Re Tricarbonyl Complexes with Ligands Containing P,N,N and P,N,O Donor Atom Sets: Synthesis and Structural Characterization

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The coordination chemistry of the heterofunctionalized phosphines HPN_2 and H_2PNO and of an analogue containing a relevant biomolecule, HPN-Pip (Pip = 4-(3-aminopropyl)-1-(2-methoxyphenyl)piperazine), was studied toward the synthon $(NEt_4)_2[ReBr_3(CO)_3]$. The complexes isolated, $[Re(CO)_3(\kappa^3\text{-}PN_2)]$, **3**, $[Re(CO)_3Br(\kappa^2\text{-}H_2PNO)]$, **4**, and $[Re(CO)_3Br(\kappa^2\text{-HPN-Pip})]$, **5**, are the first examples of Re(I) compounds stabilized by such a combination of donor atoms. All of the compounds are neutral, but the phosphines, depending on the combination of atoms, act as monoanionic and tridentate (**3**) or as neutral and bidentate (**4**, **5**). The characterization of **3**−**5** included IR, ^{1}H NMR, and ^{31}P NMR spectroscopy and X-ray crystallographic analysis. Colorless crystals of compounds **3** and **4** were obtained by slow evaporation of a methanolic solution of **3** and from a boiling acetonitrile solution of **4**. Compound **3** crystallizes with two molecules of MeOH per asymmetric unit in the monoclinic space group $P2_1/c$, $a = 10.1237(8)$ Å, $b = 9.4959(4)$ Å, $c = 28.365(2)$ Å, $\beta = 98.707(9)°$, $V = 2695.4(3)$ Å^3, $Z = 4$; **4** crystallizes in the triclinic space group $P\bar{1}$, $a = 10.0241(9)$ Å, $b = 11.2060(10)$ Å, $c = 13.0656(12)$ Å, $\alpha = 84.883(11)°$, $\beta = 71.163(10)°$, $\gamma = 63.650(9)°$, $V = 1241.19(19)$ Å^3, $Z = 2$.

Introduction

The use of organometallic complexes in biological sciences is a domain which is still in an early stage of its development.[1] However, in the radiopharmaceutical field, namely, in nuclear medicine, there are already a few examples of organometallic complexes which have found useful clinical application.[2] The organometallic Tc(I) aquo ion, *fac*-$[^{99m}Tc(OH_2)_3(CO)_3]^+$ (**1**), which is easily obtained by direct carbonylation of $[^{99m}TcO_4]^-$ under normal pressure,[3] has proven to be an useful synthon for the labeling of biomolecules, with high specific activities under retention of biological activity and specificity.[4] The suitability for labeling biomolecules arises from the high inertness of the *fac*-$[^{99m}Tc(CO)_3]$ core, the water solubility, and the good stability in aqueous solutions over a broad pH range for several hours.[4a] Complex **1** undergoes also fast replacement of the coordinated water molecules by a large variety of ligands yielding stable complexes.[5−9] However, further advances in this field still depend on the availability of new bifunctional chelating systems, which allows, on one hand, the preparation of new complexes stable in vitro and in vivo with appropriate pharmacokinetics and, on the other hand, linking of biomolecules for targeting specific receptors with retention of biological activity and specificity. Indeed there is still a need for new anchor groups in order to extend the range of potential radiopharmaceuticals labeled with **1**. As part of our ongoing studies on the development of fundamental chemistry for potential use in radiopharmaceutical applications we have shown that the tri(bi)dentate heterofunctionalized phosphines HPN_2 and H_2PNO (Chart 1) are very versatile in terms of charge and denticity toward the $[Re{=}O]^{3+}$ core.[10−12]

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(1) Jaouen, G.; Top, S.; Vessières, A.; Alberto, R. *J. Organomet. Chem.* **2000**, *600*, 23−26.
(2) Holman, B. L.; Sporn, V.; Jones, A. G.; Benjamin-Sia, S. T.; Perez-Balino, N.; Davison, A.; Lister James, J.; Kronauge, J. F.; Mitta, A. E. A.; Camin, L. L.; Cambell, S.; Williams, S. J.; Carpenter, A. T. *J. Nucl. Med.* **1987**, *28*, 13−18.
(3) (a) Aebischer, N.; Schibli, R.; Alberto, R.; Merbach, A. E. *Angew. Chem., Int. Ed.* **2000**, *39*, 254−256. (b) Alberto, R.; Schibli, R.; Waibel, R.; Abram, U.; Schubiger, A. P. *Coord. Chem. Rev.* **1999**, *190*−*192*, 901−919.
(4) (a) Egli, A.; Alberto, R.; Tannahil, L.; Schibli, R.; Abram, U.; Schaffland, A.; Waibel, R.; Tourwé, D.; Jeannin, L.; Iterbeke, K.; Schubiger, P. A. *J. Nucl. Med.* **1999**, *40*, 1913−1917. (b) Alberto, R.; Schibli, R.; Schubiger, A. P.; Abram, U.; Pietzsch, H. J.; Johannsen, B. *J. Am. Chem. Soc.* **1999**, *121*, 6076−6077. (c) Alberto, R.; Schibli, R.; Egli, A.; Schubiger, A. P.; Abram, U.; Kaden, T. A. *J. Am. Chem. Soc.* **1998**, *120*, 7987−7988. (d) Wüst, F.; Carlson, K. E.; Katzenellenbogen, J. A.; Spies, H.; Johannsen, B. *Steroids* **1998**, *63*, 665−671. (e) Hoepping, A.; Reisgys, M.; Brust, P.; Seifert, S.; Spies, H.; Alberto, R.; Johannsen, B. *J. Med. Chem.* **1998**, *41*, 4429−4432. (f) Reisgys, M.; Wüst, F.; Alberto, R.; Schibli, R.; Schubiger, A. P.; Pietzsch, H.-J.; Spies, H.; Johannsen, B. *Bioorg. Med. Chem. Lett.* **1997**, *17*, 2243−2246.
(5) (a) Pietzsch, H.-J.; Gupta, A.; Reisgys, M.; Drews, A.; Seifert, S.; Syhre, R.; Spies, H.; Alberto, A.; Abram, U.; Schubiger, P. A.; Johannsen, B. *Bioconjugate Chem.* **2000**, *11*, 414−424. (b) Schibli, R.; Alberto, R.; Abram, U.; Abram, S.; Egli, A.; Schubiger, P. A.; Kaden, T. A. *Inorg. Chem.* **1998**, *37*, 3509−3516.
(6) Schibli, R.; La Bella, R.; Alberto, R.; Garcia-Garayoa, E.; Ortner, K.; Abram, U.; Schubiger, P. A. *Bioconjugate Chem.* **2000**, *11*, 345−351.
(7) Garcia, R.; Paulo, A.; Domingos, Â.; Santos, I.; Ortner, K.; Alberto, R. *J. Am. Chem. Soc.* **2000**, *122*, 11240−11241.
(8) Abram, U.; Abram, S.; Alberto, R.; Schibli, R. *Inorg. Chim. Acta* **1996**, *248*, 193−202.
(9) (a) Schibli, R.; Katti, K. V.; Higginbotham, C.; Volkert, W. A.; Alberto, R. *Nucl. Med. Biol.* **1999**, *26*, 711−716. (b) Abram, U.; Abram, S.; Schibli, R.; Alberto, R.; Dilworth, J. R. *Polyhedron* **1998**, *17*, 1303−1309.
(10) Correia, J. D. G.; Domingos, Â; Santos, I. *Eur. J. Inorg. Chem.* **2000**, 1523−1529.
(11) Correia, J. D. G.; Domingos, Â.; Paulo, A.; Santos, I. *J. Chem. Soc., Dalton Trans.* **2000**, 2477−2482.
(12) Correia, J. D. G.; Domingos, Â; Santos, I.; Spies, H. *J. Chem. Soc., Dalton Trans.* **2001**, 2245−2250.

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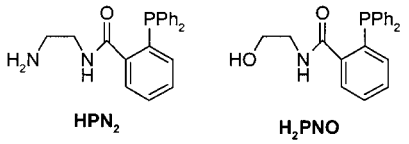
Chart 1. HPN_2 and H_2PNO Ligands



These phosphines, which can be functionalized with biologically relevant biomolecules, contain also a combination of donor atoms still unknown for the carbonyl system **1**. Thus, we studied the coordination capabilities of the HPN_2 and H_2PNO phosphines and of HPN-Pip, a phosphine bearing an arylpiperazine derivative (receptor ligand for the 5-HT_{1A} subclass of serotonergic receptors[4b]) toward the carbonyl system **1**. We herein report on the synthesis and characterization of the new compounds $[Re(CO)_3(\kappa^3\text{-}PN_2)]$, **3**, $[Re(CO)_3Br(\kappa^2\text{-}H_2PNO)]$, **4**, and $[Re(CO)_3(\kappa^2\text{-HPN-Pip})]$, **5**, which have been obtained by reacting $(NEt_4)_2[ReBr_3(CO)_3]$ with HPN_2, H_2PNO, and HPN-Pip, (Pip = 4-(3-aminopropyl)-1-(2-methoxyphenyl)piperazine), respectively.

Experimental Section

General Procedures. The reactions were carried out by standard Schlenk techniques. Chemicals and solvents were of reagent grade and were used without further purification. H_2PNO, HPN_2, *N*-[2-(diphenylphosphanyl)benzoyloxy]succinimide, $(NEt_4)_2[ReBr_3(CO)_3]$, and 4-(3-aminopropyl)-1-(2-methoxyphenyl)piperazine were prepared according to published methods.[10,13,14] ^1H and ^{31}P NMR spectra were recorded on a Varian Unity 300 MHz spectrometer; ^1H chemical shifts were referenced with the residual solvent resonances relative to tetramethylsilane and the ^{31}P NMR chemical shifts with external 85% H_3PO_4 solution. NMR spectra were run in $CDCl_3$ and d_6-DMSO. IR spectra were recorded as KBr pellets on a Perkin-Elmer 577 spectrometer and on a Biorad FTS-45 instrument. Carbon, hydrogen, and nitrogen analyses were performed on a Perkin-Elmer automatic analyzer and on a Leco CHN(S)-932 instrument.

Synthesis of *N*-[4-(3-Aminopropyl)-1-(2-methoxyphenyl)piperazine]-2-(diphenylphosphanyl)benzamide, HPN-Pip. *N*-[2-(Diphenylphosphanyl)benzoyloxy]succinimide (0.33 g, 1.32 mmol) dissolved in dry dichloromethane (5 mL) was added dropwise to a stirred solution of 4-(3-aminopropyl)-1-(2-methoxyphenyl)piperazine (0.40 g, 1.32 mmol) in the same solvent (15 mL). After 18 h at room temperature, the reaction mixture was washed with a diluted solution of HCl and the organic phase collected. The aqueous solution was extracted with dichloromethane (3 × 20 mL), and the organic phases were collected and washed with water. After drying with magnesium sulfate the solution was filtered and the solvent evaporated to dryness. A pale pink solid was obtained and used without further purification. Yield: 87%, 0.47 g. Anal. Calcd (found) for $C_{33}H_{36}N_3O_2P$: C, 73.72 (73.69); H, 6.75 (6.71); N, 7.82 (7.88). IR (KBr, ν/cm^{-1}): 1640 (C═O), 1240, 700, 750. ^1H NMR ($CDCl_3$): δ 7.70 (m, aromatic, 1H), 7.58 (t br, NH, 1H), 7.39−7.25 (m, aromatic, 12H), 7.04 (m, aromatic, 1H), 6.95−6.84 (m, aromatic, 4H), 3.83 (s, OCH_3, 3H), 3.49−3.40 (m, CH_2, 8H), 2.98 (s br, CH_2, 4H), 2.06 (s, br, 2H, CH_2). ^{31}P NMR ($CDCl_3$): δ −8.3.

Synthesis of $[Re(CO)_3(\kappa^3\text{-}PN_2)]$, 3. A solution of HPN_2 (0.023 g, 0.065 mmol) in MeOH (2 mL) was added to a stirred solution of $(NEt_4)_2[ReBr_3(CO)_3]$ (0.050 g, 0.065 mmol) in MeOH (5 mL). After 3 h under reflux the reaction mixture was allowed to cool down and water was added until no more white solid precipitated. The solid was collected by filtration, washed with water, and dried under vacuum. Colorless crystals suitable for X-ray diffraction analysis were obtained by slow evaporation of a methanolic solution. Yield: 45%, 0.018 g. Anal. Calcd (found) for $C_{24}H_{20}N_2O_4PRe\cdot 2(H_2O)$: C, 44.10 (44.69); H, 3.70 (3.40); N, 4.29 (4.31). IR (KBr, ν/cm^{-1}): 2017, 1887 (CO str), 1590, 1572 and 1544 (CONH str), 749, 699. ^1H NMR (d_6-DMSO): δ 7.88 (m, aromatic, 1H), 7.64−7.25 (m, aromatic, 13H), 6.29 (m, CH_2, 1H), 5.53 (s br NH, 1H), 4.38 (m, CH_2, 1H), 3.86 (s br, NH, 1H), 2.26 (m, CH_2, 1H), 2.15 (m, CH_2, 1H). ^{31}P NMR (d_6-DMSO): δ 14.4.

Synthesis of $[Re(CO)_3Br(\kappa^2\text{-}H_2PNO)]$, 4. A solution of H_2PNO (0.023 g, 0.065 mmol) in MeOH (2 mL) was added to a stirred solution of $(NEt_4)_2[ReBr_3(CO)_3]$ (0.050 g, 0.065 mmol) in MeOH (5 mL). After 18 h, the formed white precipitate was filtered, washed with a small amount of MeOH, and dried under vacuum. Colorless crystals suitable for X-ray diffraction analysis were obtained by recrystallization from boiling acetonitrile. Yield: 71%, 0.032 g. Anal. Calcd (found) for $C_{24}H_{20}BrNO_5PRe$: C, 41.21 (41.18); H, 2.88 (3.01); N, 2.00 (1.97). IR (KBr, ν/cm^{-1}): 2027, 1928 and 1890 (CO str), 1598 (CONH str), 748, 695. ^1H NMR (d_6-DMSO): δ 10.04 (t br, NH, 1H), 7.89 (m, aromatic, 1H), 7.77−7.57 (m, aromatic, 12H), 7.21 (m, 1H, aromatic), 6.69 (m, CH_2, 1H), 4.77 (m, CH_2, 1H), 4.09 (m, CH_2, 1H), 2.26 (m, CH_2, 1H). ^{31}P NMR (d_6-DMSO): δ 11.8.

Synthesis of $[Re(CO)_3Br(\kappa^2\text{-HPN-Pip})]$, 5. A solution of HPN-Pip (0.10 g, 0.19 mmol) in MeOH (3 mL) was added to a stirred solution of $(NEt_4)_2[ReBr_3(CO)_3]$ (0.15 g, 0.19 mmol) in MeOH (3 mL). After 18 h, partial evaporation of the solvent afforded a solid, which was collected by filtration, washed with small portions of MeOH, and dried under vacuum. Colorless crystals suitable for X-ray diffraction analysis were obtained by recrystallization from boiling methanol. Yield: 71%, 0.12 g. Anal. Calcd (found) for $C_{36}H_{36}BrN_3O_5PRe$: C, 48.71 (48.51); H, 4.09 (4.02); N, 4.73 (4.69). IR (KBr, ν/cm^{-1}): 2023, 1920, 1885 (CO str), 1600 (CONH str), 750, 700. ^1H NMR ($CDCl_3$): δ 9.48 (t br, NH, 1H), 8.15 (m, aromatic, 1H), 7.64−7.29 (m, aromatic, 12H), 7.07 (m, aromatic, 1H), 6.93−6.81 (m, aromatic, 4H), 3.86 (s, OCH_3, 3H), 3.64 (m, CH_2, 1H), 3.63−3.36 (m, 7H), 2.93 (s br, 2H), 2.81 (m, CH_2, 2H), 2.28 (s br, CH_2, 1H), 2.03 (s br, CH_2, 1H). ^{31}P NMR (d_6-$CDCl_3$): δ 14.2.

X-ray Crystal Structure Determination for Compounds 3, 4, and 5. Data for **3** and **4** were collected on a Stoe IPDS diffractometer using graphite-monochromated Mo Ka (λ = 0.71073 Å) radiation and were corrected for Lorentz, polarization, and absorption effects. Structures were solved by Patterson (**3**) and direct methods (**4**) with Shelxs97, and refined with Shelxl97 on F^2 using all data with all non-hydrogen atoms anisotropically defined.[15] The hydrogen atoms were placed in calculated positions and were refined with a riding model except for H1A and H1B of **3** respectively H1 and H2 of **4**, which were found in the difference Fourier map and isotropically refined. For **3** a numerical absorption correction was applied. For **3** and **4** a summary of the crystallographic data is given in Table 1. Data for crystal **5** were collected on an Enraf-Nonius CAD-4 diffractometer with graphite-monochromatized Mo Kα radiation, but the crystal structure was not of good quality (see Results and Discussion. Description of the Structures).

Results and Discussion

Synthesis and Characterization. The Re(I) tricarbonyl complexes $[Re(CO)_3(\kappa^3\text{-}PN_2)]$ (**3**) and $[Re(CO)_3Br(\kappa^2\text{-}H_2PNO)]$ (**4**) were synthesized by stoichiometric reaction of the precursor $(NEt_4)_2[ReBr_3(CO)_3]$ (**2**), in methanol, with HPN_2 and H_2PNO, respectively (Scheme 1).

While **4** is insoluble in MeOH, precipitating from the reaction mixture as a white solid, **3** is partially soluble in this solvent. These air and moisture stable compounds are soluble in halogenated solvents and insoluble in water. Complexes **3** and **4** have been characterized by the usual analytical techniques, including X-ray diffraction analysis. As can be seen in Scheme 1, the HPN_2 ligand provides a tridentate facial coordination geometry with deprotonation of the amide function. To the best of our knowledge this is the first time that the *fac*-$[M(CO)_3]^+$ is stabilized by an amide function. The H_2PNO ligand coordi-

(13) Alberto, R.; Schibli, R.; Schubiger, P. A.; Herrmann, W. A.; Artus, G.; Abram, U.; Kaden, T. A. *J. Organomet. Chem.* **1995**, *493*, 119−127.

(14) Scheunemann, M.; Johannsen, B. Unpublished results.

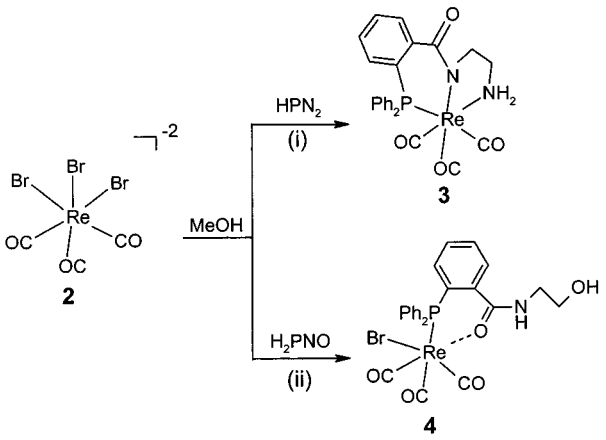
(15) (a) Sheldrick, G. M. *SHELXS97*; University of Göttingen: Göttingen, 1997. (b) Sheldrick, G. M. *SHELXL97*; University of Göttingen: Göttingen, 1997.

Table 1. Summary of Crystal Data for Compounds **3**·2MeOH and **4**

	3·2MeOH	**4**
formula	$C_{24}H_{22}N_2O_4PRe\cdot 2(CH_3OH)$	$C_{24}H_{20}BrNO_5PRe$
fw	681.67	699.49
space group	$P2_1/c$	$P\bar{1}$
a, Å	10.1237(8)	10.0241(9)
b, Å	9.4959(4)	11.2060(10)
c, Å	28.365(2)	13.0656(12)
α, deg		84.883(11)
β, deg	98.707(9)	71.163(10)
γ, deg		63.650(9)
V, Å^3	2695.4(3)	1242.19(19)
Z	4	2
D_{calcd}, g cm^{-3}	1.680	1.870
T, °C	−90	−90
μ, cm^{-1}	0.4609	0.6598
T_{min}, T_{max}	0.4499, 0.6926	0.5583, 0.7338
2θ(max), deg	52	52
reflns unique, R(int)	5195, 0.0596	4500, 0.0407
R ($I > 2\sigma(I)$)	R1[a] = 0.0299	R1[a] = 0.0304
	wR2[b] = 0.0741	wR2[b] = 0.0689
R (all data)	R1 = 0.0380	R1 = 0.0424
	wR2 = 0.0760	wR2 = 0.0706
GOF on F^2	0.811	0.877

[a] $R1 = \sum||F_o| - |F_c||/\sum|F_o|$. [b] $wR2 = \{\sum[w|F_o|^2 - |F_c|^2]^2/\sum w(F_o^2)^2\}^{1/2}$.

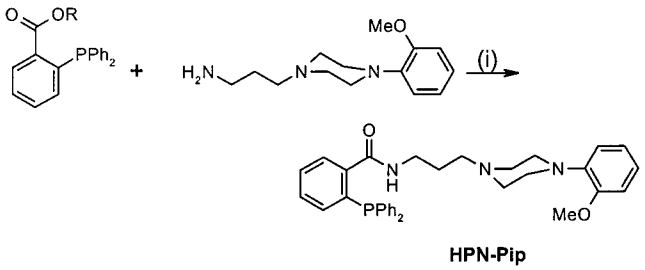
Scheme 1. Preparation of the Complexes **3** and **4**[a]



[a] (i) Methanol, reflux; (ii) methanol, room temperature.

nates as neutral and bidentate through the phosphorus and the oxygen atoms of the carbonyl. The facial arrangement of the carbonyl groups in **3** and **4** is evidenced by the CO-stretching absorptions in the IR spectra. The ν(CO) stretching bands appear at 2017 and 1887 cm^{-1} for complex **3**, and at 2027, 1928, and 1890 cm^{-1} for complex **4**. These values are within the range normally found for other complexes with the moiety "*fac*-Re(CO)$_3$". Relative to the starting material, $(NEt_4)_2[ReBr_3(CO)_3]$ (2000, 1869 cm^{-1}), the values found for **3** and **4** are higher in energy. The ν(C═O) stretching vibration of the carbonyl group of the heterofunctionalized phosphines appears at 1590 cm^{-1} for **3**, and at 1598 cm^{-1} for **4,** i.e., 30−40 cm^{-1} lower in energy relative to the corresponding free ligands, confirming the coordination to the metal center. The lowering in energy compares well with the values found for the Re(V) compounds with these ligands, previously described.[10−12] The coordination of the phosphines is also confirmed by two strong absorption bands at ca. 750 and 700 cm^{-1}, associated with the C−H and C−C out-of-plane bending vibrations of monosubstituted benzene rings.

Scheme 2. Synthesis of the Ligand HPN-Pip[a]



HPN-Pip

[a] R = *N*-succinimido. (i) Dichloromethane, room temperature

The ^{31}P NMR spectra of complexes **3** and **4** show only one singlet at δ 14.4 and δ 11.8 ppm, respectively. These resonances are significantly downfield shifted (Δ = 23.7 ppm, **3;** Δ = 21.7 ppm, **4)** relative to the free HPN_2 and H_2PNO ligands, confirming a strong σ-donor character of the phosphorus atom. The ^{1}H NMR spectra for complexes **3** and **4** present in the aromatic region a set of multiplets assigned to the protons of the aromatic rings, and another set of four signals integrating for one proton each, which reveals the diastereotopic character of the ethylenic protons (**3**, δ 6.29, 4.38, 2.26, 2.15; **4**, δ 6.69, 4.77, 4.09, 2.26). For **3** two broad singlets appear at δ 5.53 and δ 3.86 ppm, integrating for one proton each, which were assigned to the amine protons. The non-deprotonation of the amide function in complex **4** was confirmed by the presence of a broad triplet at δ 10.04 ppm.

Having in mind our interest in potential medical applications, we prepared the analogous complexes **3a** and **4a** with ^{99m}Tc, and we studied their stability in phosphate buffer.[16] Unlike **3a**, compound **4a** remains stable in solution for a long period. These results prompt us to explore the derivatization of the 4-(3-aminopropyl)-1-(2-methoxyphenyl)piperazine, which belongs to a group of molecules for the 5-HT$_{1A}$ subclass of serotonergic receptors. This moiety was functionalized as depicted in Scheme 2.

HPN-Pip was obtained in good yield (87%) after appropriate workup and was fully characterized by the usual analytical techniques. Reaction of HPN-Pip with $(NEt_4)_2[ReBr_3(CO)_3]$ at room temperature, in methanol, gave in good yield (71%) [Re(CO)$_3$(κ^2-HPN-Pip)] (**5**). This complex is air and moisture stable and soluble in halogenated solvents. In the IR spectrum, the CO stretching bands for complex **5** appear in the normal range (2023, 1930, and 1885 cm^{-1}) and, as expected, are also higher in energy relative to the corresponding starting material $(NEt_4)_2[ReBr_3(CO)_3]$. Another band appearing at 1560 cm^{-1} was attributed to the ν(C═O) stretching vibration of the carbonyl group of the ligand HPN-Pip. This band is shifted by Δ = 40 cm^{-1} relative to the corresponding stretching band in the free HPN-Pip, confirming the coordination of the oxygen atom of the carbonyl to the metal center. The two strong absorption bands associated with the monosubstituted benzene rings of the phosphines appear also at ca. 750 and 700 cm^{-1}. The ^{31}P NMR spectrum shows only one singlet at δ 14.2 ppm, downfield shifted relative to the free HPN-Pip (Δ = 22.5 ppm). The ^{1}H NMR spectrum of **5** shows also one broad triplet at δ 9.48 attributed to the amide proton of the ligand.

Description of the Structures. The structures of complexes [Re(CO)$_3$(κ^3-PN$_2$)], **3**, [Re(CO)$_3$Br(κ^2-H$_2$PNO)], **4**, and [Re(CO)$_3$Br(κ^2-HPN-Pip)], **5,** consist of discrete mononuclear units. Ellipsoid plots of **3** and **4**[17] and a diagram of **5** are given in Figures 1−3, respectively.

(16) Correia, J. D. G.; Santos, I.; Alberto, R.; Ortner, K. Unpublished results.

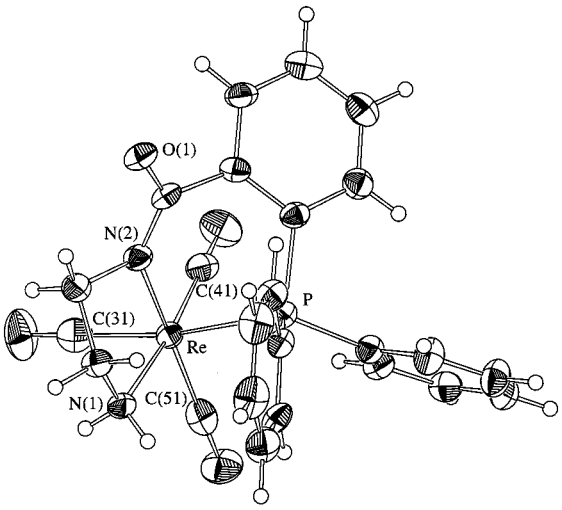


Figure 1. Ellipsoid plot of complex **3** with selected atoms numbered; thermal ellipsoids are drawn at the 50% probability level.

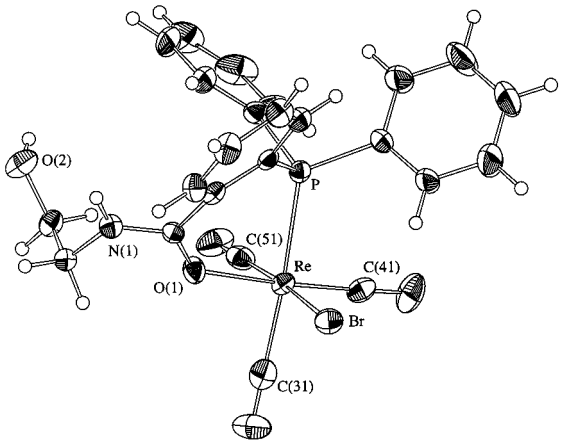


Figure 2. Ellipsoid plot of complex **4** with selected atoms numbered; thermal ellipsoids are drawn at the 50% probability level.

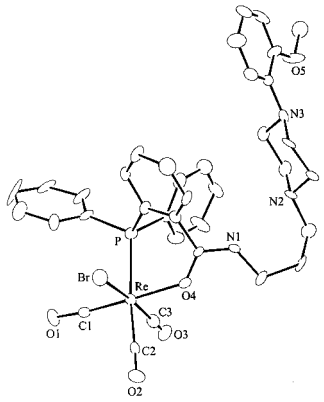


Figure 3. ORTEP drawing of complex **5** with selected atoms numbered; thermal ellipsoids are drawn at the 20% probability level.

For **5** the X-ray crystallographic analysis on a poor quality crystal did not provide an adequate data set for an accurate determination of the structure of this complex as the refinement converged to R1 = 0.1127 and wR2 = 0.1658 for 2731 reflections with $I > 2\sigma(I)$. Compound **5** crystallizes from boiling methanol as colorless crystals in the monoclinic space group $P2_1/c$ with cell parameters $a = 15.473(3)$ Å, $b = 15.128(2)$ Å, $c = 15.741(2)$ Å, $\beta = 103.670(12)°$, $V = 3580(1)$ Å^3, and $Z = 4$. However, for **5** the collected data allowed to define unambiguously the connectivities of the atoms around the Re center and to conclude that the molecular structure is, in a certain way, comparable to the structure found for complex **4**. Selected bond distances and angles for **3** and **4** are listed in Tables 2 and 3, respectively.

Table 2. Selected Bond Lengths (Å) and Angles (deg) for $[Re(CO)_3(\kappa^3\text{-}PN_2)]$ (**3**)

Re−C(41)	1.930(5)	Re−N(2)	2.192(4)
Re−C(51)	1.942(6)	Re−N(1)	2.238(4)
Re−C(31)	1.965(5)	Re−P	2.4547(11)
C(41)−Re-C(51)	91.1(2)	C(31)−Re-N(1)	87.78(18)
C(41)−Re−C(31)	88.3(2)	N(2)−Re−N(1)	76.38(14)
C(51)−Re−C(31)	91.8(2)	C(41)−Re−P	87.68(14)
C(41)−Re−N(2)	99.48(18)	C(51)−Re−P	96.21(15)
C(51)−Re−N(2)	167.90(18)	C(31)−Re−P	171.15(17)
C(31)−Re−N(2)	94.43(19)	N(2)−Re−P	78.44(10)
C(41)−Re−N(1)	174.09(18)	N(1)−Re−P	95.53(12)
C(51)−Re−N(1)	93.51(18)		

Table 3. Selected Bond Lengths (Å) and Angles (deg) for $[Re(CO)_3Br(\kappa^2\text{-}H_2PNO)]$ (**4**)

Re(1)−C(41)	1.886(8)	Re(1)−O(1)	2.164(4)
Re(1)−C(51)	1.914(8)	Re(1)−P(1)	2.4567(16)
Re(1)−C(31)	1.967(8)	Re(1)−Br(1)	2.6297(7)
C(41)−Re(1)−C(51)	91.1(3)	C(31)−Re(1)−P(1)	173.5(2)
C(41)−Re(1)−C(31)	91.0(3)	O(1)−Re(1)−P(1)	81.91(12)
C(51)−Re(1)−C(31)	89.7(3)	C(41)−Re(1)−Br(1)	95.25(19)
C(41)−Re(1)−O(1)	176.6(2)	C(51)−Re(1)−Br(1)	173.5(2)
C(51)−Re(1)−O(1)	87.8(2)	C(31)−Re(1)−Br(1)	88.65(19)
C(31)−Re(1)−O(1)	92.2(2)	O(1)−Re(1)−Br(1)	85.92(12)
C(41)−Re(1)−P(1)	95.0(2)	P(1)−Re(1)−Br(1)	88.21(4)
C(51)−Re(1)−P(1)	92.80(19)		

In the neutral complexes **3**−**5** the Re atom is six-coordinated and the coordination geometry can be described as distorted octahedral. In all the compounds the carbonyl groups occupy one triangular face of the coordination polyhedra, the other three remaining coordination sites being defined by the tridentate HPN_2 in **3** and by the bidentate H_2PNO and HPN-Pip and a bromo ligand in complexes **4** and **5,** respectively. In **3** the tridentate HPN_2 ligand is monoanionic and coordinates through the phosphorus and the two nitrogen atoms of the amide and the amine functions. In **4** and **5** the heterofunctionalized phosphines are neutral and coordinate through the phosphorus and the oxygen atom of the carbonyl group of the amide function. In all of the complexes the axial position of the octahedron is defined by the phosphorus atom of the heterofunctionalized phosphines and by one carbonyl ligand.

Deviations from the idealized octahedral geometry can be seen on the bond angles around the Re atom (Tables 2 and 3). The cis and trans bond angles are in the ranges 76.38−99.48° and 167.90−174.09° and the ranges 81.9−95.25° and 173.5−176.6° in **3** and **4**, respectively. These values indicate clearly a higher distortion in **3** than in **4**, certainly due to the tridentate coordination mode of the phosphine ligand in complex **3**.

To the best of our knowledge these are the first Re(I) carbonyl complexes isolated and structurally characterized with heterofunctionalized phosphines having such a combination of donor atoms. Therefore, a comparison of bond lengths and angles with other neutral and monomeric Re(I) complexes is difficult. However, the Re−CO bond distances in **3** (average 1.946 (6) Å) and **4** (average 1.922(8) Å) are in the range (1.89−2.03 Å) found for other neutral Re(I) tricarbonyl compounds containing monodentate, bidentate, or tridentate ligands.[5a,6,8,18] The longer value found for **3** is certainly related with the chelate coordina-

(17) Zsolnai, L.; Huttner, G. *ZORTEP*; University of Heidelberg: Heidelberg, 1994.

tion mode of the phosphine ligand and with the nature of the donor atoms. In both compounds the longer Re−CO bond distances are trans to the phosphorus, and the values are comparable (1.965(5) Å, **3**; 1.967(8) Å, **4**). This result suggests a strong σ-donor character for the phosphorus atom, which agrees with the ^{31}P NMR data. The shortest Re−CO bond distance (1.886(8) Å) is found in **4** and is trans to the carbonyl of the amide function. That carbonyl ligand is also the one which presents the longest C−O bond distance (1.169(8) Å), reflecting the π-acceptor character of the carbonyl coordinated trans to the oxygen atom of the amide function.

The Re−P bond distances found in **3** (2.4547 (11) Å) and **4** (2.4567(16) Å) are similar and do not reflect the different coordination mode of the phosphine ligands. The values are not significantly different from the Re−P bond length in other neutral complexes with monodentate phosphines, such as [Re(CO)$_3$Br(PTA)$_2$] (average 2.437 (2) Å) and [Re(CO)$_3$Br(PPhpy)$_2$] (average 2.512 Å).[19]

In **3** the Re−NH$_2$ and the Re−N bond lengths of 2.238 and 2.192 Å, respectively, are the expected values when amine and amide groups are involved.

Concluding Remarks

The complexes [Re(CO)$_3$(κ^3-PN$_2$)] (**3**), [Re(CO)$_3$Br(κ^2-H$_2$-PNO)] (**4**), and [Re(CO)$_3$Br(κ^2-HPN-Pip)] (**5**) are the first examples of *fac*-[Re(CO)$_3$]$^+$ stabilized by heterofunctionalized phosphines containing PN$_2$ and PNO donor atom sets. In **3** the ligand is tridentate and monoanionic, coordinating to the metal through the phosphorus and two nitrogen atoms of the amide and amine functions. In **4** and **5** the ligand is neutral and bidentate, through the phosphorus and the carbonyl of the amide function. Our results show the versatility of the HPN$_2$ and H$_2$-PNO ligands in terms of denticity and charge and their utility for linking to biomolecules (HPN-Pip). In order to evalute the utility of the ligands for radiopharmaceutical development, studies with the aquo ion *fac*-[^{99m}Tc(OH$_2$)$_3$(CO)$_3$]$^+$ (**1**) are in progress.

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Supporting Information Available: X-ray crystallographic files in CIF format for the structure determination of **3** and **4**. This material is available free of charge via the Internet at http://pubs.acs.org.

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(18) Abram, U.; Alberto, R.; Dilworth, J.; Zheng, Y.; Ortner, K. *Polyhedron* **1999**, *18*, 2995−3003.
(19) Schibli, R.; Katti, K. V.; Volkert, W. A.; Barnes, C. L. *Inorg. Chem.* **1998**, *37*, 5306−5312.