Synthesis, surface characterization and *in vitro* platelet compatibility study of the self-assembled monolayer with lipid-like zwitterionic phosphonylcholine terminal group

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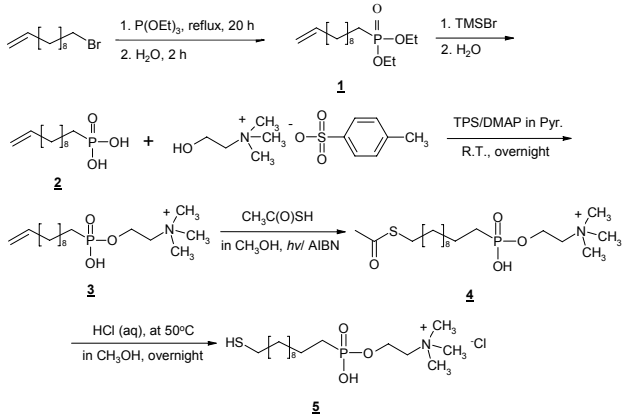
Introduction

Self-assembled monolayer (SAM) of the long-chain alkanethiols ($HS(CH_2)_nX$, n=11) with variant terminal functionalities adsorbed on Au substrate can serve as a well-oriented surface with a diverse chemical configuration for studying the blood-material interactions[1-3]. In this study, we have established a novel synthetic method for the alkanethiol with a phospholipid-like functionality, such as $–P(=O)(OH)OCH_2CH_2N^+(CH_3)_3$. In addition, the $–N^+(CH_3)_3$ and $–PO_3H_2$ terminated thiols were synthesized as well. These alkanethiols were fairly pure through the NMR and mass spectrometer measurements. Henceforth, these alkanethiols can be used to prepare the single-component as well as mixed zwitterionic SAMs for *in vitro* blood compatibility evaluations. Moreover, the "solvent" effect and "concentration" effect of thiol solutions on the SAM packing quality will also be examined.

Materials and Methods

Synthesis of 11-mercaptoundecanylphosphonyl choline ester:

The alkanethiol with $–P(=O)(OH)OCH_2CH_2N^+(CH_3)_3$ functional group was synthesized by the strategy illustrated in scheme 1. The spectral data for its structure identification were as follows: ^{1}H NMR (300 MHz, $CDCl_3$): δ 4.55 (m, 2H), 3.95 (m, 2H), 3.41 (s, 9H), 2.49-2.56 (q, *J*=7.19 Hz, 2H), 1.11-1.80 (overlapped, 21H); ^{13}C-NMR (300 MHz, $CDCl_3$): δ 66.00 (s), 59.04 (s), 54.41 (s, 3C), 33.99 (s), 30.82 (s), 30.58 (s), 29.08-29.53 (overlapped, 3C), 28.34 (s), 26.65 (s), 24.82 (s), 24.59 (s), 22.31 (s).



Scheme 1. Synthesis Procedure for $–P(=O)(OH)OCH_2CH_2N^+(CH_3)_3$ Terminal Thiol

In addition, the two alkanethiols with $–N^+(CH_3)_3$ and $–PO_3H_2$ functional groups were synthesized by the previous published strategies[4,5]. The purities of these two alkanethiols were ensured by NMR and MS spectrometers.

Surface characterization and *in vitro* blood compatibility:

A similar gold deposition procedure as our past study[6] was used for Si (111) strip and cover glass slip. The sessile-drop contact angle technique and XPS analysis were utilized to characterize the "solvent" and "concentration" effects of thiol solutions on the SAM formation. The contact activation of these zwitterionic SAMs with the whole blood or plasma was analyzed by the coagulation time (CT) or recalification time assay to evaluate the *in vitro* blood compatibility.

Results/Discussion

These three lab-synthesized alkanethiols were fairly pure through the NMR and mass spectrometer measurements. The ^{1}H-NMR spectral data of the alkanethiol with $–P(=O)(OH)OCH_2CH_2N^+(CH_3)_3$ terminal group was shown in Figure 1.

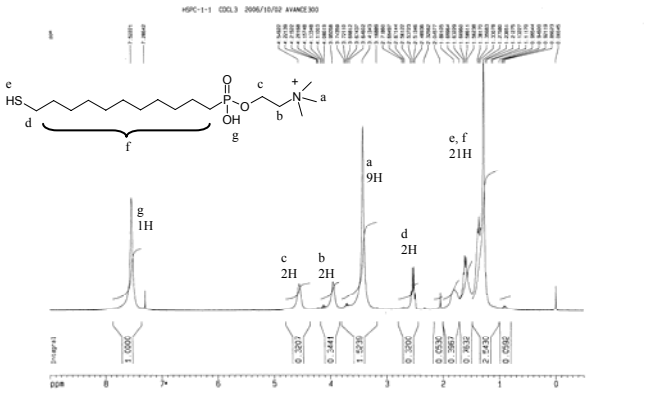


Figure 1. ^{1}H-NMR Spectrum of 11-Mercaptoundecanylphosphonyl Choline Ester

Contact angle analysis has indicated this $–P(=O)(OH)OCH_2CH_2N^+(CH_3)_3$ terminated SAM was hydrophilic. *In vitro* platelet compatibility evaluation has shown this lipid-like terminated SAM was fairly platelet compatible.

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