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Rhenium(V) and Technetium(V) Nitrido Complexes with Mixed Tridentate π-Donor and Monodentate π-Acceptor Ligands

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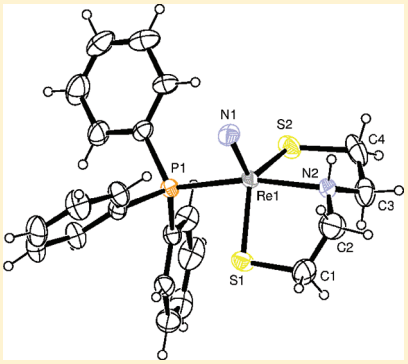
Supporting Information

ABSTRACT: Mixed-ligand $[M(N)(SNS)(PPh_3)]$ complexes (M = Tc, Re) (**1**, **2**) were prepared by reaction of the precursor $[M(N)Cl_2(PPh_3)_2]$ with ligand 2,2′-dimercaptodiethylamine $[H_2SNS = NH(CH_2CH_2SH)_2]$ in refluxing dichloromethane/ethanol mixtures. In these compounds, 2,2′-dimercaptodiethylamine acts as a dianionic tridentate chelating ligand bound to the $[M{\equiv}N]^{2+}$ group through the two π-donor deprotonated sulfur atoms and the protonated amine nitrogen atom. Triphenylphosphine completes the coordination sphere, acting as a monodentate ligand. $[M(N)(NS_2)(PPh_3)]$ complexes can assume two different isomeric forms depending on the syn and anti orientations of the hydrogen atom bound to the central nitrogen atom of the SNS ligand with respect to the M≡N moiety. X-ray crystallography of the syn isomer of complex **2** demonstrated that it has a distorted trigonal bipyramidal geometry with the nitrido group and the two sulfur atoms defining the equatorial plane, the phosphorus atom of the monophosphine and the protonated amine nitrogen of the tridentate ligand spanning the two reciprocal trans positions along the axis perpendicular to the trigonal plane. Synthesis of the analogous Tc derivatives with tris(2-cyanoethyl)phosphine, $[Tc(N)(SNS)(PCN)]$ [(PCN = $P(CH_2CH_2CN)_3$], required the preliminary preparation of the new precursor $[Tc(N)(PCN)_2Cl_2]_2$ (**3**), which was prepared by reacting $[n\text{-}NBu_4][Tc(N)Cl_4]$ with a high excess of PCN. The crystal structure of compound **3** consists of a noncrystallographic centrosymmetric dimer of Tc(V) nitrido complexes having an octahedral geometry. In this arrangement, the apical positions are occupied by two tris(2-cyanoethyl)phosphine groups and the equatorial positions by the nitrido group whereas the two Cl^- anions and one cyano ligand belong to the other octahedral component of the dimer. By reacting the new precursor $[Tc(N)(PCN)_2Cl_2]_2$ with the ligand H_2SNS the complex $[Tc(N)(SNS)(PCN)]$ (**5**) was finally obtained in acetonitrile solution. The new Tc(III) complex *trans*-$[Tc(PCN)_2Cl_4][n\text{-}NBu_4]$ (**4**) was also isolated from the reaction solution used for preparing complex **3** as side product and characterized by X-ray diffraction. The crystal structure of **4** consists of independent *trans*-$[TcCl_4(PCN)_2]^-$ anions situated on crystallographic centers of symmetry and tetrabutylammonium cations in general positions.



INTRODUCTION

Radionuclide therapy still remains one of the potentially most effective approaches for treatment of cancer.[1] In the most common accomplishment, this therapy involves intravenous administration of a radiolabeled molecule that was designed to target cancerous tissue through a specific biological mechanism selectively expressed by malignant cells. Since the very first example of this application using ^{131}I-labeled anionic iodide for the therapy of thyroid malignancies, the molecular design of the new radiotherapeutic agent has become more and more sophisticated. A common strategy entails the radiolabeling of an appropriate biologically active molecule, such as proteins, peptides, or drugs, which is known to selectively target cancerous cells. The usual challenge comes from the need to incorporate the radioactive tag within the structure of the bioactive molecule without affecting its primitive biological properties.[2] This problem becomes more relevant with metallic radionuclides, which constitutes the largest set of radioelements having suitable nuclear properties for therapeutic purposes.[3] At present, the most popular method, dubbed the 'bifunctional approach', consists of tethering a strong chelating group for the metal to a point of the bioactive molecule that is irrelevant for preserving its biological properties. The resulting bifunctional ligand would act as a bridging backbone between the biomolecule and the metal.[4]

The β-emitting radionuclide Re-188 is currently considered a very attractive candidate for development of therapeutic radiopharmaceuticals. This nuclide decays through emission of a β particle ($E_{\beta max}$ = 2.1 MeV, $t_{1/2}$ = 16.9 h) having high penetration in soft tissues.[5] Re-188 also emits a gamma photon (E_γ = 0.155 MeV) that can be conveniently used for imaging the distribution of the radiotherapeutic agent soon after its administration to the patient. This possibility can be of great help to determine the response to therapy.

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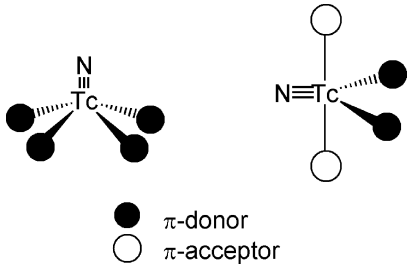
The transition metal rhenium is a congener with technetium as both belong to group 7 of the periodic table. Though their chemical properties are not completely superimposable, these two elements display many similarities. The metastable isomer ^{99m}Tc ($t_{1/2}$ = 6.06 h, E_γ = 0.140 MeV) is still the most widely used diagnostic radionuclide in nuclear medicine.[6] It has been experimentally demonstrated that a pair of technetium and rhenium compounds having exactly the same molecular geometry and ligand composition always exhibit the same in vivo biodistribution pattern.[7] This result implies that a ^{99m}Tc complex can be conveniently employed to assess the biological properties of the corresponding ^{188}Re analogue. From a practical point of view, this is of great advantage because it avoids the need of using high-dose radioactive beta-emitting radiocompounds in preclinical studies. Moreover, biodistribution data for a ^{99m}Tc analogue allow calculating dosimetry parameters that are critical to determine the effective lethal dose at the tumor. In conclusion, current trends in the search for ^{188}Re therapeutic agents always consider it to be highly useful to obtain the corresponding ^{99m}Tc counterparts whenever possible.

The chemistry of Tc and Re has been widely investigated in recent years.[8] Studies were devoted to finding strong chelating systems capable of conferring a high in vivo stability to the resulting complexes. In particular, our group focused on the study of five-coordinated complexes characterized by the presence of a terminal $[M{\equiv}N]^{2+}$ (M = Tc, Re) multiple bond.[9] An interesting feature of this class of complexes is that its structural behavior is fairly predictable simply by considering the nature of the coordinating atoms surrounding this metallic functional group.[10] In our studies, we found that a ligand system composed of four soft π-donor atoms usually affords nitrido complexes having a highly distorted umbrella-shaped, square-pyramidal geometry where the $[M{\equiv}N]^{2+}$ group lies above the basal plane. Conversely, when two π-donor and two π-acceptor atoms compose the coordination set, the preferred geometry is trigonal bipyrmidal (Scheme 1). In this arrangement, the $[M{\equiv}N]^{2+}$ core lies on the same trigonal plane occupied by the two π-donor atoms while the two π-acceptor atoms span a reciprocal trans position along the trigonal axis.[9,11]

Scheme 1



The aim of this work was to further expand our investigation on five-coordinated Tc(V) and Re(V) nitrido complexes by considering the effect on their geometrical features of the binding of three π-donor and one π-acceptor atoms. This arrangement can be accomplished by reacting the $[M{\equiv}N]^{2+}$ group with a combination of one tridentate π-donor ligand and one monodentate π-acceptor ligand (hence the acronym '3 + 1 complexes' used here). Specifically, we used here the simple ligand 2,2′-iminodiethanethiol [H_2SNS = $NH(CH_2CH_2SH)_2$], bearing a [S, N, S] π-donor atom set, and the monophosphines, tris(2-cyanoethyl)phosphine (PCN) and triphenylphosphine (PPh_3), as monodentate π-acceptor ligands for modeling this category of complexes. The results of this study will be also compared with data previously described by our group on the synthesis and structural characterization of the similar nitrido complex [$Tc(N)(ONS)(PPh_3)$] [H_2ONS = *S*-methyl-3-(2′-hydroxybenzylidene)dithiocarbazate].[12]

EXPERIMENTAL SECTION

Caution! Tc is a weak β emitter (E_β = 0.292 MeV, $t_{1/2}$ = 2.12 × 10^5 years). All manipulations were carried out in a laboratory approved for low-level radioactivity using monitored hoods and gloveboxes. When handled in milligram amounts, Tc does not present a serious health hazard since common laboratory glassware provides adequate shielding. Bremsstrahlung is not a significant problem due to the low energy of the β particles. However, proper radiation safety procedures must be used at all times to avoid contamination and inhalation of radioactive material.

Reagents. Rhenium was purchased from Sigma-Aldrich (Milan, Italy) as $KReO_4$. Technetium as $[NH_4][TcO_4]$ was obtained from Oak Ridge National Laboratory. Samples were dissolved in water and treated with excess H_2O_2 (30% v/v) at 80 °C prior to use to eliminate residual TcO_2. Solid samples of purified $[NH_4][TcO_4]$ were obtained by slow evaporation of aqueous ammonia solutions with gentle heating at 40 °C. General literature methods were employed for preparing the precursor complexes $[Re(N)Cl_2(PPh_3)_2]$,[13] $[Tc(N)Cl_2(PPh_3)_2]$,[14] and $[n\text{-}NBu_4][Tc(N)Cl_4]$.[15] Common reagents were purchased from Sigma-Aldrich (Milan, Italy) and Fluka (Milan, Italy) and used without further purification. Tris(2-cyanoethyl)phosphine [PCN = $P(CH_2CH_2CN)_3$] and triphenylphosphine [PPh_3 = $P(C_6H_5)_3$] were obtained from Sigma-Aldrich (Milan, Italy). The ligand 2,2′-iminodiethanethiol [H_2SNS = $NH(CH_2CH_2SH)_2$] was prepared using literature procedures.[16]

Physical Measurements. Elemental analyses (C, H, N, S) were performed on a Carlo Erba 1106 elemental analyzer. FTIR spectra were recorded on a Nicolet 510P Fourier transform spectrometer in the range 4000−400 cm^{-1} and in KBr mixtures using a Spectra-Tec diffuse reflectance collector accessory. ^{1}H and ^{31}P NMR spectra were collected on a Bruker AC-400 instrument using $SiMe_4$ as internal reference (^{1}H) and 85% aqueous H_3PO_4 as external reference (^{31}P). Electron-spray mass spectra in the positive-ion mode [ESI(+)MS] of rhenium and technetium compounds (ca. 10^{-6} mol dm^{-3} methanol solutions) were recorded on a LCQ instrument (Finnigan, Palo Alto, CA). Compounds were injected via a syringe pump at a flow rate of 5 μL min^{-1}. The spray capillary voltage was set at 4.5 kV, and the entrance capillary temperature and voltage were set at 240 °C and 13 V, respectively. The nebulizing gas was N_2. High-performance liquid chromatography (HPLC) was performed on a Beckman System Gold instrument equipped with a programmable solvent model 126, a sample injection valve 210A, a scanning detector Module 166, and a radioisotope detector model 170. HPLC analyses were carried out using a reversed-phase Agilent precolumn Zorbax 300SB-C18 (4.6 × 12.5 mm) and a reversed-phase Agilent column Zorbax 300SB-C18 (4.6 × 250 mm) at a flow rate of 1.0 mL/min.

Syntheses. A summary of the reactions carried out in this work is reported in Scheme 2.

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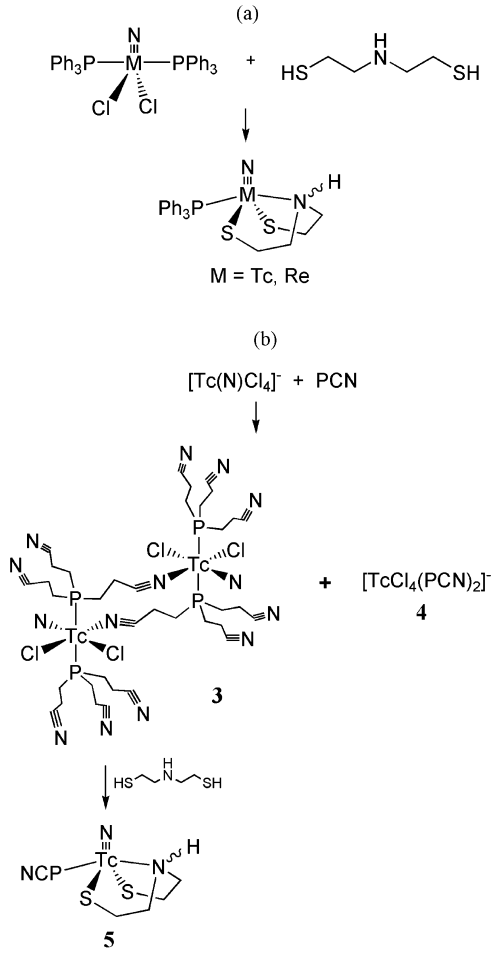
Scheme 2



*[M(N)(SNS)(PPh$_3$)] (M = Tc, **1**; M = Re, **2**).* A slight excess of the ligand H_2SNS (0.15 mmol, 0.021 g dissolved in 5 mL of EtOH) was added to a suspension containing 0.13 mmol of $[M(N)Cl_2(PPh_3)_2]$ (0.092 g for Tc; 0.10 g for Re) in 20 mL of CH_2Cl_2. The reaction mixture was heated at reflux temperature and stirred under N_2 atmosphere for 2 h. The color of the solution darkened first and then turned to bright yellow-orange after addition of excess of Et_3N (0.1 mL). After cooling, all solvents were evaporated and the crude material was washed with Et_2O. A yellow oil was collected and dried by passing a dinitrogen stream. The resulting yellow solid was crystallized by slow evaporation from an ethanol/*n*-hexane mixture yielding yellow-orange crystals of the final compound. Data for **1**. Yield: 70%. Anal. Calcd for $C_{22}H_{24}N_2PS_2Tc$: C, 51.77; H, 4.74; N, 4.49; S, 12.56. Found: C, 51.50; H, 4.65; N, 4.50; S, 12.81. IR (cm^{-1}, KBr): 1057 ν (Tc≡N), 1096 ν (Tc−P), 3067 ν(NH), 1481 ν(Ph), 1435 ν(P−Ph). ^{1}H NMR (δ, ppm, $CDCl_3$): 7.57−7.38 (m, 15H, CH_{ar}), 6.21 (s, 1H, NH), 3.22 (m, 2H, CH_2N), 3.20−2.65 (m, 2H, CH_2S), 2.27 (m, CH_2N). ^{13}C NMR (100 MHz, Me_4Si, δ, ppm, $CDCl_3$): 135.17−134.79 (6C, CH_{Ar}) 130.71 (3C, CH_{Ar}), 128.80−128.66 (6C, CH_{Ar}), 59.07 (s, CH_2S), 37.53 (s, CH_2N). ^{31}P NMR (162 MHz, −40 °C, δ, ppm, $CDCl_3$): 52.2 bs. ESI(+)MS: 511 $[MH]^+$. Data for **2**. Yield: 75%. Anal. Calcd for $C_{22}H_{24}N_2PS_2Re$: C, 44.20; H, 4.05; N, 4.69; S, 10.73. Found: C, 44.15; H, 4.11; N, 4.70; S, 10.81. IR (cm^{-1}, KBr): 1057 ν (Re≡N), 1093 ν(Re−P), 3081 ν(NH), 1481 ν(Ph), 1434 ν(P−Ph). ^{1}H NMR (δ, ppm, $CDCl_3$): 7.73 (m, 6H, CH_{ar}), 7.43 (m, 9H, CH_{ar}), 6.17 (s, 1H, NH), 3.15 (m, 2H, CH_2N), 3.15−2.87 (m, 2H, CH_2S), 2.47 (m, CH_2N). ^{13}C NMR (100 MHz, Me_4Si, δ, ppm, $CDCl_3$): 134.82−134.71 (6C, CH_{Ar}) 130.78 (3C, CH_{Ar}), 128.57−128.47 (6C, CH_{Ar}), 59.38 (s, CH_2S), 37.47 (s, CH_2N). ^{31}P NMR (162 MHz, δ, ppm, $CDCl_3$): 35.2 s. ESI(+)MS: 597, 599 $[MH]^+$. HPLC data are reported in Table 1. Compounds are soluble in chlorinated solvents, acetonitrile, acetone, and alcohols but insoluble in diethyl ether and *n*-hexane.

Table 1. HPLC Data for Selected Complexes

complex	R_f (C_{18})	retention time (min)
syn-[Re(N)(SNS)(PPh_3)]		21.04[a]
syn,anti-[^{99g}Tc(N)(SNS)PCN]	0.5[d]	14.09[b], 16.02[b]
syn,anti-[^{99g}Tc(N)(SNS)PPh_3]		20.6[a], 21.37,[a] 17.01[c]

[a] A, H_2O [containing trifluoroacetic acid (TFA, 0.1% v/v)]; B, CH_3CN [containing TFA, 0.1% v/v]. Gradient: 0−5 min, B = 30% (isocratic); 5−30 min, B = 90%; 30−35 min, B = 90% (isocratic); 35−40 min, B = 30%. [b] A, H_2O [containing TFA, 0.1% v/v]; B, CH_3CN [containing TFA, 0.1% v/v]. Gradient: 0−2 min, B = 15% (isocratic); 2−32 min, B = 20%; 32−37 min, B = 100%; 37−42 min, B = 100% (isocratic); 42−47 min, B = 15%. [c] A, H_2O [containing TFA (0.1% v/v)]; B, CH_3CN [containing TFA (0.1% v/v)]. Gradient: 0−5 min, B = 30% (isocratic); 5−20 min, B = 100%; 20−30 min, B = 100% (isocratic); 30−35 min, B = 30%. [d] H_2O [containing TFA 0.1% v/v]/CH_3CN [containing TFA (0.1% v/v)] (7:3).

*[Tc(N)(PCN)$_2$Cl$_2$]$_2$ (**3**).* To a red-orange solution containing 0.12 mmol (0.060 g) of [*n*-NBu_4][$Tc(N)Cl_4$] in 20 mL of CH_2Cl_2/EtOH (50:50% v/v), 0.48 mmol (0.093 g) of PCN, dissolved in 5 mL of CH_2Cl_2/EtOH (50:50% v/v), was added. The reaction mixture was stirred under a dinitrogen atmosphere for 1 h. The color of the solution changed to yellow. After formation of a yellow precipitate, this was filtered off and washed with diethyl ether (3 mL), ethanol (3 mL), and chloroform (3 mL). The resulting solid was dried overnight under vacuum and then dissolved in acetone. Slow diffusion of ethanol into the acetone solution afforded yellow-orange crystals suitable for X-ray diffraction. Yield: 30%. Anal. Calcd for $C_{36}H_{48}Cl_4N_{14}P_4Tc_2$: C, 37.92; H, 4.24; N, 17.20. Found: C, 37.15; H, 3.99; N, 17.01. IR (cm^{-1}, KBr): 1059 ν(Tc≡N), 1095 ν(Tc−P). ^{1}H NMR (δ, ppm, CD_3CN): 2.5 (m, 24H, CH_2CN), 2.9 (m, 24H, CH_2P). ^{31}P NMR (162 MHz, δ, ppm, CD_3CN): 23 bs. ESI(+)MS: 1139 $[MH]^+$. The compound is soluble in acetone and CH_3CN, slightly soluble in chlorinated solvents and alcohols, and insoluble in diethyl ether and *n*-pentane.

*[TcCl$_4$(PCN)$_2$][n-NBu$_4$] (**4**).* Removal of the solvent from the resulting orange supernatant collected after precipitation of compound **3** (see above) gave a yellow-orange solid residue that was filtered off and dissolved in dichloromethane. Slow evaporation of the solvent afforded orange crystals suitable for X-ray diffraction. Yield: 20%. Anal. Calcd for $C_{18}H_{24}Cl_4N_6P_2Tc$: C, 46.96; H, 6.95; N, 11.27. Found: C, 47.01; H, 7.00; N, 11.82. IR (cm^{-1}, KBr): 1098 ν(Tc−P), 356, 347 ν(Tc−Cl). ^{1}H NMR (δ, ppm, $CDCl_3$,): 1.8 (s, 12H, CH_2P), 2.6 (s, 12H, CH_2CN), 3.4−1.4 (m, 24H, $NCH_2CH_2CH_2$), 1.0 (t, 12H, NCH_3). ESI(+)MS: 649 $[Na^+ + MH]^+$, 591 $[MH - Cl]^+$, 555 $[M - 2Cl]^+$. The compound is soluble in acetone, CH_3CN, and chlorinated solvents, slightly soluble in alcohols, and insoluble in diethyl ether and *n*-pentane.

*[Tc(N)(SNS)PCN] (**5**).* To a bright orange solution containing 0.045 mmol (0.051 g) of **3** in 20 mL of CH_3CN 0.112 mmol (0.015 g) of the ligand H_2NS_2, dissolved in 5 mL of CH_3CN,

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was added. Suddenly, the color of the solution turned to yellow. The reaction mixture was stirred under a dinitrogen atmosphere for 2 h. The solvent was evaporated, and the crude material was treated with CH_2Cl_2 (2 × 3 mL). After evaporation of CH_2Cl_2, a yellow oil was collected, washed with Et_2O, and dried by passing a dinitrogen stream. Yield: 63%. Anal. Calcd for $C_{13}H_{21}N_5PS_2Tc$: C, 35.38; N, 15.87; H, 4.8. Found: C, 34.75; H, 4.6; N, 15.32. IR (cm^{-1}, KBr): 1055 ν(Tc≡N), 1092 ν(Tc−P), 3057 ν(NH). ^{1}H NMR (δ, ppm, $CDCl_3$,): 3.0 (m, 4H, CH_2N), 2.9 (m, 4H, CH_2S), 2.2 (m, 6H, CH_2CN), 2.0 (s, 1H, HN), 1.7 (m, 6H, CH_2P). ^{31}P NMR (162 MHz, δ, ppm, $CDCl_3$): 49.8 bs. ESI(+)MS: 442 $[MH]^+$. The compound is soluble in acetone and CH_3CN, slightly soluble in chlorinated solvents and alcohols, and insoluble diethyl ether and *n*-pentane.

X-ray Crystallography. Crystal data of compounds **2**, **3**, and **4** were collected on a Nonius Kappa CCD diffractometer using graphite-monochromated Mo Kα radiation (λ = 0.7107 Å) at room temperature (295 K). Data sets were integrated with the Denzo-SMN package[17] and corrected for Lorentz-polarization and absorption[18] effects. Structures were solved by direct methods (SIR97)[19] and refined by full-matrix least-squares methods with all non-hydrogen atoms anisotropically and hydrogens included on calculated positions, riding on their carrier atoms.

2. $C_{22}H_{24}N_2PReS_2$, M = 597.72, monoclinic, $P2_1/c$ (No. 14), a = 9.3975(1) Å, b = 9.6035(1) Å, c = 25.7530(5) Å, β = 97.4211(6)°, V = 2304.71(6) Å^3, Z = 4, D_c = 1.723 g cm^{-3}, μ = (Mo Kα) = 5.533 mm^{-1}, 5498 independent reflections, $\theta \leq$ 28.00°, 4200 observed reflections [$I \geq 2\sigma(I)$], R_1 = 0.0324 (observed reflections), wR_2 = 0.0792 (all reflections), GOF = 1.008, 257 parameters. Aminic H2 hydrogen atom was refined isotropically. CCDC No. 855423.

3. $C_{36}H_{48}Cl_4N_{14}P_4Tc_2$, M = 1140.39, orthorhombic, $P2_12_12_1$ (No. 19), a = 12.5552(1) Å, b = 18.1326(2) Å, c = 21.7075(3) Å, V = 4941.9(1) Å^3, Z = 4, D_c = 1.533 g cm^{-3}, μ = (Mo Kα) = 0.948 mm^{-1}, 14 343 independent reflections, $\theta \leq$ 30.00°, 11 849 observed reflections [$I \geq 2\sigma(I)$], R_1 = 0.0401 (observed reflections), wR_2 = 0.0962 (all reflections), GOF = 1.028, 537 parameters. Some CN groups of the tris(cyanoethyl)phosphine ligands were found disordered and refined isotropically over two positions. CCDC No. 855424.

4. $(C_{18}H_{24}Cl_4N_6P_2Tc)^-$ $(C_{16}H_{36}N)^+$, M = 869.56, triclinic, *P*-1 (No. 2), a = 11.9436(2) Å, b = 12.5886(2) Å, c = 16.4361(3) Å, α = 71.7489(7)°, β = 72.5811(6)°, γ = 88.9434(7)°, V = 2231.53(7) Å^3, Z = 2, D_c = 1.294 g cm^{-3}, μ = (Mo Kα) = 0.665 mm^{-1}, 10 695 independent reflections, $\theta \leq$ 28.00°, 8264 observed reflections [$I \geq 2\sigma(I)$], R_1 = 0.0353 (observed reflections), wR_2 = 0.0938 (all reflections), GOF = 1.055, 437 parameters. The asymmetric unit is built up by two independent anionic complexes situated on centers of symmetry and a tetrabutylammonium cation in general position. A number of carbon atoms of the cation moiety were found disordered and refined isotropically over two positions. CCDC No. 855425.

All calculations were performed using SHELXL-97[20] and PARST[21] implemented in the WINGX[22] system of programs. Selected bond distances and angles are reported in Tables 2, 3, and 4.

RESULTS

Synthesis and Characterization. The [M(N)(SNS)-(PPh_3)] complexes [M = Tc (**1**), Re (**2**)] were prepared in high yield from the labile precursors $[M(N)Cl_2(PPh_3)_2]$ via ligand-exchange reactions using an excess of the H_2SNS ligand. IR spectra exhibit characteristic bands at 1057 cm^{-1} assigned to the ν[M≡N] stretching vibration. Frequencies in the regions 1093−1096 and 3067−3081 cm^{-1} were assigned to the stretching vibrations of the M−PPh_3 group and of the amine group of the SNS ligand, respectively. Elemental analyses were also in good agreement with the proposed formulation. Proton spectra of complexes **1** and **2** showed relatively complex patterns consistent with their molecular structures. Complex **2** shows a sharp singlet at 35.2 ppm in the ^{31}P NMR spectrum arising from the presence of the monophosphine ligand. Conversely, the same signal was difficult to observe at room temperature for the Tc complex as a consequence of the wide broadening caused by the coupling of the quadrupolar ^{99g}Tc nucleus (I = 9/2) with the neighbor ^{31}P nucleus.[23] Figure 1a reports the HPLC chromatogram of the isomer *syn*-[Re(N)-(SNS)(PPh_3)] (see Discusssion section) eluted as a single peak at 21.04 min. The HPLC chromatogram of the complex [^{99g}Tc(N)(SNS)(PPh_3)] (Figure 1b) reveals the presence of

Table 2. Selected Bond Distances (Angstroms) and Angles (degrees) for Compound 2

bond distances			
Re1−N1	1.669(4)	Re1−S2	2.328(2)
Re1−N2	2.161(4)	Re1−P1	2.385(1)
Re1−S1	2.314(1)		
bond angles			
N1−Re1−N2	100.9(2)	N2−Re1−S2	82.9(1)
N1−Re1−S1	113.6(1)	N2−Re1−P1	165.2(1)
N1−Re1−S2	114.4(1)	S1−Re1−S2	131.63(5)
N1−Re1−P1	93.6(1)	S1−Re1−P1	89.69(4)
N2−Re1−S1	87.5(1)	S2−Re1−P1	93.24(5)
H bond			
N2−H2	0.84(4)	N2···N1	2.870(5)
H2···N1(−*x*,−*y*,−*z*)	2.04(4)	N2−H2···N1	170(4)

Table 3. Selected Bond Distances (Angstroms) and Angles (degrees) for Compound 3

bond distances			
Tc1−N1	1.630(3)	Tc2−N2	1.632(3)
Tc1−Cl1	2.632(1)	Tc2−Cl3	2.638(1)
Tc1−Cl2	2.404(1)	Tc2−Cl4	2.406(1)
Tc1−P1	2.484(1)	Tc2−P3	2.475(1)
Tc1−P2	2.454(1)	Tc2−P4	2.467(1)
Tc1−N9	2.126(3)	Tc2−N3	2.126(3)
bond angles			
N1−Tc1−Cl1	170.0(1)	N2−Tc2−Cl3	170.8(1)
N1−Tc1−Cl2	99.1(1)	N2−Tc2−Cl4	98.3(1)
N1−Tc1−P1	96.7(1)	N2−Tc2−P3	97.0(1)
N1−Tc1−P2	94.1(1)	N2−Tc2−P4	95.0(1)
N1−Tc1−N9	91.9(1)	N2−Tc2−N3	92.0(1)
Cl1−Tc1−Cl2	90.50(3)	Cl3−Tc2−Cl4	90.86(3)
Cl1−Tc1−P1	86.48(3)	Cl3−Tc2−P3	84.72(3)
Cl1−Tc1−P2	83.63(3)	Cl3−Tc2−P4	83.92(3)
Cl1−Tc1−N9	78.56(8)	Cl3−Tc2−N3	78.87(8)
Cl2−Tc1−P1	86.41(3)	Cl4−Tc2−P3	86.77(4)
Cl2−Tc1−P2	87.62(3)	Cl4−Tc2−P4	88.30(4)
Cl2−Tc1−N9	168.85(8)	Cl4−Tc2−N3	169.54(7)
P1−Tc1−P2	168.40(3)	P3−Tc2−P4	167.55(4)
P1−Tc1−N9	90.72(8)	P3−Tc2−N3	90.27(9)
P2−Tc1−N9	93.25(8)	P4−Tc2−N3	92.53(9)

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Table 4. Selected Bond Distances (Angstroms) and Angles (degrees) for Compound 4

	molecule A	molecule B		molecule A	molecule B
bond distances					
Tc1−Cl1	2.4180(5)	2.4242(5)	Tc1−P1	2.4571(5)	2.4577(7)
Tc1−Cl2	2.3722(7) 2.3542(6)				
bond angles					
Cl1−Tc1−Cl1′	180	180	Cl2−Tc1−Cl2′	180	180
Cl1−Tc1−Cl2	88.78(2)	88.82(2)	Cl2−Tc1−P1	90.01(2)	90.16(2)
Cl1−Tc1−Cl2′	91.22(2)	91.18(2)	Cl2−Tc1−P1′	89.99(2)	89.84(2)
Cl1−Tc1−P1	91.69(2)	92.42(2)	P1−Re1−P1′	180	180
Cl1−Tc1−P1′	88.31(2)	87.58(2)			

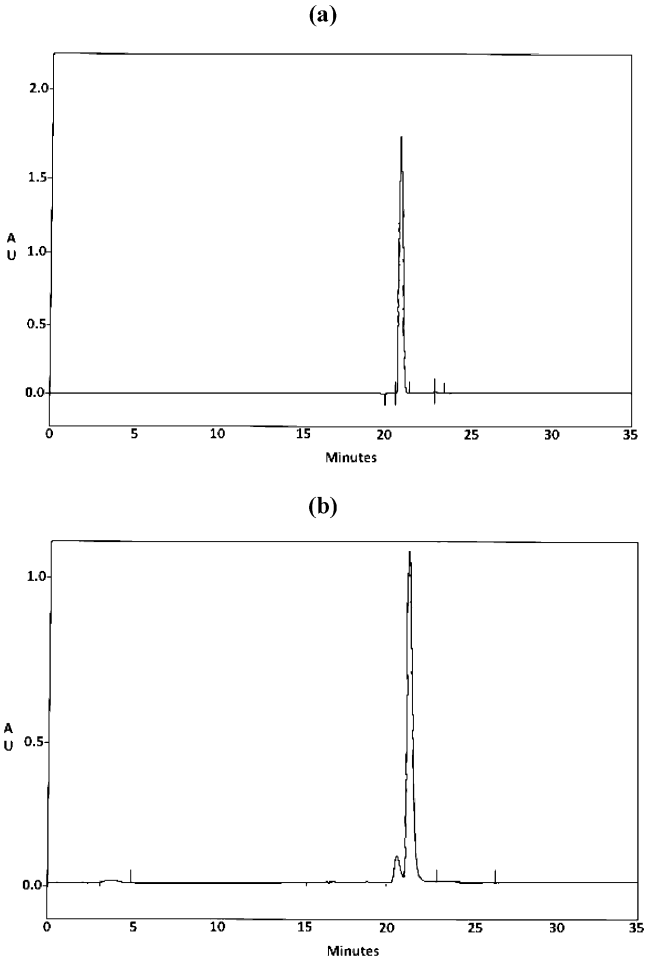

Figure 1. HPLC chromatograms of (a) *syn*-[Re(N)(SNS)(PPh_3)] (**2**) and (b) a mixture of *syn/anti*-[^{99} ^{g}Tc(N)(SNS)(PPh_3)] (**1**).

one main peak at almost the same retention time (21.37 min) of the Re analogue accompanied by another smaller peak (20.6 min). These two peaks were tentatively interpreted as corresponding to a mixture of syn and anti isomers (see also Table 1).

Attempts to prepare the analogous complexes with the monophosphine PCN by simple substitution onto the precursors [M(N)Cl_2(PPh_3)$_2$] (M = Tc, Re) with an excess of H_2SNS and PCN did not afford the complexes [M(N)(SNS)PCN] (**5**) in satisfactory yields. Similarly, reaction of the complex [Tc(N)Cl_4]$^-$ in the presence of PCN and H_2SNS failed to give the desired product (the same reaction with the Re analog [Re(N)Cl_4]$^-$ was not attempted due to the high instability of this compound). To obtain the PCN derivative, the new mixed halogeno−phosphino precursor complex [Tc(N)(PCN)$_2$$Cl_2$]$_2$ (**3**) was prepared by reacting [*n*-NBu_4][Tc(N)Cl_4] with a high excess of PCN in a CH_2Cl_2/EtOH mixture. Compound **3** was isolated by precipitation as a yellow-orange solid and then further used for preparing the complex [Tc(N)(SNS)(PCN)] (**5**) in good yield by a simple exchange reaction with H_2SNS.

Compound **3** was not the only product of the reaction of [Tc(N)Cl_4]$^-$ with PCN. Slow evaporation of the residual orange supernatant left aside after precipitation of **3** yielded orange crystals of the octahedral monoanionic Tc(III) complex *trans*-[Tc(PCN)$_2$$Cl_4$][*n*-$NBu_4$] (**4**).

The proposed formulations for complexes **3**, **4**, and **5** were confirmed by elemental analyses and spectroscopic measurements. The mass spectrum of **3** showed the parent ions and various fragments corresponding to loss of chloride ions having the expected isotopic pattern. No detectable fragmentation was observed for complex **4**, thus indicating the high stability of this dimeric structure. Whereas complexes **3** and **5** display observable ^{31}P NMR signals at room temperature in agreement with the expected phosphine coordination, no distinct ^{31}P NMR signal was detected for compound **4**. The paramagnetism of octahedral Tc(III) high-spin d^3 complexes also accounts for the broadening of signals in the ^{1}H NMR spectrum of **4**.[24]

The molecular structure of the isomeric form *syn*-[Re(N)(SNS)(PPh_3)] of complex **2** was solved by X-ray diffraction analysis, and the ORTEP[25] view of this complex is reported in Figure 2a. This five-coordinated complex exhibits a distorted trigonal bipyramidal geometry with the nitrido group and the sulfur atoms of the SNS ligand defining the equatorial plane and the phosphorus of the PPh_3 group and the nitrogen of SNS ligand occupying the axial positions. The Re1−N1 distance of 1.669(4) Å is indicative of a strong Re≡N triple bond, in agreement with other X-ray authentic trigonal bipyramidal or square pyramidal Re(V) nitrido complexes where Re−N bond lengths fall in the range 1.61−1.67 Å.[11,15,26] The overall geometrical core is very similar to those observed in Re(V)−oxo complexes containing analogous ligands.[26] In the crystal packing a pair of complexes form dimers by means of N2−H···N1(nitrido) hydrogen bonds (Figure 2b). A similar arrangement was found in the Re−oxo complex containing the same SNS ligand.[27]

The ORTEP views of complexes **3** and **4** are reported in Figures 3 and 4, respectively. Compound **3** consists of a noncrystallographic centrosymmetric dimer of Tc(V) nitrido complexes with octahedral coordination, where the apical positions are occupied by two tris(2-cyanoethyl)phosphine groups and the equatorial positions by the nitrido group, two Cl^- anions, and a cyano ligand belonging to the other octahedral component of the dimer. The Tc−N distances of

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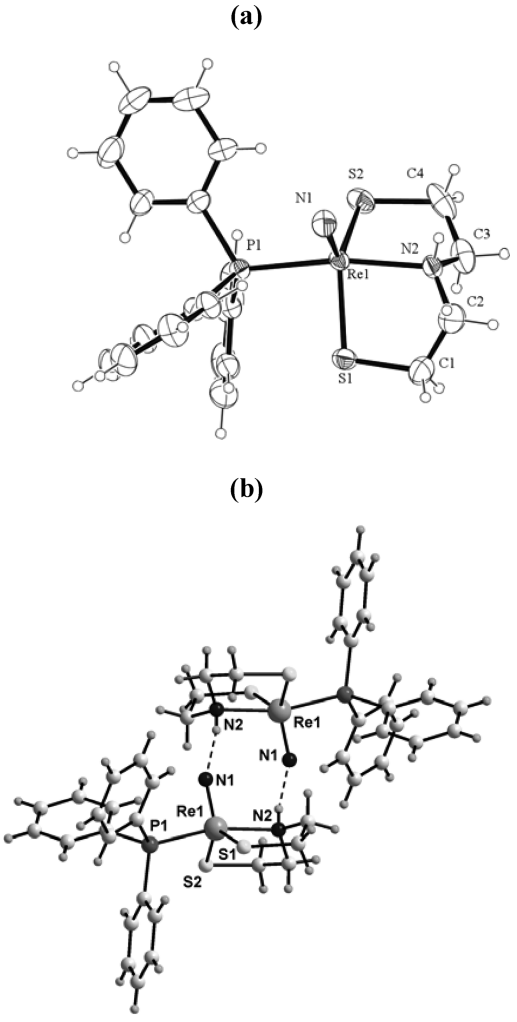

Figure 2. (a) ORTEP view of complex **2** displaying thermal ellipsoids at 30% probability. (b) View of the crystal dimer formed by complex **2** by means of a N2−H2···N1 intermolecular H bond.

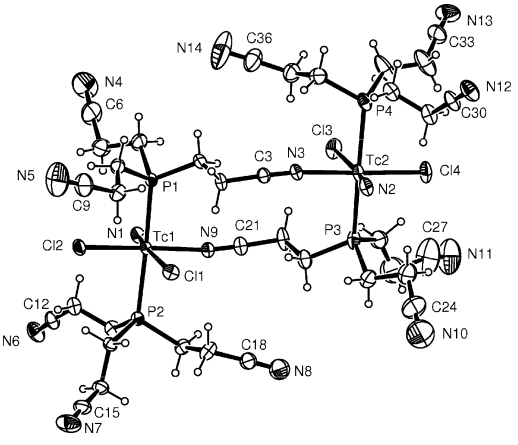

Figure 3. ORTEP view of dimeric complex **3** displaying thermal ellipsoids at 30% probability.

1.630(3) and 1.632(3) Å are consistent with the length of the triple Tc≡N bond found for other octahedral Tc(V) nitrido complexes (in the range 1.60−1.64 Å). The strong trans influence exerted by the nitrido ligand causes an extreme lengthening of the Tc−Cl(*trans*) bond distances up to 2.632(1) and 2.638(1) Å as compared to the equatorial Tc−Cl bond of

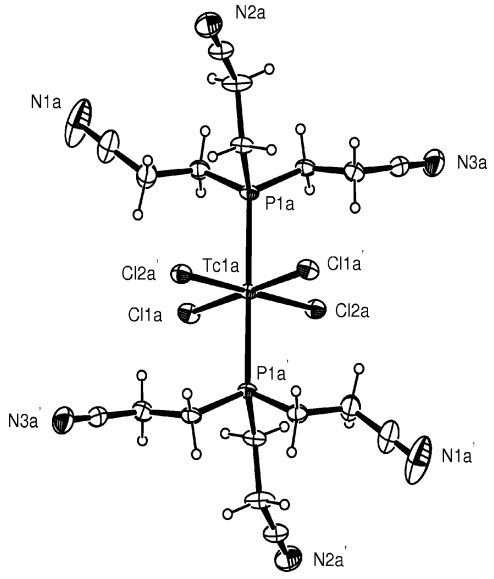

Figure 4. ORTEP view of anion complex A of compound **4** displaying thermal ellipsoids at 30% probability.

2.404(1) and 2.406(1) Å. This result is in close accordance with the structural data of other Tc(V) complexes where Tc−Cl bond distances trans to a nitrido group fall in the range 2.59−2.73 Å, whereas Tc−Cl(*cis*) distances display values from 2.41 to 2.45 Å.[28]

The crystal structure of compound **4** consists of independent *trans*-$[Tc(III)Cl_4(PCN)_2]$ anions lying on crystallographic centers of symmetry and tetrabutyl ammonium cations located in general positions. Both the independent A and B anions assume an octahedral geometry where the equatorial plane is defined by four Cl^- ligands and two PCN groups span the apical positions. Owing to the centrosymmetry, the octahedral coordination of both anions is rather regular. The Tc−Cl average bond distance of 2.392 Å is in excellent agreement with that of 2.386 Å observed in the similar octahedral structure of the anionic complex *trans*-$[Tc(III)Cl_4(Py)_2]$ (py = pyridine).[29]

DISCUSSION

The combination of the tridentate π-donor ligand 2,2′-iminodiethanethiol (H_2SNS) with a monodentate π-acceptor phosphine (PCN, PPH_3) provides a simple model for studying the behavior of five-coordinate Tc(V) and Re(V) nitrido complexes comprising a mixed coordination environment (briefly called here '3 + 1' nitrido complexes). The main interest for this study originated from the previous observation that there exists a kind of geometrical control of the structure of these complexes brought about by the nature of the coordinating atoms. Specifically, a set composed by four π-donor atoms favors a highly distorted umbrella-shaped square-pyramidal (sp) geometry, whereas a set formed by two π-donor and two π-acceptor atoms promotes the transition to trigonal bipyramidal geometry (tbp). A simple, qualitative interpretation of these findings could be obtained by considering the distribution of frontier molecular orbitals (FMO) of the metallic fragment $[M{\equiv}N]^{2+}$ (M = Tc, Re) in a five-coordinate arrangement as described in standard articles and textbooks.[30] In sp symmetry, FMOs belong to the same group formed by four antibonding orbitals pointing toward the vertexes of the basal square plane. Conversely, in a tbp symmetry, there exists a separation between FMOs involved in the π bonding along the

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axial positions and those lying on the trigonal plane. This suggests that tbp geometry can better accommodate a combination of π-acceptor and π-donor ligands. A sharp evidence of this picture comes from the observation that, in mixed phosphino−thiol Tc(V) nitrido complexes, the two π-acceptor P atoms always prefer to occupy a reciprocal trans position along the axis perpendicular to the trigonal plane.[11a] In this context, the '3 + 1' chelating system investigated here constitutes another interesting combination to add to the whole picture, particularly because it is not immediately apparent which final coordination arrangement will be the most favored.

The observed results nicely confirmed the theoretical predictions and the elegant chemical behavior of the M≡N (M = Tc, Re) functional group. Reactions of the labile precursors $[M(N)Cl_2(PPh_3)_2]$ with the ligand H_2SNS afforded the neutral complexes $[M(N)(SNS)(PPh_3)]$ (M = Tc, **1**; M = Re, **2**). In these complexes, H_2SNS binds to the M≡N moiety as a dianionic tridentate ligand through two deprotonated thiol sulfur atoms and the protonated amine nitrogen atom. A PPh_3 ligand spans the residual fourth position. Retention of the H atom bound to the amine nitrogen enable the complexes to exist in two different isomeric forms depending on the syn and anti orientations of this hydrogen with respect to the M≡N group. The crystal structure of compound **2** corresponds to the syn isomer isolated in a pure crystalline form. Results showed that **2** has a distorted tbp structure with the two sulfur atoms of the SNS ligand and the nitrido group lying on the trigonal equatorial plane. The phosphorus atom of PPh_3 occupies one axial position trans to the neutral nitrogen atom of the SNS ligand. The close correspondence between the single HPLC peak of complex **2** (Figure 1a) and the main peak observed in the HPLC chromatogram of **1** (Figure 1b) strongly indicates that both compounds are syn isomers; thus, formation of the syn arrangement is the most favored. Apparently, the presence of a small secondary HPLC signal for compound **1** (Figure 1b), tentatively assigned to the anti isomer, suggests that only a small fraction of this isomer is formed. No interconversion between the two isomeric forms was detected in the temperature range from room temperature to 100 °C.

As mentioned above, the existence of a tbp geometry for complex **2**, where the amino and phosphino groups share a reciprocal trans position, indicates that the N and P atoms overlap with the axial FMOs of the $[M{\equiv}N]^{2+}$ fragment. It might be conjectured that the sp^3 character of the protonated NH atom prevents it from behaving as a true π donor. This precludes its interaction with the π-orbital set of both sp and tbp geometries and ultimately favors a tbp arrangement. Previous structural data reported for the complex $[^{99g}Tc(N)(ONS)(PPh_3)]$[12] strongly support this interpretation. In this compound, the Schiff base H_2SNO coordinates to the $[M{\equiv}N]^{2+}$ fragment as a tridentate ligand through the negative hydroxylic oxygen atom, the neutral aldiminic nitrogen atom, and the negative thiol sulfur atom. The resulting sp geometry is consistent with the stronger π-donor character of the sp^2 nitrogen atom of the Schiff base functional moiety. The preference of a neutral sp^3 nitrogen atom to span a trans position to a π-acceptor P atom has been recently observed also in octahedral Tc(V) nitrido complexes with 2-(diphenylphosphinomethyl)aniline.[23c]

The new complexes $[^{99g}Tc(N)(PCN)_2Cl_2]_2$ (**3**) and *trans*-$[^{99g}TcCl_4(PCN)_2]^-$ (**4**) were both obtained from reaction of the Tc(VI) nitrido complex $[^{99g}Tc(N)Cl_4]^-$ with excess PCN. This reaction offers another rare example of removal of the highly stable nitrido moiety from a Tc(V) ion.[11a,31] Compound **3** is remarkable because the expected complex was the five-coordinate $[Tc(N)Cl_2(PCN)_2]$ closely analogous to the well-known precursor $[Tc(N)Cl_2(PPh_3)_2]$. Formation of a dimeric species is surprising also in view of the excess of PCN employed in the reaction. At first sight, **3** might be considered as an intermediate species formed between the starting Tc(VI) nitrido precursor and the final Tc(III) reduced compound. However, after isolation, **3** did not show the tendency to further react with PCN or convert spontaneously into complex **4** when dissolved in acetone or CH_3CN. This study was partially hampered by the low solubility of **3** in other solvents. Another tentative explanation for production of complex **4** could be attributed to the presence of some residual amount of the Tc(IV) complex, $[TcCl_6]^{2-}$,[8a,32] usually formed during preparation of the starting $[Tc(N)Cl_4][n\text{-}Bu_4]$. However, elemental analysis of the precursor Tc(VI) nitrido complex reasonably eliminated this possibility. According to these preliminary observations, formation of complexes **3** and **4** from $[Tc(N)Cl_4]^-$ seems to follow separate routes. However, further studies are required to fully determine the exact mechanism of these reactions.

■ CONCLUSIONS

The new '3 + 1' complexes $[M(N)(SNS)(PPh_3)]$ (M = Tc, Re) and $[Tc(N)(SNS)(PCN)]$ have been prepared and fully characterized. The structural characteristics of the new category of compounds could provide a convenient chemical platform for developing new diagnostic and therapeutic agents labeled with technetium-99m and rhenium-188. In fact, the relative flexibility of the coordination environment might allow a fine tuning of the biological properties of the resulting radiopharmaceuticals and essential prerequisite for development of target-specific agents for molecular imaging. Extensive studies on preparation of the corresponding Re-188 and Tc-99m '3 + 1' complexes using biologically derived SNS-type ligands have been already carried out and will be published elsewhere.

■ ASSOCIATED CONTENT

Supporting Information

X-ray crystallographic data for **2**, **3**, and **4** in cif format. This material is available free of charge via the Internet at http://pubs.acs.org.

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Notes

The authors declare no competing financial interest.

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