J. Chil. Chem. Soc., 53, Nº 1 (2008)

THE STEREOSELECTIVE SYNTHESIS OF THE WERNER COMPLEX WITH SUBSTOICHIOMETRIC SUGARS

JOSÉ PARADA, GUILLERMO LARRAZÁBAL, PEDRO AGUIRRE, SANTIAGO ZOLEZZI, CARMEN VEGA, CRISTIAN GARRIDO*

Departamento de Química Inorgánica y Analítica, Facultad de Ciencias Químicas y Farmacéutica,
Universidad de Chile. Casilla 233. Fax 7370567.
(Received: 14 March 2007 - Accepted: 26 November 2007)

ABSTRACT

A tetranuclear complex of Co(III) with hydroxo bridges, so-called "Werner Complex", was synthesized in the presence of several sugars (**1-8**) with partial resolution of this complex. The sugars in 10 mol % with respect to Co(III) induce maximum resolution of the Werner complex.

Keywords: Werner complex, hexol, sugar, Co(III), circular dichroism, dd* transition dd*, enantioselectivity.

INTRODUCTION

The present work is an example of induction of chirality from a chiral "sugar" ligand to the inorganic Werner complex (Fig.1). The Werner complex is a classic example of a chiral compound that does not contain carbon and was one of the first examples of chirality in octahedral complexes.[1, 2]

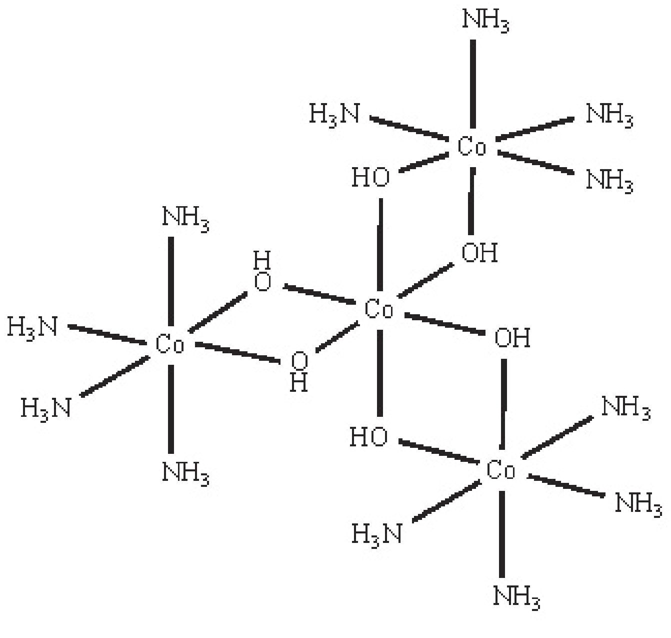
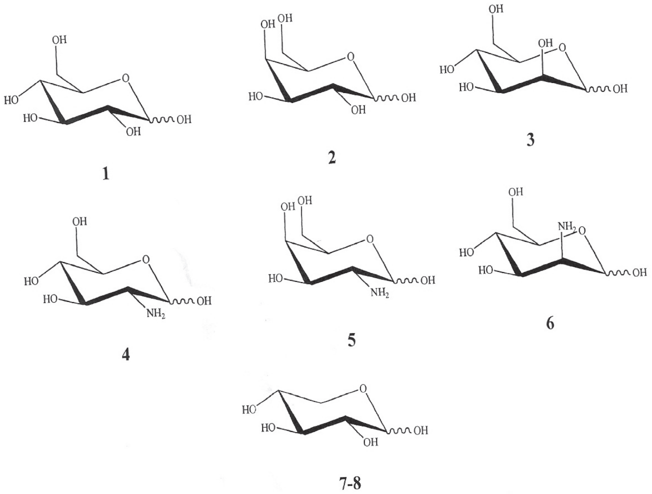


Fig. 1. Structure of Δ-$[Co[(OH)_2Co(NH_3)_4]_3]^{6+}$.

In an earlier publication[2] we showed that sugars induce stereoselective synthesis of the Werner complex, also known as "hexol". We have now extended the work by synthesizing tetranuclear complex of Co(III) in presence of several sugars (Scheme 1, **1-8**).



Sheme 1

RESULTS AND DISCUSSION

Relationship between sugar and hexol configurations

The reaction of cis-diaquotetramine Co(III) with ammonia gives the tetranuclear dodecamino-μ-hexol-tetracobalt(III) complex (Fig. 1).

$$4[Co(NH_3)_4(H_2O)_2]^{3+} + 6OH^- \rightarrow [Co[(OH)_2Co(NH_3)_4]_3]^{6+} + 4NH_3 + 8H_2O$$

These complexes have a central Co(III) ion surrounded by six OH^- with D_3 symmetry that operate as bridges to three tetramino Co(III) ions (Fig. 1). This racemic tetranuclear complex is usually called hexol. The Δ- and Λ- isomers have been separated by using potassium antimonyl tartrate.[4]

The visible absorption spectrum of the crystals initially obtained in the syntheses in the presence of sugars **(1-8)**, shows two absorption bands: one at 626 nm is assigned to the $^1T_{1g}$ state electronic transitions of the CoO_6 chromophore. The second absorption band, at 509 nm, corresponds to the $^1T_{1g}$ state of the CoN_4O_2 chromophore (Fig. 2).[5]

The circular dichroism (CD) spectra, Fig. 2, shows two signals of opposite sign: one at 685 nm, positive, and another of greater intensity at 614 nm, both under the first absorption band of hexol. At 509 nm there is a positive signal corresponding to the second absorption band (Fig. 2).

e-mail: jparada@ciq.uchile.cl.

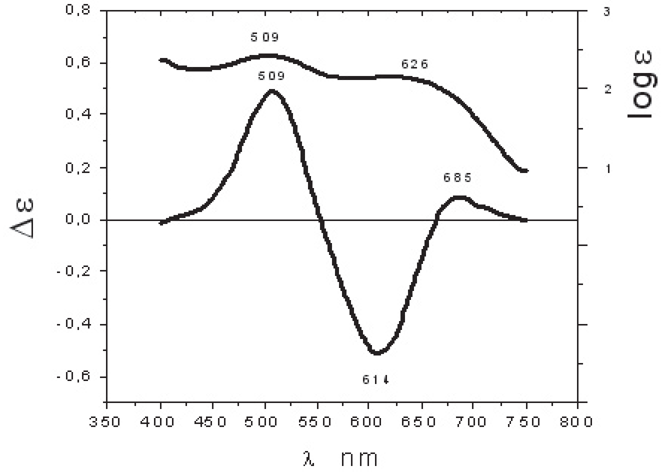


Fig.2. Absorption and circular dichroism spectra of Δ-hexol synthesized in the presence of D-galactosamine.

In order to define the stereoselectivity induced by the sugars (**1-8**) it is necessary to assign configurations by monitoring the CD signals under the absorption of the CoO$_6$ chromophore. The $^1T_{1g}$ state of Co(III), with D$_3$ symmetry, splits into two states, ^1E and $^1A_2$, where the energetic sequence is always $^1E > {}^1A_2$. The ^1E state is dominant, as regards rotatory strength, as reflected in the magnitude of the CD signal, which is greater than for the $^1A_2$ state.[6]

The $^1A_1 \rightarrow {}^1E$ transitions in trigonal compounds of Co(III), such as $[Co(ox)_3]^{3-}$ and $[Co(acac)_3]$, which correspond to the chromophore, CoO$_6$, have a positive Cotton effect, whereas the $^1A_1 \rightarrow {}^1A_2$ transition leads to a negative Cotton effect when tris-chelate complexes of Co(III) have the Λ configuration.[7] It is then possible to assign the predominant Δ configuration to the hexol crystals obtained as a sulphate in the presence of a D-sugar, whereas the Λ configuration is dominant in complexes formed in the presence of an L-sugar (Table 2).

Table 1. Elemental analyses of $[Co[(OH)_2Co(NH_3)_4]_3](SO_4)_3{\cdot}9H_2O\ H_2O$, synthesized in the presence of the sugar.

Sugar	**%N**	**%H**	**%S**	**%Co**
D-glucose (**1**)	17.2	6.3	9.4	24.0
D-galactose (**2**)	16.7	6.5	10.3	24.2
D-mannose (**3**)	16.5	5.8	10.3	23.2
D-glucosamine (**4**)	16.6	6.4	9.4	23.8
D-galactosamine (**5**)	16.8	6.3	10.3	23.7
D-mannosamine (**6**)	16.5	6.2	10.1	23.7
D-xylose (**7**)	17.3	5.9	9.8	24.4
L-xylose (**8**)	16.7	6.0	10.1	23.8
Calculated	16.9	6.1	9.7	23.8

Factors which control hexol configuration

Evidence regarding the predominant isomer and stereoselectivity in the synthesis of hexol in the presence of different substoichiometric sugars, relative to Co(III), is shown in Table 2.

Table 2. Predominant isomer and percentage of resolution (stereoselectivity) of hexol synthesized in the presence of a sugar.

	Predominant hexol isomer a)	Percentage of resolution (enantoselectivity)		
		5 mol % b)	10 mol % b)	20 mol % b)
D-glucose (**1**)	Δ	15.9	17.8	10.2
D-galactose (**2**)	Δ	14.7	15.2	11.0
D-mannose (**3**)	Δ	15.3	19.5	12.5
D-glucosamine (**4**)	Δ	17.3	25.4	17.3
D-galactosamine (**5**)	Δ	16.7	21.8	15.1
D-mannosamine (**6**)	Δ	16.6	23.1	14.1
D-xylose (**7**)	Δ	10.6	14.0	6.3
L-xylose (**8**)	Λ	10.7	14.6	6.4

a) Determined by signals sequence and sign of DC spectra. **b)** Percentage in mol with respect to Co(III).The highest optical activity of the synthesized hexol is obtained when the percentage of the sugar is of the order 10 mol % with respect to Co(III) in the formation of the hexol (see Table 2). An increase in the amount of sugar from 10 mol % to 20 mol % decreases the stereoselectivity of the hexol. The lower amounts of resolution and of formation of hexol the as amount of sugar in the reaction media is increased can be associated with formation of mononuclear complexes of the type $[Co(NH_3)_4sugar]^{3+}$ [8], that are formed in appreciable amounts as the amount of sugar is increased. This conclusion is confirmed by the absorption and CD spectra of the reaction mixture as samples of $[Co(NH_3)_4sugar]^{3+}$ are isolated.[8] Formation of these last complexes would compete with interaction of the sugar and the Werner complex, and would reduce nonbonding transmission of the sugar chirality to the hexol, thus lowering the resolution (Table 2). On the other hand, interactions of the Werner and sugar species would decrease with low sugar, and synthesis of hexol in the absence of sugar (a chiral auxiliary) leads to the racemic complex. We note that the is slated complex does not contain a sugar.

Amounts of % resolution increase in going from an hexose (**1-3**) to an amino-hexose (**4-6**) (Table 2). We postulate a relation ship involving the strength of the coordinating group of the sugar (NH$_2$ > OH), and the degree of stereoselectivity. These effects can be due to formation of a complex by an interaction between the sugar and hexol, of configuration, Δ or Λ, which is formed in small amount and remains in solution. In this interaction the reacting group of the sugar may intervene directly, and be coordinated to some extent with hexol. We also observed a decrease in stereoselectivity in going from an hexose (**1-6**) to a pentose (**7-8**), which is probably a consequence of a direct relation ship between the number of asymmetric centers of the sugar and its capacity for optical resolution of hexol (Table 2).

The D or L configuration of the sugar determines the configuration (Δ or Λ) of the hexol (Table 2), because of interactions of the chiral sugar with the preferred form of hexol.

Two experimental observations are relevant in causing this stereoselective behaviour by the sugars. We observed that on adding a crystal of racemic hexol sulphate to a solution of an aminosugar (**4-6**), e.g., D-galactosamine (**6**), the Λ isomer is solubilized, as shown by the CD spectrum of the solution. On the other hand, if the solution remaining after separating the crystal of sulphate is enriched with the isomer the Δ isomer, in this case, of the D-glucosamine (**4**), then the second portion of crystals will be enriched with the Λ isomer.

We postulate an interaction between one optical isomer of hexol, in this case the Λ isomer, with the D-sugar, which will remain in solution, as a “Werner-sugar” species, and then the hexol that crystallizes will contain more of the Δ isomer. With the L-sugar the opposite process takes place. In these compounds of the Werner-sugar type, the sugar transmits its intrinsic chirality, which depends on the number of asymmetric centers, to the coordinating group of the complex.

Association between optical isomers of Werner complexes with sugars is understandable as a stereoselective association by hydrogen bonding between the carbohydrate OH groups and the bridging OH groups of hexol, whose space disposition is helical, in agreement with crystallographic data.[9]

CONCLUSION

The presence of substoichiometric amounts of sugars (**1-8**) in the synthesis of Werner complex, are able to produce preferently one of the enantiomers. This is not observed in absence of these sugars; being aminosugars (**4-6**) those that origin a complex with a greater resolution.

EXPERIMENTAL

Synthesis of hexol ($[Co[(OH)_2Co(NH_3)_4]_3](SO_4)_3 \cdot 9H_2O$) in presence of sugars

An aqueous solution of $[Co(NH_3)_4(H_2O)_2]_2(SO_4)_3 \bullet 3H_2O$ (1 mmol) prepared as indicated in the literature[3] in 2 mL distilled water was mixed with a solution of the sugar (**1-8**) dissolved in 15 mL of O.2 M NH_3 at room temperature with strong agitation. The sugar concentrations were $6.7x10^{-3}$ M, $1.3x10^{-2}$ M and $2.7x10^{-2}$ M and correspond to 5%, 10% and 20% by weight of the sugar with respect to Co(III). The solution was kept for 2 hrs at 30 ºC, and violet crystals of the Werner complex ($[Co[(OH)_2Co(NH_3)_4]_3](SO_4)_3 \cdot 9H_2O$), separated and were filtered off and washed with water and ethanol. The crystals were dried from 24 hrs over anhydrous $CaCl_2$.

Spectral measurements

The absorption spectra (Fig.2) were measured on a Unicam UV3 spectrometer and the circular dichroism (CD) spectra were obtained on a Jobin-Ivon model CD 6 dichrograph, with 20 mg of sample in 10 mL of 0.1 M $HClO_4$ ($2x10^{-3}$ M) and a 1 cm cell.

The absorption and circular dicroism (CD) spectra in the visible region gave the absolute configuration of the Werner complex (hexol) formed in the presence of different sugars (**1-8**). We calculated the percentage resolution from the maxima in the CD spectra ($\Delta\varepsilon$ max) at 685 nm (Fig. 1), with the value of $\Delta\varepsilon$ from the literature.[4]

The cobalt content of the Werner complex was estimated by atomic absorption spectroscopy, with a Perkin Elmer 1100B spectrophotometer.

Elemental analyses, C, H and S of solid Werner complex were made on a Fisons-Carlo Erba EA 1108 micro-analyzer (Table 1).

ACKNOWLEDGEMENTS

The authors thank Dr C.A. Bunton for suggestions. The authors acknowledge financial support from the Research Department of "Universidad de Chile", Project D.I. 12 03/12-2.

REFERENCES

1. A. Werner, *Ber.* **47**, 3087 (1914).
2. a) J. Parada, G. Larrazabal, P. Aguirre, *J. Chil. Chem. Soc.* **50**, 477 (2005). b) G. Larrazabal, S. Bunel, C. Ibarra, J. Parada, *Bol. Soc. Chil. Quím.* **47**, 73 (2002).
3. A.M. Greenaway, R.J. Lancashire, *J.Chem.Ed.* **59**, 419 (1982).
4. a) H.A. Goodwin, E. C. Gyarfas, D.P. Mellor, *Aust. J. Chem.* **11**, 426 (1958). b) T. Kudo, Y. Shimura, *Bull. Chem. Soc Japan* **52**, 1648 (1979).
5. a) J. Parada, C. Ibarra, N. Gillitt, C.A. Bunton, *Polyhedron* **24**, 1002 (2005). b) J. Parada, G. Larrazabal, *Polyhedron* **23**, 1341 (2004). c) J. Parada, S. Bunel, C. Ibarra, G. Larrazábal, E. Moraga, N. Gillitt, C.A. Bunton, *Polyhedron* **21**, 2215 (2002).
6. S.F. Mason, J.W. Wood, *Chem.Commun.* 209 (1967).
7. a) R.D. Peacock, B. Stewart, *Coord. Chem. Rev.* **46**, 129 (1982). b) N.C. Moucharafiech, P.G. Eller, J.A. Bertrand, D.J. Royer, *Inorg. Chem.* **17**, 1220 (1978).
8 S. Bunel, C. Ibarra, *Polyhedron* **4**, 1537 (1985).
9. a) D.A. Dixon, R.E. Marsh, W.P. Schaefer, *Acta Cryst.* **B 34**, 807 (1978). b) I. Bernal, J. Cetrullo, S. Berhane, *J. Coord. Chem.* **53**, 185 (2000).