

Reactions of Lignan Precursors, Cinnamyl Alcohols and Cinnamic Acids, with Weitz' Aminium Salt

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Reaction of a lignans precursor, cinnamyl alcohol (2a), with Weitz' aminium salt, tris(4-bromophenyl)aminium hexachloroantimonate, in THF gave cinnamaldehyde (4), a coupling product (5), and a furofuran lignan, (±)-sesamin (6). Similar reactions using related precursors 2b, 3a, 3b gave 7, 8a, 9a, 10a, 11a, and 11b.

Key words lignan; synthesis; (±)-sesamin; Weitz' aminium salt; cinnamyl alcohol; cinnamic acid

It is well established that lignans and neo-lignans¹⁾ are formed in nature by the oxidative dimerization of various C₆C₃ phenols (1).²⁾ Indeed, some lignans and neo-lignans can be prepared from 1 either by enzymic oxidation or by using conventional oxidizing agents.³⁾

Recently, much attention has been focused on the use of mild one-electron oxidation catalysts such as Weitz' aminium salt to achieve a variety of rapid and selective organic reactions.⁴⁾ Of particular interest is a report on the radical cation-initiated Diels–Alder reaction of methylisoeugenol with Weitz' aminium salt, tris(4-bromophenyl)aminium hexachloroantimonate (BAHA),⁵⁾ to give isomers of aryltetralin neolignans, as well as trimers of the reactant. This prompted us to examine the application of the reagent to the synthesis of various lignans in connection with biosynthetic studies.⁶⁾

As substrates for our present purpose, we selected four non-phenolic compounds, (*E*)-3,4-methylenedioxycinnamyl alcohol (2a), (*E*)-3,4-methylenedioxycinnamyl acetate (2b), (*E*)-3,4,5-trimethoxycinnamic acid (3a), and methyl 3,4,5-trimethoxycinnamate (3b), and subjected them to the reaction with BAHA as follows (Table 1). Treatment of 2a with 2 eq of BAHA in tetrahydrofuran (THF) in the presence of Na₂CO₃ at 0 °C under a nitrogen atmosphere until the deep blue color of the reagent changed to light yellow gave three products, namely, cinnamaldehyde (4), a coupling product 5a between 2a and BAHA, and a furofuran lignan (±)-sesamin (6),⁷⁾ in yields of 44.2%, 3.6% and 16.2%, respectively.⁸⁾ Reaction of the acetate 2b with BAHA in the same manner as described above gave a dibenzazepine derivative 7, 8a (an analogue of 5a), and *erythro*- and *threo*-chloropropanol 9a and 10a in yields of 3.9%, 10.4%, 6.3%, and 7.8%, respectively.

Reactions of the cinnamic acids 3a and 3b with BAHA in THF in the same manner afforded the dibenzazepine

derivatives 11a and 11b in yields of 18.9% and 41.2%, respectively.

The structure of (±)-sesamin (6) was identified by comparison of the physical data with those of an authentic sample of (±)-sesamin^{7b)} and also by a ¹H-NOE experiment (Tables 3 and 4). The structures of 5a and 8a were assigned from the following chemical transformations and spectral analyses (Tables 5 and 6). (i) The IR spectrum of 5a showed the presence of hydroxyl groups (at 3432 cm⁻¹). (ii) The ¹H-NMR spectrum showed three proton signals in higher magnetic field, assigned to C₁-H (δ 4.99), C₂-H (δ 3.46–3.50), and C₃-H (δ 3.31–3.36). (iii) The ¹³C-NMR spectrum showed signals corresponding to C-1 (δ 74.7), C-2 (δ 48.1), and C-3 (δ 63.5). (iv) The molecular ion peak at *m/z* 673 was observed in the mass spectrum (MS). The MS also showed peaks at *m/z* 675 (M⁺+2), 677 (M⁺+4), and 679 (M⁺+6), and further, its high-resolution MS (HR-MS) demonstrated the presence of three bromine atoms in the molecule. These data suggested that 5a may be a compound in which a hydroxyl group and a tris(4-bromophenyl)amine group are attached to the C-1 and C-2 positions of the olefinic substrate 2a, respectively.

The signal patterns of the ¹H-NMR spectrum of 8a were very similar to those of 5a except for the proton

Table 1. Reactions of 2a, 2b, 3a, and 3b with BAHA in THF

Run	Substrate	Products (yield %)			
1	2a	4 (44.2)	5a (3.6)	6 (16.2)	
2	2b	7 (3.9)	8a (10.4)	9a (6.3)	10a (7.8)
3	3a	11a (11.9)	3a (18.9) ^{a)}		
4	3b	11b (14.5)	3b (41.2) ^{a)}		

a) Recovery.

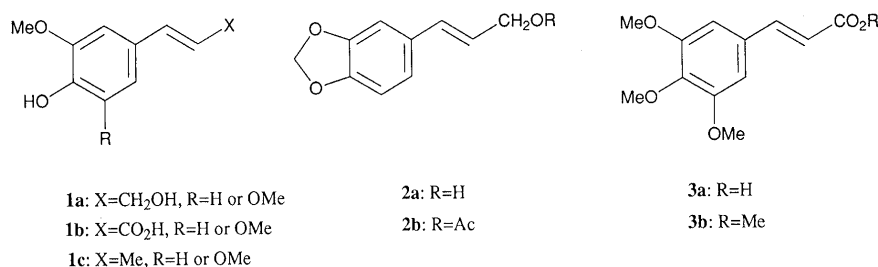


Chart 1

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signal due to the acetoxyl group at C-3 and the chemical shift of the C-3 methylene proton signals. Acetylation of **5a** and **8a** with Ac_2O -pyridine gave the diacetates **5b** and **8b**, respectively. These results suggested that **5b** and **8b** may be stereoisomers at the C-1 and C-2 positions. A *threo*-compound and its *erythro* isomer, such as **5b** and **8b** can be distinguished on the basis of the chemical shifts of C-3 methylene proton signals in the ^1H -NMR spectrum.⁹⁾

Two isomers, I and II, are possible for these compounds as shown in Chart 3, and these isomers correspond to *threo*- and *erythro*-compounds, respectively. The signals of $\text{C}_3\text{-H}$ (δ 3.49 and 4.01) of **5b** are observed at higher field in the ^1H -NMR spectrum than the corresponding

signals of **8b** (δ 3.82 and 4.28) owing to the shielding effect of the phenyl group at the C-1 position. Therefore, the structures **5a** and **5b** may be assigned to the isomer I, and **8a** and **8b** to isomer II. The structures of **9a** and **10a** were elucidated by analyses of their physical data in the same way as done in the case of **5a** and **8a** (see Tables 7 and 8).

We postulated the dibenzazepine structure for **11a**, based on analyses of its physical data with the aid of ^1H - ^{13}C shift correlation spectroscopy (COSY) and ^1H -detected heteronuclear multiple bond connectivity (HMBC) experiments (see Fig. 1, Tables 9 and 10). That is, **11a** showed a strong carboxylic acid absorption at 1695 cm^{-1} and aromatic absorption at 1585 cm^{-1} in the

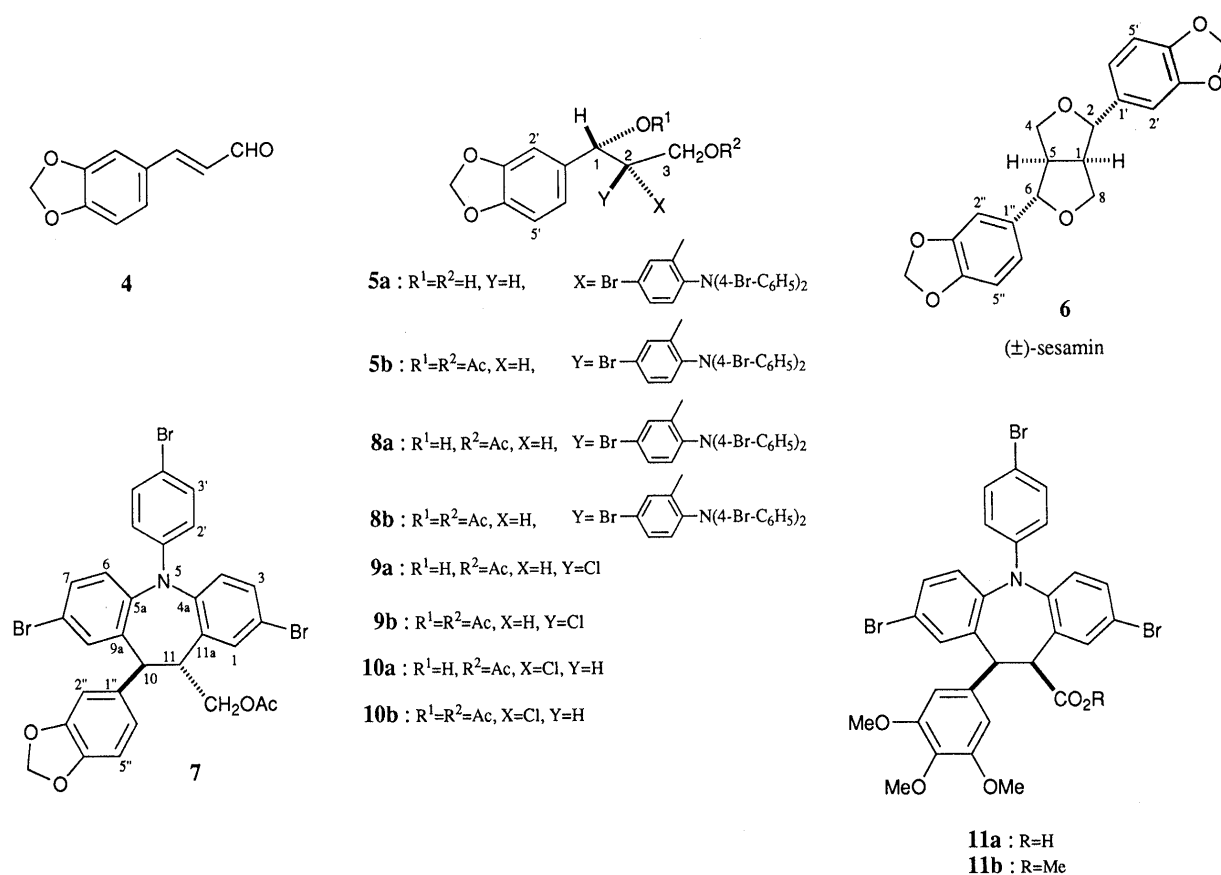
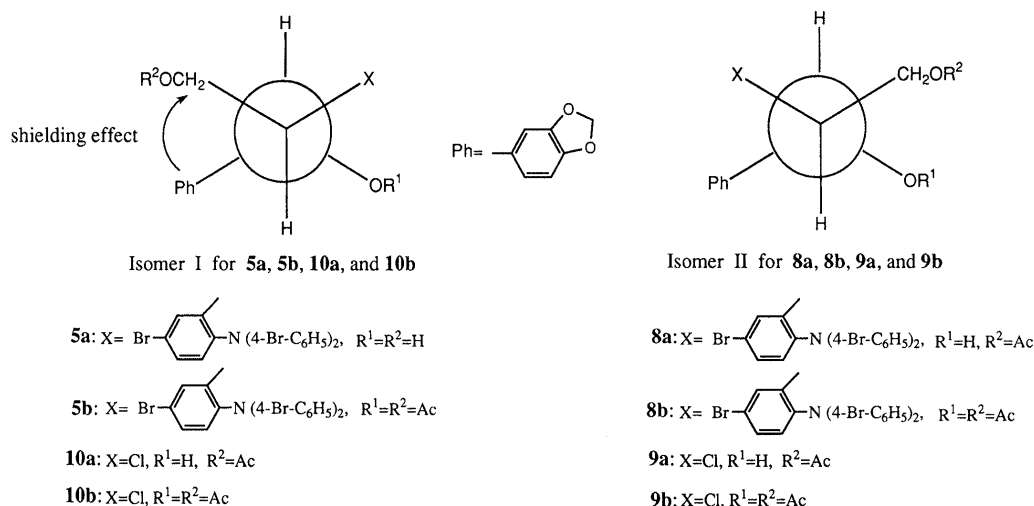


Chart 2

Chart 3. Possible Conformations for **5**, **8**, **9**, and **10**

IR spectrum. In the HMBC spectrum of **11a**, the proton at δ 4.90 (C_{10} -H) showed long-range correlations with the carbons at δ 106.3 ($C_{2''}$ and $C_{6''}$), 139.8 (C_{5a}), 139.1 (C_{9a}), 138.7 (C_{11a}), and 153.0 ($C_{3''}$ and $C_{5''}$) indicating the presence of a dibenz[*b,f*]azepine moiety, and trimethoxybenzene nuclear binding at the C_{10} position of the benzazepine nucleus with the $C_{1''}$ position of benzene. On the other hand, the proton at δ 3.77 (C_{11} -H) showed long-range correlations with the carbons at δ 142.0 (C_{4a}) and 134.9 (C_{1}), indicating that the carboxylic acid group binds at the C_{11} position of the dibenz[*b,f*]azepine moiety. Further, C_{10} -H and C_{11} -H in **11a** may have *cis* relative configuration because the coupling constant between these two protons was 3.4 Hz.

The structures of **7** and **11b** were elucidated by analyses and comparison of the IR spectra and the 1H - and ^{13}C -NMR spectra with those of **11a**, with the aid of the results of the 1H - ^{13}C COSY (see Tables 9 and 10). The stereochemistry of **7** and **11b** was postulated from the coupling constant values in the 1H -NMR spectra. That is, C_{10} -H and C_{11} -H of **7** and **11b** may have *trans* and *cis* configurations because the coupling constants between these two protons were 10.6 and 4.9 Hz, respectively.

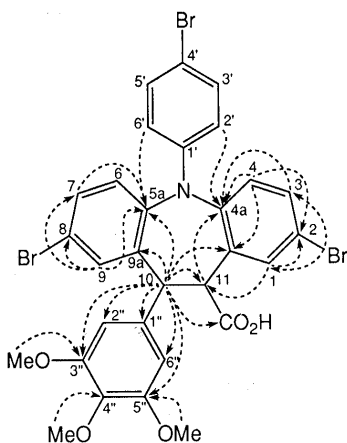


Fig. 1. Long-Range Correlations (1H ^{13}C) in the HMBC Spectrum of **11a**

Table 2. Reactions of **2a**, **2b**, **3a**, and **3b** with $Cu(OTf)_2$ - Cu_2O in MeCN

Run	Substrate	Products (yield %)	
1	2a	4 (23.8)	6 (11.7)
2	2b	12 (13.0)	13 (31.2)
3	3a	No reaction	
4	3b	No reaction	

Subsequently, we investigated reactions of **2a**, **2b**, **3a**, and **3b** with another mild one-electron oxidation reagent, copper(II) trifluoromethanesulfonate [$Cu(OTf)_2$] in the presence of Cu_2O ,¹⁰ for comparison with the reaction with BAHA (Table 2 and Fig. 2). Although reactions of **2a** and **2b** with the above reagent system gave the oxidation products, the reaction did not proceed for **3a** and **3b**. Reaction of **2a** with $Cu(OTf)_2$ - Cu_2O in MeCN gave the aldehyde **4** and ($\pm$)-sesamin (**6**) in yields of 23.8% and 11.7%, respectively. Reaction of **2b** with the same reagent system afforded the tetralins (**12** and **13**) in yields of 13% and 31.2%, respectively.

The MS and 1H -NMR of **12** and **13** suggest that they are epimeric dimers of **2b** at C_{11} . The stereochemistry of the dimers was established by analyses of the coupling constants and a 1H -NOE experiment (see Table 11).

The proton signals of C_2 -H and C_3 -H, and C_3 -H and C_4 -H in **12** and **13** suggested that they may have *trans*

Table 3. 1H -NMR Spectral Data for **6**^{a)}

Proton No.	6
H-1 α and H-5 α	3.03—3.07, m
H-2 β and H-6 β (J = Hz)	4.71, d (4.6)
H-4 α and H-8 α (J = Hz)	4.23, dd (9.2, 6.7)
H-4 β and H-8 β (J = Hz)	3.87, dd (9.2, 3.7)
H-2' and H-2'' (J = Hz)	6.84, d (1.5)
H-5' and H-5'' (J = Hz)	6.77, d (7.9)
H-6' and H-6'' (J = Hz)	6.80, dd (7.9, 1.5)
2 $\times$ OCH_2O	5.95, s

a) δ in $CDCl_3$; 1H -NMR at 270 MHz.

Table 4. ^{13}C -NMR Spectral Data for **6**^{a)}

Carbon No.	6
1 and 5	54.3
2 and 6	85.8
4 and 8	71.7
1' and 1''	135.0
2' and 2''	106.5
3' and 3''	148.0
4' and 4''	147.1
5' and 5''	108.2
6' and 6''	119.4
OCH_2O	101.1

a) δ in $CDCl_3$; ^{13}C -NMR at 125.65 MHz.

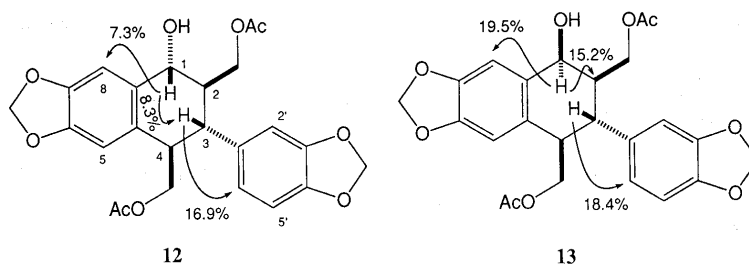


Fig. 2. Significant Enhancement of Signal Intensity in NOE Experiments on **12** and **13**

Table 5. ^1H -NMR Spectral Data for **5a**, **5b**, **8a** and **8b**^{a)}

Proton No.	5a	5b	8a	8b
H-1 ($J=\text{Hz}$)	4.99, d (5.8)	5.93, d (5.2)	4.69, d (6.7)	5.85, d (7.9)
H-2	3.46 —3.50, m	3.66, ddd (8.6)	3.43 —3.46, m	3.63, ddd (8.2)
H-3	3.31 —3.36, m	3.49, dd (11.3)	3.94, dd (11.3)	3.82, dd (11.3)
H-2'	6.57, d (1.5)	6.47, d (1.5)	6.50, d (1.5)	6.46, d (1.5)
H-5'	6.70, d (8.0)	6.69, d (7.9)	6.62, d (7.9)	6.63, d (7.9)
H-6'	6.61, dd (8.0)	6.57, dd (7.9)	6.35, dd (7.9)	6.40, dd (7.9)
OCH ₂ O ($J=\text{Hz}$)	5.92, d (1.5)	5.92, d (1.5)	5.90, d (1.5)	5.89, d (1.5)
H-3''	6.93, d (8.5)	6.98, d (8.6)	6.89, d (8.5)	6.89, d (8.6)
H-4''	7.38, dd (8.5)	7.41, dd (8.6)	7.36, dd (8.5)	7.36, dd (8.6)
H-6''	7.88, d (2.1)	7.65, d (2.4)	7.72, d (2.5)	7.69, d (2.4)
H-2''', 6''' 2''' and 6'''	6.65 —6.72, m	6.75, br d (8.5)	7.15 —7.36, m	7.26 —7.32, m
H-3''', 5''' 3''' and 5'''	7.24 —7.28, m	7.28 —7.34, m	7.15 —7.36, m	7.26 —7.32, m
C3-OCOCH ₃	—	1.98, s or 1.92, s	1.99, s	2.06, s or 1.98, s
C1-OCOCH ₃	—	1.92, s or 1.98, s	—	1.98, s or 2.06, s

All assignments were confirmed by the ^1H - ^{13}C COSY spectra. a) δ in CDCl_3 ; ^1H -NMR at 270 MHz.

Table 6. ^{13}C -NMR Spectral Data for **5a** and **8a**^{a)}

Carbon No.	5a	8a
1	74.7	74.5
2	48.1	45.5
3	63.5	63.6
1'	139.9	133.8
2'	106.7	106.5
3'	147.9	148.1
4'	147.3	147.2
5'	108.1	107.8
6'	119.1	119.8
OCH ₂ O	101.1	101.2
1''	136.5	136.2
2''	144.7	140.0
3''	131.5	131.6
4''	131.7	131.9
5''	120.3	121.1
6''	133.9	133.6
1''' and 1'''	146.6	144.1
2''', 6''', 2''' and 6'''	123.6	132.2
3''', 5''', 3''' and 5'''	132.2	132.2
4''' and 4'''	120.3	120.1
OCOCH ₃	—	20.9
OCOCH ₃	—	171.0

All assignments were confirmed by the ^1H - ^{13}C COSY spectra. a) δ in CDCl_3 ; ^{13}C -NMR at 125.65 MHz.

Table 7. ^1H -NMR Spectral Data for **9a**, **9b**, **10a** and **10b**^{a)}

Proton No.	9a	9b	10a	10b ^{b)}
H-1 ($J=\text{Hz}$)	4.84, d (5.8)	5.91, d (6.1)	5.91, d (7.3)	5.94, d (6.2)
H-2	4.23 —4.27, m	4.19 —4.24, m	4.23 —4.27, m	4.27 —4.65, m
H-3 α ($J=\text{Hz}$)	4.32, dd (11.9)	4.43 —4.42, m	3.79 —3.89, m	4.27 —4.65, m
H-3 β ($J=\text{Hz}$)	4.43, dd (12.2)	4.43 —4.42, m	3.79 —3.89, m	4.27 —4.65, m
H-2'	6.90, d (1.8)	6.87, d (1.8)	6.87, d (1.5)	6.99, d (1.8)
H-5'	6.80, d (7.9)	6.79, d (7.9)	6.79, d (7.9)	6.83, dd (8.6)
H-6'	6.84, dd (1.8)	6.84, dd (1.8)	6.86, dd (1.5)	6.96, dd (1.8)
C3-OCOCH ₃	2.09, s	2.10 or 2.11, s	2.11, s	2.03, s or 2.10, s
C1-OCOCH ₃	—	2.11 or 2.10, s	—	2.10, s or 2.03, s
OCH ₂ O	5.97, s	5.97, s	5.98, s	5.97, s

All assignments were confirmed by the ^1H - ^{13}C COSY spectra. a) δ in CDCl_3 ; ^1H -NMR at 270 MHz. b) δ in $(\text{CD}_3)_2\text{CO}$; ^1H -NMR at 90 MHz.

Table 8. ^{13}C -NMR Spectral Data for **9a**, **9b**, and **10a**^{a)}

Carbon No.	9a	9b	10a
1	75.6	74.7	74.8
2	62.9	59.7	64.4
3	64.2	64.1	63.3
1'	133.2	129.6	130.2
2'	106.9	107.7	107.7
3'	147.9	147.8	148.0
4'	147.6	148.0	147.8
5'	108.2	108.2	108.2
6'	120.2	121.4	121.5
OCH ₂ O	101.2	101.3	101.3
C-3-OCOCH ₃	20.7	20.7 or 21.0	21.0
C-1-OCOCH ₃	—	21.0 or 20.7	—
C-3-OCOCH ₃	170.9	169.4 or 170.5	169.6
C-1-OCOCH ₃	—	170.5 or 169.4	—

a) δ in CDCl_3 ; ^{13}C -NMR at 125.65 MHz.

relative configurations, based on the analyses of their coupling constants (Table 11). On the other hand, C₁-H and C₂-H of **12** and **13** may possess *trans* and *cis* configurations because the coupling constants between these two protons were 9.5 and *ca.* 0 Hz, respectively. In addition to the above data, when the signal at C₁-H (δ 4.53) in **12** was irradiated, an 8.3% increment of the C₃-H signal (δ 2.81) was observed, but irradiation of the signal at C₁-H (δ 4.64) in **13** had no influence on the signal at C₃-H (δ 3.01). These data suggested that the structures of **12** and **13** may be as shown in Fig. 2.

The products such as **5a**, **8a**, **9a**, and **10a** obtained in these reactions have a hydroxyl group at the C-1 position. This may arise from H₂O contained in the reagent, because

Table 9. ^1H -NMR Spectral Data for **7**, **11a**, and **11b**^{a)}

Proton No.	7	11a	11b
H-1 (J =Hz)	7.15, d (2.2)	7.04, d (2.1)	7.10, d (2.1)
H-3 (J =Hz)	7.43, dd (2.2)	7.51, dd (2.1)	7.52, dd (2.1)
H-4 (J =Hz)	7.27, d (8.5)	7.34, d (8.4)	7.37, d (8.5)
H-6	7.28, d (8.5)	7.22 —7.28, m	7.27 —7.33, m
H-7	7.32, dd (8.2)	7.22 —7.28, m	7.27 —7.33, m
H-9 (J =Hz)	7.50, d (2.2)	7.12, d (2.1)	7.15, d (2.1)
H-10 (J =Hz)	4.12, d (10.6)	4.90, d (3.4)	4.97, d (4.9)
H-11 (J =Hz)	3.67 —3.71, m	3.77, d (3.4)	3.81, d (4.9)
H-2' and H-6' (J =Hz)	6.62, d (9.2)	6.57, d (9.2)	6.69, d (9.2)
H-3' and H-5' (J =Hz)	7.24, d (9.2)	7.17, d (9.2)	7.24, d (9.2)
H-2''	6.51, d (1.5)	5.80, s	5.86, br s
H-5''	6.70, d (7.9)	—	—
H-6''	6.59, dd (7.9)	5.80, s	5.86, brs
C3'' and C5''-OMe	—	3.60, s	3.63, s
C4''-OMe	—	3.82, s	3.82, s
CO ₂ CH ₃	—	—	3.00, s
CH-OAc	4.02, dd (11.3)	—	—
CH-OAc	4.16, dd (11.3)	—	—
OCOCH ₃	1.98, s (4.2)	—	—
OCH ₂ O	5.92, d (1.5)	—	—
	5.94, d (1.5)	—	—

Assignments based upon ^1H - ^{13}C COSY and HMBC experiments. a) δ in CDCl_3 ; ^1H -NMR at 270 MHz.

all reactions were carried out under strictly anhydrous conditions and using deoxygenated solvent under a nitrogen atmosphere.

Experimental

All melting points are uncorrected. IR spectra were recorded with a JASCO IR-700 spectrometer, and ^1H - and ^{13}C -NMR spectra with JEOL JNM-EX90, JNM-GX270, and JNM-GSX500 spectrometers, with tetramethylsilane as an internal standard (CDCl_3 and C_6D_6 solution). Mass spectra were recorded on a JEOL JMS-D300 spectrometer. Elemental analyses were done using a Yanaco CHN-MT-3 apparatus. Wako silica gel C-200 (200 mesh) and Merck Kieselgel 60 F_{254} were used for column chromatography and thin-layer chromatography (TLC), respectively. Each organic extract was dried over Na_2SO_4 . High-performance liquid chromatography (HPLC) was performed on a Wakosil 5C4-200 column (25 cm $\times$ 4.6 mm i.d. for analytical scale or 25 cm $\times$ 20 mm i.d. for preparative scale) with aqueous methanol (40–60%), using a Shimadzu LC-6A apparatus for monitoring at 254 nm.

Reaction of **2a with BAHA in THF** Anhydrous Na_2CO_3 (7.4 g, 69 mmol), followed by BAHA⁵⁾ (3.76 g, mmol), was added to a solution

Table 10. ^{13}C -NMR Spectral Data for **7**, **11a**, and **11b**^{a)}

Carbon No.	7	11a	11b
1	135.53	134.9	134.3
2	121.0	121.1	121.2
3	131.3	131.9	131.8
4	130.5	130.68	130.77
4a	143.0	142.0	142.4
5a	141.6	139.8	140.1
6	130.3	128.5	127.9
7	130.9	130.7	130.8
8	120.7	119.3	119.5
9	132.8	136.4	136.4
9a	141.0 or 139.8	138.4	138.6
10	48.8	48.3	49.2
11	44.1	53.2	51.7
11a	139.8 or 141.0	138.7	138.6
1'	145.7	144.2	144.4
2' and 6'	113.9	115.3	115.3
3' and 5'	137.0	131.3	131.5
4'	110.5	110.9	111.2
1''	135.50	139.1	138.33
2''	108.4	106.3	106.2
3''	148.2	153.0	153.1
4''	146.8	137.1	138.4
5''	108.6	153.0	153.1
6''	121.4	106.3	106.2
C-3'', 5''-OMe	—	56.0	56.0
C-4''-OMe	—	60.9	60.9
CO ₂ R	—	174.8	170.7
CO ₂ CH ₃	—	—	53.8
CH ₂ OR	65.4	—	—
OCOCH ₃	20.8	—	—
OCOCH ₃	170.6	—	—
OCH ₂ O	101.2	—	—

Assignments based upon ^1H - ^{13}C COSY and HMBC experiments. a) δ in CDCl_3 ; ^{13}C -NMR at 125.65 MHz.

of **2a** (400 mg, 2.3 mmol) in THF (60 ml) under a nitrogen atmosphere at 0 °C. The mixture was stirred at room temperature for 30 min, when the deep blue color of the BAHA had faded. At this time, the light brown reaction mixture was passed through a short column of silica gel with AcOEt–hexane (1:2, v/v). The eluate was concentrated, and the residue was subjected to silica gel column chromatography. The first eluate with AcOEt–hexane (1:5, v/v) gave 234 mg of a mixture of **4** and **6**. The second eluate gave 55 mg (3.6%) of *threo*-2-{2-[*N,N*-bis(4-bromophenyl)amino]-5-bromophenyl]-1-(3,4-methylenedioxyphenyl)-1,3-propanediol (**5a**). The above mixture was further separated by preparative thin-layer chromatography (PTLC) on silica gel using CHCl_3 –hexane (4:1, v/v) as an eluent to give 175 mg (44.2%) of 3,4-methylenedioxycinnamaldehyde (**4**), R_f =0.63, and 60 mg (16.2%) of 2,6-bis(3,4-methylenedioxyphenyl)-3,7-dioxabicyclo[3.3.0]octane (**6**), R_f =0.38. **4**: colorless crystals, mp 77–79 °C (ether–petroleum ether). IR (KBr) cm^{-1} : 1668, 1662, 1598, 1488. ^1H -NMR (CDCl_3) δ : 6.04 (2H, s, $-\text{OCH}_2\text{O}-$), 6.56 (1H, dd, J =7.6, 15.9 Hz, $=\text{CH}-\text{CHO}$), 6.86 (1H, d, J =8.5 Hz, H-5), 7.065 (1H, d, J =1.8 Hz, H-2), 7.07 (1H, dd, J =1.8, 8.5 Hz, H-6), 7.38 (1H, d, J =15.9 Hz, Ar-CH=), 9.65 (1H, d, J =7.6 Hz, $-\text{CHO}$). HR-MS Calcd for $\text{C}_{10}\text{H}_8\text{O}_3$: 176.0473. Found: 176.0448. **5a**: colorless crystals, 92.5–94.0 °C (ether–petroleum ether). IR (KBr) cm^{-1} : 3432, 1483. Anal. Calcd for $\text{C}_{28}\text{H}_{22}\text{Br}_3\text{NO}_4$: C, 49.73; H, 3.28; N, 2.07. Found: C, 49.70; H, 3.30; N, 2.05. HR-MS Calcd for $\text{C}_{28}\text{H}_{22}\text{Br}_3\text{NO}_4$: 672.9040, 674.9079, 676.9058, 678.9037. Found: 672.8991, 674.8956, 676.8877, 678.9089. **6**: colorless crystals, mp 127.0–128.5 °C (ethanol). IR (KBr) cm^{-1} : 2878, 1500, 1488. Anal. Calcd for $\text{C}_{20}\text{H}_{18}\text{O}_6$: C, 67.79; H, 5.12. Found: C, 67.77; H, 5.10. HR-MS Calcd for $\text{C}_{20}\text{H}_{18}\text{O}_6$: 354.1103. Found: 354.1135. ^1H - and ^{13}C -NMR data for **5a** and **6** are listed in Tables 3, 4, 5, and 6.

Reaction of **2b with BAHA** Reaction of **2b** (556 mg, 2.5 mmol) was carried out at 0 °C for 1.5 h by the procedure described for the reaction of **2a** with BAHA to give a crude product (containing **7**, **8a**, **9a**, and

Table 11. ¹H-NMR Spectral Data for **12** and **13**^a

Proton No.	12	13
H-1 (<i>J</i> =Hz)	4.53β, br d (9.5)	4.64α, br s
H-2	3.20 —3.33, m	2.21 —2.27, m
H-3 (<i>J</i> =Hz)	2.81β, dd (11.6) (9.2)	3.01β, dd (12.5) (9.2)
H-4	3.20 —3.33, m	3.12 —3.16, m
H-5	6.74, s	6.79, s
H-8	7.19, s	6.82, s
H-2' (<i>J</i> =Hz)	6.67, d (1.2)	6.70, d (1.8)
H-5' (<i>J</i> =Hz)	6.77, d (7.9)	6.75, d (7.6)
H-6' (<i>J</i> =Hz)	6.65, dd (7.9) (1.2)	6.67, dd (7.6) (1.8)
2 × OCOCH ₃	2.10, s 2.09, s	2.04, s 1.94, s
C2-CH ₂ OCOCH ₃	3.60, dd (11.6) (3.4) 4.63, dd (11.6) (2.4)	3.72, dd (11.3) (4.3) 4.19, t (11.3)
C4-CH ₂ OCOCH ₃	3.98, dd (11.6) (4.6) 4.27, dd (11.3) (4.6)	4.12, dd (11.3) (4.3) 4.31, dd (11.3) (4.6)
2 × OCH ₂ O	5.96, s 5.95, s	5.96, s

^a δ in CDCl₃; ¹H-NMR at 270 MHz.

10a). This was subjected to silica gel column chromatography. The first eluate with hexane gave 68 mg (3.9%) of 5*H*-11β-acetoxymethyl-2,8-dibromo-5-(4-bromophenyl)-10β-(3,4-methylenedioxyphenyl)dibenz[*b,f*]azepine (**7**). The second eluate with AcOEt–hexane (1:10, v/v) gave 188 mg (10.4%) of *erythro*-2-{2-[*N,N*-bis(4-bromophenyl)amino]-5-bromophenyl}-3-hydroxy-3-(3,4-methylenedioxyphenyl)propyl ethanoate (**8a**). The third eluate with AcOEt–hexane (1:8, v/v) gave 40 mg (6.3%) of *erythro*-2-chloro-3-hydroxy-3-(3,4-methylenedioxyphenyl)propyl ethanoate (**9a**). The final eluate with AcOEt–hexane (1:6, v/v) gave 50 mg (7.8%) of *threo*-2-chloro-3-hydroxy-3-(3,4-methylenedioxyphenyl)propyl ethanoate (**10a**). **7**: amorphous powder, mp 191.5–193.5 °C (ether–petroleum ether). IR (KBr) cm^{−1}: 1738, 1594, 1485. *Anal.* Calcd for C₃₀H₂₂Br₃NO₄: C, 51.46; H, 3.17; N, 2.00. Found: C, 51.49; H, 3.20; N, 2.03. HR-MS Calcd for C₃₀H₂₂Br₃NO₄: 696.9100, 698.9079, 700.9058, 702.9037. Found: 696.8892, 698.8912, 700.8976, 702.9032. **8a**: colorless crystals, mp 77–79 °C (ether–hexane). IR (KBr) cm^{−1}: 3456, 1734, 1579, 1484. *Anal.* Calcd for C₃₀H₂₄Br₃NO₅: C, 50.17; H, 3.37; N, 1.95. Found: C, 50.20; H, 3.39; N, 1.93. HR-MS Calcd for C₃₀H₂₄Br₃NO₅: 714.9206, 716.9185, 718.9164, 720.9143. Found: 714.9320, 716.9328, 718.9279, 720.9267. **9a**: colorless oil. IR (KBr) cm^{−1}: 3474, 1740, 1503. HR-MS Calcd for C₁₂H₁₃ClO₅: 272.0452, 274.0432. Found: 272.0468, 274.0435. **10a**: colorless oil. IR (KBr) cm^{−1}: 3442, 1742, 1491. HR-MS Calcd for C₁₂H₁₃ClO₅: 272.0452, 274.0432. Found: 272.0416, 274.0430. ¹H- and ¹³C-NMR data for **7**, **8a**, **9a**, and **10a** are listed in Tables 5–10.

Reaction of 3a with BAHA Reaction of **3a** (500 mg, 2.1 mmol) with BAHA was carried out at 0 °C for 2.0 h by the procedure described for the reaction of **2a** to give a crude product (containing **11a** and **3a**). Purification of the crude mixture by column chromatography on silica gel using AcOEt–hexane (1:3, v/v) as an eluent to give 180 mg (11.9%) of 5*H*-2,8-dibromo-5-(4-bromophenyl)-10β-(3,4-methylenedioxyphenyl)dibenz[*b,f*]azepine-11α-carboxylic acid (**11a**) and 94.5 mg (18.9%) of recovered **3a**. **11a**: colorless crystals, mp 183–185 °C

(ether–hexane). IR (KBr) cm^{−1}: 1695, 1585, 1483. *Anal.* Calcd for C₃₀H₂₄Br₃NO₅: C, 50.17; H, 3.37; N, 1.95. Found: C, 50.18; H, 3.35; N, 1.96. HR-MS Calcd for C₃₀H₂₄Br₃NO₅: 714.9206, 720.9143. Found: 714.9105, 720.9117. ¹H- and ¹³C-NMR data for **11a** are listed in Tables 9 and 10.

Reaction of 3b with BAHA Reaction of **3b** (656 mg, 2.6 mmol) with BAHA was carried out at 0 °C for 2.5 h by the procedure described for the reaction of **2a** to give a crude product (containing **11b** and **3a**). Purification of the crude product by column chromatography on silica gel using AcOEt–hexane (1:4, v/v) as an eluent gave 275 mg (14.5%) of methyl 5*H*-2,8-dibromo-5-(4-bromophenyl)-10β-(3,4-methylenedioxyphenyl)dibenz[*b,f*]azepine-11α-carboxylate (**11b**) and 270 mg (41.2%) of recovered **3b**. **11b**: colorless crystals, mp 125–128 °C (ethanol). IR (KBr) cm^{−1}: 1730, 1598, 1502. *Anal.* Calcd for C₃₁H₂₆Br₃NO₅: C, 50.85; H, 3.58; N, 1.91. Found: C, 50.88; H, 3.60; N, 1.90. HR-MS Calcd for C₃₁H₂₆Br₃NO₅: 728.9363, 734.9300. Found: 728.9435, 734.9266. ¹H- and ¹³C-NMR data for **11b** are listed in Tables 9 and 10.

General Procedure for acetylation of 5a, 8a, 9a, and 10a Ac₂O (3 ml) was added to a solution of an alcohol (0.1 mmol) in pyridine (1 ml), and the mixture was stirred at room temperature for 4 h. The reaction mixture was poured into ice water and then extracted with ether. The organic layer was washed with 10% HCl, saturated NaHCO₃, brine, and H₂O, then dried and concentrated. The residue was purified by column chromatography on silica gel in the designated solvents. ¹H- and ¹³C-NMR data for **5b**, **8b**, **9b**, and **10b** are listed in Tables 5 and 7.

threo-2-{2-[*N,N*-bis(4-bromophenyl)amino]-5-bromophenyl}-3-ethanoyloxy-1-(3,4-methylenedioxyphenyl)propyl Ethanoate (**5b**) Compound **5b** was prepared from **5a** (67.6 mg, 0.1 mmol) and purified by column chromatography on silica gel using AcOEt–hexane (1:7, v/v) as an eluent to give 30.8 mg (40.5%) of **5b** as colorless plates (ether–petroleum ether), mp 161–162 °C. IR (KBr) cm^{−1}: 1741, 1580, 1484, 1227. MS *m/z*: 760 (M⁺).

erythro-2-{2-[*N,N*-bis(4-bromophenyl)amino]-5-bromophenyl}-3-ethanoyloxy-1-(3,4-methylenedioxyphenyl)propyl Ethanoate (**8b**) Compound **8b** was prepared from **8a** (71.8 mg, 0.1 mmol) and purified by chromatography on a silica gel column using AcOEt–hexane (1:8, v/v) as an eluent to give 67.0 mg (88.2%) of **8b** as colorless plates (ether–petroleum ether), mp 88–91 °C. IR (KBr) cm^{−1}: 1736, 1578, 1484, 1227. MS *m/z*: 760 (M⁺).

erythro-2-Chloro-3-ethanoyloxy-1-(3,4-methylenedioxyphenyl)propyl Ethanoate (**9b**) Compound **9b** was prepared from **9a** (54.4 mg, 0.2 mmol) and purified by column chromatography on silica gel using AcOEt–hexane (1:7, v/v) as an eluent to give 46.0 mg (73.2%) of **9b** as a colorless oil. IR (KBr) cm^{−1}: 1745, 1502, 1490, 1446, 1226. HR-MS Calcd for C₁₄H₁₅ClO₆: 314.0557. Found: 314.0551.

threo-2-Chloro-3-ethanoyloxy-1-(3,4-methylenedioxyphenyl)propyl Ethanoate (**10b**) Compound **10b** was prepared from **10a** (54.4 mg, 0.2 mmol) and purified by column chromatography on silica gel using benzene–acetone (100:1, v/v) as an eluent to give 26.1 mg (41.6%) of **10b** as a colorless oil. IR (KBr) cm^{−1}: 1742, 1502, 1490, 1444, 1230. HR-MS Calcd for C₁₄H₁₅ClO₆: 314.0557. Found: 314.0604.

Reaction of 2a with Cu(OTf)₂ and Cu₂O in MeCN A solution of **2a** (1 mmol) in MeCN (3.5 ml) was slowly added using a syringe pump to a solution of Cu(OTf)₂ (729 mg, 2.0 mmol) and Cu₂O (487 mg, 3.4 mmol) in MeCN (6.5 ml) at 0 °C. The mixture was stirred at 0 °C for 1 h, and then for an additional 2 h at room temperature. It was diluted with ether (30 ml), acidified with 5% HCl, and washed with brine. The organic layer was dried (Na₂SO₄), filtered, and then concentrated. The residue was subjected to silica gel column chromatography. The first eluate with benzene–acetone (15:1, v/v) gave 118 mg (23.8%) of **4**. The next eluate gave 54.2 mg (11.7%) of **6**.

Reaction of 2b with Cu(OTf)₂ and Cu₂O in MeCN Reaction of **2b** (556 mg, 2.5 mmol) was carried out at 0 °C for 1.5 h by the procedure described for the reaction of **2a** with Cu(OTf)₂ and Cu₂O to give a crude product (containing **12** and **13**). The crude product was subjected to silica gel column chromatography. The eluate with AcOEt–hexane (1:7, v/v) gave 285 mg of a mixture of **12** and **13**. The above mixture was further separated by PTLC on silica gel using benzene–acetone (4:1, v/v) as an eluent to give 75 mg (13.0%) of 2β,4β-diacetoxymethyl-1α-hydroxy-3α-(3,4-methylenedioxyphenyl)-6,7-methylenedioxytetralin (**12**) as a colorless oil (*R*_f=0.58), and 180 mg (31.2%) of 2β,4β-diacetoxymethyl-1β-hydroxy-3α-(3,4-methylenedioxyphenyl)-6,7-methylenedioxytetralin (**13**), as a colorless oil (*R*_f=0.52). **12**: IR (KBr) cm^{−1}: 3470, 1734, 1501, 1484. HR-MS Calcd for C₂₄H₂₄O₉: 456.1420.

Found: 456.1353. **13**: IR (KBr) cm^{-1} : 3488, 1732, 1502, 1484. ^{13}C -NMR (CDCl_3) δ : 21.0 and 20.9 ($2 \times \text{OCH}_3$), 39.6 (C-3), 45.7 and 44.2 (C-2 or C-4), 66.9 and 64.2 ($\text{CH}_2\text{OCOCH}_3$), 67.7 (C-1), 101.2 and 101.1 ($-\text{OCH}_2\text{O}-$), 107.7 (C-5), 107.8 (C-2'), 108.5 (C-5'), 109.5 (C-8), 121.6 (C-13), 131.5 (C-4 and C-8 or C-1'), 136.3 (C-1' or C-4 and C-8), 146.6 and 146.4 (C-6 and C-7 and/or C-3' and C-4'), 148.3 and 148.2 (C-6 and C-7 and/or C-3' and C-4'), 171.6 and 170.9 (OCOCH_3). HR-MS Calcd for $\text{C}_{24}\text{H}_{24}\text{O}_9$: 456.1420. Found: 456.1400. ^1H -NMR data for **12** and **13** are listed in Table 11.

References and Notes

- 1) Although there are two definitions of the terms lignan and neolignan,^{2a)} we defined lignans as compounds formed by the oxidative coupling of cinnamyl alcohols (**1a**) and/or cinnamic acids (**1b**), and neo-lignans as compounds formed by the oxidative coupling of propenylphenols and/or allylphenols (**1c**).
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- 8) Other solvents such as CH_2Cl_2 and MeCN were used instead of THF for the reaction of **2a** with BAHA, but gave only a complex mixture.
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