Stereoelectronic and Steric Effects in the Synthesis and Recognition of Diastereomeric Ethers by NMR and EPR Spectroscopy ☆

Manfred Mäurer[a], **Wolfgang Hiller**[b], **Bernd Müller**[c], and **Hartmut B. Stegmann***[a]

Institut für Organische Chemie der Universität Tübingen[a],
Auf der Morgenstelle 18, W-7400 Tübingen, F.R.G.

Institut für Anorganische Chemie der Universität Tübingen[b],
Auf der Morgenstelle 18, W-7400 Tübingen, F.R.G.

Institut für Physikalische Chemie der Universität Jena[c],
Lessingstraße 10, O-6900 Jena, F.R.G.

Received June 20, 1991

Key Words: Quinone methides / Stereoelectronic effects / Chiral recognition / EPR

(2,6-Di-*tert*-butyl-4-hydroxyphenyl)-alkyl-carbinols **I** are easily dehydrated in the presence of catalytic amounts of a mineral acid to form the corresponding phenyl-alkyl-carbocations **Ia**. These cations can be reversibly deprotonated to the quinone methides **Ib**, therefore, an equilibrium between both reactive compounds is assumed. In the absence of nucleophiles a reaction of these intermediates with the starting carbinol is observed leading to symmetrical ethers **Id**. In alcoholic solution the solvent acts as a nucleophilic compound and the formation of an unsymmetrical ether **Ie** is observed predominantly. If the nucleophile contains a chiral carbon atom diastereomers are formed in this reaction which are observed in variable concentrations depending on the reaction time. The assignment of these isomers to the *meso* and racemic compound has been achieved by NMR investigations in solution in combination with their solid-state structures determined by X-ray crystallography. These results indicate a remarkable thermodynamic stabilization of the symmetrical ethers in the racemic form whereas the *meso* compounds are favored if the products are formed under kinetic control. In both cases the diastereomer ratio is determined by steric repulsion and the generalized anomeric effect. − A bonding interaction of lone pairs of the ether oxygen with the π system of the corresponding phenoxyl ring was also observed by EPR investigations. This electron delocalization contributes remarkably to the mechanism responsible for the distinction of the diastereomeric radicals by different β-proton coupling constants.

The reaction of quinone methides with nucleophiles was well established in the last 20 years[1]. Recently, several authors have provided unequivocal evidence for the intermediacy of quinone methides in the chemistry of the antitumor compounds of anthracycline type[2]. In general, quinone methides with three different substituents are prochiral and converted into enantiomeric compounds by the addition of a nucleophilic substrate. If the nucleophile itself is chiral, diastereomers are formed.

For studies of the stereochemistry and particularly the influence of stereoelectronic effects on this reaction we have investigated the products formed by the reaction of quinone methides with chiral alcohols (see Scheme 1). The diastereomers obtained are investigated by ^{1}H-NMR spectroscopy as well as by EPR and ENDOR after transformation of the phenols into the corresponding phenoxyls by oxidation. A systematic investigation of diastereomeric radicals of this type has been performed very recently[3]. β-Proton coupling constants are very useful for the determination of conformers and their interconversion as demonstrated by anthracyclic semiquinones[4,5].

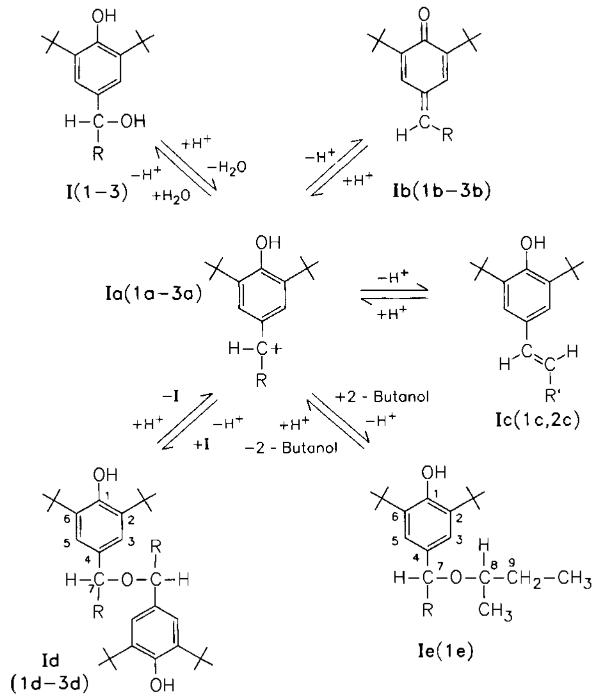
Synthesis of Diastereomeric Ethers

Quinone methides of type **Ib** are obtained by oxidation of 2,6-di-*tert*-butyl-4-alkylphenols[6]. Moreover, they are the final products of the dehydration of the corresponding carbinols **I** (Scheme 1). The carbocations **Ia** are intermediates of these reactions, and we assume an equilibrium between the quinone methides **Ib** and their protonated form **Ia** which is, furthermore, an intermediate in the reaction yielding diastereomeric ethers **Id** or **Ie**. If the alcohols bear a hydrogen atom in the α-position, then the corresponding styrene is formed in a side reaction. Addition of catalytic amounts of concentrated sulfuric acid to the phenols **I** dissolved in diethyl ether leads exclusively to the dimeric compounds **Id** whereas in solvents containing an excess of 2-butanol the asymmetric ether **Ie** is mainly formed.

Treatment of ethereal solutions of **1a** with the catalyst on a preparative scale leads to time-dependent product compositions in relation to the two diastereomers expected. The reaction was studied in NMR tubes to ensure continuous observation of the product formation. $CDCl_3$ was used as a solvent and *p*-toluene-sulfonic acid as a catalyst. Under these conditions the reaction is accelerated, compared with the preparative synthesis. The formation of the diastereomeric ethers **1d** was followed by integration of appropriate NMR signals (s. Table 2). Immediately after insertion of the sample tube into the spectrometer, small amounts (<3%) of **1b**, characterized by the signals of the *tert*-butyl protons, are observed. Within few minutes the signals of the expected products are detected.

© VCH Verlagsgesellschaft mbH, D-6940 Weinheim, 1992 0009−2940/92/0404−0857 $ 3.50+.25/0

Scheme 1



I	Ia	Ib	Id	Ie		Ic	
1	1a	1b	1d	1e	R = CH_3	1c	R' = H
2	2a	2b	2d		R = C_2H_5	2c	R' = CH_3
3	3a	3b	3d		R = t-C_4H_9		

At this time their relative concentrations are comparable. In the course of the reaction the ratio of the diastereomers reaches 3:1. After several hours additional ^{1}H-NMR peaks (δ = 6.66, J = 17.6/10.8 Hz; δ = 5.58, J = 17.6/1.1; δ = 5.05, J = 10.8/1.1) are detected. Due to the chemical shifts and the coupling constants we assign these signals to the olefinic protons of the styrene **1c**. This compound is the thermodynamically most stable product and its concentration increases with prolonged reaction time without alteration of the relative composition of the diastereomers in the NMR tube.

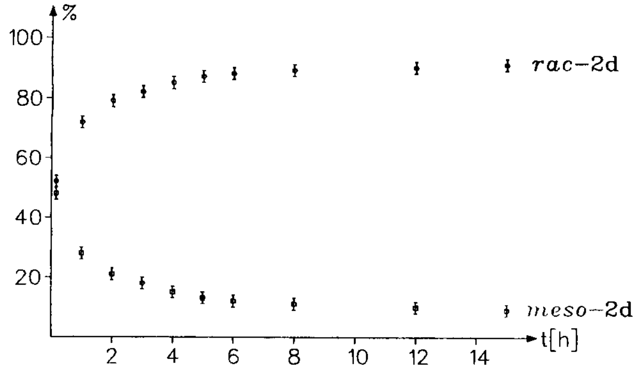


Figure 1. Dimerisation of **2** catalyzed by p-toluenesulfonic acid in $CDCl_3$. Diastereomer ratio *rac*-**2d**:*meso*-**2d** in the reaction mixture (NMR-tube experiment) versus time

The reaction of **2** under the conditions described above proceeds faster as compared with **1**. The ratio of the diastereomers is likewise 1:1 at the early beginning of the reaction. However, after several hours the product composition reaches a value of 10:1 (Table 1) as shown in Figure 1. Formation of the corresponding *trans*-styrene **2c** (δ = 6.35, J = 15.7/1.8 Hz; δ = 6.06, J = 15.7/6.6) was observed likewise.

From alcohol **3** under the same conditions only the quinone methide (< 3%) is obtained. Even prolongation of the reaction time over a period of several days does not lead to detectable amounts of the diastereomeric ethers expected. Under more rigorous reaction conditions the desired compound **3d** is finally obtained on a preparative scale. The ratio of the diastereomeric ethers is 0.43:1 (Table 1). This value is invariable with respect to alteration of the temperature and solvent applied. The product formed in excess is assigned to the *meso*-configuration in contrast to **1d** and **2d** (see below). The corresponding styrene of type **Ic** is not formed due to the lack of a hydrogen atom in the α-position.

Table 1. Diastereomer ratio in the formation of the ethers

	racemic : *meso* compound	
	kinetic contr.	thermodyn. contr.
1d	0.89	2.7
2d	1.0	10
3d	0.43	—
1e[a]	1.2	1.2

The ethers **1e** were prepared in the presence of a large excess of 2-butanol. The ratio of the diastereomers was determined to be 1.2:1. Alteration of the reaction time does not change these values.

The phenols **1d**, **2d**, **3d**, and **1e** are easily oxidized to the corresponding radicals (see below). The EPR spectra indicate unequivocally the presence of two radicals. Because of the lack of information at this time we denote the radicals and therefore the corresponding phenols, showing the smaller β-proton coupling constant, by ′ and the other diastereomers by ″. In the case of **1e** the identification given is arbitrary because the EPR and NMR spectra cannot be assigned to one another.

Configuration Analysis

The ^{1}H-NMR data observed are collected in Table 2. Comparison of these values shows significant differences for the compounds **1d**, **2d** and **3d**, due to the expected diastereomers. The chemical shifts deviate mostly in the case of the methine protons, whereas the *tert*-butyl groups, the OH groups as well as the hydrogen atoms of the aromatic rings exhibit smaller values with opposite signs. The alkyl substituents at the chiral carbon atom show only small differences. Overlooking the data of the symmetric ethers (Table 2) leads to the conclusion that obviously with increasing bulkiness of R the average shift differences $\Delta\delta$ are enhanced, probably due to more restrictions of the conformational interconversion which may avoid averaging of the individual data.

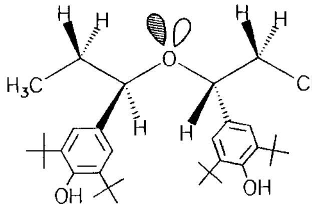
Table 2. ^{1}H-NMR data of the ethers **1d**, **2d**[a], **3d**, and **1e**[a] ($CDCl_3$, room temperature, 250 MHz)

	3,5-H	OH	7-H	2,6-t-C_4H_9	7-R	8-H	8-CH_3	9-CH_3
1d'	7.11	5.15	4.21	1.45	1.37	–	–	–
			q, 6.5 Hz		d, 6.5 Hz			
1d"	7.05	5.08	4.45	1.39	1.44	–	–	–
			q, 6.4 Hz		d, 6.4 Hz			
Δδ	0.06	0.07	−0.24	0.06	−0.07	–	–	–
2d'	7.03	5.12	3.83	1.44	0.86[b]	–	–	–
			dd, 8.4/5.0 Hz		t, 7.3 Hz			
2d"	6.90	4.99	4.17	1.34	0.91[b]	–	–	–
			t, 6.5 Hz		t, 7.3 Hz			
Δδ	0.13	0.13	−0.34	0.10	−0.05	–	–	–
3d'	7.26/6.48	5.06	3.47	1.46/1.37	0.84	–	–	–
	2 s[c]			2 s[c]				
3d"	6.98/6.57	4.92	3.99	1.31/1.24	0.88	–	–	–
	2 s[c]			2 s[c]				
Δδ	0.09[d]	0.14	−0.52	0.14[d]	−0.04	–	–	–
1e'	7.13	5.11	4.45	1.44	1.40	3.33	1.05	0.90
			q, 6.4 Hz		d, 6.5 Hz	m	d, 6.3 Hz	t, 7.4 Hz
1e"	7.11	5.11	4.46	1.44	1.41	3.20	1.11	0.83
			q, 6.4 Hz		d, 6.5 Hz	m	d, 6.0 Hz	t, 7.4 Hz
Δδ	0.02	0.00	−0.01	0.00	−0.01	0.13	−0.06	0.07

[a] The methylene protons show extended multiplets which allow no distinction of diastereomers. – [b] Signals of the CH_3 group. – [c] Broadened singlets. – [d] Average value.

According to these results merely the diastereomers **3d′** and **3d″** exhibit inequivalence of the aromatic protons and the *tert*-butyl groups in the ^{1}H-NMR spectra (Table 2), whereas an unrestricted rotation of the aromatic moiety is observed for the compounds **1d** and **2d**. At room temperature the ethers **3d** show broad absorptions for the 3,5-protons and the ring *tert*-butyl hydrogens. The latter reach coalescence slightly above room temperature and, therefore, the activation enthalpies could be estimated[7]. The values obtained are for **3d′**: $\Delta E = 67 \pm 2$ kJ mol^{-1} ($\Delta\nu = 22$ Hz; $T_c = 313$) and for **3d″**: $\Delta E = 62 \pm 2$ kJ mol^{-1} ($\Delta\nu = 49$ Hz; $T_c = 303$).

(R,R)-**2d**



The absorptions of the methine protons are systematically found at higher fields for the isomers **1d′**–**3d′** indicating an effectively higher shielding. For the interpretation of these observations we assume the preference of a conformation with these protons above or below the aromatic plane, respectively, as shown for (*R*,*R*)-**2d**. Furthermore, a staggered conformation for the alkoxy group is assumed. The ethyl groups, as example for the bulky substituents R, occupy positions opposite to each other. For this conformation a minimum of steric interactions is expected. Furthermore, for stereoelectronic reasons an energy gap is represented, too, because both electron pairs of the ether oxygen are arranged antiperiplanar with respect to the phenyl group. Therefore, the requirements for an n-σ* interaction (general anomeric effect[8]) are fulfilled.

The *meso*-configurations **1d″**–**3d″** cannot achieve a comparable energetically favored conformation. Even if a staggered arrangement is assumed, substantial non-bonding interactions occur between both chiral carbon atoms of one molecule. A configuration which allows the two lone pairs of the oxygen to donate to the σ* orbital of the sp^3-sp^2 bond is impossible. In consequence of this an energetically pronounced arrangement does not exist and, therefore, the average distances of the methine protons to the π systems are larger compared to the diastereomers as indicated by ^{1}H-NMR spectrometry.

In summary, we conclude from the NMR investigations an assignment of diastereomers **1d′**, **2d′**, and **3d′** to the (*R*,*R*) and (*S*,*S*) isomers whereas **1d″**, **2d″**, and **3d″** represent the corresponding *meso*-compounds.

The chemical shifts of the diastereomers of **1e** show significant differences merely for the protons of the *sec*-butyl group, because this group may be shielded by the magnetic anisotropic phenyl ring, but not vice versa. For this reason an assignment to different configurations is not possible.

The synthesis of **1d** on a preparative scale with subsequent separation of the diastereomers allows to determine the structures of both by X-ray crystallography. The results are given in Figure 2 as well as in Tables 7 and 8. The conformation of **1d′** (Figure 2a) in the solid state corresponds almost exactly to the low-energy form deduced from the NMR data. In the crystalline state **1d″** shows a structure without symmetry elements. As assumed, there is no pronounced low-energy conformation as indicated, for example, by the dihedral angle C2–O1–C1–C3 of 85°. The structures obtained and some other selected dihedral angles are given in Figure 2b.

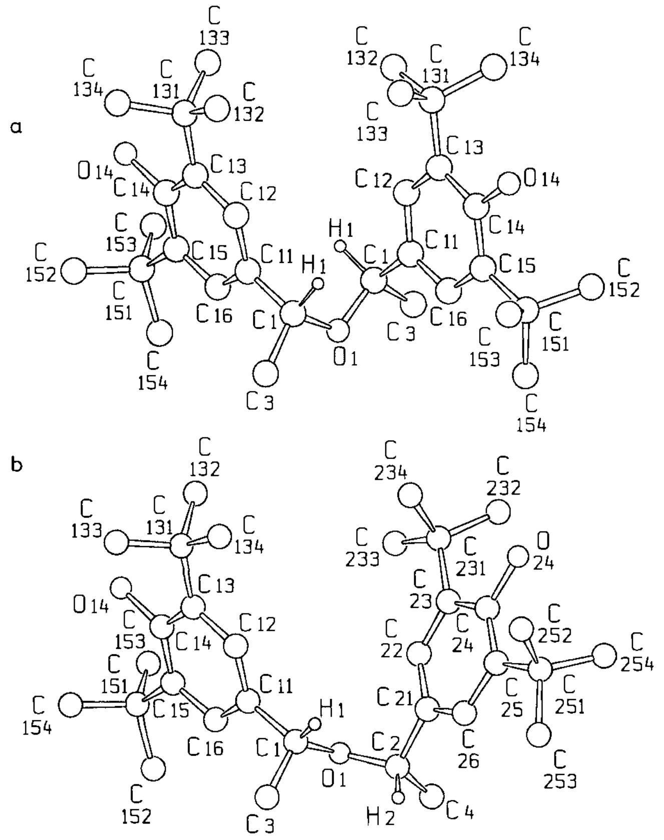


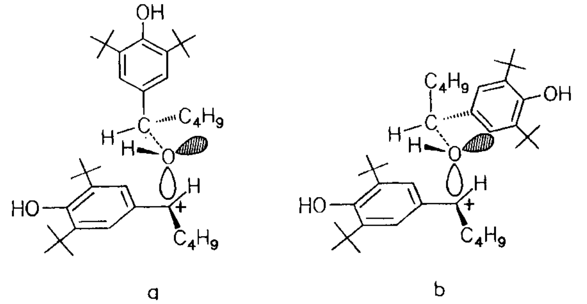
Figure 2. Crystal structure of the diastereomeric ethers **1d′** (a) and **1d″** (b); selected dihedral angles [°] (standard deviation): **1d′**: C1′–O1–C1–C3 −173.0(0.2), C1′–O1–C1–C11 64.3(0.2); **1d″**: C2–O1–C1–C3 85.2(0.6), C2–O1–C1–C11 −154.8(0.5) C1–O1–C2–C4 −161.7(0.5), C1–O1–C2–C21 74.4(0.6)

Discussion of the Diastereoselectivity

By combination of the NMR and X-ray results it is plausible that in the case of **1d** and **2d** finally the isomers of configuration (*R*,*R*) and (*S*,*S*) are formed. The difference between **1d** and **2d** with respect to the ratio of the diastereomers is due to differences in the bulkiness of the alkyl groups. In consequence of this, the non-bonding interactions increase from **1** to **2** remarkably, resulting in a decrease of the equilibrium concentration of **2d″**.

The synthesis of **3d** results in an excess of the *meso*-product under all conditions investigated. The assignment used is in complete agreement with the NMR data. But in consequence of the results obtained for the compounds **1d** and **2d** the favored formation of the racemate was expected. The contrary behavior in the case of **3d** may be explained if an exclusively kinetically controlled reaction is postulated even after prolonged reaction time and increased temperature. This requires an almost irreversible product formation, due to the *tert*-butyl group in the vicinity of the ether oxygen. For this reason, the cleavage of one C–O bond is very unlikely or at least very slow. This is consistent with the slow speed of the reaction observed by NMR spectroscopy and the observation of exclusively thermodynamically controlled product formation of the sterically hindered ethers **3d**.

For these reasons the kinetically controlled formation of the symmetric ethers may be explained by the differences of the steric and electronic properties of the alkyl and phenyl substituents of the chiral carbon atoms. For a brief discussion a simplified model will be used for the transition state representing a minimum of steric interactions and a maximum of stereoelectronic interactions. All other configurations and conformations imaginable are considered to have minor populations and will be neglected. The corresponding energetically preferred arrangements for both diastereomers of **3d** are presented in **a**, **b**.



The approach of the nucleophile with (*R*) and with (*S*) configuration to the carbocation takes place in both cases from the *Si* region[9] as shown in the transition states **a** and **b**, respectively. The products formed in this way are the (*R*,*S*) and (*S*,*S*) diastereomers. The OH group, the positively charged C atom, and the oxygen atom of the nucleophile with both lone pairs are located in the drawing plane. In this way due to the stabilization of the product by the general anomeric effect[8], interaction of the hatched lone pair with the σ* orbitals of the bond to the aromatic ring, is conceivable. For steric reasons the chiral C atom of the alcohol is located behind the drawing plane. Its smallest substituent, hydrogen, lies above the phenyl ring of the carbocation. Formula **a** represents a conformation in which both lone pairs of the ether oxygen may undergo a n-σ* interaction with the two phenyl groups whereas in **b** merely the hatched pair is able to contribute to stereoelectronic stabilization, because the *tert*-butyl group, of course in the appropriate position, is a poor electron-accepting group. With this conception the preferred formation of the thermodynamically unfavored product under kinetically controlled conditions observed in ether formation from alkylaryl-carbinols is plausible. However, an overcompensation of steric hindrance due to the location of the *tert*-butyl group opposite to the H atom in **a** by stereoelectronic effects has to be assumed. Comparable observations are already described[10].

EPR Spectroscopy

The phenols **1d** and **1e** are easily oxidized by lead dioxide to yield the corresponding phenoxyls. The half-life periods of the symmetric ether radicals are of the order of minutes whereas $\mathbf{1e}^{\bullet}$ persists several hours. Consequently, ENDOR spectra of $\mathbf{1e}^{\bullet}$ could be obtained within a temperature range from 193 to 273 K, whereas double resonance experiments with **1d**$^\bullet$ – **3d**$^\bullet$ could be performed only at certain temperatures. The diastereomers do not show any detectable difference in respect of the *g* factors but the β-proton coupling constants differ by at least 1.0 G (Table 3) and, consequently, the isomers are discernible in the EPR spectra in all examples. Figure 3 shows, for example, the superimposed spectra (doublet of triplets each) of **2d′** and **2d″**. The corresponding hyperfine lines are denoted by ′ and ″, as already defined.

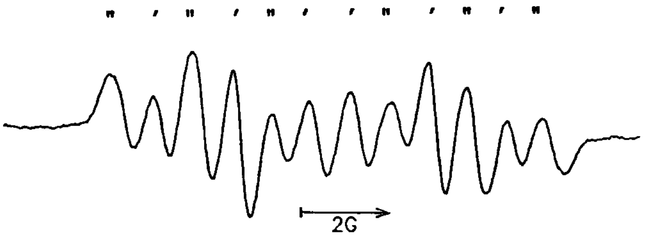


Figure 3. EPR spectrum of a diastereomeric mixture of **2d**$^\bullet$ in toluene at room temperature

Table 3. EPR[a)] and ENDOR data[b,c)] of the diastereomeric ethers

	Spectrum	Solvent	a(H_β)	a(*m*-H)	a(CH_3)	a(C_4H_9)	$g = 2.00$
1d$^{\bullet}$′	EPR	*n*-hexane	5.4		0.8		45
	ENDOR[d)]	toluene		1.69	0.81	0.08	—
1d$^{\bullet}$″	EPR	*n*-hexane	6.4		0.8		45
	ENDOR[d)]	toluene	6.66	1.69	0.81	0.08	—
2d$^{\bullet}$′	EPR	toluene	4.5	1.8	—		45
	ENDOR	toluene	4.57	1.73	—	0.08	—
2d$^{\bullet}$″	EPR	toluene	6.2	1.8	—		45
	ENDOR	toluene		1.73	—	0.08	—
3d$^{\bullet}$′	EPR	toluene	4.2	1.8	—		47
	ENDOR[e)]	toluene	4.21	1.73	—	0.08	—
3d$^{\bullet}$″	EPR	toluene	5.9	1.7	—		47
	ENDOR[e)]	toluene	6.13	1.70	—	0.07	—
1e$^{\bullet}$′	EPR	*n*-hexane	5.1		0.9		47
	ENDOR	toluene	5.30	1.72	0.82	0.09	—
1e$^{\bullet}$″	EPR	*n*-hexane	6.2		0.8		47
	ENDOR	toluene	6.68	1.72	0.82	0.09	—

[a)] EPR of separated diastereomers at room temperature. – [b)] ENDOR of diastereomeric mixtures at 253 K. – [c)] Coupling constants in Gauss. – [d)] At 213 K. – [e)] From separated diastereomers.

The radicals **1d**$^\bullet$ and **1e**$^\bullet$ exhibit an additional quartet splitting due to R = CH_3. In this case an assignment of distinct HFS components to the diastereomers has not been achieved. However, the corresponding phenols could be isolated by HPLC. The spectra of the separated two isomers together with a mixture of both are shown in Figure 4 for the compounds **1e**$^\bullet$.

The hyperfine parameters of all compounds investigated are collected in Table 3. These data show clearly the suitability of the β-proton coupling constants for the discrimination of the diastereomers whereas all other splitting constants are insensitive. The deviations observed represent the limit of error.

The radicals **3d**$^\bullet$ show merely one coupling constant for the *meta*- and *tert*-butyl protons, though according to the NMR results of **3d** the rotation of the phenyl rings is restricted leading to different chemical shifts. But if the NMR spectra indicate a slow motion for the diamagnetic precursors such a behavior is expected for the radicals too, according to the faster time scale of the EPR method. Therefore, from this result we have to conclude that in this case the spin density distribution is symmetric despite the asymmetric environment.

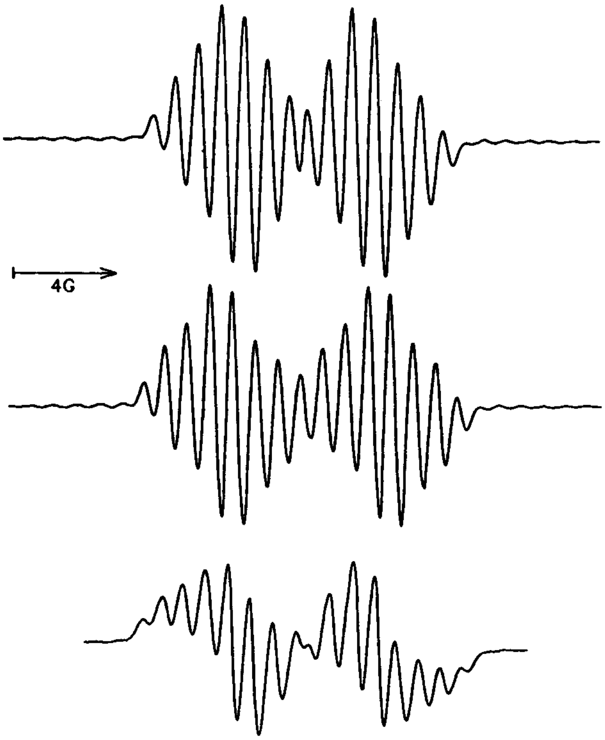


Figure 4. EPR spectra of **1e**$^\bullet$′ (a), **1e**$^\bullet$″ (b) and a mixture of both diastereomers (c) in *n*-hexane at room temperature

Table 4. Temperature dependence of the β coupling constants [G] of the diastereomeric ethers **1d**$^\bullet$ [a)], **3d**$^\bullet$ [a)], and **1e**$^\bullet$ [b)]

	1d$^\bullet$			**3d**$^\bullet$			**1e**$^\bullet$		
T [K]	a(H_β)′	a(H_β)″	Δa	a(H_β)′	a(H_β)″	Δa	a(H_β)′	a(H_β)″	Δa
183	5.92	6.52	0.60						
193	5.84	6.51	0.67	4.40	6.36	1.96	4.99	6.83	1.84
213	5.75	6.49	0.74	4.34	6.29	1.95	5.11	6.74	1.63
233	5.66	6.46	0.80	4.29	6.23	1.94	5.20	6.69	1.49
253	5.57	6.42	0.85	4.23	6.13	1.90	5.30	6.68	1.38
273	5.48	6.40	0.92	4.19	5.99	1.80	5.42	6.64	1.22
293	5.43	6.36	0.93	4.15	5.86	1.71			
313	5.39	6.35	0.96	4.12	5.74	1.62			
333	5.34	6.34	1.00	4.09	5.60	1.51			
353	5.32	6.32	1.00	4.04	5.49	1.45			

[a)] From EPR spectra of separated diastereomers in *n*-hexane, accuracy of measurement ca. 0.04 G. – [b)] From ENDOR spectra of a diastereomeric mixture in toluene, accuracy of measurement ca. 0.02 G.

The results of the temperature dependence of the β splittings are listed in Table 4. Surprising at the first glance is the diminution of the absolute values with increasing temperature for **1d**$^\bullet$ and **3d**$^\bullet$ (discussion see below). In the case of **1d**$^\bullet$ the splitting difference of the diastereomers increases by rising the temperature whereas **3d**$^\bullet$ and **1e**$^\bullet$ show the inverse behavior. These results are really remarkable. Usually, with increasing temperature the conformational interconversion leads to an averaging of the magnetic properties as indicated for the radical **3d**$^\bullet$, but not to the exceptional behavior like **1d**$^\bullet$, as mentioned in the NMR literature[11].

For these reasons a brief discussion based on already published results and the data in Tables 3 and 4 is given. All phenoxyl radicals coming into question bear in the *para*-position a carbon atom connected at least with one hydrogen atom. From the resulting β-proton coupling constant, using the Heller-McConnell equation $a_{H_\beta} = B\langle\cos^2\vartheta\rangle \cdot \varrho_{C_\alpha}$ and assuming a rigid molecule, we may calculate the torsion angle $\vartheta_{calcd.}$ as a rough estimation. The product $B \cdot \varrho_{C_\alpha}$ is known from 2,6-di-*tert*-butyl-4-methylphenoxyl (**4$^\bullet$**) and amounts to 22.2 G. The coupling constants of this radical and the angle $\vartheta_{calcd.}$ together with the corresponding values of several other phenoxyls are listed in Table 5.

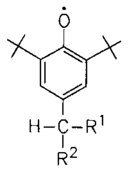


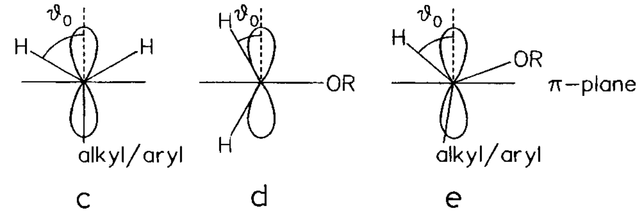
Table 5. β-Coupling constants (room temperature, [G]) and hyperconjugation angles of aroxyls substituted in the *para*-position

	R¹	R²	Solvent	a(H$_\beta$)	ϑ_{calcd}	Ref.
4$^\bullet$	H	H	toluene	11.1	45°	[13]
5$^\bullet$	H	Ph	benzene	8.7	51°	[13]
6$^\bullet$	H	Me	toluene	8.8	51°	[14]
7$^\bullet$	H	Et	toluene	8.1	53°	[14]
8$^\bullet$	H	*i*-Pr	toluene	7.2	55°	[14]
9$^\bullet$	H	*t*-Bu	toluene	5.7	60°	[14]
10$^\bullet$	H	OH	toluene	12.5	41°	[15]
11$^\bullet$	H	OMe	toluene	12.3	42°	[14]
12$^\bullet$	H	O-*t*-Bu	toluene	12.8	41°	[14]
13$^\bullet$	Ph	OH	toluene	8.4	52°	[16]
14$^\bullet$	Me	OH	toluene	7.6	54°	[16]
15$^\bullet$	*t*-Bu	OH	toluene	6.5	57°	[15]
16$^\bullet$	Me	OMe	toluene	5.8	59°	[15]
1e$^\bullet$	Me	O-*s*-Bu	*n*-hexane	5.1/6.2	61/58°	[a]
1d$^\bullet$	Me	OCH(Me)PhOH[b]	*n*-hexane	5.4/6.4	60/58°	[a]
2d$^\bullet$	Et	OCH(Et)PhOH[b]	toluene	4.5/6.2	63/58°	[a]
3d$^\bullet$	*t*-Bu	OCH(*t*-Bu)PhOH[b]	toluene	4.2/5.9	64/59°	[a]
17$^\bullet$	Ph	OMBF[c]	CCl_4	6.3/9.8	58/48°	[3]

[a] This work. – [b] PhOH = 3,5-Di-*tert*-butyl-4-hydroxyphenyl. – [c] MBF = [3a*S*-(2α,3aα,4α,7α,7aα)]-2,3,3a,4,5,6,7,7a-octahydro-7,8,8-trimethyl-4,7-methanobenzofuran-2-yl.

The alkyl- or aryl-substituted compounds **5$^\bullet$**–**9$^\bullet$** show angles between 51 and 60° and have positive temperature gradients for the β splitting as expected[12]. The results are easily interpreted on the basis of an approximation of the conformation to the rotamer **c** in Scheme 2 with decreasing temperature. In this way the steric interaction of R² with the aromatic moiety is minimized. Raising the temperature results in torsional vibrations around this low-energy conformation. An almost analogous behavior is expected for the radicals **10$^\bullet$**, **11$^\bullet$**, and **12$^\bullet$**, if only steric interactions are considered. However, these phenoxyls have considerably smaller angles and, consistent with these, negative temperature gradients[12] of the β-proton splitting. For these reasons at low temperature we assume a preferred conformation like **d** in Scheme 2 in which the oxygen atom is in proximity of the aromatic plane, represented either by a minimum of the potential energy in the plane or a double minimum above or below the aromatic ring. Such energy minima would be due to an interaction of the oxygen lone pairs with the π* orbitals of the aromatic system. In consequence of such a conformation the alkyl substituent of the oxygen is located opposite to the benzyl moiety. Because the barrier of rotation is low in these cases almost free rotation is observed at 293 K.

Scheme 2



This interpretation is confirmed by the EPR data of the secondary alcohols **13$^\bullet$**–**15$^\bullet$**. In these cases the low energy conformer is represented by the structure **e** in Scheme 2 which is obviously a compromise between the proximity of the oxygen to the aromatic plane and the steric repulsion between the phenyl ring and the aryl or alkyl group, respectively. According to the coupling constants observed the steric interactions dominate over the stereoelectronic gain of energy. Therefore, in the radicals **13$^\bullet$**–**15$^\bullet$** the minimum energy conformation is due to both steric and stereoelectronic effects. Molecules of this type are almost rigid and show β-proton coupling constants with minor temperature dependence.

If the substituents at the oxygen atom become more bulky – **16$^\bullet$**, **1e$^\bullet$**, **1d$^\bullet$**, **2d$^\bullet$**, and **3d$^\bullet$** – than their steric interaction with the phenyl ring increases particularly with rising temperature. In consequence of this the β-proton will be forced toward the aromatic plane leading to negative temperature gradients as shown for the radicals **1d$^\bullet$** and **3d$^\bullet$**. With this concept the differences of the diastereomeric pairs with respect to their β-proton coupling constants may be understood, too. The isomers with the extended steric interaction between the oxygen substituent and the phenoxyl ring, i.e. the (*R,R*) and the (*S,S*) diastereomers, have the larger torsion angle and therefore the smaller β-proton splitting constants.

This interpretation is confirmed by the results obtained for the aliphatic ethers **1e$^{\bullet\prime}$** and **1e$^{\bullet\prime\prime}$** (see Table 3) with the EPR coupling constants of 5.1 and 6.2 G. In this case the diastereomers differ significantly in the hyperconjugation parameter whereas in the ¹H-NMR parameters (Table 2) these compounds are almost indistinguishable. More striking differences are observed with diastereomeric acetals[3] (see radical **17$^\bullet$** in Table 5). These results seem to be reasonable because the isomers are different with respect to the arrangement of the alkyl groups relative to the proton at C-7. Therefore, the shielding is very similar but not the hyperconjugation angle corresponding to different steric interactions. Therefore the results obtained for the compounds

1d–**3d** and **1e** as well as the corresponding radicals clearly demonstrate the advantage of a combination of NMR and EPR results thus enabling diastereomers to be distinguished both by different NMR shieldings and EPR torsion angles.

This work was supported by the *Deutsche Forschungsgemeinschaft* and by the *Fonds der Chemischen Industrie.*

Experimental

Melting points: Büchi apparatus (Dr. Tottoli). – Elemental analyses: Microanalytical Laboratory, Chemisches Institut der Universität Tübingen, *W. Bock.* – 250-MHz ^{1}H and 62.9-MHz ^{13}C NMR: Bruker AC 250. – IR (KBr): Perkin-Elmer IR 281 B. – MS (70 eV): Varian MAT-711 A. – EPR: Varian E 12, Bruker ESP 300. – ENDOR: Varian E-Line-Century EPR spectrometer equipped with a Bruker ER 810 ENDOR unit (500 W amplifier) and a Bruker ER 140 data system. – HPLC: Waters 501 HPLC pump; Rheodyne injection system; Grom HPLC column Nucleosil Si 100, 5 µm, 250 × 4.6 mm; Biotronic UV detector BT 3030; Shimadzu C-R5A-Cromatopac data system.

The racemates of the alcohols 1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)ethanol (**1**), 1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-1-propanol (**2**), and 1-(3,5-di-*tert*-butyl-4-hydroxyphenyl)-2,2-dimethyl-1-propanol (**3**) were synthesized according to well-known methods by Friedel-Crafts acylation from 2,6-di-*tert*-butylphenol[17] and subsequent reduction with $NaBH_4$[18]. 2,6-Di-*tert*-butyl-1,4-benzoquinone ethide (**1b**) was prepared by oxidation of 2,6-di-*tert*-butyl-4-ethylphenol[6].

EPR Measurements: A sample of the phenol (10–100 µg) was placed in the EPR tube and dissolved in an inert non-polar solvent. After flushing with nitrogen for 10 min it was oxidized to the corresponding phenoxyl with a very small amount of lead dioxide.

Fractions of the diamagnetic precursors purified by HPLC were collected in the EPR tube directly after leaving the UV detector and bubbled with nitrogen for 30 min in order to remove oxygen and the ether of the mobile phase (*n*-hexane/0.8–2% diethyl ether). If the linewidth was too large due to high radical concentration the sample was diluted and again flushed with nitrogen for 10 min.

General Method for the Preparation of **1d**, **2d**, *and* **3d**: 4 mmol of the alcohols **1**, **2**, and **3** was dissolved in 20 ml of absol. diethyl ether and 1 drop of conc. sulfuric acid was added. In the case of **1** and **2** the mixture was stirred for 6 h and 30 min., respectively, for **3** it was refluxed for 24 h. The diastereomeric ratio was affected by the reaction time and the amount of catalyst used. Some sodium sulfate and sodium hydrogen carbonate were added in order to stop the reaction. After 1 h the salts were filtered off, and the solvent was removed. The crude reaction product consisted of the ethers desired and some starting material. The diastereomeric ethers were separated from remaining alcohol by filtration [silica gel, deactivated with triethylamine, petroleum ether/ether (20:1)]. The products obtained from the liquid phase were purified by recrystallisation from *n*-hexane. In the course of purification the racemates were accumulated in all cases.

Ether	Yield	M.p. [°C]	Formula (Mol. weight)	Elemental analysis
1d	50%	181[a)] 155[b)]	$C_{32}H_{50}O_3$ (482.7)	Calcd. C 79.62 H 10.44 Found C 79.18 H 10.67
2d	48%	166[a)]	$C_{34}H_{54}O_3$ (510.8)	Calcd. C 79.95 H 10.66 Found C 79.67 H 10.59
3d	43%	192–197[c)]	$C_{38}H_{62}O_3$ (566.9)	Calcd. C 80.51 H 11.02 Found C 80.54 H 11.11

[a)] Racemic compound. – [b)] *meso*-Compound. – [c)] Diastereomeric mixture.

Bis[1-(3,5-di-tert-butyl-4-hydroxyphenyl)ethyl] Ether (**1d**): IR: $\tilde{\nu}$ = 3640 cm^{-1} (OH), 3080 (aromat. CH), 2960/2920/2870 (aliphat. CH), 1080 (CO). – MS: *m/z* (%) = 482 (2) [M^+], 249 (9), 235 (25), 234 (38), 233 (61), 217 (28), 177 (100), 57 (33). – ^{1}H NMR ($CDCl_3$): diastereomer **1d′**: δ = 7.11 (s, 2H, aromat. H), 5.15 (s, 1H, OH), 4.21 (q, *J* = 6.5 Hz, 1H, HCO), 1.45 (s, 18H, C_4H_9), 1.37 (d, *J* = 6.5 Hz, 3H, CH_3); diastereomer **1d″**: δ = 7.05 (s, 2H, aromat. H), 5.08 (s, 1H, OH), 4.45 (q, *J* = 6.4 Hz, 1H, HCO), 1.39 (s, 18H, C_4H_9), 1.44 (d, *J* = 6.4 Hz, 3H, CH_3). – ^{13}C NMR ($CDCl_3$, noise-decoupled): diastereomer **1d′**: δ = 152.8 [C-4 (C_6H_2)], 135.7 [C-3, -5 (C_6H_2)], 135.0 [C-1 (C_6H_2)], 122.8 [C-2,-6 (C_6H_2)], 74.6 (CO), 34.4 [*C*(CH_3)$_3$], 30.5 [C(*C*H_3)$_3$], 25.0 (CH_3); diastereomer **1d″**: δ = 152.7 [C-4 (C_6H_2)], 135.4 [C-3,-5 (C_6H_2)], 135.0 [C-1 (C_6H_2)], 123.0 [C-2,-6 (C_6H_2)], 75.1 (CO), 34.3 [*C*(CH_3)$_3$], 30.4 [C(*C*H_3)$_3$], 23.1 (CH_3). – EPR (*n*-hexane): diastereomer **1d**$^{\bullet\prime}$: *g* = 2.0045, *a* = 5.4 G (H_β), 0.8 (CH_3); diastereomer **1d**$^{\bullet\prime\prime}$: *g* = 2.0045, *a* = 6.4 G (H_β), 0.8 (CH_3). – ENDOR (toluene, 213 K): diastereomer **1d**$^{\bullet\prime}$: *a* = 1.69 G (*m*-H), 0.81 (CH_3), 0.08 (C_4H_9); diastereomer **1d**$^{\bullet\prime\prime}$: *a* = 6.66 G (H_β), 1.69 (*m*-H), 0.81 (CH_3), 0.08 (C_4H_9).

Table 6. Crystallographic data of isomers **1d′** and **1d″**

		1d'	**1d"**
Formula		$C_{32}H_{50}O_3$	$C_{32}H_{50}O_3$
Molecular mass		482.75	482.75
F(000)		1064	2128
Crystal size		0.1 × 0.2 × 0.2 mm	0.1 × 0.25 × 0.2 mm
Crystal system		monoclinic	orthorhombic
Space group		C2/c (No. 15)	Pbca (No. 61)
Lattice parameters	a	2803.90(6) pm	1046.7(2) pm
	b	992.35(3) pm	1079.3(2) pm
	c	1162.81(4) pm	5385.6(8) pm
	α	90°	90°
	β	107.115(1)°	90°
	γ	90°	90°
Volume	V	$3092.2 \cdot 10^6$ pm^3	$6084.6 \cdot 10^6$ pm^3
Formula units	Z	4	8
Density	ρ_x	1.037 g · cm^{-3}	1.054 g · cm^{-3}
Temperature		20°C	20°C
Diffractometer		CAD4	CAD4
Radiation	λ	Cu-K_α	Cu-K_α
Monochromator		graphite	graphite
Scan		ω/θ	ω/θ
Θ-range	Θ_{max}	65°	69°
h k l		0 → 32	0 → 12
		0 → 11	0 → 13
		-13 → 13	0 → 65
Absorption coeffizient	μ	4.662 cm^{-1}	4.739 cm^{-1}
Absorption correction		empirical	empirical
max/min		1.181/0.779	1.261/0.479
Reflections measured		2763	6380
Reflections observed $I \geq 3\sigma(I)$		2154	2355
No. of parameters		160	317
R-values	R	0.063	0.076
	R_w	0.063	0.074
Structur solution		direct methods	direct methods
Refinement		full matrix (F)	full matrix (F)
H-Atoms		from difference fourier synthesis	
Programs used		see ref. [20]	see ref. [20]

Bis[1-(3,5-di-tert-butyl-4-hydroxyphenyl)propyl] Ether (**2d**): IR: $\tilde{\nu}$ = 3640 cm^{-1} (OH), 3080 (aromat. CH), 2960/2920/2870 (aliphat. CH), 1090 (CO). – MS: *m/z* (%) = 510 (1) [M$^+$], 248 (19), 247 (100), 190 (11), 57 (8). – ^{1}H NMR (CDCl$_3$): Diastereomer **2d′**: δ = 7.03 (s, 2H, aromat. H), 5.12 (s, 1H, OH), 3.83 (dd, *J* = 8.4/5.0 Hz, 1H, HCO), 1.44 (s, 18H, C$_4$H$_9$), 0.86 (t, *J* = 7.3 Hz, 3H, CH$_3$); diastereomer **2d″**: δ = 6.90 (s, 2H, aromat. H), 4.99 (s, 1H, OH), 4.17 (t, *J* = 6.5 Hz, 1H, HCO), 1.34 (s, 18H, C$_4$H$_9$), 0.91 (t, *J* = 7.3 Hz, 3H, CH$_3$). – EPR (*n*-hexane): diastereomer **2d**$^{\bullet\prime}$: *g* = 2.0045, *a* = 4.1 G (H$_\beta$), 1.8 (*m*-H); diastereomer **2d**$^{\bullet\prime\prime}$: *g* = 2.0045, *a* = 5.7 G (H$_\beta$), 1.8 (*m*-H). – ENDOR (toluene, 253 K): diastereomer **2d**$^{\bullet\prime}$: *a* = 4.57 G (H$_\beta$), 1.73 (*m*-H), 0.08 (C$_4$H$_9$); diastereomer **2d**$^{\bullet\prime\prime}$: *a* = 1.73 G (*m*-H), 0.08 (C$_4$H$_9$).

Bis[1-(3,5-di-tert-butyl-4-hydroxyphenyl)-2,2-dimethylpropyl] Ether (**3d**): IR: $\tilde{\nu}$ = 3640 cm^{-1} (OH), 3080 (aromat. CH), 2950/2910/2870 (aliphat. CH), 1080 (CO). – MS (FD, 50°C): *m/z* (%) = 567 (40), 566 (100) [M$^+$], 509 (74). – ^{1}H NMR (CDCl$_3$): diastereomer **3d′**: δ = 7.26/6.48 [2 s (broadened), 2H, aromat. H], 5.06 (s, 1H, OH), 3.47 (s, 1H, HCO), 1.46/1.37 [2 s (broadened), 18H, C$_4$H$_9$-Ar], 0.84 (s, 9H, C$_4$H$_9$CO); diastereomer **3d″**: δ = 6.98/6.57 [2 s (broadened), 2H, aromat. H], 4.92 (s, 1H, OH), 3.99 (s, 1H, HCO), 1.31/1.24 [2 s (broadened), 18H, C$_4$H$_9$–Ar], 0.88 (s, 9H, C$_4$H$_9$CO). – EPR (toluene): diastereomer **3d**$^{\bullet\prime}$: *g* = 2.0047, *a* = 4.2 G (H$_\beta$), 1.8 (*m*-H); diastereomer **3d**$^{\bullet\prime\prime}$: *g* = 2.0047, *a* = 5.9 G (H$_\beta$), 1.7 (*m*-H). – ENDOR (toluene, 253 K): diastereomer **3d**$^{\bullet\prime}$: *a* = 4.21 G (H$_\beta$), 1.73 (*m*-H), 0.08 (C$_4$H$_9$–Ar); diastereomer **3d**$^{\bullet\prime\prime}$: *a* = 6.13 G (H$_\beta$), 1.70 (*m*-H), 0.07 (C$_4$H$_9$–Ar).

Crystal Structure Determination of **1d′** *and* **1d″**: In order to obtain single crystals of both diastereomers of **1d** the general procedure given above was modified. In the case of **1d′** the reaction mixture was stirred for 60 h, in the case of **1d″** only for 2 h. Pure crystals of the racemic compound **1d′** could be easily obtained by twofold recrystallizing (*n*-hexane). **1d″** could be accumulated up to 90% by column chromatography [silica gel, deactivated with triethylamine, petroleum ether/ether (20:1)] and further purified by several recrystallizations from *n*-hexane. The crystallographic data are given in Table 6. Table 7 and 8 contain atomic coordinates and thermal parameters[19].

Table 7. Atomic coordinates and thermal parameters B_{eq} [Å^2] of **1d′** with standard deviation in units of the last significant figure in parentheses. $B_{eq} = 4/3\,[B_{11}a^2 + B_{22}b^2 + B_{33}c^2 + B_{12}ab \cdot \cos\gamma + B_{13}ac \cdot \cos\beta + B_{23}bc \cdot \cos\alpha]$

	x	y	z	B_{eq}
O1	0.500	0.1582(3)	0.750	3.15(6)
O14	0.31842(8)	−0.2271(3)	0.7300(2)	6.21(6)
C1	0.47552(9)	0.0786(3)	0.6463(2)	3.18(6)
C3	0.4577(1)	0.1778(3)	0.5427(3)	4.72(8)
C11	0.43311(9)	−0.0038(3)	0.6674(2)	2.83(5)
C12	0.4316(1)	−0.1421(3)	0.6514(2)	3.06(6)
C13	0.3935(1)	−0.2206(3)	0.6706(2)	3.33(6)
C14	0.3566(1)	−0.1531(3)	0.7073(2)	3.82(6)
C15	0.35612(9)	−0.0131(3)	0.7224(2)	3.37(6)
C16	0.39558(9)	0.0591(3)	0.7027(2)	3.20(6)
C131	0.3940(1)	−0.3750(3)	0.6553(3)	4.51(8)
C132	0.4353(2)	−0.4197(3)	0.6040(4)	6.4(1)
C133	0.4033(2)	−0.4434(4)	0.7786(3)	6.9(1)
C134	0.3442(2)	−0.4265(4)	0.5683(3)	6.5(1)
C151	0.3141(1)	0.0602(4)	0.7569(3)	4.61(7)
C152	0.2634(1)	0.0351(5)	0.6614(3)	6.0(1)
C153	0.3110(1)	0.0147(6)	0.8810(3)	7.6(1)
C154	0.3221(1)	0.2132(4)	0.7634(4)	7.3(1)

sec-Butyl 1-(3,5-Di-tert-butyl-4-hydroxyphenyl)ethyl Ether (**1e**): A solution of 0.5 g (2.2 mmol) of **1b** in 20 ml of absol. diethyl ether was mixed with 1.6 g (22 mmol) of 2-butanol and about 0.1 mg of *p*-toluenesulfonic acid. After refluxing for 1 h some sodium sulfate and sodium hydrogen carbonate were added, and the mixture was filtered 1 h later. The solvent as well as the main fraction of 2-butanol were removed by distillation. The diastereomeric ethers were separated from the remaining alcohol by filtration [silica gel, deactivated with triethylamine, petroleum ether/ether (20:1)]. Removal of the solvent yielded 0.60 g (2 mmol, 91%) of a pale yellow oil containing the products desired in more than 95% purity (measured by ^{1}H NMR). – ^{1}H NMR (CDCl$_3$), characteristic shifts: diastereomeric mixture **1e′**/**1e″**: δ = 7.13/7.11 (s, 2H, aromat. H), 5.11 (s, 1H, OH), 4.45/4.46 (q, *J* = 6.4 Hz, 1H, HC-Ar), 3.33/3.20 (m, 1H, *H*CCH$_2$), 1.44 (s, 18H, C$_4$H$_9$), 1.40/1.41 (d, *J* = 6.5 Hz, 3H, CH$_3$C–Ar), 1.05/1.11 (d, *J* = 6.3/6.0 Hz, 3H, C*H*$_3$CCH$_2$), 0.90/0.83 (t, *J* = 7.4 Hz, 3H, C*H*$_3$CH$_2$). – EPR (*n*-hexane): diastereomer **1e**$^{\bullet\prime}$: *g* = 2.0047, *a* = 5.1 G (H$_\beta$), 0.9 (CH$_3$); diastereomer **1e**$^{\bullet\prime\prime}$: *g* = 2.0047, *a* = 6.2 G (H$_\beta$), 0.8 (CH$_3$). – ENDOR (toluene, 253 K): diastereomeric mixture **1e**$^{\bullet\prime}$/**1e**$^{\bullet\prime\prime}$: *a* = 5.30/6.68 G (H$_\beta$), 1.72 (*m*-H), 0.82 (CH$_3$), 0.09 (C$_4$H$_9$).

Table 8. Atomic coordinates and thermal parameters B_{eq} [Å^2] of **1d″** with standard deviation in units of the last significant figure in parentheses. B_{eq} see Table 7

	x	y	z	B_{eq}
O1	0.3209(4)	0.2723(4)	0.12258(7)	4.7(1)
O14	−0.0692(4)	0.2959(4)	0.03519(7)	4.8(1)
O24	−0.0519(4)	0.3858(4)	0.21309(8)	5.0(1)
C1	0.2929(6)	0.3908(6)	0.1111(1)	4.7(2)
C2	0.3614(6)	0.2838(6)	0.14761(9)	4.4(1)
C3	0.4068(7)	0.4529(9)	0.1006(1)	7.5(2)
C4	0.4258(7)	0.1667(8)	0.1541(1)	6.2(2)
C11	0.1967(6)	0.3636(5)	0.09016(9)	3.7(1)
C12	0.0814(6)	0.4219(5)	0.0906(1)	3.7(1)
C13	−0.0104(6)	0.4027(5)	0.0724(1)	3.4(1)
C14	0.0216(6)	0.3196(5)	0.0530(1)	3.4(1)
C15	0.1394(5)	0.2597(5)	0.05187(9)	3.2(1)
C16	0.2261(6)	0.2830(6)	0.0707(1)	3.9(1)
C21	0.2471(6)	0.3146(6)	0.16438(9)	3.7(1)
C22	0.1277(6)	0.2678(5)	0.15982(9)	3.9(1)
C23	0.0241(6)	0.2899(5)	0.1756(1)	3.5(1)
C24	0.0490(6)	0.3642(5)	0.1967(1)	3.5(1)
C25	0.1679(6)	0.4159(5)	0.20185(9)	3.4(1)
C26	0.2657(6)	0.3893(5)	0.18472(9)	3.6(1)
C131	−0.1378(6)	0.4722(6)	0.0730(1)	4.2(1)
C132	−0.2487(8)	0.3798(8)	0.0754(2)	8.0(2)
C133	−0.1549(7)	0.5497(7)	0.0497(1)	5.8(2)
C134	−0.1459(8)	0.5593(7)	0.0956(1)	6.5(2)
C151	0.1737(6)	0.1726(6)	0.0300(1)	4.0(1)
C152	0.3107(7)	0.1241(7)	0.0321(1)	6.4(2)
C153	0.0859(8)	0.0588(7)	0.0298(1)	6.0(2)
C154	0.1644(7)	0.2414(7)	0.0052(1)	5.5(2)
C231	−0.1112(6)	0.2376(6)	0.1705(1)	4.3(1)
C232	−0.1585(7)	0.1548(7)	0.1920(1)	6.4(2)
C233	−0.1127(8)	0.1616(8)	0.1469(1)	7.4(2)
C234	−0.2033(7)	0.3434(8)	0.1664(2)	7.5(2)
C251	0.1928(6)	0.4938(5)	0.2253(1)	3.8(1)
C252	0.1095(7)	0.6102(6)	0.2257(1)	5.1(2)
C253	0.3317(7)	0.5431(7)	0.2254(1)	6.6(2)
C254	0.1731(7)	0.4158(6)	0.2484(1)	5.3(2)

CAS-Registry-Nummern

1: 104438-67-7 / **1a**: 138694-85-6 / **1b**: 6738-27-8 / **1d′** (*R**,*R**): 138694-86-7 / **1d″** (*R**,*S**): 138694-87-8 / **1d**$^{\cdot\prime}$: 138694-89-0 / **1d**$^{\cdot\prime\prime}$: 138694-88-9 / **1e′** (*R**,*R**): 138694-90-3 / **1e″** (*R**,*S**): 138694-91-4 / **1e**$^{\cdot\prime}$: 138694-92-5 / **1e**$^{\cdot\prime\prime}$: 138694-93-6 / **2**: 138694-94-7 / **2a**: 138694-95-8 / **2b**: 7019-90-1 / **2d′** (*R**,*R**): 138694-96-9 / **2d″** (*R**,*S**): 138694-97-0 / **2d**$^{\cdot\prime}$: 138694-98-1 / **2d**$^{\cdot\prime\prime}$: 138694-99-2 / **3**: 138721-99-0 / **3a**: 138695-00-8 / **3b**: 10316-31-1 / **3d′** (*R**,*R**): 138695-01-9 / **3d″** (*R**,*S**): 138721-75-2 / **3d**$^{\cdot\prime}$: 138694-02-0 / **3d**$^{\cdot\prime\prime}$: 138695-03-1

☆ Herrn Professor *Ernst Bayer* zum 65. Geburtstag gewidmet.

[1] P. Grünanger, *Methoden Org. Chem. (Houben-Weyl) 4th Ed.*, **1979**, vol. 7/3b, p. 397.

[2] G. Gaudiano, T. H. Koch, *J. Am. Chem. Soc.* **1990**, *112*, 9423–9425, and references cited therein.

[3] M. Mäurer, H. B. Stegmann, *Chem. Ber.* **1990**, *123*, 1679–1685.

[4] T. Jülich, K. Scheffler, P. Schuler, H. B. Stegmann, *Magn. Reson. Chem.* **1988**, *26*, 701–706.

[5] T. Jülich, H. B. Stegmann, K. Krohn, A. Eickhoff, *Magn. Reson. Chem.* **1991**, *29*, 178–183.

[6] C. D. Cook, B. E. Norcross, *J. Am. Chem. Soc.* **1959**, *81*, 1176–1180.

[7] H. Günther, *NMR-Spektroskopie*, Georg Thieme-Verlag, Stuttgart, **1983**, p. 229.

[8] A. J. Kirby, *The Anomeric Effect and Related Stereoelectronic Effects at Oxygen*, Springer Verlag, Berlin, **1983**.

[9] F. Vögtle, J. Franke, W. Bunzel, *Kontakte (Darmstadt)* **1985** (1), 28–39.

[10] A. S. Cieplak, *J. Am. Chem. Soc.* **1981**, *103*, 4540–4552.

[11] A. L. Cholli, A. Galdes, D. J. Pennino, Z. Kosarych, *J. Magn. Reson.* **1989**, *84*, 379–382.

[12] K. Scheffler, private communication.

[13] W. Uber, H. B. Stegmann in *Landolt-Börnstein, Zahlenwerte und Funktionen aus Naturwissenschaft und Technik* (Ed.: H. Fischer), vol. II/9c2, Springer, Berlin, **1979**, p. 64.

[14] D. Klotz, G. Deuschle, H. B. Stegmann in ref.[13], vol. II/17e, Springer, Berlin, **1989**, p. 75.

[15] M. Mäurer, Dissertation, Universität Tübingen, **1991**.

[16] H. Wendel, Wissenschaftliche Zulassungsarbeit, *Universität Tübingen,* **1986**.

[17] N. V. Portnykh, A. A. Volod'kin, V. V. Ershov, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1966**, 2243–2244.

[18] A. A. Volod'kin, N.V. Portnykh, V. V. Ershov, *Izv. Akad. Nauk SSSR, Ser. Khim.* **1968**, 220–222.

[19] Further details of the crystal structure investigations are available on request from the Fachinformationszentrum Karlsruhe, Gesellschaft für wissenschaftlich-technische Information mbH, D-7514 Eggenstein-Leopoldshafen 2, on quoting the depository numbers CSD-55049 (**1d′**) and CSD-55349 (**1d″**), respectively, the names of the authors and the journal citation.

[20] Enraf Nonius, *MolEN, Program Package for Crystal Structure Determinations*, Delft, Holland; G. M. Sheldrick, *SHELXS, Program for Crystal Structure Solution*, Universität Göttingen; E. Keller, *SCHAKAL, Programm zur Darstellung von Molekülstrukturen*, Universität Freiburg, modified by M. Kretschmer, W. Hiller, Universität Tübingen; W. Hiller, *HIPAS, Programm-Interface zum Datenaustausch zwischen Programmpaketen*, Universität Tübingen.

[244/91]