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Oxorhenium(V) '3+2' mixed-ligand complexes carrying the SNO/SN donor and C_{60}

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Abstract

Fullerenes based Schiff bases are prepared and used to stabilise the $[ReO]^{3+}$ core. We show, for this purpose, that ligand exchange reactions of $[NBu_4][ReOCl_4]$ with bidentate SN and tridentate Schiff bases derived from the condensation of ketones or aldehydes with dithiocarbazic acid methyl ester ($H_2N-NH-C(=S)SCH_3$) produce new '3+2' mixed-ligand complexes carrying the SNO/SN donor atom set.

Keywords: Rhenium; Schiff bases; Fullerenes; Mixed ligand complexes; Radiopharmaceuticals

1. Introduction

Biomedical applications of fullerenes are one field that focus attention for yielding viable fullerene-based products [1,2]. Various in vivo biological properties for C_{60} and its functionalized derivatives such as, for instance, carboxymethano-C_{60} [3–8], fullerenols [9–15] or, more recently, hexasulfobutyl[60]fullerene (FC_4S) [16–20], have been demonstrated during the last decade. Especially, its relatively non-toxicity towards various cells series showed the feasibility of C_{60} based compounds for medicinal applications. Among potential domains, radiomedicine and diagnostic purposes appear to be an interesting field of possible development for both empty or endohedral metallofullerenes derivatives [21,22]. Considering these precedents and our studies on the synthesis of rhenium and technetium compounds for nuclear medicine, we decided to synthesize new ligands with the C_{60} moiety and suitable to chelate Re and/or Tc. Two aspects must be considered: first, the connection between C_{60} with the other part of molecule and then, the chelating system around the metallic center.

Based on some recent works in our laboratory, we report, in this first paper, the synthesis and the structural characterisation of original oxorhenium(V) '3+2' mixed-ligand complexes carrying both a common 'SNO' tridentate ligand and a 'SN' bidentate ligand. C_{60} moiety connecting by Bingle cyclopropanation has been conveniently introduced via a well designed 'SN' ligand.

2. Experimental

2.1. General

$[NBu_4][ReOCl_4]$ [23,24] and *S*-methyl dithiocarbazate (MDTCZ) [25] were prepared according to literature methods. Other compounds are available from Aldrich (Saint Quentin Fallavier, France). Solvents were purified according to classical methods [26].

Carbon, hydrogen and oxygen analysis were performed by I.C.S.N. (91198 Gif sur Yvette, France) on a Carlo–Erba elemental analyser model-1106. IR spectra were obtained by a Nicolet 205 instrument in KBr pellets (4000–500 cm^{-1}). Mass spectrometry was carried out by C.R.M.P.O. (35700 Rennes, France) on a Zabspect TOF (Micromass) spectrometer (FAB^+, NBA matrix). ^1H- and ^{13}C-NMR were recorded with a Bruker ARX 400 at 400.13 and 100.62 MHz, respectively.

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Chemical shift values are referred to $CHCl_3$ (7.26 ppm: ^{1}H-NMR and 77.1 ppm: ^{13}C-NMR).

2.2. Preparation of 5

5a: 1.4 ml of freshly distilled ethyl malonyl chloride (10.1 mmol), was added to a solution of 2.12 g of pentane-1,5-diol (20.3 mmol) and 1.4 ml of Et_3N, in 200 ml of dry CH_2Cl_2 under nitrogen, at 0 °C. After stirring (2 h) at room temperature (r.t.), usual extracting processes and chromatography (CH_2Cl_2–AcOEt, 8/2 then 1/1, v/v) afford a light yellow oil (yield = 63%). R_f (CH_2Cl_2–AcOEt, 8/2, v/v) = 0.30. ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.25 (t, 3H, J = 7.1 Hz, CH_3); 1.43 (m, 2H, CH_2); 1.57 (quint, 2H, CH_2); 1.66 (quint, 2H, CH_2); 1.75 (s, 1H, OH); 3.34 (s, 2H, $COCH_2CO$); 3.61 (t, J = 6.4 Hz, 2H, CH_2OH); 4.14 (t, J = 6.4 Hz, 2H, CO_2CH_2); 4.16 (q, J = 7.1 Hz, 2H, CO_2CH_2). ^{13}C-NMR ($CDCl_3$), δ (ppm): 14.1 (CH_3); 22.1 (CH_2); 28.2 (CH_2); 32.2 (CH_2); 41.7 ($COCH_2CO$); 61.6 (CH_2); 62.5 (CH_2OH); 65.4 (CO_2CH_2); 166.7 (C=O); 166.8 (C=O).

2.3. Preparation of 7

To 286 mg (0.4 mmol) of C_{60} in toluene (300 ml) under stirring and a N_2 atmosphere, were added consecutively **5a** (91 mg, 0.42 mmol), I_2 (101 mg, 0.40 mmol) and DBU (0.80 mmol). After 4 h and 30 min, filtration over silica gel (toluene then CH_2Cl_2) gave unreacted C_{60}. Then, residue obtained from elution with a mixture of CH_2Cl_2 and AcOEt, 8/2, v/v) was washed ($Na_2S_2O_3$aq, 20%, w/w) and dried over $MgSO_4$. Evaporation of solvents afforded **7a** (158 mg, yield = 43%). R_f (CH_2Cl_2–AcOEt, 8/2, v/v) = 0.55. Spectrometry (FAB): m/z = 936.0993: $[ReO(SNO–CH_3)Cl]^{+\bullet}$. ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.26–1.35 (m, 3H, CH_3); 1.49 (m, 2H, CH_2); 1.67 (s, 2H, CH_2); 1.66 (quint, 2H, CH_2); 1.75 (s, 1H, OH); 3.34 (s, 2H, $COCH_2CO$); 3.61 (t, J = 6.4 Hz, 2H, CH_2OH); 4.14 (t, J = 6.4 Hz, 2H, CO_2CH_2); 4.16 (q, J = 7.1 Hz, 2H, CO_2CH_2). ^{13}C-NMR ($CDCl_3$), δ (ppm): 14.35 (CH_3), 22.36 (CH_2), 28.44 (CH_2), 32.28 (CH_2), 42.09 (CH_2CO_2), 62.75 (OCH_2), 63.57 (CH_2OH), 67.32 (CH_2O), 71.66 (C); 139.02, 139.15, 141.04, 141.97, 141.99, 142.28, 143.06, 143.10, 143.18, 143.97, 144.69, 144.77, 144.96, 145.23, 145.26, 145.35, 145.42 (C); 163.71 (C=O), 163.78 (C=O).

2.4. Oxidation of alcohols 5 and 7

6a: to a CH_2Cl_2 solution (20 ml) of **5a**, 730 mg of pyridinium chlorochromate (PCC) was added under stirring at r.t. After 3 h, diethyl ether (10 ml) was added before filtration on silica gel. Removing of solvents and chromatography (CH_2Cl_2–AcOEt, 8/2, v/v) gave us 215 mg (yield = 76%) of **6a** as a colorless oil. ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.27 (t, 3H, J = 7.1 Hz, CH_3), 1.65–1.75 (m, 2H, CH_2), 2.45–2.52 (m, 2H, CH_2), 3.37 (s, 2H, CH_2), 4.15 (t, 2H, J = 6.1 Hz, CH_2O), 4.18 (q, 2H, J = 7.1 Hz, CH_2O), 9.77 (br s, 1H, CHO). ^{13}C-NMR ($CDCl_3$), δ (ppm): 14.45 (CH_3), 18.79 (CH_2), 28.23 (CH_2), 41.99 (CH_2CO_2), 43.62 (CH_2CHO), 61.99 (OCH_2), 65.33 (OCH_2), 166.97 (C=O), 167.05 (C=O), 202.28 (CH=O).

8a: dark brown solid after chromatography (CH_2Cl_2). Yield = 83%. R_f (CH_2Cl_2–AcOEt, 8/2, v/v) = 0.90. ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.49 (t, 3H, J = 7.1 Hz, CH_3); 1.80–1.90 (m, 4H, CH_2); 2.58 (t, J = 6.6 Hz, 2H, CH_2CHO); 4.52 (t, J = 7.1 Hz, 2H, CO_2CH_2); 4.56 (q, J = 7.1 Hz, 2H, CO_2CH_2); 9.81 (s, 1H, CHO). ^{13}C-NMR ($CDCl_3$), δ (ppm): 14.40 (CH_3); 18.58 (CH_2); 28.03 (CH_2); 43.33 (CH_2CHO); 52.2 (CH_2); 63.6 (CH_2OCO); 66.8 (CH_2O); 71.6 (C); 71.64 (C), 138.98, 139.18, 141.95, 141.98, 142.25, 142.28, 143.06, 143.09, 143.10, 143.97, 144.71, 144.72, 144.77, 144.97, 145.20, 145.21, 145.25, 145.27, 145.35; 163.6 (C=O); 163.7 (C=O); 201.68 (CHO).

2.5. Preparation of Schiff bases

2.5.1. Without a C_{60} moiety, i.e. 9a

MDTCZ (118 mg, 0.97 mmol) was stirring in EtOH (10 ml) at reflux. Then, aldehyde **6a** in EtOH (10 ml) was added. After 10 h at reflux, evaporation of solvent afforded the Schiff base as a yellow oil in a nearly quantitative yield. ^{1}H-NMR ($CDCl_3$), δ (ppm): 1.25 (t, 3H, J = 7.1 Hz, CH_3); 1.62–1.75 (m, 4H, CH_2); 2.37 (dt, J = 6.8 × 5.1 Hz, 2H, CH_2C=N); 2.60 (s, 3H, SCH_3); 3.37 (s, 2H, CH_2CO); 4.10–4.25 (m, 4H, OCH_2); 7.36 (t, J = 5.1 Hz, 1H, CH=N); 10.66 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$): 14.15 (CH_3); 17.68 (SCH_3); 22.35 (CH_2); 27.89 (CH_2); 31.63 (CH_2); 41.68 (CH_2C=O); 61.70 (OCH_2); 65.06 (OCH_2); 149.71 (C=N); 166.71 (C=O); 166.74 (C=O); 200.18 (CS_2).

2.5.2. With a C_{60} moiety, i.e. 10a

Aldehyde **8a** (37 mg), MDTCZ (10.2 mg) and molecular sieves (4 Å) (10 mg) were mixed in dry toluene at reflux for 2 h. Filtration (Celite) with freshly distilled (over P_2O_5) CH_2Cl_2 before concentration under vacuum, afforded a residue which was chromatographied using CH_2Cl_2. Yield = 63%, brown solid, R_f (CH_2Cl_2) = 0.60. ^{1}H-NMR ($CDCl_3$): 1.48 (t, 3H, J = 7.1 Hz, CH_3), 1.75–1.85 (m, 2H, CH_2CH_2CH=), 1.90–2.00 (m, 2H, OCH_2CH_2), 2.40–2.50 (m, 2H, CH_2CH=), 2.60 (s, 3H, SCH_3), 4.55 (t, 2H, OCH_2), 4.57 (q, 2H, OCH_2), 7.36 (t, 1H, J = 5.1 Hz, CH=), 10.21 (br s, 1H, NH). ^{13}C-NMR ($CDCl_3$): 14.40 (CH_3), 17.87 (SCH_3), 22.50 (CH_2CH_2CH=), 28.03 (CH_2CH_2O), 31.59 (CH_2CH=), 52.25 (C), 63.62 (OCH_2), 66.81 (OCH_2), 71.60 (C), 71.64 (C), 138.81, 139.28, 141.03, 141.05, 142.27, 143.03, 143.08, 143.09, 143.17, 143.95, 144.70, 144.76, 144.96, 145.16, 145.24,

145.25, 145.34, 145.41, 148.68 (CH=), 163.66 (C=O), 163.75 (C=O), 200.32 (C = S).

2.6. Preparation of complex 3

To an acetone solution (10 ml) of $[NBu_4][ReOCl_4]$ (0.100 g, 0.17 mmol), *S*-methyl-β-*N*-(2-hydroxyphenylethylidene)dithiocarbazate (0.09 g, 0.34 mmol) in acetone (20 ml) was added dropwise and solution was stirred at r.t. for 12 h. Solvent was removed by evaporation under vacuum and residue was dissolved in dichloromethane, chromatographied (PE–CH_2Cl_2: 6/4, v/v). Obtained powder was recrystallized to afford 0.062 g (62%) of **3**.

Molecular formula: $C_{14}H_{17}O_2N_4ReS_4$. Anal. Found: C, 28.57; H, 2.93; S, 21.82. Calc. for: C, 28.60; H, 2.90; S, 21.80%. Selected IR bands (cm^{-1}): 1605 (S, ν(C=N)), 1561 (m), 1527 (s), 1491 (m), 1421 (w), 1407 (w), 1312 (w, ν(C–O)), 1224 (m), 1007 (s, $\nu(CS_2)$), 993 (s, ν(Re=O)), 755 (s). Spectrometry (FAB): $m/z = 441.0$: $[ReO(SNO–CH_3)Cl]^{+\bullet}$.

^{1}H-NMR ($CDCl_3$), δ (ppm): 1.99 (s, 3H, CH_3C=); 2.26 (s, 3H, CH_3C=); 2.71 (s, 3H, SCH_3); 2.80 (s, 3H, SCH_3); 6.62 (d, $J = 7.6$ Hz, 1H, CH); 7.03 (t, $J = 7.6$ Hz, 1H, CH); 7.39 (t, $J = 7.6$ Hz, 1H, CH); 7.56 (d, $J = 7.6$ Hz, 1H, CH); 8.71 (s, 1H, HC=N). ^{13}C-NMR ($CDCl_3$), δ (ppm): 18.5 (SCH_3), 19.4 (CH_3), 20.8 (SCH_3), 122.2, 122.4, 131.5 and 137.5 (4 $C_{aro}H$), 122.2 ($C_{aro}C$=), 169.6 ($C_{aro}O$), 178.6 (CH_3C=N), 191.8 (CS_2).

2.7. Preparation of complexes 4

4d: **1** (9.5 mg, 39 μmol) in 2 ml of CH_2Cl_2 was added to a red solution of $[ReOCl_4][NBu_4]$ (23.2 mg, 39 μmol) in CH_2Cl_2 (2 ml). Under stirring, solution turned to green before **10a** (41 mg, 39 μmol) in a CH_2Cl_2 + MeOH (10 ml/2 ml) was added dropwise. Solution was stirred at r.t. for 2 h. Solvent was removed by evaporation under vacuum and residue was dissolved in CH_2Cl_2, chromatographied (CH_2Cl_2). Complex **4d** was isolated as a brown powder (yield = 45%). Selected IR bands (cm^{-1}): 1740.3 (m, ν(C=O)), 1590.2 (m, ν(C=N)), 1230.7 (S), 993.0 (m, ν(C–S)), 951.0 (m, ν(Re=O)). Mass spectrometry (FAB): $m/z = 1479.0434$: $[ReO(SNO)(SN)]^{+\bullet}$.

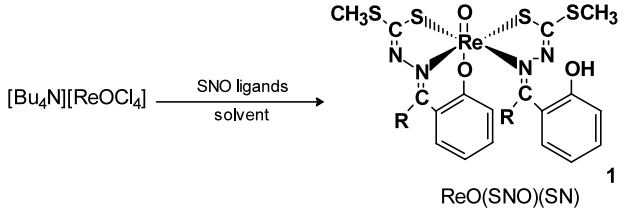
^{1}H-NMR ($CDCl_3$), δ (ppm): 1.20–1.35 (m, 2H, CH_2CH_2C=); 1.48 (t, 3H, CH_3); 1.60–1.70 (m, 2H, CH_2CH_2CO); 2.15–2.25 (m, 1H, CHC=); 2.45–2.60 (m, 1H, CH′C=); 2.73 (s, 3H, SCH_3); 2.79 (s, 3H, SCH_3); 3.36 (s, 3H, CH_3C=); 4.40 (t, $J = 6.2$ Hz, 2H, OCH_2); 4.55 (q, $J = 7.1$ Hz, 2H, OCH_2); 6.56 (d, $J = 8.2$ Hz, 1H, CH); 7.04 (t, $J = 5.6$ Hz, CH=); 7.07 (t, $J = 7.6$ Hz, 1H, CH); 7.37 (t, $J = 7.6$ Hz, 1H, CH); 7.78 (d, $J = 8.2$ Hz, 1H, CH). ^{13}C-NMR ($CDCl_3$), δ (ppm): 14.4 (OCH_2CH_3), 18.56 (CH_3S), 18.76 (CH_3S), 19.41 (CH_3C=), 22.10 (CH_2CH_2C=), 28.24 (CH_2CH_2O), 29.10 (CH_2CH_2C=), 52.19 [C(C=O)$_2$], 63.37 (OCH_2CH_3), 66.37 ($CO_2CH_2CH_2$), 71.53 and 77.30 [CC(C=O)$_2$], 119.84 (CH_{aro}), 120.14 (CH_{aro}), 124.55 ($C_{aro}C$=), 129.71 (CH_{aro}), 135.26 (CH_{aro}), 138.70, 138.72, 139.23, 141.05, 141.08, 141.79, 141.81, 141.93, 142.25, 143.02, 143.05, 143.07, 143.08, 143.11, 143.16, 143.21, 143.95, 144.55, 144.68, 144.71, 144.76, 144.96, 145.00, 145.04, 145.11, 145.27, 145.31, 161.33 (C=N), 163.62 (C=O), 163.70 (C=O), 168.64 (CH_3C=N), 169.42 ($C_{aro}O$), 191.84 (CS_2), 194.19 (CS_2).

3. Results and discussions

3.1. Synthesis of ligands

We think that studies aiming at the synthesis of mixed Tc or Re/C_{60} may be interesting to nuclear medicine, both for diagnostic (^{99m}Tc/γ-emitter) and therapeutic ($^{186/188}$Re/β-emitter) purposes. Despite the rich chemistry exhibited by fullerenes, mixed rhenium/C_{60} or technetium/C_{60} complexes have appeared only times in the literature [27]. With the aim to prepare potential radiopharmaceuticals, we plan first to connect C_{60} with cold rhenium at milligrams scale. Recently, we showed that ligand exchange reactions of various oxorhenium(V) precursors with bidentate (SN) and tridentate (SNO) Schiff bases derived from the condensation of ketones or aldehydes with $H_2NNHC(=S)SCH_3$ (MDTCZ) [25] produce novel '3+2' mixed-ligand complexes carrying the SNO/SN donor atom set [28–30]. Various complexes were obtained depending on stoechiometry, additives (Ph_3P),.... Among them, complexes **1** are obtained by exchange reactions between $[Bu_4N][ReOCl_4]$ and two equivalents of SNO ligands in CH_2Cl_2 (Scheme 1).

For these complexes, the observed high stability could be also explained through the π-stacking interactions between the two aromatic rings as shown in the thermal



Scheme 1. Synthesis of symmetrical complexes **1**.

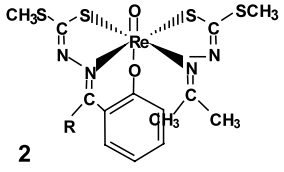
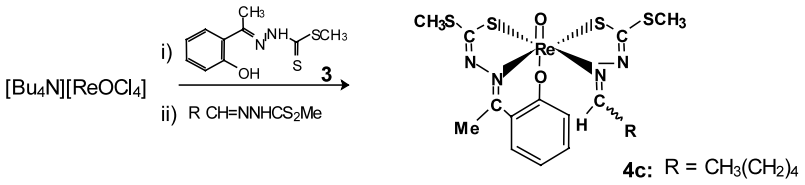
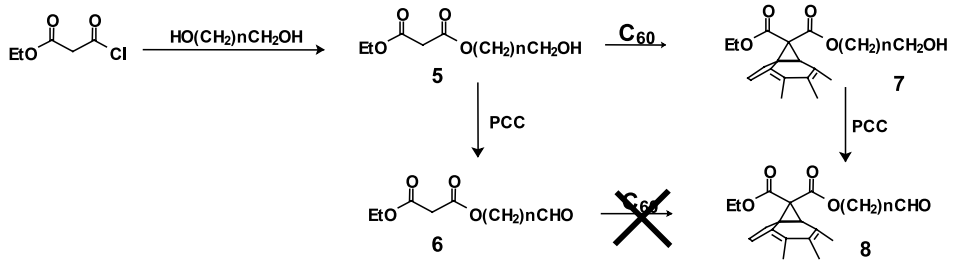


Fig. 1. Mixed complex **2** from reaction between **1** and acetone.



Scheme 2. Synthesis of mixed complex **4c**.



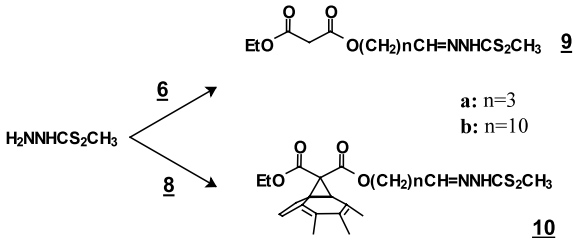
Scheme 3. Synthesis of C_{60}-aldehydes **8**.

ellipsoid diagram of the molecular structures [29]. But, nevertheless, during this study, we showed that on trying to perform this reaction in acetone, the main isolated product was **2**, probably obtained from in situ exchange reaction between acetone and SNO ligand. This fact prompts us to develop a new approach using alkyl SN type ligand to connect complexes with various vectors (Fig. 1).

As preliminary experiments, we show that the direct preparation of such mixed complexes was possible using an equimolar mixture of SNO-type ligand **3**, from 2′-hydroxyacetophenone and MDTCZ, and alkyl Schiff base synthesized from simple hexylaldehyde (Scheme 2).

For this work, we then used only **3** as SNO ligand for each complex described below. To connect C_{60}, among the large variety of available reactions for fullerene functionalization, we choose cyclopropanation, known as Bingel reaction [31,32] to introduce a side-chain on the C_{60} core. This reaction begins by the generation of a carbon nucleophile by deprotonation of α-halo esters, conveniently in situ generated, and leads to a clean cyclopropanation of C_{60} after a S_Ni mechanism. Required synthons **8** were prepared according to Scheme 3 from mono esterification of ethyl malonyl chloride with alkanediols.

Direct oxidation of **5** using pyridium chlorochromate (PCC) [33,34] gave aldehyde **6** that did not react with C_{60} under Bingel conditions (I_2/DBU) probably due to side reactions with carbonyl function in basic conditions. Then, **8** was obtained conveniently by first reaction cyclopropanation reaction of C_{60} with **5** following by oxidation with PCC. In literature, condensation of MDTCZ on aldehydes or ketones was performed in ethanol [35–37]. Due to the low solubility of C_{60} in most of solvents [38], we prefer toluene for this reaction with **8**. In this case, added molecular sieves (4 Å) appeared then necessary to promote the elimination



Scheme 4. SN ligands.

of water of intermediate N-substituted hemiaminals (Scheme 4).

3.2. Synthesis of Re-complexes

Rhenium SNO/SN complexes were obtained from reaction between $[Bu_4N][ReOCl_4]$ and one equivalent of **1** and one equivalent of the adequate SN ligand. This reaction can be carried out one pot but, in this case, yields were lower and final purification was difficult. Then, a two step procedure was followed: first, addition of one equivalent of **1** to a red solution of $[Bu_4N][ReOCl_4]$ in the adequate solvent led to a green solution of the diamagnetic complex ReO(SNO)Cl [28]. Then, addition of the SN ligand afforded mixed complexes after a preparative chromatography with silica gel. Previous works showed us that best yields were obtained with ethanol and/or CH_2Cl_2 as solvents. With C_{60} ligands, only pure CH_2Cl_2 was used due again to lower solubility (Fig. 2).

3.3. Structural analysis of complexes

All our complexes are air stable and their structure is supported by correct elementary analysis and MSFAB spectra. Observed diamagnetic character is in accor-

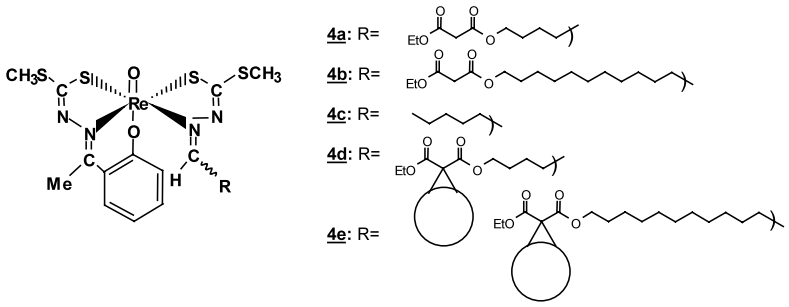


Fig. 2. Mixed SNO/SN complexes **4**.

dance with the behaviour of all oxo complexes of Re(V) in a distorted octahedral environment. The infra-red spectroscopic data reveal the presence of C=N (1590–1598 cm^{-1}) and C–S (992–993 cm^{-1}) bands in each complex **4**. Moreover, the ν(Re=O) stretching vibration is observed (951.0–952.5 cm^{-1}) in accordance with six-coordinate oxorhenium compounds with a phenolic oxygen *trans* to Re=O multiple bond [39].

NMR spectra of ligands before and after complexation are also especially useful to prove coordination of rhenium and homogeneity of the structures.

^{1}H-NMR spectra analysis: first, NH and OH signals of **1** (respectively, at 9.99 and 11.38 ppm) disappeared in complexes spectra. Influence of complexation was shown too for CH_3C=N singlets of **1** which appeared always strongly deshielded of about 0.80 ppm between free ligands and mixed complexes (Table 1). For the SN ligands, difference was more important because, after complexation, we observe two massifs for each hydrogen of the methylene group CH_2C=N. Due to chelation, rotation is probably restricted and, then, the two geminal protons have two different chemical shifts (about 0.25 ppm) because of the anisotropic effect of the aromatic ring of the SNO ligand [29]. Finally, ^{1}H-NMR spectra exhibit the CH=N imino-group protons of the bidentate Schiff bases at lower shift (6.98–7.08 vs.

Table 1
Selected ^{1}H-NMR data for free ligands and complexes

Ligands		1	10a	10b	11	9a	9b
SCH_3	Free ligand	2.95	2.60	2.65	2.61	2.60	2.62
	Complexes **4**	[a]	2.72/2.82	2.71/2.80	–	2.71/2.80	2.71/2.80
CH_3C=N	Free ligand	2.60	–	–	–	–	–
	Complexes **4**	[a]	3.39	3.37	–	3.37	3.38
CH_2CH=N	Free ligand	–	2.40	2.32	2.38	2.37	2.33
	Complexes **4**	–	2.10–2.20	2.15–2.25	2.10–2.20	2.15–2.25	2.15–2.25
			2.35–2.45	2.35–2.45	2.35–2.45	2.35–2.45	2.40–2.50
CH_2CH=N	Free ligand	–	7.29	7.35	7.28	7.36	7.27
	Complexes **4**	–	7.05	7.06	7.03	6.98	7.08

[a] Signals from **1** and SN ligands were not attributed.

Table 2
Selected ^{13}C-NMR data for free ligands and complexes

Ligands		1	10a	10b	11	9a	9b
CS_2	Free ligand	199.32	200.32	200.10	199.99	200.18	200.27
	Complexes **4**	[a]	191.84/194.19	191.95/193.26	192.17/193.41	191.92/193.90	191.97/193.23
SCH_3	Free ligand	18.11	17.87	–	17.70	17.68	17.79
	Complexes **4**	[a]	18.56/18.76	18.53/18.70	18.88/19.05	18.66/19.35	18.49/18.65
CH_3C=N	Free ligand	153.32	–	–	–	–	–
	Complexes **4**	–	168.64	169.29	169.76	169.01	169.31
CH_3C=	Free ligand	13.21	–	–	–	–	–
	Complexes **4**	–	19.41	19.33	19.37	19.35	19.30
CH_2C=N	Free ligand	–	148.68	–	151.00	149.71	150.41
	Complexes **4**	–	161.33	161.30	160.71	161.33	161.30
CH_2C=	Free ligand	–	31.59	–	32.21	31.63	30.92
	Complexes **4**	–	29.53	30.25	30.58	29.64	30.25

[a] Signals from **1** and SN ligands were not attributed.

7.27–7.36 ppm) as observed again previously [29]. Moreover, coupling constants observed between these protons and vicinal methylene group were significatly higher (5.1 Hz in the free ligand vs. 5.6 Hz in the complex).

^{13}C-NMR spectra analysis: signals for carbons directly concerned by chelation are strongly shifted (Table 2). For **1**, the imino-group carbon signal is deshielded from 153.32 in the free ligand to 168.6–169.3 in complexes. For SN ligands, the same behaviour is observed with about 6ppm of shifting. The vicinal carbon shift is also modified. But, if we observed again a strong deshielding of about 15 ppm for the SNO ligand **1**, in opposite, a smooth shielding is observed for SN ligands (about 1–2 ppm). On an other hand, complexes exhibit two characteristic CS_2 signals at lower fields (191–194 ppm) compared to those of the ligands ($\approx$200 ppm) indicating that co-ordination via the charged thiolic sulphur atom has occurred.

As a conclusion, this work is, to our knowledge, the first report of synthesis of mixte C_{60}/Re complexes for radiopharmaceuticals purposes. Now, the in vivo biodistribution of these molecules is under investigation. Moreover, the followed synthetic pathway used a new way to stabilize and functionnalize Re=O chelates that could be suitable for labelling others molecules.

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