# Gateway Reactions to Diverse, Polyfunctional Monolayer-Protected Gold Clusters

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**Abstract:** Amide and ester coupling reactions of $\omega$-functionalized monolayer-protected gold cluster molecules (MPCs) are an exceptionally efficient avenue to a diverse variety of polyfunctionalized MPCs starting from a small subset of $\omega$-functionalized materials. In this paper, coupling reactions have been employed to produce 13 MPCs bearing multiple copies of a diverse variety of structural groups. Detailed features of three of the 13 polyfunctionalized products are highlighted: (*a*) stepwise coupling and deprotection reactions result in an MPC surrounded by ca. eight pendant tripeptides, (*b*) a preliminary Steady-State Electron Paramagnetic Resonance (SSEPR) experiment is described for MPCs bearing multiple spin labels (ca. 13/cluster), and (*c*) a polyelectron electrochemical reaction is described for an MPC bearing multiple (ca. 7/cluster) coupled phenothiazine derivatives. The coupling reactions substantially expand the available diversity of MPCs as polyfunctionalized chemical reagents platformed on a nanometer-sized central core.

## Introduction

Molecules bearing multiple copies of a given functional group or structural moiety are widely prepared and used in chemistry. Linear and hyperbranched polymers are well-known examples of polyfunctionality, to which dendrimers[1] add the important aspect of spatial organization. Cluster molecules consisting of central cores supporting functionalized monolayers are *potential analogues of dendrimers*, but such materials thus far are undeveloped as polyfunctional reagents. Alkanethiolate/Au monolayer-protected clusters[2] (MPCs) are particularly attractive in this regard owing to their stability, tunable solubility, and relative ease of characterization.[3] Moreover, understanding cluster reactivity is a prerequisite for their use in a variety of applications, including catalysis, chemical sensing,[4] and nanoscale electronics. One level of polyfunctionalization has been previously demonstrated using place-exchange reactions[5−7] of nanometer-sized MPCs with $\omega$-functionalized-alkanethiols, but the additional step of using the latter, or other, cluster molecules as building blocks to prepare structurally diverse polyfunctional clusters has received only scant attention.[8−11] To that end, we recently reported the polyreactivity of alkylamines with $\omega$-Br-alkanethiolate/Au MPCs, observing as many as 20 $S_N2$ displacements per cluster molecule.[11]

This paper describes a more general synthetic route, based on amide and ester coupling reactions,[12,13] to alkanethiolate/Au-based MPCs bearing multiple copies of a diverse selection of structural groups, starting from a small and readily prepared (by place-exchange[5−7]) *subset* of $\omega$-functionalized MPC materials. The coupling reactions[14] are those of alcohols or amines with MPC $\omega$-carboxylic acid groups and of carboxylic acids with MPC $\omega$-alcohol groups, a synthetic strategy offering several important features: (a) amide and ester formation are versatile, well-known reactions[12,13] and powerful activating agents are readily available,[14] (b) a tremendous variety of target substituents with amine, carboxylic acid, or alcohol groups can be obtained, and (c) the alternate, place-exchange pathway, involving synthesis of $\omega$-functionalized alkanethiol derivatives, is often not facile (*vide infra*).

The materials produced herein provide the groundwork for numerous studies, including investigation of various aspects of chemical reactivity and spectroscopic chararacterization as a

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**Table 1.** Coupling Reactions of $\omega$-Functionalized MPCs (−COOH, −OH) with a Variety of Reagents

| # | MPC[a] | reagent coupled to MPC | % conv.[b]/ca. no. coupled[c] | interest |
|---|---|---|---|---|
| 1 | C12:C11COOH (4:1) | 4-amino-TEMPO | 95/13 | spin label |
| 2 | C12:C11COOH (4:1) | 4-(aminomethyl)pyridine | 95/9.5 | metal ligand |
| 3 | C12:C11COOH (10:1) | glutamic acid di-*tert*-butyl ester | 90/4 | amino acid |
| 4 | C12:C11COOH (6:1) | 1-aminopyrene | 95/7 | chromophore; fluorophore |
| 5 | C12:C11COOH (4:1) | 2-(aminomethyl)-15-crown-5 | 80/8 | ionophore |
| 6 | C12:C11COOH (6:1) | benzylamine | 95/7 | group conversion |
| 7 | C12:C11COOH (2.7:1) | 2-naphthaleneethanol | 85/11.5 | chromophore |
| 8 | C12:C11COOH (4:1) | ferrocene methanol | 50/5 | electroactive |
| 9 | C12:C11COOH (2.7:1) | α-D-glucose | 35/5 | sugar |
| 10 | C12:C11COOH (2.7:1) | uridine | 60/8 | nucleotide |
| 11 | C12:C11OH (3:1) | 10*H*-(phenothiazine-10)propionic acid | 65/7.4 | electroactive |
| 12 | C12:C11OH (4:1) | anthraquinone-2-carboxylic acid | 75/7.5 | electroactive; chromophore |

[a] MPC nomenclature is CX:CYZ (a:b), where X specifies the alkanethiolate chain-length and Y the chain-length of the place-exchanged $\omega$-Z-alkanethiol (Z = COOH, OH), and (a:b) specifies the mole ratio of X and Y chains in the cluster, as determined from the methyl/$-CH_2R$ $^1$H NMR spectral ratio in solutions of $I_2$-decomposed clusters[11] (R = COOH) or intact MPCs (R = OH). [b] Conversion determined from methyl/$-CH_2R$ (R = COOR, CONHR) $^1$H NMR spectral ratios in solutions of reacted MPCs, except for 4-amino-TEMPO, which was monitored with FTIR. [c] Average number coupled[15] given[7] a 145 atom Au core with 50 alkanethiolate ligands.

function of coverage on the particle surface, gold core size, and relative chain-lengths of the connecting alkanethiol and diluent ligands.

## Results and Discussion

We previously described a versatile synthetic route to $\omega$-functionalized alkanethiolate gold cluster compounds based on simple place-exchange reactions.[5] Importantly, this strategy allows for cluster functionalization while avoiding concurrent changes in the dimensions of the Au core which potentially could occur when employing functionalized alkanethiols in a *de novo* synthetic fashion.[8] A later study described the synthesis and characterization of polyhetero-$\omega$-functionalized MPCs and the steric effect of terminal substituents on the extent of place-exchange.[6] While polyfunctionalization can thus be achieved by synthesizing the alkanethiol derivative of interest and performing place-exchange reactions, an attractive alternate pathway is to employ place-exchange reactions to prepare a small-subset of easily obtained starting materials for coupling to a diverse selection of structural groups in a second reaction step.

Besides having importance in demonstrating that MPCs participate in chemical reactions in a predictable fashion,[11] the functionalization strategy described herein offers several important advantages over the place-exchange route.[5−7] The amide and ester coupling reactions could be performed to attach interesting structural groups to the free alkanethiol, followed by place-exchange onto the gold core. This route would, however, involve protection of the thiol (via a disulfide or other appropriate protecting group) prior to the coupling reaction, then extractions or chromatography to remove reactants and side products and, finally, deprotection to again afford the thiol. The coupling method described herein relies on $\omega$-functionalized alkanethiols firmly affixed to the gold core which alleviates the need for protecting/deprotecting the thiol functionality. Moreover, unreacted materials and reagents are simply removed by filtration. Thus, except in the case where residual, unreacted terminal groups would pose problems for subsequent experiments, coupling reactions on the clusters represent a simple and powerful route to achieve polyfunctionalized MPCs containing a wide variety of structural groups.

The results in Table 1 demonstrate that multiple copies[15] of diverse substituents can be coupled to MPCs by amide and ester-forming reactions (entries #1−6, $\omega$-amide formation, #7−12, $\omega$-ester formation). The synthetic details and product analysis are found in the Experimental Section. The deliberate diversity of product materials portrays how the generality of the coupling reaction provides entree into various avenues of polyfunctional MPC chemistry. Features of three of the 13 different MPC products are highlighted below.

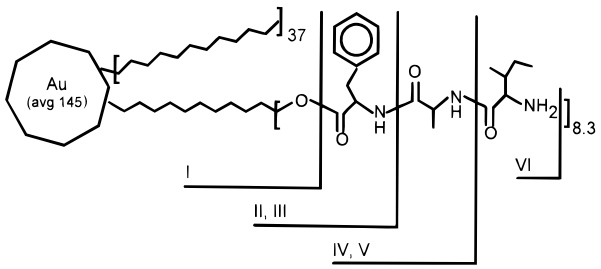


**Figure 1.** Cartoon representation of the multistep synthesis of a tripeptide-functionalized MPC. Steps I, III, and V are coupling reactions, and Steps II, IV, and VI are deprotection reactions. Truncated peptide products resulting from incomplete coupling reactions are not shown in the figure. The complete cluster product makeup is: (a) C12SH: 37, (b) HOC11SH: 1.7, (c) Ile-Ala-Phe-C11SH: 8.3, (d) Ala-Phe-C11SH: 1.3, (e) Phe-C11SH: 1.4 (total of ca. 50 thiolates/MPC).

First, as has been shown recently, considerable benefits can accrue to melding of nanoparticle and biologically relevant chemistries.[16] In Table 1, #3 (amino acid), #9 (sugar), and #10 (nucleotide) comprise examples where multiple copies of simple biomolecules are coupled to MPCs. Figure 1 shows a further example (not in Table 1) of using multiple reaction steps to construct MPCs with a more complex biological moiety. Specifically, sequential couplings (of BOC-phenylalanine, BOC-alanine, and BOC-isoleucine) and deprotections (20% TFA in $CH_2Cl_2$) lead to an MPC surrounded by ca. eight pendant tripeptides in 67% overall yield. This example demonstrates the feasibility and tolerance of MPCs with multistep reaction sequences and lays the groundwork for the preparation of a variety of biofunctionalized MPCs.

Second, Table 1 illustrates several examples of MPCs with multiple spectroscopic labels (e.g., chromophores, fluorophores, spin labels). Preliminary steady-state electron paramagnetic resonance (SSEPR) experiments have been accomplished on the spin labeled (TEMPO) MPC. Figure 2 shows an EPR

(15) Just as place-exchange reactions should yield[5] a statistical distribution of $\omega$-functionalized alkanethiolates/cluster, so should the subsequent coupling reactions. Details of this distribution are as yet unknown. Thus, NMR measurements in reaction #1 (Table 1) refer to the *average* number (13) of TEMPO sites per cluster.

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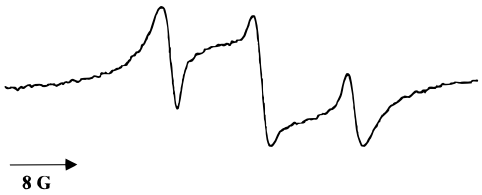


**Figure 2.** Room-temperature SSEPR solution spectra of TEMPO-functionalized MPC (ca. 13 TEMPO/cluster) at a concentration of $10^{-3}$ M (in spin label) in methyl-THF.

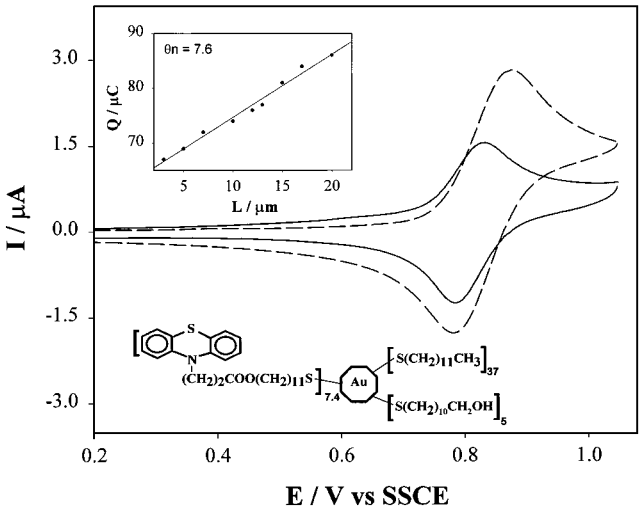


**Figure 3.** Electrochemical characterization of 10*H*-(phenothiazine-10)-propionic acid -functionalized MPC (lower inset). Cyclic voltammetry of 0.8 mM (in phenothiazine) 10*H*-(phenothiazine-10)propionic acid -functionalized MPC (–) and of 1 mM 10*H*-(phenothiazine-10)propionic acid (- -) in 2:1 toluene/$CH_3CN$ (v/v) at 100 mV/s. Upper inset: Thin layer coulometry charge $Q$ vs cell length $L$ ($r^2 = 0.98$, slope $= 11.47 \times 10^{-3}$ C/cm).

spectrum of a polyTEMPO MPC bearing an average of ca.13 radicals per cluster in which hyperfine splitting due to the $M_I = -1, 0, +1$ spin states of the nitrogen nucleus is apparent. The line shape, however, is not completely symmetrical which may be due to a superposition of spectra resulting from a distribution in the actual number of spins on individual clusters.[15] Additionally, results so far indicate that the spin label has little or no interaction with the underlying gold core (ca. 145 atoms). EPR studies of the spin labeled MPCs as a function of spin loading, gold core size, and length of the connecting alkanethiolate chain are presently underway.

Third, while MPCs bearing multiple redox groups have been formed via place-exchange reactions with redox-alkanethiols,[5−7] we are interested in alternate routes to polyredox MPCs that facilitate exploration of their electrocatalytic properties and possible roles in charge-transfer complexes. As part of the present study, we coupled multiple copies of a phenothiazine derivative to an MPC (see lower inset, Figure 3). A solution of this cluster exhibits oxidative voltammetry (Figure 3, solid line) nearly identical to that of phenothiazine monomer (Figure 3, dashed line). (Currents for the MPC are smaller owing to its slower diffusion.) Coulometry in thin-layer cells[17] as a function of their thickness, $L$, (Figure 3, upper inset) showed[18] that the average number of electroactive phenothiazines per cluster was 7.6, a result consistent with $^1$H NMR data (Table 1) which gives an average of 7.4 phenothiazines per cluster. The coulometry provides both an independent measure of cluster loading and a confirmation that all attached phenothiazines are electroactive.

The generality of the amide/ester coupling strategy is amply illustrated by the above experiments, which open the way to investigations and uses of MPCs as a new kind of polyfunctionalized material. In summary, these results provide a pathway for the investigation of (a) "nanofactory" MPCs, in which combinations of appropriate groups exhibit mutually supporting chemical and redox catalytic reactivities, (b) the synthesis of MPCs containing complex biomolecules including those capable of participating in molecular recognition, and (c) studies employing MPCs functionalized with spectroscopic labels that should allow for more detailed investigations of label/label or label/core interactions with coverage, relative chain-lengths of connecting and diluent alkanethiols, and gold core size.

## Experimental Section

**Chemicals.** $HAuCl_4 \cdot xH_2O$[19] and 10*H*-(phenothiazine-10)-propionic acid[20] were synthesized according to literature procedures. 11-Mercaptoundecanoic acid and 11-mercapto-undecanol were either synthesized according to the procedure of Bain[21] or purchased from Aldrich (95% and 97% purity, respectively). Tetrahydrofuran (J. T. Baker, <16 ppm water content) was used for all coupling reactions. The MPC synthesis (*average* core of 145 Au atoms and ca. 50 protecting alkanethiolate chains)[3] and place exchange reactions[5−7] were accomplished as described earlier. All other reagents were used as received.

**Spectroscopy.** $^1$H NMR spectra (in $C_6D_6$, $CD_2Cl_2$, or $CDCl_3$) were obtained with a Bruker AMX 200 MHZ spectrometer. A line broadening factor of 1 Hz was used to improve S/N of MPC NMR data. Infrared absorbance spectra of clusters as thin films were acquired using a Bio-Rad 6000 FTIR spectrometer. Reported IR bands are those that are unique to each modified MPC (a C12 MPC spectra was used for background subtraction). Steady-state EPR (in methyl-THF) were obtained with a JEOL JES RE-1X EPR spectrometer.

**Analysis of ω-Carboxylic Acid-Alkanethiolate Functionalized MPCs Using $I_2$-Decomposition.** In a typical reaction, approximately 50 mg of the ω-carboxylic acid-alkanethiolate functionalized MPC was dissolved in dichloromethane and stirred with approximately 3 mg of iodine for 1 h. Following disulfide formation, which could be monitored by a change in solution color from dark brown to clear violet, the insoluble brown residue (actual identity of insoluble materials not identified) was removed and the sample rotovapped to dryness. NMR of $I_2$-decomposed C12:C11COOH (4:1) (in $CDCl_3$): $\delta$ (ppm) = 0.85 (t, 5.5 H), 1.25 (m, 35.4 H), 1.66 (m, 5.3 H), 2.35 (t, 1 H), 2.65 (t, 4 H). Analogous NMR results were obtained for other MPCs with different mole ratios of methyl/-$CH_2COOH$ and will thus not be detailed.

**Coupling of Amines to C12:C11COOH (a:b) (#1−6).** Coupling reactions were performed after the manner of McCafferty et al.[14] In a typical reaction, ca. 100 mg of the acid MPC (C12:C11COOH MPC (4:1)) was treated with 5 equiv (relative to mol of MPC acid groups) of BOP (60 mg), HOBt (18 mg), NMM (14 μL), and DMAP (16 mg) in low water THF (concentration of 2 mg cluster/mL), and, following a brief

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(18) The number of electrons/cluster $\theta$n is calculated from the slope of charge $Q$ versus $L$ since $Q/L = \theta n$FAC.

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activation period (10 min), 5 equiv of the amine were added to the reaction mixture and the solution stirred at room temperature for 15 h. Solvent was removed under vacuum, and the reacted MPC was collected on a frit where unreacted materials were removed by washing with 500 mL of acetonitrile followed by sonication/decanting with 50 mL of acetonitrile (3×).

***(#1)* 4-Amino-TEMPO.** IR: 2851 ($d^+$), 2922 ($d^-$), 1641, 1537 $cm^{-1}$.

***(#2)* 4-(Aminomethyl)pyridine.** NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.89 (br, 15.6 H), 1.28 (br, H), 1.74 (br, H), 2.21 (br, 3.1 H), 4.32 (br, 1.9 H), 7.12 (br, 2.3 H), 8.43 (br, 2 H). IR: 2850 ($d^+$), 2920 ($d^-$), 1653, 1602, 1539 $cm^{-1}$.

***(#3)* Glutamic Acid Di-*tert*-butyl Ester.** NMR (in $C_6D_6$): $\delta$ (ppm) = 1.02 (br, 27 H), 1.4 (br, 218 H), 2.3 (br, 28 H), 4.8 (br, 2 H). IR: 2850 ($d^+$), 2920 ($d^-$), 1734, 1680, 1650, 1536, 1392, 1367, 1155 $cm^{-1}$.

***(#4)* 1-Aminopyrene.** NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.85 (br, 3 H), 1.3 (br, 15 H), 1.85 (br, 1.9 H), 3.35 (br, 0.33 H), 3.55 (br, 0.31 H), 7.15 (br, 0.02 H), 7.45 (br, 0.04 H), 7.7 (br, 0.06 H), 8.0 (br, 0.18 H). IR: 2851 ($d^+$), 2921 ($d^-$), 1735, 1700, 1655, 1601, 1558, 1517 $cm^{-1}$.

***(#5)* 2-(Aminomethyl)-15-crown-5.** NMR (in $C_6D_6$): $\delta$ (ppm) = 0.75 (br, 0.8 H), 1.0 (br, 3 H), 1.45 (br, 18 H), 2.25 (br, 2 H), 3.6 (br, 3.8 H). IR: 2949 ($d^+$), 2922 ($d^-$), 1734, 1650, 1543, 1122 $cm^{-1}$.

***(#6)* Benzylamine.** NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.90 (br, 31 H), 1.3 (br, 141 H), 2.2 (br, 4 H), 4.4 (br, 3 H), 7.3 (br, 5 H). IR: 2850 ($d^+$), 2920 ($d^-$), 1734, 1646, 1547 $cm^{-1}$.

**Coupling of Alcohols to C12:C11COOH (a:b) (#7−10).** In a typical reaction, ca. 100 mg of the acid MPC (C12:C11COOH (4:1)) was treated with 5 equiv (relative to the mol of MPC acid groups) of BOP (60 mg), HOBt (18 mg), NMM (14 $\mu$L), and DMAP (16 mg) in low water THF (concentration of 2 mg cluster/mL), and, following a brief activation period (10 min), 5 equiv of the alcohol were added to the reaction mixture and the solution was stirred at room temperature for 15 h. Solvent was removed under vacuum, and the reacted MPC was collected on a frit where unreacted materials were removed by washing with 500 mL of acetonitrile followed by sonication/decanting with 50 of mL acetonitrile (3×).

***(#7)* 2-Naphthalene-Ethanol.** NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.92 (br, 10 H), 1.3 (br, 69 H), 2.25 (br, 2 H), 3.4 (br, 1.1 H), 3.6 (br, 2 H), 5.9 (br, 0.10 H), 6.5 (br, 0.11 H), 7.15 (br, 0.05 H), 7.4 (br, 0.17 H), 7.8 (br, 0.18 H) IR: 2851 ($d^+$), 2922 ($d^-$), 1739, 1653, 1118, 1070 $cm^{-1}$.

***(#8)* Ferrocene-Methanol.** NMR (in $C_6D_6$): $\delta$ (ppm) = 1.0 (br, 27 H), 1.5 (br, 226 H), 3.9 (br, 5 H), 4.2 (br, 1.3 H), 4.8 (br, 0.9 H) IR: 2851 ($d^+$), 2922 ($d^-$), 1727, 1680, 1594, 1268, 1244IR: 2851 ($d^+$), 2922 ($d^-$), 1737, 1710, 1653, 1616 $cm^{-1}$.

***(#9)* α-D-Glucose.** The same synthesis and purification method was employed except that the solvent was 5:1 THF/DMF to aid glucose solubility. NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.9 (br, 3 H), 1.3 (br, 17 H), 2.9 (br, 0.34 H) IR: 2850 ($d^+$), 2920 ($d^-$), 1815, 1733, 1647, 1612, 840, 781, 769, 740 $cm^{-1}$.

***(#10)* Uridine.** The same synthesis and purification method was employed except that the solvent was 5:1 THF/DMF to aid uridine solubility. NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.9 (br, 3 H), 1.3 (br, 17 H), 2.9 (br, 0.85 H) IR: 2851 ($d^+$), 2921 ($d^-$), 1817, 1733, 1700, 1633, 1616, 1491, 1411, 843, 782, 764, 742 $cm^{-1}$.

**Coupling of Carboxylic Acids to C12:C11OH (a:b) (#11−12).** In a typical reaction, 5 equiv (relative to mol of MPC alcohol) of the acid was treated with 5 equiv of BOP (60 mg), HOBt (18 mg), NMM (14 $\mu$L), and DMAP (16 mg) in low water THF (concentration of 2 mg cluster/mL), and, following a brief activation period (10 min), ca. 100 mg of the alcohol (C12:C11OH (4:1)) was added and the solution was stirred at room temperature for 15 h. Solvent was removed under vacuum, and the reacted MPC was collected on a frit where unreacted materials were removed by washing with 500 mL of acetonitrile followed by sonication/decanting with 50 mL acetonitrile (3×).

***(#11)* 10H-(Phenothiazine-10)propionic Acid.** NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.9 (br, 17 H), 1.3 (br, 150 H), 2.75 (br, 0.2 H), 4.0 (br, 2 H), 4.1 (br, 2 H), 6.8 (br, 5.9 H), 7.1 (br, 5.9 H) IR: 2851 ($d^+$), 2921 ($d^-$), 1817, 1733, 1700, 1633, 1616, 1491, 1411, 843, 782, 764, 742 $cm^{-1}$. Electrochemistry of this MPC derivative is shown in Figure 3.

***(#12)* Anthraquinone-2-carboxylic Acid.** NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.88 (br, 17 H), 1.3 (br, 119 H), 1.8 (br, 14 H), 3.55 (br, 1.8 H), 4.3 (br, 2 H), 7.8 (br, 1.8), 8.3 br, 3.4 H), 8.8 (br, 0.93 H) IR: 2851 ($d^+$), 2922 ($d^-$), 1727, 1680, 1594, 1268, 1244 $cm^{-1}$.

**Synthesis of Tripeptide-Terminated MPC.** Coupling (steps I, III, V) and deprotection (steps II, IV, VI) reactions are described below.

***(Step I)* Coupling of BOC-Phenylalanine.** Five molar equiv of BOC-phenylalanine (168 mg) were activated (10 min) by treatment with 5 equiv of BOP (280 mg), HOBt (87 mg), NMM (128 $\mu$L), and DMAP (77 mg) in THF (concentration of 2 mg cluster/mL), 200 mg of 3:1 C12:C11OH was added, and the solution was stirred at room temperature for 15 h. Solvent was removed under vacuum, and the reacted MPC was collected on a frit where unreacted materials were removed by washing with 500 mL of acetonitrile followed by sonication/decanting with 50 mL of acetonitrile (3×). The above procedure was repeated on the same material to afford an 87% conversion to the BOC−Phe-terminated MPC. NMR (in $C_6D_6$): $\delta$ (ppm) = 0.88 (br, 12.8 H), 1.35 (br, 48 H), 3.05 (br, 1.75 H), 3.55 (br, 2.2 H), 4.1 (br, 1.7 H), 4.5 (br, 0.3 H), 7.2 (d, 5 H).

***(Step II)* Deprotection of BOC−Phe-Terminated MPC.** To a solution of 1.0 g of BOC−Phe-terminated MPC in 30 mL $CH_2Cl_2$ was added 7.5 mL of trifluoroacetic acid. The reaction was stirred at room temperature for 2 h after which the reaction mixture was diluted with 100 mL of distilled $H_2O$. The organic phase was separated, and the aqueous phase was further washed with 100 mL of $CH_2Cl_2$. The combined organic phases were washed with 2 × 100 mL of 10% $NaHCO_3$ and then removed in vacuo. The precipitate was then washed with copious quantities of acetonitrile and air-dried. NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.88 (br, 26 H), 1.35 (br, 192 H), 7.2 (d, 5 H).

***(Step III)* Coupling of BOC-Alanine.** BOC-alanine was coupled to the N-terminus of phenylalanine as in reactions #1−7 above (five molar excess of reagents). NMR (in $C_6D_6$): $\delta$ (ppm) = 0.85 (br, 13.6 H), 1.35 (br, 115 H), 3.05 (br, 2.6 H), 4.1 (br, 2.5 H), 4.7 (br, 0.6 H), 7.2 (d, 5 H).

***(Step IV)* Deprotection of BOC−Ala-Phe-Terminated MPC.** BOC-alanine was deprotected as in Step II above. NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.85 (br, 16.8 H), 1.35 (br, 156 H), 3.05 (br, 3.4 H), 4.1 (br, 1.9 H), 4.7 (br, 0.7 H), 7.2 (d, 5 H) 7.65 (br, 0.12 H).

***(Step V)* Coupling of BOC-Isoleucine.** BOC-isoleucine was coupled to the N-terminus of alanine as in reactions #1−7 above (five molar excess of reagents). NMR (in $C_6D_6$): $\delta$ (ppm) = 0.85 (br, 18 H), 1.35 (br, 147 H), 3.05 (br, 2.6 H), 4.1 (br, 2.4 H), 4.7 (br, 0.02 H), 7.2 (d, 5 H). IR: 3063, 3029, 2848 ($d^+$), 2917 ($d^-$), 1738, 1718, 1687, 1644, 1513, 1497, 1164 $cm^{-1}$.

***(Step VI)* Deprotection of BOC−Ile-Ala-Phe-Terminated MPC.** BOC-isoleucine was deprotected as in Step II above. NMR (in $CD_2Cl_2$): $\delta$ (ppm) = 0.85 (br, 16.8 H), 1.35 (br, 156 H), 3.05 (br, 3.4 H), 4.1 (br, 1.9 H), 4.7 (br, 0.7 H), 7.2 (d, 5 H) 7.65 (br, 0.12 H). The final product was analyzed by $I_2$-induced decomposition which indicated 87% conversion for the coupling of both Ile and Ala to give a 67% overall conversion in three steps to the tripeptide. NMR of $I_2$-induced decomposition product (in $CD_2Cl_2$): $\delta$ (ppm) = 0.88 (t, 13.3 H), 1.32 (br, 32.8 H), 1.45 (d, 6.64 H), 1.75 (q, 18 H), 2.68 (t, 23 H), 2.87 (t, 0.79 H), 3.1 (br, 2.4 H), 3.6 (t, 0.72 H), 4.06 (t, 4 H), 4.34 (br, 0.85 H), 4.73 (br, 1.2 H), 5.05 (br, 0.76 H), 6.6 (br, 1.5 H), 7.1−7.4 (q, 9.56 H).

**Steady-State Electron Paramagnetic Resonance Spectroscopy (SSEPR).** The solution spectrum (Figure 2) of the TEMPO-labeled cluster was acquired using a JEOL JES RE−1X EPR spectrometer. Spectra were collected by scanning for 2 min at a center field of 3370 G (sweep width of 80 G) using a field modulation of 1 G and spectrometer microwave frequency of 9.45 GHz. A $10^{-4}$ M ($10^{-3}$ M in spin label) solution of the TEMPO-labeled MPC in methyl-THF was employed for all measurements.

**Electrochemical Measurements.** (a) Cyclic voltammetry (Figure 3) was performed using a BAS 100B electrochemical analyzer. Electrode materials and preparation were as follows: (1) A platinum 3 mm diameter working electrode was polished with 0.5 $\mu$m diamond (Buehler) paste followed by rinsing with water, ethanol, and acetone prior to each experiment, and (2) a Pt coil counter electrode and saturated calomel reference electrode resided in the same cell compartment as the working electrode. Solutions (2:1 Tol/$CH_3CN$[6]) of the phenothiazine-MPC (0.8 mM in phenothiazine) and of phenothiazine monomer (1 mM) were degassed and then bathed throughout with solvent-saturated $N_2$. (b) Thin-layer coulometry (Figure 3) was performed using a BAS 100B electrochemical analyzer. Electrode materials and preparation were as follows: (1) a 4.3 mm diameter Pt working electrode was polished with 0.5 $\mu$m diamond (Buehler) paste followed by rinsing with water, ethanol, and acetone, and toluene prior to each experiment, and (2) a Pt wire counter electrode and Ag wire quasi-reference electrode (AgQRE) resided in a locally designed thin-layer cell.[16,17] A Mitutoyo digital micrometer (1−2", 0.00005"resolution) was fitted to the cell and used to define the thin-layer cell thickness, $L$. Charge-time measurements were performed for cell thicknesses of 2−30 $\mu$m, and $Q$ values of zero-time intercepts extrapolated from the longer time plateaus (20−32 s) of each charge-time plot. The product of the number of phenothiazines per cluster, $\theta$, and of electrons per phenothiazine, n, is obtained from the slope of a $Q$ versus $L$ plot ($Q/L = \theta n\mathrm{FAC} = 11.47 \times 10^{-3}$ $C$/cm, $C = 1.07 \times 10^{-7}$ mol/cm$^3$).

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