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Raman spectroscopic evidence for bent metallocene fragments $[M(Cp)_2]^{2+}$

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Raman spectroscopy was used as a very simple and convenient tool for the detection of bent metallocene fragments $[M(Cp)_2]^{2+}$ (Cp = η^5-cyclopentadienyl ring; M = early transition metal) both in solid state and in solution. The rules were formulated and tested on the group of titanium complexes containing one or two η^5-bonded cyclopentadienyl rings, as well as on a series of model α-amino acid complexes of antitumour active titanocene and vanadocene dichlorides. Copyright © 2004 John Wiley & Sons, Ltd.

KEYWORDS: bent metallocene fragment; Raman spectroscopy; titanocene dichloride; amino acid complexes

INTRODUCTION

Bent metallocenes of early transition metals have been studied extensively after the discovery of their antitumour properties.[1,2] Several bent metallocene complexes of amino acids and various DNA building blocks, particularly with titanocene, vanadocene and molybdenocene dichlorides ($[M(Cp)_2Cl_2]$, M = Ti, V, Mo), have been synthesized and characterized, with a view, in part, to explain the mechanism of antitumour action of the bent metallocenes, which is still not fully understood.[3–12] These complexes contain either the bent metallocene fragment $[M(Cp)_2]^{2+}$, which comprises two η^5-bonded cyclopentadienyl rings and plays a crucial role in the antitumour action,[3,4,8,9] or, less commonly, the monocyclopentadienyl fragment $[M(Cp)]^{3+}$.[4,7] Despite many spectroscopic (such as multinuclear NMR, electron paramagnetic resonance, UV–Vis), X-ray crystallography and other methods (capillary electrophoresis[7]) applicable for studying the model complexes containing relevant bioligands and their behaviour in the aqueous solution, it is not an easy task to decide unambiguously, whether they contain $[M(Cp)_2]^{2+}$ or $[M(Cp)]^{3+}$ fragments.[3–9] This problem arises from the fact that in many cases it is not simple to follow the life-path of bent metallocene or its consecutive metabolites or even to isolate, separate and further characterize resulting compounds, in particular when experimental conditions are close to physiological conditions (pH 6–7). This situation commonly gives rise to complex mixtures of structurally similar fragments.[7]

In our research group we have been interested recently in the synthesis and structural characterization of model α-amino acid complexes of antitumour active titanocene[13] and vanadocene dichlorides.[14] We have found that Raman spectroscopy can be used as a very simple and convenient probe for the detection of bent metallocene fragments $[M(Cp)_2]^{2+}$ in such complexes. Our findings prompted us to formulate simple rules for determination of the presence of the bent $[M(Cp)_2]^{2+}$ units. Applicability of these rules was tested on a series of titanium- and vanadium-based compounds, largely on $[M(Cp)_2Cl_2]$ α-amino acid complexes.

EXPERIMENTAL

Materials

All of the manipulations were performed under a dry, oxygen-free argon atmosphere using standard Schlenk and glovebox techniques. Solvents were purified by standard methods and freshly distilled prior to use. Complex $[Nb(Cp)_2Cl_2]$

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was purchased from Fluka and was purified by sublimation at reduced pressure. All other complexes were prepared according to literature methods: $[Ti(Cp)X_3]$ ($X = Cl$, Br, I),[15] $[M(Cp)_2X_2]$ ($M = Ti$, Zr; $X = Br$ or I),[16] $[M(Cp)_2F_2]$ ($M = Ti$, Zr),[17] $[Ti(Cp)F_3]$,[17] $[V(Cp)_2Cl_2]$,[18] $[V(Cp)Cl_3]$,[19] $[Ti(Cp)_{0.31}O_{0.30}(OH)]$,[20] $[Ti(Cp)_2Cl(CH_3CN)][FeCl_4]$,[21] [Ti (Cp)O(2-MeAla)]$_n$,[22] $[[V(Cp)_2A]X]$ (A = glycine, L-alanine, L-valine; $X = Cl, PF_6$).[14]

Synthesis of $[Nb(Cp)_2Br_2]$

A 1 g (3.40 mmol) quantity of sublimed niobocene dichloride was dissolved in 120 ml of dichloromethane. To the vigorously stirred solution, 0.24 ml (2.47 mmol) of boron tribromide was added. After 20 min of stirring, the reaction mixture was evaporated to dryness at reduced pressure. The solid residue was washed by 3 × 10 ml of n-hexane and sublimed at 220 °C, affording 0.42 g (32%) of brown crystals. Anal. Found: C, 31.0; H, 2.5; Br, 41.8%. Calc. for $C_{10}H_{10}Br_2Nb$.: C, 31.4; H, 2.6; Br, 41.7%.

Synthesis of $[V(Cp)_2Br_2]$

A 0.28-ml (2.91 mmol) aliquot of boron tribromide was added to a vigorously stirred solution of 1 g (3.96 mmol) of vanadocene dichloride in 150 ml of dichloromethane. After 20 min of stirring the reaction mixture was evaporated to dryness at reduced pressure. The residual solid was extracted first by n-hexane to remove impurities and then by dichloromethane. The dichloromethane extract was cooled at −78 °C to give dark-green crystals, which were separated and dried *in vacuo*. Yield is 0.5 g (37%). Anal. Found: C, 35.2; H, 2.99; Br, 46.6%. Calc. For $C_{10}H_{10}Br_2V$: C, 35.5; H, 2.98; Br, 46.7%.

Synthesis of $[V(Cp)Br_3]$

To a stirred solution of 0.83 g (3.7 mmol) of cyclopentadienyl vanadium(IV) trichloride in 40 ml of dichloromethane, 3.0 g (12 mmol) of BBr_3 was added via a septum. The colour of the solution changed immediately from violet to dark green. After 20 min of stirring, the reaction mixture was evaporated to dryness at reduced pressure. The crude solid product was washed with 2 × 10 ml of n-hexane and sublimed at 105 °C and 10^{-4} Pa to yield 1.20 g (88%) of dark-green crystals. Anal. Found: C, 16.71; H, 1.32%. Calc. for $C_5H_5Br_3V$: C, 16.87; H, 1.41%.

Syntheses of α-amino acid complexes $[Ti(Cp)_2A_2]Cl_2$

The titanocene amino acid complexes were prepared by modification of the published procedure:[10] $[Ti(Cp)_2Cl_2]$ (1.00 g, 4 mmol) was stirred with the appropriate α-amino acid (8 mmol) and water (8 mmol) in 3–5 ml of methanol until the orange precipitate was formed (30 min to 3 h). Crystalline material was filtered off, washed several times with CH_2Cl_2 and vacuum dried to yield 65–95% of analytically pure products.

Spectroscopic measurements

Raman spectra were recorded on an FT spectrometer Bruker IFS-55 with FRA 106 FT Raman equipment using a diode-pumped Nd : YAG laser (1064 nm) and a nitrogen-cooled Ge detector (power of incident light for solid-state measurements, 100 mW mm^{-2}; and for saturated solution measurements, 150 mW mm^{-2}; resolution usually 2 cm^{-1}).

RESULTS AND DISCUSSION

Considering assignments of vibrational modes in the spectra of the parent complexes $[M(Cp)_2X_2]$ and monocyclopentadienyl complexes $[M(Cp)X_3]$ (M = early transition metal; X = halide),[23,24] we have found that for the evidence of the bent $[M(Cp)_2]^{2+}$ fragments the following two easily identifiable vibrations are of interest: ring breathing of the η^5-bonded cyclopentadienyl ring and a_1 symmetric cyclopentadienyl ring tilting of the C_{2v} bent metallocene fragments $[M(Cp)_2]^{2+}$ (Fig. 1). The former vibration gives rise to prominent strongly polarized Raman bands at ~1100 cm^{-1}. This peak occurs in any complex containing one or more η^5-bonded cyclopentadienyl rings and it can be considered the most evident η^5-bonded cyclopentadienyl ring frequency.[25] For each cyclopentadienyl complex its frequency varies slightly in dependence on the nature and number of other ligands, as well as on the central metal atom. For example, the ring breathing frequency differences for $[Ti(Cp)X_3]$ and $[Ti(Cp)_2X_2]$ complexes average 6 cm^{-1} (Table 1). The latter vibration—a_1 symmetric ring tilting—is significant only for complexes containing the C_{2v} bent metallocene fragment $[M(Cp)_2]^{2+}$. The a_1 symmetric ring tilting mode shows a strongly polarized peak of very high intensity in Raman spectra of such complexes. Although the frequency of this peak is expected to be nearly constant for a certain metal, its dependence on halogen atoms can be observed. As shown in Table 1, its frequency ranges in a narrow interval up to 10 cm^{-1} for a certain metal. Following the previous considerations, simple rules can be formulated. If the Raman spectrum shows:

(i) one peak at ~1100 cm^{-1} and a peak at ~270 cm^{-1}, then the $[M(Cp)_2]^{2+}$ fragment is present,

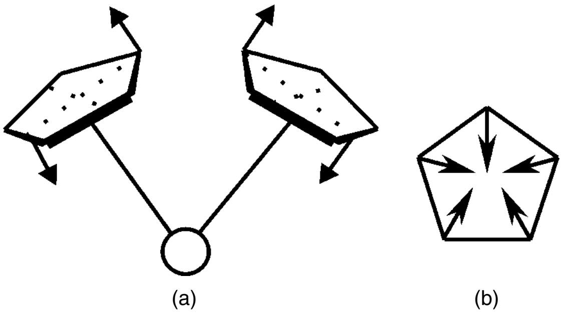

Figure 1. Graphical representation of the a_1 ring tilting mode (a) and the ring breathing vibrational modes (b).

Table 1. Wavenumbers (cm^{-1}) and relative intensities (in parentheses) of ring breathing and a_1 tilting modes for [M(Cp)$_2$Cl$_2$] and [M(Cp)Cl$_3$] complexes in solid state

Compound	Ring breath	a_1 Ring tilt	Compound	Ring breath	a_1 Ring tilt
Ti(Cp)$_2$F$_2$	1132 (5.6)	259 (10)	Zr(Cp)$_2$I$_2$	1127 (10)	272 (8.2)
Ti(Cp)$_2$Cl$_2$	1134 (8.1)	257 (10)	Nb(Cp)$_2$Cl$_2$	1125 (7.1)	295 (10)
Ti(Cp)$_2$Br$_2$	1132 (7.8)	268 (10)	Nb(Cp)$_2$Br$_2$	1127 (6.4)	303 (10)
Ti(Cp)$_2$I$_2$	1131 (7.6)	267 (10)	Ti(Cp)F$_3$	1138 (10)	—
V(Cp)$_2$Cl$_2$	1131 (5.9)	295 (10)	Ti(Cp)Cl$_3$	1128 (10)	—
V(Cp)$_2$Br$_2$	1129 (4.8)	296 (10)	Ti(Cp)Br$_3$	1126 (10)	—
Zr(Cp)$_2$F$_2$	1127 (7.6)	268 (10)	Ti(Cp)I$_3$	1124 (10)	—
Zr(Cp)$_2$Cl$_2$	1128 (10)	268 (9.9)	V(Cp)Cl$_3$	1122 (10)	—
Zr(Cp)$_2$Br$_2$	1127 (8.3)	274 (10)	V(Cp)Br$_3$	1122 (10)	—

(ii) one peak at ~1100 cm^{-1} and no peak at ~270 cm^{-1}, then the [M(Cp)]$^{3+}$ fragment is present,

(iii) two peaks at ~1100 cm^{-1} and a peak at ~270 cm^{-1}, then the complex contains both the bent [M(Cp)$_2$]$^{2+}$ metallocene and [M(Cp)]$^{3+}$ fragments.

Applicability of these rules was tested on a series of titanium cyclopentadienyl complexes: [Ti(Cp)$_2$A$_2$]Cl$_2$ (A = glycine, *N*-methylglycine, 2-methylalanine, L-alanine, D-alanine, D,L-alanine, L-phenylalanine, D-phenylalanine, D,L-phenylalanine, L-valine, D-valine, D,L-norvaline, L-leucine, L-isoleucine, D,L-norleucine, L-cysteine, L-*S*-methylcysteine, L-*S*-phenylcysteine, L-methionine, D-methionine, ^{13}C-glycine, *N*-d_3-glycine); [Ti(Cp)O(2-MeAla)]$_n$, [Ti(Cp)$_{0.31}$O$_{0.30}$(OH)], [Ti(Cp)$_2$Cl(CH$_3$CN)][FeCl$_4$]) and vanadocene amino acid complexes [V(Cp)$_2$A]X (A = glycine, L-alanine, L-valine; X = Cl, PF$_6$); and an equimolar mixture of [Ti(Cp)$_2$Cl$_2$] and [Ti(Cp)Cl$_3$] complexes in molar ratio 1 : 1 (Table 2).

Solid-state as well as aqueous solution Raman spectra of the [Ti(Cp)$_2$A$_2$]Cl$_2$ amino acid (Fig. 2) and [Ti(Cp)$_2$(Cl)CH$_3$CN]-[FeCl$_4$] complexes show one peak at ~1130 cm^{-1} and a peak at ~265 cm^{-1}, both of high intensity, hence they contain

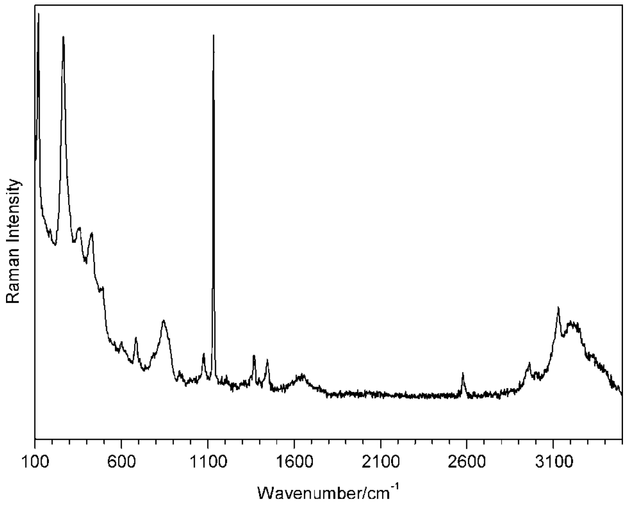

Figure 2. Raman spectrum of aqueous solution of the complex [Ti(Cp)$_2$(L-Cys)$_2$]Cl$_2$.

Table 2. Wavenumbers (cm^{-1}) and relative intensities (in parentheses) of ring breathing and a_1 tilting modes for the tested complexes

Compound	Ring breath	a_1 Ring tilt
[Ti(Cp)$_2$(Gly)$_2$]Cl$_2$	1132 (7)	268 (10)
[Ti(Cp)$_2$(*N*-MeGly)$_2$]Cl$_2$	1131 (10)	261 (8.3)
[Ti(Cp)$_2$(2-MeAla)$_2$]Cl$_2$	1132 (3.5)	266 (10)
[Ti(Cp)$_2$(L-Ala)$_2$]Cl$_2$	1132 (7.9)	264 (10)
[Ti(Cp)$_2$(D-Ala)$_2$]Cl$_2$	1133 (8.5)	262 (10)
[Ti(Cp)$_2$(D,L-Ala)$_2$]Cl$_2$	1134 (5.6)	270 (10)
[Ti(Cp)$_2$(L-Phe)$_2$]Cl$_2$	1132 (8.5)	264 (10)
[Ti(Cp)$_2$(D-Phe)$_2$]Cl$_2$	1134 (7.9)	263 (10)
[Ti(Cp)$_2$(D,L-Phe)$_2$]Cl$_2$	1134 (8.0)	261 (10)
[Ti(Cp)$_2$(L-Val)$_2$]Cl$_2$	1134 (8.1)	261 (10)
[Ti(Cp)$_2$(D-Val)$_2$]Cl$_2$	1134 (10)	260 (7.5)
[Ti(Cp)$_2$(D,L-Nva)$_2$]Cl$_2$	1136 (4.0)	272 (10)
[Ti(Cp)$_2$(L-Leu)$_2$]Cl$_2$	1133 (10)	261 (7.5)
[Ti(Cp)$_2$(L-Ile)$_2$]Cl$_2$	1128 (5.8)	264 (10)
[Ti(Cp)$_2$(D,L-Nle)$_2$]Cl$_2$	1132 (8.1)	261 (7.1)
[Ti(Cp)$_2$(L-Cys)$_2$]Cl$_2$	1132 (7.5)	267 (10)
[Ti(Cp)$_2$(L-*S*-MeCys)$_2$]Cl$_2$	1134 (6.6)	268 (10)
[Ti(Cp)$_2$(L-*S*-PheCys)$_2$]Cl$_2$	1132 (10)	266 (8.1)
[Ti(Cp)$_2$(L-Met)$_2$]Cl$_2$	1132 (4.9)	261 (10)
[Ti(Cp)$_2$(D-Met)$_2$]Cl$_2$	1132 (5.1)	260 (10)
[Ti(Cp)$_2$(^{13}C-Gly)$_2$]Cl$_2$	1132 (5.0)	270 (10)
[Ti(Cp)$_2$(*N*-d_3-Gly)$_2$]Cl$_2$	1132 (8.0)	263 (10)
[Ti(Cp)$_2$Cl(CH$_3$CN)][FeCl$_4$]	1131 (6.5)	268 (6.7)
[V(Cp)$_2$(Gly)]Cl	1131 (9.1)	287 (10)
[V(Cp)$_2$(L-Ala)]Cl	1132 (10)	280 (8.0)
[V(Cp)$_2$(L-Val)]Cl	1132 (10)	283 (7.4)
[V(Cp)$_2$(Gly)]PF$_6$	1132 (10)	288 (9.9)
[V(Cp)$_2$(L-Ala)]PF$_6$	1132 (9.2)	284 (10)
[V(Cp)$_2$(L-Val)]PF$_6$	1135 (8.4)	279 (10)
[Ti(Cp)$_{0.31}$O$_{0.30}$(OH)]	1128 (10)	—
[Ti(Cp)O(2-MeAla)]$_n$	1129 (10)	—

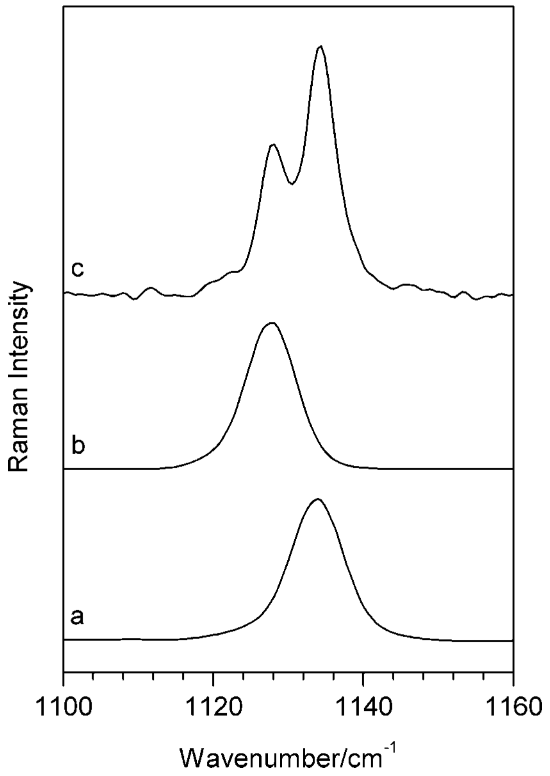

Figure 3. Ring breathing vibrations of $[Ti(Cp)_2Cl_2]$ (a), $[Ti(Cp)Cl_3]$ (b) and an equimolar chemical mixture of $[Ti(Cp)_2Cl_2]$ and $[Ti(Cp)Cl_3]$ (c).

the bent $[Ti(Cp)_2]^{2+}$ metallocene fragment. The vanadocene amino acid complexes contain bent fragment $[V(Cp)_2]^{2+}$, because their spectra show one peak at ~1130 cm^{-1} and a peak at ~280 cm^{-1}. In the case of the $[Ti(Cp)O(2\text{-}MeAla)]_n$ and $[Ti(Cp)_{0.31}O_{0.30}(OH)]$ complexes, one peak was found at 1129 cm^{-1} and 1128 cm^{-1}, respectively, giving evidence of the $[Ti(Cp)]^{3+}$ fragment. As expected, Raman spectra of an equimolar mixture of $[Ti(Cp)_2Cl_2]$ and $[Ti(Cp)Cl_3]$ show two peaks at 1134 and 1129 cm^{-1} and one peak at 259 cm^{-1} (Fig. 3). Thus, in terms of the rules, it is possible to decide whether reactions of metallocene dihalides are accompanied by full η^5-bonded cyclopentadienyl ring elimination or the bent metallocene fragments $[M(Cp)_2]^{2+}$ remain unaffected. In particular, this method allows the bent metallocene fragments $[M(Cp)_2]^{2+}$ to be detected in aqueous solutions under conditions that are very close to physiological conditions. It is evident that Raman spectroscopy is a very simple and sensitive tool for the detection of bent metallocene fragments $[M(Cp)_2]^{2+}$, both in solid state and in solution.

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REFERENCES

1. Köpf H, Köpf-Maier P. *Angew. Chem. Int. Ed.* 1979; **18**: 477.
2. Köpf H, Köpf-Maier P, Hesse B. *J. Cancer Res. Clin. Oncol.* 1980; **96**: 43.
3. Köpf-Maier P. *Met. Complexes Cancer Chemother.* 1993; 259.
4. Murray JH, Harding MM. *J. Med. Chem.* 1994; **37**: 1936.
5. Prout K, Critchley SR. *Acta Crystallogr.* 1977; **B33**: 456.
6. Cardin CJ, Roy A. *Inorg. Chim. Acta* 1985; **107**: L37.
7. Wittrisch H, Sröer HP, Vogt J, Vogt C. *Electrophoresis* 2000; **19**: 3012.
8. Kuo LY, Lin AM, Marks TJ. *Metal Ions Biol. Syst.* 1996; **33**: 53.
9. Lovejoy DB, Richardson DR. *Exp. Opin., Invest. Drugs* 2000; **9**: 6.
10. Klapötke TM, Köpf H, Tornieporth-Oetting IC, White PS. *Organometallics* 1994; **13**: 3628.
11. Klapötke TM, Köpf H, Tornieporth-Oetting IC, White PS. *Angew. Chem.* 1994; **14**: 106.
12. Tornieporth-Oetting IC. *Organometallics* 1995; **14**: 1632.
13. Bína R, Císařová I, Pavlík I. *Appl. Organometal. Chem.* 2004; **18**: 71.
14. Vinklárek J, Paláčková H, Honzíček H. *Collect. Czech. Commun.* 2004; **69**: 811.
15. Herrmann WA, Zybill CE. *Synthetic Methods of Organometallic and Inorganic Chemistry*, Herrmann WA, Saltzer A (eds), vol. 1. Georg Thieme: Stuttgart, 1996; 94.
16. Zybill CE. *Synthetic Methods of Organometallic and Inorganic Chemistry*. Herrmann WA, Saltzer A (eds), vol. 8. Georg Thieme: Stuttgart, 1997; 31–33.
17. Murphy EF, Murugavel R, Roesky HW. *Chem. Rev.* 1997; **97**: 3425.
18. King RB. *Organometallic Synthesis*, vol. 1. Academic Press: New York, 1965; 75–78.
19. Oswald L, Thiele K-H. *Z. Anorg. Allg. Chem.* 1976; **423**: 231.
20. Toney JH, Marks TJ. *J. Am. Chem. Soc.* 1985; **107**: 947.
21. Meirim MG., Neuse EW. *Trans. Met. Chem.* 1984; **9**: 337.
22. Carraher CE Jr, Tisinger LG, Tisinger WH. *J. Macromol. Chem.* 1985; 177.
23. Balduci G, Bencivenni L, De Rosa G, Gigli R, Martini B, Nunziante Cesaro S. *J. Mol. Struct.* 1980; **64**: 163.
24. Spoliti M, Bencivenni L, Farina A, Martini B, Nunziante Cesaro S. *J. Mol. Struct.* 1980; **65**: 105.
25. Diana E, Rossetti R, Stanghellini PL, Kettle SFA. *Inorg. Chem.* 1997; **36**: 382.