the flavonostilbenes (stilbenoid and flavonoid) [5]. The different kinds of linkages to heterocyclic units are responsible for the variation of stilbenoid structures.

Experimental Part

General. Anal. TLC: *Merck* silica gel F_{254} (0.25 mm). Prep. TLC: *Merck* silica gel F_{254} (0.5 mm). Column chromatography (CC): *Merck* silica gel *60* (70–230 mesh), *Sephadex LH-20*. Vacuum liquid chromatography (VLC): *Merck* silica gel *60* $PF_{254+366}$. M.p.: *Yanagimoto* micro melting-point apparatus; uncorrected. Optical rotation: *Jasco P-1020* polarimeter. UV Spectra: *Shimadzu UV-2200* spectrophotometer; λ_{max} in nm. IR Spectra: *Jasco FT-IR-8000* spectrophotometer; KBr microplate; in cm^{-1}. ^1H- and ^{13}C-NMR Spectra: *Jeol JNM-A-500*,

-EX-400, or *-LA-300* spectrometer; at r.t., (D_6)acetone soln.; δ in ppm rel. to $SiMe_4$ as an internal reference; coupling constants *J* in Hz. FAB-MS: *Jeol-JMS-DX-300* spectrometer; in *m/z*.

Plant Material. Stem bark of *Shorea hemsleyana* was collected in Indonesia in October 1997.

Extraction and Isolation. The dried and ground stem bark of *S. hemsleyana* (1 kg) was successively extracted with acetone (3 × 3 l), MeOH (3 × 3 l), and 70% MeOH (3 × 3 l) at r.t. Evaporation gave the respective residues (47 g (acetone), 42 g (MeOH), and 26 g (70% MeOH)). Part (40 g) of the acetone extract was subjected to CC (silica gel, $CHCl_3$/MeOH of increasing polarity): *Fractions 1–34. Fr. 25* (with $CHCl_3$/MeOH 8:1; 1.5 g) was submitted to VLC ($CHCl_3$/MeOH). The $CHCl_3$/MeOH 8:1 fraction afforded **1** (270 mg) after purification by *Sephadex LH-20*, CC (MeOH), and prep. TLC (AcOEt/$CHCl_3$/MeOH/H_2O 80:40:11:2).

Shorealactone (=*6-[3-(3,5-Dihydroxyphenyl)-2,3-dihydro-6-hydroxy-2-(4-hydroxyphenyl)benzofuran-4-yl]-tetrahydro-3,5a-dihydroxy-7-(4-hydroxyphenyl)-2*H*-difuro[3,2-*b*:2′,3′-*c*]furan-5(5a*H*)-one*; **1**). Pale yellow amorphous powder. UV: 217, 280 (sh), 285, 293 (sh). IR: 3358, 1788, 1454. $[\alpha]_D = -200$ (*c* = 0.1, MeOH). ^{1}H- and ^{13}C-NMR: *Tables 1* and *2*, resp. FAB-MS (neg.): 627 ($[M-H]^-$. HR-FAB-MS (neg.): 627.1510 ($[M-H]^-$, $C_{34}H_{27}O_{12}^-$; calc. 627.1502).

Shorealactone Heptaacetate (=*3,5a-Bis(acetyloxy)-6-[6-(acetyloxy)-2-[4-(acetyloxy)phenyl]-3-[3,5-bis(acetyloxy)phenyl]-2,3-dihydrobenzofuran-4-yl]-7-[4-(acetyloxy)phenyl]-tetrahydro-2*H*-difuro[3,2-*b*:2′,3′-*c*]furan-5(5a*H*)-one*; **1a**). A soln. of **1** (10 mg) in pyridine (0.5 ml) and Ac_2O (0.5 ml) was kept at r.t. for 24 h. Workup in the usual manner and purification of the resulting crude product (12 mg) by prep. TLC (hexane/AcOEt 1:1) afforded **1a** (10 mg). Colorless amorphous powder. ^{1}H-NMR ((D_6)acetone, 400 MHz)[1]): 6.99 (*d*, *J* = 8.6, H–C(2a), H–C(6a)); 7.09 (*d*, *J* = 8.6, H–C(3a), H–C(5a)); 5.38 (*d*, *J* = 8.4, H–C(7a)); 3.22 (br. *d*, *J* = 8.4, H–C(8a)); 6.63 (br. *s*, H–C(10a), H–C(14a)); 6.90 (*t*, *J* = 2.0, H–C(12a)); 7.20 (*d*, *J* = 8.8, H–C(2b), H–C(6b)); 7.05 (*d*, *J* = 8.8, H–C(3b), H–C(5b)); 5.34 (*d*, *J* = 11.0, H–C(7b)); 3.22 (*d*, *J* = 11.0, H–C(8b)); 6.69 (*d*, *J* = 2.0, H–C(12b)); 7.41 (br. *d*, H–C(14b)); 4.88 (*d*, *J* = 2.0, H–C(4′)); 5.22 (*ddd*, *J* = 5.8, 4.0, 2.0, H–C(5′)); 4.04 (*dd*, *J* = 10.2, 4.0, H–C(6′)); 4.24 (*dd*, *J* = 10.2, 5.8, H–C(6′)); 2.09, 2.25, 2.26, 2.26, 2.27, 2.28, 2.31 (7 AcO). FAB-MS (neg.): 921 ($[M-H]^-$).

*6-[3-(3,5-Dimethoxyphenyl)-2,3-dihydro-6-methoxy-2-(4-methoxyphenyl)benzofuran-4-yl]-tetrahydro-3,5a-dihydroxy-7-(4-methoxyphenyl)-, 6-[3-(3,5-Dimethoxyphenyl)-2,3-dihydro-6-methoxy-2-(4-methoxyphenyl)benzofuran-4-yl]-tetrahydro-3-hydroxy-5a-methoxy-7-(4-methoxyphenyl)-, and 6-[3-(3,5-Dimethoxyphenyl)-2,3-dihydro-6-methoxy-2-(4-methoxyphenyl)benzofuran-4-yl]-tetrahydro-3,5a-dimethoxy-7-(4-methoxyphenyl)-2*H*-difuro[3,2-*b*:2′,3′-*c*]furan-5(5a*H*)-one* (**1b**, **1c**, and **1d**, resp.). Compound **1** (100 mg) was treated with K_2CO_3 (2 g) and MeI (0.5 g) in dry acetone under reflux for 6 h. Workup in the usual manner and purification of the crude product (105 mg) by prep. TLC (hexane/AcOEt 1:1) afforded **1b** (24 mg), **1c** (65 mg), and **1d** (7 mg).

Pentamethyl Ether **1b**: Colorless amorphous powder. ^{1}H-NMR ((D_6)acetone, 400 MHz)[1]): 6.82 (br. *s*, H–C(2a), H–C(6a)); 6.82 (br. *s*, H–C(3a), H–C(5a)); 3.79 (*s*, MeO–C(4a)); 5.19 (*d*, *J* = 7.3, H–C(7a)); 3.17 (*d*, *J* = 7.3, H–C(8a)); 6.04 (br. *d*, H–C(10a), H–C(14a)); 3.72 (*s*, MeO–C(11a), MeO–C(13a)); 6.34 (*t*, *J* = 2.0, H–C(12a)); 7.03 (*d*, *J* = 8.3, H–C(2b), H–C(6b)); 6.84 (*d*, *J* = 8.3, H–C(3b), H–C(5b)); 3.75 (*s*, MeO–C(4b)); 5.36 (*d*, *J* = 10.7, H–C(7b)); 3.19 (*d*, *J* = 10.7, H–C(8b)); 6.37 (*d*, *J* = 2.0, H–C(12b)); 3.82 (*s*, MeO–C(13b)); 7.30 (br. *d*, H–C(14b)); 5.43 (br. *s*, OH–C(2′)); 4.35 (br. *s*, H–C(4′)); 4.24 (br. *s*, H–C(5′)); 4.82 (br. *d*, OH–C(5′)); 4.00 (*dd*, *J* = 10.2, 4.2, 1 H–C(6′)); 4.08 (*dd*, *J* = 10.2, 2.4, 1 H–C(6′)). ^{13}C-NMR ((D_6)acetone, 100 MHz; * overlapping)[1]): 133.7 (C(1a)); 128.5 (C(2a), C(6a)); 114.7 (C(3a), C(5a)); 160.7 (C(4a)); 55.7 (*Me*O–C(4a)); 93.8 (C(7a)); 57.4 (C(8a)); 145.6 (C(9a)); 106.5 (C(10a), C(14a)); 162.4 (C(11a), C(13a)); 55.6* (*Me*O–C(11a), *Me*O–C(13a)); 100.7 (C(12a)); 131.2 (C(1b)); 128.1 (C(2b), C(6b)); 114.5 (C(3b), C(5b)); 160.0 (C(4b)); 55.6* (*Me*O–C(4b)); 89.8 (C(7b)); 56.8 (C(8b)); 131.9 (C(9b)); 123.7 (C(10b)); 161.4 (C(11b)); 95.9 (C(12b)); 161.9 (C(13b)); 55.8 (*Me*O–C(13b)); 109.9 (C(14b)); 172.1 (C(1′)); 81.1 (C(2′)); 118.9 (C(3′)); 89.5 (C(4′)); 74.8 (C(5′)); 75.8 (C(6′)). FAB-MS (neg.): 697 ($[M-H]^-$). HR-FAB-MS (neg.): 697.2295 ($[M-H]^-$, $C_{39}H_{38}O_{12}^-$; calc. 697.2285).

Hexamethyl Ether **1c**: Colorless amorphous powder. ^{1}H-NMR ((D_6)acetone, 400 MHz)[1]): 6.85 (*d*, *J* = 8.8, H–C(2a), H–C(6a)); 6.88 (*d*, *J* = 8.6, H–C(3a), H–C(5a)); 3.81 (*s*, MeO–C(4a)); 5.23 (*d*, *J* = 6.8, H–C(7a)); 3.26 (br. *s*, H–C(8a)); 6.03 (br. *d*, H–C(10a), H–C(14a)); 3.72 (*s*, MeO–C(11a), MeO–C(13a)); 6.36 (*t*, *J* = 2.0, H–C(12a)); 7.00 (*d*, *J* = 8.3, H–C(2b), H–C(6b)); 6.83 (*d*, *J* = 8.3, H–C(3b), H–C(5b)); 3.76 (*s*, MeO–C(4b)); 5.32 (*d*, *J* = 10.2, H–C(7b)); 3.29 (*d*, *J* = 10.2, H–C(8b)); 6.40 (*d*, *J* = 2.0, H–C(12b)); 3.84 (*s*, MeO–C(13b)); 7.08 (br. *d*, H–C(14b)); 3.40 (br. *s*, MeO–C(2′)); 4.35 (br. *s*, H–C(4′)); 4.35 (br. *s*, H–C(5′)); 4.88 (br. *d*, OH–C(5′)); 4.07 (*dd*, *J* = 9.5, 5.2, 1 H–C(6′)); 4.20 (*dd*, *J* = 9.5, 4.6, 1 H–C(6′)). ^{13}C-NMR ((D_6)acetone, 100 MHz; * overlapping)[1]): 133.8 (C(1a)); 128.2 (C(2a), C(6a)); 114.5 (C(3a), C(5a)); 160.9 (C(4a)); 55.7 (*Me*O–C(4a)); 93.6 (C(7a)); 57.3 (C(8a)); 145.5 (C(9a)); 106.4 (C(10a), C(14a)); 162.3 (C(11a), C(13a)); 55.5* (*Me*O–C(11a), *Me*O–C(13a)); 100.5 (C(12a)); 131.2 (C(1b)); 127.9 (C(2b), C(6b));

114.4 (C(3b), C(5b)); 160.5 (C(4b)); 55.5* (*Me*O–C(4b)); 89.7 (C(7b)); 56.4 (C(8b)); 132.1 (C(9b)); 123.5 (C(10b)); 161.4 (C(11b)); 95.7 (C(12b)); 161.8 (C(13b)); 55.9 (*Me*O–C(13b)); 109.9 (C(14b)); 169.4 (C(1′)); 86.3 (C(2′)); 55.5* (*Me*O–C(2′)); 119.4 (C(3′)); 89.9 (C(4′)); 75.4 (C(5′)); 74.5 (C(6′)). FAB-MS (neg.): 711 ($[M-H]^-$). HR-FAB-MS (neg.): 711.2455 ($[M-H]^-$, $C_{40}H_{40}O_{12}^-$; calc. 711.2441).

Heptamethyl Ether **1d**: Colorless amorphous powder. ^{1}H-NMR ((D$_6$)acetone, 400 MHz)[1]): 6.85 (*d*, *J* = 8.8, H–C(2a), H–C(6a)); 6.88 (*d*, *J* = 8.8, H–C(3a), H–C(5a)); 3.81 (*s*, MeO–C(4a)); 5.26 (*d*, *J* = 6.9, H–C(7a)); 3.29 (br. *s*, H–C(8a)); 6.06 (br. *d*, H–C(10a), H–C(14a)); 3.74 (*s*, MeO–C(11a), MeO–C(13a)); 6.34 (*t*, *J* = 2.0, H–C(12a)); 7.00 (*d*, *J* = 8.3, H–C(2b), H–C(6b)); 6.83 (*d*, *J* = 8.3, H–C(3b), H–C(5b)); 3.76 (*s*, MeO–C(4b)); 5.33 (*d*, *J* = 10.3, H–C(7b)); 3.30 (*d*, *J* = 10.3, H–C(8b)); 6.40 (*d*, *J* = 2.0, H–C(12b)); 3.83 (*s*, MeO–C(13b)); 7.06 (br. *d*, H–C(14b)); 3.40 (br. *s*, MeO–C(2′)); 4.38 (*d*, *J* = 2.2, H–C(4′)); 4.02 (*ddd*, *J* = 5.7, 4.7, 2.2, H–C(5′)); 3.43 (*s*, MeO–C(5′)); 4.09 (*dd*, *J* = 9.6, 4.7, H–C(6′)); 4.30 (*dd*, *J* = 9.6, 5.7, H–C(6′)). ^{13}C-NMR ((D$_6$)acetone, 100 MHz ** interchangeable, * overlapping[1]): 133.8 (C(1a)); 128.2 (C(2a), C(6a)); 114.6 (C(3a), (5a)); 160.9 (C(4a)); 55.7 (*Me*O–C(4a)); 93.6 (C(7a)); 57.4** (C(8a)); 145.6 (C(9a)); 106.5 (C(10a), C(14a)); 162.4 (C(11a), C(13a)); 55.5* (*Me*O–C(11a), *Me*O–C(13a)); 100.4 (C(12a)); 131.1 (C(1b)); 127.9 (C(2b), C(6b)); 114.5 (C(3b), C(5b)); 160.6 (C(4b)); 55.5* (*Me*O–C(4b)); 89.8 (C(7b)); 57.7** (C(8b)); 132.0 (C(9b)); 123.6 (C(10b)); 161.4 (C(11b)); 95.8 (C(12b)); 161.9 (C(13b)); 56.0 (*Me*O–C(13b)); 109.8 (C(14b)); 169.2 (C(1′)); 86.4 (C(2′)); 55.5* (*Me*O–C(2′)); 119.3 (C(3′)); 87.6 (C(4′)); 83.7 (C(5′)); 73.2 (C(6′)). FAB-MS (neg.): 725 ($[M-H]^-$). HR-FAB-MS (neg.): 725.2615 ($[M-H]^-$, $C_{41}H_{42}O_{12}^-$; calc. 725.2598).

*4-Bromobenzoic Acid 6-[3-(3,5-Dimethoxyphenyl)-2,3-dihydro-6-methoxy-2-(4-methoxyphenyl)benzofuran-4-yl]-hexahydro-5a-methoxy-7-(4-methoxyphenyl)-5-oxo-2*H*-difuro[3,2-*b*:2′,3′-*c*]furan-3-yl Ester* (**1e**). A soln. of **1c** (20 mg) in pyridine (5 ml) and 4-bromobenzoyl chloride (100 mg) was kept at 80° for 2 h. Workup in the usual manner and recrystallization of the crude product (24 mg) from $CHCl_3$/EtOH gave **1e** (18 mg). Colorless prisms. M.p. 203°. ^{1}H-NMR ((D$_6$)acetone, 300 MHz)[1]): 6.82 (*d*, *J* = 8.8, H–C(2a), H–C(6a)); 6.87 (*d*, *J* = 8.8, H–C(3a), H–C(5a)); 3.80 (*s*, MeO–C(4a)); 5.25 (*d*, *J* = 6.8, H–C(7a)); 3.24 (br. *s*, H–C(8a)); 6.03 (br. *d*, H–C(10a), H–C(14a)); 3.73 (*s*, MeO–C(11a), MeO–C(13a)); 6.38 (*t*, *J* = 2.0, H–C(12a)); 6.98 (*d*, *J* = 8.3, H–C(2b), H–C(6b)); 6.79 (*d*, *J* = 8.3, H–C(3b), H–C(5b)); 3.74 (*s*, MeO–C(4b)); 5.42 (*d*, *J* = 10.1, H–C(7b)); 3.35 (*d*, *J* = 10.1, H–C(8b)); 6.41 (*d*, *J* = 2.0, H–C(12b)); 3.85 (*s*, MeO–C(13b)); 7.09 (br. *d*, H–C(14b)); 3.49 (br. *s*, MeO–C(2′)); 4.60 (br. *d*, H–C(4′)); 5.49 (*ddd*, *J* = 4.9, 3.1, 1.6, H–C(5′)); 8.01, 7.77 (2*d*, *J* = 8.8, 4 arom. H (4-BrC_6H_4CO)); 4.52 (*dd*, *J* = 10.1, 4.9, H–C(6′)); 4.42 (*dd*, *J* = 10.1, 3.1, H–C(6′)).

X-Ray Crystal-Structure Analysis of **1e**. A colorless prism crystal of **1e** having the dimensions of *ca*. 0.22 × 0.20 × 0.05 mm was mounted on a glass fiber. All measurements were made on a *Rigaku-AFC-7R* diffractometer with graphite monochromated Cu-K_α radiation. Of the 7957 reflections collected, 3980 were unique (R_{int} = 0.013). No decay correction was applied. An empirical absorption correction based on azimuthal scans of three reflections was applied, which resulted in transmission factors ranging from 0.72 to 1.0. The structure was solved by direct methods [6] and expanded by *Fourier* techniques [7]. The non-H-atoms were refined anisotropically. H-Atoms were included, but not refined. The final cycle of full-matrix least-squares refinement was based on 3980 observed reflections and 551 variable parameters, and converged with unweighted and weighted agreement factors of $R = 0.054$, $R_w = 0.108$. The maximum and minimum peaks on the final difference *Fourier* map corresponded to 0.27 and -0.36 e$^-$/A^3, resp. The absolute configuration of the molecule was determined based on *Flack*'s parameter, 0.026 (22), and confirmed by the method of *Bijvoet* inequality relationships. Comparing $|F_o(hkl)|/|F_o(h\bar{k}\bar{l})|$ and $|F_c(hkl)|/|F_c(h\bar{k}\bar{l})|$ for 326 *Friedel* pairs for which the differences $||F_c(hkl)|-|(h\bar{k}\bar{l})||/(\sigma(F_o(hkl))^2+\sigma(F_o(h\bar{k}\bar{l}))^2)^{1/2}$ are greater than 1.0, 314 pairs showed consistently the absolute configuration given in *Fig. 3*. All calculations were performed with the teXsan crystallographic software package of *Molecular Structure Corporation*.

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