Pergamon

Tetrahedron 57 (2001) 1489–1495

TETRAHEDRON

The triphenylmethyl group as thiol protection during ruthenium-promoted synthesis of tetraalkyl-*p*-phenylenediamine systems having alkanethiol side chains

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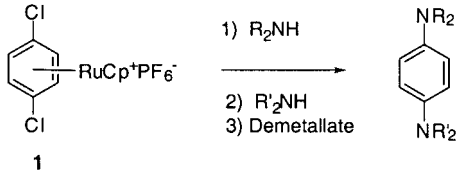
Received 3 November 2000; accepted 6 December 2000

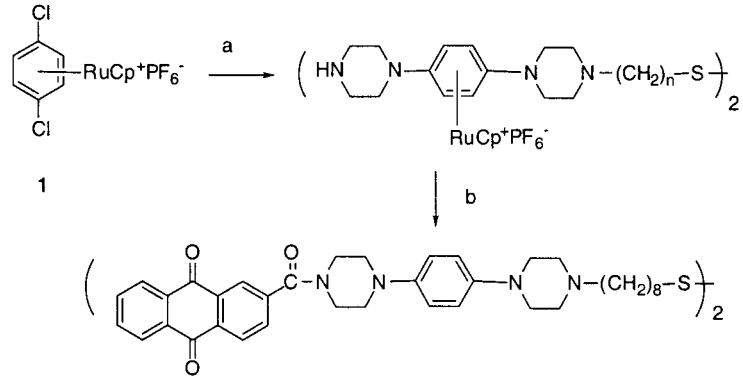
Abstract—The use of triphenylmethyl as thiol protecting group during the construction of thioalkyl-substituted tetraalkyl-*p*-phenylenediamine derivatives, via arene–ruthenium chemistry, is reported.

N,*N*,*N*′,*N*′-Tetramethyl-*p*-phenylenediamine (TMPD), is a powerful organic donor molecule, first described in 1879 by Wurster,[1] the redox properties of which have received considerable attention.[2] The first and only self-assembled monolayers (SAMs) of TMPD derivatives, having a single *N*-thioalkyl side chain, have been shown to be more easily oxidized, by electrochemical methods, than TMPD itself.[3] Because of difficulties in their preparation using standard methodology, very few functionalized tetraalkyl-*p*-phenylenediamine (TAPD) derivatives are readily available.[4] Over the past several years we have developed an approach to the synthesis of a wide range of these molecules, using transition-metal promoted S_NAr reactions of chloroarenes,[5] and we have reported on their redox properties,[6] as well as the photoinduced electron transfer characteristics of Donor–σ–Acceptor (D–σ–A) systems that use the TAPD as the donor unit.[7] The general reaction is outlined in Eq. (1). The use of a transition metal moiety for this process has several advantages, among which is protection of the readily oxidizable TAPD system during numerous synthetic operations.



(1)

Recently, we reported[8] an approach to the construction of D–σ–A molecules that have thioalkyl side chains, via sequential S_NAr reactions on [(1,4-dichlorobenzene)-RuCp]$^+$[PF_6]$^-$ (**1**), summarized in Scheme 1. Such compounds, and related systems, might be useful as, e.g. unimolecular rectifiers,[9] currently under investigation in



Scheme 1.

Keywords: *N*,*N*,*N*′,*N*′-tetramethyl-*p*-phenylenediamine; self-assembled monolayers; arene–ruthenium.
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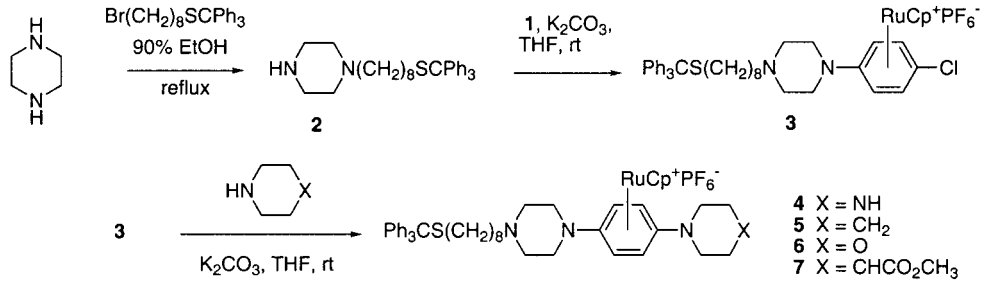
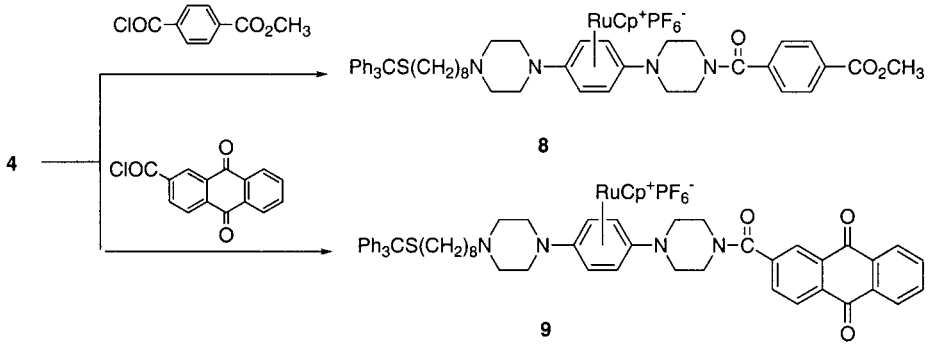
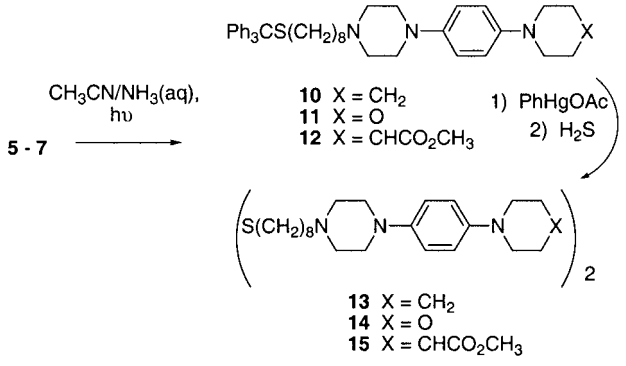


Scheme 2.



Scheme 3.

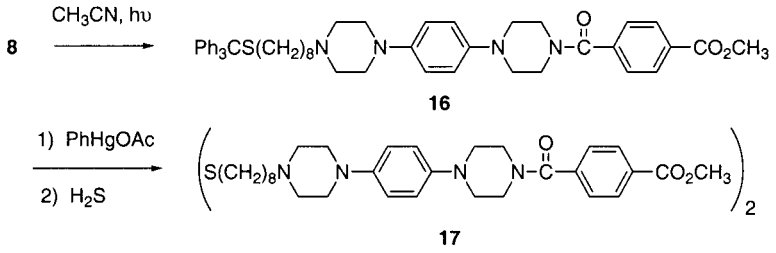
our laboratories, since they can be used to construct monolayers on, e.g. nanostructured gold[10] or platinum[11] surfaces. The approach we described earlier, in which bis(piperazinoalkyl)disulfides are used as the latent thiol groups, suffers the disadvantage of requiring very long reaction times (>17 d) for high-yielding bis(arylation) of the long-chain diamine, the reasons for which are presently unknown. In order to access the ultimate product D–σ–A compounds more conveniently, we have investigated an approach that uses alternative thiol protection during the S_NAr reactions. We describe herein the use of the triphenylmethyl group, which we have found to be well-suited for this purpose, with the advantage that its removal can be effected in the presence of the arene–RuCp system, thereby maintaining protection of the sensitive TAPD molecule until it is released by controlled demetallation.



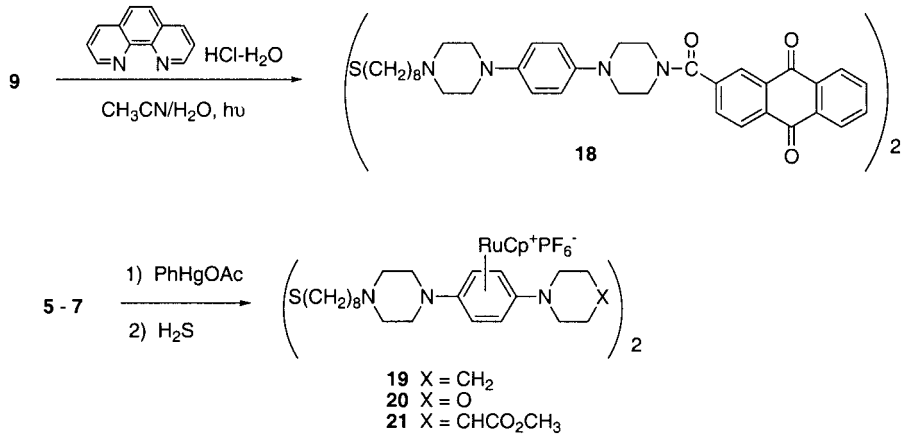
Scheme 4.

For these studies we have used, as the first nucleophile, 1-(8-triphenylmethylthiooctyl)piperazine (**2**), obtained in 98% yield by reacting the known 1-bromo-8-triphenylmethylthiooctane[12] with excess piperazine in EtOH at reflux. Reaction of **2** with **1** proceeded smoothly at room temperature, and required only 90 h for completion (in contrast to >400 h for the aforementioned disulfide derivative). The product **3** was obtained in 91% yield. Complex **3** was reacted with several cyclic amine nucleophiles to afford the TAPD complexes **4**–**7** (Scheme 2). In addition, the piperazine derivative **4** was readily converted to the *N*-acyl (acyl=acceptor) systems **8** and **9** (Scheme 3); the triphenylmethyl thioether was stable during all of these transformations, as expected.

Deprotection of the thiol might be accomplished either on



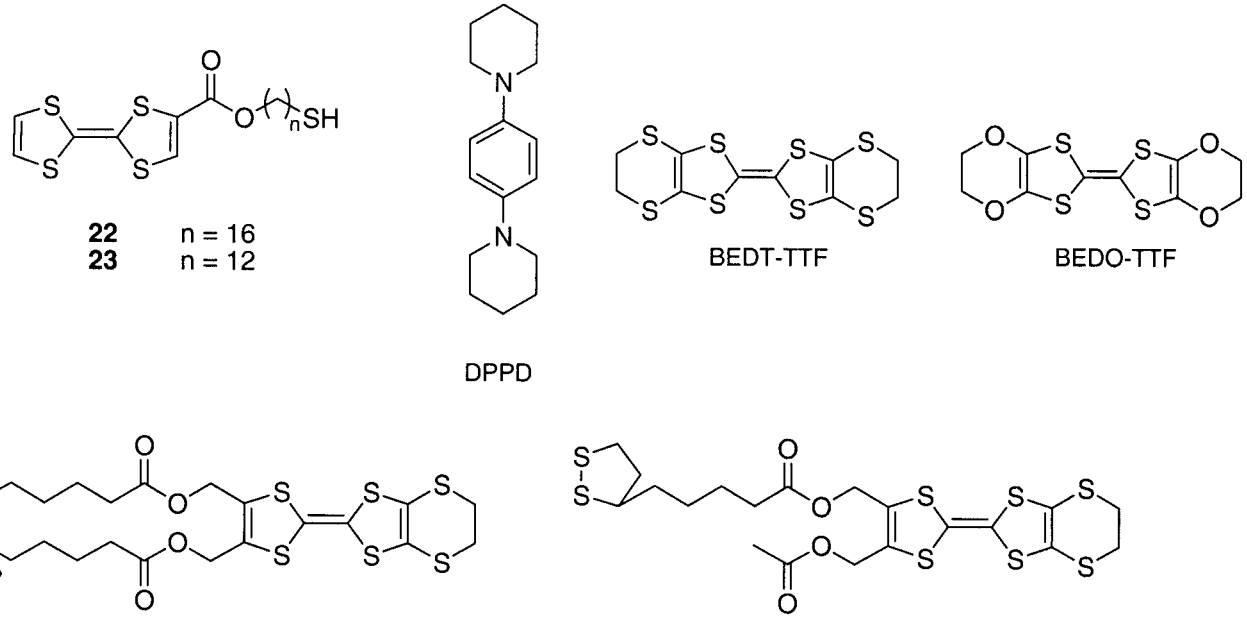
Scheme 5.



Scheme 6.

the complexes or on the TAPD derivatives that result from demetallation. Initially, the decomplexation of complexes **5**–**7** was performed prior to trityl removal, by exposure of the complexes to UV light (Rayonet reactor) in aqueous ammonia–acetonitrile. This was accompanied in some cases by concomitant partial or complete loss of the trityl group; further treatment of the crude products with PhHgOAc, then H_2S in CH_2Cl_2–CH_3OH,[13] completed the

Table 1. Redox potential of derivatized *p*-phenylenediamines and TTFs



	$E_{1,1/2}$[a] (mV)		
p-phenylenediamine		TTF	
TMPD	174	TTF	401
DPPD	230		380[b]
			420[c]
13	289	BEDO-TTF	400[b]
14	389	BEDT-TTF	485[b]
15	342	**22**	590[c]
17	418	**23**	540[c]
18	423	**24**	650[d]
		25	730[d]

[a] Experimental conditions: 1 mM substrate, 0.1 M Bu_4NPF_6 vs Ag/AgCl in CH_2Cl_2.
[b] Ref. 14(a), vs Ag/AgCl in CH_2Cl_2, first oxidation potential.
[c] Ref. 14(b), vs Ag/AgCl in benzonitrile.
[d] Ref. 14(a,c), vs Ag/AgCl in THF, SAM.

deprotection to afford the disulfides shown (formed as a result of oxidation of the thiols during isolation and purification). Thus, decomplexation of **5** and **6** afforded directly the disulfides **13** and **14**, respectively, with no isolation of **10** or **11**, while **7** gave a mixture of **12** and **15**, and **8** gave **16**, the latter without loss of the trityl group (Schemes 4 and 5).

Conversion of the **12/15** mixture to **15**, and of **16** to **17** was straightforward. It may be noted that disulfides can be used directly for the construction of surface-attached monolayers, so this is quite acceptable. We found that it is also possible to detatch the triphenylmethyl group *before* demetallation, and in several cases this allows easier removal of (ether-soluble) triphenylmethyl byproducts, as the ruthenium complexes are generally insoluble in diethyl ether. The arene–ruthenium system is sufficiently stable to survive the deprotection conditions (PhHgOAc then H_2S in CH_2Cl_2–CH_3OH), and the product complexes are again obtained as disulfides. Examples are shown here for the conversion of **5**–**7** to **19**–**21**. Subsequent decomplexation reactions were effected by the usual photochemical procedure in the presence of aqueous ammonia to free the residual Ru(II) products from the piperazine diamine in the product molecule, as detailed in Section 1[6,8] (Scheme 6).

We have carried out some preliminary cyclic voltammetry studies on these compounds, and the results are summarized in Table 1. The noteworthy feature of these data is that functionalization of the TAPD system does not lead to changes in redox potential of a magnitude that would prevent utilization of the compounds as powerful electron donors. This is in contrast to TTF systems, which generally are less easily functionalized with retention of useful donor capability, some examples of which are included in the table for comparison.[14] Thus, we anticipate that the arene–ruthenium chemistry described herein will allow access to a range of interesting molecules that have useful donor–acceptor properties.

1. Experimental

1.1. General procedures

All reactions were performed under an inert atmosphere (using dry, oxygen-free argon). All solvents used in the reactions were freshly distilled under nitrogen as follows: tetrahydrofuran from sodium/benzophenone, and methylene chloride and acetonitrile from CaH_2. Column chromatography was performed on aluminium oxide (Aldrich neutral or basic alumina (Brockman I)) or flash grade silica gel and the eluting solvents are reported as V/V percent mixtures. Thin layer chromatography was performed on E. Merck silica gel 60 F_{254} 0.25 mm or Aluminium oxide 60 F_{254} 0.25 mm plates and visualized with UV light. NMR (^1H or ^{13}C) spectra were recorded on a Varian Gemini-300 (300 MHz) spectrometer using $CDCl_3$ or acetone-d_6 as solvent. Infrared spectra were recorded for solutions in methylene chloride or chloroform using a NaCl cell on a Nicolet Impact 400 FTIR spectrophotometer. Accurate masses (HRMS) are reported for the ^{102}Ru isotope. All new compounds were judged to be at least 95% pure according to their ^1H NMR spectra. Cyclopentadienyl-(1,4-dichlorobenzene)ruthenium hexafluoro-phosphate[8] and 8-(triphenylmethylthio)-1-bromooctane[12] were prepared by literature procedures. Demetallation was performed in a Rayonet apparatus (350 mm). Mercury residues from deprotection reactions are generally set aside for collection and disposal by insitutional safety services personnel.

Cyclic voltammetry was carried out using a CH Instruments electrochemical analyzer. The supporting electrolyte (0.1 M nBu$_4$NPF$_6$) was prepared using CH_2Cl_2 (HPLC grade) and degassed for 30 min before use. nBu$_4$NPF$_6$ (electrochemical grade) was purchased from Fluka Co. and used as received. A glassy carbon (GC, ϕ 3 mm) was used as a working electrode, the counter electrode was a platinum wire, and a Ag/AgCl electrode was used as the reference electrode. Both the counter and the reference electrodes were directly immersed in the electrolyte solution. The scan rate was 50 mV/sec. The potential of the regular ferrocene/ferricinium couple was 470 mV under our experimental conditions.

1.1.1. 1-(8-Triphenylmethylthiooctyl)-piperazine (2). A mixture of piperazine (1.4 g, 16.2 mmol, 5 equiv.), 8-(triphenylmethylthio)-1-bromooctane (1.512 g, 3.23 mmol) in 55 mL 90% ethanol was refluxed overnight. After removing the ethanol under reduced pressure, the residue was made strongly alkaline with 1 M NaOH, extracted with ether four times and dried over Na_2SO_4 to give product as an oil (1.5 g, 98%). ^1H NMR (300 MHz, $CDCl_3$) δ 7.18–7.43 (15H), 2.94 (t, J=4.7 Hz, 2H), 2.45 (br s, 4H), 2.30 (t, J=7.7 Hz, 2H), 2.14 (t, J=7.1 Hz, 2H), 1.21–1.50 (15H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.0, 129.5, 127.7, 126,4, 66.3, 59.2, 53.8, 45.6, 31.9, 29.2, 29.0, 28.9, 28.5, 27.4, 26.5; HRMS Calcd for MH^+ ($C_{31}H_{41}N_2S$) 473.2990. Found: 473.2990.

1.1.2. (η^5-Cyclopentadienyl)(η^6-(1-chloro-4-(4-(8-triphenylmethylthiooctyl)-piperazino)-benzene]ruthenium hexafluorophosphate (3). Cyclopentadienyl(1,4-dichlorobenzene)ruthenium hexafluorophosphate (**1**, 0.615 g, 1.34 mmol) was stirred with K_2CO_3 (195 mg, 1.41 mmol, 1.05 equiv) and compound **2** (1.27 g, 2.68 mmol, 2 equiv) in 27 mL THF at rt for 90 h. After removing THF under reduced pressure, ether was added. The mixture was stirred for several hours, ether was decanted and fresh ether was added. The procedure was repeated until all unreacted 1-(8-triphenylmethyl-thiooctyl)-piperazine was removed. Then the precipitate was collected, dissolved in acetone, filtered, and the solvent was removed in vacuo to give the product as an amorphous powder (1.094 g, 91%). ^1H NMR (300 MHz, d^6-Acetone) δ 7.26–7.45 (15H), 6.55 (d, J=6.6 Hz, 2H), 6.17 (d, J=6.6 Hz, 2H), 5.57 (s, 5H), 3.22 (t, J=5.0 Hz, 4H), 2.57 (t, J=5.0 Hz, 4H), 2.37 (t, J=7.2 Hz, 2H), 2.19 (t, J=7.2 Hz, 2H), 1.24–1.50 (12H); ^{13}C NMR (75 MHz, d^6-Acetone) δ 146.0, 130.3, 128.6, 127.4, 126.4, 101.7, 85.9, 81.2, 69.3, 67.1, 58.8, 52.7, 47.9, 32.1, 29.3, 29.0, 28.9, 28.5, 27.4, 26.5; FAB HRMS Calcd for M–PF_6^-($C_{42}H_{48}N_2ClSRu$, ^{102}Ru) 749.2770. Found: 749.2259.

1.1.3. (η^5-Cyclopentadienyl)(η^6-1-(piperazino)-4-(4-(8-triphenylmethylthiooctyl)-piperazino)benzene]ruthenium hexafluorophosphate (4). Complex **3** (800 mg, 0.89 mmol) was stirred with piperazine (308 mg, 3.58 mmol, 4 equiv)

and K_2CO_3 (247 mg, 1.78 mmol, 2 equiv) in THF (18 mL) for 22 h at rt. After removing THF under reduced pressure, ether was added. The mixture was stirred for several hours, the ether was decanted and fresh ether was added. The procedure was repeated until all unreacted piperazine was removed. Then the precipitate was collected, dissolved in acetone, filtered, and the solvent was removed in vacuo to give the product as an amorphous powder (715 mg, 85%). ^{1}H NMR (300 MHz, d^6-Acetone) δ 7.23–7.42 (15H), 5.80 (s, 4H), 5.42 (s, 5H), 3.03 (t, J=4.7 Hz, 4H), 2.95 (br, 8H), 2.53 (t, J=4.7 Hz, 4H), 2.32 (t, J=7.2 Hz, 2H), 2.15 (t, J=7.2 Hz, 2H), 1.19–1.50 (12H); ^{13}C NMR (75 MHz, d^6-Acetone) δ 146.2, 130.5, 128.9, 127.6, 123.8, 123.1, 77.6, 68.4, 68.2, 67.3, 59.1, 53.1, 49.4, 48.6, 46.1, 32.7,31.9, 29.2, 29.0, 28.9, 28.2, 27.6; FAB HRMS Calcd for M–PF_6^-($C_{46}H_{57}N_4SRu$, ^{102}Ru) 799.3347. Found: 799.3363.

1.1.4. (η^5-Cyclopentadienyl)(η^6-1-(piperidino)-4-(4-(8-triphenylmethylthiooctyl)-piperazino)benzene]ruthenium hexafluorophosphate (5). Complex **3** (269 mg, 0.3 mmol) was stirred with piperidine (297 μL, 3 mmol, 10 equiv) and K_2CO_3 (83 mg, 0.6 mmol, 2 equiv) in THF (5 mL) for 48 h at rt. The solvent was removed and the residue was pumped in vacuo for overnight. Then ether was added, the precipitate was collected and washed with ether several times. The residue was dissolved in acetone and filtered, and the filtrate was evaporated in vacuo to give the product as an amorphous powder (259 mg, 91%). ^{1}H NMR (300 MHz, d^6-Acetone) δ 7.27–7.47 (15H), 5.89 (s, 4H), 5.48 (s, 5H), 3.16 (t, J=4.9 Hz, 4H), 3.09 (t, J=4.9 Hz, 4H), 2.58 (t, J=4.9 Hz, 4H), 2.37 (t, J=7.2 Hz, 2H), 2.19 (t, J=7.2 Hz, 2H), 1.26–1.74 (18H); ^{13}C NMR (75 MHz, d^6-Acetone) δ 146.0, 130.4, 128.7, 127.5, 124.0, 122.7, 77.5, 68.3, 67.8, 67.2, 58.9, 53.0, 49.0, 48.4, 32.5, 29.9, 29.7, 29.6, 29.2, 28.0, 27.5, 25.4, 24.0; FAB HRMS Calcd for M–PF_6^-($C_{47}H_{58}N_3SRu$, ^{102}Ru) 798.3395. Found: 798.3390.

1.1.5. (η^5-Cyclopentadienyl)(η^6-1-(morpholino)-4-(4-(8-triphenylmethylthiooctyl)-piperazino)benzene]ruthenium hexafluorophosphate (6). The procedure is the same as for compound **5**. Complex **3** (235 mg, 0.263 mmol) was treated with morpholine (230 μL, 2.6 mmol, 10 equiv) and K_2CO_3 (73 mg, 0.528 mmol, 2 equiv) in THF (5 mL) for 68 h at rt to give the product as an amorphous powder (220 mg, 88%). ^{1}H NMR (300 MHz, d^6-Acetone) δ 7.27–7.47 (15H), 5.86 (s, 4H), 5.49 (s, 5H), 3.84 (t, J=4.9 Hz, 4H), 3.02–3.08 (m, 8H), 2.58 (t, J=4.9 Hz, 4H), 2.37 (t, J=7.2 Hz, 2H), 2.19 (t, J=7.2 Hz, 2H), 1.26–1.74 (12H); ^{13}C NMR (75 MHz, d^6-Acetone) δ 146.0, 130.4, 128.7, 127.5, 123.3, 122.8, 77.6, 68.5, 68.2, 67.2, 66.4, 58.9, 53.0, 48.4 (2C), 32.5, 29.9, 29.7, 29.5, 29.2, 28.0, 27.5; FAB HRMS Calcd for M–PF_6^-($C_{46}H_{56}N_3OSRu$, ^{102}Ru) 800.3200. Found: 800.3196.

1.1.6. (η^5-Cyclopentadienyl)(η^6-1-(4-methoxycarbonyl-piperidino)-4-(4-(8-triphenylmethylthiooctyl)piperazino)-benzene]ruthenium hexafluorophosphate (7). A solution of complex **3** (380 mg, 0.425 mmol), (4-methoxycarbonyl)-piperidine hydrochloride (305 mg, 1.70 mmol, 4 equiv), with NaOH (68 mg, 1.70 mmol, 4 equiv) and K_2CO_3 (235 mg, 1.70 mmol, 4 equiv) in 7 mL THF was purged with Ar for 30 min. The mixture was sealed in a pressure tube and heated to 65–70°C for 60 h. After removing the THF under reduced pressure, CH_2Cl_2 was added. The organic phase was washed with 1 M NaOH, H_2O, and brine and dried over Na_2SO_4 to give **7** as a powder (360 mg, 85%) ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.17–7.42 (15H), 5.65 (d, J=7 Hz, 2H), 5.61 (d, J=7 Hz, 2H), 5.24 (s, 5H), 3.70 (s, 3H), 3.52 (br m, 2H), 2.93 (br s, 4H), 2.63 (br, 1H), 2.55 (br s, 6H), 2.33 (t, J=7.2 Hz, 2H), 2.13 (t, J=7.2 Hz, 2H), 1.80–2.02 (4H), 1.21–1.43 (12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6, 145.1, 129.6, 127.8, 126.6, 122.6, 121.8, 77.3, 67.4, 67.1, 66.4, 58.5, 52.1, 52.0, 47.7, 47.0, 39.8, 32.0, 29.3, 29.2, 29.0, 28.6, 27.4, 26.8, 26.5; IR (CH_2Cl_2) 1740 cm^{-1}; FAB HRMS Calcd for M–PF_6^-($C_{49}H_{60}N_3O_2SRu$, ^{102}Ru) 856.3450. Found: 856.3456.

1.1.7. (η^5-Cyclopentadienyl)(η^6-1-(4-(4-methoxycarbonyl-benzoyl)piperazino)-4-(4-(8-triphenylmethylthiooctyl)-piperazino)benzene]ruthenium hexafluorophosphate (8). The acid chloride from *mono* methyl terephthalate (245 mg, 1.36 mmol, 3 equiv) and K_2CO_3 (188 mg, 1.36 mmol, 3 equiv) were stirred in 10 mL CH_2Cl_2. Complex **4** (418 mg, 0.44 mmol) in 15 mL CH_2Cl_2 was added and the mixture was stirred at rt for 18 h. Then 1 M NaOH solution and CH_2Cl_2 were added and the mixture was stirred for another 12 h. The organic phase was separated and washed with 1 M NaOH, H_2O, brine, and dried over Na_2SO_4 and evaporated to give complex **8** as a powder (465 mg, 92%).^{1}H NMR (300 MHz, $CDCl_3$) δ 8.08 (d, J=8.2 Hz, 2H), 7.51 (d, J=8.2 Hz, 2H), 7.17–7.42 (15H), 5.70 (d, J=6.7 Hz, 2H), 5.60 (d, J=6.7 Hz, 2H), 5.27 (s, 5H), 3.91 (s, 3H), 3.50–3.90 (br, 4H), 3.00 (br s, 4H), 2.93 (br s, 4H), 2.54 (br s, 4H), 2.32 (t, J=7.2 Hz, 2H), 2.13 (t, J=7.2 Hz, 2H), 1.21–1.41 (12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 169.4, 166.3, 145.1, 139.1, 131.6, 130.0, 129.6, 127.8, 127.4, 126.6, 122.3, 121.4, 77.3, 68.5, 67.3, 66.4, 58.5, 52.4, 52.0 (2C), 47.6 (2C), 32.0, 29.3, 29.2, 29.0, 28.6, 27.4, 26.8; IR (CH_2Cl_2) 1723, 1647 cm^{-1}; FAB HRMS Calcd for M–PF_6^- ($C_{55}H_{63}N_4O_3SRu$, ^{102}Ru) 961.3665. Found: 961.3661.

1.1.8. (η^5-Cyclopentadienyl)(η^6-1-(4-(anthraquinone-2-carboxy)piperazino)-4-(4-(8-triphenylmethylthiooctyl)-piperazino)benzene]ruthenium hexafluorophosphate (9). The procedure is the same as for compound **8**. Complex **4** (385 mg, 0.406 mmol), the acid chloride from anthraquinone 2-carboxylic acid (308 mg, 1.22 mmol, 3 equiv) and K_2CO_3 (168 mg, 1.22 mmol, 3 equiv) gave **9** as a powder (393 mg, 82%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.22–8.33 (4H); 7.77–7.89 (3H); 7.17–7.42 (15H); 5.67 (d, J=6.6 Hz, 2H), 5.55 (d, J=6.6 Hz, 2H), 5.26 (s, 5H), 3.80–3.95 (br, 2H), 3.5–3.7 (br, 2H), 3.03 (br, 4H), 2.90 (br s, 4H), 2.53 (br s, 4H), 2.32 (t, J=7.2 Hz, 2H), 2.13 (t, J=7.2 Hz, 2H), 1.20–1.43 (12H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 182.2 (2C), 168.4, 145.1, 140.4, 134.5 (2C), 134.1, 133.6, 133.3 (2C), 132.8, 129.6, 127.8, 127.4 (2C), 126.6, 126.0, 122.2, 121.3, 77.4, 68.4, 67.2, 66.4, 58.5, 52.0 (2C), 47.6 (2C), 32.0, 29.3, 29.2, 29.0, 28.6, 27.4, 26.8; IR (CH_2Cl_2) 1679, 1642 cm^{-1}; FAB HRMS Calcd for M–PF_6^- ($C_{61}H_{63}N_4O_3SRu$, ^{102}Ru) 1033.3664. Found: 1033.3654.

1.1.9. (1-(4-(4-Methoxycarbonylbenzoyl)piperazino))(4-

(4-(8-triphenylmethylthiooctyl)piperazino))benzene (16). A solution of complex **8** (56 mg, 0.05 mmol) in CH_3CN/TMEDA (12 mL/3 mL) was degassed for 30 min and irradiated under UV light for 47 h. Basic alumina (Brockman I) was added to the solution. After removing the solvent, the alumina residue was dried in vacuo. This was placed atop a short basic alumina column and the product was eluted with chloroform. Further purification by TLC (Merck Al_2O_3 plate) with $CHCl_3$ afforded analytically pure product as a film (21 mg, 53%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 8.10 (d, J=8.2 Hz, 2H), 7.50 (d, J=8.2 Hz, 2H), 7.18–7.44 (15H), 6.90 (s, 4H), 3.95 (s, 3H), 3.94 (br, 2H), 3.60 (br, 2H), 3.16 (br, 6H), 3.01 (br, 2H), 2.64 (br, 4H), 2.40 (t, J=7.2 Hz, 2H), 2.15 (t, J=7.2 Hz, 2H), 1.22–1.60 (12H); IR (CH_2Cl_2) 1740, 1651 cm^{-1}; FAB HRMS Calcd for M ($C_{50}H_{58}N_4O_3S$) 794.4293. Found: 794.4228.

1.1.10. Bis[8-[4-[4-(anthraquinone-2-carbonyl)piperazino)-phenyl)]piperazino]octyl]disulfide (18). To a CH_3CN–H_2O (19:1) solution of the 1,10-phenanthroline–HCl–H_2O (34 mg, 0.14 mmol, 2 equiv) was added Ru complex **9** (85 mg, 0.07 mmol). The mixture was degassed for 30 min and irradiated under UV light for 16 h. Basic alumina (Brockman I) was added to the intense red solution. After removing the solvent, the alumina residue was dried in vacuo. This was placed atop a short basic alumina column and the product was eluted with $CHCl_3$. Any remaining phenanthroline was then removed by washing the chloroform solution with 0.05 M HCl solution and water, then the organic phase was dried over Na_2SO_4. Further purification by TLC (Merck Al_2O_3 plate) with $CHCl_3$ afforded **18** (16 mg, 35%), identical to the same compound previously reported by us.[8]

1.1.11. Bis[8-[4-[4-(piperidino)phenyl)]piperazino]octyl] disulfide (13). The procedure is the same as for compound **16**. A solution of complex **5** (82 mg, 0.087 mmol) in CH_3CN/NH_3(aq) (17 mL/3 mL) was degassed for 30 min and irradiated under UV light for 48 h to give the product as a film (crude weight 14 mg, crude yield 41%). Further purification by TLC (Merck Al_2O_3 plate) with $CHCl_3$ afforded an analytical sample. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.89 (s, 8H), 3.13 (br s, 8H), 3.03 (t, J=5.2 Hz, 8H), 2.68 (t, J=7.3 Hz, 4H), 2.63 (br, 8H), 2.40 (t, J=7.3 Hz, 4H), 1.20–1.80 (m, 36H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 146.6, 145.0, 118.2, 117.7, 58.8, 53.4, 51.9, 50.2, 39.2, 29.5, 29.2 (2C), 28.5, 27.6, 26.8, 26.1, 24.3; FAB HRMS Calcd for M^+ ($C_{46}H_{76}N_6S_2$) 776.5573. Found: 776.5574.

1.1.12. Bis[8-[4-[4-(morpholino)phenyl)]piperazino]octyl] disulfide (14). The procedure is the same as for compound **16**. A solution of complex **6** (145 mg, 0.153 mmol) in CH_3CN/NH_3(aq) (17 mL/3 mL) was degassed for 30 min and irradiated under UV light for 48 h, to give the product as a film (40 mg, crude yield 67%). Further purification by TLC (Merck Al_2O_3 plate) with $CHCl_3$ afforded pure **14**. ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.91 (d, J=9.3 Hz, 4H), 6.87 (d, J=9.3 Hz, 4H), 3.85 (t, J=4.7 Hz, 8H), 3.14 (br, 8H), 3.07 (t, J=4.7 Hz, 8H), 2.68 (t, J=7.2 Hz, 4H), 2.63 (br, 8H), 2.41 (t, J=7.2 Hz, 4H), 1.33–1.68 (24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 145.6, 145.3, 117.8, 117.3, 67.1, 58.8, 53.4, 50.5, 50.2, 39.2, 29.4, 29.2, 28.5, 27.6, 26.8; FAB HRMS Calcd for M^+ ($C_{44}H_{72}N_6O_2S_2$) 780.5158. Found: 780.5143.

1.1.13. Bis[8-[4-[4-(4-methoxycarbonylpiperidino)phenyl)]-piperazino]octyl] disulfide (15). The procedure is the same as for compound **16**. A solution of complex **7** (100 mg, 0.10 mmol) in CH_3CN/NH_3(aq) (10 mL/1.5 mL) was degassed for 30 min and irradiated under UV light for 48 h to give **12** (20 mg, 22% yield) and **15** (9 mg, 20% yield). **12**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 7.18–7.45 (15H), 6.90 (s, 4H), 3.71 (s, 3H), 3.50 (m, 2H), 3.12 (t, J=4.7 Hz, 4H), 2.69 (m, 2H), 2.59 (t, J=4.7 Hz, 4H), 2.35 (m, 3H), 2.13 (t, J=7.2 Hz, 2H), 1.81–2.04 (m, 4H), 1.15 (12H); IR (CH_2Cl_2) 1740 cm^{-1}; **15**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 6.90 (s, 8H), 3.70 (s, 6H), 3.50 (br m, 4H), 3.10 (m, 8H), 2.69 (m, 8H), 2.60 (br, 8H), 2.37 (m, 6H), 1.81–2.05 (m, 8H), 1.26–1.79 (24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 175.5, 145.8, 145.3, 118.3, 117.7, 58.8, 53.4 (2C), 51.8, 50.5, 50.1, 40.9, 39.2, 29.4, 29.2, 28.5, 28.4, 27.5, 26.7; IR (CH_2Cl_2) 1726 cm^{-1}; FAB HRMS Calcd for M^+ ($C_{50}H_{80}N_6O_4S_2$) 892.5682. Found: 892.5642.

1.1.14. Bis[8-[4-[(4-(4-methoxycarbonylbenzoyl)piperazino)phenyl)]piperazino]octyl] disulfide (17). Compound **16** (27 mg, 0.034 mmol) was stirred with PhHgOAc (38 mg, 0.113 mmol, 3.3 equiv) in CH_2Cl_2–CH_3OH (2 mL, 1:1) at rt for 6 h. After removing solvent under reduced pressure, the residue was redissolved in 4 mL CH_2Cl_2 and purged with H_2S for 2 h. Neutral alumina (Brockman I) was added to the solution, the solvent was removed by rotary evaporation and the alumina residue was dried in vacuo. This was placed atop a short neutral alumina column and the product was eluted with $CHCl_3$. Further purification by TLC (Merck Al_2O_3 plate) with $CHCl_3$ afforded **17** (13 mg, 70%), identical to the same compound previously reported by us.

1.2. Deprotection followed by demetallation reactions

1.2.1. Bis[8-[4-[4-(piperidino)phenyl)]piperazino]octyl] disulfide (13). *Deprotection:* Complex **5** (163 mg, 0.173 mmol) was stirred with PhHgOAc (192 mg, 0.570 mmol, 3.3 equiv) in CH_2Cl_2–CH_3OH (4 mL, 1:1) at rt for 7 h. After removing solvent under reduced pressure, the residue was redissolved in 10 mL CH_2Cl_2 and purged with H_2S for 3 h. Neutral alumina (Brockman I) was added to the solution. The solvent was removed by rotary evaporation and the alumina/residue was dried in vacuo. This was placed atop a short neutral alumina column and the side product was eluted with $CHCl_3$ then $CHCl_3$–CH_3OH (1:1). The solvent was evaporated and $CHCl_3$ was added. The organic solution was washed with H_2O and dried over Na_2SO_4 to give product **19** (111 mg), which was not purified.

Decomplexation: A solution of complex **19** (111 mg) in CH_3CN-NH_3(aq) (17 mL/3 mL) was degassed for 30 min and then irradiated under UV light for 48 h. Basic alumina (Brockman I) was added to the solution. The solvent was removed by rotary evaporation and the alumina residue was dried in vacuo. This was placed atop a short basic alumina column and the TAPD derivative was eluted with $CHCl_3$. Then the procedure was repeated by using silica gel with

$CHCl_3$ then 4% methanol in chloroform to give the product **13** (12 mg, 18% yield over two steps).

1.2.2. Bis[8-[4-[4-(4-methoxycarbonylpiperidino)phenyl)]-piperazino]octyl] disulfide (15). The procedure is the same as for conversion of **16** to **17**. Compound **12** (105 mg, 0.152 mmol) was stirred with PhHgOAc (169 mg, 0.502 mmol, 3.3 equiv) in CH_2Cl_2–CH_3OH (3 mL, 1:1) at rt for 10 h. After removing solvent under reduced pressure, the residue was redissolved in 8 mL CH_2Cl_2 and purged with H_2S for 3 h to give product **15**, isolated in the usual way as a solid film (33 mg, 48% yield).

1.2.3. Bis[8-[4-[4-(morpholino)phenyl)]piperazino]octyl] disulfide (14). *Deprotection:* The procedure is the same as for compound **19**. Complex **6** (205 mg, 0.217 mmol) was stirred with PhHgOAc (241 mg, 0.716 mmol, 3.3 equiv) in CH_2Cl_2–CH_3OH (4 mL, 1:1) at rt for 7 h. After removing solvent under reduced pressure, the residue was redissolved in 14 mL CH_2Cl_2 and purged with H_2S for 3 h to give product **20** (150 mg).

Decomplexation: The procedure is the same as for compound **13**. A solution of complex **20** (150 mg) in CH_3CN/NH_3 (17 mL/3 mL) was degassed for 30 min and irradiated under UV light for 48 h to give the product **14** (20 mg, 24% yield over two steps).

1.2.4. Bis[8-[4-[η^6-4-(4-methoxycarbonylpiperidino)piperazino)phenyl)(η^5-cyclo-pentadienyl)ruthenium(II)]-piperazino]octyl] disulfide hexafluorophosphate (21). The procedure is the same as for compound **19**. Complex **7** (218 mg, 0.218 mmol) was stirred with PhHgOAc (260 mg, 0.772 mmol, 3.5 equiv) in CH_2Cl_2–CH_3OH (4 mL, 1:1) at rt for 7 h. After removing solvent under reduced pressure, the residue was redissolved in 10 mL CH_2Cl_2 and purged with H_2S for 3 h to give product **21** (130 mg, 79%). ^{1}H NMR (300 MHz, $CDCl_3$) δ 5.73 (s, 8H), 5.19 (s, 10H), 3.63 (s, 6H), 3.50 (br m, 4H), 2.91 (br, 8H), 2.42–2.61 (18H), 2.29 (t, J=7.1 Hz, 4H), 1.81–2.02 (m, 8H), 1.23–1.60 (24H); ^{13}C NMR (75 MHz, $CDCl_3$) δ 174.6, 122.5, 121.7, 77.4, 67.7, 67.4, 58.4, 52.0, 51.9, 47.7, 47.0, 39.8, 39.1, 33.9, 29.4, 29.1, 29.0, 27.4, 26.6, 26.4; IR ($CHCl_3$) 1741 cm^{-1}; FAB HRMS Calcd for M–PF_6^- ($C_{60}H_{90}N_6O_4S_2Ru_2PF_6$, ^{102}Ru) 1371.4200. Found: 1371.4191. This complex was converted to **15** as described above: A solution of complex **21** (80 mg, 0.053 mmol) in CH_3CN–NH_3(aq) (17 mL/3 mL) was degassed for 30 min and irradiated under UV light for 48 h to give the product **15** (20 mg, 41% yield).

Acknowledgements

We are grateful to the National Institutes of Health, General Medical Sciences, for financial support, and to David Sopchak and Professor Chung-Chiun Liu for helpful discussions concerning the electrochemical measurements.

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