Electronic Supplementary Information

Configuration and stability of naturally occurring *all-cis*-tetrahydrofuran lignans from *Piper solmsianum*

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Table S8. Relative energies and structures of the stereoisomers for THFs lignans (pairs of enantiomers: **2a**, **3a**, **7** and **8**; *meso* **6** and **1a**)

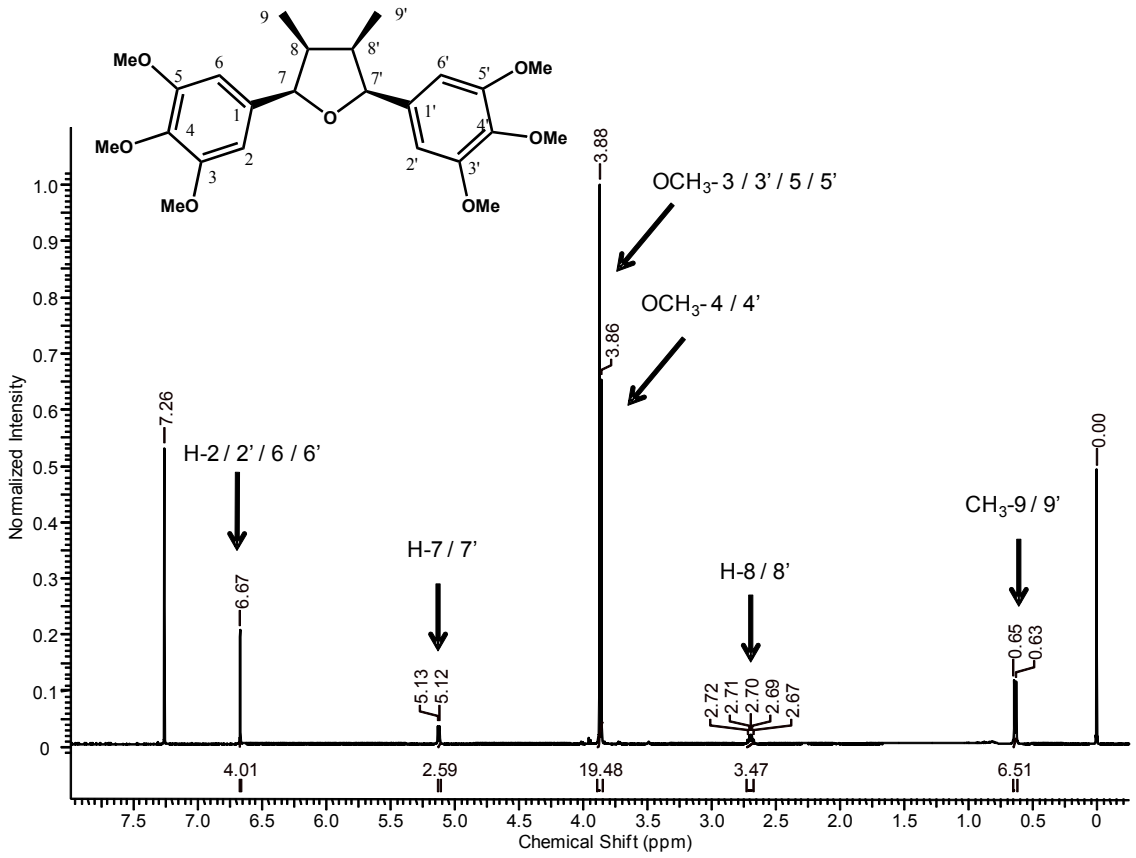


Figure S1. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of compound **1a**.

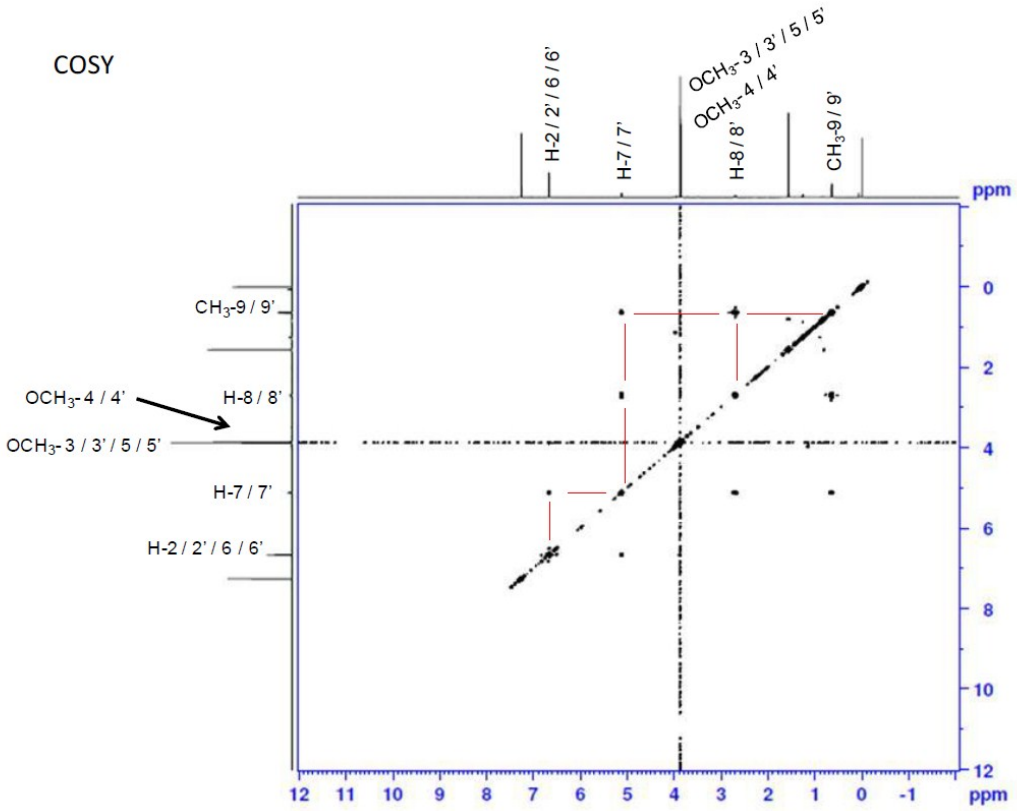


Figure S2. COSY correlation for **1a**.

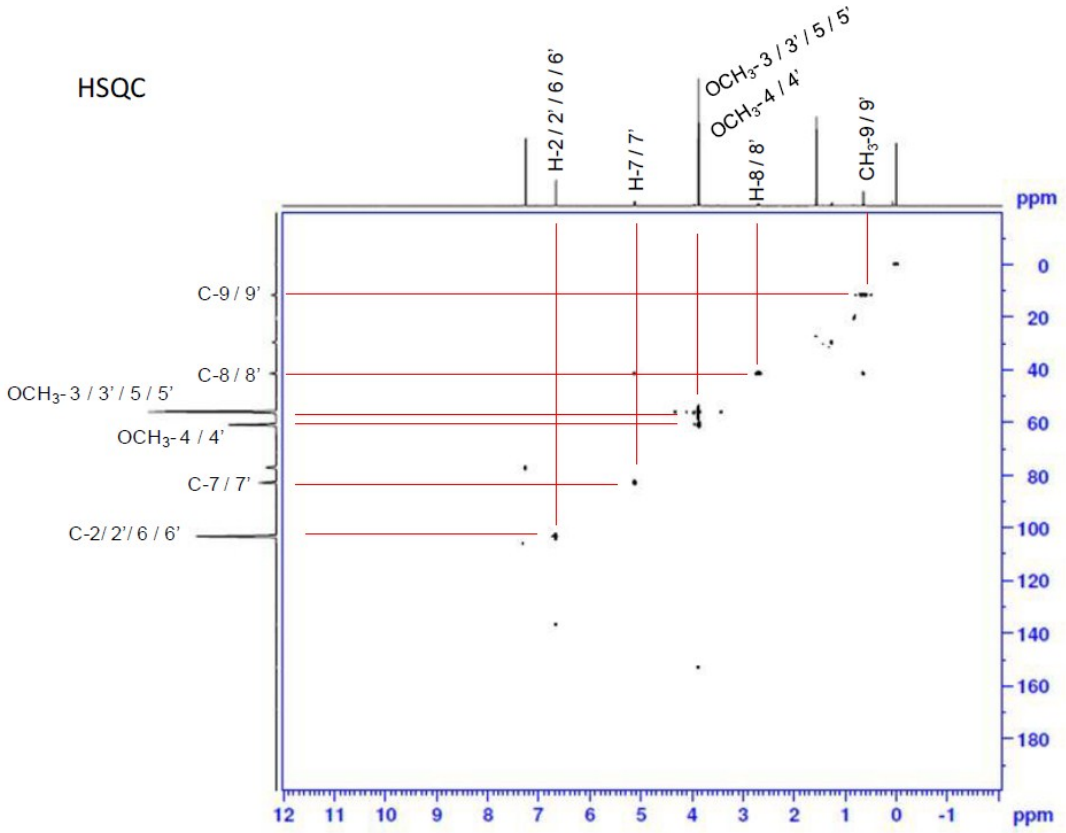


Figure S3. HSQC correlation for **1a**.

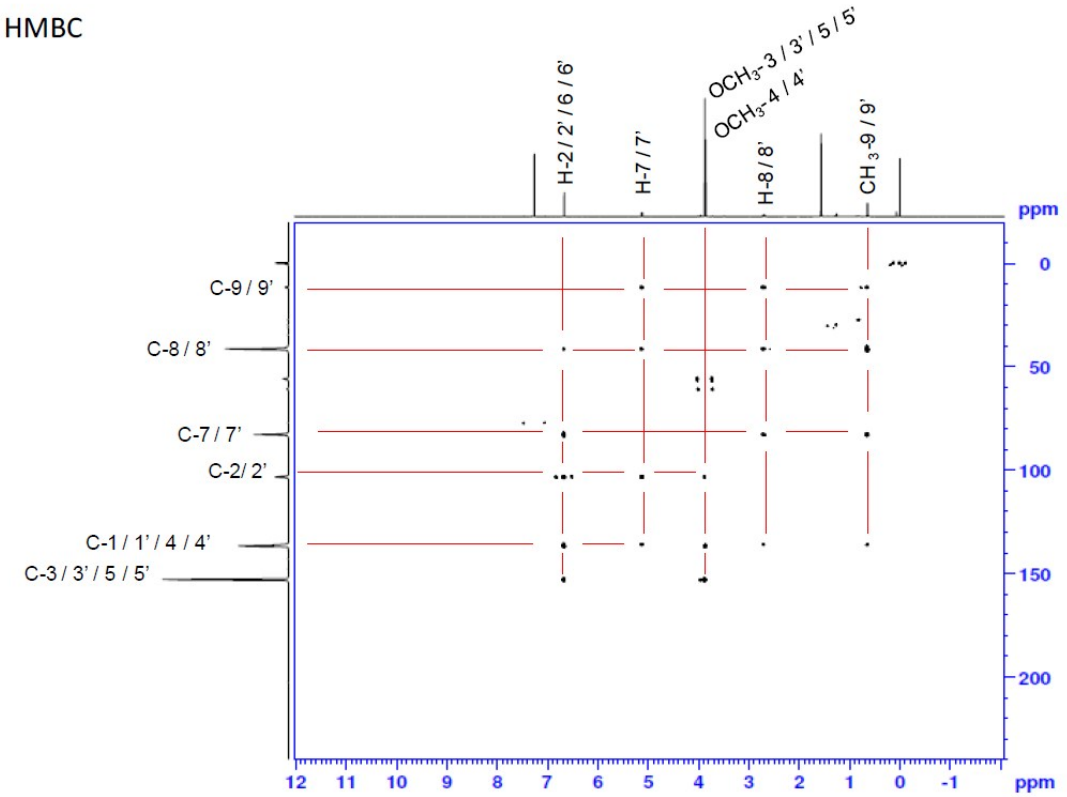


Figure S4. HMBC correlation for **1a**.

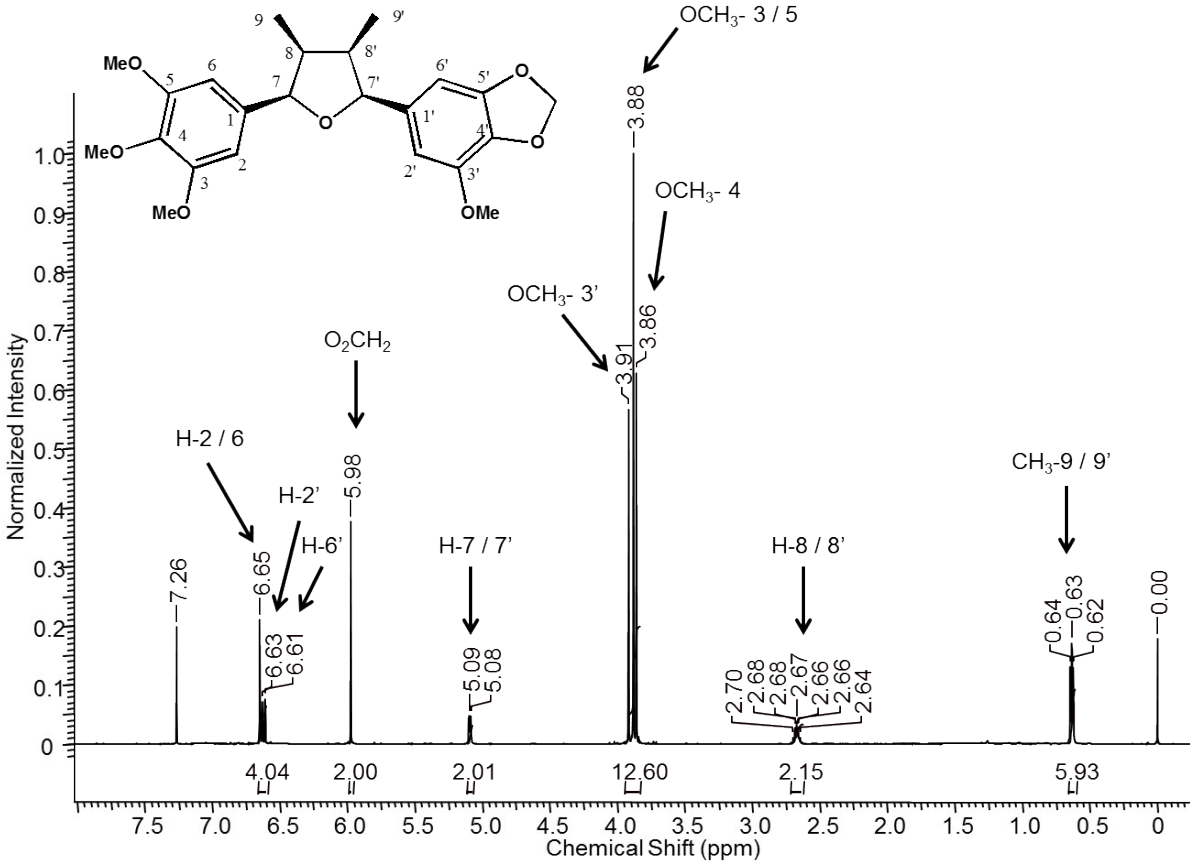


Figure S5. ^{1}H NMR (500 MHz, $CDCl_3$) spectrum of **1b**.

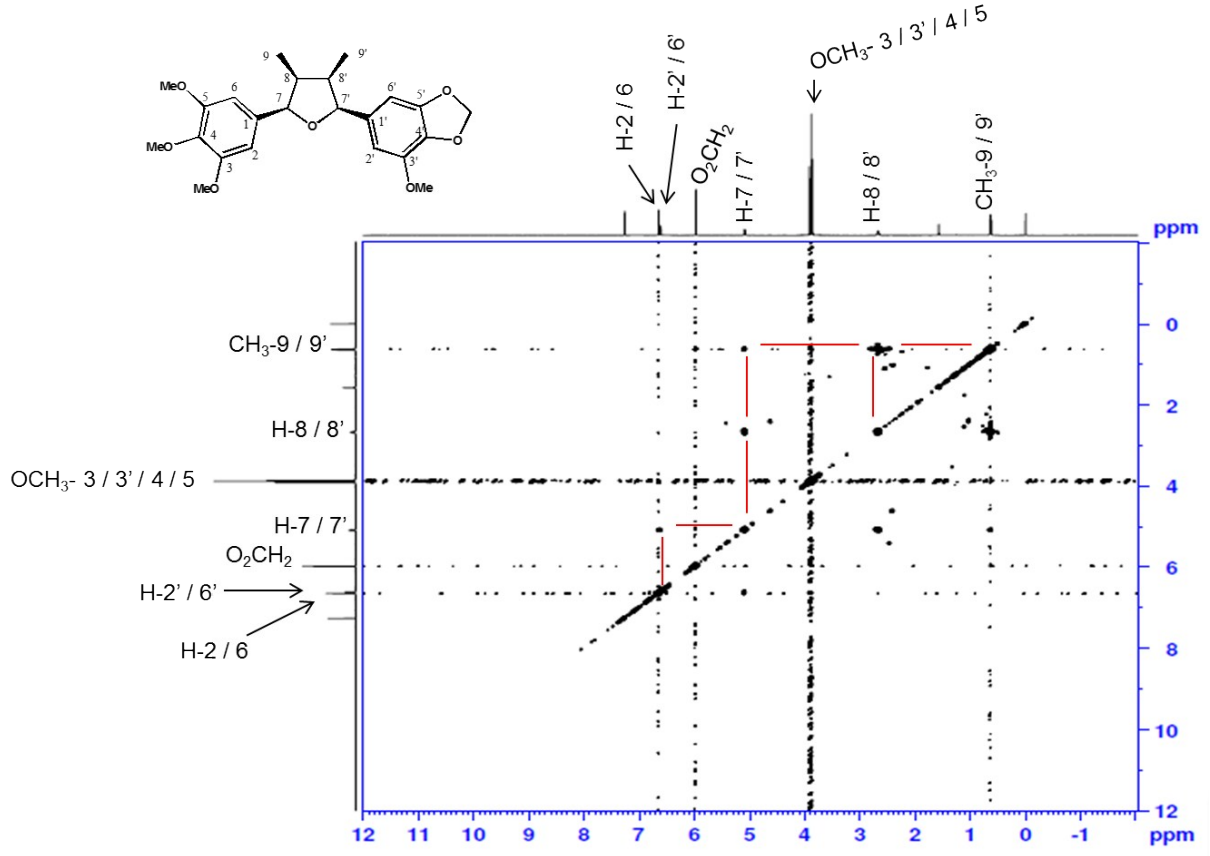


Figure S6. COSY correlation for **1b**.

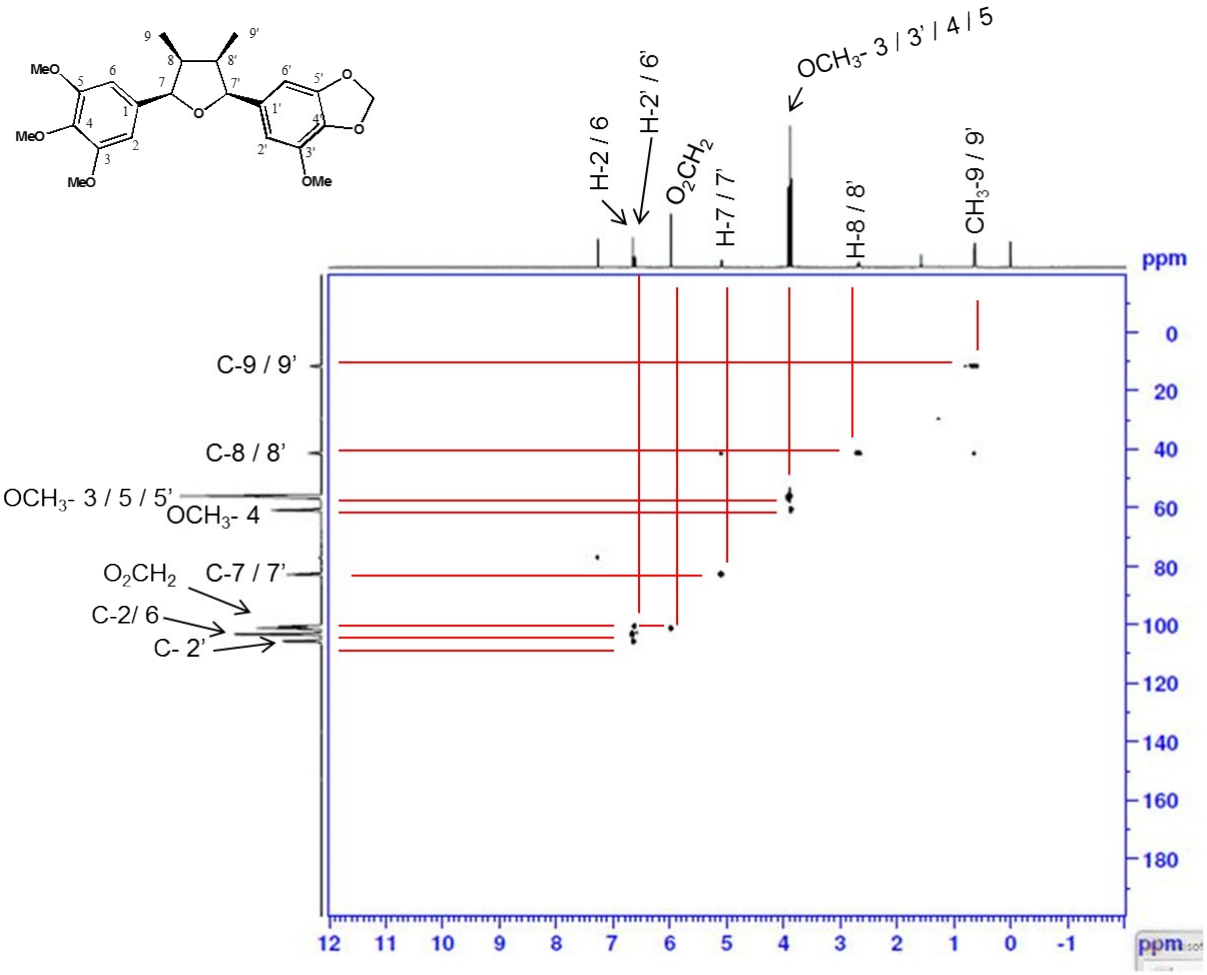


Figure S7. HSQC correlation for **1b**.

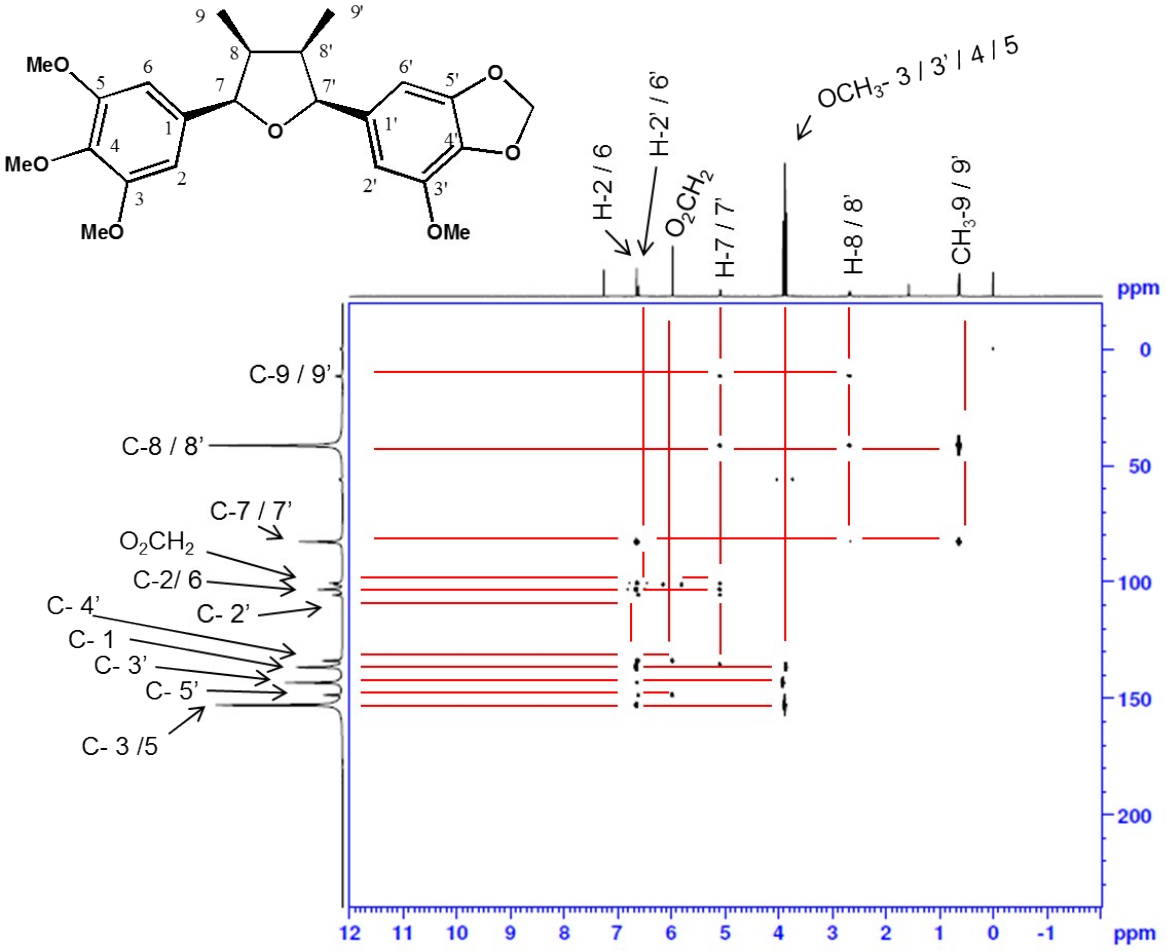


Figure S8. HMBC correlation for **1b**.

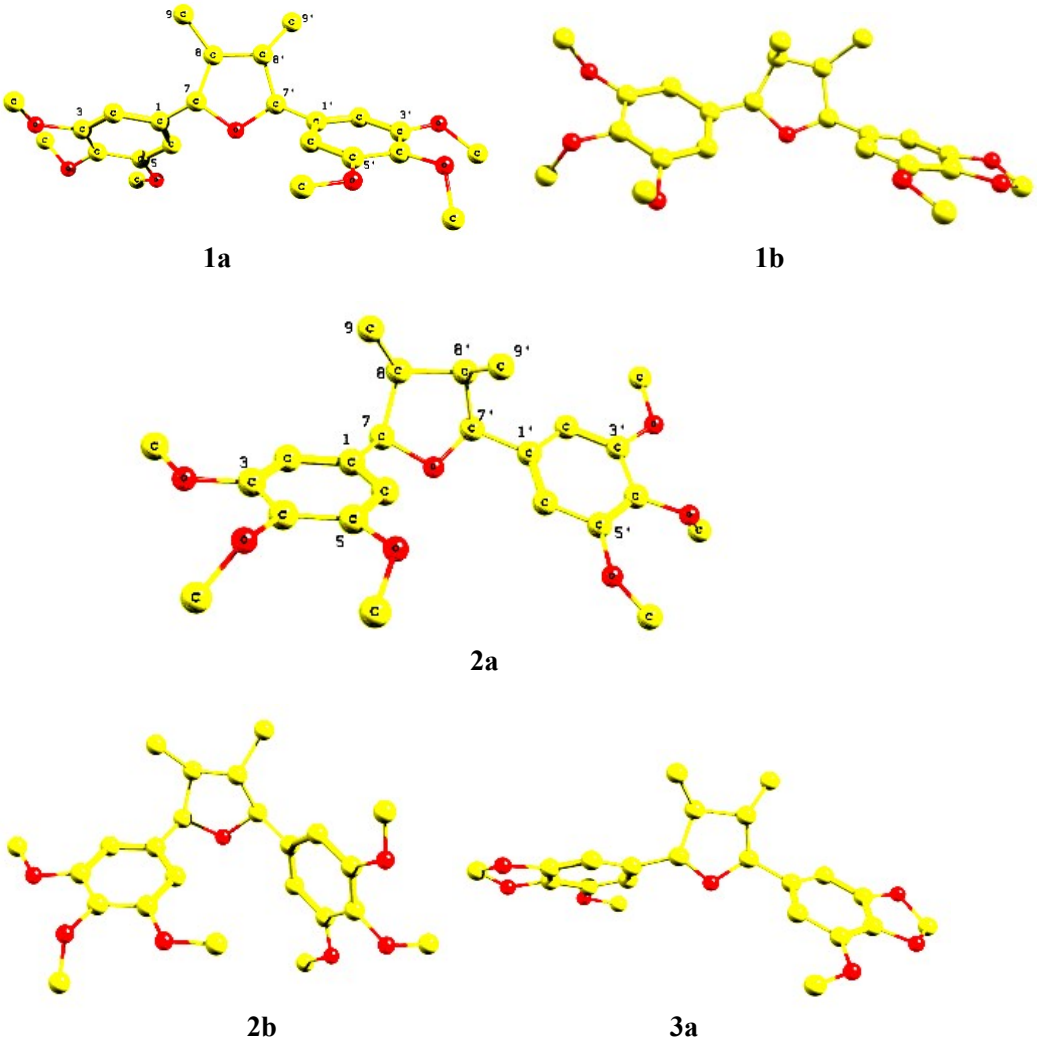


Figure S9. Calculated geometrical structures of lignans **1a** - **3a** (hydrogens not shown).

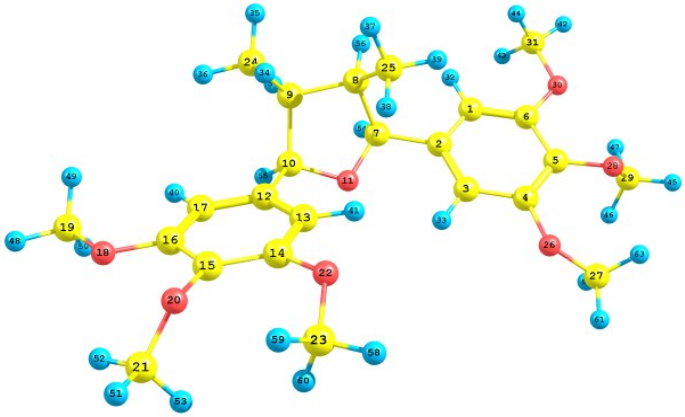
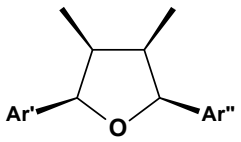


Figure S10. Numbering for lignan **2a** showing all hydrogen atoms.

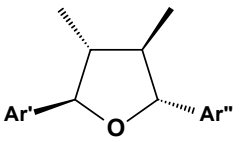
Table S1. ^{1}H and ^{13}C NMR data[a] for tetrahydrofuran lignans with different substitution patterns and stereochemistries

compounds	7 and 7'		8 and 8'		9 and 9'		$[\alpha]_D^{21}$	ref
	$^{1}H_{(\delta, J)}$	$^{13}C_{(\delta)}$	$^{1}H_{(\delta, J)}$	$^{13}C_{(\delta)}$	$^{1}H_{(\delta, J)}$	$^{13}C_{(\delta)}$		
1c	5.06 (d, 6.6)	84.3	2.60 (m)	42.7	0.56 (d, 7.0)	12.6	0	32, 37
5	4.38 (d, 6.5)	88.3	2.20 (m)	45.7	0.99 (m)	13.1	0	32, 37
3c	4.59 (d, 9.1)	88.7	1.74 (m)	51.9	1.01 (d, 5.8)	13.9	-	32, 37
4	5.44 (d, 6.0)	83.2	2.26 (m)	43.7	0.71 (d, 6.4)	14.4	-38.2º	40
2a	4.67 (d, 8.8)	88.4	1.75 (m)	50.9	1.08 (d, 8.8)	13.9	-51.1º	35
2b	4.50 (d, 9.0)	88.4	1.68 (m)	51.0	0.96 (d, 6.3)	13.9	-10.1º	36
2c	4.52 (d, 7.2)	88.3	1.67 (m)	50.8	0.96 (d, 7.2)	13.8	-4.5º	35
		88.4		51.1		13.9		
3a	5.05 (d, 8.5)	83.1	2.26 (m)	48.2	0.68 (d, 7.0)	15.0	-25.6º	20
	4.33 (d, 9.0)	87.4	1.72 (m)	45.9	1.06 (d, 7.0)	14.9		
3b	5.02 (d, 8.5)	83.2	2.16 (m)	45.8	0.61 (d, 7.5)	15.0	-30.7º	20
	4.30 (d, 9.0)	87.3	1.68 (m)	47.8	1.01 (d, 6.5)	14.8		

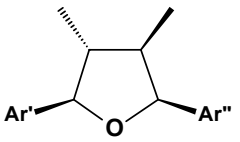
[a] Compounds dissolved in $CDCl_3$; δ in ppm relative to TMS, J in Hz.



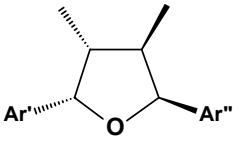
1a Ar'=Ar"=Ar_2
1b Ar'=Ar_2; Ar"=Ar_3
1c Ar'=Ar"=Ar_1



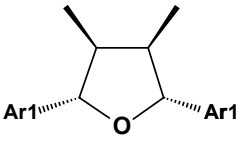
2a Ar'=Ar"=Ar_2
2b Ar'=Ar"=Ar_3
2c Ar'=Ar_2; Ar"=Ar_3



3a Ar'=Ar"=Ar_3
3b Ar'=Ar_2; Ar"=Ar_3
3c Ar'=Ar"=Ar_1



4 Ar'=Ar"=Ar_4



5

Ar_1= 4-hydroxyphenyl
Ar_2= 3,4,5-trimethoxyphenyl
Ar_3=3,4-methylenedioxy-5-methoxyphenyl
Ar_4=3-hydroxy-4-methoxyphenyl

Table S2. Calculated energies (gas phase) for the lignans with geometries optimized according to B3LYP/6-31G(d,p) and zero-point energies (ZPE) added.

Lignans	energy + ZPE (Hartree/particule)	relative energy (Hartree/particule)	relative energy (kcal mol^{-1})
1a	- 1459.800437	0.010359	6.5
3a	- 1459.810119	0.000677	0.42
2a	- 1459.810796	0.0	0.0
1b	- 1419.337431		
2b	- 1378.883505		

Table S3. Conformer energy* of lignans in water (ε=78.3) and cyclohexane (ε=2.0) media.

	Isomers Lignans Energy (Hartree/particule)			**Relative Energy**	
Medium	**1a**	**2a**	**3a**	**$\Delta E^{(2a-1a)}$**	**$\Delta E^{(2a-3a)}$**
				(kcal mol^{-1})	
Gas Phase	-1460.329755	-1460.339709	-1460.339364	- 6.25	- 0.22
Water	-1460.351951	-1460.361272	-1460.361762	- 5.85	+ 0.31
Cyclohexane	-1460.332939	-1460.342804	-1460.342544	- 6.19	- 0.16

	Isomers Lignans Energy (Hartree/particule)	
Medium	**1b**	**2b**
Gas Phase	-1419.816936	-1379.314216
Water	-1419.837997	-1379.340329
Cyclohexane	-1419.819695	-1379.317854

* PCM/(B3LYP/6-31G(d,p))SCRF models

Table S4**.** Selected Bond Lengths[a] in Lignans **1a** – **3a** Calculated using the B3LYP/6-31G(d,p) Method

Bond	**1a**	**1b**	**2a (crystal)[b]**	**2b**	**3a**
O-C7	1.436	1.426	1.430 (1.431)	1.437	1.432
O-C7’	1.435	1.430	1.425 (1.426)	1.437	1.442
C7-C8	1.545	1.549	1.546 (1.534)	1.546	1.554
C8-C9	1.526	1.532	1.528 (1.515)	1.526	1.527
C7'-C8'	1.547	1.580	1.550 (1.549)	1.546	1.541
C8'-C9'	1.526	1.528	1.532 (1.506)	1.526	1.532
C7-C1	1.516	1.512	1.516 (1.511)	1.515	1.522
C7'-C1'	1.514	1.518	1.511 (1.503)	1.515	1.525
C_{ring}-$O_{(MeO)}$	~1.37[a]	1.374	~1.37[a] (1.365)	1.361	1.372
$C_{(MeO)}$-$O_{(MeO)}$	~1.43[a]	1.434	~1.43[a] (1.431)	1.420	~1.42[a]
C_{ring}-O_{MeO}		1.378		1.377	
$(C\text{-}O)_{epoxy}$		1.433		1.428	

[a] Average values in Å; For numbering see Figure S9
[b] ref. 14

Table S5. Selected Dihedral Angles[a] in Lignans **1a - 3a**

Bond	**1a**	**1b**	**2a**	**2b**	**3a**
O-C7'-C1'-C6'	38.8	26.7	11.1	31.3	– 34.9
C8-C7-C1-C2	90.7	– 69.5	– 87.0	89.5	– 89.0
O-C7-C1-C6	32.0	– 9.1	– 28.0	31.0	– 29.0
O-C7'-C8'-C9'	156.5	– 138.3	– 81.6	157.0	147.0
O-C7-C8-C9	157.5	81.5	137.8	156.5	158.7
O-C7-C8-C8'	32.6	– 41.8	8.92	31.4	31.9
O-C7'-C8'-C8	30.4	– 9.46	41.7	32.1	24.6

[a] Dihedral angles in °; For numbering see Figure S9

Table S6. Lengths of Selected Hydrogen Bonds[a] in Lignans **1a – 3a** Calculated using the B3LYP/6-31G(d,p) level of theory.

Bond[b]	**1a**	**1b**	**2a**	**2b**	**3a**
O11 – H38			2.87481		
O11 – H33	2.53065	2.47395	2.40684	2.44379	2.41733
O29 – H63	2.40625		2.41130		
O30 – H47	2.32478		2.32082		3.00064
O11 – H41	2.47677	2.39822	2.51029	2.44094	2.50649
O18 – H52			2.31947		
O20 – H59			2.40968		
O11 – H14		2.87041			

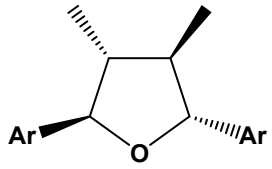
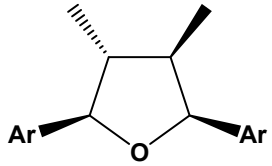
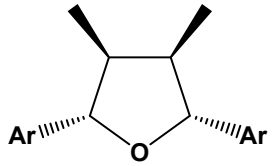
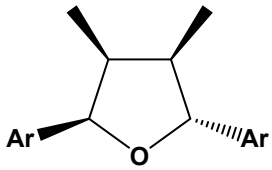
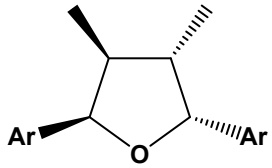
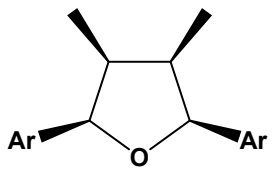
[a] Values in Å; [b] For numbering see Figure S9

Table S7. Selected Bond Angles[a] in Lignans **1a** – **3a** Calculated using the B3LYP/6-31G(d,p) Method.

Bond[b]	**1a**	**1b**	**2a** (crystal)[c]	**2b**	**3a**
O11-C7-C2	110.8	110.0	110.6 (111.9)	110.8	109.1
O11-C10-C12	110.6	110.4	110.6 (110.3)	110.4	111.7
C12-C10-C9	114.8	117.2	116.4 (117.1)	115.1	115.8
C7-C8-C25	114.3	116.4	113.8 (111.2)	114.4	114.2
C14-O22-C23	118.0	115.0	120.9 (117.2)	117.6	117.9
C15-O20-C21	116.4	113.6	116.4 (115.3)		114.4
C16-O18-C19	120.7	115.7	118.2 (118.6)		118.0
C4-O26-C27	121.3	118.8	121.0 (118.2)	117.6	118.0
C5-O28-C29	116.3		116.4 (113.7)		114.4
C6-O30-C31	118.2		118.1 (117.3)		118.2
C7-C2-C3	120.8	121.3	121.7 (121.7)	119.9	118.0
C10-C12-C13	120.3	121.6	121.8 (120.7)	119.9	120.9
C10-C9-C24	114.3	113.8	116.4 (112.5)	114.4	116.7

[a] Bond angles in °; [b] For numbering see Figure S10; [c] ref. 14.

Table S8. Relative energies and structures of ten possible stereoisomers for THFs lignans (pairs of enantiomers: **2a**, **3a**, **7** and **8**; *meso*: **6** and **1a**)

Lignans	Relative energies (Kcal/mol)
 **2a**	0.0
 **3d**	2.5
 **6** (*meso*)	3.1
 **7**	4.1
 **8**	4.4
 **1a** (*meso*)	5.6

Ar = phenyl