X-ray Structure of a Trimeric 5,5′-Biaryl/*erythro*-β-*O*-4-ether Lignin Model: Evidence for Through-Space Weak Interactions

Jean-Philippe Roblin,[a] Hubert Duran,[a] Elisabeth Duran,[a] Liliane Gorrichon,*[a] and Bruno Donnadieu[b]

Abstract: The crystal structure of a trimeric lignin model **1** presenting the characteristic pattern of biphenyl (5,5′) and aryl-alkyl-ether (β-O-4) linkages has been determined. The crystal system is triclinic and the crystallographic unit cell consists of two monomeric molecules. These results are compared with crystal data from the literature of simple models of the 5,5′ and β-O-4 structure type. The availability of a terminal aldehyde function on the model affords some interesting intermolecular interactions by weak hydrogen bonding which controls the conformation of the molecule and the aromatic ring orientation in particular; an unexpected *cisoïd* conformation of the biaryl unit is observed based on the 64.4° value found for the torsion angle between the two 5,5′ aromatic rings.

Keywords: aryl-alkyl-ether · biaryls · conformational analysis · lignin model · X-ray absorption spectroscopy

Introduction

Lignins, complex polyphenolic polymers found in all plants which have developed vascular systems, are the second most abundant polymers in the biomass after cellulose, and promise to be an interesting renewable material.[1] The complexity of these polymers lies in the diversity of the intermonomeric linkages, which mainly occur during the biosynthesis, from the random radical coupling of three different *p*-hydroxycinnamyl alcohols (Figure 1). It has also been postulated from recent NMR studies that some other phenylpropane units, such as coumaroyl or feruloyl-esters, participate to the radical processes.[2] The mechanisms and the roles of different peroxidase enzyme classes in radical initiation and polymerization/depolymerization are under extensive study.[3] Due to their complexity, lignin polymers are considered to be an amorphous three dimensional network.[4] However, this concept has been discussed[5] and appears to be too simple to explain some recent scientific results. Monolignol coupling and lignin formation has just been proposed to operate under the control of a "dirigent" protein which offers specific lignol radical binding sites.[5a] Some years ago it was also pointed out in Raman micro-spectrophotometric experiments by Atalla et al.[5b] that hydrophobic interactions between aromatic rings give rise to a certain organizational level in lignins. Therefore, the structural investigation of models by means of X-ray diffraction studies gives pertinent information concerning the orientation of the different substituents and the weak interactions which may be involved in the through-space organization of lignin monomer units.

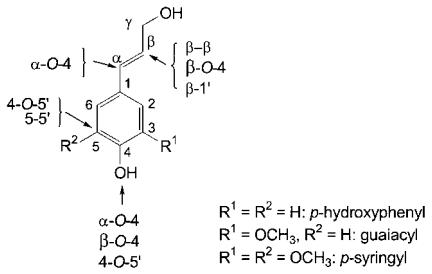


Figure 1. Momomeric units and principal linkages found in lignin polymers.

To provide a better understanding of lignin structure and reactivity many mimics have been developed of the different substructures units of lignins.[6] Aryl-alkyl-ether bonds (β-O-4) are the commonest linkages found in lignins no matter what the nature of the lignified plant tissues. When compared with other linkages, 5,5′-diaryl bonds appeared to be responsible for lignin increased stabilities towards pulping conditions; the content in biaryl units was estimated to be in the range 9 to 17% in softwoods and only 4.5% in hardwoods[1f] while it was proposed by Pew[7] to represent 25% in coniferous lignins;

[a] Dr. L. Gorrichon, Dr. J.-P. Roblin, Dr. H. Duran, Dr. E. Duran
Laboratoire de Synthèse et Physicochimie
de Molécules d'Intérêt Biologique, associé au CNRS
Université Paul-Sabatier, 118 route de Narbonne
31062 Toulouse cedex 4 (France)
Fax: (+33) 5 61 55 60 11
E-mail: spco@iris.ups-tlse.fr

[b] Dr. B. Donnadieu
Laboratoire de Chimie de Coordination, CNRS UPR 8241
205 route de Narbonne, 31077 Toulouse cedex 4 (France)

  0947-6539/00/0607-1229 $ 17.50+.50/0

these results were obtained from an early determination based on an UV comparison between lignin models and spruce lignin. Recently, new results were obtained by Brunow's group.[8] They announced the discovery of dibenzodioxocins, a 5,5′-biaryl type structure covalently linked on the phenolic functions by a C(6)-C(3) unit, as being a substantial part of the lignin building blocks. When submitted to pulping degradation conditions, dibenzodioxocins give 5,5′-bicreosol moieties.[9] Argyropoulos et al.[10] have also shown that milled wood lignin subjected to Kraft pulping conditions liberated large amounts of stable 5,5′-bicreosol moieties, which indicates that dibenzodioxocins are an integral part of the native lignins and their degradation products (5,5′-bicreosol type moieties) an integral part of residual Kraft lignin structure. As such the significance of these biaryl moieties in understanding native and industrially produced lignins becomes apparent.

In order to study the chemical behaviour, the reactivity and the possible template or anchor effects of biaryl units in both solution and on polymer-supported state, we synthesized several oligolignols. We were interested by an unsymmetrical new trilignol **1** (Figure 2) composed of β-O-4, an 5,5′ biaryl

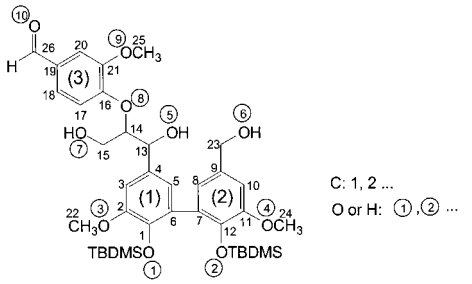


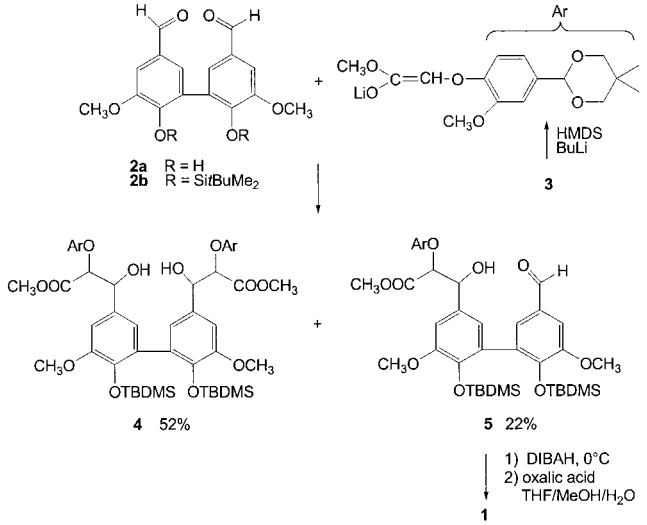
Figure 2. Trimeric lignin model **1**.

intermonomeric bonds and an aldehyde function. In a model of spruce lignin, Adler[1b] assumed the presence of carbonyl moieties in the polymer. The presence of this function has also been postulated in ^{13}C-NMR studies on native lignin extracts.[2a] In this paper we would like to report its crystal structure which is the first one to exhibit this particularly important bonding pattern.

Abstract in French: *La structure cristalline d'un modèle trimérique de lignine **1** présentant le motif caractéristique de liaisons biphényle (5,5′) et aryl-alkyl-ether a été détermine. Le cristal est triclinique et la maille cristalline possède deux molécules monomères. Ce résultat est comparé avec les données de la littérature de modèles simples 5,5′ et β-O-4. La disponibilité de la fonction aldéhyde terminale dans ce modèle donne à ce motif quelques interactions intermoléculaires intéressantes par liaison hydrogène faible qui contrôle la conformation de la molécule et l'orientation des noyaux aromatiques; en particulier, une conformation cisoïde inattendue des unités biaryle est observée, une valeur de 64,4° est trouvée pour l'angle de torsion entre les deux noyaux aromatiques 5 – 5′.*

Results and Discussion

Working on a recurrent synthetic pathway to obtain β-O-4 oligolignols[11] we were interested in the synthesis of mixed oligolignols containing both 5,5′ and β-O-4 linkages. We decided to synthesize the biaryl unit prior to the condensation step based on the Nakatsubo procedure with some modifications.[12] The key step in the synthesis of compound **1** is an aldol condensation between the bis-vanillin **2** with protected phenolic functionalities and the lithium enolate of the α-phenoxy ester **3** (Scheme 1). The aldehyde functionality in **3**



Scheme 1. Synthesis of the biaryl lignin model **1**.

was masked and can be further unmasked if necessary thereby allowing the recurrent synthesis to oligolignols to continue; these models can also be grafted onto a solid support for further studies. Some improvements to the methodology have been made concerning the choice of the base to generate the enolate moiety and the choice of protective groups.

When lithium bis-(trimethylsilyl)amide, which lacks a proton in α-position to the nitrogen, was used as a base instead of lithium diisopropylamide, reduction of the protected bis-vanillin to the corresponding benzyl alcohol, as observed in previous studies, was avoided. The aldehyde from the α-phenoxy ester **3** was protected as a cyclic six-membered acetal with 2,2-dimethylpropanediol. Although three diastereoisomers can be expected in the condensation step, only two compounds were obtained: Bis-β-hydroxyester **4** (52%) was isolated as a mixture of the *erythro-erythro* and *erythro-threo* diastereoisomers in a 4:1 ratio, and monoadduct **5** (22%) which was further reduced and deprotected to give compound **1**; the *erythro* isomer was the only one observed. When a *tert*-butyldimethylsilyl group was used instead of the classical benzyl group for the protection of the phenolic functions, compound **1** was isolated as a crystalline solid (Figure 3).

Tables 1 to 3 list the crystal and experimental data, the interatomic distances and bond angles for compound **1**. Study of the aryl-alkyl-ether part of the molecule confirms the *erythro* configuration first determined by ^{1}H-NMR spectroscopy.[13]

0947-6539/00/0607-1230 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 7

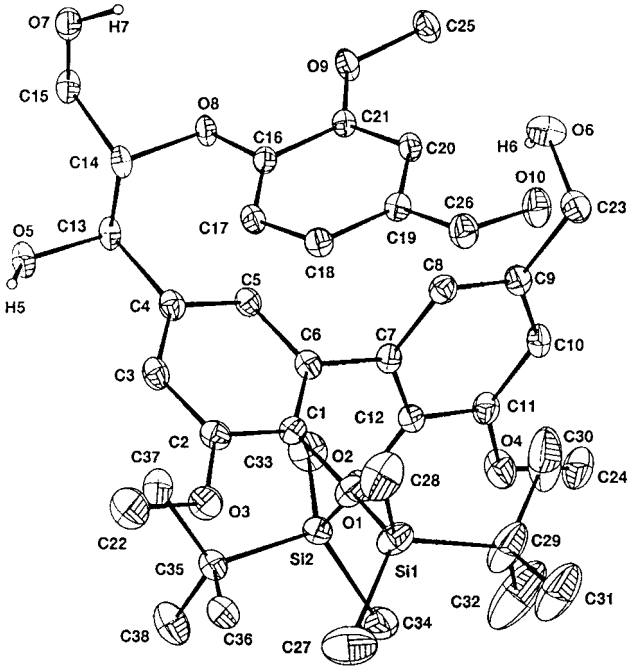


Figure 3. Crystal structure of **1**.

Weak hydrogen bonds are given in Table 3. The crystal system is triclinic and the unit cell consists of two monomeric molecules of 1-[3-methoxy-4-*tert*-butyldimethylsilyloxy-5-(2-*tert*-butyldimethylsilyloxy-3-methoxy-5-hydroxymethylphenyl)-phenyl]-2-(4-formyl-2-methoxyphenoxy)-1,3-propanediol, held together by weak hydrogen bonds ($OH(6)\cdots CH_3O(9')$) as depicted in Figure 4. Interactions with other trimeric units in the adjacent cell occur through π stacking and also weak hydrogen bonds ($OH(7)\cdots C{=}O(10')$). This latter interaction is dependent on the *erythro* configuration of the diastereoisomer studied, since the primary hydroxyl function (OH(7)) involved in the hydrogen bonding will be oriented different on the carbon-β-(C14) in the *threo* isomer. The three rings are planar (the maximum deviation of the aromatic carbon atoms from their respective least squares plane is 0.013 Å). The angles between mean planes of the aromatic rings are 37.8° for rings (1), (3) of the β-O-4 part, 65.1° for rings (1), (2) of the biphenyl part and 87.0° for rings (2), (3) (Table 4).

It is interesting to compare the crystal data for compound **1** with the crystal parameters of simple *erythro* β-O-4-**7**[14] and 5,5′-**8**[15] structure models, which have already been published (Figure 5).

In the case of compound **7**, Stomberg and Lundquist[14] described two conformational orientations due to the disordered CH_2OH group; in our study the use of low temperature X-ray determination afforded only one conformation. The torsion angle between C(4)-C(13)-C(14)-C(15) (169.92°) is close to the value found for **7** (175.35°). The main difference between structures **7** and **1** arises from the relative plane orientation of the aromatic rings (the angle between rings A and B is 87.5°). In the case of compound **1**, aromatic rings (1) and (3) present a much smaller angle value (37.8°) in such a way that interactions between π orbitals of C(16)-C(4) and C(17)-C(3) of the aromatic rings could occur ($C(16)\cdots C(4) =$ 3.20 Å, $C(17)\cdots C(3) = 3.39$ Å). This particular difference may be induced by favourable intermolecular π stacking and/or weak hydrogen bonding.

In the case of the biphenyl moiety, the length of the bond connecting the two aromatic rings is the same for both compounds **1** and **8** (1.491(3) Å and 1.491(2) Å). However, the main difference between these two structures lies in the

Table 1. Crystal data, data collection and refinement parameters.

Crystal data	
unit asymetric	$C_{38}H_{56}O_{10}Si_2$
molecular weight	729.03
ρ_{calcd} [g cm^{-3}]	1.19
μ [cm^{-1}]	1.33
F(000)	784.51
crystal system	triclinic
space group	$P\bar{1}$
a [Å]	9.8999(2)
b [Å]	11.399(2)
c [Å]	18.309(4)
α [°]	92.17(2)
β [°]	95.84(2)
γ [°]	97.63(2)
V [Å^3]	2034.1(9)
Z	2
crystal size [mm]	0.5 × 0.5 × 0.2
crystal shape	block
crystal color	colourless
data collection	
radiation type	$Mo_{K\alpha}$
wavelength [Å]	0.71073
tube power [kW]	1.50
collimator size [mm]	0.5
temperature [K]	160
detector distance [mm]	80.0
2θ range [°]	2.9–48.4
ϕ movement mode	rotation
ϕ start [°]	0.0
ϕ end [°]	200
ϕ incr [°]	1.5
exposures	167
measurement duration [h]	19
irradiation/exposures [min]	2.5
used reflections for cell post-refinement	5000
measured reflections	15958
independent reflections	5967
merging R value	0.034
completeness of data set [%]	92
refinement parameters	
Refinement on	F_{obs}
R[a]	0.038
R_w[b]	0.041
$\Delta\rho_{max}$, $\Delta\rho_{min}$ [e Å^3]	0.46, −0.37
G.O.F (S)[c]	0.6
weighting scheme[d]	Chebyshev
using parameters	1.82, −1.38, 0.648, −0.826
abs corr	None
reflections used [$I > \sigma(I)$]	4316
parameters used	492

[a] $R = \Sigma(||F_o| - |F_c||)/\Sigma(|F_o|)$. [b] $R_w = [\Sigma_w(||F_o| - |F_c||)^2/\Sigma_w(|F_o|)^2]^{1/2}$. [c] Goodness of fit $= [\Sigma(|F_o| - |F_c|)^2/(N_{obs} - N_{parameters})^{1/2}$. [d] $W =$ [weight] · $[1 - \Delta F/6\sigma F)^2]^2$ where weight is calculated from following expression weight $= 1/\Sigma(r = 1,n)$ArTr(X), where Ar are the coefficients for the Chebyshev polyniomal Tr(X) with $X = F_c/F_c$(max) according to J. R. Carruthers, D. J. Watkin (Chebychev Weighting) *Acta Crystallogr. Sect. A35* **1979**, 698–699.

Table 2. Selected interatomic distances [Å] and angles [°] for **1** with standard deviations in parentheses.

Si(1)−O(1)	1.654(2)	C(13)-O(5)-H(5)	110(2)
Si(2)−O(2)	1.651(2)	C(23)-O(6)-H(6)	107(3)
O(1)−C(1)	1.358(3)	C(15)-O(7)-H(7)	110(3)
O(2)−C(12)	1.360(3)	C(14)-O(8)-C(16)	121.9(2)
O(3)−C(2)	1.371(3)	C(3)-C(4)-C(13)	121.8(2)
O(3)−C(22)	1.418(3)	C(5)-C(4)-C(13)	119.3(2)
O(4)−C(11)	1.372(3)	C(1)-C(6)-C(7)	121.2(2)
C(4)−C(13)	1.514(3)	C(5)-C(6)-C(7)	119.3(2)
O(4)−C(24)	1.406(3)	C(6)-C(7)-C(8)	119.9(2)
O(5)−C(13)	1.429(3)	C(5)-C(6)-C(7)	119.3(2)
O(5)−H(5)	0.95(3)	C(6)-C(7)-C(12)	120.8(2)
C(6)−C(7)	1.491(3)	O(5)-C(13)-C(4)	113.9(2)
O(6)−C(23)	1.421(3)	C(4)-C(13)-C(14)	112.9(2)
O(6)−H(6)	0.91(5)	O(8)-C(14)-C(13)	112(2)
O(7)−H(7)	0.84(4)	O(8)-C(14)-C(15)	104.3(2)
O(7)−C(15)	1.417(3)	O(5)-C(13)-C(14)	107.2(2)
O(8)−C(16)	1.360(3)	O(8)-C(14)-C(15)	105.3(2)
O(8)−C(14)	1.447(3)	O(8)-C(14)-H(141)	108(2)
O(9)−C(21)	1.362(3)	C(13)-C(14)-H(141)	112(2)
C(9)−C(23)	1.502(3)	O(7)-C(15)-C(14)	112.8(2)
O(9)−C(25)	1.431(3)	O(8)-C(16)-C(17)	126.4(2)
O(10)−C(26)	1.220(3)	O(8)-C(16)-C(21)	113.4(2)
C(13)−C(14)	1.541(3)	C(18)-C(19)-C(26)	118.3(2)
C(14)−C(15)	1.514(3)	C(20)-C(19)-C(26)	122.1(2)
C(19)−C(26)	1.443(4)	O(9)-C(21)-C(16)	114.7(2)
		O(9)-C(21)-C(20)	125.2(2)
		C(16)-C(21)-C(20)	120.2(2)
		O(6)-C(23)-C(9)	112.7(2)
		O(10)-C(26)-C(19)	126.7(3)
		O(10)-C(26)-H(261)	119(2)
		C(19)-C(26)-H(261)	115(2)

Table 3. Full list of distances and angles() for O-H···H bonded (with e.s.d.'s in parentheses)

O(9)···H(6i)	2.20(6)	O(9)···H(6i)−O(6i)	160.0(2)
O(10)···H(7j)	2.10(4)	O(10)···H(7j)−O(7j)	145.7(2)
O(9)···O(6i)	3.076(3)		
O(10)···O(7j)	2.840(3)		

Table 4. Equation of the planes, angles between mean planes

Plane 1: C(1)-C(2)-C(3)-C(4)-C(5)-C(6):	
$6.109x - 8.734y + 6.372z - 3.517 = 0.0$	
Plane 2: C(7)-C(8)-C(9)-C(10)-C(11)-C(12):	
$4.744x - 6.981y - 12.7542 + 2.563 = 0.0$	
Plane 3: C(16)-C(17)-C(18)-C(19)-C(20)-C(21):	
$0.528x - 8.167y + 13.242z - 5.451 = 0.0$	
Angles between mean planes:	1 and 2: 65.1°
	1 and 3: 37.8°
	2 and 3: 87.0°

relative orientation of the aromatic rings. Despite the fact that angle values of the aromatic mean planes are rather similar (59.8° for **8** and 65.1° for **1**) and agree with what is usually found for *o*,*o*′-substituted biphenyls, the torsion angle between C(1)-C(6)-C(7)-C(12) for **1** is about 64.4°, corresponding to a *cisoïd* conformation (compared with 120.7° for the corresponding angle for **8** which fits with a *transoïd* conformation).[15, 16] Nevertheless, *cisoïd* conformations are not unprecedented in biaryl compounds;[17] the angle values for bridged biphenyl cyclooctadienes,[17a] in which the biaryl unit is included in an eight-membered ring in the same way as in dibenzodioxocins,[8b] were found equal to 56.5° and 62.0° (depending on the stereoisomer considered) and they can be compared to the 64° torsion angle determined for compound **1**. Silylation in **1**, compared with acetylation in **8**, contribute to an increase in the apparent size of the phenolic function. The steric factors probably play a role in the conformational change observed. This point is not disconnected from the well known ability of the lignin phenolic functions to bind to other molecules such as carbohydrates[1f] or ions (silicates, calcium)[18]; if a chain elongation based on a 5,5′-diphenolic unit occurs during lignin formation, a conformational change in the relative orientation

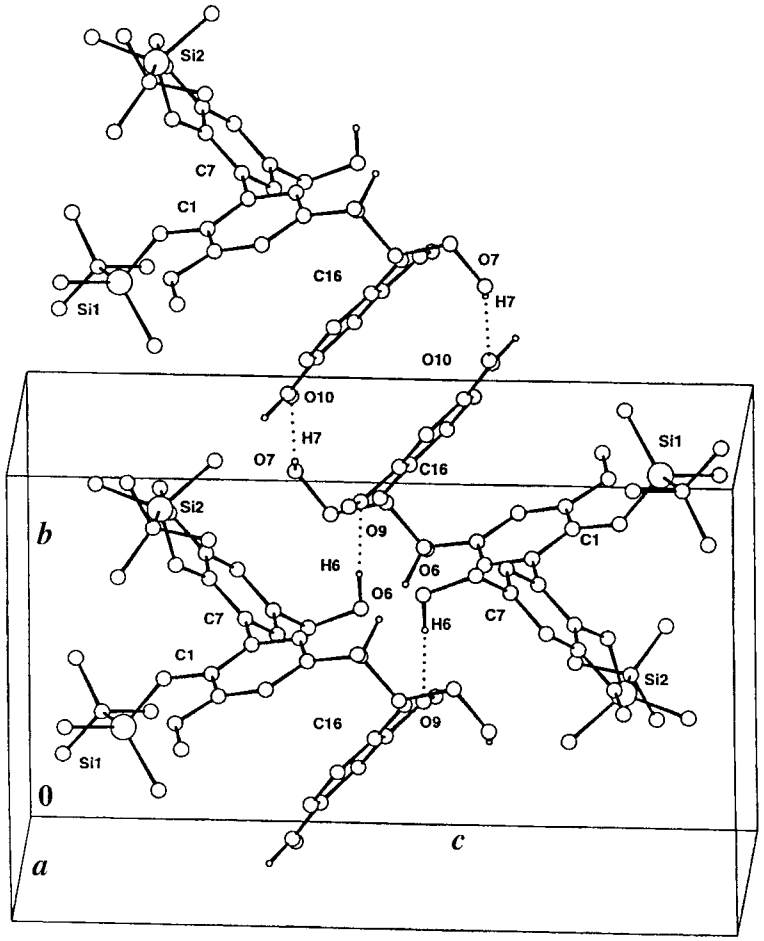


Figure 4. Unit cell and weak hydrogen bonding.

0947-6539/00/0607-1232 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 7

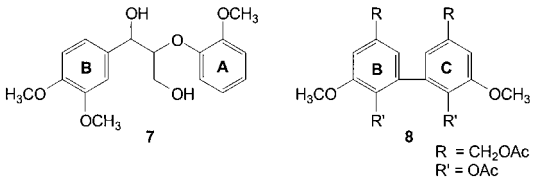


Figure 5. Simple dimeric lignin models for which X-ray data are available.

of the aromatic rings will induce a modified spatial organization for branches and further regions on the lignin network.

An important feature which has also to be pointed out is the role of weak hydrogen bonding and "π" stacking in the inter- and intramolecular organization of compound **1**. These interactions contribute to give a parallel orientation of the aromatic rings in the mixed β-O-4 ether and 5,5′-biaryl model; a result in excellent agreement with the conclusions of Atalla et al.[19] who predicted that at the molecular level the lignin will be more highly organized than has been previously recognized.

Conclusion

It is still generally agreed upon that lignins cannot be crystalline because of their great complexity compared with other vegetable biopolymers.[20] However, some studies have shown there can be a certain organizational level between the different monomeric units of lignin polymers.[1f, 5a, 5b] Weak hydrogen bonding[5f] as well as hydrophobic interactions may play an important role in this organization and also in the biodegradation process. We were interested in a trilignol model **1** which presents a β-O-4 ether structure and a biaryl unit. The importance of biaryl units in lignin chemistry is well documented and recently implemented by the discovery of new biaryl moieties like dibenzodioxocins[8] in native lignin or 5,5′-bicreosol type units in residual Kraft lignins. As shown in the crystal structure of the trimeric lignin model **1** the biaryl unit presents the same preferential *cisoïd* conformation on that bridged biaryl compound, and not the *transoïd* previously observed for some other 5,5′-biaryl lignin models. Intramolecular interactions by weak hydrogen bonding also play an important role in the orientation of the aromatic ring planes and could therefore influence the lignification process and possible organization of lignin polymers.

Experimental Section

Materials: Commercially available chemicals were used as received. The solvents were distilled prior to use: THF was distilled from sodium, dichloromethane from calcium hydride; acetone when distilled, was stored over molecular sieves 4 Å. All purifications were made on silica gel 6–35 μm with a Jobin–Yvon Miniprep apparatus. ^{1}H- and ^{13}C-NMR spectroscopy spectra were recorded on a Bruker AC250 (250 MHz for proton, 63 MHz for carbon); all spectra were carried out in $CDCl_3$. IR spectra were recorded on a Perkin–Elmer 833 instrument; all spectra were realized in KBr plates.

5,5′-Bis(4-*tert*-butyldimethylsilyloxy-3-methoxybenzaldehyde) (2b): *tert*-Butyldimethylsilyl chloride (11.9 mmol) was added to a suspension of bisvanillin[21] (5 mmol) in DMF (15 mL), under nitrogen atmosphere. Then, imidazole (24.8 mmol) was added to the reaction mixture under stirring at the room temperature. After 3 h, the reaction mixture was neutralized with aqueous $NaHCO_3$ (5%) and extracted with EtOAc. The combined organic extracts were dried ($MgSO_4$) and concentrated in vacuo. The crude product was recrystallized from Et_2O (1.9 g, 72%). IR: $\tilde{\nu}$ = 1691 (CHO), 1586 (C=C) cm^{-1}; ^{1}H NMR: δ = 0.02 (s, 2 × 6H, $Si(CH_3)_2$), 0.61 (s, 2 × 9H, $C(CH_3)_3$), 3.89 (s, 2 × 3H, CH_3O), 7.40 (d, 2 × 1H, J_{meta} = 1.94 Hz, ArH), 7.45 (d, 2 × 1H, J_{meta} = 1.94 Hz, ArH), 9.84 (s, 1H, CHO); ^{13}C NMR: δ = −4.28 ($Si(CH_3)_2$), 18.33 (CSi), 25.17 ($(CH_3)_3$), 55.19 (OCH_3), 108.69 (CH), 129.39 (CH), 129.46 (C), 129.66 (C), 149.11 (C), 151.06 (C), 190.96 (CHO); $C_{28}H_{42}O_6Si_2$ (580.8): calcd C 63.41, H 7.99; found C 63.36, H 7.98.

5,5-Dimethyl-2(4-hydroxy-3-methoxyphenyl)-1,3-dioxane (3a): Vanillin (9 g, 59 mmol) and 2,2-dimethylpropan-1,3-diol (18,5 g, 178 mmol) were dissolved in toluene (300 mL) containing *p*-toluene sulfonic acid (687 mg, 3 mmol). The mixture was refluxed with a Dean–Stark apparatus for 4 h. The reaction mixture was neutralized with $NaHCO_3$, washed with water and dried over Na_2SO_4 and evaporated in vacuo. The yellow oil was recrystallized from diisopropyl ether (76% yield). IR: $\tilde{\nu}$ = 3390, 3300 (OH), 1282 (C-O-C) cm^{-1}; ^{1}H NMR: δ = 0.80, 1.30 (s, 6H, 2CH_3 dioxane), 3.70 (AB syst, 4H, J_{AB} = 11.1 Hz, 2OCH_2 dioxane), 3.91 (s, 3H, OCH_3), 5.32 (s, 1H, CH dioxane), 5.67 (s, 1H, OH), 6.88–7.06 (m, 3H, CHar); ^{13}C NMR: δ = 21.89, 23.12 (2CH_3 dioxane), 30.20 (C_{IV} dioxane), 55.92 (OCH_3), 77.68 (2OCH_2 dioxane), 101.79 (CH dioxane), 108.44 (CHar), 114.04 (CHar), 119.5 (CHar), 130.79 (C_{IV}), 146.13 (C_{IV}), 146.43 (C_{IV}).

Methyl-[4-(4,4-dimethyl-2,6-dioxacyclohexyl)-3-methoxyphenoxy]ethanoate (3): Compound **3a** (9 g, 37.6 mmol), methylchloroacetate (12.2 g, 112.9 mmol), potassium iodide (8.1 g, 48.9 mmol) were stirred in acetone (300 mL), and was refluxed for 5 h. Inorganic salts were filtered over Celite. The combined filtrate was washed with water. The organic layer was dried over Na_2SO_4 and evaporated in vacuo. A viscous oily substance was recrystallized from diisopropyl ether (97%). IR: $\tilde{\nu}$ = 1767 (COO), 1443, 1391 (C-O-C); ^{1}H NMR: δ = 0.79, 1.27 (s, 6H, 2CH_3 dioxane), 3.69 (AB syst, 4H, J_{AB} = 10.8 Hz, 2OCH_2 dioxane), 3.76 (s, 3H, $COOH_3$), 3.90 (s, 3H, OCH_3); 4.68 (s, 2H, OCH_2), 5.33 (s, 1H, CH dioxane), 6.80–7.09 (m, 3H, CHar); ^{13}C NMR: δ = 21.89, 23.12 (2CH_3 dioxane); 30.20 (C_{IV} dioxane), 52.25 ($COOCH_3$), 55.89 (OCH_3), 66.49 (OCH_2), 77.68 (2OCH_2 dioxane), 101.45 (CH dioxane), 109.74 (CHar), 113.79 (CHar), 118.61 (CHar), 133.08 (C_{IV}), 147.49 (C_{IV}), 149.53 (C_{IV}), 169.41 (COO); $C_{16}H_{22}O_6$ (310.34): calcd C 61.48, H 7.08; found C 61.92, H 7.15.

Procedure for the synthesis of β-hydroxyesters 4 and 5: BuLi (2 mL, 3.1 mmol, 1.6 M in hexane) was slowly added at −10 °C under nitrogen atmosphere to HMDS (hexamethyldisilazane) (3.1 mmol, 0.5 mL). The reaction mixture was cooled at −78 °C, then a solution of **3** (4.56 mmol) in THF (9 mL) was added dropwise at the same temperature. After 15 min, a solution of **2b** (2.07 mmol) in THF (10 mL) was slowly added at the same temperature. The reaction was stirred for 15 min at −78 °C and hydrolyzed by addition of CH_3COOH (1.0 mL, 3.1 mmol) at −78 °C, washed with saturated NH_4Cl and allowed to warm up to room temperature. The combined organic extracts were washed with water, dried over Na_2SO_4 and concentrated in vacuo. The crude material was purified by column chromatography HPLC (silica gel 15–40 μm, petroleum ether/CH_2Cl_2/EtOAc 2:6.4:1.6) to give *erythro-erythro*/*erythro-threo* (80:20) (52%); only the *erythro-erythro* isomer of **4** was isolated (40%); and **5** (22%).

***erythro* 5,5′-Bis{methyl-3-(3-methoxy-4-*tert*-butyldimethylsilyloxyphenyl)-2-[4-(4,4-dimethyl-2,6-dioxacyclohexyl)-2-methoxyphenoxy]-3-hydroxypropanoate} (4)**: IR: $\tilde{\nu}$ = 1756 (CHO); 1606 (C=C) cm^{-1}; ^{1}H NMR: δ = −0.20, −0.15, −0.14, −0.10, −0.09, −0.05, −0.04, −0.007 (s, 12H, $Si(CH_3)_2$), 0.64, 0.66, 0.67 (s, 18H, $(CH_3)_3$), 0.78 (s, 6H, CH_3 dioxane), 1.27 (s, 6H, CH_3 dioxane), 3.61 (s, 3H, $COOCH_3$), 3.61–3.74 (AB syst., 2 × 2H, J_{AB} = 11.11 Hz, CH_2 dioxane), 3.78 (s, 6H, OCH_3), 3.83, 3.84 (s, 2 × 3H, OCH_3), 4.70 (d, 1H, $J_{\alpha\beta}$ = 5.10 Hz, C_βH), 5.10 (d, 1H, $J_{\alpha\beta}$ = 5.10 Hz, C_αH), 5.31 (s, 1H, CH dioxane), 6.79–7.05 (m, 10H, ArH); ^{13}C NMR: δ = −4.66, −4.48, −4.36 ($Si(CH_3)_2$), 18.33 (CSi), 21.87, 23.09 (CH_3 dioxane), 25.44 ($(CH_3)_3$), 30.20 (C_{IV} dioxane), 52.02 (CH_3OCO), 55.15 (CH_3O); 55.84 (CH_3O), 73.92 (C_βH), 77.63 (OCH_2 dioxane), 83.45 (C_αH), 101.35 (CH dioxane), 108.83–122.59 (CH), 130.15–150.37 (C), 169.82 (COO).

***erythro* Methyl-3-[3-methoxy-4-*tert*-butyldimethylsilyloxy-5-(2-*tert*-butyldimethylsilyl-oxy-3-methoxy-5-formylphenyl)phenyl]-2-[4-(4,4-dimethyl-2,6-dioxacyclohexyl)-2-methoxyphenoxy]-3-hydroxypropanoate (5)**: IR: $\tilde{\nu}$ = 3432 (OH), 1756 (C=O) cm^{-1}; ^{1}H NMR: δ = −0.10–0.00 (m, 12H, $Si(CH_3)_2$), 0.59, 0.61, 0.62 (s, 18H, $(CH_3)_3$), 0.79 (s, 6H, CH_3 dioxane),

1.26 (s, 6H, CH_3 dioxane), 3.65 (s, 3H), 3.59–3.90 (16H, CH_2 dioxane, $COOCH_3$, OCH_3), 4.70 (brs, 1H, $C_\beta H$), 5.12 (d, 1H, $J_{\alpha\beta}=5.10$ Hz, $C_\alpha H$), 5.31 (s, 1H, CH dioxane), 6.79–7.05 (m, 10H, ArH); ^{13}C NMR: $\delta=-4.48$, -4.36, -4.19 ($Si(CH_3)_2$), 18.29 (CSi), 21.87, 23.09 (CH_3 dioxane), 25.32 ($(CH_3)_3$), 30.21 (C_{IV} dioxane), 52.04 (CH_3OCO), 55.15, 55.80, 55.89 (CH_3O), 73.85 ($C_\beta H$), 77.65 (OCH_2 dioxane), 83.45 ($C_\alpha H$), 101.31 (CH dioxane), 107.91–122.21 (CH), 129.27–151.13 (C), 169.82 (COO), 191.30 (CHO).

1-[3-Methoxy-4-*tert*-butyldimethylsilyloxy-5-(2-*tert*-butyldimethylsilyloxy-3-methoxy-5-hydroxymethylphenyl)phenyl]-2-[4-(4,4-dimethyl-2,6-dioxacyclohexyl)-2-methoxyphenoxy]-1,3-propanediol (**6**): *Procedure for the reduction*: DIBAH (1M in toluene, 3 mL, 2.93 mmol) was added dropwise at 0 °C under argon to a solution of **5** (0.44 mmol) in dry CH_2Cl_2 (6 mL). Methanol, water and aqueous 10% HCl were successively added to the resulting mixture. The reaction mixture was filtered, washed and dried over Na_2SO_4. The crude product was purified by column chromatography HPLC (silica gel 15–40 μm; EtOAc/CH_2Cl_2 5:5) to furnish **6** (72%). IR: $\tilde{\nu}=3601$, 3495 (OH), 1597 (C=C) cm^{-1}; ^{1}H NMR: $\delta=-0.12$, -0.06, -0.05, -0.10, -0.03, 0.00 (s, 12H, $Si(CH_3)_2$), 0.61, 0.64 (s, 18H, $(CH_3)_3$), 0.80 (s, 6H, CH_3 dioxane), 1.29 (s, 2×3H, CH_3), 3.64–3.76 (AB syst., 2×2H, $J_{AB}=10.94$ Hz, CH_2 dioxane), 3.80 (s, 2×3H, OCH_3), 3.87 (m, 2H, $CH_2\gamma O$), 3.89 (s, 3H, OCH_3), 4.12 (brs, 1H, $C_\beta H$), 4.56 (s, 2H, CH_2OH), 4.96 (brs, 1H, $C_\alpha H$), 5.35 (s, 1H, CH dioxane), 6.69–7.11 (m, 7H, ArH); ^{13}C NMR: $\delta=-4.49$, -4.24 ($Si(CH_3)_2$), 18.36 (CSi), 20.91, 23.12 (CH_3 dioxane), 25.40 ($(CH_3)_3$), 30.25 (C_{IV} dioxane), 55.15 (CH_3O), 55.22 (CH_3O), 55.92 (CH_3O), 60.60 ($CH_{2\gamma}$), 72.85 ($C_\alpha H$), 77.69 (OCH_2 dioxane), 87.32 ($C_\alpha H$); 101.34 (CH dioxane), 107.85–122.98 (CH), 130.53–151.43 (C).

1-[3-Methoxy-4-*tert*-butyldimethylsilyloxy-5-(2-*tert*-butyldimethylsilyloxy-3-methoxy-5-hydroxymethylphenyl)phenyl]-2-(4-formyl-2-methoxyphenoxy)-1,3-propanediol (**1**): Oxalic acid (0.38 g, 4.23 mmol) was added to a solution of **6** (0.07 mmol) in THF/MeOH/H_2O (5:3:2, 6 mL). After 3 h, 30 min at room temperature, the reaction mixture was neutralized with aqueous $NaHCO_3$ (5%), washed with water, dried over Na_2SO_4 and concentrated to furnish pure **1** (97%). IR: $\tilde{\nu}=3598$, 3452 (OH), 1695 (CHO) cm^{-1}; ^{1}H NMR: $\delta=-0.10$, -0.06 (s, 26H, $Si(CH_3)_2$), 0.63 (s, 2×9H, $(CH_3)_3$), 3.80 (s, 3×3H, OCH_3), 3.87 (m, 2H, $CH_2\gamma O$), 4.43 (m, 1H, CH_β); 4.57 (s, 2H, CH_2OH), 4.99 (d, 1H, $J_{\alpha\beta}=5.48$ Hz, CH_α), 6.74–7.37 (m, 7H, ArH), 9.83 (s, 1H, CHO); ^{13}C NMR: $\delta=-4.49$, -4.24 ($Si(CH_3)_2$), 18.36 (CSi), 20.91, 23.12 (CH_3 dioxane), 25.40 ($(CH_3)_3$), 30.25 (C_{IV} dioxane), 55.15 (CH_3O), 55.22 (CH_3O), 55.92 (CH_3O), 60.60 ($CH_{2\gamma}$), 72.85($C_\beta H$), 77.69 (OCH_2 dioxane), 87.32 ($C_\alpha H$), 101.34 (CH dioxane), 107.85–122.98 (CH), 130.53–151.43 (C).

X-ray determination: X-ray diffraction analyses on $C_{38}H_{56}O_{10}Si_2$ ($MW=729.03$) were carried out on a STOE I.P.D.S. (Imaging Plate Diffraction System) equipped with an Oxford Cryosystems Cooler Device. The crystal-to-detector distance was 80 mm. 125 exposures were obtained with $0<\varphi<200°$ with the crystal oscillating through 1.5° in φ. Coverage of the unique set was >92% complete to at least $2\theta=48.4°$. Crystal decay was monitored by measuring 200 reflections per image. The final unit cell was obtained by least-squares refinement of 5000 reflections using $Mo_{K\alpha}$ radiation ($\lambda=0.71073$ Å). Only statistical fluctuations were observed in the intensity monitors over the course of the data collection. No absorption corrections were applied to the data.

The structure was determined from a triclinic crystal of dimensions: $0.5\times0.5\times0.17$ mm^3 (space group $P\bar{1}$, with unit cell; $a=9.8999(2)$ Å, $b=11.399(2)$ Å, $c=18.309(2)$ Å, $\alpha=92.17(2)°$, $\beta=95.84(2)°$, $\gamma=97.63(2)°$, $V=2034.1(9)$ Å^3. It has two molecules per cell, $\rho_{calcd}=1.19$ g cm^{-3}, $\mu=1.33$ cm^{-1}, $F(000)=784.51$. A total of 15958 reflections was measured (5967 independent) with $R_{average}=0.034$.

The structure was solved by direct methods (SIR92)[22] and refined by least-square procedures on F_{obs}. Hydrogen atoms were located on various Fourier maps, but were introduced into calculation in idealized positions (d(C–H) = 0.96 Å) and their atomic coordinates were recalculated after each cycle of refinement. They were given isotropic thermal parameters 20% higher than those of the carbon atom to which they were attached, except for the specific hydrogens able to form a O-H···H bonds. Least-squares refinements were carried out by minimizing the function $\Sigma w(|F_o|-|F_c|)^2$, where F_o and F_c were the observed and calculated structures. A weighting scheme was used.[23] The calculations were carried out with the aid of the CRYSTALS package programs[24] running on the PC. The drawing of the molecule was achieved with CAMERON,[25] with thermal ellipsoids at the 50% probability level. The atomic scattering factors were taken from the international tables for X-ray crystallography.[26]

Crystallographic data (excluding structure factors) for the structure reported in this paper have been deposited with the Cambridge Crystallographic Data Centre as supplementary publication no. CCDC-127301. Copies of the data can be obtained free of charge on application to CCDC, 12 Union Road, Cambridge CB21EZ, UK (fax: (+44) 1223-336-033; e-mail: deposit@ccdc.cam.ac.uk).

Acknowledgment

Financial support by MESR and CNRS is gratefully acknowledged. We are extremely grateful to Prof. K. Douglas for helpful discussions and for critical reading of the manuscript. Fruitful discussions with Prof. Dimitris S. Argyropoulos are also gratefully acknowledged.

[1] For reviews see a) K. Freudenberg, A. C. Neish, *Constitution and Biosynthesis of Lignin*, Springer, **1968**, pp. 78; b) E. Adler, *Wood Sci. Technol.* **1977**, *11*, 169–218; c) B. Monties, *Methods in Plant Biochemistry*, *Vol. 1* (Eds.: R. M. Day, J. B. Harborne), Academic Press, **1989**, pp. 113–157; d) H. Grisebach, *The Biochemistry of Plants*, *Vol. 7* (Ed.: E. E. Conn), Academic Press, **1981**, pp. 457–478; e) D. H. Northcote, *Plant Cell Wall Polymers Biogenesis and Biodegradation*, No. 399, Ch. 1 (Eds.: N. G. Lewis, M. G. Paice), ACS Symposium Series **1989**, pp. 1–15; f) D. S. Argyropoulos, S. B. Menachem, *Adv. Biochem. Eng. Biotechnol.* **1997**, *57*, 128–158.

[2] a) R. F. Helm, J. Ralph, *J. Agri. Food Chem.* **1993**, *41*, 570–576; b) J. Ralph, R. D. Hatfield, S. Quideau, R. F. Helm, J. H. Graber, H. J. G. Jung, *J. Am. Chem. Soc.* **1994**, *116*, 9448–9456; c) C. Lapierre, B. Monties, E. Guittet, J. Y. Lallemand, *Holzforschung* **1987**, *41*, 51–58; d) A. Scalbert, B. Monties, E. Guittet, J. Y. Lallemand, *Holzforschung* **1986**, *40*, 119–127; e) A. Scalbert, B. Monties, J. Y. Lallemand, E. Guittet, C. Rolando, *Phytochem.* **1985**, *24*, 1359–1362.

[3] a) G. Labat, B. Meunier, *Bull. Soc. Chim. Fr.* **1990**, *127*, 553–564 and references therein; b) J. J. Bono, P. Goulas, J. F. Boe, N. Portet, J. F. Seris, *Eur. J. Biochem.* **1990**, *192*, 189–193; c) E. Lang, F. Nerud, F. Zachazil, *FEMS Microbiol. Lett.* **1998**, *167*, 239–244; d) K. Ambert-Balay, S. M. Fuchs, M. Tien, *Biochem. Biophys. Res. Commun.* **1998**, *251*, 283–286; e) C. Crestini, D. S. Argyropoulos, *Bioorg. Med. Chem.* **1998**, *6*, 2161–2169; f) W. A. Doyle, W. Blodig, N. C. Veitch, K. Piontek, A. T. Smith, *Biochemistry* **1998**, *37*, 15097–15105.

[4] D. A. I. Goring, *Polymer Properties of Lignin and Lignin Derivatives in Lignins: Occurrence and Formation* (Eds.: K. V. Sarkanen, C. H. Ludwig), Wiley, New York, **1971**, Chp. 17, pp. 695–768.

[5] a) D. R. Gang, M. A. Costa, M. Fujita, A. T. Dinkova-Kostava, H. B. Wang, B. Burlat, W. Martin, S. Sarkanen, L. B. Davin, N. G. Lewis, *Chem. Biol.* **1999**, *6*, 143–151; b) H. R. Atalla, U. P. Agarwal, *Science* **1985**, *227*, 636–638; c) A. P. Karmanov, S. P. Kutzenov, D. V. Matveev, *Eur. Workshop Lignocellul. Pulp 5th* **1998**, 145–148; d) A. P. Karmanov, L. S. Kocheva, V. Y. Belaev, T. A. Marchenko, *Adv. Lignocellul. Ecol. Friendly Pulping Bleaching Technol.*, *Eur. Workshop Lignocellul. Pulp 5th* **1998**,149–152; e) K. Radotic, J. Budinski-Simendic, M. Jeremic, *Hem. Ind.* **1998**, *52*, 347–350 [*Chem. Abstr.* **1999**, *130*, 53831f]; f) J. P. Simon, K. E. L. Erikson, *J. Mol. Struct.* **1996**, *384*, 1–7.

[6] a) T. Higuchi, F. Nakatsubo, *Kemia Kemi* **1980**, *9*, 481–489; b) T. Ahvonen, G. Brunow, P. Kristerson, K. Lundquist, *Acta Chem. Scand.* **1983**, *B37*, 845–849; c) M. Hauteville, M. C. Duclos-Jordan, *Holzforschung* **1986**, *40*, 293–298; d) J. A. Hyatt, *Holzforschung* **1987**, *41*, 363–370; e) J. Ralph, S. Quideau, J. H. Grabber, R. D. Hatfield, *J. Chem. Soc. Perkin Trans. 1* **1994**, 3485–3498; f) I. Kilpeläinen, A. Tervila-Wilo, H. Peräkyla, J. Matikainen, G. Brunow, *Holzforschung* **1994**, *48*, 381–386; g) K. Syrjanen, G. Brunow, *J. Chem. Soc. Perkin Trans 1* **1998**, 3425–3430; h) S. Baffoni, L. Banci, A. Brard, *J. Chem. Soc. Perkin Trans 1* **1998**, 3207–3218.

[7] J. C. Pew, *J. Org. Chem.* **1963**, *28*, 1048–1054.

[8] a) P. Karhunen, P. Rummakko, J. Sipilä, G. Brunow, I. Kilpeläinen, *Tetrahedron Lett.* **1995**, *36*, 169–170; b) P. Karhunen, P. Rummakko, J.

  0947-6539/00/0607-1234 $ 17.50+.50/0 *Chem. Eur. J.* **2000**, *6*, No. 7

Sipilä, G. Brunow, I. Kilpeläinen, *Tetrahedron Lett.* **1995**, *36*, 4501–4504.
[9] P. Karhunen, J. Mikkola, G. Brunow, *Proc. 9th Int. Symp. Wood Pulp. Chem.*, Montreal, June **1997**, R1,1–R1,3.
[10] B. C. Ahvazi, G. Pageau, D. Argyropoulos, *Can. J. Chem.* **1998**, *76*, 506–512.
[11] J.-P. Roblin, H. Duran, E. Duran, V. Banuls, L. Gorrichon, *Bioorg. Med. Chem. Lett.* **1996**, *6*, 2355–2358; J.-P. Roblin, *Thesis*, University Paul-Sabatier, Toulouse (France), **1998**.
[12] F. Nakatsubo, K. Sato, T. Higuchi, *Holzforschung* **1975**, *29*, 165–168.
[13] M. Hauteville, K. Lundquist, S. von Unge, *Acta Chem. Scand.* **1986**, *B40*, 31–35.
[14] R. Stomberg, K. Lundquist, *Acta Chem. Scand.* **1986**, *A40*, 705–710.
[15] G. Brunow, P. Karhunen, K. Lundquist, S. Olson, R. Stomberg, *J. Chem. Crystallogr.* **1995**, *25*, 1–10.
[16] C. Andraud, T. Brotin, C. Garcia, F. Pellé, P. Goldner, B. Bigot, A. Collet, *J. Am. Chem. Soc.* **1994**, *116*, 2094–2102.
[17] a) B. Borecka, T. S. Cameron, A. Linden, P. Rashidi-Ranjbar, J. Sandström, *J. Am. Chem. Soc.* **1990**, *112*, 1185–1190; b) L. Eshdat, E. Shabtai, S. A. Saleh, T. Sternfeld, M. Saito, Y. Okamoto, M. Rabinovitz, *J. Org. Chem.* **1999**, *64*, 3532–3537.
[18] a) H. Maischner, *Mineral Nutrition of Higher Polants*, Academic Press, **1995**, pp. 417–426; b) A. Weiss, A. Herzog, *Biochemistry of Silicon and Related Problems* (Eds.: G. Bendz, I. Lundquist), Plenum Press, New York, **1978**, pp. 109–127.
[19] R. H. Atalla, U. P. Agarwal, *Science* **1985**, *227*, 636–638.
[20] J. Ralph, *Magn. Reson. Chem.* **1993**, *31*, 357–363.
[21] K. Elbs, H. Lerch, *J. Prakt. Chem.* **1916**, *93*, 1.
[22] A. Altomare, G. Cascarano, G. Giacovazzo, A. Guargliardi, M. C. Burla, G. Polidori, M. Camalli, SIR92 a program for automatic solution of crystal structures by direct methods, *J. Appl. Crystallogr.* **1994**, *27*, 435.
[23] E. Prince, *Mathematical Techniques in Crystallography*, Springer, Berlin, **1982**.
[24] D. J. Watkin, J. R. Carruthers, P. W. Betteridge, *CRYSTALS User Guide*, Chemical Crystallography Laboratory, University of Oxford, Oxford, **1985**.
[25] D. J. Watkin, C. K. Prout, L. J. Pearce, CAMERON, Chemical Crystallography Laboratory, University of Oxford, Oxford, **1996**.
[26] *International Tables for X-ray Crystallography*, *Vol. 4*, Kynoch Press, Birmingham, England, **1974**.

Received: April 2, 1999
Revised version: July 13, 1999 [F1716]