CONFORMATIONAL ANALYSIS OF TETRAHYDROFUROFURAN LIGNANS: SESAMOLIN

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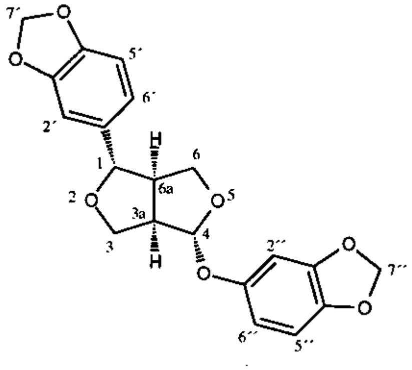
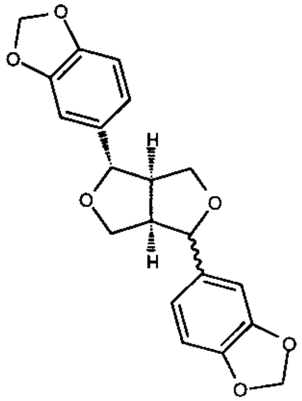
Abstract — The stereochemistry of sesamolin (**1**), an aryl-aryloxy-tetrahydrofurofuran derivative comprising a main component of the lignans isolated from *Sesamum indicum*, was investigated. The favoured conformation was determined using several methods of conformational analysis: nuclear Overhauser effect (NOE), lanthanide induced shifts (^{1}H-LIS), molecular mechanics (force-field) calculations (FF), and X-ray crystal structure determination. The conformation was found to deviate from the more common analoguous diaryltetrahydrofurofuran derivatives. The reason is the anomeric effect of the cyclic acetal favouring a pseudo-axial position of the aryloxy substituent.

In continuation of our interest in the stereochemistry of tetrahydrofurofuran lignans[1,2] we investigated the conformation of sesamolin (**1**) in solution and in the solid state. Two further lignans of known conformation, sesamin (**2**) and episesamin (**3**) were used for comparison. All three lignans have been isolated from the oil of *Sesamum indicum* DC. (= *S. indicum* L. + *S. orientale* L.).

Diaryltetrahydrofurofurans have attracted much attention concerning their relative and absolute stereochemistries[1-12] and their chemical[13-18] and biological activities.[18-24] Especially the lignans from the widely used sesame oil were the subject of extensive investigations, recently mainly by Japanese authors.[18-22, 24] The stability of sesame oil towards oxidation is attributed to the antioxidant properties of lignans.[13-18] However, these antioxidants have also been shown to possess most interesting bioactive properties, including anticholesterenic[19-21] and anticancer activity.[18,22-24]



1 Sesamolin "eq/eq"



2 Sesamin "eq/eq"
3 Episesamin "eq/ax"

The conformational behaviour of the two five-membered rings of the tetrahydrofurofuran skeleton is rather interesting. The oxolane ring annelation is always *cis* and the two rings form an envelope conformation, with the oxygen atom out of the plane of the other four (carbon) atoms. Depending on the relative position of the aryl substituents at C-1 and C-4, the oxygen atoms O-2 and/or O-5 may either be bent away from the other oxolane five-ring (*exo* topology or chair conformation; e.g. Figure 1, compound **2**: two chairs, **3**: left ring only) or they may point towards the second five-ring (*endo* or boat; e.g. **3**: right ring). Consequently, the eight atoms of the annelated two-ring system (8-membered main ring, with a zero-bridge from C-3a to C-6a in the bicyclic 3,7-dioxabicyclo[3.3.0]octane system) may either form a chair/chair (e.g. **2**), a chair/boat (e.g. **3**), or a boat/boat conformer (e.g. compound **3** in Ref.[2]). This chair or boat conformations of the half molecule in relation to the other half are governed by the 1,4-aryl substituents, which adopt generally a pseudo-equatorial position.[1] In the literature, however, the relative positions of the two aryl substituents of diarylfurofurans are usually characterized as being either "axial" or "equatorial", presuming a chair/chair conformation of the dioxabicyclooctane system (e.g. Ref.[8]). This denotation is only correct in the case of "eq/eq" aryl substitution at C-1 and C-4 (and chair/chair conformation). In all other cases ("eq/ax" and "ax/ax") these terms are convenient but misleading, because the five-ring with the "axial" aryl substituent flips, forming a boat conformation with the former "axial" substituent in an actually equatorial (or better pseudo-equatorial) position. "Ax/ax" derivatives have even a preferred conformation of boat/boat topology and both substituents are again positioned pseudo-equatorial.[2] Therefore the diaryltetrahydrofurofurans which are classically denoted as "eq/eq" may also be called chair/chair isomers, "eq/ax" corresponds to the correct expression chair/boat, and "ax/ax" is actually best described as the boat/boat isomer with all substituents pseudo-equatorial. The suggested denotation using "boat" and "chair" with the supplementary note "all substituents in pseudo-eq. position" describes the conformation and the relative configurations at C-1 and C-4 correct, clear and illustrative. (For description of the relative configurations only, one should use *cis* and *trans* relative to some reference, but not the conformationally determined terms axial or equatorial.)

All these considerations concerning the conformational behaviour are valid for the widespread simple diarylfurofuran lignans, where the aryl rests are directly linked to the tetrahydrofurofuran system (e.g. **2** or **3**). However, matters seem to be different for the less common aryloxy-substituted tetrahydrofurofurans. One of these rare aryloxy-tetrahydrofurofurans is sesamolin (**1**) which comprises a main component of the lignans isolated from *Sesamum indicum*. The ^{1}H-nmr spectrum of the "eq/eq" sesamolin (methylenedioxyphenyl-methylenedioxyphenyloxy-tetrahydrofurofuran) shows some unusual shift and coupling parameters in comparison with "eq/eq" diphenyltetrahydrofurofurans. The chiroptical properties differ as well. Usually the $[\alpha]_D$ values for "eq/eq" diaryl lignan derivatives are +60° ± 10 (+120° ± 10 for "eq/ax", and +300° ± 20 for "ax/ax").[11] For the "eq/eq" sesamolin $[\alpha]_D$ is +218°.[25a] The CD spectrum, on the other hand, with maxima at 292 nm ($\Delta\varepsilon$ = +0.7) and 237 nm (+2.8) is very similar to the one of sesamin (**2**) (see Exp. and Ref.[12]). For the correlation of the absolute stereochemistries of sesamolin and sesamin see Ref.[26], for the absolute configurations within the (+)-diaryltetrahydrofurofuran series see Ref.[27].

Especially the unexpected coupling constants in the ^{1}H-nmr spectrum prompted us to investigate the favoured conformation (and relative configuration) of this compound, using several methods of conformational analysis: evaluation of vicinal coupling constants, nuclear Overhauser effect (NOE), lanthanide induced shifts (^{1}H-LIS), molecular mechanics (force-field) calculations (FF), and X-ray crystal structure determination.

^{1}H-Nmr: Chemical Shifts and Coupling Constants

The ^{1}H-nmr spectrum of the "eq/eq" type sesamolin (**1**) shows some unexpected features in comparison with the "eq/eq" sesamin (**2**). If the basic tetrahydrofurofuran systems of sesamolin and sesamin were comparable, the chemical shifts and coupling constants of protons not too close to the acetal position C-4 should also be comparable. However, the chemical shifts and especially the conformationally significant coupling constants of **1** agree much better with the corresponding values of the "eq/ax" episesamin (**3**): $J(6\beta,6a)$ = 1 Hz for **1** compares very well with $J(6\beta,6a)$ ~ 0 Hz for **3** ($J(6\beta,6a)$ = 6.9 Hz for **2**), $J(6\alpha,6a)$ is 6.0 Hz for **1** and 6.1 Hz for **3** (3.6 Hz for **2**), $J(1,6a)$ = 7.6 Hz for **1** and 7.1 Hz for **3** (4.4 Hz for **2**) (see Table 1 and Figure 1). There is only one characteristic deviation in the coupling constants between compounds (**1**) and (**3**), namely the coupling constant of the acetalic proton 4-H; $J(3a,4)$ ~ 0 Hz for **1**, but 5.3 Hz for **3**. The most striking hypothesis to explain these data is to assume a similar topology for **1** and **3** with a pseudo-equatorial position of the C-4 aryl substituent in **3** [1,2] and a pseudo-axial position of the C-4 aryloxy-substituent in sesamolin (**1**) (compare Figure 1).

This assumption is consistent with the postulated so-called "eq/eq" configuration of sesamolin.[25b] However, the overall conformation of the tetrahydrofurofuran system resembles the one of the "eq/ax" episesamin, namely chair/boat and not chair/chair (like the "eq/eq" sesamin). Table 2 shows all relevant configurational and conformational interrelations. It shows also that only in the case of sesamin the characterization of the relative configurations as "eq/eq" is identical with the real positions of the aryl rests at the tetrahydrofurofuran system.

Table 1. ^{1}H-Nmr data for compounds (**1–3**) (δ/ppm, $CDCl_3$, TMS).

No.	**1**	**2**	**3**	No.	**1**	**2**	**3**
1	4.40 d	4.72 d	4.39 d	2′	6.88 br.s	6.85 br.s	6.86 br.s
3α	4.45 dd	3.87 dd	3.8 m	5′	6.78 d	6.77 d	6.8 br.m
3β	3.64 dd	4.23 dd	3.3 m	6′	6.83 dd	6.81 d	6.8 br.m
3a	3.31 ddd	3.05 m	3.3 m	7′	5.96 s	5.95 s	5.96 s*
4	5.50 s	4.72 d	4.83 d	2″	6.62 d	6.85 br.s	6.86 br.s
6α	4.13 dd	3.87 dd	3.82 dd	5″	6.71 d	6.77 d	6.8 br.m
6β	3.96 dd	4.23 dd	4.09 br.d	6″	6.50 dd	6.81 d	6.8 br.m
6a	2.95 dddd	3.05 m	2.86 m	7″	5.92 s	5.95 s	5.95 s*

* Interchangeable

Coupling constants: **1** : *J*(1,6a) = 7.6 Hz, *J*(3α,3β) = 9.1 Hz, *J*(3α,3a) = 8.9 Hz, *J*(3β,3a) = 7.4 Hz, *J*(3a,4) < 0.2 Hz, *J*(3a,6a) = 9.0 Hz, *J*(6α,6β) = 9.2 Hz, *J*(6α,6a) = 6.0 Hz, *J*(6β,6a) = 1.0 Hz, *J*(5′,6′) = 7.9 Hz, *J*(5″,6″) = 8.4 Hz; **2** : *J*(1,6a) = *J*(3a,4) = 4.4 Hz, *J*(3α,3β) = *J*(6α,6β) = 9.2 Hz, *J*(3α,3a) = *J*(6α,6a) = 3.6 Hz, *J*(3β,3a) = *J*(6β,6a) = 6.9 Hz, *J*(5′,6′) = *J*(5″,6″) = 8.2 Hz; **3**: *J*(1,6a) = 7.1 Hz, *J*(3a,4) = 5.3 Hz, *J*(6α,6β) = 9.4 Hz, *J*(6α,6a) = 6.1 Hz, *J*(6β,6a) < 0.2 Hz. NOE **1**: 3β → 1, 3β → 3α (strong), 3β → 4 (st.); 3a → 3α (st.), 3a → 4, 3a → 6a (st.); 4 → 3β (st.), 4 → 3a, 4 → 2″ (st.), 4 → 6″ (st.); 6α → 6β (st.), 6α → 6a (st.); 6β → 1 (st.), 6β → 6α (st.); 6a → 3a (st.), 6a → 6α (st.); 6a → 2′ (st.).

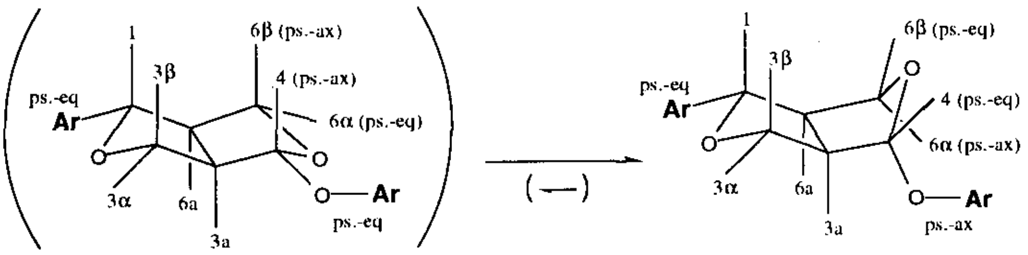
Table 2. Classical stereochemical denotation of substituted tetrahydrofuran lignans, actual conformations of the bridged ring system, and real positions of the aryl moyeties.

	Relative configuration	Conformations of the ring systems	Real positions of the aryl rests
Sesamolin (**1**)	"eq/eq"	chair / boat	ps.-eq / ps.-ax
Sesamin (**2**)	"eq/eq"	chair / chair	ps.-eq / ps.-eq
Episesamin (**3**)	"eq/ax"	chair / boat	ps.-eq / ps.-eq

So far the stereochemistry of **1** outlined above is mainly based on direct comparison of ^{1}H coupling constants of cyclic ethers (**2**, **3**) with a cyclic acetal (**1**). However, chemical shifts and – to a less extent – coupling constants may be influenced by the additional hetero-atom, especially in the close vicinity of the acetal position C-4. The derived conclusions need therefore additional support. Further pieces of evidence were provided by NOE measurements and ^{1}H-LIS data.

Nuclear Overhauser Effects

Irradiation at 4-H of sesamolin (**1**) gave a clear NOE on the resonance of 3a-H and *vice versa* (3a ↔ 4). This implies that 4-H is positioned in a ps.-eq position, because there are usually no NO-effects between *trans*-orientated axially positioned vicinal protons (e.g. no NOE between 3β and 3a). The strong effects between 6β → 1, 3β ↔ 4, and 3β → 1 are clearly in favour of a so called "eq/eq" substituted tetrahydrofurofuran derivative with 1-H and 4-H (and aryl and aryloxy) in a relative *cis* configuration, but they do not allow to discriminate between both possible conformers of **1** (compare Figure 1). However, following the former finding, the O-Ar substituent is clearly in ps.-ax position (4-H ps.-eq), which in turn implies that the conformations of the aryl- and aryloxy-substituted five-rings are in a chair/boat and not in a chair/chair arrangement. All NOE data (Table 1) are compatible with the assumed overall chair/boat conformation with O-Ar pseudo-axial. However, with the exception of the NOE 4 ↔ 3a all other data are compatible with the other conformer as well (compare Figure 1). Unfortunately, the expected NOEs 6a → 6β or 6β → 6a ("symmetrical" to 3a ↔ 4) are not observable. Further evidence for an unambiguous conformational analysis of **1** was furnished by measurement of lanthanide induced shift data.



"eq/eq" chair/chair

Sesamolin (**1**)
"eq/eq" chair/boat

Sesamin (**2**)
"eq/eq" chair/chair

Episesamin (**3**)
"eq/ax" chair/boat

Figure 1. Stereoformulas of **1** - **3**. In the case of sesamolin (**1**), the possible conformational equilibrium is shown for a direct comparison of the chair/chair geometry of **1** with **2** and the actually present chair/boat geometry of **1** with **3** (Note: no evidence for the chair/chair conformer of **1** with O-Ar ps.-eq was found).

Lanthanide Induced Shifts (LIS)

In a previous paper[2] we have observed that in the case of a chair/chair type tetrahydrofurofuran there seems to occur some kind of bidentate complexing with the cyclic ether oxygen atoms co-ordinated to the europium shift reagent. Since this is not the case for chair/boat or boat/boat conformations, this method should help to discriminate between the two possible conformations chair/chair or chair/boat of sesamolin (**1**, Figure 1). Figure 2 shows the lanthanide induced shift values (LIS) for compounds (**1**-**3**). For better comparison the LIS data are normalized to a value of 1.00 for protons 4-H in all three compounds. The most striking result of the LIS experiment is the very good agreement of the LIS values of sesamolin (**1**, "eq/eq"-type) with the corresponding data of episesamin (**3**, "eq/ax"-type, chair/boat conformation); the only differences are – for obvious reasons – within the aryloxy moiety. The data for sesamin (**2**, "eq/eq"-type, chair/chair conformation) differ very much from the data of **1** and **3**, and they agree very well with the data for a previously analyzed "eq/eq"-type tetrahydrofurofuran with chair/chair topology.[2] The only reasonable conclusion of these findings is that the ring conformations of **2** and **3** are both of chair/boat type. This result is primarily valid for the complex species. However, since the progressive complexation (see Exp. Part) does not cause any changes in the coupling constants of the ring protons, a change of ring conformations in the complex can be excluded. Therefore the complex geometry of sesamolin is identical with the free substrate, namely chair/boat conformation with a pseudo-equatorial aryl rest at C-1 and a pseudo-axial aryloxy rest at C-4. The direct comparison of the LIS values (Figure 2) is rather convincing, and the derived chair/boat conformation of **1** in solution agrees fully with all other evidence derived so far.

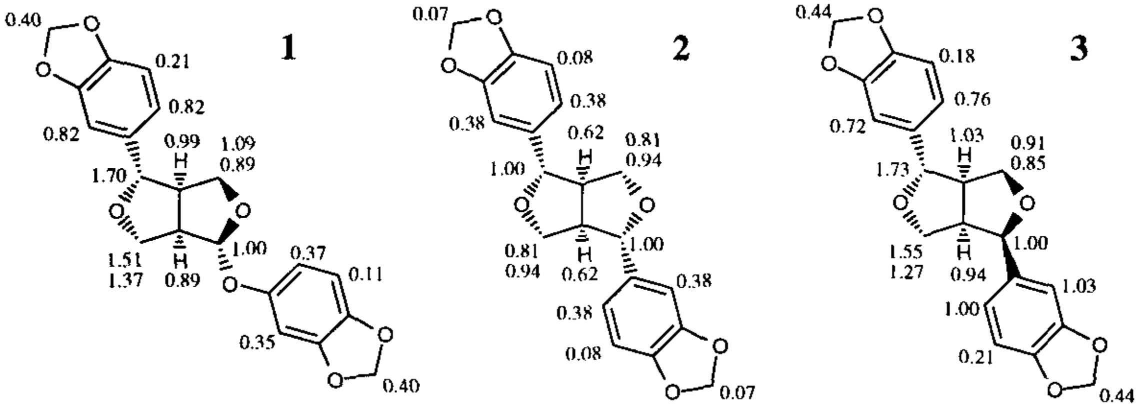


Figure 2. ^{1}H-Nmr LIS data for compounds (**1** - **3**), normalized to the value of 1.00 ppm for 4-H in the 1:1 complex of sesamolin (**1**). The normalization factor is 3.00 for **2** and 0.3 for **3** (complexation of **2** is three times better than **1**, complexation of **3** three times worse).

Force Field Calculations

Next we were interested, if a simple force field calculation was able to describe the conformational behaviour of tetrahydrofurofuran lignans properly. The calculations (programme PCMODEL 4.0, "gas phase" calculation) gave the expected energy minimum conformations of chair/chair for sesamin and chair/boat for sesamolin. Even if the calculations started from a hypothetical chair/chair for sesamolin, no local energy minimum was found for this geometry and the molecule changed unequivocally into the chair/boat conformation; generally, no local minima for less favoured conformations were found, therefore no estimates of energy differences can be given.

X-Ray Structure Analysis

The crystal structure of sesamolin (**1**) (Figure 3 and Tables 3 and 4) supports fully the results of conformational analysis in solution. The two five-rings of the tetrahydrofurofuran structure exhibit a clear envelope conformation with the four atoms C-1-C-6a-C-3a-C-3 and C-4-C-3a-C-6a-C-6 almost in plane (compare entries 2 and 7 in Table 4). The oxygen atoms are bent either *exo* (O-2) or *endo* (O-5) relative to the second five-ring. The former is the case for the aryl-substituted ring (ring "A" in Table 4, forming a chair-like partial structure), the lattter happens with the aryloxy-substituted ring (ring "B", boat-like). The result is a chair/boat conformation for the tetrahydrofurofuran system with the aryl rest pseudo-equatorial and the aryloxy rest pseudo-axial (compare Figure 3). The ring puckering angles of the two 5-ring systems (folding angles between the planes defined by atoms 1,2,3 and 1,6a,3a,3 in ring "A", and 4,5,6 and 4,3a,6a,6 in ring "B") were found to be 43° in ring "A" and 39° in ring "B". Similar results (42 ± 1°) were found for the diaryltetrahydrofurofurans of Ref.[1].

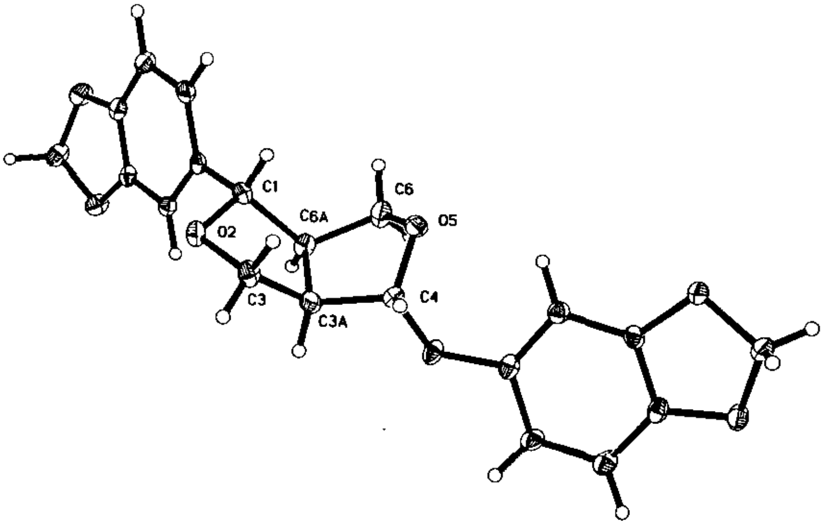


Figure 3. The asymmetric unit in the crystal structure of sesamolin (**1**).

Table 3. Atomic coordinates (x 10^4) and equivalent isotropic displacement parameters ($Å^2$ x 10^3) for the atoms in the crystal structure of sesamolin (**1**). Estimated standard deviations in parentheses. Hydrogen positions have been computed on the basis of stereochemical plausibility and included into the refinement with fixed isotropic displacement parameters. U_{eq} is defined as one third of the trace of the orthogonalized U_{ij} tensor.

	X/a	Y/b	Z/c	U_{eq}		X/a	Y/b	Z/c	U_{eq}
C1	2137(2)	4137(5)	7370(2)	15(1)	C6′	2157(2)	7260(5)	8338(2)	17(1)
C1-H	2367(2)	5206(5)	7066(2)	80	C6′-H	2456(2)	8016(5)	7989(2)	80
O-2	2751(1)	2524(3)	7667(1)	16(1)	C7′	1039(2)	5907(5)	10557(2)	21(2)
C3	2790(2)	1399(5)	6910(2)	18(1)	C7′-Ha	1452(2)	5434(5)	11059(2)	80
C3-Hα	3062(2)	40(5)	7054(2)	80	C7′-Hb	530(2)	6176(5)	10718(2)	80
C3-Hβ	3089(2)	2215(5)	6579(2)	80	C3′-O	910(1)	4305(3)	9891(1)	19(1)
C3a	1882(2)	1092(5)	6405(2)	16(1)	C4′-O	1310(1)	7793(3)	10219(1)	21(1)
C3a-H	1667(2)	-265(5)	6530(2)	80	C4-O	1023(1)	212(3)	5052(1)	18(1)
C4	1726(2)	1452(4)	5442(2)	15(1)	C1″	805(2)	24(5)	4167(2)	16(1)
C4-H	2199(2)	1021(4)	5240(2)	80	C2″	973(2)	1589(4)	3621(2)	15(1)
O-5	1579(1)	3645(3)	5324(1)	18(1)	C2″-H	1252(2)	2902(4)	3835(2)	80
C6	1085(2)	4254(5)	5899(2)	22(1)	C3″	713(2)	1151(5)	2756(2)	15(1)
C6-Hα	509(2)	3909(5)	5656(2)	80	C4″	301(2)	-659(5)	2440(2)	16(1)
C6-Hβ	1133(2)	5765(5)	6015(2)	80	C5″	126(2)	-2220(5)	2972(2)	18(1)
C6a	1438(2)	2981(5)	6717(2)	16(1)	C5″-H	-172(2)	-3499(5)	2744(2)	80
C6a-H	1009(2)	2503(5)	6978(2)	80	C6″	392(2)	-1855(5)	3852(2)	18(1)
C1′	1913(2)	5178(5)	8119(2)	14(1)	C6″-H	293(2)	-2922(5)	4247(2)	80
C2′	1476(2)	4029(4)	8621(2)	14(1)	C7″	574(2)	1085(5)	1346(2)	19(1)
C2′-H	1291(2)	2585(4)	8479(2)	80	C7″-Ha	255(2)	1858(5)	853(2)	80
C3′	1330(2)	5064(5)	9314(2)	15(1)	C7″-Hb	1070(2)	550(5)	1216(2)	80
C4′	1568(2)	7144(5)	9517(2)	16(1)	C3″-O	781(1)	2454(3)	2091(1)	21(1)
C5′	1987(2)	8296(5)	9040(2)	18(1)	C4″-O	96(1)	-649(3)	1554(1)	20(1)
C5′-H	2159(2)	9747(5)	9185(2)	80					

Conclusions

Contrary to the "eq/eq" 1,4-diaryltetrahydrofurofuran lignans which prefer a chair/chair conformation of the bicyclic tetrahydrofurofuran skeleton resulting in a pseudo-equatorial configuration for the two aryl rests, all evidence is in favour of a chair/boat conformation with aryl pseudo-equatorial and aryloxy pseudo-axial in the "eq/eq" 1-aryl-4-aryloxytetrahydrofurofuran derivative sesamolin (**1**). The sterically unfavourable pseudo-axial position of O-Ar in **1** is obviously favoured due to an electronic interaction, namely the anomeric effect. This effect is well known from other cyclic acetalic compounds, especially in carbohydrate chemistry. The reason is an overlap of a non-bonded orbital of the ring oxygen with a σ^* orbital of the acetalic C-atom.[28-31] This stabilizing n-σ^* interaction is only possible in a conformation with the aryloxy substituent pseudo-axial. A consequence of this overlap is a partial double bond character of the bond O-5–C-4. The corresponding bond shortening can be observed in the X-ray data: the bond length of O-5–C-4 is 1.39 Å, compared to 1.42-1.43 Å for all other O–C bonds in the two five-rings (O-5–C-6, O-2–C-1, and O-2–C-3). According to the orbital theory of the anomeric effect, the exocyclic C–O bond (C-4–4-O in **1**) should be elongated. It is found to be 1.41 Å in sesamolin (**1**), which may be explained by the fact that the next C–O bond (4-O–C-1") is again of partial double bond character (aromatic C–O bond, 1.38 Å) *resulting in the "conjugated" sequence* O-5$\overset{\cdots}{-}$C-4—4-O$\overset{\cdots}{-}$C-1" *with corresponding bond legths* 1.39/1.41/1.38 (compared to 1.43 Å for a paraffinic C–O bond).[32] Together with all other evidence, the bond shortening of the cyclic C-4–O-5 bond to 1.39 Å proves clearly the presence of an anomeric effect causing a chair/boat conformation for sesamolin (**1**) with the aryloxy substituent pseudo-axial in solution and in the solid phase.

Table 4. Selected torsional angles (°) of sesamolin (1): comparison of X-ray data and calculated values (PC-MODEL).

Torsional angle	X-ray	PC-MODEL	Torsional angle	X-ray	PC-MODEL
Ring A			Ring B		
1. O2-C1-C6a-C3a	-24.9	-20.2	6. O5-C4-C3a-C6a	24.2	25.2
2. C1-C6a-C3a-C3	- 0.7	- 4.1	7. C4-C3a-C6a-C6	- 0.9	- 3.0
3. C6a-C3a-C3-O2	26.2	27.2	8. C3a-C6a-C6-O5	-21.9	-20.2
4. C3a-C3-O2-C1	-43.6	-41.6	9. C6a-C6-O5-C4	39.0	37.6
5. C3-O2-C1-C6a	42.8	38.8	10. C6-O5-C4-C3a	-39.7	-39.5
Linking Ring A and B					
11. C1-C6a-C3a-C4	-120.0	-123.3	12. C6-C6a-C3a-C3	118.4	116.2

In the force field calculation (PC-MODEL) the overall chair/boat conformation of the cyclic tetrahydrofurofuran system of **1** (caused by the anomeric effect) is reproduced very well (Table 4), although this geometry puts the O-Ar substituent in the generally less favoured pseudo-axial position. In the case of sesamolin, the balance between steric and electronic interactions is reproduced correctly by the programme. The calculated torsional angles characterizing the topology of the bicyclic tetrahydrofurofuran system agree also very well with the corresponding data of the experimental X-ray structure analysis (Table 4). Concerning the bond length, the PC-MODEL calculation assumes standard C-O bond lengths of 1.42 Å for all four C-O bonds in the ring system showing no bond shortening due to the anomeric effect (the aromatic C-O bond is standardized to the length of 1.37 Å).

EXPERIMENTAL

Nmr: Bruker AM 400 WB (400 MHz) and Bruker WM 250 (250 MHz). – CD: Jobin-Yvon CD 6.

Compounds (**1-3**) were isolated from sesame oil (Sesamöl hell, "Naturgarten", Naturkostladen G.m.b.H. A-8462 Gamlitz, Japanese origin). 50 g oil was extracted with 5 x 80 ml of methanol. After concentration to 25 ml the extract was allowed to rest in the refrigerator overnight for the separation of rests of the oily phase (some drops of oil). The remaining solution was evaporated to dryness and separated by means of medium pressure chromatography on silica gel with petrol ether : ethyl acetate = 85 : 15 as eluent. After repeated purification cycles 250 mg of sesamin (**2**) (0.5 %), 100 mg of sesamolin (**1**) (0.2 %), and 15 mg of episesamin (**3**) (0.03 %) were isolated. For the crystal structure analysis sesamolin was slowly crystallized from ether (refrigerator, 3 weeks).

CD spectrum of **1** (EtOH, $c = 0.8 \cdot 10^{-4}$ mol/l, 20 °C) λ ($\Delta\varepsilon$) = 292 nm (+0.7, max.), 258 (0.0, min.), 240 (+2.8, max.), 218 (+1.2, min.), < 218 (strong positive effect).

^{1}H-LIS data of **1-3**: Increasing amounts of Eu(dpm)$_3$ were added to solutions of ca. 6 mg substrate in 0.5 ml of CDCl$_3$. The LIS for the concentration ratio R_0:S_0 = 1:1 ("1:1 complex") were obtained by extrapolation of 5-7 different reagent concentrations in the range of R_0:S_0 = 0.0-0.7 : 1. No changes in the coupling constants were observed, indicating that no changes in the substrate conformations occurred in the course of complexation with the shift reagent.

X-Ray crystal structure analysis of sesamolin (**1**): Colourless crystals obtained from diethyl ether were investigated on a locally constructed 4-circle diffractometer at 85(3) K using MoK$_\alpha$ radiation (λ = 0.71073 Å). A crystal specimen of 0.5 x 0.5 x 0.2 mm was used for all diffraction experiments. Unit cell dimensions were obtained by least-squares against the setting angles of 51 reflections between $4 \le 2\theta \le 10$: Monoclinic, C2, $Z = 4$ for $C_{20}H_{18}O_7$, a = 16.609(3) Å, b = 6.2370(10) Å, c = 16.015(3) Å, β = 104.75(3)°, V = 1604.3(5) Å^3, $F(000) = 776$. 2997 symmetry independent and 2573 significant ($I > 2\sigma(I)$) intensity values were measured (ω-scan, $\Delta\omega = 1.2°$, $3.14 \le \theta \le 27.54$, $-19 \le h \le 19$, $-7 \le k \le 8$, $-1 \le l \le 19$, no absorption correction, $\mu = 0.117$) and used for direct-methods structure solution and least-squares refinement (244 parameters refined against 2993 intensity observations), which converged at $wR_2 = [\Sigma[w(F_o^2 - F_c^2)^2] / \Sigma[w(F_o^2)^2]]^{1/2} = 0.1161$ (all 2997 reflections), $R_1 = \Sigma||F_o| - |F_c|| / \Sigma|F_o| = 0.0571$ (all reflections) and $R_1 = 0.0442$ (2573 significant reflections). Residual features up to ±0.336 eÅ^{-3} were observed in a final difference map. All computations were performed with version 5.03 of the SHELXTL PC program system (Siemens Analytical Instruments, Inc., 1994).

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