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TETRAHEDRON: *ASYMMETRY*

$[Rh_2(OCOCF_3)_4]$ as an auxiliary chromophore in chiroptical studies on steroidal alcohols

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Abstract

The circular dichroism (CD) of in situ formed complexes of steroidal substituted secondary and tertiary alcohols with $[Rh_2(OCOCF_3)_4]$ have been investigated. The applicability of the bulkiness rule, developed for unsubstituted secondary alcohols and connecting the sign of the E band at ca. 350 nm with the absolute stereochemistry of an alcohol, is extended to substituted secondary and tertiary alcohols. The rule works well for secondary and tertiary alcohols containing a double bond, alkoxy, ester or amide groups, halogen substituents as well as additional primary hydroxy groups in a molecule. The influence of other substituents present at the stereogenic center, e.g. a keto-, amino-, azido- or additional hydroxy groups, on CD is also described. It is demonstrated that alcohol molecules bind to the Rh-core at axial positions to form 1:2 adducts of the general formula $[Rh_2(OCOCF_3)_4(alcohol)_2]$.

1. Introduction

Determination of the absolute configuration of compounds transparent in the UV–vis region by the CD technique is one of the most important challenges for physical-organic and organic chemists, especially in the case of monofunctional compounds. CD spectroscopy is a very convenient and sensitive method for the determination of the absolute configuration, provided the structures studied are non-racemic and absorb in an accessible frequency range. In order to obtain CD spectra of substances which are optically active, but transparent in the range of accessible wavelengths, cottonogenic derivatives have to be prepared, in which CD will be induced by its chiral environment. One of the procedures consists of the in situ formation of chiral complexes by mixing a solution of an achiral transition metal complex with an optically active substance which is transparent in the UV–vis region.

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In 1974 two complexing agents forming chiral in situ complexes were developed for the determination of the absolute configuration of chiral alcohols. Andersen et al.[1] found that europium tris(6,6,7,7,8,8,8-heptafluoro-2,2-dimethyl-3,5-octanedionate) [Eu(fod)$_3$] forms 1:2 complexes [Eu(fod)$_3$(ROH)$_2$] with secondary and tertiary alcohols. Their CD effects, at ca. 525 nm, correlate with the geometry of the investigated alcohol. However, the measurements require relatively concentrated substrate solutions, ca. 40–170 mM. Moreover, this method cannot be applied to polyfunctional compounds. Another in situ method was proposed by Dillon and Nakanishi.[2] They used copper hexafluoroacetylacetonate [Cu(hfac)$_2$] as an electrophilic component for alcohol complexes. The experimental sign of the Cotton effect (CE) observed at ca. 330 nm, directly reflects the bulk relationship between the substituents at the stereogenic center.

Recently, a very convenient method involving in situ complexes of dirhodium tetrakis(trifluoroacetate) [Rh$_2$(OCOCF$_3$)$_4$] was developed by Snatzke and Gerards[3] and applied to the determination of the absolute stereochemistry of chiral secondary alcohols. It was also found that olefins, ethers (including epoxides) and ketones ligate to the Rh-core in its axial positions.[3,4] Although numerous natural and synthetic chiral alcohols, such as gibberellins,[5] phyto- or mycosterols,[6,7] etc., possess other functional groups or substituents, no systematic studies were undertaken on such polyfunctional compounds, and to date application of the method elaborated by Snatzke and Gerards is limited. Further investigations on secondary alcohols derived from sugars and α-hydroxyacids demonstrated that direct application of the Snatzke and Gerards empirical bulkiness rule to these compounds is not straightforward.[8]

These facts encouraged us to study further the application of the perfluorinated Rh-complex in the assignment of the absolute configuration of functionalized secondary alcohols. Moreover, we decided to examine the possibility of an extension of this in situ method to tertiary alcohols. In this paper, we describe the usefulness of [Rh$_2$(OCOCF$_3$)$_4$] for the determination of the absolute configuration of a variety of optically active secondary (Fig. 1), and tertiary (Fig. 2), steroidal and related alcohols containing additional substituents such as acetoxy-, bromo-, azido-, amino-, methoxy-, methoxycarbonyl-, amido- or ketone oxo groups.

2. Results and discussion

2.1. UV–vis spectra

The UV–vis spectra of the [Rh$_2$(OCOCF$_3$)$_4$] in hexane[3] and chloroform are very similar and differ only slightly in band positions. Weak absorption bands I and II are located at 609 nm and 459 nm in hexane, whereas in chloroform they appear at 613 nm and 444 nm, respectively. When dichloromethane is used as a solvent, band I lies at 605 nm and band II is seen only as a shoulder at ca. 450 nm. In all solvents discussed, the weak absorption band III is not clearly visible and appears as a shoulder on the short-wavelength side of band II. The well-shaped band IV, of moderate intensity, appears only in dichloromethane at 331 nm. The strong absorption bands V and VI can be observed at ca. 263 nm (shoulder) and 223 nm in hexane, at 250 nm in chloroform (in this solvent, band VI lies out of the measurement range), and at ca. 258 nm (shoulder) and 227 nm in dichloromethane, respectively.

The shapes of the UV–vis spectra of [Rh$_2$(OCOCF$_3$)$_4$] with axially coordinated unsubstituted secondary monohydroxy alcohols **1** and **2** are similar to those of the Rh-cluster measured in the same solvent. Their long wavelength band I lies at 591 or 592 nm (Table 1), and shows a characteristic blue shift of around 18 nm as compared with the Rh-cluster alone, whereas absorption band II is only insignificantly shifted from 459 nm to 461 or 458 nm, respectively. For other alcohols studied which

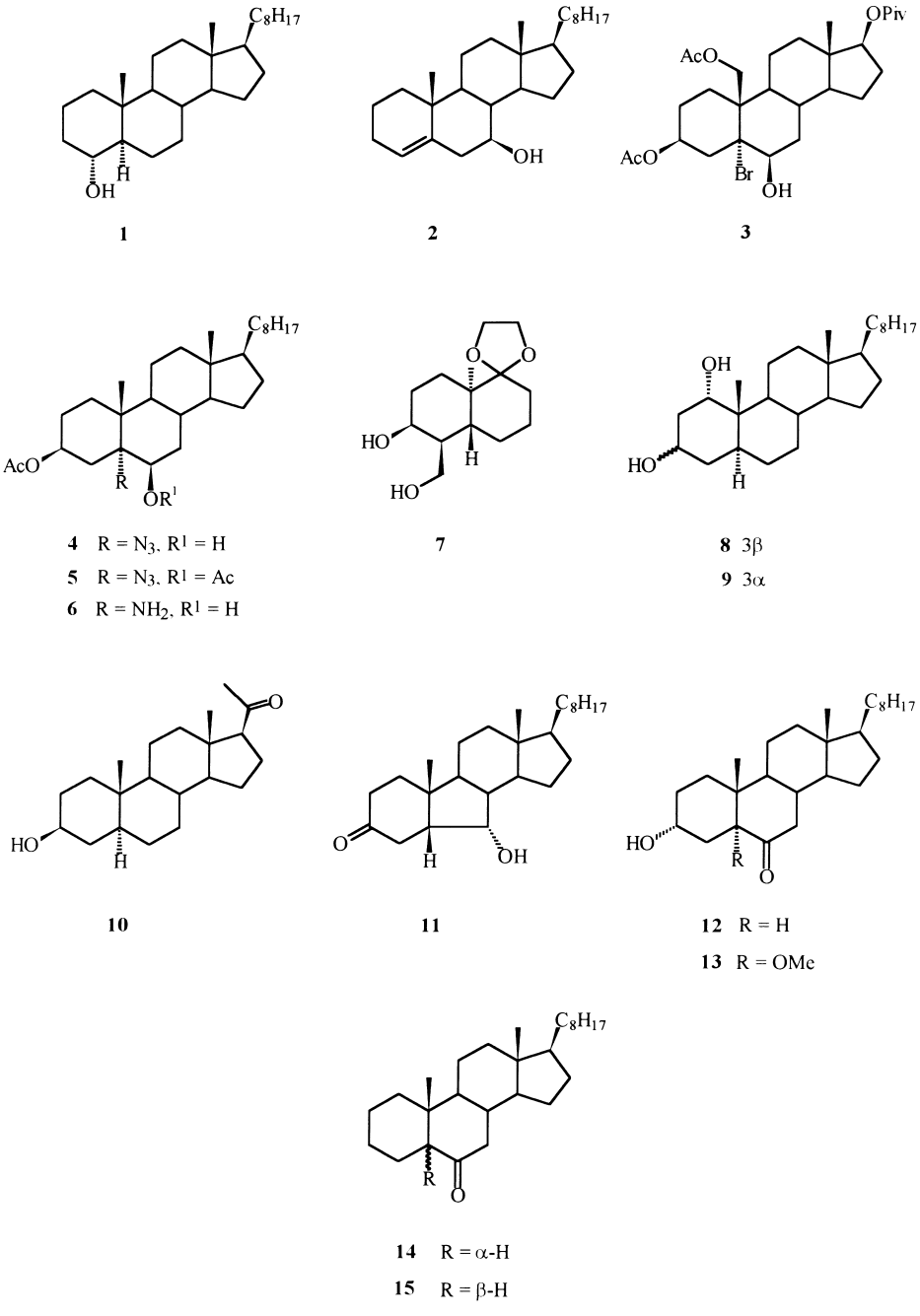
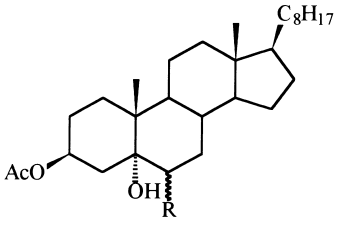
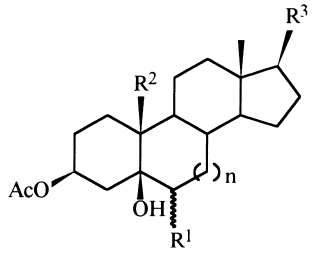


Figure 1. Investigated compounds **1**–**15**

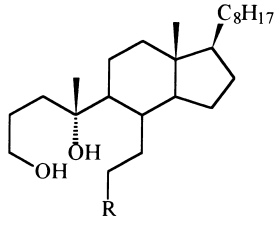
contain an additional substituent in the molecule, band I appears in the range 580–599 nm in hexane or 578–605 nm in chloroform showing a blue shift of around 10–29 nm in hexane or 8–35 nm in chloroform (Table 1). Absorption band II is seen in the range of 455–463 nm in hexane or 457–460 nm in chloroform. On the basis of the results presented above, one can conclude that substitution of the adjacent carbon atom of the secondary and tertiary alcohols by for example, an acetoxy-, methoxy- or azido group has practically no influence on the absorption spectrum. Moreover, the blue color of the



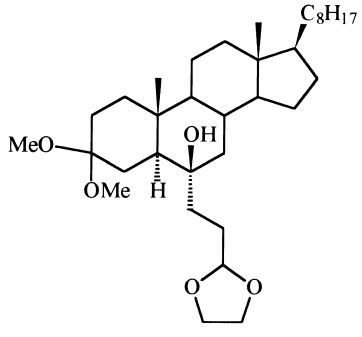
16 R = β-Me
17 R = H
18 R = β-Br
19 R = β-OAc
20 R = β-OMe
21 R = α-OAc
22 R = β-N_3



	R^1	R^2	R^3	n
23	H	Me	C_8H_{17}	1
24	α-Br	CH_2OAc	OPiv	1
25	α-N_3	Me	C_8H_{17}	1
26	α-OAc	Me	C_8H_{17}	0
27	β-OAc	Me	C_8H_{17}	1
28	β-CH_2OAc	Me	C_8H_{17}	0
29	β-COOMe	Me	C_8H_{17}	0



30 R = CH_2OH
31 R = $CONH_2$



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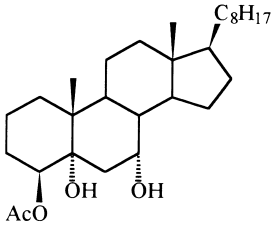

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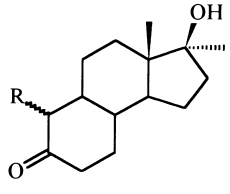

34 R = β-Me
35 R = α-Me

Figure 2. Investigated compounds **16**–**35**

complex solutions, observed in a majority of the investigated compounds, indicates axial ligation through the hydroxyl oxygen, in agreement with the literature data.[9a,b] The characteristic shapes of the UV–vis spectra of the representative in situ formed chiral Rh-complexes, in the 345–800 nm range, are shown in Fig. 3.

The blue-colored hexane solutions of the Rh-complexes of ketones **14** and **15** absorb at 583 or 585

Table 1
Positions of selected absorption bands in nm of in situ formed Rh-complexes of compounds **1**–**35** recorded in hexane (h) and/or chloroform (ch) and/or methylene chloride (mc)

Comp.	Solvent	Band II	Band I	Comp.	Solvent	Band II	Band I	Comp.	Solvent	Band II	Band I
1	h	461	591	**11**	h	458	578	**24**	ch	450^{sh}	605
2	h	458	592	**12**	h	462	585	**25**	h	460	585
3	ch	432^{sh}	600	**13**	h	459	584	**26**	h	458	596
4	ch	448^{sh}	596	**14**	h	461	585	**27**	h	460	597
5	ch	447^{sh}	595	**15**	h	462	583	**28**	h	460	595
6	ch	470^{sh}	541	**16**	h	458	596	**29**	h	458	599
7	ch	458	592	**17**	h	456	594	**30**	ch	458	578
8	h	450^{sh}	590	**18**	h	455^{sh}	599	**31**	ch	457	583
	ch	459	590	**19**	h	458	594	**32**	h	458	589
9	h	456	585	**20**	h	458	596	**33**	h	460	587
	ch	460	583	**21**	h	460	597	**34**	ch	455	588
10	mc	452^{sh}	596	**22**	h	455	593	**35**	ch	453	595
10a[a]	mc	449^{sh}	597	**23**	h	458	599				

^{sh} shoulder;
[a] compound **10a** is the 2 : 1 complex of alcohol **10** with $[Rh_2(OCOCF_3)_4]$ isolated in a crystalline form from *in situ* formed hexane solution.

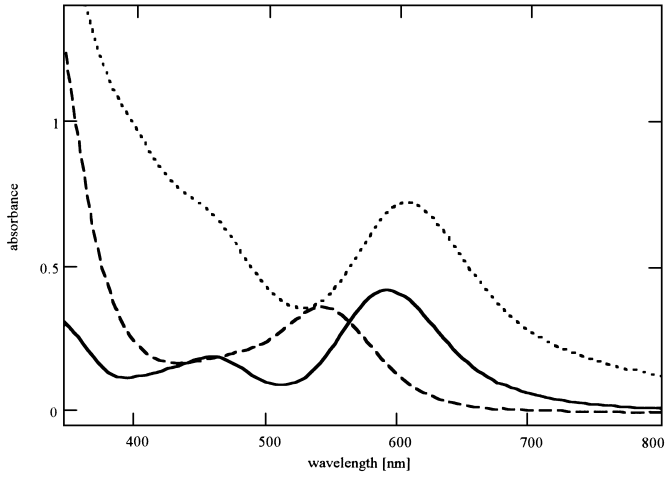

Figure 3. UV–vis spectra of in situ formed Rh-complexes of compounds **6** (– – –), **8** (—) and **24** (· · ·) recorded in chloroform

nm (band I) and 461 or 462 nm (band II), respectively. Thus, the UV–vis spectra as well as the colors of their complexes with Rh-core are similar to those of unsubstituted alcohols and do not allow us to distinguish between ligation through a hydroxyl or a carbonyl group for hydroxyketones **10**–**13**, **34** and **35**. In spite of that, the complexation mode of hydroxyketone **10** is known, as we have succeeded in isolating its chiral rhodium complex in a crystalline form from the hexane solution. The structure of the adduct formed has been determined by X-ray diffraction analysis.[10] As expected, compound **10** forms a 1:2 adduct of the general formula $[Rh_2(OCOCF_3)_4][\mathbf{10}]_2$ as in the case of olefins.[4] In addition, X-ray data demonstrate that in the crystalline state, ligation of hydroxyketone **10** to the rhodium atoms occurs exclusively through the hydroxy group (Fig. 4).

An exceptional behavior, however, is displayed by alcohol **6** with an amino group in the vicinity of a

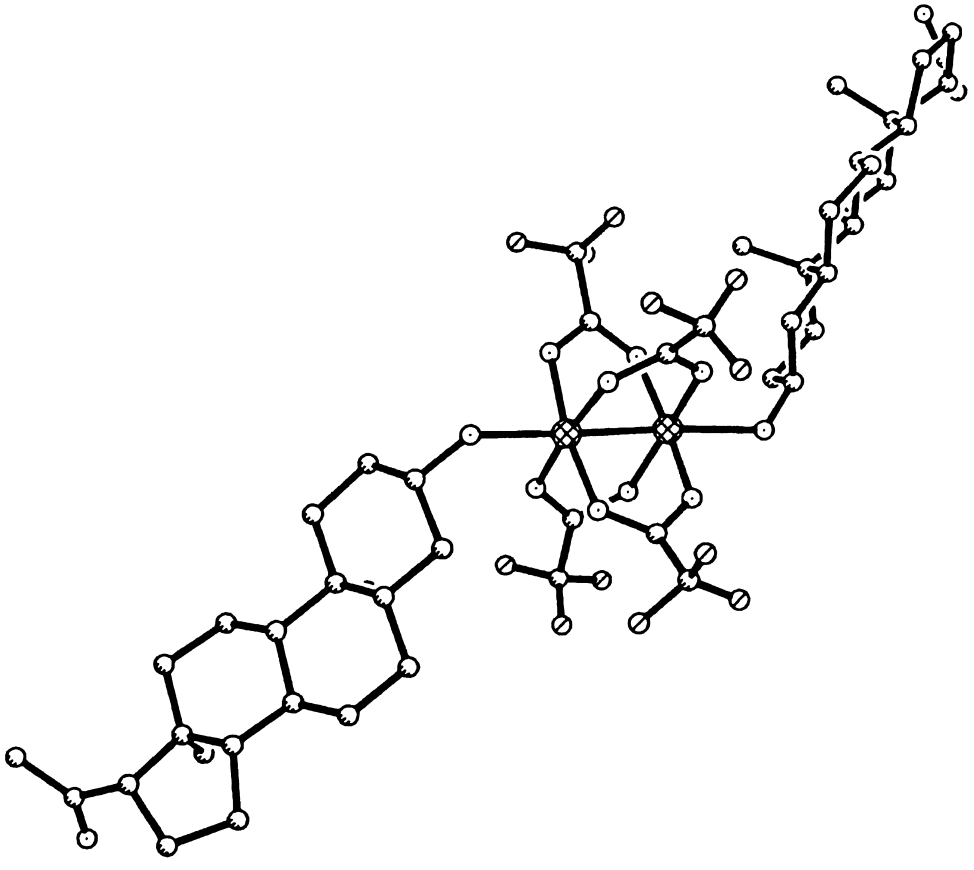

Figure 4. ORTEP diagram of the chiral Rh-complex of compound **10**[10]

hydroxy function. The pink-colored solution of the chiral Rh-complex of **6** shows absorption band I at 541 nm (Table 1 and Fig. 3) with a large blue shift (72 nm) in comparison to the Rh-complex devoid of axial ligands. In spite of the presence of two possible coordination sites, the color of the complex formed as well as the band I position determines the identity of the donor atom in the axial ligand as the nitrogen.[9]

2.2. CD spectra

2.2.1. Secondary alcohols

CD data of compounds **1**–**15** are collected in Table 2. In general, up to six CEs A–F can be found in the CD spectra of the in situ formed Rh-complexes of compounds **1**–**15** in the 600–270 nm range. It was demonstrated[3] that the E band, appearing at ca. 350 nm, can be used for correlation of its sign and the stereochemistry of secondary alcohols, applying the bulkiness rule presented in Fig. 5.

According to the bulkiness rule, compounds **1** and **2** with the stereochemistry 'b*R*' for **1** and 'b*S*' for **2**, display a negative and a positive E band, respectively. Substitution of the adjacent carbon atom in secondary alcohols **3** and **4** by bromo- and azido groups, respectively, does not change the expected signs of the E bands. Thus, both compounds possessing 'b*R*' bulk relationship show negative signs of this band. In order to prove that the CEs of compound **4** do not come from a chiral complex formed by the azido group, a CD spectrum of compound **5** with an acetylated hydroxy group at C-6 was measured

Table 2
CD data of in situ formed Rh-complexes of compounds **1**–**15** measured in hexane (h) and/or chloroform (ch) and/or methylene chloride (mc). Values are given as $\Delta\varepsilon'$(nm)*

Comp.	Solvent	Band F	Band E	Band D	Band C	Band B	Band A
1	h	+0.03 (311)	–0.01 (354)	+0.04 (385)[a]		–0.03 (512)	–0.03 (578)
2	h		+0.01 (371)		–0.01 (448)	+0.02 (513)	
3	ch		–0.07 (359)	–0.01 (403[sh])	+0.04 (457)	+0.02 (535[sh])	+0.01 (592[sh])
4	ch	–0.65 (298)	–0.05 (352[sh])	+0.20 (398)	+0.22 (450)		+0.03 (605)
5	ch		+0.12 (331)	+0.06 (390)	+0.04 (452[sh])	–0.01 (515)	+0.01 (573)
6	ch		+0.06 (346)[b]	–0.04 (462)	+0.02 (497)	–0.02 (544)	+0.01 (611)
7	ch	+0.20 (295)	+0.08 (342)		+0.03 (468)	–0.01 (521)	
8	h		–0.05 (357)	–0.03 (389[sh])	+0.03 (460)	–0.02 (507)	
	ch		–0.02 (351)	–0.01 (402)	+0.01 (451)	–0.02 (511)	
9	h	–0,29 (274)	+0.17 (352)	+0.05 (398[sh])		–0.04 (512)	
	ch		+0.19 (353)	+0.06 (406[sh])	+0.02 (458[sh])	–0.05 (513)	+0.04 (580)
10	mc		+0.21 (351)	+0.10 (397[sh])	–0.01 (475)		–0.02 (574)
10a[d]	mc		+0.17 (359)	+0.04 (411[sh])	–0.002 (456)	+0.01 (500)	–0.01 (568)[c]
11	h		–0.38 (350)	–0.12 (415)		+0.11 (524)	–0.06 (590)
12	h		+0.12 (346)	+0.06 (412)	+0.04 (454[sh])	–0.02 (515)	+0.02 (578)
13	h		+0.01 (360)		+0.09 (446)	–0.02 (515)	+0.02 (576)
14	h		+0.69 (346)	+0.41 (412)	+0.23 (460[sh])	–0.08 (513)	+0.11 (576)
15	h		+0.04 (339)	+0.10 (421[sh])	+0.13 (453)	–0.02 (515)	+0.05 (577)

* for explanation of the term $\Delta\varepsilon'$ see experimental.
[sh] shoulder ;
[a] an additional band –0.007 (419nm) ; [b] additional bands: -0.005 (399nm) and +0.003 (429nm);
[c] an additional band -0.03 (612nm) ; [d] compound **10a** is the crystalline 2:1 complex of alcohol **10** with $[Rh_2(OCOCF_3)_4]$.

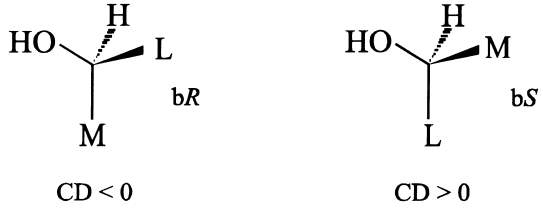

Figure 5. Bulkiness rule for correlation of the alcohol geometry with the sign of the CD band E according to Gerards and Snatzke[3]

in the presence of $[Rh_2(OCOCF_3)_4]$. The positive sign of the E band clearly shows that, in the absence of a hydroxy group at C-6, ligation through an azido or an acetoxy substituent takes place. Thus, the negative sign of the E band in compound **4** indicates ligation through a hydroxy group. However, an exchange of a bromo- or azido group for an amino substituent, as in compound **6**, inverts the sign of the E band. Taking into consideration the position of absorption band I at 541 nm and the pink color of the complex solution,[9] a ligation through an amino group should be assumed for **6**. However, having at hand

Table 3
Selected data of ^{1}H and ^{13}C NMR spectra of **8**, **9**, **10** and their in situ formed Rh-complexes recorded in $CDCl_3$

Comp.	^{1}H NMR								^{13}C NMR	
	18-H	19-H	26-H	27-H	21-H	1β-H	3ξ-H	17α-H	C-1	C-3
8	0.653 s	0.811 s	0.859 d	0.864 d	0.898 d	3.816 t	4.008 br tt 3α		73.13	66.64
Rh+8	0.645 s	0.875 s	0.837 d	0.842 d	0.869 d	4.038 m	4.525 m 3α		74.23	69.68
9	0.652 s	0.748 s	0.857 d	0.861 d	0.896 d	3.732 nm	4.075 nm 3β		72.81	67.92
Rh+9	0.654 s	0.871 s	0.835 d	0.839 d	0.848 d	4.258 m	4.536 m 3β		75.51	70.79
10	0.579 s	0.783 s			2.082 d		3.567 m 3α	2.489 m		71.13
Rh+10	0.663 s	0.851 s			2.279 d		4.081 m 3α	2.701 m		74.17

s - singlet; d - doublet; t - triplet; tt - triplet of triplets; m - multiplet; nm - narrow multiplet; br - broad;

CD data of only one Rh-complex with primary steroidal amine, we are unable to correlate its absolute stereochemistry with the signs of the observed CEs.

In the case of the diol **7**, only one (secondary) hydroxy group is directly connected to a stereogenic center at C-7. A complexation through the primary hydroxy group, also present in the molecule, does not give any considerable contribution to the CD. Therefore, a positive sign of the E band can unambiguously be correlated with the 'b*S*' stereochemistry of the secondary alcohol.

For compounds **8** and **9**, bearing two hydroxy substituents, a complexation through the less hindered 3β- or 3α-hydroxy group, respectively, was expected. As seen in Table 2, compound **8** gives a negative, and compound **9**, a positive E band in accord with the bulkiness estimated for these alcohols. In the case of the diol **8**, the privileged complexation through 3β-hydroxy group was deduced also from the comparison of ^{1}H and ^{13}C NMR spectra of the diol **8** and its formed in situ Rh-complex. The selected ^{1}H and ^{13}C NMR data are collected in Table 3. As seen in Table 3, complexation of **8** to the Rh-cluster leads to considerable shifts and broadening of ^{1}H NMR signals derived from the protons in the vicinity of Rh atoms. The large deshielding effect observed for the 3α-H signal (+0.517 ppm) is very similar to that found earlier for simple unsubstituted primary or secondary alcohols (from +0.54 to +0.69),[11] and strongly suggests ligation through the 3β-hydroxy group in compound **8**. In the ^{13}C NMR spectrum of Rh-complex of **8**, C-1 and C-3 carbon signals are broadened, but much stronger broadening is observed for the C-3 atom. Moreover, both signals are shifted downfield (C-1, $\Delta\delta$=+1.10 and C-3, $\Delta\delta$=+3.04) in comparison to the spectrum of a non-complexed **8**. Thus, both the ^{1}H and ^{13}C NMR spectra indicate the predominating ligation of compound **8** through the 3β-hydroxy group.

The ^{1}H NMR spectra of compound **9** and its Rh-complex presented in Table 3 show nearly equal downfield shift of 1β-H (+0.526) and 3β-H (+0.461). A larger downfield shift (+0.123) is also observed for C-19 methyl protons. The ^{13}C NMR spectra of **9** and its Rh-complex demonstrate shifts of the C-1 and C-3 carbon signals of $\Delta\delta$=+2.70 and $\Delta\delta$=+2.87, respectively, both of the signals being broadened to the same extent. Thus, the NMR spectra indicate the presence of two possible complexes in the solution formed by binding to the Rh-core through 3α- or 1α-hydroxy groups. On the basis of the bulkiness rule, the formation of an Rh-complex through a 1α-hydroxyl ('b*R*' configuration) should cause a negative sign of the E band and the one formed through a 3α-hydroxyl ('b*S*' configuration) should cause a positive sign

of this band. The observed positive sign of the E band points to predominant binding of 3α-OH group to the Rh-core.

Besides a hydroxy group, compounds **10**–**13** possess an additional binding site, i.e. the ketone group. Moreover, hydroxyketone **13** bears a 5α-methoxy substituent, but due to its steric hindrance it is not suitable for binding to the Rh-cluster through the ether oxygen atom. The complexation of compounds **10**–**13** through a hydroxy group should lead to a positive E band for compound **10** and a negative one for compounds **11**–**13**, as predicted by the bulkiness rule. Indeed, the observed signs of the E band for compounds **10** and **11** agree with the aforementioned prediction. A comparison of the ^{1}H NMR spectra of the compound **10** and its in situ Rh-complex (Table 3), shows deshielding of 17α-H by +0.212 and of 3α-H by +0.514. Similarly, in the ^{13}C NMR spectrum of the chiral complex of compound **10** (Table 3), the C-3 signal is deshielded by 3.04 ppm from 71.13 to 74.17 ppm, respectively. On this basis it can be deduced, by analogy with compound **8**, that the ligation through the C-3 hydroxy group predominates in the solution. The isolation of the formed in situ Rh-complex of compound **10** in a crystalline form confirms unequivocally the ligation of two alcohol molecules in axial positions of the Rh-cluster (Fig. 4). In addition, it is worth noting that the CD curve of the isolated crystalline complex **10a** is very similar to that obtained for the complex formed in situ (Table 2). This fact indicates predominating ligation of hydroxyketone **10** to the Rh-core through 3β-hydroxy group also in a solution.

According to the 'b*R*' bulkiness of C-3 carbon atom in **12** and **13**, the expected sign of the E bands for these compounds should be negative, as in the case of cholest-5-en-3α-ol.[3] The observed positive sign of E bands for **12** and **13** (Table 2), which contradicts the one predicted on the basis of the bulkiness rule, suggests complexation through a ketone oxo group. In order to confirm this assumption, we measured the CD of the in situ formed Rh-complexes with 6-oxosteroids **14** and **15**. Both ketones give positive E bands and the shapes of their CD curves are analogous to those of hydroxyketones **12** and **13**. At first sight identical signs of CEs for Rh-complexes of both C5 epimeric ketones seem to be surprising. As there is so far no rule derived for Rh-complexes of ketones correlating CEs signs with their stereochemistry, the results obtained cannot be discussed in more detail at the moment.

2.2.2. Tertiary alcohols

In order to prove that tertiary alcohols are able to form chiral complexes with a Rh-cluster, we studied a variety of differently substituted compounds **16**–**35** (Fig. 2). The bulk relationship for tertiary alcohols was estimated considering the possible direction of the Rh-cluster approach to the lone electron pairs of the hydroxyl oxygen. It was assumed that the approach takes place from the less hindered side of the alcohol molecule, i.e. between S (small) and M (medium) substituents attached to the stereogenic center. Thus, for instance, the 'b*R*' or 'b*S*' configuration for investigated tertiary alcohols is ascribed as follows:

(i) 'b*R*'configuration — for all 5α-hydroxy steroids **16**–**22** and **33** resulting from the α-side approach between C-10 (M substituent) and C-4 (S substituent);
(ii) 'b*S*' configuration — for 5β-hydroxy steroids with 6β-hydrogen **23**–**26** resulting from the β-side approach between C-4 (M substituent) and C-6 (S substituent);
(iii) 'b*R*'configuration — for 6β-substituted 5β-hydroxy steroids **27**–**29** resulting from the β-side approach between C-6 (M substituent) and C-4 (S substituent)]; etc.

The CD data obtained for compounds **16**–**35** are presented in Table 4. The results collected for two series of 5-hydroxy steroids substituted at the adjacent carbon atom, i.e. 5α-hydroxysteroids **16**–**21** and 5β-hydroxysteroids **23**–**29** (Fig. 2, Table 4), clearly demonstrate that, regardless of the absolute *R*/*S* configuration at C-5, the bulkiness of these alcohols determines the sign of the E band. In agreement with this statement, 5α-hydroxysteroids **16**–**21** show a negative E band due to their 'b*R*' bulkiness. The C-6 unsubstituted and 6α-substituted 5β-hydroxysteroids **23**–**26** display a positive E band, whereas 6β-

Table 4
CD data of in situ formed Rh-complexes of compounds **16**–**35** recorded in hexane (h) and/or chloroform (ch). Values are given as $\Delta\varepsilon'$(nm)*

Comp.	Solvent	Band F	Band E	Band D	Band C	Band B	Band A
16	h	−0.18 (312)	−0.17 (345)	−0.10 (405^{sh})	−0.06 (450^{sh})	+0.03 (512)	−0.02 (594)
17	h	+0.20 (271)	−0.06 (352)	−0.02 (412)		+0.04 (502)	−0.05 (582)^{a}
18	h		−0.05 (366)	−0.04 (402^{sh})	−0.02 (457^{sh})	+0.01 (514)	−0.01 (586)
19	h	+0.39 (283)	−0.06 (353)		−0.08 (454)	+0.04 (516)	−0.06 (585)
20	h	+0.04 (285)	−0.11 (350)	−0.06 (412)	−0.04 (453^{sh})	+0.02 (513)	−0.02 (585)
21	h	+0.08 (292)	−0.22 (350)	−0.09 (406)	+0.006 (468)	−0.02 (517)	−0.02 (601)
22	h		+0.08 (365)	+0.07 (401)		+0.02 (509)	−0.02 (592)
23	h	−0.004 (317)	+0.02 (367)		+0.03 (439)	−0.07 (513)	+0.04 (589)
24	ch	−0.02 (324)	+0.01 (352^{sh})	+0.04 (426)		+0.01 (529)	
25	h		+0.59 (380)		+0.35 (447)	+0.03 (548)	−0.15 (630)
26	h		+0.02 (347)	−0.03 (400^{sh})	−0.07 (455)	+0.08 (511)	−0.02 (590)
27	h		−0.18 (353)	−0.08 (408)	+0.04 (483)	+0.03 (528^{sh})	
28	h		−0.03 (341)	−0.01 (404)		+0.05 (506)	−0.01 (587^{sh})^{a}
29	h		−0.20 (353)	−0.08 (404)	+0.01 (470)		−0.004 (582)
30	ch		−0.11 (331^{sh})		+0.07 (455)	−0.04 (518)	
31	ch		−0.02 (351)	−0.002 (396)	+0.02 (462)	−0.01 (511)	
32	h		−0.03 (359)		−0.02 (458)	+0.02 (511)	−0.01 (575)
33	h	−0.08 (293)	−0.19 (355)	−0.07 (396^{sh})	+0.07 (455)	−0.02 (512)	
34	ch		+0.07 (349)	+0.02 (403)	−0.002 (461)	+0.001 (514)	+0.002 (600)
35	ch		−0.27 (351)	−0.14 (403)	+0.005 (478)	−0.004 (519)	−0.002 (618)

* for explanation of the term $\Delta\varepsilon'$ see experimental.
sh shoulder ;
a an additional band -0.03 (650nm).

substituted 5β-hydroxysteroids **27**–**29** show a negative E band, in accordance with their ‘b*S*’ or ‘b*R*’ bulkiness, respectively (Fig. 6).

Azido-alcohol **22** represents the only exception in this series of compounds. The shape of its CD curve, as well as the sign of the E band, differ from those for **16**–**21**. Most probably, this compound undergoes ligation to the Rh-core through an azido group. However, we have no proof for this assumption.

The estimated bulkiness for C-10 (compounds **30**–**31**) and C-6 (compound **32**) atoms bearing tertiary hydroxy groups is ‘b*R*’. Thus, all of them cause a negative sign of the E band following the bulkiness rule. The presence of additional functional groups in compounds **30** and **31** does not significantly influence the CD due to their remote position with respect to the stereogenic centers. For the same reason the methoxy groups at C-3 as well as the ether oxygens of the 1,3-dioxolane ring in the alcohol **32** do not contribute to CD.

In the series of tertiary alcohols, compound **33** possesses a secondary hydroxy group at C-7 in addition to the tertiary OH group at C-5. In this case, 7α-hydroxyl is less hindered in comparison to the 5α-hydroxyl and thus the preferred ligation through the oxygen atom of the former group is expected.

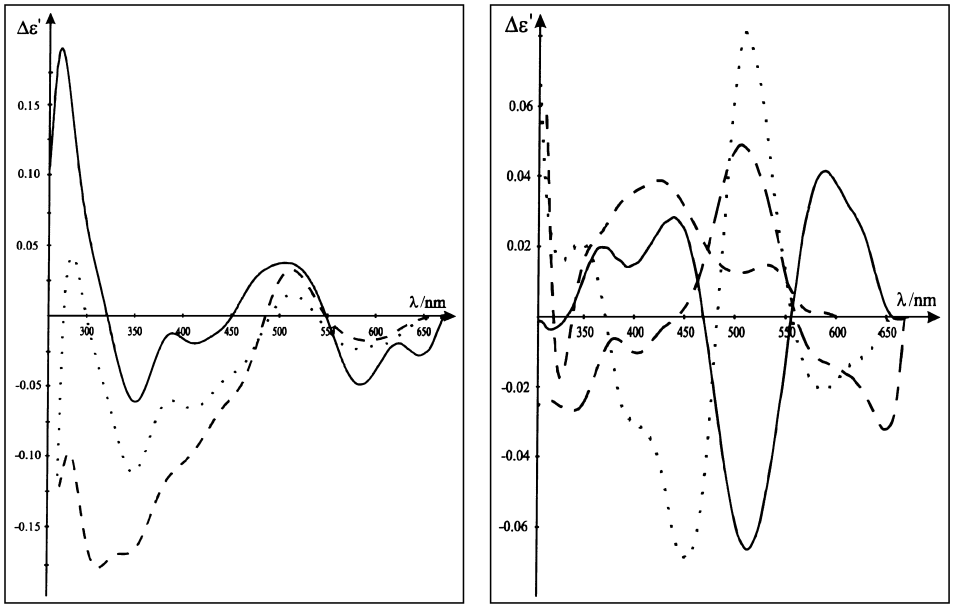

Figure 6. CD spectra of in situ formed Rh-complexes of **16** (– – –), **17** (—), and **20** (· · ·) (left) and **23** (—), **24** (– – –), **26** (· · ·) and **28** (— – —) (right)

However, an equilibrium of complexes formed through 7α- and 5α-hydroxyls cannot be excluded. The X-ray analysis of the in situ formed Rh-complex of compound **33**, isolated in the crystalline form from the hexane solution (Fig. 7), shows the presence of one type of a complex only; namely a 2:1 complex with two alcohol molecules ligated to the Rh-core through a 7α-hydroxyl. A negative sign of the E band is in agreement with the 'b*R*' bulkiness of C-7 carbon atom and indicates predominating ligation through the 7α-hydroxy group also in solution.

In addition to the tertiary 17β-hydroxy function of the 'b*S*' configuration, the last two compounds studied, namely **34** and **35**, bear a remote ketone oxo group with an adjoining stereogenic center at C-10. Although the position of the lowest energy bands in their absorption spectra is quite similar and amounts to 588 nm for **34** and 593 nm for **35** (Table 1), the colors of their solutions differ slightly. According to the literature data,[3] the blue color of the complex of **34** suggests complexation through a hydroxy group. This assumption seems to be supported by the positive sign of the E band which is in accordance with the bulkiness of the 17β-alcohol. On the other hand, the blue-green color of the Rh-complex of **35** suggests a complexation through the carbonyl oxygen.[3] Indeed, the CD spectrum of this complex shows a negative E band in contradiction to the 'b*S*' configuration at C-17 thus excluding coordination through the 17β-OH group. Having at hand very few compounds with a keto group only, we are not able to draw a conclusion concerning the relationship between the stereostructure of ketones and CE signs of their Rh-complexes.

3. Conclusion

Results of this study show that the in situ method, developed for the determination of the absolute configuration of unsubstituted secondary alcohols, can be successfully extended to substituted secondary as well as to tertiary alcohols. Furthermore, investigations carried out on the series of 5α- and 5β-hydroxysteroids, substituted at the adjacent carbon atom, prove a correlation between the E band sign and

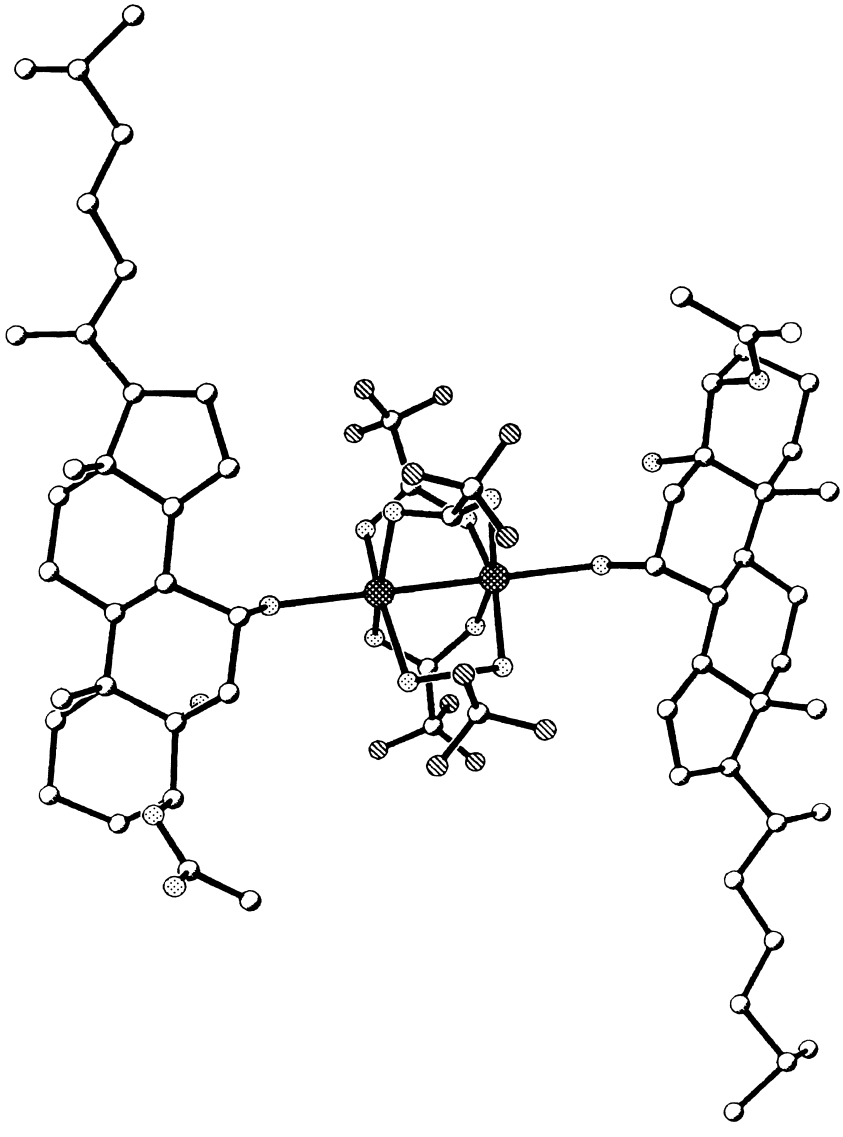

Figure 7. ORTEP diagram of the in situ formed Rh-complex of compound **33**[10]

the bulkiness of an alcohol. The in situ method can be applied successfully to the absolute configurational assignment for most of the substituted alcohols.

In some bifunctional compounds, such as diols, hydroxyketones, aminoalcohols and azidoalcohols, both groups present in the molecule are able to form chiral complexes with the Rh-core. Therefore, a competition in ligation to the Rh-cluster may occur between them. It was demonstrated that the in situ method does not give unambiguous results with alcohols containing an additional functional group connected to the stereogenic center, i.e. azido, hydroxyl or keto group. In such cases, the ^{1}H and ^{13}C NMR spectroscopy may be helpful in the assessment of the complexation site. It was also shown that aminoalcohol **6** undergoes an axial ligation to the Rh-cluster through the nitrogen atom of an amino substituent.

Moreover, for the first time, Rh-complexes with chiral alcohol molecules acting as ligands were iso-

lated in a crystalline form and their structures determined by the X-ray method, thus giving information about the complexation mode.

4. Experimental

^{1}H and ^{13}C NMR spectra were recorded with a Bruker AM 500 spectrometer. UV–vis spectra were measured on a Cary 1E spectrophotometer in hexane, chloroform and methylene chloride. CD spectra were measured between 700 and 230 nm at room temperature with a spectrophotometer AVIV 62D using hexane, chloroform and methylene chloride solutions in cells of 1 cm path length (spectral band width 2 nm, sensitivity 10×10^{-6} or 20×10^{-6} ΔA-unit/nm). Depending on the S:N-ratio the λ-scan speed was 0.2 or 0.5 nm/s.

For CD measurements the solid chiral alcohol (1–3 mg) was dissolved in a dry solution of the stock [$Rh_2(OCOCF_3)_4$] complex (6–7 mg) in hexane, chloroform or methylene chloride (10 ml) so that the molar ratio of the stock complex to ligand was about 1:0.3 to 1:0.7. As the true concentrations of the individual optically active complexes are not known, apparent $\Delta\varepsilon'$-values are given, calculated from the total ligand concentration on the assumption of 100% complexation. On the other hand, for determination of the absolute configuration from CD only the signs of CEs are required. Therefore, qualitative values of $\Delta\varepsilon'$ are of no relevance for the operating bulkiness rule. Some of the $\Delta\varepsilon'$-values are very small, but nevertheless the signal-to-noise ratio in each case was better then at least 10:1. At room temperature solutions of the complexes are stable for a very long time. The CD spectra of alcohols with a Rh-core taken from the solutions kept for several days differ only in a magnitude of CEs which slightly rise.

[$Rh_2(OCOCF_3)_4$] was commercially available from Aldrich and was used without further purification.

Source of compounds: Compounds **1**,[12] **2**,[13] **4**,[14] **5**,[14] **6**,[15] **8**,[16] **9**,[16] **11**,[17] **12**,[18] **14**,[19] **15**,[12] **16**,[20] **17**,[21] **18**,[22] **19**,[23] **20**,[24] **21**,[25] **22**,[26] **23**,[27] **25**,[14] **26**,[28] **27**,[29] **28**,[30] **29**,[30] were obtained according to the literature data. Compound **10** was commercially available from Sigma. Compounds **30** and **31** were synthesized starting from (*E*)-5-hydroxyimino-3,5-seco-4-norcholestan-3-oic acid methyl ester[31] by abnormal Beckmann rearrangement using thionyl chloride, followed by cyclization of seco-nitriles with HBr/AcOH and reduction of lactone-amide formed with $LiBH_4$. Stereochemistry of compounds **30** and **31** was established by spectroscopic and chemical correlation methods.[32]

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32. (10*R*)-3,5;5,10-Bissecocholestanetriol-3,5,10 (**30**); m.p. 133–134°C (Et_2O–hexane); $[\alpha]_D^{24}$=+7.8; IR (KBr): ν_{max}=3500–3300 (OH) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=0.67 (s, 3H, 18-H_3), 1.18 (s, 3H, 19-H_3), 3.45–3.75 (br m, 4H, 3H_2 and 5-H_2); $C_{26}H_{50}O_3$ (410.66): calcd C 76.04, H 12.27%; found C 76.02, H 12.28%. (10*R*)-3,10-Dihydroxy-3,5;5,10-bissecocholestane-5-amide (**32**); m.p. 160–162°C (Me_2CO); $[\alpha]_D^{25}$=+2.8; IR (KBr): ν_{max}=3450–3350 (OH and NH_2), 1680 (C=O, amide) cm^{-1}; ^{1}H NMR ($CDCl_3$): δ=0.66 (s, 3H, 18-H_3), 1.18 (s, 3H, 19-H_3), 3.63 (m, 3H, 3-H_2 and OH), 5.60 and 6.16 (each 1H, $CONH_2$); $C_{26}H_{49}O_3N$ (423.66): calcd C 73.71, H 11.66, N 3.31%; found C 73.62, H 11.59, N 3.30%.