

Structural and ^{99}Tc NMR Investigations of Complexes with $\text{fac-}[\text{Tc}(\text{CO})_3]^+$ Moieties and Macrocyclic Thioethers of Various Ring Sizes: Synthesis and X-ray Structure of the Complexes $\text{fac-}[\text{Tc}(\text{9-ane-S}_3)(\text{CO})_3]\text{Br}$, $\text{fac-}[\text{Tc}_2(\text{tosylate})_2(18\text{-ane-S}_6)(\text{CO})_6]$, and $\text{fac-}[\text{Tc}_2(20\text{-ane-S}_6\text{-OH})(\text{CO})_6][\text{tosylate}]_2$

Roger Schibli,[†] Roger Alberto,[‡] Ulrich Abram,[§] Sonja Abram,[§] André Egli,[‡]
P. August Schubiger,^{*,‡} and Thomas A. Kaden^{||}

Center for Radiological Research, University of Missouri, Columbia, Missouri 65211, Division of Radiopharmacy, Paul Scherrer Institute, CH-5232 Villigen, Switzerland, Forschungszentrum Rossendorf, Institute of Radiochemistry, c/o Dresden University of Technology, D-01062 Dresden, Germany, and Institute of Inorganic Chemistry, Spitalstrasse 51, CH-4056 Basel, Switzerland

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Starting originally from the organometallic precursor $[\text{NET}_4]_2[\text{TcBr}_3(\text{CO})_3]$ (**1b**), substitution reactions were performed with the macrocyclic thioethers 1,4,7-trithiacyclononane (9-ane-S₃), 1,4,7,10,13,16-hexathiacyclooctadecane (18-ane-S₆), and 3,6,9,13,16,19-hexathiacycloicosanol (20-ane-S₆-OH). The corresponding complexes $\text{fac-}[\text{Tc}(\text{9-ane-S}_3)(\text{CO})_3]\text{Br}$ (**2**), $\text{fac-}[\text{Tc}_2(\text{tosylate})_2(18\text{-ane-S}_6)(\text{CO})_6]$ (**3**), and $\text{fac-}[\text{Tc}_2(20\text{-ane-S}_6\text{-OH})(\text{CO})_6][\text{tosylate}]_2$ (**5**) were isolated in good yields and characterized spectroscopically by IR, ^1H , ^{99}Tc NMR, and X-ray diffraction methods. In the case of 18-ane-S₆ and 20-ane-S₆-OH the formation of the 1:2 as well as the 1:1 complex could be observed in the ^{99}Tc NMR experiment, depending on the ligand to metal ratio. Complex **2** crystallizes in the monoclinic space group $P2_1/c$, $a = 14.79(2)$ Å, $b = 11.691(2)$ Å, $c = 16.94(2)$ Å, $\beta = 94.88(6)^\circ$, $Z = 8$. The tripodal ligand is coordinated through the sulfur atoms to the metal center, forming three favorable five-membered chelate rings. Complex **3** crystallizes in the monoclinic space group $C2/c$, $a = 26.073(4)$ Å, $b = 9.288(1)$ Å, $c = 17.898(3)$ Å, $\beta = 99.84(1)^\circ$, $Z = 4$. The binuclear unit is formed by two $\text{fac-}[\text{Tc}(\text{tosylate})(\text{CO})_3]$ moieties which are trans, bidentate coordinated to the macrocyclic ligand. Compound **5** crystallizes in the monoclinic space group Pc , $a = 25.737(4)$ Å, $b = 14.009(1)$ Å, $c = 26.479(3)$ Å, $\beta = 149.56(2)^\circ$, $Z = 4$. In the case of the dicationic compound **5**, the two Tc(I) centers are tripodal, cis coordinated toward the thia crown ether. A detailed analysis of the ring conformation in the solid state structure explained to a certain extent the formation of only one isomer (trans in the case of **3** and cis in the case of **5**, respectively) during the substitution reaction.

Introduction

Macrocyclic thioethers have been a topic of interest because of the σ - and π -donating and the π -accepting properties in addition to their increased thermodynamic stability over open-chain analogues due to the macrocyclic effect.¹ Furthermore, thioethers are resistant toward aerial oxidation, hydrolysis, and protonation. These facts play an important role for the stability of corresponding complexes when tested under challenging *in vivo* conditions. Therefore, Tc-99m, Re-186, or Ag-111 labeled complexes based on a thiamacrocyclic skeleton are of interest for radiopharmaceutical applications. Numerous publications have documented the high affinity of technetium toward sulfur atoms in thiols, thiolates, and thioethers and in particular macrocyclic thioethers.² However, reports of compounds with cyclic thioethers and technetium in lower oxidation states and in particular organometallic technetium complexes are rare.³ Furthermore, none of the later species have ever been structur-

ally characterized. This lack of examples is striking since the chemistry of $^{99}\text{Tc}(\text{I})$ with other σ -donating and π -accepting ligand systems such as phosphines and isonitriles has been widely explored.⁴ The compounds **2**, **3**, and **5** presented in this paper are the first fully characterized representatives of this class of interesting compounds. Although there are examples of rhenium(I)-carbonyl complexes of the general formula $\text{fac-}[\text{ReX}_n(\text{L})(\text{CO})_3]^{(1-n)+}$ ($X = \text{Cl, Br}$; $n = 0, 1$) with L being

* Author for correspondence. E-mail: schubiger@psi.ch. Fax: (0)56-310-2849.

[†] Center for Radiological Research, University of Missouri—Columbia.

[‡] Division of Radiopharmacy, Paul Scherrer Institute.

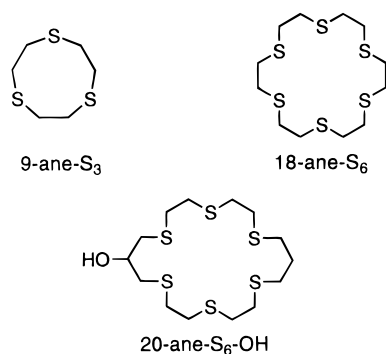
[§] Forschungszentrum Rossendorf, Institute of Radiochemistry, Dresden University of Technology.

^{||} Institute of Inorganic Chemistry, University of Basel.

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Scheme 1



thiamacrocycles of different ring size and various numbers of sulfur atoms,¹ no examples of polynuclear metal–carbonyl complexes of group 7b elements with large macrocycles (S_6 or S_8) can be found in the literature. Our group recently reported a convenient synthesis of *fac*-[NET_4]₂[$\text{TcX}_3(\text{CO})_3$] ($X = \text{Cl}$ (**1a**), Br (**1b**)) on the macroscopic level with Tc-99 as well as on the no-carrier-added level with Tc-99m.⁵ **1** and its corresponding rhenium analogue have proved to be excellent synthons for selective substitution reactions with a variety of ligand systems under ambient reaction conditions.⁶ In the presented work we combined the pronounced capacity of thioether ligands to bind technetium with the kinetical inertness of the organometallic *fac*-[$\text{Tc}(\text{CO})_3$]⁺ moiety. We reacted **1** with the three macrocyclic thioethers 9-ane- S_3 , 18-ane- S_6 , and 20-ane- S_6 -OH, which have the potential to be attached to biologically relevant molecules after further derivatization (Scheme 1). We describe herein the synthesis and the structure of the complexes *fac*-[$\text{Tc}(9\text{-ane-S}_3)(\text{CO})_3$ Br] (**2**), *fac*-[$\text{Tc}_2(\text{tosylate})_2(18\text{-ane-S}_6)(\text{CO})_6$] (**3**), and *fac*-[$\text{Tc}_2(20\text{-ane-S}_6\text{-OH})(\text{CO})_6$][tosylate]₂ (**5**). The substitution reactions with 18-ane- S_6 and 20-ane- S_6 -OH were monitored by means of ⁹⁹Tc NMR, and the formation of 1:2 as well as 1:1 species was detected.

Experimental Section

All reactions were carried out by standard Schlenk techniques. Chemicals and solvents were of reagent grade, were purchased from Fluka AG Buchs, and were used without further purification. 1,4,7-Trithiacyclononane and 1,4,7,10,13,16-hexathiacyclooctadecane were purchased from Aldrich. 3,6,9,13,16,19-Hexathiacycloicosanol was prepared according to the literature.⁷ The starting material **1a/b** was synthesized by procedures reported previously.^{5a} FT-IR spectra were recorded on a Perkin-Elmer 16 PC FT-IR spectrometer as KBr pellets. The ¹H and ⁹⁹Tc NMR spectra were recorded on a Varian Gemini 2000 system (operating at 300 MHz). ¹H chemical shifts are reported relative to residual solvent protons as a reference (3.30 ppm for methanol-*d*₄, 2.49 ppm for DMSO-*d*₆). For the ⁹⁹Tc chemical shifts NH_4TcO_4 (0 ppm, in D₂O) was used as the external reference. Acquisition parameters of the ⁹⁹Tc NMR spectra: The pulse frequency was set to

67.5224 MHz with a pulse angle of 54.8°. The spectrum width was set to 100 kHz. All spectra were recorded with an acquisition time of 0.3 s/scan and an addition of 1000 scans/spectrum. The line broadening was 1 Hz.

CAUTION! ⁹⁹Tc is a weak β -emitter. Although radiation from small amounts of material is completely absorbed by glass walls, all operations have been carried out in specially equipped laboratories to avoid contamination or ingestion.

Synthesis of *fac*-[$\text{Tc}(9\text{-ane-S}_3)(\text{CO})_3$ Br] (2**).** [NET_4]₂[$\text{TcBr}_3(\text{CO})_3$] (88 mg, 0.13 mmol) was dissolved in 5 cm³ of methanol. 1,4,7-Trithiacyclononane (23 mg, 0.13 mmol) was added, and the reaction mixture was stirred at ambient temperature overnight. A white precipitate was formed, which was filtered, washed with ether, and dried in vacuo. Yield: 50 mg (87%). Crystals of X-ray quality were obtained from a warm, saturated methanolic solution. IR (cm⁻¹, KBr): 3420 (w), 3356 (w), 2904 (w), 2050 (vs), 1980 (vs), 1410 (w), 1190 (w), 1050 (w), 622 (m), 594 (w), 512 (m). ¹H NMR (δ , methanol-*d*₄): 3.1 (broad s). ⁹⁹Tc NMR (δ , methanol-*d*₄): -1656 (s, $\Delta\nu_{1/2}$ = 150 Hz).

Synthesis of *fac*-[$\text{Tc}_2(\text{tosylate})_2(18\text{-ane-S}_6)(\text{CO})_6$] (3**).** [NET_4]₂[$\text{TcBr}_3(\text{CO})_3$] (129 mg, 0.19 mmol) was dissolved in 5 cm³ of methanol. Silver tosylate (153 mg, 0.55 mmol) was dissolved in 3 cm³ of methanol and added. After filtration of AgBr, 1,4,7,10,13,16-hexathiacyclooctadecane (34 mg, 0.08 mmol) was added to the methanolic solution and the reaction mixture was stirred overnight at ambient temperature. The solvent was removed in vacuo, and 2 cm³ of CH₂Cl₂ was added to the colorless, oily residue to remove [NET_4][tosylate]. After separation of the CH₂Cl₂ layer, the residue was redissolved in 1 cm³ of hot methanol and the solution was kept at -30 °C. Within 2 days white crystals were formed, which were collected, washed with ether, and dried in vacuo. Yield: 82 mg (84% based on Tc). Crystals of X-ray quality were obtained by slow diffusion of ether into a methanolic solution of **3**. IR (cm⁻¹, KBr): 2960 (w), 2042 (vs), 1958 (vs), 1924 (vs), 1384 (s), 1184 (w), 1036 (s), 644 (w). ¹H NMR (δ , methanol-*d*₄): 2.41 (s, 6H, CH₃), 2.70–3.20 (m, 24H, CH₂), 7.17–7.21 (m, 4H, aromatic), 7.65–7.68 (m, 4H, aromatic). ⁹⁹Tc NMR (δ , methanol-*d*₄): -1488 (s, $\Delta\nu_{1/2}$ = 210 Hz).

Synthesis of *fac*-[$\text{Tc}_2(20\text{-ane-S}_6\text{-OH})(\text{CO})_6$][tosylate]₂ (5**).** Complex **5** was synthesized and purified according to the method described for compound **3**. Yield: 72% based on Tc. Crystals of X-ray quality were obtained by slow diffusion of ether into a methanolic solution of **5**. IR (cm⁻¹, KBr): 3441 (m), 2926 (w), 2054 (vs), 1949 (vs), 1628 (w), 1412 (w), 1213 (m), 1122 (m), 1033 (m), 1010 (m), 684 (w), 568 (w). ¹H NMR (δ , DMSO-*d*₆): 2.35 (s, 6H, CH₃), 2.55–3.92 (m, 27H, CH₂), 7.22–7.26 (m, 4H, aromatic), 7.67–7.70 (m, 4H, aromatic). ⁹⁹Tc NMR (δ , DMSO-*d*₆): -1468 (s, $\Delta\nu_{1/2}$ = 360 Hz).

X-ray Data Collection and Processing. The intensities for the X-ray determination were collected on an automated single-crystal diffractometer of the type CAD4 (Enraf-Nonius) using Mo K α (**2**, **5**) and Cu K α (**3**) radiation, respectively, with ω scans. The unit cell dimensions were determined from the angular settings of 25 high-angle reflections. The structures were solved by heavy-atom Patterson synthesis using SHELXS-86.⁸ Refinement was performed with SHELXL-93.⁹ All non-hydrogen atoms were located from successive Fourier maps and refined with anisotropic thermal parameters. In the case of complex **3** the hydrogen atoms were fully refined whereas in **2** and **5** the hydrogen atoms were placed at the calculated positions and refined using the "riding model" option of SHELXL-93. Crystal data and more details of the collection and refinements are contained in Table 1.

Results and Discussion

The complexes *fac*-[$\text{Tc}_2(\text{tosylate})_2(18\text{-ane-S}_6)(\text{CO})_6$] (**3**) and *fac*-[$\text{Tc}_2(20\text{-ane-S}_6\text{-OH})(\text{CO})_6$][tosylate]₂ (**5**) were obtained by previous substitution of the halides in **1** with silver tosylate and

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Table 1. Crystallographic Data for Complexes **2**, **3**, and **5**

	2	3	5
formula	C ₉ H ₁₂ BrO ₃ S ₃ Tc	C ₃₂ H ₃₈ S ₈ O ₁₂ Tc ₂	C ₃₅ H ₄₆ O ₁₄ S ₈ Tc ₂
fw	442.28	1067.10	1143.2
cryst size (mm)	0.6 × 0.2 × 0.1	0.5 × 0.2 × 0.1	0.2 × 0.2 × 0.05
space group	<i>P2₁/c</i>	<i>C2/c</i>	<i>Pc</i>
<i>a</i> (Å)	14.79(2)	26.07(3)	25.737(4)
<i>b</i> (Å)	11.691(2)	9.28(8)	14.009(1)
<i>c</i> (Å)	16.94(2)	17.89(7)	26.479(3)
β (deg)	94.88(6)	99.84(5)	149.56(2)
<i>V</i> (Å ³)	2918(5)	4270(1)	4837(1)
<i>Z</i>	8	4	4
temp (K)	203(2)	213(3)	203(2)
<i>D_c</i> (g/cm ³)	2.014	1.660	1.569
μ (mm ⁻¹)	4.147	9.40	0.974
<i>F</i> (000)	1728	2160	2326
radiation	Mo Kα	Cu Kα	Mo Kα
wavelength (Å)	0.709 30	1.541 84	0.710 73
2θ range (deg)	3.19–28.89	5.02–64.93	3.02–25.00
no. of collected reflns	8048	3927	18 103
no. of indep reflns	7128	3585	17 032
no. of obsd reflns	4990	2654	12 857
GOF	1.155	1.031	1.047
wR2/R1 ^a (%)	7.79/4.83	10.28/4.01	18.07/7.34

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

subsequent addition of 0.5 equiv of the corresponding ligand to the filtered solution. Attempts to isolate and recrystallize the dimeric complexes with the halides as counterions were not successful. Only previous exchange of the halides by the more bulky tosylate ions enabled us to separate the product from byproducts. However, exchange of the bromides by tosylates had no significant influence on the substitution reactions with the macrocyclic thioethers; this was confirmed in the ⁹⁹Tc NMR experiment. For the matter of consistency, all further experiments were performed with tosylate as the anion. The formation of complexes **3** and **5** was relatively slow (*T*_{1/2} = 30 min). This is not surprising for low-spin d⁶ metal centers, which usually show slow reaction kinetics. The reactions of [NEt₄]₂[TcBr₃(CO)₃] (**1b**) with 9-ane-S₃ in methanol at room temperature produced the mononuclear complex *fac*-[Tc(9-ane-S₃)(CO)₃]Br (**2**) in 87% yield. The reaction was completed within 30 min, which was concluded from the ⁹⁹Tc NMR experiment. This is significantly faster than in the case of the formation of complexes **3** and **5**. The faster reaction kinetics with 9-ane-S₃ is unexpected since in all complexes the metal centers have a low-spin d⁶ configuration. Therefore, the differences must be ligand related. 9-ane-S₃ reveals an all-endo orientation of the lone pairs of the three donor atoms, which is ideal for facial coordination. No reorientation of the sulfur lone pairs is necessary for a direct and fast tripodal coordination of the ligand to the technetium center. Contrary to this situation, the larger thiamacrocycles reveal a mixed exo, endo orientation of the sulfur lone pairs which demands a structural reorganization before a dipodal or tripodal coordination can be achieved. Details of the ring conformation analysis will be discussed later. Complexes **2**, **3**, and **5** are air-stable, white, crystalline solids. They are only sparingly soluble in acetonitrile and methanol and almost insoluble in water. Their facial geometry is evidenced by the CO-stretch absorption as detected in the IR spectra. The frequencies of the CO vibrations of the three complexes increase with their charge. In the case of the neutral complex **3**, the CO stretch absorptions were observed at 2042, 1958, and 1924 cm⁻¹, which is significantly lower than in the dicationic complex **5** (2054 and 1949 cm⁻¹). This can undoubtedly be explained by the stronger metal-to-carbonyl back-bonding in **3**. In the case of **2**, the CO-stretch bands were found

at 2050 and 1980 cm⁻¹, which is significantly higher than in the corresponding rhenium complex (2010 and 1940 cm⁻¹).¹⁰

⁹⁹Tc NMR Spectroscopy. In the past years, ⁹⁹Tc NMR spectroscopy has found increased application as a tool to study reactions and electronic properties of this element in different valencies. The high receptivity of the ⁹⁹Tc nucleus (0.275 relative to ¹H) and the wide range of chemical shifts as a function of ligand and oxidation state enable the observation of almost any compound, although the nucleus possesses an appreciable quadrupole moment, which leads to substantial line broadening. It has been shown elsewhere¹¹ that the half line widths of the ⁹⁹Tc resonances systematically depend on the symmetry of electron distribution around the nucleus and the oxidation state. Thus, the more asymmetric the distribution, the shorter the relaxation time, and consequently, the lines broaden. Nevertheless, the observation of the ⁹⁹Tc resonances is possible and is an important tool in the detection of intermediates. Also, information about symmetry and electronic properties of the products may be obtained.

The use of ⁹⁹Tc NMR spectroscopy for the detection of intermediates is exemplified by the reaction of **1** with 9-ane-S₃, 18-ane-S₆, and 20-ane-S₆-OH. In coordinating solvents the anionic ligands [X]⁻ (e.g., X = Cl, Br, tosylate) of **1** are partially substituted by solvent molecules (sol). Depending on the relative strength of coordination ability of the solvent and the anion, respectively, **1** can be present as any combination of [TcX_{*m*}(sol)_{3-*m*}(CO)₃]^{(1-*m*)⁺ (*m* = 0–2). It has been reported previously,^{6a} that the equilibrium in water lies completely on the side of [Tc(OH₂)₃(CO)₃]⁺ for most of the common anions such as halides or tosylate. In contrast, a methanolic solution of **1** (0.1 M) containing the tosylate ions exhibits an equilibrium of three products as determined by ⁹⁹Tc NMR spectroscopy (spectrum I of Figure 1). A strong peak at -744 ppm (Δ*ν*_{1/2} = 67 Hz) is assigned to the completely solvated cationic [Tc(sol)₃(CO)₃]⁺ whereas the weak peak at -804 ppm (Δ*ν*_{1/2} = 70 Hz) is attributed to the less electron deficient neutral [Tc-(tosylate)(sol)₂(CO)₃]. The very small peak at -796 ppm likely}

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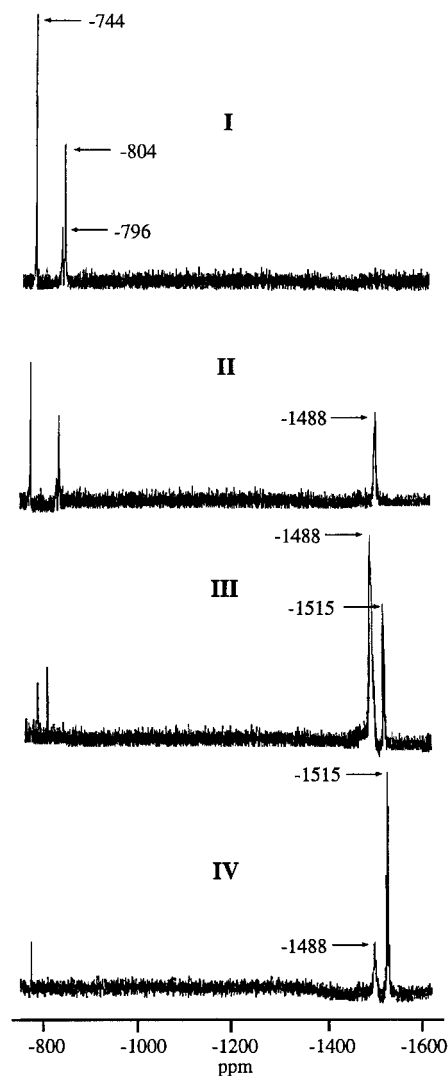


Figure 1. ^{99}Tc NMR spectra as a function of the concentration of 18-ane- S_6 .

represents the *fac*- $[\text{Tc}(\text{CO})_3]^+$ moiety coordinated to two tosylate anions. All substitution reactions monitored by ^{99}Tc NMR spectroscopy were carried out directly in NMR tubes. Addition of 1 equiv of 9-ane- S_3 to the methanolic solution of **1** revealed after 30 min the complete disappearance of the educts, and only one single peak at -1656 ppm ($\Delta\nu_{1/2} = 150$ Hz) for complex **2** could be observed.

In contrast to the straightforward reaction with 9-ane- S_3 , the situation was different with 18-ane- S_6 . Since more than one *fac*- $[\text{Tc}(\text{CO})_3]^+$ moiety can coordinate to the thia crown, the chemical shift and the number of observed signals depend on the ligand to metal ratio. Addition of 0.4 equiv of 18-ane- S_6 showed in the ^{99}Tc NMR after 30 min the resonances of starting material and a high-field-shifted peak at -1488 ppm ($\Delta\nu_{1/2} = 210$ Hz) (spectrum II of Figure 1). The peak at -1488 ppm was tentatively assigned to the resonance of **3** and unambiguously confirmed by comparison with a spectrum recorded from an analytically pure sample of **3** in methanol. After addition of another 0.6 equiv of 18-ane- S_6 , the resonances associated with the solvated species disappeared, the intensity of the signal associated with the 1:2 complex was enhanced, and a new signal at -1515 ppm ($\Delta\nu_{1/2} = 130$ Hz) (spectrum III, Figure 1) appeared. Since the additional 0.6 equiv corresponded to a total of 1 equiv, this peak should represent a 1:1 product, presumably the neutral complex $[\text{Tc}(\text{tosylate})(18\text{-ane-S}_6)(\text{CO})_3]$ (**4**) with a

bidentate-coordinated 18-ane- S_6 and a tosylate attached to the metal center. The structurally comparable rhenium complex $[\text{ReBr}(14\text{-ane-S}_4)(\text{CO})_3]$ with a bidentate-coordinated macrocyclic thioether and one coordinated bromide has been reported in the literature.¹

Initial addition of 1 equiv of 18-ane- S_6 to a methanolic solution of **1** revealed in the low-field region the same two resonances but in opposite intensities. After 2 h the ratio between the peaks at -1515 and -1488 ppm remained constant (spectrum IV, Figure 1). Due to the formation of the 1:2 product, free 18-ane- S_6 must still be present, but even heating of the sample did not lead to the complete formation of the 1:1 complex, demonstrating the kinetically controlled formation and inertness of **3**. By further addition of metal precursor this ratio changed. Thus, the resonance signal of the 1:1 complex at -1515 ppm decreased, while that of the 1:2 complex at -1488 ppm increased. Attempts to isolate the mononuclear complex $[\text{Tc}(\text{tosylate})(18\text{-ane-S}_6)(\text{CO})_3]$ (**4**) from the reaction with a 1:1 metal to ligand ratio failed.

The reaction of **1** with 20-ane- $\text{S}_6\text{-OH}$ was more difficult to follow since complex **5** is only sparingly soluble in methanol. In the ^{99}Tc NMR spectra obtained from a metal to ligand ratio of 1:1 or 1:2, three peaks at -1474 ppm ($\Delta\nu_{1/2} = 360$ Hz), -1495 ppm ($\Delta\nu_{1/2} = 250$ Hz), and -1506 ppm ($\Delta\nu_{1/2} = 310$ Hz) were observed after 15 min. Extended heating at 60°C over an 8 h period caused the disappearance of the signal at -1495 ppm. This observation was accompanied by the formation of a white precipitate of the 1:2 complex in the NMR tube. Dissolution of **5** in DMSO showed a single resonance peak at -1468 ppm. Thus, we assign the resonance signal at -1474 ppm in methanol to complex **5** and the resonance at -1506 ppm to the 1:1 complex $[\text{Tc}(20\text{-ane-S}_6\text{-OH})(\text{CO})_3]$ -[tosylate], respectively. The intermediate at -1495 ppm observed in the beginning of the reaction might represent a complex coordinated only bidentate to the macrocyclic ligand, which, upon heating, loses the eventually coordinated tosylate anion and converts to either of the two facially coordinated complexes. The reaction equations resulting from these spectroscopic investigations are outlined in Scheme 2.

Surprisingly, the resonance signal of the dicationic complex **5** appears closer to those of the neutral complexes formed with 18-ane- S_6 than to the signal of the cationic complex **2**. Thus, it seems that not only slightly changed electronic properties of the ligand but also the chelate effect is responsible for this observation. The ^{99}Tc NMR resonances of the two complexes with the general formula $[\text{Tc}(\text{CO})_3(\text{CH}_3\text{CN})(\text{P}_2)]$ show comparable shifts caused mainly by the chelate effect. When P_2 represents two monodentate coordinating triphenylphosphine ligands, the ^{99}Tc resonates at -3213 ppm. The resonance dramatically shifts to higher field (-3517 ppm) when the monodentate phosphines are replaced by the bidentate phosphine dppe.¹² In the case of **2** the electron distribution around the metal center is determined by the three rigid five-membered chelates. In the case of the larger macrocycles, only one or two five-membered chelates are formed, which leave the coordination geometry and, thus, the electron distribution much more flexible.

Description of the Structures. *fac*- $[\text{Tc}(9\text{-ane-S}_3)(\text{CO})_3]\text{Br}$ crystallizes in the monoclinic space group $P2_1/c$. An ORTEP²¹

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Scheme 2

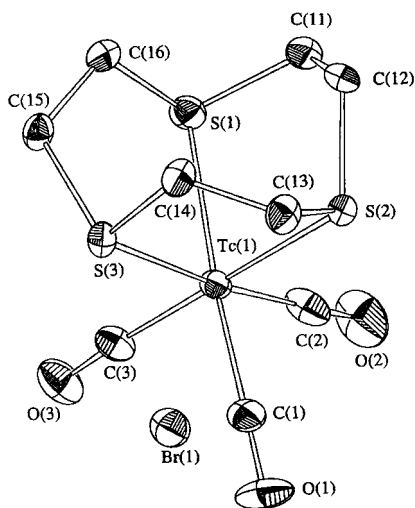
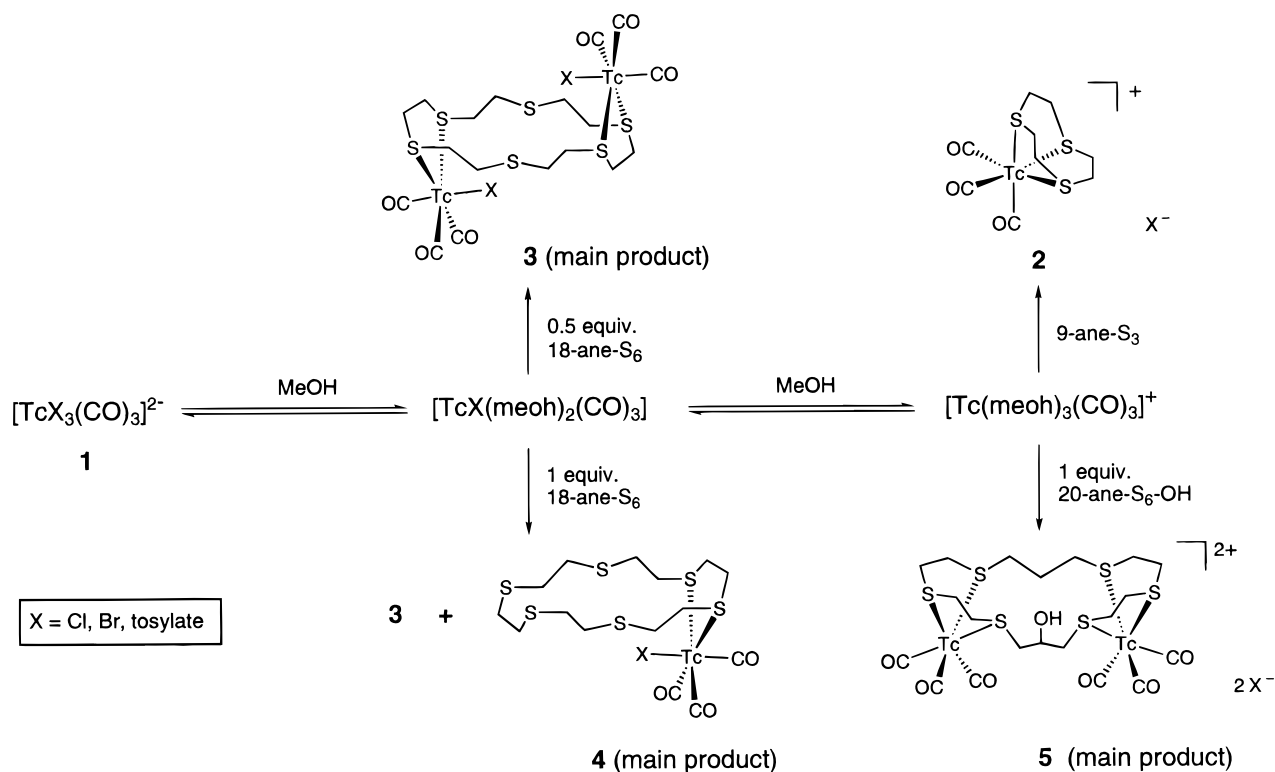


Figure 2. ORTEP plot of **2**. Hydrogen atoms are omitted for clarity. Ellipsoids are drawn at the 30% probability level.

view of **2** along with the corresponding atom-numbering scheme is given in Figure 2. Selected bond lengths and angles are summarized in Table 2. The metal center has an almost ideal octahedral coordination sphere with a facial arrangement of the

Table 2. Selected Bond Lengths (Å) and Angles (deg) for **2** and **3**

2			
Tc(1)–C(102)	1.931(6)	Tc(1)–S(2)	2.447(2)
Tc(1)–C(2)	1.910(7)	Tc(1)–S(3)	2.465(2)
Tc(1)–C(3)	1.933(6)	S(1)–C(11)	1.823(6)
Tc(1)–S(1)	2.448(3)	S(2)–C(12)	1.821(6)
C(2)–Tc(1)–C(1)	89.1(3)	C(1)–Tc(1)–S(2)	90.4(2)
C(2)–Tc(1)–C(3)	88.7(3)	C(3)–Tc(1)–S(2)	179.0(2)
C(1)–Tc(1)–C(3)	89.0(2)	S(2)–Tc(1)–S(1)	85.52(7)
C(2)–Tc(1)–S(2)	92.1(2)		
3			
Tc–C(30)	1.938(7)	Tc–O(11)	2.171(4)
Tc–C(40)	1.891(6)	Tc–S(1)	2.479(2)
Tc–C(50)	1.917(7)	S(7)–Tc ^{#a}	2.502(2)
C(50)–Tc–C(30)	91.9(3)	O(11)–Tc–S(1)	87.10(10)
C(40)–Tc–C(50)	86.4(3)	S(1)–Tc–S(7) [#]	84.23(5)
C(40)–Tc–C(30)	86.2(2)	O(11)–Tc–S(7) [#]	85.86(10)
C(50)–Tc–O(11)	94.9(2)	C(40)–Tc–O(11)	177.4(2)
C(30)–Tc–O(11)	95.9(2)		

^a (#) Symmetry transformation used: $-x + 0.5$; $-y + 0.5$; $-z$.

three carbonyl groups. The coordinated macrocyclic ligand forms three five-membered rings with the metal center. The S–Tc–S and the C–Tc–C angles have average values of 85.2(3)° and 88.9(2)°, respectively. Therefore, they only slightly deviate from the expected ideal 90° for an octahedron. The Tc–C bond lengths possess a mean distance of 1.92(1) Å and are about 0.05 Å shorter than in *fac*-[Re(9-ane-S₃)(CO)₃]Br.¹⁰ The mean Tc–S distance is 2.45(1) Å, which is almost equal to the Re–S bond lengths (2.46(1) Å) in the corresponding rhenium complex.¹⁰ However, they are significantly longer than in the homoleptic Tc(II) and Re(II) complexes [Tc(9-ane-S₃)₂]²⁺ (2.38(1) Å) and [Re(9-ane-S₃)₂]²⁺ (2.37(1) Å), respectively.^{2b} *fac*-[Tc₂(tosylate)₂(18-ane-S₆)(CO)₆] crystallizes in the monoclinic space group C2/c with half a molecule per asymmetric unit. The molecule is completed by inversion through the center of the molecule. The technetium centers are bidentate and exo

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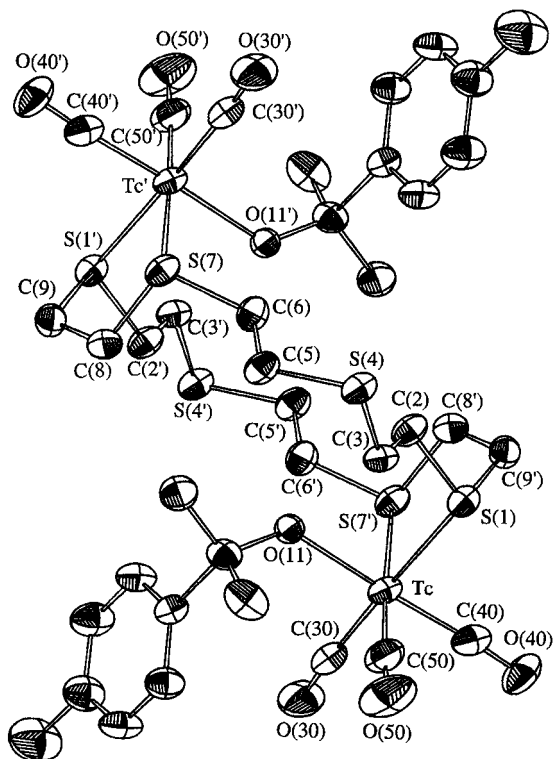


Figure 3. ORTEP plot of the neutral complex **3**. Hydrogen atoms are omitted for clarity. Ellipsoids are drawn at the 30% probability level.

Table 3. Selected Bond Lengths (Å) and Angles (deg) for **5**

Tc(1)–C(102)	1.97(2)	Tc(2)–S(5)	2.453(5)
Tc(1)–C(103)	1.94(2)	Tc(2)–S(8)	2.446(5)
Tc(1)–C(101)	1.90(2)	Tc(2)–S(11)	2.482(4)
Tc(1)–S(18)	2.460(4)	Tc(2)–C(106)	1.86(2)
Tc(1)–S(1)	2.482(4)	Tc(2)–C(105)	1.89(2)
Tc(1)–S(15)	2.478(4)	Tc(2)–C(104)	1.89(2)
C(102)–Tc(1)–C(103)	88.9(8)	C(106)–Tc(2)–C(105)	87.3(8)
C(102)–Tc(1)–C(101)	89.4(7)	C(105)–Tc(2)–C(104)	93.7(8)
C(103)–Tc(1)–C(101)	89.9(8)	C(106)–Tc(2)–C(104)	88.5(9)
S(18)–Tc(1)–S(1)	83.1(1)	S(5)–Tc(2)–S(11)	90.0(1)
S(18)–Tc(1)–S(15)	84.4(1)	S(8)–Tc(2)–S(5)	83.9(2)
S(1)–Tc(1)–S(15)	91.6(1)	S(8)–Tc(2)–S(11)	84.5(2)

coordinated to the 18-ane-S₆ ring system, which is very similar to the rhodium(III) centers in the complex [Rh₂Cl₂(C₅Me₅)₂-(18-ane-S₆)].¹³ The Tc(1) center exhibits a slightly distorted octahedral coordination. The S–Tc–S bond angle (84.2(1)°) is comparable to those in complex **2**. The C(30)–Tc–C(50) angle is 91.9(3)°, which is significantly larger than the other two C–Tc–C angles with an average of 86.3(2)°. The Tc–S bond lengths are 2.479(2) and 2.502(2) Å, which are slightly larger than the values in complex **2**. Due to the stronger π -back-bonding induced by the coordinated anion in the trans position, the Tc–C(40) bond length (1.891(6) Å) is shorter than the Tc–C bonds trans to the sulfur atoms (1.938(7) Å and 1.917(7) Å). The Tc···Tc' distance is 8.55 Å. An ORTEP²¹ view of **3** with the corresponding atom numbering is given in Figure 3. Selected bond lengths and angles are summarized in Table 2.

fac-[Tc₂(20-ane-S₆-OH)(CO)₆][tosylate]₂·MeOH crystallizes in the monoclinic space group *Pc* with two independent formula units per asymmetric unit. One methanol molecule cocrystallized with the complex. The structures of the two independent molecules are only slightly different. Therefore, selected bond lengths and angles in Table 3 are given for only one molecule. In contrast to complex **3**, the *fac*-[Tc(CO)₃]⁺ moieties are tripodal, endo and cis coordinated toward the macrocycle. The

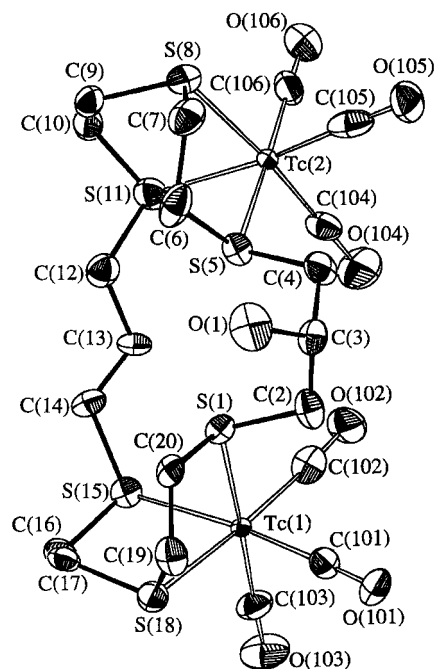


Figure 4. ORTEP plot of the complex cation of compound **5**. Hydrogen atoms are omitted for clarity. Ellipsoids are drawn at the 30% probability level.

coordinated atoms are only in a slightly distorted octahedral arrangement around the metal centers. Two of the S–Tc–S angles at each of the four technetium centers are in the range between 83.1° and 84.5° and are comparable to those in complexes **2** and **3**. The third S–Tc–S angle in all cases is significantly larger, with an angle of approximately 90°. The distance between the two technetium centers in both molecules is 6.77 Å. The Tc–C and Tc–S bond lengths have averages of 1.91(3) and 2.46(1) Å, respectively. An ORTEP²¹ view of complex **5** with the corresponding atom numbering is given in Figure 4.

Analysis of the Ring Conformations. The conformation of macrocyclic thioethers is controlled by the preferred gauche placement and an antipathy for the anti placement at the C–S linkages. The ring conformation of cyclic thioethers can therefore be specified by the torsion angles around the C–C, C–S, and S–C bonds.^{14,15} Furthermore, in macrocyclic thioethers the sulfur atoms generally reveal an exo-dentate orientation, which is in contrast to the oxa and aza macrocycles. However, not all crown thioethers follow this rule. In violation of the exo generalization, all sulfur atoms in 9-ane-S₃ and two sulfur atoms in 18-ane-S₆ are endo oriented.^{16,17} To explain the structural differences of **2**, **3**, and **5** we compared the torsion or dihedral angles of the crown thioethers with those of the uncoordinated ligands as well as with those in structurally comparable complexes, respectively.

The conformation of 9-ane-S₃ in **2** is only slightly different from that of the free ligand (Table 4). This is not surprising since the free ligand has already an ideal endo orientation of the sulfur atoms for a facial, tripodal coordination. The transannular S···S distance of 3.32 Å is significantly smaller than in the free ligand (3.45 Å). This can be explained by a lack of repulsion of the lone pairs of the sulfur atoms due to the coordination to the metal center.

The free ligand 18-ane-S₆ crystallizes with a (g⁺ag[−], g⁺g[−]g[−], g⁺ag⁺) sequence,^{18,19} whereas the ligand in **3** shows a (aag[−], g⁺ag⁺, a^{*}g[−]g[−]) sequence (Figure 5). The torsion angles of 18-ane-S₆ in **3** are listed in Table 5. Structure A in Figure 5 of the

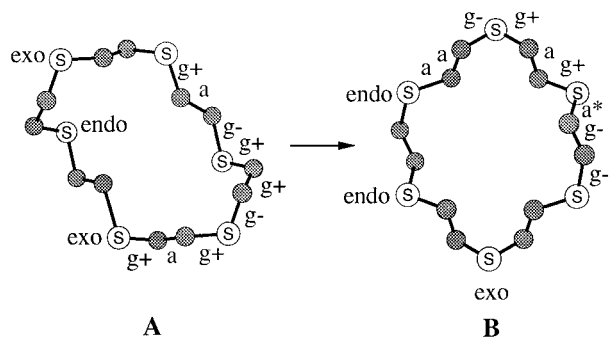


Figure 5. Ring conformation of 18-ane-S₆ uncoordinated (A) and in complex **3** (B).

Table 4. Ligand Torsion Angles (deg) for **2** and Free 9-ane-S₃

	2	9-ane-S ₃
S(3)–C(14)–C(13)–S(2)	–48.2	–58.5
C(12)–C(11)–S(1)–C(16)	–64.8	–55.1
C(16)–C(15)–S(3)–C(14)	131.7	131.1
S(2)–C(12)–C(11)–S(1)	–48.5	
C(14)–C(13)–S(2)–C(12)	130.5	
C(15)–C(16)–S(1)–C(11)	134.2	
S(3)–C(15)–C(16)–S(1)	–52.1	
C(13)–C(14)–S(3)–C(15)	–63.8	
C(11)–C(12)–S(2)–C(13)	–68.2	

Table 5. Ligand Torsion Angles (deg) for **3**

S(7)–C(6)–C(5)–S(4)	156.8
S(4)–C(3)–C(2)–S(1)	–163.0
C(6)–C(5)–S(4)–C(3)	90.3
C(2)–C(3)–S(4)–C(5)	–84.0
C(5)–C(6)–S(7)–C(8)	–170.7
C(3)–C(2)–S(1)–C(9')	–74.2
S(1')–C(9)–C(8)–S(7)	–53.0
C(8)–C(9)–S(1')–C(2')	137.0
C(9)–C(8)–S(7)–C(6)	–68.2

free ligand reveals only gauche C–S linkages. Furthermore, only two of the sulfur atoms show an endo orientation as earlier mentioned. In contrast to this situation, structure **B** of the macrocyclic ring system in **3** is characterized by four anti and one unfavored anticlinal linkages as well as four endo sulfur atoms. Only four of the six sulfur atoms are involved in the metal coordination. The identical structural features can also be found in the dinuclear complex [Rh₂(C₅Me₅)₂Cl₂(18-ane-S₆)] [BPh₄]₂.¹³

Although the X-ray structures of the free ligands 20-ane-S₆ and 20-ane-S₆-OH are not known, the same preference for gauche placements at the C–S linkages and exo orientation of the sulfur atoms can be expected. The macrocycle in **5** shows six gauche placements, two anti placements, one angle of 91° and one of 97°, respectively, and only two pure anticlinal placements (Table 6). Only half of the C–S interactions in **5** are in the preferred gauche placement. Furthermore, from a steric point of view a trans coordination of the technetium centers seems to be favored compared to a cis coordination. However, analysis of the ring system in the complex *trans*-[Rh₂(COD)₂(20-ane-S₆)] [PF₆]₂ (COD = cyclooctadiene) with a tripodal but trans coordination of the Rh(I) centers revealed an even more unfavored ring conformation.²⁰ Four anti, two anticlinal, two placements with angles around 90° but only four preferred gauche placements can be observed in the crystal structure of *trans*-[Rh₂(COD)₂(20-ane-S₆)] [PF₆]₂. The two additional energetically favored gauche interactions found in **5** and the minor steric requirement of the *fac*-[Tc(CO)₃]⁺ moieties (compared to the [Rh(COD)] moieties) might be an explanation why in the case of 20-ane-S₆-OH only the cis and not a trans

Table 6. Ligand Torsion Angles (deg) for **5**

C(6)–S(5)–C(4)–C(3)	82.6
C(4)–S(5)–C(6)–C(7)	91.8
C(20)–S(1)–C(2)–C(3)	–83.3
C(2)–S(1)–C(20)–C(19)	–97.2
C(17)–S(18)–C(19)–C(20)	–56.4
C(19)–S(18)–C(17)–C(16)	150.1
C(10)–S(11)–C(14)–C(13)	–176.8
C(14)–S(15)–C(16)–C(17)	–73.7
C(10)–S(11)–C(12)–C(13)	166.8
C(12)–S(11)–C(10)–C(9)	72.7
C(7)–S(8)–C(9)–C(10)	–142.4
C(9)–S(8)–C(7)–C(6)	62.8
S(5)–C(4)–C(3)–C(2)	65.6
C(4)–C(3)–C(2)–S(1)	–78.6
S(1)–C(20)–C(19)–S(18)	–44.1
S(18)–C(17)–C(16)–S(15)	–63.4
S(15)–C(14)–C(13)–C(12)	–176.7
C(14)–C(13)–C(12)–S(11)	–175.1
S(11)–C(10)–C(9)–S(8)	–53.7
S(8)–C(7)–C(6)–S(5)	–34.5

isomer is formed during the substitution reaction. Another remarkable structural feature of **5** can be found at the propylene bridges of the macrocycle. The derivatized propylene bridge (bearing the OH group) reveals two gauche C–C linkages whereas the underivatized bridge shows two anti conformations. Therefore, the thioether in **5** is not in a “crown” but in a twisted “inside-out” conformation which is known to be a particularly favorable, low-energy state.

The results of the structural and the ring conformation analyses of the compounds **3** and **5** as listed below explain to a certain extent the different binding of the *fac*-[Tc(CO)₃]⁺ cores to the macrocycles 18-ane-S₆ and 20-ane-S₆-OH: (1) Although the *fac*-[Tc(CO)₃]⁺ is a relatively small moiety, the thiomacrocyclic 18-ane-S₆ is too small to host two metal centers in a cis/dipodal or a cis/tripodal coordination. Therefore, steric hindrance prohibits a corresponding coordination. (2) A trans/tripodal coordination would induce a strong ring deformation and ring contraction of 18-ane-S₆, which are incompatible with the mentioned gauche and exo preference of macrocyclic thioethers. (3) The ligand 20-ane-S₆-OH is larger and more flexible than 18-ane-S₆. A tripodal coordination (compared to a dipodal coordination) of the two *fac*-[Tc(CO)₃]⁺ moieties is from a steric point of view possible and obviously preferred by the metal center. (4) Furthermore, as shown by the ring conformation analysis of *trans*-[Rh₂(COD)₂(20-ane-S₆)] [PF₆]₂, a trans/tripodal coordination of the metal centers forces the ring system to a structural rearrangement, which is less favored than the one found in complex **5** with a cis/tripodal coordination.

Conclusions

The reactions of 18-ane-S₆ and 20-ane-S₆-OH with **1** resulted in the formation of novel dinuclear complexes of transition metal carbonyls with interesting structural characteristics. Complexes **3** and **5** underline the high tendency of macrocyclic thioethers to bridge metal centers and show the rich coordination chemistry of these large macrocyclic rings. Although only 20-ane-S₆-OH in complex **5** is already bifunctionalized, **2** and **3** and/or the corresponding ligands 9-ane-S₃ and 18-ane-S₆ can be regarded as model complexes/ligands in order to model suitable compounds for a given nuclear medical application. It is known that charge, size, and lipophilicity of a bifunctional chelator and/or complex have major influences on the bioactivity and biodistribution of a pharmacophore. In this report we have shown that the *fac*-[Tc(CO)₃]⁺ moiety combined with macrocyclic thioethers offers an excellent tool to control the properties

of a bioconjugate by the formation of neutral, mono- and dicationic complexes. The high stability of the corresponding complexes **2**, **3**, and **5** on the macroscopic level substantiates the promising starting point for our ongoing in vitro and in vivo studies with these ligand systems labeled with the *fac*-[^{99m}Tc-(CO)₃]⁺ moiety.

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Supporting Information Available: Tables giving complete crystallographic experimental details, bond distances and angles, positional parameters for all atoms, anisotropic thermal parameters, and hydrogen atom coordinates for all three complexes (30 pages). Ordering information is given on any current masthead page.

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