

Determination of the Absolute Configuration of Chiral 1,3-Diols by CD Spectroscopy of their $[\text{Mo}_2(\text{OAc})_4]$ Complexes. ¹⁾

Jadwiga Frelek

Warsaw (Poland), Institute of Organic Chemistry of the Polish Academy of Sciences

Wojciech Szczepek

Warsaw (Poland), Pharmaceutical Research Institute

Wolfgang Voelter

Tübingen, Abteilung für Physikalische Biochemie, Physiologisch-chemisches Institut der Universität

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Abstract. Bidentate complexes between $[\text{Mo}_2(\text{OAc})_4]$ and 1,3-diols (**1–16**) show several CD bands in the 250–600 nm range. A previously published sector rule for the prediction of the sign of band II at ca. 400 nm for rigid cyclic 1,3-diols is extended to open-chain (**7–12**) as well as "semi-rigid" 1,3-

glycols (**1–6** and **14–16**). Their absolute configuration can be correlated with the sign of this CD band. This *in situ* complexation needs minute amounts of substance and therefore is a very convenient tool for the determination of the absolute configuration of such class of compounds.

The 1,3-diol fragment is frequently present in many natural or synthetic products, e.g. cortisone, sugar derivatives, macrolide antibiotics as e.g. griseoviridin [1], diterpenes as e.g. aphidicolin [2] etc. The stereochemistry of this type of chiral diols can be determined by various spectroscopic methods including circular dichroism (CD) techniques, such as the "dibenzoate chirality method" [3, 4, 5] or complexing with $\text{Ni}(\text{acac})_2$ [6], $\text{Pr}(\text{dpm})_3$ [7] as well as with Cupra A [8]. However, in many cases applicability of these methods is limited, especially in the case of complexing techniques, e.g. the Cupra A method requires water as solvent, and Cotton effects (CE's) of Pr complexes depend strongly on the concentration used.

Since 1981 it is known that the acetate ligands of the dimolybdenum tetraacetate $[\text{Mo}_2(\text{OAc})_4]$ can easily be exchanged in solution by chiral 1,3-diols [9–13]. The optically active *in situ* complexes thus formed show several CD bands useful for the empirical determination of the absolute configuration of such diols. We have recently published [14] a sector rule, proposed on the ba-

sis of the results obtained for conformationally rigid steroidal 1,3-diols, correlating the molecular structure of 1,3-diols acting as ligands with the sign of the Cotton effect around 400 nm (CD band II). Moreover, we have found that only an axial orientation of both hydroxyl groups of 1,3-diols allows the formation of a chiral complex thus leading to Cotton effects within the absorption bands of the $[\text{Mo}_2\text{O}_8]$ chromophore. Our sector rule has been successfully applied in confirming of the absolute configuration assignment at C(5) for heptofuranose derivatives having free hydroxyl groups at C(5) and C(7) (*prim-sec* diols) or at C(3) and C(5) (*sec-sec* diols) [15].

The aim of this work is to discuss the applicability of the *in situ* method and the validity of our empirical sector rule [14] for conformationally flexible open-chain 1,3-diols. Moreover, the use of chiral molybdenum complexes with "semi-rigid" 1,3-glycols for the determination of their absolute configuration is also tested. These two classes of 1,3-diols are of particular interest from the experimental point of view because

¹⁾ This paper is a continuation of our studies initiated under inspiration of the late Professor G. Sznatzke on the application of transition metal complexes to chiroptical studies of compounds transparent above 200 nm.

in their structural analysis some difficulties arise due to their high conformational flexibility. In general the analysis of such systems is more complex than that of cyclic ones.

Results and Discussion

The hexopyranose derivatives **1–3** and bicyclic compounds **4–6** may be assumed to be “semi-rigid” 1,3-diols because there exists only one conformer with syn-parallel orientation of the hydroxyl groups as in the case of conformationally rigid steroidal 1,3-diols. Thus the easy formation of chiral complexes with $[\text{Mo}_2(\text{OAc})_4]$ leading to the Cotton effects within absorption bands of the metal cluster was expected. In fact, the glucopyranose derivatives **1, 2** and mannopyranose derivative **3** (*prim–sec* 4eq,6-diols, Figure 1) show CD curves similar to those described earlier [12, 13] with a negative band I above 520 nm (if observed) and also a negative band II around 420 nm (Table 1). The sign of the band

Table 1 CD data of the diols **1** through **16** with $[\text{Mo}_2(\text{OAc})_4]$ in DMSO. Values are given as $\Delta\epsilon'$ (λ/nm).

Comp.	Band I	Band II	Band III	Band IV	Band V
1	–0.01 (538)	–0.03 (420)			
2		–0.01 (428)			
3	–0.02 (538)	–0.10 (420)			
4		–0.09 (391)		–0.19 (322)	
5		–0.12 (384)		–0.60 (298)	
6		–0.36 (390)		–0.30 (317)	+0.20 (279)
7	+0.01 (518)	+0.03 (418)			–0.33 (279)
8		+0.08 (393)			
9		+0.002 (444)	–0.002 (386)		
10	–0.006 (502)	+0.001 (427)	–0.02 (376)	–0.05 (307)	
11			no CD		
12			no CD		
13			no CD		
14			no CD		
15			no CD		
16			no CD		

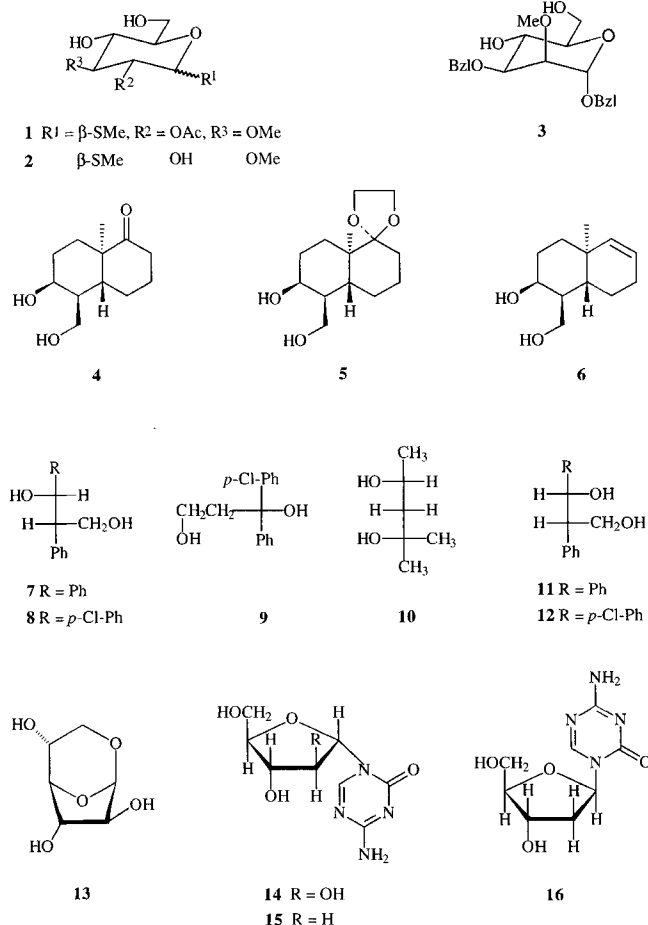


Fig. 1 Investigated 1,3-diols

II CE of these compounds is negative because the greater part of the molecule in all three cases occupies the negative sector as shown in Figure 2a. A negative band II CE has also been expected (Figure 2b) for the three bicyclic compounds **4–6**. These compounds were tested in order to prove that “semi-rigid” *prim–sec* 1,3-diols with axial secondary hydroxyl and equatorial hydroxymethyl groups attached to a six-membered ring follow the sector rule. The observed band II of the *in situ* formed complexes of the diols **4–6** shows a negative sign. Moreover, all of them produce a negative band IV around 300–320 nm. A positive band V at 279 nm was observed only for diol **6**.

We have also investigated the chiroptical properties of the *in situ* formed complexes of some flexible open-chain 1,3-diols with *prim–sec*, *prim–tert* or *sec–tert* diol units. Among the 1,2-diphenylethane derivatives **7, 8, 11** and **12** (Figure 1) only the *threo* isomers **7** and **8** formed *in situ* chiral complexes showing the positive band II CE around 400 nm. An additional positive band I at 518 nm and negative band V at 279 nm (Table 1) was observed only for the diol **7**. Compounds **11** and **12** probably do not form complexes with Mo cluster as they do not give the induced CD in 650–250 nm range. These facts are in accord with our MMX calculations [16],

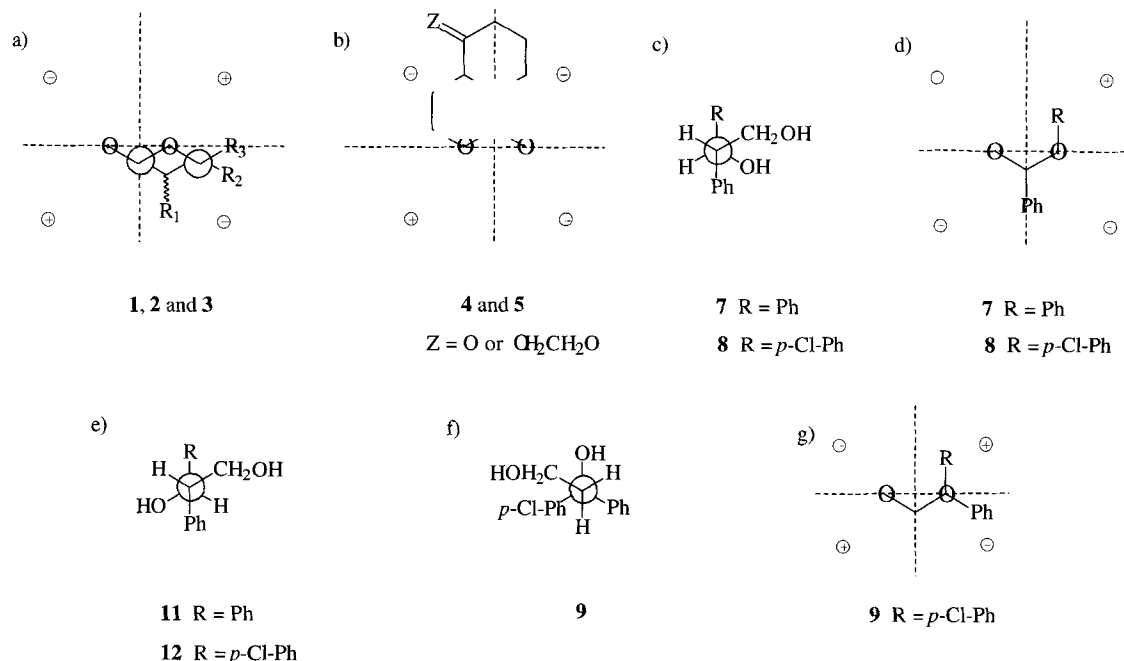


Fig. 2 Sector rule for compounds 1–3 a); sector rule for compounds 4 and 5 b); Newman projection c) and sector rule d) for preferred conformers of compounds 7 and 8; Newman projection for least energy conformers of compounds 11 and 12 e); Newman projection for preferred conformer f) and its sector projection g) of compound 9.

which showed that preferred conformers of the diols 7 and 8 are those with antiparallel oriented phenyl substituents (Figure 2c) whereas the least energy conformers of the diols 11 and 12 are those with antiparallel oriented hydroxyl and hydroxymethyl substituents (Figure 2e). This steric arrangement of hydroxyl groups in 11 and 12 explains the inability in forming chiral complexes by these compounds. The observed positive sign of band II Cotton effect of the diols 7 and 8 is consistent with the sign of the sector occupied by the greater part of the molecules (Figure 2d).

The *prim-tert* diol 9 underwent complexation and its chiral *in situ* complex exhibits two very weak bands, positive at 444 nm (band II) and negative at 386 nm (band III) as shown in Table 1 and Figure 3. The preferred conformer of compound 9, as obtained from energy minimization, is shown in Figure 2f and its sector projection represents Figure 2g. Very low intensity of the observed Cotton effects is due to the presence of very similar groups in the sectors of opposite signs: *p*-chlorophenyl substituent in the positive sector and phenyl substituent in the negative one.

Four very weak CD bands were obtained for the complex of the *sec-tert* diol 10. Positive CD band II was observed at 427 nm and three negative bands I, III and IV appeared at ca. 500, 380 and 310 nm, respectively. In this case one of the positive sectors is occupied only by a small methyl substituent and thus it defines the

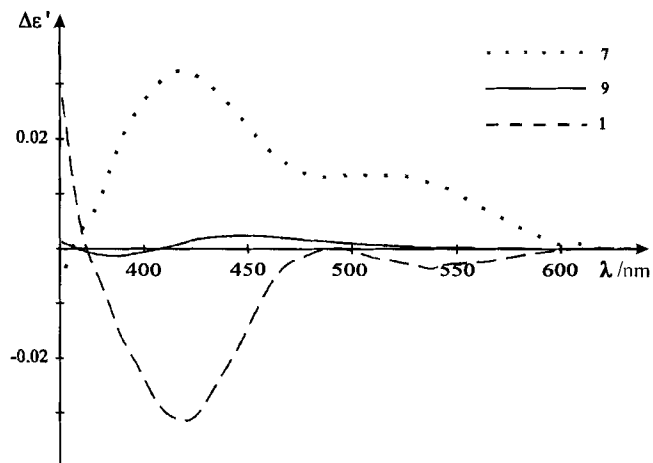


Fig. 3 CD spectra of *in situ* [Mo₂(OAc)₄] complexes of 1, 7 and 9 in the range 350–600 nm

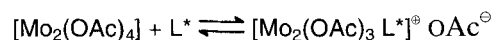
sign of the band II Cotton effect. The amplitude of this band reflects a small contribution of the methyl substituent to the CD.

Among other investigated compounds neither the bridged sugar derivative 13 nor the D-ribose or 2-deoxy-D-ribose derivatives 14–16 show Cotton effects in the presence of the dimolybdenum cluster. An inspection of Dreiding models as well as the MMX calculations [16] shows that in these cases the distance between two hydroxyl groups in 1,3-diol moieties is too long for formation of a chiral complex with Mo-core.

A comparison of these results and the literature [9–13] obtained so far for 1,3-diols, indicates that the λ_{\max} values of bands I–VI fall in the ranges 550–440, 450–380, 390–330, 330–300, 290–270 and 260–250 nm, respectively. Analysis of the relation between the observed signs of the CE's and structure of the investigated compounds, evidently shows that only the sign of band II can be taken for the structure–CD correlation because it is the only one observed for all *in situ* complexes of chiral 1,3-diols. The frequently appearing band I and band III cannot be used for this purpose as they show in some cases the same sign and in other cases the opposite sign to that of band II thus being influenced by additional structural features. The same behavior is observed for bands IV and V. Although always of the same sign as band II, band VI must also be excluded from structure–CD correlation because of its rare appearance. It is worth noting that in about 30% of the known data, band II was the only one observed and its λ_{\max} values are in the 440–380 nm range.

Among the many different structures of dimolybdenum complexes described in the literature, one group was of particular interest to us. These are the mixed alkoxide/alcoholate complexes of the general formula $[\text{Mo}_2(\text{OR})_4(\text{ROH})_4]$ with a quadruple Mo–Mo bond [17]. The x-ray crystal structure of these compounds shows that all ligands are equatorially arranged in this type of cluster. No axial ligation of alcohol molecule(s) was found. These data are in good agreement with the fact [9, 11] that $[\text{Mo}_2(\text{OAc})_4]$ does not complex with chiral monoalcohols which act as monodentate ligands and thus does not induce CD.

Although the $[\text{Mo}_2(\text{OAc})_4]$ cluster is thermodynamically stable, in DMSO solution its acetate ligands can be exchanged by other bidentate ligands e.g. 1,3-diols. For approximately 1:1 molar ratio of the ligand to “stock” complex, $[\text{Mo}_2(\text{OAc})_3\text{L}^*]^+ \text{OAc}^-$ is expected to be the only chiral complex, as shown in the equation:



where L^* is a chiral bidentate ligand. So far we have no proof whether 1,3-diols ligate in the newly formed chiral $[\text{Mo}_2(\text{OAc})_3(1,3\text{-diol})]^+ \text{OAc}^-$ complex in a “perpendicular” or “parallel” mode of complexation as it was proposed for complexes of 1,2-diols with the same Mo-cluster [12]. Our efforts to obtain this type of complexes in the crystalline form for x-ray structure determination have failed. However, independent of the complexation mode, 6-membered (“perpendicular” mode) or 7-membered (“parallel” mode) rings formed by the O–C(1)–C(2)–C(3)–O unit and one or two molybdenum atom(s), respectively, should be achiral because a “local symmetry plane” exists for the moieties as shown in Figure 4. Thus, the $[\text{Mo}_2\text{O}_8]$ chromophore is incorpo-

rated into the achiral rings (“achiral second sphere”) and the CD of such complexes should therefore be mainly governed by a “sector rule” and not by a “helicity rule” as for complexes of chiral 1,2-diols. Thus it is comprehensible that the measured $\Delta\varepsilon'$ values for the complexes of the 1,3-diols are relatively small, but nevertheless the signal-to-noise ratio in each case was better than at least 5:1. It is worth to note at this stage that the same rule can be applied in correlating the sign of the CE and the structure of the ligand independent of the type of the complex formed. The existence of both types of complexes (“parallel” and “perpendicular”) might explain the earlier observed time-dependent shift of the band II λ_{\max} value of (6*E*)-6-hydroxyimino-5 β -cholestane-3 β ,5-diol (initial value at 405 nm shifts to 380 nm after 5h) [14].

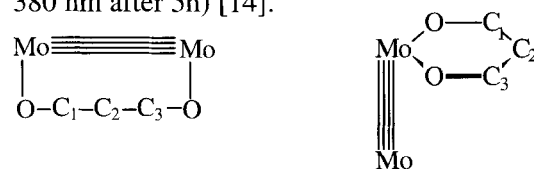


Fig. 4 Modes of complexation of 1,3-diols to $[\text{Mo}_2(\text{OAc})_4]$: “parallel” (left) and “perpendicular” (right)

Conclusions

The results presented in this paper clearly show that not only rigid but also “semi-rigid” and flexible 1,3-diols exchange acetate group(s) of the $[\text{Mo}_2(\text{OAc})_4]$ cluster if they can act as bidentate ligands. Additionally, exchange of the ligand inducing circular dichroism within the absorption bands of the $[\text{Mo}_2\text{O}_8]$ chromophore requires *syn*-parallel orientated hydroxyl groups in the complexing 1,3-diol. Thus, diols with non-parallel orientation of hydroxyl groups or with too distant hydroxyl oxygens do not give CD in the presence of dimolybdenum tetraacetate as it was observed in the case of compounds **13–16** (see Figure 1 and Table 1).

In general, band shapes but not band positions in the CD spectra depend on the type of the 1,3-diol (*prim-sec*, *prim-tert*, *sec-sec*, *sec-tert*). The sign of the band II CE directly reflects the stereochemical surroundings of the 1,3-diol moiety giving information about the absolute configuration.

Ambiguities in the structure–CD correlation are expected, if sectors of opposite sign are occupied by substituents of the same or nearly the same bulkiness. Such a case is exemplified by compound **9** (Figure 2g).

As demonstrated, the applicability of our method covers all types of chiral 1,3-diols i.e. *prim-sec prim-tert*, *sec-sec* and *sec-tert*. In the case of 1,3-diols containing a tertiary hydroxyl group, this fast *in situ* technique exceeds the well-known “dibenzoate method” as it avoids derivatisation, which in the case of tertiary

hydroxyl group is not facile and therefore limits the use of the exciton chirality method. Compared to complexing with Ni(acac)₂, Pr(dpm)₃ or Cupra A, it is more profitable because these methods are limited to *prim-sec* diols [6, 7, 8].

Summarizing our results on circular dichroism of chiral dimolybdenum complexes with rigid, "semi-rigid" and flexible 1,3-diols we can conclude that our technique is supplementary to that of exciton chirality method and especially useful for rigid 1,3-diols with *syn*-parallel arrangement of hydroxyl groups as well as for flexible open-chain diols which predominantly exist in relative *syn*-configuration. Such steric arrangement of two hydroxyl groups cannot give the necessary twisting of the interacting chromophores after derivatisation, making no exciton chirality [4, 18].

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Experimental

CD spectra were measured between 650 and 230 nm at room temperature with a Jobin-Yvon ISA dichrograph Mark III, connected on-line to a PDP-8/e computer, using DMSO solutions in cells of 0.1, 0.2 and 1 cm path length (spectral band width 1.5 nm, sensitivity 5×10^{-6} or 10×10^{-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 diol (1–3 mg) was dissolved in a solution of the stock [Mo₂(OAc)₄] complex (6–7 mg) in DMSO (10 ml) so that the molar ratio of the stock complex to diol was about 1:0.3 to 1:0.7. As the true concentrations of the individual optically active complexes are not known, apparent $\Delta\epsilon'$ values are given, calculated from the total ligand concentration and assuming 100% complexation.

[Mo₂(OAc)₄] and DMSO (Uvasol) were commercially available from Fluka AG and E. Merck, respectively, and were used without further purification.

Compounds **1** [19], **2** [19], **13** [20], **14** [21], **15** [22], **16** [22] were obtained according to the known procedures.

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Address for correspondence:

Dr. Jadwiga Frelek
Institute of Organic Chemistry of
the Polish Academy of Sciences
Kasprzaka 44
01-224 Warsaw, Poland