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Coordination of Coenzyme M and Its Derivatives on Ni^{II}(tetraazacycle) Complexes: A Model for the Active Site of Methyl Coenzyme M Reductase

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A series of tetraazamacrocyclic nickel(II) complexes coordinated by methyl coenzyme M (MeSCoM), coenzyme M (HSCoM), and 3-methylthiopropionate (Metp) have been synthesized as structural models of the active site of methyl coenzyme M reductase in the oxidized MCR_{silent} state. They include *RSRS*-[Ni(tmc)(L)](OTf) {L = MeSCoM (**2**), HSCoM (**4**), and Metp (**5**)} (tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane) and [Ni(pyc)(L)](OTf) {L = MeSCoM (**6**), HSCoM (**7**), Metp (**8**), pyc = 5-oxo-7-(2-pyridyl)-1,4,8,11-tetraazacyclotetradecane}. The X-ray crystal analysis revealed that MeSCoM, HSCoM, and Metp are bound to Ni in an η^1 manner through interactions with one O atom of each ligand. The tmc complexes assume a pentacoordinate geometry, which is in between a square pyramid and a trigonal bipyramid, while the pyc complexes are octahedral with coordination of the pendant pyridine at the site *trans* to the sulfonate or carboxylate ligand.

Introduction

Methyl-coenzyme M reductase (MCR) in methanogenic Archaea is the nickel enzyme, which plays an important role in biological methane formation. The enzyme catalyzes the reaction between methyl-CoM (MeSCoM) and *N*-7-mercaptoheptanoyl threonine phosphate (HSCoB), generating methane and a disulfide species (CoBS-SCoM) in the final step of methanogenesis [Equation (1)].[1]

$$CH_3SCoM + HSCoB \longrightarrow CH_4 + CoBS{-}SCoM \quad (1)$$
$$\Delta G^{0'} = -30\ kJ\ mol^{-1}$$

Recently, the structures of inactive states of MCR have been determined by crystallographic analysis, and those of MCR_{silent} and $MCR_{ox1\text{-}silent}$ from *Methanobacterium thermoautrophicum* are shown in Figure 1 (a and b).[2] The active site contains a nickel tetrahydrocorphinoid cofactor F_{430} as a prosthetic group (Figure 2),[2–4] and the nickel is additionally coordinated at an axial position by a sulfonate oxygen of the heterodisulfide CoBS-SCoM for the MCR_{silent} or a thiolato (or thiol) sulfur of the coenzyme M for the $MCR_{ox1\text{-}silent}$. At the other axial position, Gln147 is weakly interacting with the nickel atom, while the coordination mode of the glutamine residue has not been established. The electron density map derived from X-ray analysis suggests the coordination of an oxygen atom,[2,3] while both nitrogen and oxygen atoms appear to be bound to nickel according to the EXAFS data.[5]

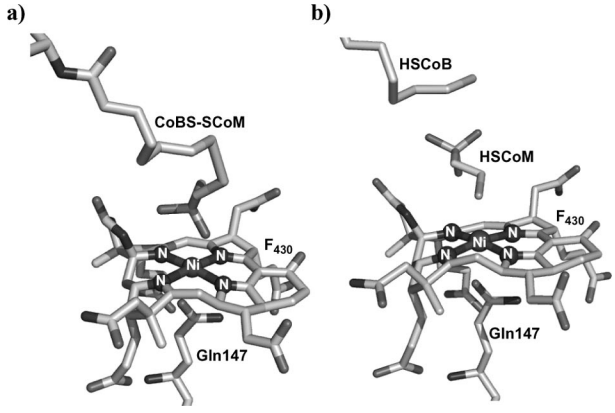

Figure 1. The active site structures of methyl coenzyme M reductase; a: MCR_{silent}, b: $MCR_{ox1\text{-}silent}$.

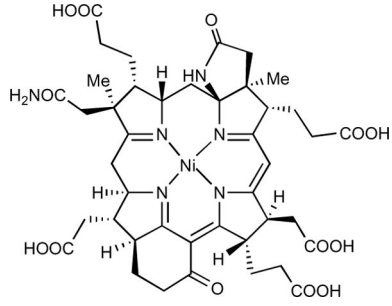

Figure 2. Schematic view of cofactor F_{430} in MCR.

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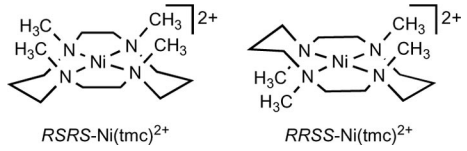
Although nickel complexes of N_4 macrocycles have been reported as models of the MCR active site,[6,7] attempts to synthesize those containing methyl coenzyme M (MeSCoM) and coenzyme M (HSCoM) remain very limited.[6,8] For instance, Riordan and co-workers have demonstrated the formation of $[Ni^{II}(tmc)(MeSCoM)]^+$ (tmc = 1,4,8,11-tetramethyl-1,4,8,11-tetraazacyclotetradecane)[9] in situ, and they proposed that MeSCoM is bound at a sulfonate oxygen atom on the basis of the IR and ^1H NMR data.[6] However, the MeSCoM complex has not been isolated, and the X-ray structure analysis is as yet unavailable. We herein report the isolation and structures of nickel(II) tetraazamacrocycles, $[Ni(tmc)]^{2+}$ and $[Ni(pyc)]^{2+}$ {pyc = 5-oxo-7-(2-pyridyl)-1,4,8,11-tetraazacyclotetradecane},[10] which carry methyl coenzyme M (MeSCoM), coenzyme M (HSCoM), and 3-(methylthio)propionate (Metp) at an axial position.

Results and Discussion

Synthesis of *RSRS*-[Ni(tmc)(L)](OTf) {L = MeSCoM (2), HSCoM (4), $MeS(CH_2)_2CO_2$ (5)}

The tetramethyltetraazacyclotetradecane ligand in $[Ni(tmc)]^{2+}$ may have two major conformations, *RSRS*- and *RRSS*-$[Ni(tmc)]^{2+}$, as shown in Scheme 1.[11]



Scheme 1. Two major stereoisomers of $Ni(tmc)^{2+}$.

The *RSRS*-conformer is more appropriate for modeling the active site of methyl coenzyme M reductase, because it can take an axial ligand to assume a square-pyramidal structure.[12,13] Thus, *RSRS*-[Ni(tmc)(Cl)](Cl) was prepared by the reaction of $NiCl_2{\cdot}6H_2O$ with tmc, and the chloride complex was treated with an excess amount of Na[MeSCoM] in water.[14] However, the chloride ligand coordinated at Ni remained intact and the counter-anion was replaced by the MeSCoM sulfonate, resulting in the formation of *RSRS*-[Ni(tmc)(Cl)](MeSCoM) (**1**) in 55% yield as a brownish-green crystalline powder. The structure was determined by X-ray crystallography. As shown in Figure 3, the complex assumes a square-pyramidal geometry at Ni, which is similar to the structure of *RSRS*-[Ni(tmc)(OAc)].[13a]

In an attempt to remove the chloride ligand on Ni, complex **1** was treated with silver triflate in acetonitrile. After removing AgCl, *RSRS*-[Ni(tmc)(MeSCoM)](OTf) (**2**) was isolated in 76% yield as green crystals. The X-ray analysis confirmed that MeSCoM coordinates at Ni through an interaction with an oxygen atom of sulfonate. The UV/Vis spectra of **2** in THF exhibits two d-d* bands at 403 and 680 nm, which are consistent with the UV data reported for square-pyramidal Ni^{II} complexes with a tmc ligand, in which two d-d* bands appear at 380–430 and 600–720 nm.[12,15] In contrast, the square planar Ni^{II} complexes of tmc show one d-d* band at 490–560 nm.[12,15] Thus, the pentacoordinate structure of **2** is likely to be retained in solution (Scheme 2).

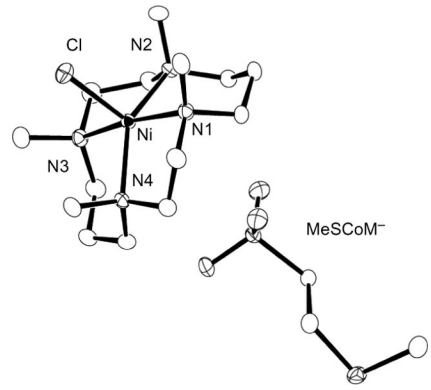
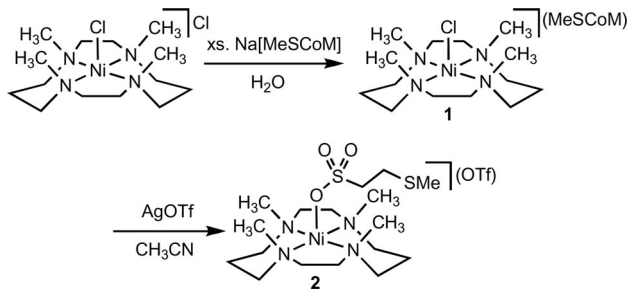
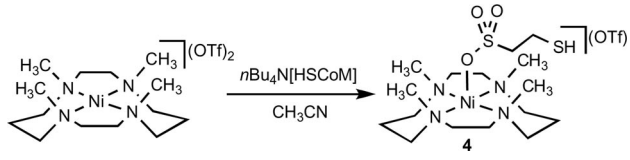


Figure 3. Structure of **1** with 50% probability ellipsoids.



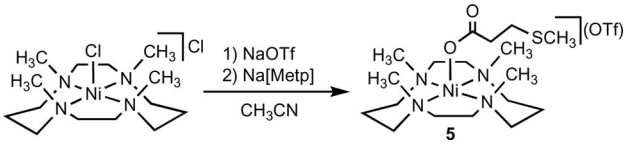
Scheme 2. Synthesis of complex **2**.

Next we attempted to synthesize the HSCoM analogue of the MeSCoM complex **2**, *RSRS*-[Ni(tmc)(HSCoM)](OTf) (**4**), by a procedure similar to the synthesis of **2**. Thus, *RSRS*-[Ni(tmc)(Cl)](HSCoM) (**3**) was prepared from the reaction of sodium sulfonate salt of HSCoM and *RSRS*-[Ni(tmc)(Cl)](Cl) in water, which was then allowed to react with silver triflate. Although the desired complex **4** was obtained, the yield was as low as ca. 10%, and a considerable amount of *RSRS*-[Ni(tmc)(Cl)](OTf) was generated. Therefore, *RSRS*-$[Ni(tmc)](OTf)_2$ was prepared as an alternative precursor, and it was treated with 1 equiv. of (nBu_4N)-[HSCoM] in acetonitrile. From this procedure, **4** was isolated in 48% yield as green crystals, and the pentacoordination structure was determined by X-ray analysis. The UV/Vis spectrum of **4** in THF shows two d-d* bands at 403 and 677 nm, indicating that the pentacoordination geometry is retained in solution also for the HSCoM complex (Scheme 3).



Scheme 3. Synthesis of complex **4**.

The 3-methylthiopropionate (Metp) complex, *RSRS*-[Ni(tmc)(Metp)](OTf) (**5**), was also synthesized. In this case, *RSRS*-[Ni(tmc)(Cl)](Cl) was found to be effective as a precursor, and the treatment of the chloride complex with sodium 3-methylthiopropionate (NaMetp) and sodium triflate in acetonitrile afforded **5** in 83% yield as green powder. Recrystallization from a THF/Et_2O solution provided crystals suitable for X-ray analysis. The UV/Vis spectrum of **5** in THF again indicates a pentacoordinate geometry in solution, exhibiting two d-d* transition bands at 397 and 640 nm as were observed in the spectra of **2** and **4**. The IR band at 1599 cm^{-1}, which arises from the carboxylate group in **5**, is substantially shifted to a lower frequency compared with that of HMetp (1713 cm^{-1}), conforming to a Mept coordination at the carboxylate site of Metp (Scheme 4).

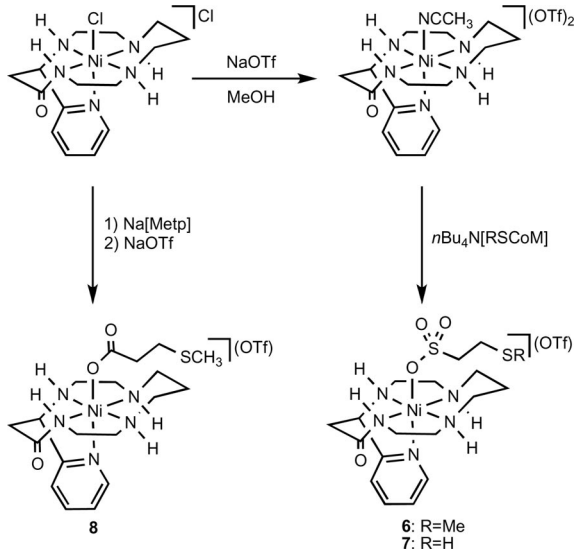


Scheme 4. Synthesis of complex **5**.

Synthesis of [Ni(pyc)(L)]OTf {L = MeSCoM (6), HSCoM (7), $MeS(CH_2)_2CO_2$ (8)}

At the MCR active site, a glutamine residue (Gln147) is weakly bound to the Ni atom, as shown in Figure 1. In order to mimic this sixth coordination at the site *trans* to MeSCoM or HSCoM, we prepared MCR model complexes which have the tetraazamacrocyclic ligand with a pyridine pendant, pyc.

The chloride complex [Ni(pyc)(Cl)](Cl) was prepared from pyc and $NiCl_2 \cdot 6H_2O$, and it was converted into the triflate complex [Ni(pyc)($NCCH_3$)]$(OTf)_2$ by treatment with sodium triflate in methanol followed by extraction with CH_3CN.[16] The reaction of the triflate complex with 1 equiv. of ($n$$Bu_4N$)[MeSCoM] in acetonitrile afforded [Ni(pyc)(MeSCoM)](OTf) (**6**) as purple crystals in 53% yield. The positive ESI-TOF-MS spectrum of **6** shows the signals attributable to $[Ni(pyc)(MeSCoM)]^+$, indicating the coordination of MeSCoM at the nickel center. The UV/Vis spectrum of **6** in acetonitrile exhibits one d-d* band at 528 nm, which is similar to the spectrum of $[Ni(L')(OH_2)](ClO_4)_2$ {L′ = 7-(2-pyridyl)-1,4,8,11-tetraazacyclotetradecane} showing an absorption at 523 nm.[17] The octahedral coordination structure of **6** was confirmed by X-ray analysis. The HSCoM and Metp complexes, [Ni(pyc)(HSCoM)](OTf) (**7**) and [Ni(pyc)(Metp)](OTf) (**8**), were also synthesized by similar procedures using ($n$$Bu_4N$)[HSCoM] and Na(Metp), respectively. Their UV spectra are similar to that of **6**, indicating octahedral coordination at nickel (Scheme 5).



Scheme 5. Synthesis of complexes **6**–**8**.

Molecular Structures of the MCR Model Complexes

The molecular structures of **1**–**8** have been determined by X-ray analysis. In Figure 4, the ORTEP plots of the complex cations of **2**, **4**, and **5** are shown, and their metric parameters are listed in Table 1, along with those of **1** for comparison. The sulfonate groups in **2** and **4**, and the carboxylate group in **5**, are bound to Ni through an interaction with one O atom. In the pentacoordination geometries of these complexes and **1**, the N atoms of tmc are not coplanar. The N1–Ni–N3 bonds are substantially bent (145°–152°), while the N2–Ni–N4 bonds are nearly linear (172°–175°). Therefore, the coordination geometry at Ni can be described either as a distorted square pyramid with O or Cl occupying the apical position, or a distorted trigonal bi-

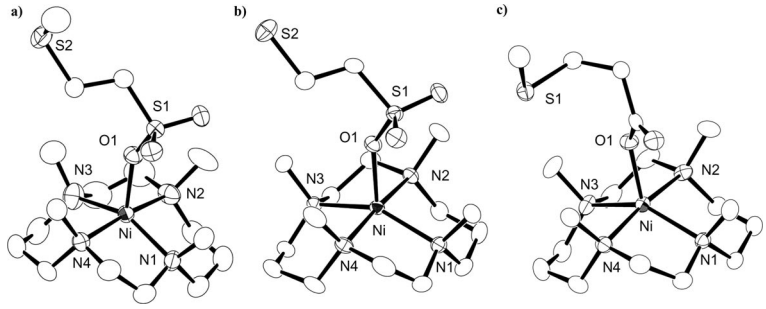


Figure 4. Structures of the complex cations of a) **2**, b) **4**, and c) **5** with 50% probability ellipsoids. The hydrogen atoms and anions are omitted for clarity.

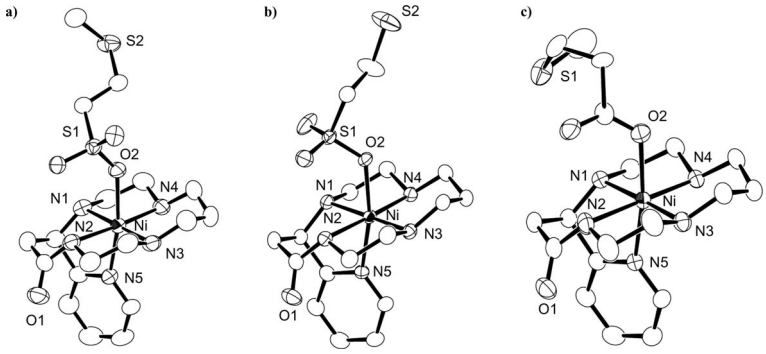


Figure 5. Structures of the pyc complex cations of a) **6**, b) **7**, and c) **8** with 50% probability ellipsoids. The hydrogen atoms are omitted for clarity. The major components of the disordered positions for **7** and **8** are depicted.

pyramid where N2 and N4 are at the axial positions. The longer Ni–O bond lengths of the sulfonato complexes **2** and **4** relative to that of **5** indicate weaker coordination of the sulfonate group than the carboxylate group.

Table 1. Selected bond lengths [Å] and angles [°] of **1**, **2**, **4**, and **5**.

	1		**2**	**4**	**5**
Ni–Cl	2.3074(17)	Ni–O1	2.017(2)	2.0196(19)	1.9710(18)
Ni–N1	2.099(5)	Ni–N1	2.111(2)	2.114(2)	2.142(2)
Ni–N2	2.181(4)	Ni–N2	2.129(2)	2.145(2)	2.1475(18)
Ni–N3	2.132(5)	Ni–N3	2.112(3)	2.117(2)	2.132(2)
Ni–N4	2.133(5)	Ni–N4	2.130(2)	2.135(2)	2.1258(18)
Cl–Ni–N1	108.30(14)	O1–Ni–N1	108.42(8)	110.92(9)	116.26(8)
Cl–Ni–N2	93.05(14)	O1–Ni–N2	93.29(9)	91.39(8)	90.57(7)
Cl–Ni–N3	106.57(14)	O1–Ni–N3	99.76(10)	99.50(9)	97.27(8)
Cl–Ni–N4	95.13(14)	O1–Ni–N4	94.26(9)	93.77(8)	96.91(7)
N1–Ni–N3	145.12(19)	N1–Ni–N3	151.82(11)	149.57(8)	146.39(9)
N2–Ni–N4	171.82(19)	N2–Ni–N4	172.41(10)	174.84(8)	172.49(8)

The ORTEP drawings of the complex cations of **6**–**8** are shown in Figure 5, and the metric parameters are summarized in Table 2. In these complexes, the pendant pyridine is bound to Ni, and four N atoms of the cyclam ring with an *RSRS* configuration are nearly coplanar. Their coordination geometries are octahedral, where the sulfonate or carboxylate group of **6**, **7**, and **8** coordinates at Ni in an η^1 manner. The Ni–O2 distances are within a range of Ni–O lengths of the known octahedral (sulfonato)nickel(II) complexes (2.04 to 2.17 Å),[18] while they are 0.12–0.13 Å longer than the corresponding pentacoordinate tmc complexes **2**, **4**, and **5** because of the pyridine coordination at the *trans* position. The *O*-coordination of the carboxylato complex **8** is again stronger than those of the sulfonato complexes **6** and **7**.

Table 2. Selected bond lengths [Å] and angles [°] of **6**–**8**.

	6	**7**	**8**
Ni–O2	2.142(2)	2.1330(19)	2.090(2)
Ni–N1	2.054(3)	2.068(2)	2.069(2)
Ni–N2	2.208(3)	2.2408(19)	2.229(2)
Ni–N3	2.072(3)	2.044(2)	2.061(2)
Ni–N4	2.057(3)	2.0590(19)	2.051(2)
Ni–N5	2.118(3)	2.114(2)	2.145(2)
O2–Ni–N1	89.39(13)	91.72(8)	88.81(10)
O2–Ni–N2	89.75(12)	88.20(7)	93.13(10)
O2–Ni–N3	89.43(13)	87.55(8)	91.65(11)
O2–Ni–N4	86.77(12)	89.55(7)	87.18(10)
O2–Ni–N5	167.94(13)	168.72(7)	166.46(10)
N1–Ni–N3	176.96(14)	177.74(7)	177.05(10)
N2–Ni–N4	176.51(14)	177.75(8)	179.27(10)
N1–Ni–N5	78.78(14)	78.71(8)	77.65(10)

Structural Comparison of the Model Complexes and the Active Site of MCR_{silent}

We have synthesized a series of penta- and hexa-coordinate tetraazamacrocyclic nickel complexes having methyl coenzyme M, coenzyme M, and 3-methylthiopropionate. Among them, the pyc complexes **6** and **7** resemble the active site of MCR_{silent} most, in that MeSCoM and HSCoM coordinate to Ni at the sulfonate site, and in that the coordination geometry at Ni is octahedral with the pendant pyridine being *trans* to the sulfonate group. In the MCR_{silent} state, a relatively weak interaction between Ni and Gln147 could tune the strength of the coenzyme coordination. However, this coordination mode differs from that of $MCR_{ox1\text{-}silent}$, in which HSCoM is bound to Ni at the thiol sulfur. The preference of sulfonate coordination over thiol coordination in **7** may imply that the sulfonate group is tightly bound to HSCoB, preventing the sulfonate from coordination at Ni. Or the *S*-coordination of coenzyme M in $MCR_{ox1\text{-}silent}$ could occur as a thiolate anion rather than a form of thiol. With this possibility in mind, we examined deprotonation of the HSCoM ligand in **4** and **7**, but the reactions led to precipitation of insoluble brown materials and characterization of the product is not possible. Further investigation is underway.

Experimental Section

General: All reactions and manipulations of air-sensitive compounds were conducted under an inert atmosphere of dry nitrogen by employing standard Schlenk techniques or in a glove box. Ether, THF, and acetonitrile were degassed and purified by the method described by Grubbs, where the solvents were passed over columns of activated alumina and supported copper catalyst supplied by Hansen & Co. Ltd. Methanol and ethanol were distilled from Mg under a nitrogen atmosphere. CH_3NO_2 and water were bubbled

with nitrogen prior to use. IR spectra were recorded with a JASCO FT/IR-410 spectrometer. UV/Vis spectra were recorded in 10-mm quartz glass cells with a JASCO V560 spectrometer. Electrospray ionization time-of-flight mass spectrometry (ESI-TOF-MS) spectra were obtained from a Micromass LCT TOF-MS spectrometer. Elemental analyses for C, H, N, and S were performed on a LECO CHNS-932 elemental analyzer where the samples were sealed in silver capsules. Nickel(II) halides, nickel(II) triflate, and the other reagents were purchased and used without further purification. The following compounds were prepared according to literature procedures: tmc,[9] pyc,[10] Na[MeSCoM],[19] (nBu$_4$N)[MeSCoM],[6] and (nBu$_4$N)[HSCoM].[20]

Synthesis

***RSRS*-[Ni(tmc)(Cl)](Cl):** To an aqueous solution (20 mL) of $NiCl_2{\cdot}6H_2O$ (1.19 g, 5.0 mmol) was added an ethanol solution (30 mL) of tmc (1.22 g, 4.8 mmol) and the mixture was then stirred for 3 h. The red solution was evaporated in vacuo and extracted with $CHCl_3$. The green solution was dried with $MgSO_4$ and evaporated to give a green powder of [Ni(tmc)(Cl)](Cl). The *RSRS*-isomer was purified by recrystallization from acetone solution in 42% yield. The isomeric structure was confirmed by X-ray structural analysis. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 349.1 (100) $[M]^+$. UV/Vis (CH_2Cl_2, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 423 (105), 707 (55). $C_{14}H_{32}Cl_2N_4Ni$ (386.03): calcd. C 43.56, H 8.36, N 14.51; found C 43.69, H 8.25, N 14.24.

***RSRS*-[Ni(tmc)(Cl)](MeSCoM) (1):** To an aqueous solution (5 mL) of *RSRS*-[Ni(tmc)(Cl)](Cl) (124 mg, 0.32 mmol) was added sodium 2-methylthioethanesulfonate (284 mg, 1.6 mmol) and the mixture was stirred at room temp. for 30 min. The red solution was concentrated and extracted with CH_3NO_2. The solution was dried with $MgSO_4$ and the solvents evaporated to dryness. The residue was recrystallized from CH_3CN/Et_2O to give **1** as brownish-green crystalline powder in 55% yield. The green crystals suitable for X-ray structural analysis were obtained from acetonitrile solution layered with Et_2O at room temp. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 349.1 (100) $[M]^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 430 (160), 720 (56). $C_{17}H_{39}ClN_4NiO_3S_2$ (505.80): calcd. C 40.37, H 7.77, N 11.08, S 12.68; found C 40.52, H 7.33, N 11.13, S 12.52.

***RSRS*-[Ni(tmc)(MeSCoM)](OTf) (2):** To an acetonitrile solution (10 mL) of **1** (202 mg, 0.40 mmol) was slowly added an acetonitrile solution (5 mL) of AgOTf (102 mg, 0.40 mmol). The white precipitate of AgCl was filtered off and the solution was evaporated to dryness. The residue was recrystallized from THF/Et_2O to give green crystals of **2** in 76% yield. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 469.1 (100) $[M]^+$, 463.1 (5) [M – (MeSCoM) + OTf]$^+$. UV/Vis (THF, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 403 (79), 680 (21). $C_{18}H_{39}F_3N_4NiO_6S_3$ (619.42): calcd. C 34.90, H 6.35, N 9.05, S 15.53; found C 35.38, H 6.34, N 9.06, S 15.35.

***RSRS*-[Ni(tmc)(Cl)](HSCoM) (3):** The synthesis of **3** was carried out as described for **1**, but using *RSRS*-[Ni(tmc)(Cl)](Cl) (154 mg, 0.40 mmol) and sodium 2-mercaptoethanesulfonate (354 mg, 2.2 mmol). Complex **3** was isolated as green crystals in 48% yield. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 349.2 (100) $[M]^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 435 (116), 717 (61). $C_{16}H_{37}ClN_4NiO_3S_2$ (491.77): calcd. C 39.08, H 7.58, N 11.39, S 13.04; found C 39.54, H 7.45, N 11.41, S 12.72.

***RSRS*-[Ni(tmc)](OTf)$_2$:** *RSRS*-[Ni(tmc)](OTf)$_2$ was prepared by the treatment of *RSRS*-[Ni(tmc)(Cl)](Cl) (385 mg, 1.0 mmol) with NaOTf (520 mg, 3.0 mmol) in aqueous solution (15 mL). The product was extracted with CH_3NO_2 and dried with $MgSO_4$. The solution was evaporated and recrystallized from acetone/Et_2O to give red crystals of *RSRS*-[Ni(tmc)](OTf)$_2$ in 75% yield. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 157.1 (10) $[M]^{2+}$, 177.6 (20) [M + $CH_3CN]^{2+}$, 463.1 (100) [M + OTf]$^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 381 (160), 610 (48). $C_{16}H_{32}F_6N_4NiO_6S_2$ (613.27): calcd. C 31.34, H 5.26, N 9.14, S 10.46; found C 31.94, H 4.96, N 9.04, S 10.54.

***RSRS*-[Ni(tmc)(HSCoM)](OTf) (4):** To an acetonitrile solution (10 mL) of *RSRS*-[Ni(tmc)](OTf)$_2$ (122 mg, 0.20 mmol) was added an acetonitrile solution (5 mL) of (nBu$_4$N)[HSCoM] (80 mg, 0.21 mmol). The solution was stirred at room temp. for 1 h and the solvents evaporated in vacuo. The residue was washed with Et_2O and recrystallized from CH_3CN/Et_2O to give green crystals of **4** in 48% yield. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 455.0 (100) $[M]^+$, 463.1 (3) [M – (HSCoM) + OTf]$^+$. UV/Vis (THF, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 403 (170), 677 (77). $C_{17}H_{37}F_3N_4NiO_6S_3$ (605.39): calcd. C 33.73, H 6.16, N 9.25, S 15.89; found C 34.05, H 5.86, N 9.32, S 15.33.

***RSRS*-[Ni(tmc)(Metp)](OTf) (5):** To an acetonitrile solution (10 mL) of *RSRS*-[Ni(tmc)(Cl)](Cl) (116 mg, 0.30 mmol) was added NaOTf (52 mg, 0.30 mmol) and sodium 3-methylthiopropionate (43 mg, 0.30 mmol). The mixture was stirred for 3 h at room temp. and the white precipitate was removed by centrifuging. After the solution was evaporated in vacuo, **5** was obtained as a green powder in 83% yield. Green crystals suitable for X-ray structural analysis were obtained from a THF/Et_2O mixed solution of **5**. IR (KBr): $\tilde{\nu}$ = 1599 cm^{-1}. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 433.1 (100) $[M]^+$. UV/Vis (THF, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 397 (60), 640 (26). $C_{19}H_{39}F_3N_4NiO_5S_2$ (583.36): calcd. C 39.12, H 6.74, N 9.60, S 10.99; found C 38.77, H 6.66, N 9.72, S 10.53.

[Ni(pyc)(Cl)](Cl): To a methanol solution (10 mL) of $NiCl_2{\cdot}6H_2O$ (190 mg, 0.80 mmol) was added a methanol solution (5 mL) of pyc (232 mg, 0.80 mmol) and the mixture was stirred at room temp. for 3 h. The solution was evaporated and the residue was recrystallized from $MeOH/Et_2O$ to give purple crystals of [Ni(pyc)(Cl)](Cl) in 82% yield. ESI-TOF-MS (MeOH): *m*/*z* (%) = 383.9 (50) $[M]^+$, 347.9 (100) [M – HCl]$^+$. UV/Vis (MeOH, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 303 (510), 475 (14). $C_{15}H_{25}Cl_2N_5Ni$ (421.00): calcd. C 42.80, H 5.99, N 16.64; found C 42.60, H 6.19, N 16.52.

[Ni(pyc)(NCCH$_3$)](OTf)$_2$: To a methanol solution (10 mL) of [Ni(pyc)(Cl)](Cl) (210 mg, 0.50 mmol) was added a methanol solution (5 mL) of NaOTf (172 mg, 1.0 mmol) and the mixture was stirred at room temp. for 3 h. The solution was evaporated and extracted with acetonitrile. After the solution was concentrated, Et_2O was slowly added to give a purple crystalline powder of [Ni(pyc)(NCCH$_3$)](OTf)$_2$ in 82% yield. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 195.3 (20) $[M]^{2+}$, 215.8 (40) [M + $(CH_3CN)]^{2+}$, 498.2 (100) [M – (CH_3CN) + OTf]$^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 501 (49). $C_{19}H_{28}F_6N_6NiO_7S_2$ (689.28): calcd. C 33.11, H 4.09, N 12.19, S 9.30; found C 33.13, H 4.13, N 12.16, S 9.12.

[Ni(pyc)(MeSCoM)](OTf) (6): To an acetonitrile solution (5 mL) of [Ni(pyc)(NCCH$_3$)](OTf)$_2$ (139 mg, 0.20 mmol) was added an acetonitrile solution (2 mL) of (nBu$_4$N)[MeSCoM] (78 mg, 0.20 mmol) and the mixture was stirred at room temp. for 30 min. The solution was evaporated and washed with Et_2O. The crude product was purified by recrystallization from CH_3CN/Et_2O to give purple crystals of **6** in 53% yield. ESI-TOF-MS (CH_3CN): *m*/*z* (%) = 504.1 (100) $[M]^+$, 498.0 (3) [M – (MeSCoM) + OTf]$^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 528 (17). $C_{19}H_{32}F_3N_5NiO_7S_3$ (654.38): calcd. C 34.87, H 4.93, N 10.70, S 14.70; found C 34.82, H 4.95, N 10.57, S 14.74.

[Ni(pyc)(HSCoM)](OTf) (7): The synthesis of **7** was carried out as described for **6**, but using $[Ni(pyc)(NCCH_3)](OTf)_2$ (120 mg, 0.17 mmol) and (nBu$_4$N)[HSCoM] (67 mg, 0.17 mmol) with 42% yield. ESI-TOF-MS (CH_3CN): m/z (%) = 490.0 (100) $[M]^+$, 498.0 (2) $[M - (HSCoM) + OTf]^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 524 (14). $C_{18}H_{30}F_3N_5NiO_7S_3$ (640.35): calcd. C 33.76, H 4.72, N 10.94, S 15.02; found C 33.92, H 4.83, N 10.94, S 14.32.

[Ni(pyc)(Metp)](OTf) (8): To a methanol solution (5 mL) of [Ni(pyc)(Cl)](Cl) (119 mg, 0.28 mmol) was added a methanol solution (3 mL) of NaOTf (48 mg, 0.28 mmol) and sodium 3-methylthiopropionate (40 mg, 0.28 mmol). The mixture was stirred at room temp. for 30 min and the solvents were evaporated in vacuo. The residue was extracted with acetonitrile and the solvents evaporated to dryness. The purple powder of **8** was obtained in 73% yield. Purple crystals suitable for X-ray structural analysis were obtained from acetonitrile solution layered with Et_2O at room temp. ESI-TOF-MS (CH_3CN): m/z (%) = 467.9 (100) $[M]^+$, 348.0 (20) $[M - MetpH]^+$. UV/Vis (CH_3CN, room temp.; λ_{max}, nm) (ε [cm^{-1}] M^{-1}): 523 (11). $C_{20}H_{32}F_3N_5NiO_6S_2$ (618.32): calcd. C 38.85, H 5.21, N 11.33, S 10.37; found C 38.77, H 5.03, N 11.31, S 10.21.

Table 3. Crystal data for **1**–**8**, *RSRS*-[Ni(tmc)(Cl)](Cl), [Ni(pyc)(Cl)](Cl), and $[Ni(pyc)(NCCH_3)](OTf)_2$.

	1	**2**	**3**	**4**	**5**	**6**
Formula	$C_{17}H_{39}N_4ClNiO_3S_2$	$C_{18}H_{39}N_4F_3NiO_6S_3$	$C_{16}H_{37}N_4ClF_3NiO_3S_2$	$C_{17}H_{37}N_4F_3NiO_6S_3$	$C_{19}H_{39}N_4F_3NiO_5S_2$	$C_{19}H_{32}N_5F_3NiO_7S_3$
Formula weight	505.79	619.40	491.77	605.38	583.36	654.37
Crystal system	monoclinic	orthorhombic	orthorhombic	monoclinic	triclinic	orthorhombic
Space group	$P2_1$ (No. 4)	*Pbca* (No. 61)	*Pbca* (No. 61)	$P2_1$ (No. 4)	$P\bar{1}$ (No. 2)	*Pbca* (No. 61)
a [Å]	8.500(5)	10.3006(15)	9.5276(12)	8.617(2)	8.680(3)	10.4216(15)
b [Å]	9.300(5)	19.501(3)	21.014(3)	16.352(4)	10.560(4)	18.386(3)
c [Å]	14.853(9)	26.912(4)	22.193(3)	9.771(2)	14.529(5)	28.940(4)
α [°]	90	90	90	90	95.694(3)	90
β [°]	102.804(7)	90	90	108.241(3)	102.726(6)	90
γ [°]	90	90	90	90	99.320(4)	90
V [Å^3]	1144.9(11)	5406.0(13)	4443.4(10)	1307.6(5)	1269.1(8)	5545.2(14)
Z	2	8	8	2	2	8
ρ_{calcd} [g cm^{-1}]	1.467	1.522	1.470	1.537	1.526	1.567
μ [cm^{-1}]	11.717	10.100	12.053	10.420	9.884	9.932
F(000)	540	2608	2096	636	616	2720
$2\theta_{max}$ [°]	55.0	55.0	55.0	54.9	55.0	55.0
Refl. collected	9187	41436	49457	10305	15128	43020
Indep. (R_{int})	4488 (0.044)	6178 (0.035)	5089 (0.089)	5354 (0.021)	5788 (0.032)	6344 (0.071)
Parameters	254	371	254	312	308	344
R_1[a]	0.0589	0.0613	0.0478	0.0352	0.0446	0.0698
wR_2[b]	0.1472	0.1670	0.1523	0.0741	0.1173	0.2137
GOF on F^2[c]	1.082	1.099	1.090	1.035	1.126	1.082
Flack parameters	–0.01(2)	–	–	–0.020(10)	–	–
CCDC	779878	779879	779880	779881	779882	779883

Complex	**7**	**8**	*RSRS*-[Ni(tmc)(Cl)](Cl)·2(H_2O)	[Ni(pyc)(Cl)](Cl)·CH_3OH	$[Ni(pyc)(NCCH_3)](OTf)_2$
Formula	$C_{18}H_{30}N_5F_3NiO_7S_3$	$C_{20}H_{32}N_5F_3NiO_6S_2$	$C_{14}H_{36}N_4Cl_2NiO_2$	$C_{16}H_{28}N_5Cl_2NiO_2$	$C_{19}H_{28}N_6F_6NiO_7S_2$
Formula weight	640.34	618.32	422.07	452.04	689.28
Crystal system	monoclinic	monoclinic	monoclinic	monoclinic	monoclinic
Space group	$P2_1/c$ (No. 14)	$C2/c$ (No. 15)	$P2_1/c$ (No. 14)	$P2_1/c$ (No. 14)	Cc (No. 9)
a [Å]	9.0478(15)	10.143(5)	8.9533(11)	9.520(3)	12.157(3)
b [Å]	30.802(5)	20.438(9)	11.9505(15)	11.335(3)	13.635(3)
c [Å]	9.6572(16)	28.360(13)	18.453(2)	19.029(5)	33.840(8)
α [°]	90	90	90	90	90
β [°]	101.070(2)	116.098(7)	91.228(3)	99.676(4)	98.944(3)
γ [°]	90	90	90	90	90
V [Å^3]	2641.3(8)	5279(4)	1974.0(4)	2024.2(9)	5541(2)
Z	4	8	4	4	8
ρ_{calcd} [g cm^{-1}]	1.610	1.556	1.420	1.483	1.652
μ [cm^{-1}]	10.406	9.594	12.669	12.429	9.419
F(000)	1328	2576	904	948	2832
$2\theta_{max}$ [°]	54.9	55.1	54.9	55.0	55.0
Refl. collected	20634	21688	15598	24038	31579
Indep. (R_{int})	6051 (0.036)	6033 (0.033)	4497 (0.042)	4640 (0.048)	12271 (0.074)
Parameters	344	380	225	245	740
R_1[a]	0.0464	0.0564	0.0258	0.0395	0.0635
wR_2[b]	0.1285	0.1631	0.0626	0.1003	0.1868
GOF on F^2[c]	1.098	1.100	1.058	1.079	1.047
Flack parameters	–	–	–	–	0.290(14)
CCDC	779884	779885	779886	779887	779888

[a] $R1 = \Sigma||F_o| - |F_c||/\Sigma|F_o|$ [$I > 2\sigma(I)$]. [b] $wR2 = \{[\Sigma w(|F_o| - |F_c|)^2/\Sigma wF_o^2]\}^{1/2}$ (all data). [c] GOF = $[\Sigma w(|F_o| - |F_c|)^2/(N_o - N_v)]^{1/2}$ (N_o = number of observations, N_v = number of variables).

Crystal Structure Determination: Crystallographic data and refinement parameters for **1**–**8**, *RSRS*-[Ni(tmc)Cl](Cl), [Ni(pyc)(Cl)](Cl), and $[Ni(pyc)(NCCH_3)](OTf)_2$ are summarized in Table 3. Single crystals were mounted on a loop using oil (CryoLoop, Immersion Oil, Type B or Paraton, Hampton Research Corp.) and set on a Rigaku AFC-8 {for **1**, **3**–**8**, and *RSRS*-[Ni(tmc)(Cl)](Cl)} or AFC-10 {for **2**, [Ni(pyc)(Cl)](Cl), and $[Ni(pyc)(NCCH_3)](OTf)_2$} instrument equipped with a Mercury CCD detector (for **3**–**7**) or with a Saturn CCD detector {for **1**, **2**, **8**, *RSRS*-[Ni(tmc)(Cl)](Cl), [Ni-(pyc)(Cl)](Cl), and $[Ni(pyc)(NCCH_3)](OTf)_2$}. The measurements were made using graphite-monochromated Mo-K_α radiation (λ = 0.71070 Å) under a cold nitrogen stream. The frame data were integrated and corrected for absorption with the Rigaku/MSC CrystalClear program package. The structures were solved using direct methods (SIR-92 or SIR-97) and standard difference map techniques and were refined with full-matrix least-squares procedures on F^2 by the Rigaku/MSC CrystalStructure package. Anisotropic refinement was applied to all non-hydrogen atoms. The counter anion $CF_3SO_3^-$ in **2**, $HSCoM^-$ in **3**, the thiol SH in **7**, $CH_3SCH_2CH_2CO_2^-$ in **8**, and crystalline solvent MeOH in [Ni-(pyc)(Cl)](Cl) were disordered over several positions, in which the respective ratio was refined freely, while the total occupancy of the components was constrained to unity. The hydrogen atom of SH in **4** and H_2O in *RSRS*-[Ni(tmc)(Cl)](Cl) were assigned from the Fourier map and refined isotropically. All of the other hydrogen atoms were placed at calculated positions.

CCDC numbers are shown in Table 3.

Supporting Information (see also the footnote on the first page of this article): Figure S1–S3 show ORTEP plots of *RSRS*-[Ni(tmc)(Cl)](Cl), [Ni(pyc)(Cl)](Cl), and $[Ni(pyc)(NCCH_3)](OTf)_2$, respectively.

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