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On the nuclearity of tricarbonylrhenium(I) complexes with N,O,O-donating Schiff bases derived from amino acids

Sérgio M. Soares [a], Sebastião S. Lemos [a,*], Maria José A. Sales [a], Robert A. Burrow [b]

[a] Instituto de Química, Universidade de Brasília, 70910-900 Brasília, DF, Brazil
[b] Departamento de Química, Universidade Federal de Santa Maria, 97105-900 Santa Maria, RS, Brazil

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ABSTRACT

The reaction of $[ReBr(CO)_5]$ with $AgOOCCH_3$ followed with *N*-(2-hydroxynaphtalidene)-β-alanine ($bala2hnH_2$); $NEt_4[ReBr_3(CO)_3]$ with the potassium salt of *N*-(2-hydroxynaphtalidene)-(D,L)-β-phenylalanine ($bphala2hnH_2$), or with *N*-(5-bromine-2-hydroxysalicylidene)-(D,L)-β-phenylalanine ($bphalabrsalH_2$) gave the complexes [*fac*-$\{Re(bala2hnH)(CO)_3\}_2$] (**1**), (H_3O)[Re(*fac*-bphala2hn)$(CO)_3$]·$CHCl_3$·H_2O (**2**), K[*fac*-Re(bphala2hn)$(CO)_3$]·$^1/_3$ $CHCl_3$·$2H_2O$ (**3**) and K[*fac*-Re(bphalabrsal)$(CO)_3$]·$2H_2O$ (**4**), respectively. Single crystal X-ray crystallography showed that the neutral dinuclear complex **1** is centrosymmetric with each rhenium(I) atom having an octahedral coordination geometry comprising of three terminal carbonyl ligands, in a *fac* configuration, and both ligands bala2hnH are bridging and chelating the two rhenium(I) centers. In the anionic mononuclear complexes **2** and **3**, $bphala2hn^{2-}$ acts as a N,O,O tridentate ligand to the *fac*-$\{Re(CO)_3\}^+$ fragment giving rise an octahedral geometry around the rhenium(I) atom.

1. Introduction

The $\{M(CO)_3\}^+$ synthon (M = Tc or Re) has been largely exploited in the development of new generation radiopharmaceuticals [1]. The coordination chemistry of rhenium has been spurred because of its resemblance with radioactive technetium analogs and feasible application as β-emitting $^{186/188}Re$ for both diagnostic and radiotherapy. The chemical robustness of the *fac*-$\{M(CO)_3\}^+$ moiety in physiological media has been demonstrated in the production of radiolabeled $^{99m}Tc(CO)_3$-biomolecules [2]. The ^{99m}Tc-isotope, a γ-emitter, is routinely employed in diagnostic imaging due to its ideal nuclear characteristics. Its complexes are extensively used for medical imaging from organs like ^{99m}Tc-EHIDA (EHIDA = *N*-2,6-diethylacetanilido)iminodiacetic acid to diagnosis in the hepatobiliary system and $[^{99m}Tc(glucoheptonate)_2]^-$ to produce images of the kidneys [1,3]. The tricabonylrhenium(I) complex with [(4-nitrobenzyl)(pyridin-2-ylmethyl)amin acetic acid has been prepared and structurally characterized and its technetium-99m congener was evaluated as a new radiopharmaceuticals for imaging hypoxia [4].

Schiff bases have shown biological activities as fungicide, bactericide, cytotoxic and antineoplasic [5]. Derivative from pyridine-2-carboxaldehyde and β-alanine afford the neutral diimine (*N*,*N*)-chelating ligand bromotricarbonylrhenium(I) complex where the carboxylic acid pendant arms self-interact, giving a centrosymmetric dimeric arrangement [6]. It is worth noting that the reaction of $[Re(CO)_3(H_2O)_3]^+$ with the respective ligands derived from glycine or α-alanine have produced a dinuclear complex where the chelate-diimine coordinates to a rhenium(I) atom and the carboxylate group coordinates to another rhenium center [7].

Although many neutral tricarbonylrhenium(I) complexes chelating ligands with (N,N,O) donor atoms have been thoroughly characterized [4,6–8] there is a scarcity of complexes containing ligands with (N,O,O) donor atoms in the literature [9,10]. Here, we report the synthesis and structural characterization of a neutral and three anionic complexes where LH_2 is a Schiff base derived from β-amino acids and an ortho-hydroxyaldehyde, [{*fac*-Re(bala2hnH)$(CO)_3\}_2$] (**1**), (H_3O)[*fac*-Re(bphala2hn)$(CO)_3$]·$CHCl_3$·H_2O (**2**), K[*fac*-Re(bphala2hn)$(CO)_3$]·$^1/_3$ $CHCl_3$·$2H_2O$ (**3**) and K[*fac*-Re(bphalabrsal)$(CO)_3$]·$2H_2O$ (**4**). We also discuss the fine tuning of the ligand in order to control the nuclearity and the availability of an anchoring group, i.e., the carboxyl group that could possibly interact with some biomolecules or some specific tissue.

2. Experimental

2.1. Materials

Chemicals and solvents were purchased from commercial sources and used without further purification. The rhenium(I) precursors $[ReBr(CO)_5]$ and $NEt_4[ReBr_3(CO)_3]$ were prepared by

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* Corresponding author.
E-mail address: sslemos@unb.br (S.S. Lemos).

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reported methods [11]. ^1H and $^{13}C\{^1H\}$ NMR spectra were recorded in DMSO-d_6 solutions at room temperature at 300 and 75 MHz, respectively, on a Varian Mercury plus 7.04 T spectrometer. Chemical shifts (δ) are given in ppm relative to $SiMe_4$ (internal reference for both ^1H and ^{13}C). Infrared spectra were recorded on an FT-IR Bomem BM100 spectrometer as KBr pellets in the 4000–400 cm^{-1} region. Thermal studies were performed on a Shimadzu Thermogravimetric Analyzer DTG-60H in platinum crucibles at a heating rate of 5 °C/min under a nitrogen atmosphere (30 mL/min).

The single crystal X-ray diffraction data for compounds **1**, **2** and **3** were collected at room temperature on a Bruker X8 Smart APEX2 diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.71073 Å). Data collection: APEX2 (Bruker, 2009); cell refinement: SAINT (Bruker, 2009) and data reduction: SAINT (Bruker, 2009) [12]. Data were corrected for absorption effects using the multi-scan method (SADABS) [13]. The structures were solved with SHELXS by direct methods [14]. All non-hydrogen atoms were refined with anisotropic displacement parameters with SHELXL [14]. Hydrogen atoms were refined with isotropic atomic displacement parameters with SHELXL. The Diamond 3.2i for Windows [15] was used to prepare the molecular graphics. More detailed information about the structure determinations is given in Table 1.

Table 1
Crystallographic data for **1**, **2** and **3**.

	1	**2**	**3**
Molecular formula	$C_{34}H_{24}N_2O_{12}Re_2$	$C_{24}H_{19}Cl_3NO_7Re$	$C_{70}H_{46}Cl_3K_3N_3O_{24}Re_3$
Formula weight (g/mol)	1024.95	725.95	2095.35
Crystal system	Monoclinic	Trigonal	Trigonal
Space group	$P2_1/c$	P-3c1	P-3c1
Unit cell dimensions			
a (Å)	13.7516(9)	22.9278(6)	22.8668(2)
b (Å)	11.0178(7)	22.9278(6)	22.8668(2)
c (Å)	11.8176(8)	16.1518(5)	16.1059(2)
α (°)	90	90	90
β (°)	115,425(3)	90	90
γ (°)	90	120	120
Volume (Å^3)	1617.10(18)	7353.2(4)	7293.34(16)
Z	2	12	4
D_{calc} (Mg/m^3)	2.105	1.967	1.908
Absorption coefficient (mm^{-1})	7.549	5.331	5.329
Reflns meas.	26,581	81,732	107,108
$2\theta_{max}$	58.00°	61.06°	61.05°
R_{int}/R_{sig}	0.0547/0.0499	0.1113/0.0979	0.0787/0.0388
Data/Parameters	4267/227	7107/280	7461/337
Goodness-of-fit on F^2	1.079	0.983	1.016
Final R indices [$I > 2\sigma(I)$]	$R_1 = 0.039$ $wR_2 = 0.084$	$R_1 = 0.0532$ $wR_2 = 0.1175$	$R_1 = 0.0421$ $wR_2 = 0.0924$

2.2. Syntheses

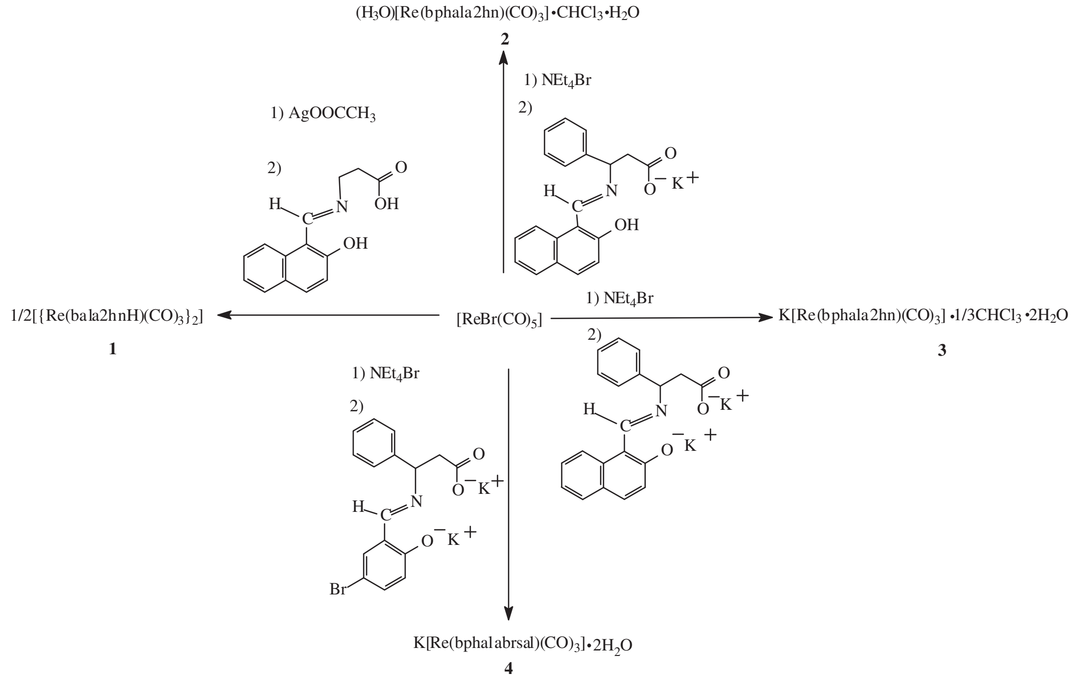
The Schiff bases bphala2hnH$_2$ and bphalabrsalH$_2$ were prepared according to the reported procedure for bala2hnH$_2$, only changing the solvent methanol for ethanol to improve the yield [16].

2.2.1. Synthesis of bphalabrsalH$_2$

To an aqueous solution (5 mL) of (D,L)-β-phenylalanine (165.2 mg, 1 mmol), under reflux for 30 min, a methanolic solution (20 mL) containing 5-bromine salicylaldehyde (201.0 mg, 1 mmol) was added and the reflux was continued for 1 h. After cooling, the golden precipitate was filtered off, washed with cold water (5 mL) and methanol (5 mL) and dried in air. Yield: 313 mg (90%). M.p.: 162 °C. IR (KBr, cm^{-1}) 3459 (ν OH), 1628 (ν C=N), 1705 (ν COOH), 1269 (ν CO$_{phenol}$). ^1H NMR δ 13.11 (s, COOH), 12.15 (s, COH), 8.66 (s, 1H, CH=N), 7.72 (d, 1H, CH$_{arom.}$, J = 2.7 Hz), 7.50 (dd, 1H, CH$_{arom.}$, J = 8.7 Hz) 7.50–7.34 (m, 5H, CH$_{arom.}$); 6.92 (d, CH$_{arom.}$, J = 8.7 Hz), 4.86 (dd, 1H, CH, J = 8.25 Hz); 3.01–2.86 (m, 2H, CH$_2$). $^{13}C\{^1H\}$ NMR δ 172.2; 164.7; 159.9; 142.0; 135.4; 134.0; 129.1; 128.0; 127.3; 120.9; 119.4; 110.0; 69.3; 42.4.

2.2.2. Synthesis of [{Re(bala2hnH)(CO)$_3$}$_2$] (**1**)

To a solution of [ReBr(CO)$_5$] (40.6 mg, 0.1 mmol) in acetonitrile (15 mL), maintained at reflux, a methanolic solution (5 mL) of silver



Scheme 1. Preparation of the tricarbonylrhenium(I) complexes with Schiff bases LH$_2$.