Disulfide-Strapped Porphyrins for Monolayer Formation on Gold
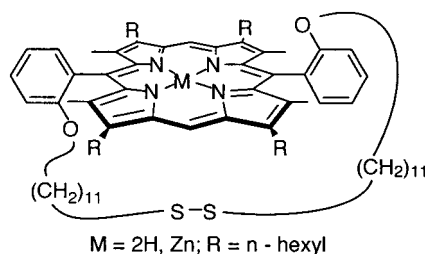
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ABSTRACT

M = 2H, Zn; R = n - hexyl

Porphyrins with a disulfide-containing strap have been prepared as an alternative to dithiols for self-assembled monolayer formation on gold surfaces. The strapped porphyrins have the advantage of greater air stability than their dithiol analogues. *Cis* and *trans* atropisomers of a strapped porphyrin were isolated. Gold electrodes modified with dithiol and disulfide porphyrins were not identical as evidenced by contact angle or electrochemical measurements.

The attachment of metalloporphyrins to gold surfaces by way of a gold−sulfur interaction has afforded self-assembled monolayers (SAMs) with potential applications ranging from electrocatalysis to the sensing of volatile analytes.[1−14] Porphyrins carrying a single alkanethiol group are believed to pack in SAMs in an offset face-to-face manner with the plane of the porphyrin tilted with respect to the surface normal.[9,11,13] However, multiple alkanethiol substituents around the porphyrin periphery constrain the porphyrin to lie parallel to the surface.[7−9,11] The monolayer packing has important consequences for its function, as stacking may block access to the porphyrin metal center.[3,11] Thiol-substituted porphyrins are known to undergo facile photosensitized aerial oxidation to disulfides,[10,15] a reaction which may be especially problematic for polythiols due to the formation of insoluble polymeric products.[16] Here we present the synthesis and properties of porphyrins with a disulfide "strap" intended to combine the surface binding properties of dithiols with the greater oxidative stability of disulfides.

We chose to prepare strapped porphyrins by condensation of a dialdehyde with a dipyrromethane.[17,18] Alkyl thioacetate

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substituted benzaldehydes **3** and **7** were prepared according to Scheme 1 by alkylation of hydroxybenzaldehyde with

Scheme 1[a]
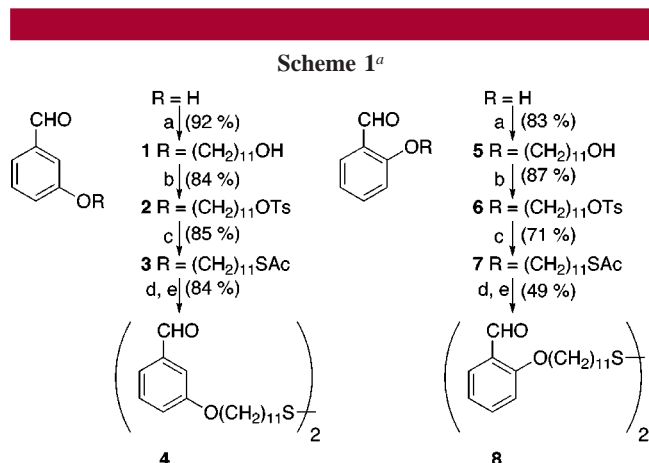
[a] (a) Cs$_2$CO$_3$, HO(CH$_2$)$_{11}$Br, DMF; (b) TsCl, Et$_3$N, DCM; (c) KSAc, PEG 400; (d) K$_2$CO$_3$, MeOH; (e) I$_2$, CHCl$_3$.

bromoundecanol, followed by conversion of the alcohol to a thioacetate[19] via a tosylate. The resulting aldehydes could be used directly for TFA-catalyzed porphyrin synthesis[20] to afford thioacetate-protected porphyrins **9** and **10**.

10 mixture of atropisomers
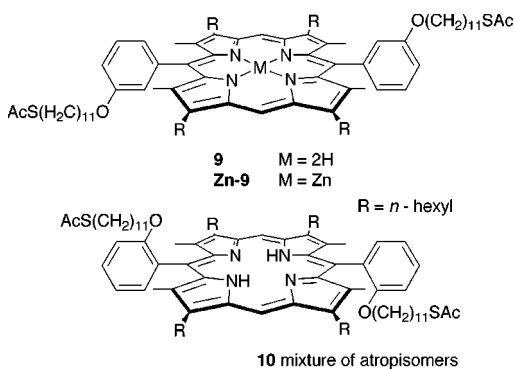
The *ortho* aryl substituted porphyrin **10** was obtained as a mixture of *cis* and *trans* atropisomers which proved inseparable on a preparative scale, although their presence was revealed by TLC and ^{1}H NMR. **9** and **10** also exist as atropisomers, although these interconvert sufficiently rapidly that only a single spot is observed by TLC.

Cleavage of the thioacetate groups of **3** and **7** under basic conditions, followed by iodine oxidation without isolation of the intermediate thiol, afforded dialdehydes **4** and **8**. Dialdehyde **4** was condensed with a dipyrromethane using conditions similar to those used to prepare **9**, but at higher dilution. Oxidation of the porphyrinogen intermediate with DDQ afforded strapped porphyrin **11** in an isolated yield of 53%. Evidence for the cyclic structure is found in the ^{1}H NMR spectrum as the strap is constrained to lie in the

shielding region over the face of the porphyrin. The C*H*$_2$S resonance is not observed at the typical chemical shift of 2.7 ppm but is shielded and overlaps with the hexyl-H^2 resonance at 2.21 ppm as judged by the 12H integral of this multiplet. A single porphyrin *meso* resonance is indicative of a single atropisomer or rapid atropisomerization on the NMR chemical shift time scale. The monomeric nature of the product was confirmed by the high-resolution electrospray mass spectrum which displayed a molecular ion at *m/z* 1257.8930 compared to a calculated mass for [M + H]$^+$ of 1257.8925. The zinc metalated derivative **Zn-11** was prepared, and the ^{1}H NMR spectrum of this compound clearly displays the shielded C*H*$_2$S triplet at 2.07 ppm.
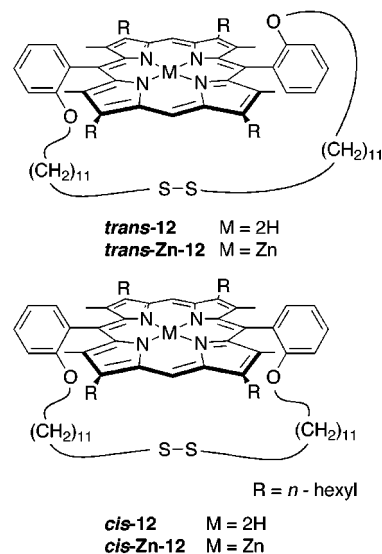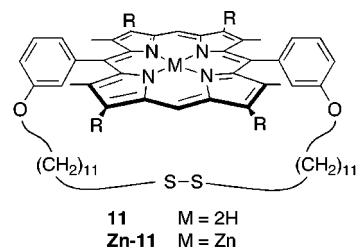
Condensation of **8** with dipyrromethane followed by DDQ oxidation afforded two major products with very similar R_f values on silica gel TLC with all common solvent systems. However, after metalation with zinc, the products were separated chromatographically, and on the basis of ^{1}H NMR evidence we propose that these are a pair of *cis* and *trans* atropisomers of **Zn-12**. Isolated yields of the *cis* and *trans* forms were 25 and 14%, respectively. Inspection of a CPK model of *trans*-**Zn-12** shows that the strap is long enough to span the aryl groups around the periphery of the porphyrin without considerable distortion of the porphyrin but with some loss of conformational freedom of the strap. The compound assigned to the *cis* isomer displayed a shielded C*H*$_2$S triplet at 2.48 ppm in the ^{1}H NMR spectrum, whereas this multiplet occurred at 2.88 ppm in the *trans* isomer, consistent with the CPK model which requires the central portion of the strap to lie in the deshielding region around the porphyrin periphery. The dispersion of the strap reso-

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nances is greater in **Zn-11** than *cis*-**Zn-12** as in the former the *meta* aryl substitution forces the strap to lie on average closer to the porphyrin plane. No unusual features, such as a red-shifted Soret band,[21] were observed in the UV/visible spectra of any of these compounds, suggesting that the porphyrins are not considerably distorted from planarity by the strap. Although *trans*-**Zn-12** is a crystalline solid, so far we have been unable to obtain crystals of sufficient quality for an X-ray diffraction study.

13   M = 2H
Zn-13 M = Zn

R = *n* - hexyl
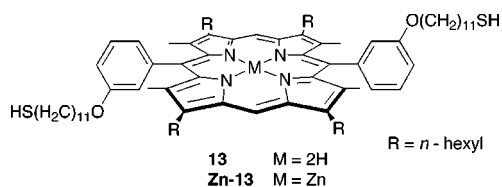
Deprotection of the thioacetate groups of **9** and **Zn-9** by aminolysis[22] afforded dithiols **13** and **Zn-13**. These compounds were found to be sensitive to a combination of light and oxygen, with solutions developing a precipitate of presumably polymeric disulfides within several hours of exposure to ambient conditions. Exclusion of light was found to substantially slow this oxidation process. Oxidation of dilute (<0.1 mM) solutions of **13** and deprotected **10**, as a mixture of atropisomers, with I_2 in DCM, followed by zinc metalation, afforded **Zn-11** and *cis*-**Zn-12** in isolated yields of 87 and 9%, respectively. In each case the ^{1}H NMR spectrum of the product was identical to that produced by the dialdehyde route. It seems likely that oxidative cyclization to *trans*-**Zn-12** is sufficiently slow to allow competition from polymer formation, accounting for the poor yield of *cis*-**Zn-12** and the apparent absence of the *trans* isomer. More rapid rotation about the *meso*-aryl bonds of **13** permits conversion of the *trans* to the *cis* atropisomer which is able to cyclize. The dialdehyde route to **11** is superior as dithiols and oxidative polymerization are avoided at all stages.

The thermal atropisomerization of *cis*- and *trans*-**Zn-12** was investigated by ^{1}H NMR spectroscopy. A sample of *trans*-**Zn-12** in $C_2D_2Cl_4$ solution was heated, and spectra were acquired at regular temperature intervals. After several minutes at 107 °C the resonances of *cis*-**Zn-12** appeared. The resonances of both species remained sharp at a temperature of 117 °C. After further heating at 117 °C, the resonances of *trans*-**Zn-12** disappeared entirely and were replaced with those of *cis*-**Zn-12**, indicating that the *trans* atropisomer has only kinetic stability.

A sample of *trans*-**Zn-12** was demetalated by treatment with TFA. The atropisomerization rates of *trans*-**12** and *trans*-**Zn-12** were measured at 110 °C in $C_2D_2Cl_4$. ^{1}H NMR spectra (Figure 1) were quantified by normalization of the total porphyrin *meso* integral for each spectrum and integration of the C*H*$_2$S resonance of the *trans* atropisomer. Data
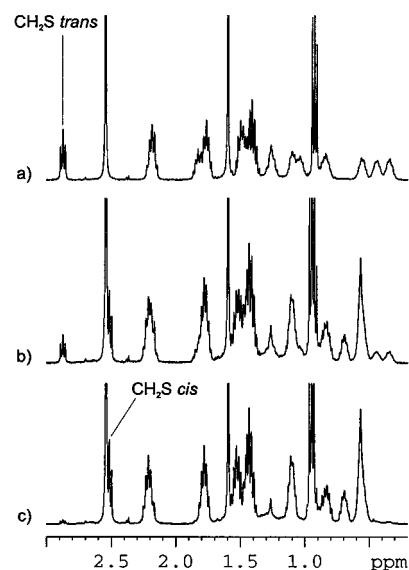
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Figure 1. 400 MHz ^{1}H NMR spectra of *trans*-**Zn-12** in $C_2D_2Cl_4$ after heating at 110 °C for (a) 0 min, (b) 28 min, (c) 76 min.

were fitted to a first-order model, and from the average of two independent determinations rate constants of 0.038 and 0.11 min^{-1} were obtained for *trans*-**Zn-12** and *trans*-**12**, respectively. The greater rate of atropisomerization of free-base porphyrins over their zinc counterparts has been noted by other authors and ascribed to a rigidification of the porphyrin on zinc metalation.[23]

Preliminary studies of the structures of adlayers of these compounds on gold surfaces have been carried out using water contact angle measurements and electrochemistry. Details of the experimental procedures have been reported previously.[24] Advancing and receding contact angles are summarized in Table 1. Layers of **13** and **Zn-13** were found

Table 1. Advancing and Receding Water Contact Angles (θ_a, θ_r),[a] Differential Capacitance[b] (*C*), and Charge-Transfer Resistance[b] (R_{ct}) of Porphyrin-Modified Gold Electrodes

	θ_a/deg	θ_r/deg	$C/\mu F\ cm^{-2}$	R_{ct}/kΩ
11	99 ± 1	63 ± 4	9.8	0.8
Zn-11	92 ± 1	50 ± 6	10.5	0.5
cis-**Zn-12**	93 ± 3	59 ± 4	10.3	0.3
trans-**Zn-12**	90 ± 1	54 ± 7	12.7	0.3
13	105 ± 1	77 ± 2	5.1	34
Zn-13	102 ± 2	57 ± 6	4.9	16
bare gold	79 ± 3	0	39	0.08

[a] A contact angle of 0 indicates a low and ill defined angle. [b] Errors estimated as <50%.

to be more hydrophobic than their cyclic analogues **11** and **Zn-11**, which implies that structural differences exist between the layers of the two classes of compounds. To electrochemically probe the thickness and permeability of the adlayers,

the differential capacitance of functionalized electrodes was measured at -0.35 V with respect to Hg/Hg_2SO_4 with a 0.1 M $NaClO_4$ electrolyte. Additionally the charge-transfer resistance of the layers to the $Fe(CN)_6^{3-/4-}$ redox couple was investigated by impedance analysis using an equivalent circuit model.[25] The results are also displayed in Table 1. The dithiol porphyrins display lower capacitance and higher resistance than their strapped analogues, indicating the former layers to be thicker and/or less permeable to ions.[26]

The higher charge-transfer resistance of the layers of **13** and **Zn-13** is also reflected in the cyclic voltammograms (Figure 2) obtained with these modified electrodes and the
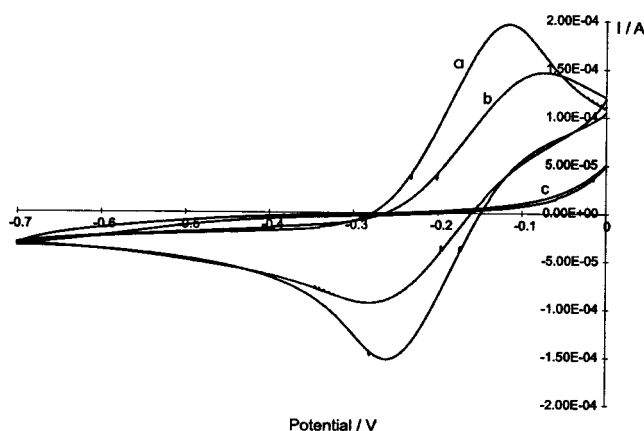

Figure 2. Cyclic voltammograms obtained with bare gold and porphyrin-modified gold electrodes and the $Fe(CN)_6^{3-/4-}$ redox couple: (a) bare Au; (b) Au$-$**11**; (c) Au$-$**13**. Potential is with respect to Hg/Hg_2SO_4.

$Fe(CN)_6^{3-/4-}$ redox couple. Relative to a bare gold electrode, electrodes modified with **11** and **Zn-11** displayed a reduced peak current and increased peak separations, consistent with

a partially blocked electrode.[27] Peaks were absent entirely when electrodes modified with **13** and **Zn-13** were used, implying that these layers effectively insulate the electrode from the redox probe. These electrochemical results corroborate the contact angle values which indicate that the structures of adlayers of the dithiol porphyrins and their strapped analogues are not identical. The differences may arise from incomplete binding of dithiols to the surface[8,28] or adsorption of disulfide polymers despite care to exclude light from solutions of the porphyrins during incubation with gold electrodes to avoid accelerating the oxidation process. Both sulfur atoms of the strapped compounds will contact the gold surface simultaneously, so incomplete binding of sulfur groups is not anticipated. After further surface characterization and optimization of the adsorption conditions, disulfide-strapped porphyrins should be a valuable alternative to porphyrin dithiols.

In summary, porphyrins with disulfide straps have been prepared and have the advantage of greater air stability over their dithiol analogues, and consequently easier handling. *Cis* and *trans* atropisomers of *ortho* aryl substituted strapped porphyrins were isolated, and it was demonstrated that the *trans* isomer has only kinetic stability. Surface derivatization experiments have revealed that monolayers of the strapped porphyrins on gold surfaces are not identical to those prepared from analogous dithiols.

Supporting Information Available: Experimental details and characterization of compounds **1**$-$**13**. This material is available free of charge via the Internet at http://pubs.acs.org.

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