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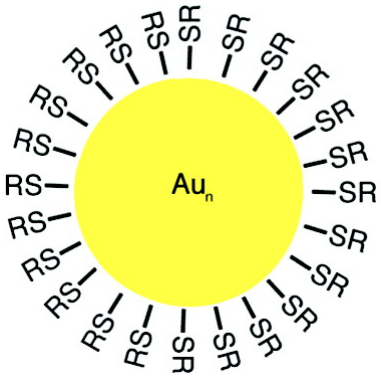

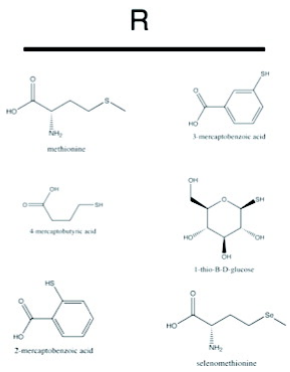

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Thiolate Ligands for Synthesis of Water-Soluble Gold Clusters

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Organothiolate monolayer-protected gold clusters (MPCs) have been a focus of intensive research since they were first described, just over 10 years ago. Of three common synthetic methods for generating water-soluble, thiolate-protected gold nanoparticles,[1] the one- and two-phase syntheses of Brust et al.[2] have attracted the most attention,[3,4] due to synthetic control over particle size, dispersity, and surface functionality, to size-dependent optical, catalytic, and capacitance properties, and to the extraordinary stability of the resultant thioalkane-protected products to air, long-term storage, solvents, temperature, and concentration extremes.

Other synthetic routes to water-soluble MPCs, notably, a two-phase method[5] for replacing the triphenylphosphine ligands on clusters, such as undecagold and "Au_{55}", have been reported. Insofar as these clusters have been analyzed, they have properties similar to those of clusters made by the method of Brust et al.

Early work employing the Brust MPC synthesis focused exclusively on MPCs soluble in nonaqueous solvents. This work showed that straight chain ligands at least as large as pentanethiol were needed to confer the remarkable stability of MPCs,[6] unique among aurous and nonaurous metal clusters. The stability was lower for clusters formed with C3 to C4 straight chain alkanethiolates and increased with increasing chain length.[3] Alkanethiolate-protected MPCs with chain lengths shorter than C3 have not been described.

The first reports of water-soluble Brust MPCs came four years after the initial synthesis.[7−9] Although the work has been extended,[10−14] no systematic attempt has been made to demonstrate minimal ligand requirements for water-soluble MPCs, as was done for alkanethiolate MPCs. Here, we report on the results of Brust synthesis with many commercially available, water-soluble thiolate ligands. For some thiols, a thioether, and also a non-thiol chalcogenide that did not yield stable MPCs in the Brust synthesis, we tested the capacity to stabilize preformed "Au_{55}" cores through thiolate-for-phosphine exchange and phase transfer. The Brust MPC synthesis produces a cluster core whose size, shape, and atomic packing properties are determined in large part by the thiolate[11] and the thiolate-to-gold ratio used.[6] Conversely, the generation of MPCs by thiolate replacement of triphenylphosphine begins with a preformed cluster core. This approach sometimes does[5] and

Table 1. Water-Soluble Thiolates and Their Ability to Passivate Gold Clusters

compound name	published synthesis	diameter (nm)[k]	soluble product	stability	synthetic method[a]	behavior in HD–PAGE gel
3-mercaptopropionic acid	ref 21	undetermined[j]	yes	days to weeks	Brust	did not enter matrix in HD or LD−PAGE[i]
4-mercaptobutyric acid	no	4.0 ± 1.2	yes	weeks	Brust	not tested
3-mercapto-1,2-propanediol	ref 14[b]	4.7 ± 1.2	yes	days	Brust	single diffuse band in HD−PAGE
cysteine	ref 12[c]	1.6 ± 0.3	yes	days	Brust[f]	entered gel matrix as single band; stalled; single band in LD−PAGE
methionine	no	2.4 ± 1.0	yes	weeks	Hutchison	did not enter matrix in HD or LD−PAGE
thiomalate	ref 13[d]	2.1 ± 1.4	yes	weeks	Brust	single tight band surrounded by large halo
2-mercaptobenzoic acid	no	2.1 ± 0.9	yes	minutes	Brust	did not enter matrix in HD or LD−PAGE
3-mercaptobenzoic acid	no	1.6 ± 0.6	yes	days	Brust	did not enter matrix; single band in LD−PAGE
4-mercaptobenzoic acid	ref 7[e]	1.8 ± 0.4	yes	months	Brust	2 tight bands
tiopronin	ref 9	1.9 ± 0.7	yes	months	Brust[f]	single diffuse pink band in HD or LD−PAGE
selenomethionine	no	1.6 ± 0.4	yes	days	Hutchison	did not enter matrix in HD or LD−PAGE
1-thio-β-D-glucose	no	2.1 ± 0.5	yes[g]	months	Brust[f]	single band in LD−PAGE
glutathione	ref 8	1.4 ± 0.4	yes	months	Brust	5 bands
ITCAE pentapeptide[h]	no	1.4 ± 0.4	yes	days	Hutchison	not tested

[a] Brust synthesis was in 1:1 water:methanol with a 3:1 thiolate:gold ratio. Typical concentrations were 10 mM gold and 30 mM thiolate. A 5-fold molar excess of $NaBH_4$ in a volume of water ~10% of the reaction volume was added to complete the cluster formation. Reactions denoted Hutchison were performed as described (ref 5). [b] A 1:1 ratio of thiolate:Au(III) and a 9-fold BH_4^- excess. [c] Cystine was used as the starting material to create cysteine MPCs. [d] Highest organothiolate:Au(III) ratio used was 5:2, with equimolar $NaBH_4$ to $HAuCl_4$, likely resulting in incomplete reduction. [e] A 1.8:1 thiolate:Au(III) ratio was used. [f] These compounds failed to form soluble products in 1:1 water:methanol, but did so under similar conditions in 6:1 methanol:acetic acid. [g] This compound formed product that remained in suspension following low-speed centrifugation, indicating cluster formation, but failed to redissolve after methanol precipitation; this product was not repeatably precipitable in methanol, but could be purified from starting materials by gel filtration and, otherwise, behaved as a stable water-soluble MPC. [h] The pentapeptide had the sequence Ile-Thr-Cys-Ala-Glu. [i] LD−PAGE was a standard 12% SDS−PAGE gel. [j] Particles form aggregates within which individual particle diameters cannot be measured. [k] See Supporting Information for images, histograms, and further analysis.

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sometimes does not[15] preserve the cluster core, which, in any case, never reaches the narrow dispersity that can be achieved following purification of products of a Brust MPC synthesis.[11] The phase transfer approach allows more promiscuous use of thiolate side chains than does the Brust MPC synthesis, while generating thiolate-protected gold particles that are typically more stable than the precursors.

The Brust synthesis proceeds in two steps:[11,16]

$$\mathrm{Au(III)} + 3\ \mathrm{RSH} \rightarrow (-\mathrm{Au(I)/SR}-)_n(\mathrm{polymer}) + \mathrm{RSSR}$$

$$(-\mathrm{Au(I)/SR}-)_n + \mathrm{BH_4^-} \rightarrow \mathrm{Au}_x(\mathrm{SR})_y$$

The particle size of the product (value of x) depends on the thiolate-to-Au(III) ratio in the first step.[6] Decreasing the thiolate load results in a larger value of x, but also in a more polydisperse product.[16] Increasing the amount of borohydride reductant favors the formation of larger core sizes without great loss of the narrow dispersity characteristic of the Brust synthesis.[11] The synthesis usually yields a set of discrete products, each corresponding to a closed shell cluster.[17] The distribution of products obtained, as well as many of the properties of an MPC, including the chemical and thermal stability, solubility, capacitance, and reactivity toward place exchange,[18] depends on the nature of the thiolate used.

We performed Brust MPC synthesis with various water-soluble thiolates, using a 3:1 ratio of thiolate:gold throughout, and a 5-fold excess of $NaBH_4$ as reductant. Syntheses were done in a 1:1 water: methanol system, except where noted. Hutchison phase transfer syntheses were performed with 1.0 mg of "Au_{55}" dissolved in 5 mL of methylene chloride and a 10-fold or greater molar excess of replacement ligand over total ligand in the "Au_{55}" preparation. We used Schmid's original formula of $Au_{55}PPh_{12}Cl_6$, rather than the formulas arrived at by other analyses,[5,19] for calculation of the number of ligands in an Au_{55} preparation. Cluster formation was verified by UV−vis spectroscopy and high-resolution transmission electron microscopy (HR-TEM). Most clusters showed a featureless spectrum, rising smoothly from the visible into the UV, characteristic of sub-2 nm gold clusters.[6] For HR-TEM analysis, samples were dried onto Formvar- or carbon-coated EM grids, which had been glow-discharged in either water or amylamine. Particle images and sizes may be found in the Supporting Information. Many gold cluster preparations were amenable to purification by high-density polyacrylamide gel electrophoresis,[11] and the number and quality of bands in the gel were noted. Examples may be found in the Supporting Information.

It can be assumed that virtually any ligand that succeeds in the Brust synthesis will also do so in phase transfer synthesis. We tested 22 water-soluble organothiols which failed to yield stable water-soluble products in the Brust single phase synthesis.[20]

From the results for 36 ligands, we could draw the following conclusions: (1) Small positively charged ligands do not support the production of MPCs in the Brust synthesis. (2) The smallest negatively charged thiolate yielding a Brust MPC was mercapto-propionic acid. Larger acidic organic thiolates were also effective passivants. (3) The smallest uncharged organothiolate yielding a Brust MPC was 3-mercapto-1,2-propanediol, which formed clusters that remained in solution for days, but which did not exhibit long term stability. Thioglucose, also neutral, produced clusters with longer stability. Short polyglycol ligands recently reported,[10] but not commercially available, may yield more stable MPCs with neutral monolayers. (4) Larger organothiolates were generally better stabilizers. (5) Penicillamine did not form soluble clusters, which was surprising in view of the success of cysteine. (6) Thus, the ligand size/cluster stability trend previously reported for alkanethiolate MPCs also applies to water-soluble MPCs, but with notable exceptions.

In summary, we have screened 36 water-soluble organothiolates for their ability to form water-soluble MPCs. We report 13 such MPCs, 6 of which are novel, and 4 of which have been reported with nonstandard stoichiometries of ligand or borohydride in previous syntheses. While all clusters reported here were repeatably precipitable with methanol, most did not exhibit the extraordinary stability of alkanethiolate MPCs; a few exceptional ligands formed clusters that remained in solution indefinitely. We suggest that our survey of water-soluble MPCs affords a toolkit for future applications of such compounds. Further work is needed to characterize the gel-purified clusters with respect to core size, place exchange, capacitance, and other properties known to vary with monolayer composition.

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Supporting Information Available: Additional figures. This material is available free of charge via the Internet at http://pubs.acs.org.

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