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Synthesis of fluorescent long-chain thiols/disulfides as building-blocks for self-assembled monolayers preparation

Rapid Communication

Sushilkumar A. Jadhav[1,2]

[1]Department of Material Science and Chemical Engineering,
Politecnico di Torino, 10129 Torino, Italy

[2]Italian Interuniversity consortium for Materials Science
and Technology, 50121 Firenze, Italy#

Abstract: New symmetrical disulfides together with the corresponding thiols bearing fluorescent end-groups have been synthesized as building-blocks for self-assembled monolayers (SAMs). The synthesis has been accomplished starting from aromatic nitrogen heterocycles in three steps. The conversion of the tosylated intermediate into the final disulfide is accomplished by use of sodium hydrogen sulfide (NaSH). Both products (thiols and disulfides) were isolated and characterized.

Keywords: Symmetrical disulfides • Thiols
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1. Introduction

Self-assembled monolayers (SAMs) are molecular assemblies formed by the chemisorptions of organic compounds from solution or gas phase onto the surface of a substrate [1,2]. The building-blocks of SAMs are organic compounds possessing three important parts they are the head-group, spacer chain and the end-group. The head group is with a specific affinity for the surface of the substrate (such as metal, metal oxide or semiconductor). Organosulfur compounds are suitable materials as building-blocks for SAMs as sulfur has been found to be the best head group for reasons that it presents in its reduced state, high affinity towards metals, particularly silver or gold [3] but also towards other metals. Both two- (2D) and three-dimensional (3D) monolayers (Fig. 1) can be prepared by chemisorptions of thiols and disulfides. Further the properties of resulting monolayers and underlaying nanostructures can be modified by changing the chemical nature of the terminal (end) group of the carbon chain: accordingly, these classes of organic compounds can be used to prepare highly ordered monolayers for their use in micro- and nano-fabrication in biomaterials and biological assays,

in molecular electronics, in analytical and sensory applications, templates for crystal nucleation and growth [4 and references therein].

In this respect, the interest for the use and hence for the relevant synthesis of thiols or disulfides as building blocks for assemblies on noble-metal surfaces through chemisorptions has been boosted [5a-c]. Newer and easier techniques of organic synthesis of these classes of compounds are welcomed which will assist the material chemists. The points which must be taken into account during the synthesis of organosulfur compounds as building-blocks for SAMs are represented by the end-group itself and the length of the spacer chain: for instance, a chain length of 10-12 carbon atoms has been found to give good crystalline SAMs from solution [6]. The aromatic head-groups of the SAM can react with one another to give polymerized monolayer which intern generates a conjugated layer around the nanostructures making the resulting hybrid materials applicable in energy conversion and conduction devices [7]. Long-chain organic compounds bearing fluorescent groups are attractive as fluorescent labels in construction of mixed monolayers on metallic nanostructures in sensory and analytical applications. Further SAMs constructed

* E-mail: sushil.unige@gmail.com
#Consorzio Interuniversitario Nazionale per la Scienza e Tecnologia dei Materiali (INSTM), 50121 Firenze, Italy
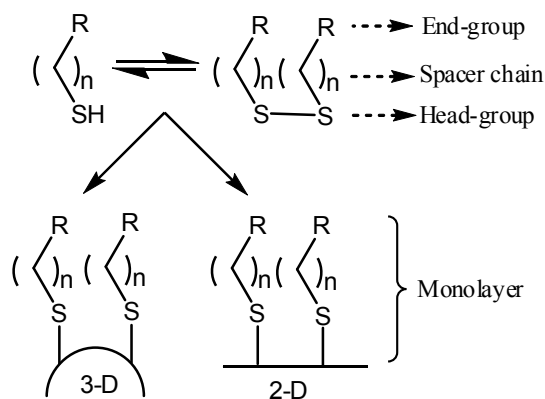
Figure 1. Chemisorption of alkane thiols or disulfides on gold.

from aromatic thiols have higher conductivity and rigidity compared to aliphatic thiols which makes them attractive compounds for monolayer formations [8].

2. Experimental procedure

Petroleum ether and light petroleum refer to the fractions boiling in the range of 40-60°C and 80-110°C, respectively. Solvents used as eluents were distilled prior to use. Toluene, ethanol, THF, 11-bromo-1-undecanol, 9*H*-carbazole, benzotriazoles and light petroleum were extra pure commercial products and were used as received. Anhydrous methylene chloride was syringed under argon. Pyridine was twice distilled prior to use, first from KOH pellets and then from CaH_2. The ^{1}H NMR and ^{13}C Spectra were recorded at 300 MHz.

11-(9-Carbazolyl)-1-undecanol (2a) (Scheme 1, step *i*).

9*H*-Carbazole (4 g, 23.91 mmol) was dissolved in warm toluene (250 mL). The solution was left under stirring for 30 minutes, Then 11-bromo-1-undecanol (7.2 g, 28.70 mmol), tetrabutylammonium bromide (0.385 g, 1.195 mmol), and 50% aqueous NaOH (20 mL) were added. The mixture was then stirred at 80°C till the completion of the reaction (*i.e.,* approximately for 24 h), monitoring the progress of the reaction by TLC. The mixture was then acidified to *p*H 1 by adding 37% HCl, diluted with water, and extracted with Et_2O. The organic layer was washed to neutrality with water and then dried over Na_2SO_4. Evaporation of the solvent gave a yellowish white residue which was flash-chromatographed on a silica-gel column using as eluent petroleum ether/ethyl acetate mixtures of varying composition. The chromatographic separation yielded a white crystalline product (6.69 g, 83%), mp 76.4 – 76.6°C.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.19-1.34 (14H, m), 1.52 (2H, quint., *J* = 6.3), 1.86 (2H, quint., *J* = 7.2), 3.62 (2H, t, *J* = 6.3), 4.3 (2H, t, *J* = 7.2), 7.26 (2H, m), 7.40-7.47 (4H, m), 8.1 (2H, d, *J* = 7.8). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 25.95, 27.56, 29.22, 29.61, 29.65, 29.71, 29.76, 33.02, 43.31, 63.32, 108.89, 118.91, 120.58, 123.03, 125.79, 140.65.

11-(1H-Benzo[d][1,2,3]triazol-1-yl)undecan-1-ol (2b) and ***11-(2H-benzo[d][1,2,3]triazol-2-yl)undecan-1-ol (2c)*** (Scheme 1, step *i*).

Compounds **2b** and **2c** were synthesized by the same procedure described above for the preparation of **2a**. Both of them were obtained as isomers from the same reaction of benzotriazole (**2**) with 11-bromoundecanol.

11-(1H-benzo[d][1,2,3]triazol-1-yl)undecan-1-ol (2b): white crystalline solid (61%), mp. 57.7-57.9°C. H^1 NMR (300 MHz, $CDCl_3$): δ = 1.25-1.33 (14H, m), 1.55 (2H, quint., *J* = 6.6), 2.0 (2H, quint., *J* = 7.2), 3.63 (2H, t, *J* = 6.6), 4.64 (2H, t, *J* = 7.2), 7.32-7.38 (1H, m), 7.45-7.51 (2H, m), 8.05 (1H, d, *J* = 6.6). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 25.92, 26.88, 29.18, 29.51, 29.55, 29.67, 29.87, 33, 48.45, 63.23, 109.54, 120.26, 123.98, 127.33, 133.17, 146.23.

11-(2H-benzo[d][1,2,3]triazol-2-yl)undecan-1-ol (2c): waxy solid (25%), mp 36°C. H^1 NMR (300 MHz, $CDCl_3$): δ = 1.25-1.34 (14H, m), 1.55 (2H, quint., *J* = 7.2), 2.11 (2H, quint., *J* = 6.6), 3.63 (2H, t, *J* = 7.2), 4.72 (2H, t, *J* = 6.6), 7.37 (2H, dd, J_1 = 3.0, J_2 = 6.6), 7.85 (2H, dd, J_1 = 3.0, J_2 = 6.6). ^{13}C NMR (300 MHz, $CDCl_3$): δ = 25.94, 26.74, 29.2, 29.59, 29.71, 30.26, 33, 56.86, 63.17, 118.12, 126.38, 144.46.

11-(9-Carbazolyl) p-toluenesulfonate (3a) (Scheme 1, step *ii*).

Dry pyridine (4.3 mL) was added to a magnetically stirred solution of 11-(9-carbazolyl)-1-undecanol (6 g, 17.80 mmol) in dry CH_2Cl_2 (220 mL) which was then cooled to 10°C and added with *p*-tosylchloride (5.091 g, 26.7 mmol) in small portions. After standing for additional 10 min at the same temperature the mixture was allowed to reach room temperature, left under stirring for 40 h, poured into a mixture of 37% HCl (50 mL) and crushed ice, and finally extracted with ethyl ether. The organic layer was washed repeatedly with water, dried over anhydrous sodium sulphate, and the solvent was removed under reduced pressure to give a residue which was flash-chromatographed on a silica-gel column (eluent: petroleum ether/ethyl acetate mixtures of varying compositions). The crude product from the chromatographic separation yielded 6.22 g (71%) of an faint-orange oil which was not further purified.

^{1}H NMR (300 MHz, $CDCl_3$): δ = 1.18-1.37 (14H, m), 1.56 (2H, quint., *J* = 6.6), 1.86 (2H, quint., *J* = 7.2),

4.0 (2H, t, *J* = 6.6), 4.3 (2H, t, *J* = 7.2), 7.20-7.26 (2H, m), 7.39-7.49 (4H, m), 7.78 (2H, d, *J* = 8.1), 8.1 (2H, d, *J* = 7.5). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 21.88, 25.54, 27.54, 29.04, 29.11, 29.22, 29.54, 29.62, 29.63, 29.65, 43.30, 70.96, 108.91, 118.93, 120.58, 123.03, 125.81, 128.12, 130.05, 133.43, 140.66, 144.88.

Compounds **3b** and **3c** were synthesized following the same procedure described above for the preparation of **3a**.

11-(1H-Benzo[d][1,2,3]triazol-1-yl)undecyl p-toluenesulfonate (3b)

Colourless oil (58%). H^1 NMR (300 MHz, CDCl$_3$): δ = 1.18-1.31 (14H, m), 1.61 (2H, quint., *J* = 6.6), 2.0 (2H, quint., *J* = 7.2), 4.0 (2H, t, *J* = 6.6), 4.63 (2H, t, *J* = 7.2), 7.31-7.36 (3H, m), 7.45-7.53 (2H, m), 7.77 (2H, d, *J* = 8.4), 8.05 (2H, d, *J* = 8.2). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 11.18, 14.27, 21.85, 23.20, 23.97, 25.51, 26.9, 29, 29.2, 29.5, 29.89, 30.59, 38.96, 48.45, 68.38, 70.91, 109.55, 120.26, 123.98, 127.35, 128.1, 129, 130, 131.1, 144.84.

11-(2H-Benzo[d][1,2,3]triazol-2-yl)undecyl p-toluenesulfonate (3c)

White crystalline solid (78%), mp 53.5-53.7°C. H^1 NMR (300 MHz, CDCl$_3$): δ = 1.19-1.33 (14H, m), 1.60 (2H, quint., *J* = 6.6 Hz), 2.07 (2H, quint., *J* = 7.2 Hz), 4.0 (2H, t, *J* = 6.6 Hz), 4.72 (2H, t, *J* = 7.2 Hz), 7.31-7.39 (4H, m), 7.78 (2H, d, *J* = 7.5 Hz), 7.84-7.88 (2H, m). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 21.85, 25.52, 26.74, 29.02, .09, 29.19, 29.5, 29.52, 30.26, 56.85, 70.79, 118.16, 126.36, 128.1, 130, 133.51, 144.5, 144.81.

11-(9-Carbazolyl)-1-undecanethiol (5a) and 11-(9-carbazolyl)-1-undecyl disulfide (4a) (Scheme 1, step iii).

The tosylated product (4.6 g. 9.36 mmol) was dissolved in the minimum absolute ethanol, sodium hydrogen sulphide (3.147 g. 56.2 mmol) was added and the mixture was sonicated at 50°C for 10 h. The solution was diluted with chloroform and washed with 1N HCl and then with water. The organic phase was dried over sodium sulphate. Rotoevaporation of the solvent gave a colourless thick liquid which was purified by chromatography, allowing the separation of the thiol and of the corresponding disulfide.

11-(9-Carbazolyl)-1-undecyl disulfide (4a).

Colourless solid (48%), mp 38.5-38.6°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.24-1.35 (14H, m), 1.65 (2H, quint., *J* = 7.5), 1.86 (2H, quint., *J* = 7.2), 2.67 (2H, quint., *J* = 7.5), 4.29 (2H, t, *J* = 7.2), 7.20-7.26 (2H, m), 7.39-7.49 (4H, m), 8.1 (2H, d, *J* = 0.6). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 27.55, 28.73, 29.21, 29.43, 29.65, 29.66, 29.70, 39.38, 43.30, 108.88, 118.90, 120.57, 123.01, 125.78, 140.63.

11-(9-Carbazolyl)-1-undecanethiol (5a).

Colourless oil (7%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.24-1.36 (14H, m), 1.55- 1.64 (3H, m), 1.87 (2H, quint., *J* = 7.5), 2.51 (2H, q, *J* = 6.6), 4.30 (2H, t, *J* = 7.5), 7.21-7.25 (2H, m), 7.40-7.49 (4H, m), 8.10 (2H, d, *J* = 7.5). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 24.9, 27.55, 28.58, 29.21, 29.26, 29.64, 29.67, 29.69, 34.27, 43.31, 108.88, 118.90, 120.57, 123.08, 125.78, 140.64.

Compounds **4b-c** and **5b-c** were synthesized following the same procedure described above for the preparation of **4a** and **5a**, respectively.

11-(1H-Benzo[d][1,2,3]triazol-1-yl)-1-undecyl) disulfide (4b).

White crystalline solid (20%), mp 80.8-81°C. ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.24-1.33 (14H, m), 1.65 (2H, quint., *J* = 7.35), 2.0 (2H, quint., *J* = 7.2), 2.66 (2H, t, *J* = 7.35), 4.63 (2H, t, *J* = 7.2), 7.35-7.39 (1H, m), 7.48-7.54 (2H, m), 8.06 (1H, d, *J* = 8.4). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 26.94, 28.71, 29.24, 29.41, 29.56, 29.63, 29.91, 39.38, 48.47, 109.53, 117.9, 123.97, 127.33.

11-(1H-Benzo[d][1,2,3]triazol-1-yl)-1-undecanethiol (5b).

White crystalline solid (7%), mp 42.5-42.7°C. H^1 NMR (300 MHz, CDCl$_3$): δ = 1.24-1.35 (14H, m), 1.54- 1.64 (3H, m), 2.0 (2H, quint., *J* = 6.9), 2.52 (2H, q, *J* = 7.5), 4.64 (2H, t, *J* = 6.9), 7.35-7.39 (1H, m), 7.46-
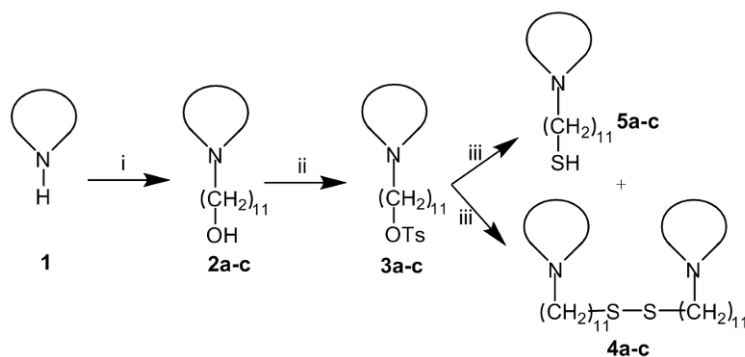
Scheme 1. Synthesis of long-chain thiols and/or symmetrical disulfides bearing N-heterocyclic end-groups. **i**) 11-Bromo-1-undecanol, NaOH, 80 °C; **ii**) p-tosylchloride, pyridine; **iii**) NaSH, EtOH, 45°C.

Table 1. Yields of intermediates and final products from Scheme 1.

1	2 (Yield %)	3 (Yield %)	4 (Yield %)	5 (Yield %)
	2a (83)	**3a** (71)	**4a** (48)	**5a** (7)
	2b (61)	**3b** (58)	**4b** (20)	**5b** (7)
	2c (25)	**3c** (78)	**4c** (48)	**5c** (10)

[a] Both tautomers present as substrates in the same run.

7.52 (2H, m), 8.06 (1H, d, J = 8.1). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 24.88, 26.94, 28.56, 29.24, 29.56, 29.64, 29.92, 34.25, 48.48, 109.55, 120.3, 123.99, 127.34, 133.16, 146.26.

11-(2H-Benzo[d][1,2,3]triazol-2-yl)-1-undecyl disulfide (4c). Waxy solid (48%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.24-1.42 (14H, m), 1.64 (2H, quint., J = 7.5), 2.1 (2H, quint., J = 6.9), 2.65 (2H, t, J = 7.5), 4.70 (2H t, J = 6.9), 7.35 (2H, dd, J_1 = 3.0, J_2 = 6.6), 7.85 (2H, dd, J_1 = 3.0, J_2 = 6.6). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 26.76, 28.72, 29.22, 29.41, 29.43, 29.54, 29.63, 30.27, 39.40, 56.85, 118.16, 126.35, 144.50.

11-(1H-Benzo[d][1,2,3]triazol-2-yl)-1-undecanethiol (5c). Colourless oil (10%). ^{1}H NMR (300 MHz, CDCl$_3$): δ = 1.23-1.37 (14H, m), 1.52-1.62 (3H, m), 2.1 (2H, quint., J = 7.2), 2.48 (2H, q, J = 7.2), 4.70 (2H, t, J = 7.2), 7.35 (2H, dd, J_1 = 3.0, J_2=6.6), 7.83 (2H, dd, J_1 = 3.0 , J_2=6.6 Hz). ^{13}C NMR (300 MHz, CDCl$_3$): δ = 24.85, 26.75, 28.56, 29.15, 29.21, 29.32, 29.52, 29.61, 29.63, 30.26, 34.24, 118.16, 126.34, 129.02.

3. Results and discussion

In an process of attachment of a chemical functionality of the general formula X-(CH$_2$)$_n$-OH where X= Halogen atom (such as Cl, Br, I) containing long chain of methylene units to the fluorescent head groups we have selected the aromatic nitrogen heterocycles as precursors because of the ease of the substitution electrophilic reactions at the nitrogen atom. The synthetic route to amino-functionalized thiols and/or disulfides is shown in Scheme 1. It involves the reaction of a aromatic heterocycle of nitrogen (**1**) like 9-H carbazole or benzotriazole with 11-bromo-1-undecanol under basic conditions to obtain the amino alcohol (**2**) followed by tosylation of the alcohol group with *p*-tosyl chloride and then conversion of the tosylated intermediate (**3**) into the final disulfide (**4**) and thiol (**5**) in a single step using sodium hydrogen sulfide which involves a simple nucleophilic substitution of the tosylate group by $^-$SH group. The final step yields the disulfide (major) and the thiol (minor) products. The yields of all intermediates and final products (*i.e.,* thiols and the corresponding disulfides, which have both characterized in any case) are summarized in Table 1. Proton NMR spectroscopy is used to differentiate between the thiols and disulfides both these compounds are normally difficult to separate as thiols can be easily oxidised to disulfides even in air at room temperature, flash chromatography is used to separate them. All the thiols separated have shown a quartet in proton NMR spectra for the methylene group attached to the sulphur atom of the thiol (-CH$_2$-S-H) group. The same methyele group in the corresponding disulfides (-CH$_2$-S-S-CH$_2$-) disappear and shows a triplet in the H^1 NMR confirming the oxidation (refer to NMR data and [4]).

To add more significance to the results, it should be stressed, at this regard, that thiols and disulfides are generally equivalent as building blocks for the fabrication of the monolayer on metallic surfaces (cf. Fig. 1). Particular ligand structures and/or experimental procedures or specific applications might anyway require preferentially either thiols or disulfides: as a matter of fact, while the interconversion between thiols and disulfides can be performed in a rather simple way by means of a number of literature methodologies [9,10].

4. Conclusions

In summary, symmetrical disulfides and the corresponding thiols were synthesized from easily available starting materials and employing a simple and convenient procedure which could be applied to the synthesis of other items with chains of varying nature or lengths and/or bearing different end-groups. The compounds synthesized herein bear fluorescent end-groups, which makes them attractive in the field of functionalization of nanostructures and construction of SAMs for photonics and sensoristic applications and also as fluorescent labels in mixed monolayer constructions. Studies on construction of monolayers from the compounds mentioned above and their characterization are in progress.

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