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Bifunctional Single Amino Acid Chelates for Labeling of Biomolecules with the $\{Tc(CO)_3\}^+$ and $\{Re(CO)_3\}^+$ Cores. Crystal and Molecular Structures of $[ReBr(CO)_3(H_2NCH_2C_5H_4N)]$, $[Re(CO)_3\{(C_5H_4NCH_2)_2NH\}]Br$, $[Re(CO)_3\{(C_5H_4NCH_2)_2NCH_2CO_2H\}]Br$, $[Re(CO)_3\{X(Y)NCH_2CO_2CH_2CH_3\}]Br$ (X = Y = 2-pyridylmethyl; X = 2-pyridylmethyl, Y = 2-(1-methylimidazolyl)methyl; X = Y = 2-(1-methylimidazolyl)methyl), $[ReBr(CO)_3\{(C_5H_4NCH_2)NH(CH_2C_4H_3S)\}]$, and $[Re(CO)_3\{(C_5H_4NCH_2)N(CH_2C_4H_3S)(CH_2CO_2)\}]$

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The reactions of a series of potentially tridentate ligands, derived from single amino acids or amino acid analogues, with $[NEt_4]_2[ReBr_3(CO)_3]$ have been investigated. The model compounds $[Re(CO)_3Br\{(2\text{-pyridylmethyl})NH_2\}]$ (**1**) and $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NH\}]Br$ (**2**) were also prepared and structurally characterized. With ligands possessing two pyridyl appendages, $(2\text{-pyridylmethyl})_2NX$ (X = $-CH_2CO_2H$, $-CH_2CO_2Et$, $-CH_2CH_2CO_2H$, $-CH_2CH_2CO_2Et$, $-CH_2CH_2CH_2CH_2$-$CH(NHCO_2{}^tBu)CO_2H$), complexes of the type $[Re(CO)_3(ligand)]Br$ (**3**–**6**) were isolated. All possess the *fac*-$\{Re(CO)_3N_3\}$ coordination geometry in the cationic molecular unit. Similarly, the ligands with the imidazolyl arms (2-pyridylmethyl)$\{$2-(1-methylimidazolyl)methyl$\}NCH_2CO_2Et$ and $\{$2-(1-methylimidazolyl)methyl$\}_2NCH_2CO_2Et$, complexes **7** and **8** of the same $[Re(CO)_3(ligand)]Br$ type, were prepared. Replacement of one pyridyl arm with a thiophene group yielded the complex $[Re(CO)_3\{(2\text{-pyridylmethyl})N(CH_2CO_2)(2\text{-thiophenemethyl})\}]$ (**9**), while additional substitution of X = –H for $-CH_2CO_2H$ yielded $[Re(CO)_3Br\{(2\text{-pyridylmethyl})NH(2\text{-thiophenemethyl})\}]$ (**10**). In both **9** and **10**, the thiophene is uncoordinated and pendant, and the derivatives display *fac*-$\{Re(CO)_3N_2O\}$ and *fac*-$\{Re(CO)_3N_2Br\}$ coordination geometries, respectively. Crystal data: $C_9H_8BrN_2O_3Re$ (**1**), triclinic $P\bar{1}$, $a = 8.156(1)$ Å, $b = 12.077(1)$ Å, $c = 12.945(2)$ Å, $\alpha = 92.183(3)°$, $\beta = 107.848(3)°$, $\gamma = 100.955(7)°$, $V = 1185.1(3)$ Å, $Z = 4$; $C_{15}H_{13}BrN_3O_3Re$ (**2**), tetragonal $P4_1$, $a = 8.6095(3)$ Å, $c = 22.228(1)$ Å, $V = 1646.9(1)$ Å^3, $Z = 4$; $C_{17}H_{14}BrN_3O_5Re{\cdot}CH_3OH$ (**3**), monoclinic $P2_1/m$, $a = 7.4425(3)$ Å, $b = 9.7596(4)$ Å, $c = 14.0646(6)$ Å, $\beta = 97.753(1)°$, $V = 1012.26(7)$ Å^3, $Z = 2$; $C_{19}H_{19}BrN_3O_5Re$ (**4**), tetragonal $P\bar{4}2_1c$, $a = 16.895(3)$ Å, $c = 15.042(3)$ Å, $V = 4293.7(13)$ Å^3, $Z = 8$; $C_{18}H_{20}BrN_4O_5Re{\cdot}CH_3OH{\cdot}H_2O$ (**7**), monoclinic $P2_1/c$, $a = 10.2816(4)$ Å, $b = 30.386(1)$ Å, $c = 14.5810(6)$ Å, $\beta = 99.868(1)°$, $V = 4488.03(3)$ Å^3, $Z = 8$; $C_{17}H_{21}BrN_5O_5Re{\cdot}0.5CH_2Cl_2{\cdot}0.5H_2O$ (**8**), triclinic $P\bar{1}$, $a = 11.5363(6)$ Å, $b = 13.1898(6)$ Å, $c = 16.4933(8)$ Å, $\alpha = 89.356(1)°$, $\beta = 74.907(1)°$, $\gamma = 76.216(1)°$, $V = 2349.8(2)$ Å^3, $Z = 4$; $C_{16}H_{13}N_2O_5ReS$ (**9**), monoclinic $P2_1/c$, $a = 17.2072(7)$ Å, $b = 8.5853(4)$ Å, $c = 11.5607(5)$ Å, $\beta = 101.73(1)°$, $V = 1672.2(1)$ Å^3, $Z = 4$; and $C_{14}H_{12}N_2O_3BrReS$ (**10**), triclinic $P\bar{1}$, $a = 7.5585(3)$ Å, $b = 9.7713(4)$ Å, $c = 11.7103(4)$ Å, $\alpha = 109.566(1)°$, $\beta = 98.298(1)°$, $\gamma = 100.925(1)°$, $V = 779.73(5)$ Å^3, $Z = 2$.

Introduction

The significant contemporary interest in the chemistry of technetium and rhenium reflects the importance of the radioisotopes ^{99m}Tc and ^{186,188}Re in the development of diagnostic and therapeutic radiopharmaceuticals, respectively.[1,2] The established methods for radiolabeling of target-specific biomolecules with ^{99m}Tc or ^{188}Re exploit the coordination preferences of the metals in specific oxidation states and ligand environments. In this regard, it is noteworthy that all formal oxidation states of rhenium and

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technetium between −I and VII are represented by characterized compounds.[2] The most stable and readily accessible oxidation states are often characterized by chemically robust core structures that may be exploited as platforms for the development of radiopharmaceutical reagents. This strategy is well-represented by the $\{MO\}^{3+}$ core (M = Tc or Re) in conjunction with tetradentate N,S-donor bifunctional chelating agents[3] and by the Tc-hydrazino-nicotinamide core that has been adapted for the labeling of polyclonal IgG,[4,5] chemotactic peptides,[5−7] stealth liposomes,[8] antisense oligonucleotides,[9] GPIIb/IIIa receptor antagonist[10a] and somatostatin analogues,[11,12] and fibronectin receptor antagonist for tumor imaging.[10b] More recently, the organometallic approach pioneered by Jaouen et al.[13] has led to the development of $\{Tc(CO)_3\}^+$ and $\{Re(CO)_3\}^+$ cores for the development of novel target-specific radiopharmaceuticals.[14−16]

The M(I)-tricarbonyl cores (M = Tc or Re) exhibit several useful properties for the development of radiopharmaceuticals. The small size of the core allows labeling of low-molecular weight biomolecules with high specific activities with retention of biological activity and specificity. The precursor complexes to the radioconjugates, *fac*-$[M(CO)_3(H_2O)_3]^+$, may be readily prepared in aqueous-based kit formulations. The water molecules of the precursor complex are readily substituted by a variety of functional groups, including amines, thioethers, imines, thiols, and phosphines. Furthermore, the *fac*-$[M(CO)_3]^+$ core is chemically robust, low-spin d^6, providing a convenient platform for drug development.

Previous studies on the coordination chemistry of the $\{M(CO)_3\}^+$ core established that chelating ligands incorporating amine, aromatic N-heterocycles, and carboxylate donors were most effective.[14f] This observation suggested the design of bifunctional chelators constructed from amino acids, so as to provide a donor set for effective coordination of the $\{M(CO)_3\}^+$ and a linker group for attachment to a biomolecule. Consequently, we have developed a family of bifunctional chelators based on pyridyl, imidazole, carboxylate, and thiophene derivatized amino acids, modified so as to incorporate a tridentate chelation terminus (A), as well as a

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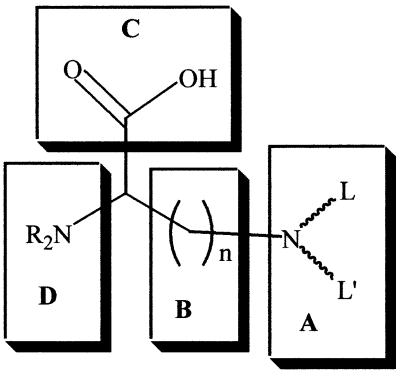
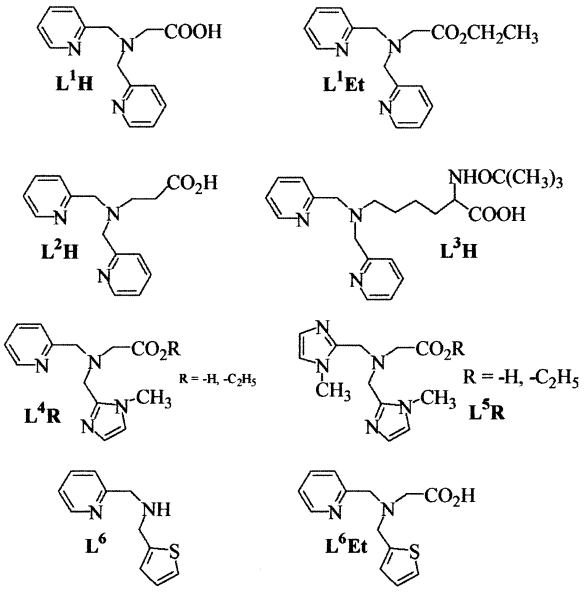
Scheme 1



Scheme 2



terminus (C) for conjugation to peptides, exploiting solid-phase synthesis or acylation to larger polypeptides and proteins (Scheme 1). Inclusion of the amino terminus (D) allows insertion at any position along the peptide sequence and suggests the use of these novel single-amino acid chelates (SAAC) in conventional solid-phase peptide synthesis.[17] The optimal design of the tether (B) may also be investigated. As part of these continuing studies, we report the syntheses of the ligands **L^{1}R**−**L^{6}R** (R = −H, $-C_2H_5$) (Scheme 2) and of their complexes with the $\{Re(CO)_3\}^+$ subunit. The structures of the model compounds $[ReBr(CO)_3\{(2\text{-pyridylmethyl})NH_2\}]$ (**1**) and $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NH\}]Br$ (**2**) and of the novel ligand complexes $[Re(CO)_3\{X(Y)NCH_2CO_2CH_2CH_3\}]Br$, (X = Y = 2-pyridylmethyl (**4**); X = 2-pyridylmethyl, Y = {2-(1-methylimidazolyl)methyl} (**7**); X = Y = {2-(1-methylimidazolyl)methyl} (**8**)), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NCH_2CO_2H\}]Br$ (**3**), $[Re(CO)_3\{(2\text{-pyridylmethyl})N(2\text{-thiophenemethyl})(CH_2CO_2)\}]$ (**9**), and $[ReBr(CO)_3\{(2\text{-pyridylmethyl})NH(2\text{-thiophenemethyl})\}]$ (**10**) are discussed.

Experimental Section

General Methods. All reagents and organic solvents used in this study are reagent grade and were used without further purification. $[NEt_4]_2[ReBr_3(CO)_3]$[18] was prepared according to the literature method. ^{1}H and ^{13}C NMR spectra were recorded on a Bruker DPX 300 spectrometer; all peak positions are relative to TMS. IR spectra were recorded as KBr pellets with a Perkin-Elmer Series 1600 FT-IR spectrometer in the region of 400−4000 cm^{-1} with polystyrene as a reference. Electrospray mass spectrometry (ESMS) was performed on a Fisons Platform quadrupole instrument where samples were dissolved in 50:50 CH_3CN/H_2O. For compounds analyzed in positive ion mode, one drop of 0.1% trifluoroacetic acid was added. For compounds run in negative mode, one drop of 0.10 M NH_4OH was added. Carbon, hydrogen, and nitrogen analyses were carried out by Oneida research services, Whitesboro, NY.

Ligand Syntheses. (Bis(2-pyridylmethyl)amino)acetic Acid (L^{1}H). The following procedure is based on literature procedures[19] with a slight modification. 2-Chloromethylpyridine hydrochloride (9.2 g, 56.0 mmol) and glycine (2 g, 26.6 mmol) were dissolved in water (30 mL) and stirred at room temperature for 5 days, with addition of 5 mol dm^{-3} aqueous NaOH solution at intervals to maintain the pH at 8−10. The resulting dark red solution was extracted with ethyl acetate, and the aqueous phase was acidified to pH 6, extracted with chloroform, and concentrated under vacuum. Pale yellow crystals of the pure ligand were obtained from dichloromethane. Yield: 2.87 g (42%). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.29 (d, J = 5.1 Hz, 2H, PyH), 7.60 (t, J = 9.0 Hz, 2H, PyH), 7.30 (d, J = 7.8 Hz, 2H, PyH), 7.12 (t, J = 6.2 Hz, 2H, PyH), 4.10 (s, 4H, $PyCH_2$), 3.39 (s, 2H, NCH_2). ^{13}C NMR (δ (ppm), MeOH-d_4): 173.05 (C, CO_2H), 156.10 (2C, Py), 149.76 (2CH, Py), 139.31 (2CH, Py), 125.15 (2CH, Py), 124.77 (2CH, Py), 59.77 (2C, $PyCH_2$), 57.77 (C, NCH_2).

Ethyl (Bis(2-pyridylmethyl)amino)acetate (L^{1}Et). (Bis(2-pyridylmethyl)amino)acetic acid (L^{1}H) (1 g, 3.89 mmol) was dissolved in saturated ethanolic HCl (20 mL) and refluxed for 3 h. The reaction was quenched with triethylamine and the mixture concentrated. The residue was dissolved in dichloromethane, washed with water, dried (Na_2SO_4), and concentrated. The crude product was purified by silica gel column chromatography using methanol/chloroform (3:97) to give **L^{1}Et** as a viscous liquid. Yield: 910 mg (82%). ^{1}H NMR (δ (ppm), $CDCl_3$): 8.49 (d, J = 3.0 Hz, 2H, PyH), 7.96 (t, J = 4.2 Hz, 2H, PyH), 7.53 (d, J = 7.8 Hz, 2H, PyH), 7.12 (t, J = 5.7 Hz, 2H, PyH), 3.97 (s, 4H, $PyCH_2$), 3.42 (s, 2H, NCH_2), 4.12 (q, 2H, OCH_2), 1.22 (s, 3H, CH_3). ^{13}C NMR (δ (ppm), $CDCl_3$): 171.05 (C, CO_2R), 158.80 (2C, Py), 148.80 (2CH, Py), 136.32 (2CH, Py), 122.93 (2CH, Py), 121.88 (2CH, Py), 59.70 (2C, CH_2Py), 54.67 (C, NCH_2), 60.21 (OCH_2), 13.99 (CH_3).

Bis(2-pyridylmethyl)amino)propionic Acid (L^{2}H). This compound was synthesized by a similar procedure as described above in the case of **L^{1}H** except that 3-aminopropionic acid was used instead of glycine. Starting from 2-chloromethylpyridine hydrochloride (7.73 g, 47.2 mmol) and 3-aminopropionic acid (2 g, 22.4 mmol), pale red crystals of (bis(2-pyridylmethyl)amino)propionic acid were obtained from dichloromethane. Yield: 2.74 g (45%). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.40 (d, J = 5.1 Hz, 2H, PyH), 7.73 (t, J = 9.0 Hz, 2H, PyH), 7.51 (d, J = 7.8 Hz, 2H, PyH), 7.24 (t, J = 6.0 Hz, 2H, PyH), 3.39 (s, 4H, $PyCH_2$), 2.96 (t, J = 6.9 Hz, 2H, NCH_2), 2.5 (t, J = 6.9 Hz, 2H, CH_2CO_2). ^{13}C NMR (δ (ppm), MeOH-d_4): 176.79 (C, CO_2H), 158.20 (2C, Py), 149.72 (2CH, Py), 138. 98 (2CH, Py), 125.29 (2CH, Py), 124.37 (2CH, Py), 60.22 (2C, $PyCH_2$), 51.90 (C, NCH_2), 33.15 (C, CH_2).

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***N*-α-(*tert*-Butoxycarbonyl)-*N*-*ω*-bis(2-pyridylmethyl)-L-lysine (L^{3}H).** 2-Chloromethylpyridine hydrochloride (1.4 g, 8.53 mmol) and *N*-α-(*tert*-butoxycarbonyl)-L-lysine (1 g, 4.06 mmol) were dissolved in water (25 mL) and stirred at room temperature for 5 days, with addition of 5 mol dm^{-3} aqueous NaOH solution at intervals to maintain the pH at 8−10. The resulting dark red solution was extracted with ethyl acetate, and then the aqueous phase was acidified to pH 6 using 1 mol dm^{-3} HCl, extracted with chloroform, and concentrated under vacuum. The residue was purified by column chromatography (SiO_2) using MeOH/$CHCl_3$ (1:9) to yield **L^{3}H** as a red viscous liquid (950 mg, 55%). ^{1}H NMR (δ (ppm), $CDCl_3$): 8.51 (d, J = 5.1 Hz, 2H, PyH), 7.64 (t, J = 7.5 Hz, PyH), 7.48 (d, J = 7.8 Hz, 2H, PyH), 7.15 (t, J = 6.3 Hz, 2H, PyH), 4.24 (t, H, $NCHCO_2$), 3.86 (s, 4H, $PyCH_2$), 2.57 (t, 2H, NCH_2), 1.62−1.26 (m, 6H, CH_2), 1.41 (s, 9H, ^{t}Bu). ^{13}C NMR (δ (ppm), MeOH-d_4): 177.49 (C, CO_2H), 157.71 (2C, Py), 149.72 (2CH, Py), 138.93 (2CH, Py), 125.11 (2CH, Py), 124.34 (2CH, Py), 80.06 (CH, NCH), 60.12 (2C, $PyCH_2$), 55.50 (2C, NCH_2, $NCHCO_2$), 33.15 (C, CH_2), 28.93 (3C, ^{t}Bu), 26.66 (C, CH_2), 24.31 (C, CH_2).

Ethyl [(2-Pyridylmethyl)-2-(1-methylimidazolylmethyl)]aminoacetate (L^{4}Et). To a solution of 1-methylimidazole-2-aldehyde (5 g, 45.1 mmol) in 80 mL of methanol was added slowly a solution of 2-picolylamine (4.88 g, 45.1 mmol) in 20 mL of methanol, and the solution was stirred for 2 h. At this time, the reactants were completely consumed. To this reaction mixture was added $NaBH_4$ (1.7 g, 45.1 mmol) in portions, and the solution was stirred for another 3 h, whereupon the solution was evaporated to dryness and the residue was extracted with chloroform and concentrated. This residue was dissolved in anhydrous dimethylformamide (40 mL). Potassium carbonate (7.53 g, 45.1 mmol) and ethyl bromoacetate (6.23 g, 45.1 mmol) were added to the solution under an argon atmosphere. The resulting suspension was protected from light and allowed to stir at 30 °C, under argon, for 32 h. The reaction mixture was filtered, and the filtrate was evaporated to dryness. The resulting red oil was purified by silica gel column chromatography using a MeOH/$CHCl_3$ (5:95) solution to give 7.80 g of the product. Yield: 60%. ^{1}H NMR (δ (ppm), MeOH-d_4): 8.33 (d, J = 4.2 Hz, 1H, PyH), 7.67 (t, J = 7.5 Hz, 1H, PyH), 7.36 (d, J = 8.1 Hz, 1H, PyH), 7.18 (t, J = 6.9 Hz, 1H, PyH), 6.89 (d, J = 1.2 Hz, 1H, ImH), 6.71 (d, J = 1.2 Hz, 1H, ImH), 3.86 (s, 2H, $PyCH_2$), 3.83 (s, 2H, $ImCH_2$), 3.58 (s, 3H, NCH_3), 3.22 (s, 2H, NCH_2), 3.99 (q, J = 14.4 Hz, 2H, OCH_2), 1.13 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (δ (ppm), MeOH-d_4): 172.23 (C, CO_2Et), 159.93 (C, Py), 149.72 (CH, Py), 146.26 (C, Im), 138.69 (CH, Py), 127.22 (CH, Py), 125.01 (CH, Py), 123.99 (CH, Im), 123.71 (CH, Im), 60.66 (C, $PyCH_2$), 55.54 (C, $ImCH_2$), 51.39 (C, NCH_3), 33.56 (C, NCH_2), 61.62 (C, OCH_2), 14.73 (C, CH_3).

Ethyl [Bis{2-(1-methylimidazolylmethyl)}amino]acetate (L^{5}Et). The preparation of **L^{5}Et** is based on literature procedures[20] with minor modifications.

(a) Preparation of Bis(2-(1-methylimidazolyl)methyl)amine (L^5). A solution of methyl-2-imidazolcarboxaldehyde oxime[20] (5 g, 40 mmol) in methanol (120 mL) was hydrogenated at atmospheric pressure and room temperature with 10% palladium charcoal for 5 days. The catalyst was filtered through Celite, and the filtrate was evaporated to give a white powder as **L^5**. Yield: 78%. ^{1}H NMR (δ (ppm), MeOH-d_4): 6.85 (d, J = 1.2 Hz, 2H, ImH), 6.70 (d, J = 1.2 Hz, 2H, ImH), 3.67 (s, 4H, $ImCH_2$), 3.48 (s, 6H, NCH_3). ^{13}C NMR (δ (ppm), methanol-d_4): 147.71 (2C, Im), 127.25 (2CH, Im), 123.31 (2CH, Im), 45.23 (2C, $ImCH_2$), 33.37 (2C, NCH_3).

(b) Preparation of L^{5}Et. Potassium carbonate (2.43 g, 17.56 mmol) and ethyl bromoacetate (1.76 g, 10.54 mmol) were added to a solution of bis(2-(1-methylimidazolyl)methyl)amine (**L^5**) (1.8 g, 8.78 mmol) in dimethylformamide under an argon atmosphere. The resulting suspension was sheltered from light and allowed to stir at room temperature for 5 days. Water was added to the resulting mixture, and the solution was extracted with chloroform (3 × 50 mL). After the solvent was evaporated, the resulting oil was purified by silica gel column chromatography using a MeOH/$CHCl_3$ (5:95) solution to give **L^{5}Et** as white powder. Yield: 1.05 g (41%). ^{1}H NMR (δ (ppm), MeOH-d_4): 6.87 (d, J = 1.2 Hz, 2H, ImH), 6.79 (d, J = 1.2 Hz, 2H, ImH), 4.06 (q, J = 14.4 Hz, 2H, OCH_2), 3.75 (s, 4H, $ImCH_2$), 3.51 (s, 6H, NCH_3), 3.35 (s, 2H, NCH_2CO_2), 1.19 (t, J = 7.2 Hz, 3H, CH_3). ^{13}C NMR (δ (ppm), MeOH-d_4): 172.09 (C, CO_2Et), 146.24 (2C, Im), 127.17 (2CH, Im), 123.79 (2CH, Im), 61.73 (C, OCH_2), 55.03 (2C, $ImCH_2$), 52.37 (2C, NCH_3), 33.24 (C, NCH_2), 14.67 (C, CH_3).

{(2-Pyridylmethyl)(2-thiophenemethyl)}amine (L^6). 2-Thiophenecarboxaldehyde (10.25 g, 91.40 mmol) and 2-pyridylmethylamine (11.72 g, 91.40 mmol) were dissolved in 50 mL of methanol and stirred under argon at room temperature for 1 h. Sodium borohydride (3.46 g, 91.40 mmol) was added to the solution, and the reaction mixture was stirred under argon for another 3 h. After concentration under vacuum, the residue was dissolved in a minimum amount of dichloromethane, washed with water, dried over sodium sulfate, and concentrated. The crude ligand was purified by silica gel column chromatography using MeOH/CH_2Cl_2 (7:93) to give the pure product as a viscous liquid. Yield: 9.15 g (44.79 mmol, 78%). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.47 (d, J = 5.1 Hz, 1H, PyH), 7.73 (t, J = 4.2 Hz, 1H, PyH), 7.40 (d, J = 7.8 Hz, 1H, PyH), 7.22 (m, 2H, PyH, ThH), 6.93 (m, 2H, ThH), 3.93 (s, 2H, $PyCH_2$), 3.85 (s, 2H, $ThCH_2$). ^{13}C NMR (δ (ppm), MeOH-d_4): 160.43 (C, Py), 149.93 (CH, Py), 144.00 (C, Th), 138.65 (CH, Py), 127.90 (CH, Py), 126.98 (CH, Py), 125.90 (CH, Th), 124.12 (CH, Th), 123.75 (CH, Th), 54.39 (C, $PyCH_2$), 48.34 (C, $ThCH_2$).

Ethyl [{(2-Pyridylmethyl)(2-thiophenemethyl)}amine] Acetate (L^{6}Et). {(2-Pyridylmethyl)(2-thiophenylmethyl)}amine (**L^6**) (3.00 g, 14.68 mmol) was dissolved in 40 mL of DMF with stirring under argon gas. Ethyl bromoacetate (2.51 g, 15 mmol) and potassium carbonate (2.07 g, 15 mmol) were added to the solution. The reaction mixture was protected from light with aluminum foil and stirred under argon for 6 days. After concentration under vacuum, the residue was dissolved in a minimum amount of dichloromethane, washed with water, dried over sodium sulfate, and concentrated. The crude ligand was purified by silica gel column chromatography using methanol/dichloromethane (6:94) to give the pure product as a viscous liquid. Yield: 1.44 g (5.25 mmol, 48%). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.41 (d, J = 5.1 Hz, 1H, PyH), 7.83 (t, J = 4.2 Hz, 1H, PyH), 7.71 (d, J = 7.8 Hz, 1H, PyH), 7.29 (m, 2H, PyH, ThH), 6.93 (m, 2H, ThH), 6.95 (m, ThH), 4.05 (s, 2H, $PyCH_2$), 3.98 (s, 2H, $ThCH_2$), 3.38 (s, 2H, NCH_2), 4.13 (q, OCH_2), 1.26 (t, CH_3). ^{13}C NMR (δ (ppm), MeOH-d_4): 171.0 (C, CO_2Et), 158.6 (C, Py), 149.4 (CH, Py), 139.4 (CH, Py), 135.9 (C, Th), 126.5 (CH, Py), 125.0 (CH, Py), 123.4 (CH, Th), 123.0 (CH, Th), 120.6 (CH, Th), 59.2 (C, OCH_2), 58.7 (C, $PyCH_2$), 56.7 (C, $ThCH_2$), 53.4 (NCH_2), 13.6 (CH_3).

Synthesis of [Re(CO)$_3$Br(H$_2$NCH$_2$C$_5$H$_4$N)] (1). A solution of $[NEt_4]_2[Re(CO)_3Br_3]$ (0.358 g, 0.465 mmol) and 2-methylaminopyridine (0.050 g, 0.465 mmol) in methanol (20 mL) was refluxed for 6 h. After cooling to room temperature, the reaction mixture was filtered, and the filtrate was evaporated to dryness. The residue was dissolved in dichloromethane and layered with hexane. Light yellow plates were obtained in 74% yield. Anal. Calcd (found) for $C_9H_8BrN_2O_3Re$: C, 23.6 (23.4); H, 1.75 (1.79); N, 6.11 (6.00). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.80 (d, J = 6.0 Hz, 2H, PyH), 7.98

(t, $J = 6.9$ Hz, 2H, PyH), 7.63 (d, $J = 7.8$ Hz, 2H, PyH), 7.20 (t, $J = 6.0$ Hz, 2H, PyH), 5.7 (s, 2H, NH_2), 4.75, 4.33 (m, 2H, $PyCH_2$).

Synthesis of [Re(CO)$_3${(2-pyridylmethyl)$_2$NH}]Br (2). Compound **2** was prepared and crystallized using a procedure analogous to that described for **1**. Anal. Calcd (found) for $C_{15}H_{13}BrN_3O_2Re$: C, 32.8 (32.6); H, 2.37 (2.30); N, 7.64 (7.33). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.87 (d, $J = 5.1$ Hz, 2H, PyH), 7.97 (t, $J = 4.2$ Hz, 2H, PyH), 7.26 (d, $J = 7.8$ Hz, 2H, PyH), 7.20 (t, $J = 7.0$ Hz, 2H, PyH), 4.75, 4.30 (m, 4H, $PyCH_2$).

Synthesis of the Rhenium Complexes of the Ligands L^{n}R. The complexes **3**−**6** were prepared by the same general procedure. A representative synthesis for complex **3** is presented.

(a) [Re(CO)$_3$(L^{1}H)]Br (3). To a stirred solution of $[NEt_4]_2[Re(CO)_3Br_3]$ (0.101 g, 0.13 mmol) in 20 mL of methanol was added L^1H (0.033 g, 0.13 mmol) in 2 mL of methanol, whereupon the solution was refluxed for 5 h. After being cooled to room temperature, the solution was filtered and evaporated to dryness to give a colorless residue. Recrystallization from methanol gave colorless plates suitable for X-ray crystallography. Yield: quantitative. Anal. Calcd (found) for $C_{17}H_{15}BrN_3O_5Re$: C, 33.82 (33.62); H, 2.41 (2.49); N, 6.83 (6.92). (^{1}H NMR (δ (ppm), MeOH-d_4): 8.76 (d, $J = 5.1$ Hz, 2H, PyH), 7.94 (t, $J = 7.8$ Hz, 2H, PyH), 7.58 (d, $J = 8.1$ Hz, 2H, PyH), 7.36 (t, $J = 6.6$ Hz, 2H, PyH), 5.37 (dd, $J = 17$ Hz, $PyCH_2$), 4.85 (dd, $J = 17$ Hz, $PyCH_2$), 4.69 (s, 2H, NCH_2). ^{13}C NMR (δ (ppm), MeOH-d_4): 195.06, 194.49 (*fac*-Re−CO_3), 169.51 (C, CO_2H), 160.76 (2C, Py), 151.43 (2CH, Py), 140.13 (2CH, Py), 125.39 (2CH, Py), 123.19 (2CH, Py), 67.77 (2C, $PyCH_2$), 67.26 (C, NCH_2). Mass spectrum (ESIMS): $m/z = 528.2$ $[Re(CO)_3(L^1H)]^+$. IR (KBr, ν/cm^{-1}): 2026, 1939, 1907 (*fac*-Re−CO_3); 1737 (ν_{as}(C═O)), 1186 (ν_{sym}(C═O)) of the ligand carboxylic acid group.

[Re(CO)$_3$(L^{1}Et)] (4). Single crystals were obtained from a carefully layered solution of dichloromethane with hexane. Anal. Calcd (found) for $C_{19}H_{19}BrN_3O_5Re$: C, 35.91 (36.10); H, 3.01 (3.07); N, 6.61 (6.66). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.87 (d, $J = 5.0$ Hz, 2H, PyH), 7.96 (t, $J = 6.0$ Hz, 2H, PyH), 7.57 (d, $J = 7.8$ Hz, 2H, PyH), 7.39 (t, $J = 6.0$ Hz, 2H, PyH), 5.27 (dd, $J = 15$ Hz, 2H, $PyCH_2$), 4.73 (dd, $J = 15$ Hz, 2H, $PyCH_2$), 4.73 (s, 2H, NCH_2), 4.32 (q, 2H, OCH_2), 1.33 (t, 3H, CH_3). ^{13}C NMR (δ (ppm), MeOH-d_4): 195.28, 194.68 (*fac*-Re−CO_3), 168.32 (C, CO_2Et), 160.89 (2C, Py), 151.76 (2CH, Py), 140.90 (2CH, Py), 125.67 (2CH, Py), 123.98 (2CH, Py), 68.09 (2C, $PyCH_2$), 67.52 (NCH_2), 61.72 (C, OCH_2), 13.11 (CH_3). IR (KBr, ν/cm^{-1}): 2030, 1925 (*fac*-$Re(CO)_3$); 1739 (ν_{as}(C═O)), 1204 (ν_{sym}(C═O)) of the ester group.

[Re(CO)$_3$(L^{2}H)] (5). Anal. Calcd (found) for $C_{18}H_{17}BrN_3O_5Re$: C, 34.78 (34.90); H, 2.71 (2.91); N, 6.76 (6.66). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.82 (d, $J = 5.1$ Hz, 2H, PyH), 7.90 (t, $J = 7.9$ Hz, 2H, PyH), 7.54 (d, $J = 7.8$ Hz, 2H, PyH), 7.33 (t, $J = 6.0$, 2H, PyH), 4.92 (dd, $J = 17$ Hz, 2H, $PyCH_2$), 4.79 (dd, $J = 17$ Hz, 2H, $PyCH_2$), 4.12 (t, $J = 6.9$ Hz, 2H, NCH_2), 2.99 (t, $J = 6.9$ Hz, 2H, CH_2). ^{13}C NMR (δ (ppm), MeOH-d_4): 197.24, 196.44 (*fac*-$Re(CO)_3$), 173.79 (C, CO_2H), 162.05 (2C, Py), 153.25 (2CH, Py), 141.77 (2CH, Py), 127.08 (2CH, Py), 124.86 (2CH, Py), 68.51 (2C, $PyCH_2$), 66.94 (C, NCH_2), 30.78 (C, CH_2). Mass spectrum (ESIMS): $m/z = [Re(CO)_3(\mathbf{L^2H})]^+ = 542.2$. IR (KBr, ν/cm^{-1}): 2026, 1925, 1907 (ν(*fac*-$Re(CO)_3$)); 1739 (ν_{as}(C═O)), 1120(ν_{sym}-(C═O)) of the acid group.

[Re(CO)$_3$(L^{3}H)] (6). Anal. Calcd (found) for $C_{24}H_{32}BrN_4O_7Re$: C, 38.20 (38.67); H, 4.20 (4.34); N, 7.42 (7.40). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.93 (d, $J = 5.1$ Hz, 2H, PyH), 8.0 (t, $J = 6.9$ Hz, 2H, PyH), 7.69 (d, $J = 7.8$ Hz, 2H, PyH), 7.46 (t, $J = 6.0$ Hz, 2H, PyH), 5.10 (d, $J = 17.5$ Hz, 2H, $PyCH_2$), 4.93 (d, $J = 17.5$ Hz, 2H, $PyCH_2$), 4.20 (t, $J = 5.1$, 1H, $NCHCO_2$), 3.9 (t, $J = 4.8$ Hz, 2H, NCH_2), 2.15−1.50 (m, 6H, CH_2), 1.49 (s, 9H, ^{t}Bu). ^{13}C NMR (δ (ppm), methanol-d_4): 197.44, 196.59 (*fac*-Re−CO_3), 177.20 (C, CO_2H), 162.31 (2C, Py), 153.14 (2CH, Py), 141.69 (2CH, Py), 127.05 (2CH, Py), 124.95 (2CH, Py), 80.51 (C, O^{t}Bu), 71.79 (NCH_2), 68.87 (2C, $PyCH_2$), 54.79 ($NCHCO_2$), 32.58 (C, CH_2), 28.90 (3C, ^{t}Bu), 25.81 (C, CH_2), 24.30 (C, CH_2).

[Re(CO)$_3$(L^{4}Et)]Br (7). To a stirred solution of $[NEt_4]_2[Re(CO)_3Br_3]$ (0.358 g, 0.465 mmol) in 40 mL of methanol was added **L^{4}Et** (0.134 g, 0.465 mmol) in 4 mL of methanol, and the solution was refluxed for 5 h. After cooling to room temperature, the solution was filtered and evaporated to dryness. The residue was dissolved in dichloromethane and carefully layered with hexane to give colorless crystals suitable for X-ray crystallography. Yield: 82%. Anal. Calcd (found) for $C_{18}H_{20}BrN_4O_5Re$: C, 33.86 (33.79); H, 3.16 (3.46); N, 8.77 (8.69). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.80 (d, $J = 5.4$ Hz, 1H, PyH), 8.04 (t, $J = 6.3$ Hz, 1H, PyH), 7.72 (d, $J = 7.8$ Hz, 1H, PyH), 7.45 (t, $J = 6.6$ Hz, 1H, PyH), 7.14 (d, $J = 1.8$ Hz, 1H, ImH), 7.11 (d, $J = 1.5$ Hz, 1H, ImH), 5.43 (d, $J = 16.2$ Hz, 2H, $PyCH_2$), 4.85 (d, $J = 11.7$ Hz, 2H, $ImCH_2$), 4.71 (d, $J = 4.2$ Hz, 2H, NCH_2), 4.33 (q, $J = 14.4$ Hz, 2H, OCH_2), 3.60 (s, 3H, NCH_3), 1.36 (t, $J = 7.2$ Hz, 3H, CH_3). ^{13}C NMR (δ (ppm), MeOH-d_4): 196.91, 195.96 (*fac*-Re−CO_3), 170.05 (CO_2Et), 160.84 (C, Py), 153.92 (C, Im), 153.34 (CH, Py), 141.72 (CH, Py), 128.75 (CH, Py), 127.17 (CH, Py), 125.66 (CH, Im), 125.43 (CH, Im), 70.69 (C, $PyCH_2$), 68.67 (C, $ImCH_2$), 63.17 (C, NCH_2), 59.15 (C, OCH_2), 34.89 (C, NCH_3), 14.51 (C, CH_3). IR (KBr, ν/cm^{-1}): 2022, 1922, 1906 (ν(*fac*-$Re(CO)_3$)); 1746 (ν_{as}(C═O)), 1208 (ν_{sym}(C═O)) of the acid group.

Preparation of [Re(CO)$_3$(L^{5}Et)] (8). The same procedure as for $[Re(CO)_3$(**L^{4}Et**)] was employed. Yield: 66%. Anal. Calcd (found) for $C_{17}H_{21}BrN_5O_5Re$: C, 31.83 (31.99); H, 3.30 (3.46); N, 10.92 (10.93). ^{1}H NMR (δ (ppm), MeOH-d_4): 7.29 (d, $J = 1.5$ Hz, 2H, ImH), 7.17 (d, $J = 1.5$ Hz, 2H, ImH), 5.29, 4.88 (dd, $J = 16.5$ Hz, 4H, $ImCH_2$), 4.79 (s, 2H, NCH_2), 4.44 (q, $J = 14.4$ Hz, 2H, OCH_2), 3.86 (s, 6H, NCH_3), 1.43 (t, $J = 7.2$ Hz, 3H, CH_3). ^{13}C NMR (δ (ppm), methanol-d_4): 197.15, 195.90 (*fac*-$Re(CO)_3$), 169.97 (C, COOEt), 152.40 (2C, Im), 128.58 (2CH, Im), 125.26 (2CH, Im), 68.77 (C, NCH_2), 63.12 (C, OCH_2), 61.18 (2C, $ImCH_2$), 35.39 (2C, NCH_3), 14.56 (C, CH_3). IR (KBr, ν/cm^{-1}): 2022, 1922, 1901 (ν(*fac*-$Re(CO)_3$)); 1743 (ν_{as}(C═O)), 1212 (ν_{sym}(C═O)) of the carboxylate group.

[Re(CO)$_3$L^{6}Et] (9). Yield: 78%. Anal. Calcd (found) for $C_{16}H_{13}N_2O_5ReS$: C, 36.15 (36.60); H, 2.46 (2.58); N, 5.27 (5.26). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.90 (d, $J = 5.1$ Hz, 1H, PyH), 7.96 (t, $J = 4.2$ Hz, 1H, PyH), 7.46 (d, $J = 7.8$ Hz, 1H, PyH), 7.31 (d, 2H, $J = 6.6$ Hz, ThH), 6.99 (t, 1H, $J = 4.6$ Hz, PyH), 6.91 (d, $J = 4.5$ Hz, ThH), 6.88 (m, ThH), 5.05, 4.44 (dd, $J = 14.4$ Hz, CH_2CO_2), 4.75, 4.25 (dd, $J = 15.5$ Hz, $PyCH_2$), 4.90, 3.2 (dd, $J = 15.1$ Hz, CH_2Th). ^{13}C NMR (δ (ppm), MeOH-d_4): 207, 206, 196 (*fac*-$Re(CO)_3$), 188.0 (CO_2), 161.6 (CH, Py), 150.0 (CH, Py), 143.5 (C, Th), 141.8 (2CH, Py), 138.2 (CH, Th), 136.9 (CH, Py), 135.5 (CH, Th), 133.8 (CH, Th), 77.2 (C, CH_2CO_2), 74.9 (C, $PyCH_2$), 70.5 (C, $ThCH_2$).

[Re(CO)$_3$(L^6)Br] (10). The same procedure as that used to prepare **5** was employed. Yield: 82%. Anal. Calcd (found) for $C_{14}H_{12}BrN_2O_3ReS$: C, 30.33 (31.01); H, 2.18 (2.22); N, 5.05 (5.16). ^{1}H NMR (δ (ppm), MeOH-d_4): 8.81 (m, 1H, PyH), 7.97 (m, 1H, PyH), 7.71 (m, 1H, PyH), 7.50 (m, 3H, 1PyH, 2ThH), 7.09 (m, 1H, ThH), 4.74 (dd, $J = 16$ Hz, 2H, $PyCH_2$), 4.47 (m, 2H, $ThCH_2$). ^{13}C NMR (δ (ppm), MeOH-d_4): 208, 209 (*fac*-$Re(CO)_3$), 163.0 (C, Py), 153.68 (CH, Py), 140.84 (CH, Py), 139.4 (C, Th), 130.05 (CH, Py), 128.6 (CH, Py), 127.7 (CH, Th), 125.8 (CH, Th), 124.0 (CH, Th), 57.55 (C, $PyCH_2$), 53.1 (C, $ThCH_2$).

Table 1. Summary of Crystal Data for the Structures of $[Re(CO)_3Br(H_2NCH_2\text{-}2\text{-pyridine})]$ (**1**), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NH\}]Br$ (**2**), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NCH_2CO_2H\}]Br\cdot CH_3OH$ (**3**), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NCH_2CO_2Et\}]Br$ (**4**), $[Re(CO)_3\{(2\text{-pyridylmethyl})(methylimidazolylmethyl)NCH_2CO_2Et\}]Br\cdot CH_3OH\cdot H_2O$ (**7**), $[Re(CO)_3\{(methylimidazolylmethyl)_2NCH_2CO_2Et\}]Br\cdot 0.5CH_2Cl_2\cdot 0.5H_2O$ (**8**), $[Re(CO)_3\{(2\text{-pyridylmethyl})N(CH_2CO_2)(CH_2\text{-thiophene})\}]$ (**9**), and $[Re(CO)_3Br\{(2\text{-pyridylmethyl})NH(CH_2\text{-thiophene})\}]$ (**10**)

	1	**2**	**3**	**4**	**7**	**8**	**9**	**10**
formula	$C_9H_8BrN_2O_3Re$	$C_{15}H_{13}BrN_3O_3Re$	$C_{18}H_{19}BrN_3O_6Re$	$C_{19}H_{19}BrN_3O_5Re$	$C_{19}H_{26}BrN_4O_7Re$	$C_{17.5}H_{23}BrClN_5O_{5.5}Re$	$C_{16}H_{13}N_2O_5ReS$	$C_{14}H_{12}BrN_2O_3ReS$
fw	458.29	549.39	639.47	635.48	688.55	692.97	531.54	554.43
space group	$P\bar{1}$	$P4_1$	$P2_1/m$	$P42_1c$	$P2_1/c$	$P\bar{1}$	$P2_1/c$	$P\bar{1}$
T, K	90(3)	86(2)	90(2)	90(2)	90(2)	90(2)	90(2)	90(2)
a, Å	8.156(1)	8.6095(3)	7.4425(3)	16.895(3)	10.2816(4)	11.5363(6)	17.2072(7)	7.5585(3)
b, Å	12.077(1)	8.6095(3)	9.7596(4)	16.895(3)	30.386(1)	13.1898(6)	8.5853(4)	9.7713(4)
c, Å	12.945(2)	22.218(1)	14.0646(6)	15.042(3)	14.5810(6)	16.4933(8)	11.5607(5)	11.7103(4)
α, deg	92.183(3)	90.0	90.0	90.0	90.0	89.356(1)	90.0	109.566(1)
β, deg	107.848(3)	90.0	97.753(1)	90.0	99.868(1)	74.907(1)	101.73(1)	98.298(1)
γ, deg	100.955(3)	90.0	90.0	90.0	90.0	76.216(1)	90.0	100.925(1)
V, Å^3	1185.1(3)	1646.9(1)	1012.26(7)	4293.7(13)	4488.0(3)	2349.8(2)	1672.2(1)	779.73(5)
Z	4	4	2	8	8	4	4	2
D_{calc}, g cm^{-3}	2.569	2.216	2.098	1.966	2.038	1.959	2.111	2.361
μ, mm^{-1}	13.618	9.822	8.016	7.556	7.244	7.025	7.422	10.500
R1[a] (all data)	0.036	0.025	0.0384	0.049	0.0467	0.0478	0.0293	0.0375
wR2[b]	0.078	0.059	0.0885	0.0987	0.0729	0.0694	0.0564	0.0903

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

Table 2. Comparison of Selected Bond Lengths (Å) and Angles (deg) for the Structures of $[Re(CO)_3Br(H_2NCH_2\text{-}2\text{-pyridine})]$ (**1**), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NH\}]Br$ (**2**), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NCH_2CO_2H\}]Br$ (**3**), $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NCH_2CO_2Et\}]Br$ (**4**), $[Re(CO)_3\{(2\text{-pyridylmethyl})(methylimidazolylmethyl)NCH_2CO_2Et\}]Br\cdot CH_3OH\cdot H_2O$ (**7**), $[Re(CO)_3\{(methylimidazolylmethyl)_2NCH_2CO_2Et\}]Br\cdot 0.5CH_2Cl_2\cdot 0.5\ H_2O$ (**8**), $[Re(CO)_3\{(2\text{-pyridylmethyl})N(CH_2CO_2)(CH_2\text{-thiophene})\}]$ (**9**), $[Re(CO)_3Br\{(2\text{-pyridylmethyl})NH(CH_2\text{-thiophene})\}]$ (**10**), and Related Examples

	1	**2**	**3**	**4**	**7**	**8**	**9**	**10**	$[Re(CO)_3Br(tppz)]$	$[Re(CO)_3\{O_2CCH(NH_2)CH_2\text{-imidazole}\}]$	$[Re(CO)_3Br(\{\text{-}CH_2S(CH_2)_2Cl\}_2)]$
Re−C, range	1.904(6)−1.919(6)	1.901(6)−1.926(7)	1.909(5)−1.915(4)	1.914(6)−1.928(7)	1.915(6)−1.918(6)	1.895(2)−1.926(2)	1.905(3)−1.913(3)	1.911(4)−.927(4)	1.873(11)−1959(11)	1.900(6)−1.910(6)	1.917(11)−1.979(6)
Re−N amine	2.230(5)	2.187(4)	2.237(4)	2.232(4)	2.268(4)	2.294(2)	2.242(2)	2.233(3)		2.188(5)	
Re−N pyridine or imidazole	2.190(5)	2.177(5) 2.183(5)	2.161(4) × 2	2.161(6) 2.174(5)	2.155(5) 2.179(5)	2.136(2) 2.143(2)	2.176(2)	2.190(3)	2.249(7) 2167(7)	2.192(4)	
Re−O							2.113(2)			2.147(4)	
Re−S											2.525(3) 2.537(2)
Re−Br	2.6462(7)							2.6270(4)	2.618(1)		2.608(1)
C−Re−X trans angles	173.2(2)−178.2(2)	171.5(2)−174.5(2)	170.0(2)−175.0(2)	174.7(3)−175.4(2)	169.2(2)−175.9(2)	170.6(1)−174.7(1)	172.8(1)−175.1(1)	170.6(2)−75.1(1)	169.2(4)−178.6(2)	not reported	173.2(2)−177.3(2)

X-ray Crystal Structure Determinations of 1−4 and 7−10. The selected crystals of **1**−**4** and **7**−**10** were studied on a Bruker diffractometer equipped with the SMART CCD system using graphite-monochromated Mo Kα radiation ($\lambda = 0.71073$ Å).[21] The data collections were carried out at 90(3) K. The data were corrected for Lorentz polarization effects, and absorption corrections were made using SADABS.[22] All calculations were performed using SHELXTL.[23] The structures were solved by direct methods, and all of the non-hydrogen atoms were located from the initial solution. After all the non-hydrogen atoms in the structures were located, the models were refined against F^2 initially using isotropic and later anisotropic thermal displacement parameters until the final values of Δ/σ_{max} were less than 0.001. At this point the hydrogen atoms were located from the electron density difference maps, and final cycles of refinements were performed until the final values of Δ/σ_{max} were again less than 0.001. No anomalies were encountered in the refinement of the structures. The relevant parameters for crystal data, data collection, structure solution, and refinement are summarized in Table 1, and important bond lengths and bond angles are summarized in Table 2. A complete description of the details of the crystallographic methods is given in the Supporting Information.

Results and Discussion

Synthesis and Spectroscopic Properties. All the complexes were prepared in excellent yields by refluxing equivalent amounts of each ligand and $[NEt_4]_2[ReBr_3(CO)_3]$ in methanol for a few hours. Slow cooling of the concentrated

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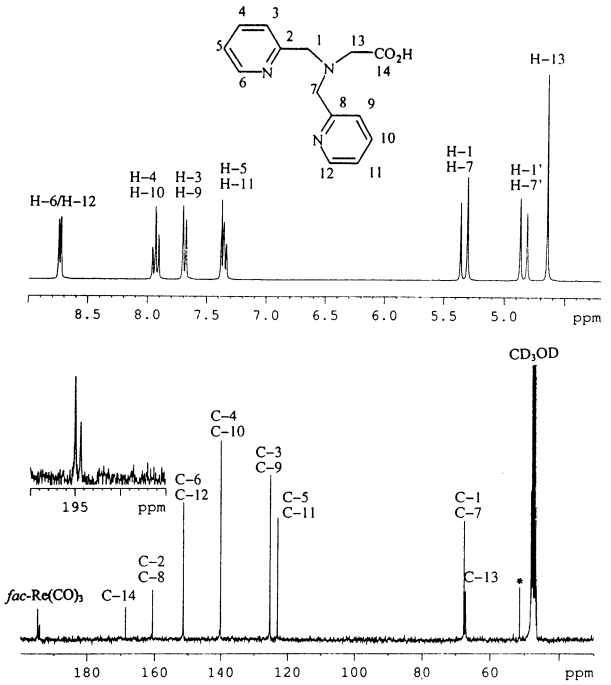

Figure 1. ^{1}H and ^{13}C NMR spectra of [Re(CO)$_3${(2-pyridyl-CH$_2$)$_2$N(CH$_2$-CO$_2$H)}]Br (**3**).

reaction mixture separates the products as white crystalline precipitates from the side product tetraethylammonium bromide.

The IR spectra of these complexes contain three strong bands in the region of 2030−1907 cm^{-1} indicating the presence of the *fac*-{Re(CO)$_3$}$^+$ core.[24−27] The complexes **3**, **5**, and **6** exhibit two strong absorptions in the regions of 1737−1734 and 1177−1230 cm^{-1}, corresponding to the two vibrations of the carboxylate group, ν_{as}(C═O) and ν_{sym}(O−C−O), respectively. Thus, since the Δ value ($\Delta = \nu_{as} - \nu_{sym} = 300$ cm^{-1}) is greater than 200 cm^{-1}, the possibility of a bidentate coordination that usually exhibits a Δ value of 40−80 cm^{-1} is excluded.

^{1}H and ^{13}C NMR spectroscopy indicate that the cationic complexes **3**−**6** retain their solid-state structure in solution. The assignments of all protons in all the ligands and the corresponding complexes are based on intensity, spin−spin splitting structure, and ^{1}H−^{1}H COSY and ^{1}H−^{13}C HMQC experiments and are presented in the Experimental Section. As an example, the ^{1}H and ^{13}C spectra of **3** are shown in Figure 1. Crystallographic data indicate that the complex cations of **3** and **4** exhibit mirror symmetry along one of the three facial carbonyl groups and the aliphatic amine side chain. This feature is reflected in their ^{1}H NMR spectra: the proton signals of methylene group adjacent to the pyridine are split into two sets of doublets with coupling constants

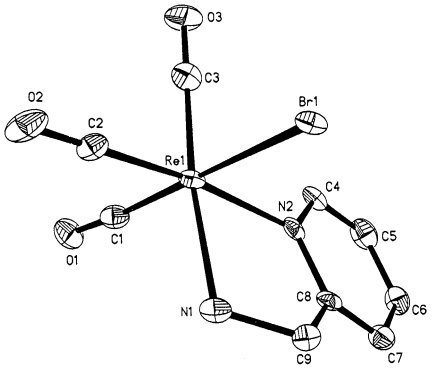

Figure 2. View of the structure of [ReBr(CO)$_3${(2-pyridyl-CH$_2$)NH$_2$}] (**1**), showing the atom-labeling scheme and 50% thermal ellipsoids.

consistent with geminal coupling (17−20 Hz). Also, there is only one set of pyridine protons. Analysis of the ^{13}C data of the complexes reveals that there are only two Re−CO peaks near 194−198 ppm instead of the three peaks expected for the *fac*-{Re(CO)$_3$}$^+$ moiety. The characteristic 2:1 peak height for these carbonyl resonances indicates that two CO groups are magnetically equivalent because of the mirror symmetry along the axis formed by the Re with one CO group. The ^{13}C NMR data show only one set of pyridine carbons, an observation consistent with these symmetry considerations. The fact that all complexes **3**−**6** retain the same geometry and structure in solution suggests that they are not only nonfluxional at room temperature but also chemically robust in a variety of solvents, including methanol, ethanol, acetonitrile, and dimethylformamide.

The data obtained from the mass spectra of the complexes are consistent with the formulations from elemental analysis and from spectroscopic evidence. For example, in the ESMS mass spectrum of [Re(CO)$_3$(**L^{2}H**)]Br (**5**), the most prominent *m*/*z* peak occurs at 527 and is assigned to [Re(CO)$_3$(**L^{2}H**)]$^+$ on the basis of the isotopic distribution of ^{185,187}Re. In addition, a higher mass peak at *m*/*z* 606 corresponds to (**5**-H)$^+$. Similarly, for the derivative [Re(CO)$_3${(2-C$_5$H$_4$NCH$_2$)$_2$-NCH$_2$CH$_2$CO$_2$H}]Br (**6**), prominent *m*/*z* peaks are observed at *m*/*z* 542 and 621, corresponding to [Re(CO)$_3${(2-C$_5$H$_4$-NCH$_2$)$_2$NCH$_2$CH$_2$CO$_2$H}]$^+$ and (**6**-H)$^+$, respectively.

Crystallographic Studies. The X-ray structural results confirm that all the rhenium(I) complexes of this study exhibit the chemically robust *fac*-{Re(CO)$_3$}$^+$ core and distorted octahedral geometries. The model compound [Re(CO)$_3$Br(2-pyridylmethyl)NH$_2$)] (**1**), shown in Figure 2, possesses the common {Re(I)(CO)$_3$X} (X = halide or another anionic ligand) neutral subunit that occurs with bidentate coligands or with multidentate ligands that prefer meridional to facial coordination modes.[14a,28−35] The remain-

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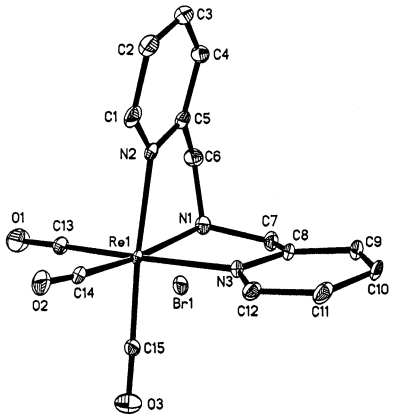

Figure 3. View of the structure of $[Re(CO)_3\{(2\text{-pyridyl-}CH_2)_2NH\}]Br$ (**2**), showing the atom-labeling scheme and 50% thermal ellipsoids.

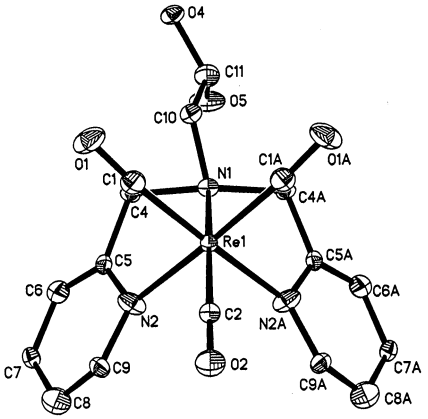

Figure 4. View of the structure of $[Re(CO)_3\{(2\text{-pyridyl-}CH_2)_2NCH_2CO_2H\}]Br$ (**3**), showing the atom-labeling scheme and 50% thermal ellipsoids.

ing coordination sites are occupied by the amine nitrogen donor N1 and the pyridyl nitrogen N2 of the 2-pyridylmethylamine ligand.

The Re−carbonyl bond distances (1.904−1.919(6) Å) are consistent with those found in similar complexes,[35] as is the Re−Br bond length of 2.6462(7) Å. The Re−N1 distance of 2.230(5) Å is somewhat longer than that of 2.190(5) Å for Re−N2, consistent with sp^3- and sp^2-hybridized nitrogen donors, respectively. The trans angles fall in the range of 173.2(2)−177.0(2)°, showing only minor deviations from the idealized octahedral limit. The most significant angular distortion is associated with the N1−Re−N2 angle of 75.5(2)°, which is a consequence of the formation of the strained five-membered chelate ring.

As anticipated, the incorporation of a second methylpyridine arm in the tridentate ligand $(2\text{-pyridylmethyl})_2NH$ results in displacement of all bromide ligands from the rhenium(I) coordination sphere to give $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NH\}]Br$ (**2**). The structure consists of discrete Br^- anions and $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NH\}]^+$ cations, shown in Figure 3. The distorted octahedral environment of the Re(I) in the molecular cation is defined by the three facially bound CO groups and the amine and pyridyl nitrogen donors of the ligand. As shown in Table 2, the metrical parameters are unexceptional for a structure of this type.

The structure of the cation of $[Re(CO)_3\{2\text{-pyridylmethyl})_2NCH_2CO_2H\}]Br$ (**3**) illustrates that the $\{Re(CO)_3N_3\}$ core geometry of **2** is maintained upon introduction of the $-CH_2CO_2H$ pendant arm (Figure 4). The structure also confirms that the $\{Re(CO)_3\}^+$ core exhibits a coordination preference for pyridyl nitrogen donors rather than the carboxylate unit of the pendant arm. As shown in Table 2, the bond lengths and angles associated with **3** are similar to those of **2**. The structure of the ethyl ester derivative $[Re(CO)_3\{(2\text{-pyridylmethyl})_2NCH_2CO_2Et\}]Br$ (**4**) is analogous to that of **3**, and the metrical parameters of the Re(I) site are unexceptional (Table 2). The structural consequences of replacing the pyridyl donor arms of **4** with methylimidazole groups were assessed by preparing and structurally characterizing the complexes $[Re(CO)_3(\mathbf{L^4Et})]Br$ (**7**) and $[Re(CO)_3(\mathbf{L^5Et})]Br$ (**8**). As shown in Figure 5, the structures of **7** and **8** are analogous to that of **4**. The metrical parameters for **7** and **8** are unexceptional for the $\{Re(CO)_3N_3\}^+$ core.

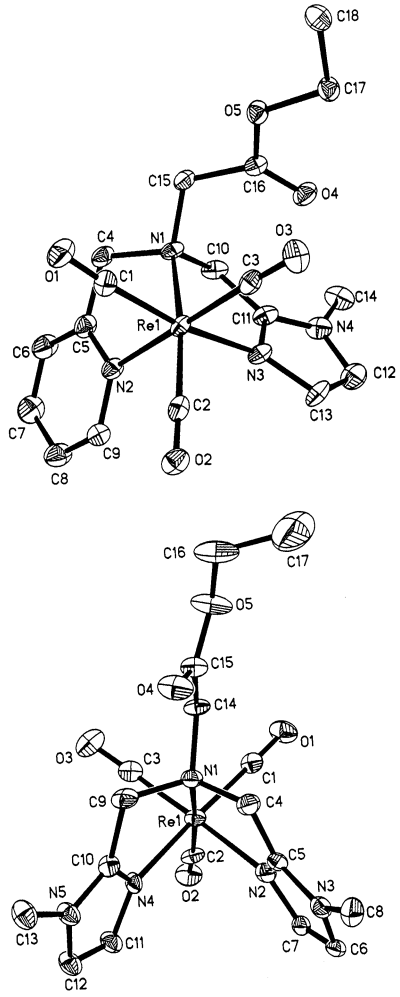

Figure 5. Structures of $[Re(CO)_3(\mathbf{L^4Et})]Br$ (**7**) and $[Re(CO)_3(\mathbf{L^5Et})]Br$ (**8**), showing the atom-labeling schemes and 50% thermal ellipsoids.

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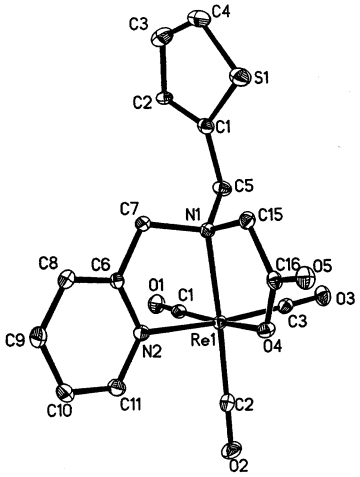

Figure 6. View of the structure of $[Re(CO)_3\{(2\text{-pyridyl-}CH_2)N(CH_2CO_2)(CH_2\text{-thiophene})\}]$ (**9**), showing the atom-labeling scheme and 50% thermal ellipsoids.

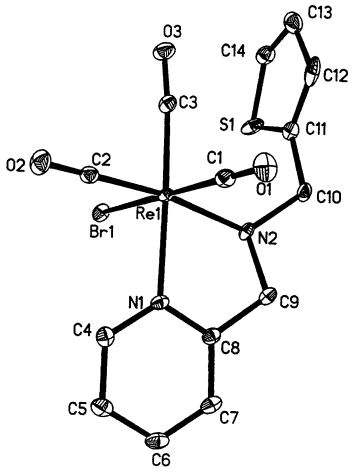

Figure 7. View of the structure of $[ReBr(CO)_3\{(2\text{-pyridyl-}CH_2)NH(CH_2\text{-thiophene}\}]$ (**10**), showing the atom-labeling scheme and 50% thermal ellipsoids.

To evaluate the coordination preferences of the $\{Re(CO)_3\}^+$ core with respect to other potential donor groups, one pyridyl arm of the glycine-based tridentate ligand type was replaced with a thiophene group, resulting in the isolation of the complex $[Re(CO)_3\{(2\text{-pyridylmethyl})N(2\text{-thiophenemethyl})(CH_2CO_2)\}]$ (**9**), shown in Figure 6. In this case, a carboxylate oxygen binds to the *fac*-$\{Re(CO)_3\}^+$ core along with the amine and pyridyl nitrogen donors. Consequently, the thiophene arm is pendant. Deprotonation of the carboxylate provides an anionic ligand and an overall neutral molecular species.

Both carboxylate and thioether donors have been demonstrated to act as effective ligands for the $\{Re(CO)_3\}^+$ core, as illustrated by $[Re(CO)_3\{O_2CCH(NH_2)CH_2\text{-imidazole}\}]$[14f] and $[Re(CO)_3Br\{CH_2S(CH_2)_2Cl\}_2]$,[14a] respectively. However, on the basis of the observations of this study, the apparent coordination preference of the $\{Re(CO)_3\}^+$ core is pyridyl nitrogen > carboxylate > thiophene sulfur. While thioether sulfur atoms may be effective donors in general, as suggested by the examples cited, thiophene is an especially weak ligand.

Removal of the carboxylate arm of the ligand in (2-pyridylmethyl)NH(2-thiophenemethyl) does not result in sulfur coordination, as illustrated by the structure of $[Re(CO)_3Br\{(2\text{-pyridylmethyl})NH(2\text{-thiophenemethyl})\}]$ (**10**), shown in Figure 7. In this case, the remaining coordination sites about the *fac*-$\{Re(CO)_3\}^+$ core are occupied by the amine and pyridyl nitrogen donors of the bidentate ligand and a bromide. The thiophene arm of the ligand is pendant, establishing that the halide is a more effective ligand than the thioether group.

Conclusions

A series of potentially tridentate ligands derived from simple amino acids have been prepared. These ligands react cleanly and in high yield with $[NEt_4]_2[ReBr_3(CO)_3]$ to give complexes of the types $[Re(CO)_3(ligand)]Br$ and $[Re(CO)_3Br(ligand)]$, depending on the nature of the donor groups. Tridentate ligation is observed when three or two nitrogen donors and a carboxylate group are available. In contrast, thioether sulfur donors do not appear to be as effective in ligation to the $\{Re(CO)_3\}^+$ core. A qualitative order of the coordination preferences for these complexes is pyridyl nitrogen > carboxylate > halide > thioether. Furthermore, these ligands represent a novel class of bifunctional chelates, namely, SAAC that can be exploited for the creation of peptide libraries and derivatized peptides and proteins, which can be subsequently complexed with $[M(CO)_3L_3]$ reagents for radiolabeling.

Acknowledgment. This work was supported by a grant from the Department of Energy (DOE), Office of Health and Environmental Research (D2-FG02-99ER62791).

Supporting Information Available: Tables of complete crystal data, final coordinates, temperature factors, distances, and angles for the crystallographic study of **1**−**4** and **7**−**10** in CIF format. This material is available free of charge via the Internet at http://pubs.acs.org.

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