Inorganica Chimica Acta 362 (2009) 1781–1786

Contents lists available at ScienceDirect

Inorganica Chimica Acta

journal homepage: www.elsevier.com/locate/ica

Bismuth(III) complexes with tetra-pyridylmethyl-cyclen

Jean-François Morfin, Raphaël Tripier, Michel Le Baccon, Henri Handel *

UMR CNRS 66521 'Chimie, Electrochimie Moléculaires et Chimie Analytique', 6, Avenue Victor Le Gorgeu, 29200 Brest, France

ARTICLE INFO

Article history:
Received 3 June 2008
Received in revised form 16 July 2008
Accepted 22 August 2008
Available online 28 August 2008

Keywords:
Cyclen
Bismuth
NMR spectroscopy
X-ray diffraction

ABSTRACT

Bimuth(III) complexes with 1,4,7,10-tetrakis(2-pyridylmethyl)-1,4,7,10-tetraazacyclododecane have been prepared in dichloromethane and ethanol and investigated. These complexes have been characterized structurally by X-ray diffraction and NMR-2D studies. They present different coordination scheme depending on the reaction conditions: according to the nature of solvent, bismuth coordinates from six to eight nitrogen atoms and forms in the solid state a chiral structure which is maintained in solution.

1. Introduction

The coordination chemistry of bismuth(III) is rather sparse when compared with that of other metals. However, recently bismuth complexes have attracted much attention due to their potential applications in medicine: ^{212}Bi or ^{213}Bi are alpha-emitting isotopes and show great promise in radio-immunotherapy when attached to monoclonal antibodies using a complexing ligand. The half-life time of ^{213}Bi is very attractive (46 min) for a cancer therapy, but consequently a successful use of this isotope necessitates not only a thermodynamically and kinetically stable complex but also a chelating agent able to associate rapidly the Bi(III) ion. A variety of coordination modes have been reported in complexes involving this ion well known to assume various high coordination number with irregular geometries: six to ten-coordinate environment are known [1], according to the character of multi-dentate ligand system, cation–anion interactions and nature of the solvent. In addition bismuth(III) metal ions hydrolyze very easily in aqueous solutions and a relatively strong acid medium is required to avoid hydrolysis products [2]. However, bismuth(III) exhibits a high affinity for nitrogen-donor ligands, so the incorporation of this heteroatom into the host framework should enhance the complex stability [3].

Tetraazacycloalkanes bearing pyridylmethyl arms have been previously used for bismuth coordination [4]. Recently, the DNA-binding properties and the antitumor activity of Bi(III) complex with 1,4,7,10-tetrakis(2-pyridylmethyl)-1,4,7,10-tetraazacyclododecane (**TPC**) were reported [5] and authors suggested that the coordination number of Bi(III) complex in solution may be higher than eight and labile coordination sites may exist. Moreover the authors showed that the Bi**TPC** complex is able to induce conformational changes of DNA under physiological conditions. However, the complex was only basically characterized and, for this reason, it seems to us interesting to report here the synthesis, detailed NMR characterization and crystal structure of Bi(III) complexes with **TPC** (Fig. 1). The role of the pyridyl arms and the influence of the macrocyclic moiety in Bi(III) binding process are investigated according to the nature of the solvent, dichloromethane or water.

2. Experimental

2.1. Materials

All reagents as bismuth chloride ($BiCl_3$) and bismuth nitrate ($Bi(NO_3)\cdot 5H_2O$) were of commercial quality and solvents were dried using standard procedures. Elemental analyses were performed at the Service de Microanalyse, CNRS, 91198 Gif sur Yvette, France.

2.2. X-ray investigations

Single-crystal X-ray diffraction data were collected by François Michaud (Université de Bretagne Occidentale) at 170 K on an X-CALIBUR-2 CCD 4-circle diffractometer (Oxford Diffraction) with graphite-monochromatized Mo Kα radiation ($\lambda = 0.71073$ Å).

Analysis of compound [Bi**TPC**Cl_2]Cl, $2CH_2Cl_2$: colorless rod shape crystals were obtained from an evaporated mixture of chloroform and dichloromethane. Crystal data and structure refinement for [Bi**TPC**Cl_2]Cl, $2CH_2Cl_2$ are summarized in Table 1.

* Corresponding author. Fax: +33 2 98 01 70 01.
E-mail address: henri.handel@univ-brest.fr (H. Handel).

0020-1693/$ - see front matter © 2008 Elsevier B.V. All rights reserved.
doi:10.1016/j.ica.2008.08.013

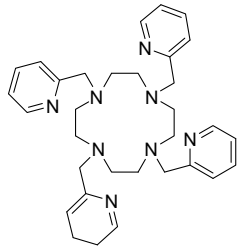

Fig. 1. Tetra-pyridylmethyl-cyclen **TPC** ligand.

Analysis of compound [Bi**TPC**]$(NO_3)_3$, $2CH_3OH$: colorless rod shape crystals were obtained from an evaporated ethanolic solution. Crystal data and structure refinement for [Bi**TPC**]$(NO_3)_3$, $2CH_3OH$ are summarized in Table 1.

Unit-cell determination and data reduction, including interframe scaling, Lorentz, polarization, empirical absorption and detector sensitivity corrections, were carried out using attached programs of CRYSALIS software (Oxford Diffraction) [6]. Structure was solved by direct method and refined by full matrix least squares method on F^2 with, respectively, SIR92 [7] and SHELXL 97 [8] suites of programs. The hydrogen atoms were identified at the last steps and refined under geometrical restraints and isotropic U-constraints.

Table 1
Crystal data and structure refinement for [Bi**TPC**Cl_2]Cl, $2CH_2Cl_2$[a] and for [Bi**TPC**]$(NO_3)_3$[c]

Empirical formula	$C_{34}H_{44}BiCl_7N_8$ (=$C_{32}H_{40}BiCl_3N_8$, $2CH_2Cl_2$)	$C_{34}H_{48}BiN_{11}O_{11}$ ($C_{32}H_{40}BiN_8^{3+}$, $3(NO_3^-)$, $2(CH_3OH)$)
Formula weight (g mol^{-1})	1021.9	995.81
Sample dimensions (mm)	0.28 × 0.23 × 0.10 (mm)	0.41 × 0.34 × 0.28 (mm)
Crystal system/ space group	monoclinic, *C*12/*c*1	monoclinic, *P*121/*n*1
Z	4	4
a (Å)	20.9778(9)	10.7202(4)
b (Å)	15.8153(8)	16.9823(7)
c (Å)	12.6086(10)	23.0492(10)
$\alpha = \gamma$ (°)	90	90
β (°)	104.874(4)	97.187 (4)
v (Å^3)	4043.0(3)	4163.2(3)
T (K)	170(2)	170(2)
λ (Å)	0.71073	0.71073
μ (mm^{-1})	4.86	4.304
D_x (Mg m^{-3})	1.679	1.589
Measured reflections	18987	29578
Unique reflections	4971; 4098 with $I > 2\sigma$(I)	8992; 6083 with $I > 2\sigma$(I)
F(000)	2024	2000
θ	3.07° < θ < 31.08°	2.73° < θ < 28.93°
$R_{int.}$	0.0255	0.0353
h	−29 → 29	−14 → 14
k	−16 → 15	−20 → 20
l	−17 → 17	−31 → 30
R_1 [$I > 2\sigma$ (*I*) and all data]	0.0270 and 0.0371	0.0367 and 0.0698
wR_2 [$I > 2\sigma$ (I) and all data]	0.0711 and 0.0757	0.1016 and 0.1171
S	1.047	1.076
w [$I > 2\sigma$ (*I*)]	1/ $[\sigma^2 + (0.0486P)^2 + 0.9010P]$[b]	1/$[\sigma^2 + (0.0600P)^2 + 4.4714P]$[d]
$\Delta\rho_{max}$ (e Å^{-3})	0.99	1.929
$\Delta\rho_{min}$ (e Å^{-3})	−1.114	−0.069

[a] Refinement on all F^2, 227 parameters, 0 restraint, 4971 data, rejected, with $I > 2\sigma(I)$.
[b] $P(F_o^2 + 2F_c^2)/3$.
[c] Refinement on all F^2, 502 parameters, 67 restraint, 8992 data, rejected, with $I > 2\sigma(I)$.
[d] $P(F_o^2 + 2F_c^2)/3$.

2.3. Ligand and complexes syntheses

1,4,7,10-Tetrakis(2-pyridylmethyl)-1,4,7,10-tetraazacyclododecane (**TPC**) were obtained as previously described [9].

2.4. Preparation of [Bi**TPC**Cl_2]Cl, $2CH_2Cl_2$

To a solution of 200 mg (0.37 mmol) of **TPC** in 20 ml of dry dichloromethane, was added 129 mg (0.41 mmol) of $BiCl_3$ and the mixture was refluxed. After 16 h of stirring, the solution was filtered and evaporated. A solution mixture of chloroform and dichloromethane was added to the obtained residue and a slow evaporation leads to colorless crystals suitable the following analyses and for X-ray investigations (yield = 73%). ^{1}H NMR (CD_2Cl_2, 253 K, 500 MHz): δ = 3.08 (2H, d, CH_2–CH_2, ^2J = 15.2 Hz), 3.23 (2H, d, CH_2–CH_2, ^2J = 13.6 Hz), 3.24 (2H, dd, CH_2–CH_2, ^2J = 13.7 Hz, ^3J = 13.5 Hz), 3.33 (2H, d, CH_2–CH_2, ^2J = 13.7 Hz), 3.41 (2H, d, CH_2–CH_2, ^2J = 15.0 Hz), 3.56 (2H, dd, CH_2–CH_2, ^2J = 13.6 Hz, ^3J = 14.3 Hz), 3.61 (2H, d, CH_2–Py, ^2J = 14.2 Hz), 4.18 (2H, dd, CH_2–CH_2, ^2J = 15.0 Hz, ^3J = 13.6 Hz), 4.38 (2H, dd, CH_2–CH_2, ^2J = 15.2 Hz, ^3J = 14.3 Hz), 4.68 (2H, d, CH_2–Py, ^2J = 15.0 Hz), 4.99 (2H, d, CH_2–Py, ^2J = 14.2 Hz), 5.27 (2H, d, CH_2–Py, ^2J = 15.0 Hz), 7.18 (2H, d, H_{Py}, ^3J = 7.7 Hz), 7.20 (2H, t, H_{Py}, ^3J = 7.7 Hz), 7.39 (2H, t, H_{Py}, ^3J = 7.6 Hz), 7.54 (2H, d, H_{Py}, ^3J = 7.8 Hz), 7.64 (2H, t, H_{Py}, ^3J = 7.5 Hz), 7.96 (2H, t, H_{Py}, ^3J = 7.7 Hz), 8.44 (2H, d, H_{Py}, ^3J = 4.6 Hz), 9.53 (2H, d, H_{Py}, ^3J = 4.8 Hz). ^{13}C NMR (CD_2Cl_2, 253 K, 500 MHz): δ = 45.56 (2C), 51.91 (2C), 57.96 (2C–Py), 61.73 (2C–Py), 123.7 ($2C_{Py}$), 124.35 ($2C_{Py}$), 124.47 ($2C_{Py}$), 126.32 ($2C_{Py}$), 136.43 ($2C_{Py}$), 139.17 ($2C_{Py}$), 149.41 ($2C_{Py}$), 149.55 ($2C_{Py}$), 154.09 ($2C_{Py}$), 156.36 ($2C_{Py}$). ^{15}N NMR (CD_2Cl_2, 253 K, 500 MHz): δ = −321.81 (2N), −319.23 (2N), −95.08 ($2N_{py}$), −60.43 ($2N_{py}$). *Anal.* Calc. for $C_{34}H_{44}Cl_7N_8Bi$ (1021.92): C, 39.96; H, 4.34; N, 10.97; Cl, 24.28; Bi, 20.45. Found: C, 39.44; H, 4.43; N, 10.82; Cl, 23.97; Bi, 20.10%.

2.5. Preparation of [Bi**TPC**]$(NO_3)_3$, $2CH_3OH$

To a solution of 200 mg (0.37 mmol) of **TPC** in 10 ml of ethanol, was added 200 mg (0.41 mmol) of $Bi(NO_3)_3 \cdot 5H_2O$ and the melange was stirred 4 h. Then the solution was filtered and evaporated to give a white powder. Methanol was added and slowly evaporated to yield colorless crystals suitable for the following analyses for X-ray investigations (yield = 65%). ^{1}H NMR (CD_3OD, 263 K, 500 MHz): δ = 3.48 (4H, dd, ^2J = 14.5 Hz, ^3J = 13.6 Hz, CH_2–CH_2), 3.75 (4H, d, CH_2–CH_2, ^2J = 14.4 Hz), 3.93 (4H, d, CH_2–CH_2, ^2J = 14.5 Hz), 4.05 (4H, dd, ^2J = 14.4 Hz, ^3J = 13.6 Hz, CH_2–CH_2), 4.55 (4H, d, ^2J = 16.5 Hz, CH_2–Py), 5.21 (4H, d, ^2J = 16.5 Hz, CH_2–Py), 7.18 (4H, t, ^3J = 4.5 Hz, H_{Py}), 7.43 (4H, t, ^3J = 6.5 Hz, H_{Py}), 7.75 (4H, d, ^3J = 7.7 Hz, H_{Py}), 8.19 (4H, t, ^3J = 6.5 Hz, H_{Py}). ^{13}C NMR (MeOD, 298 K, 400 MHz): δ = 53.30 (4C), 55.30 (4C), 61.88 (4C–Py), 127.07 ($8C_{Py}$), 142.83 ($4C_{Py}$), 149.44 ($4C_{Py}$), 157.84 ($4C_{Py}$). *Anal.* Calc. for $C_{32}H_{40}N_{11}O_9Bi$ (931.71): C, 41.25; H, 4.33; N, 16.54; Bi, 22.43. Found: C, 41.05; H, 4.36; N, 16.46; Bi, 22.32%.

2.6. NMR measurements

^{1}H NMR spectra were recorded with a Bruker 500 MHz spectrometer. The 2D ^{1}H–^{1}H homonuclear and ^{1}H–^{13}C heteronuclear correlations and homonuclear decoupling experiments, allow us to fully assign the ^{1}H and ^{13}C signals. Table 2 presents the ^{1}H NMR data for **TPC** and [Bi**TPC**Cl_2]$^+$ in CD_2Cl_2 at 253 K and data for **TPC** and [Bi**TPC**]$^{3+}$ in CD_3OD at 298 K.