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Highly photostable silicon(IV) phthalocyanines containing adamantane moieties: synthesis, structure, and properties

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ABSTRACT

Two new axially disubstituted silicon(IV) phthalocyanines **1** and **2** have been synthesized by treating silicon phthalocyanine dichloride with 1-adamantanemethanol or 1-adamamtaneethanol, respectively. The crystal structure of compound **2** has been characterized by X-ray diffraction analysis. Both compounds are efficient singlet-oxygen generator with a quantum yield of 0.40–0.43. With two rigid bulky adamantane moieties at the axial positions, these phthalocyanines not only are essentially non-aggregated in common solvents, but also exhibit a high photostability. They are about 100 times more stable than zinc phthalocyanine under the same irradiation conditions. With the goal of enhancing the biocompatibilities, interactions and conjugations of these two compounds with bovine serum albumin have also been investigated.

1. Introduction

Over the past few decades, phthalocyanines (Pcs) have attracted great attention because of their versatile applications.[1] One of their most promising aspects is functioning as photosensitizers for photodynamic therapy of cancer or photodegradation of pollutants.[2,3]

The most fundamental property of a photosensitizer is able to generate reactive oxygen species (ROS), in particular singlet oxygen, under light irradiation.[2] The photosensitized ROS production of phthalocyanines is strongly affected by the nature of their central metal ions.[4] The phthalocyanines coordinated with closed shell, diamagnetic ions (such as Zn^{2+}, Si^{4+}, Al^{3+}, Ga^{3+}) were found to possess high ROS yield.[4] Otherwise, the photosensitizing efficiency of the phthalocyanine is largely influenced by its molecular aggregation.[2–4] Molecular aggregation of phthalocyanines, which is an intrinsic property of these large π-conjugated systems, provides an efficient non-radiative energy relaxation pathway, thereby shortening the excited state lifetimes and greatly reducing the photosensitizing efficiency.[4b,5]

Because silicon center allows the introduction of two appropriate axial ligands to inhibit the π–π staking tendency of phthalocyanine rings, and moreover give the macrocycles desirable photophysical characteristics, silicon(IV) phthalocyanines (SiPcs) have emerged to be one of the most promising classes of Pc-based photosensitizers.[2c,4b,6] However, the unsatisfactory photostabilities of the SiPcs limited their total application potentials to some degree. For example, Kenney et al. reported[6a] that solutions of a SiPc photosensitizer, $CH_3SiPcOSi(CH_3)_2(CH_2)_3N(CH_3)_2$, in solvent such as toluene were rapidly photolyzed by light. Ng et al. also mentioned[7] that the stability of the SiPc was in general lower than that of its competitor zinc(II) phthalocyanine. Therefore, how to improve the photostability is an important issue for the practical use of this kind of phthalocyanine.

We describe herein the synthesis and properties of two new SiPcs axially containing adamantine moieties. Adamantine is a kind of rigid spherical alkyl group and shows large steric hinderance.[8] Also, it is a biological active group and has been investigated for potential application as carrier group for anti-cancer drugs.[9] By introduction two adamantine-containing substituents at the axial positions of a SiPc, we hope to inhibit the self-aggregation and increase biocompatibilities of these compounds. More importantly in this work, we aim to improve the photostabilities of the SiPcs through the addition of these rigid bulky moieties. Such approach has been used to enhance the stabilities of the polymers. For example,[8a,10] adamantane has also been incorporated into the backbones of polyamides and phenylenevinylene, and subsequently producing increased stability. But in the field of photosensitzer, this strategy has not been carried out.

Only several phthalocyanines peripherally modified by adamantanes have been reported. Kobayashi et al.[11] firstly prepared the phthalocyanines peripherally containing adamantane units and examined their spectroscopic properties. Afterward, in order to

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obtain the analogues having more red-shifting in their UV–vis absorption spectra, Causey et al.[12] synthesized the magnesium, nickel, and metal-free phthalocyanines substituted with adamantine moieties. Vior et al.[13] also prepared four zinc phthalocyanines replaced with oxygen and sulfur linked adamantine groups. However, to the best of our knowledge, no silicon phthalocyanines containing adamantine moieties have been reported in the literature.

2. Results and discussion

2.1. Synthesis

Scheme 1 shows the synthetic pathway of the adamantine-containing phthalocyanines **1** and **2**. This is a type approach to obtain silicon phthalocyanine axially disubstituted with alkoxy groups using dichlorosilicon phthalocyanine as the starting material.[14] The nucleophilic substitution reaction of 1-adamantanemethanol or 1-adamantaneethanol with silicon(IV) phthalocyanine dichloride in the presence of NaH led to axial substitution, giving the compound **1** or **2** in moderate yield. Two products are highly soluble in common organic solvents and could be readily purified by column chromatography. These new compounds were characterized by MS, ^{1}H NMR, and FTIR spectroscopic methods together with elemental analysis.

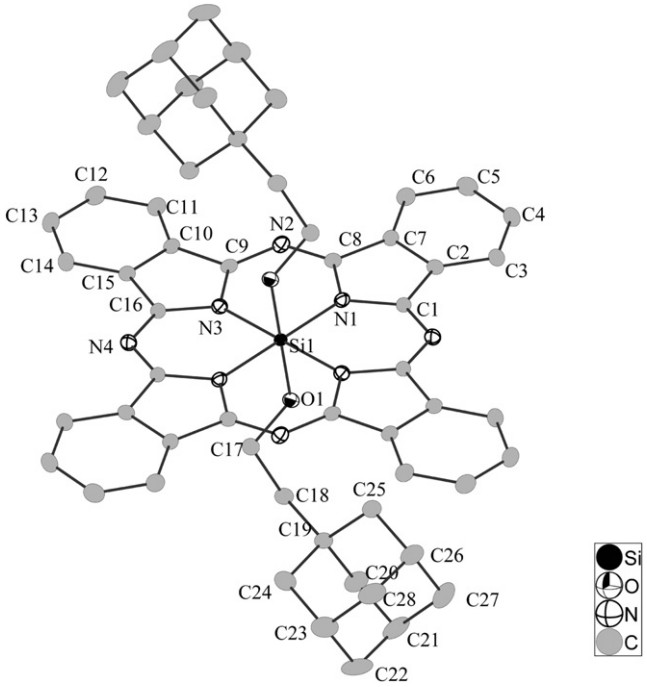
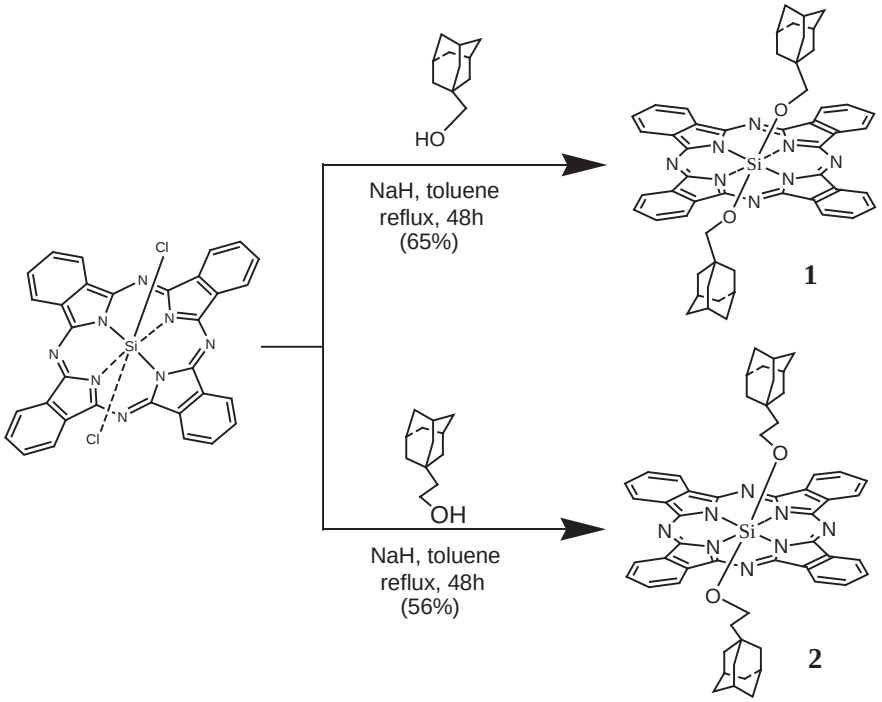


Fig. 1. An ORTEP diagram of the molecular structure of **2**.



Scheme 1. Preparation of compounds **1** and **2**.

2.2. X-ray crystal structure of compound 2

Compound **2** was also characterized structurally by X-ray diffraction analysis. The single crystal of **2** was obtained by recrystallization of **2** in $CHCl_3$/DMF solution. Fig. 1 shows a perspective view of the molecular structure of **2**, which contains an inversion center (at the silicon atom) relating two halves of the molecule. Selected bond distances and angles are given in Table 1. The central Si(IV) ion is six-coordinated by four nitrogen atoms from Pc ligand and two oxygen atoms from two substituents. The mean distances of Si–N bond and Si–O bond are 1.92 Å and 1.71 Å, respectively. These bond lengths are similar to that for other $SiPc(OR)_2$ molecules.[6c]

As shown in Fig. 2, compound **2** contains infinite stair-like stacks of phthalocyanine moieties. Here stacks of Pc ring are separated by layers of axial adamantanes with a distance of ca. 9.46 Å between Pc layers. This distance is more large than that of other SiPc derivatives (3.38–3.50 Å),[15] which should be attributed to the large hinderance effect of adamantine moieties.

Table 1
Selected geometrical parameters (Å, °)

Bond lengths			
Si1–O1	1.7057(11)	N4–C1	1.321(2)
Si1–N1	1.9190(13)	N4–C16	1.326(2)
Si1–N3	1.9302(13)	C7–C8	1.457(2)
O1–C17	1.4099(19)	C9–C10	1.450(2)
N1–C8	1.3805(19)	C4–C5	1.403(2)
N1–C1	1.3810(19)	C1–N4	1.321(2)
N2–C9	1.321(2)	C1–C2	1.451(2)
N2–C8	1.323(2)	C2–C3	1.396(2)
N3–C16	1.3768(19)	C2–C7	1.397(2)
N3–C9	1.3834(19)	C15–C16	1.447(2)
C17–C18	1.532(2)		
Bond angles			
O1–Si1–N1	86.79(5)	C8–N1–Si1	126.40(10)
O1–Si1–N1	93.21(5)	C1–N1–Si1	126.30(10)
O1–Si1–N3	88.06(5)	C16–N3–Si1	126.14(10)
O1–Si1–N3	91.94(5)	C9–N3–Si1	126.19(10)
N1–Si1–N3	90.02(6)	O1–C17–C18	110.51(13)
N1–Si1–N3	89.98(6)	O1–C17–H17A	109.5
C17–O1–Si1	130.11(10)	O1–C17–H17B	109.5

With the addition of 0.5% THF, compounds **1** and **2** could become soluble in PBS (phosphate buffer solution, pH=7.4). As shown in Fig. 3, both two compounds show a broad and weak Q-band peaking at ca. 682 nm in PBS. This indicates that they are highly aggregated in PBS. However, their Q-bands became intense and sharp when the PBS solution was added with 1% Cremophor EL. Cremophor EL has usually been used as a nontoxic surfactant to formulate a photosensitizer for in vitro and in vivo applications. Although the absorption intensity is still lower than that in DMF, the absorption basically follows the Lambert–Beer law for both compounds, suggesting that they mainly exist as a non-aggregated form in the 1% Cremophor EL solution.

Upon excitation at the 610 nm, these compounds showed a high fluorescence emission at 679–680 nm with a quantum yield (Φ_F) of 0.46–0.50 in DMF, while exhibited a lower fluorescence emission at 681–682 nm with a Φ_F of 0.22–0.24 in 1% Cremophor EL solution (Table 2 and Fig. 4). However, both compounds hardly presented the fluorescence emission in PBS, which is mainly due to their aggregated nature[15,16] in PBS as reflected by their absorption spectra.

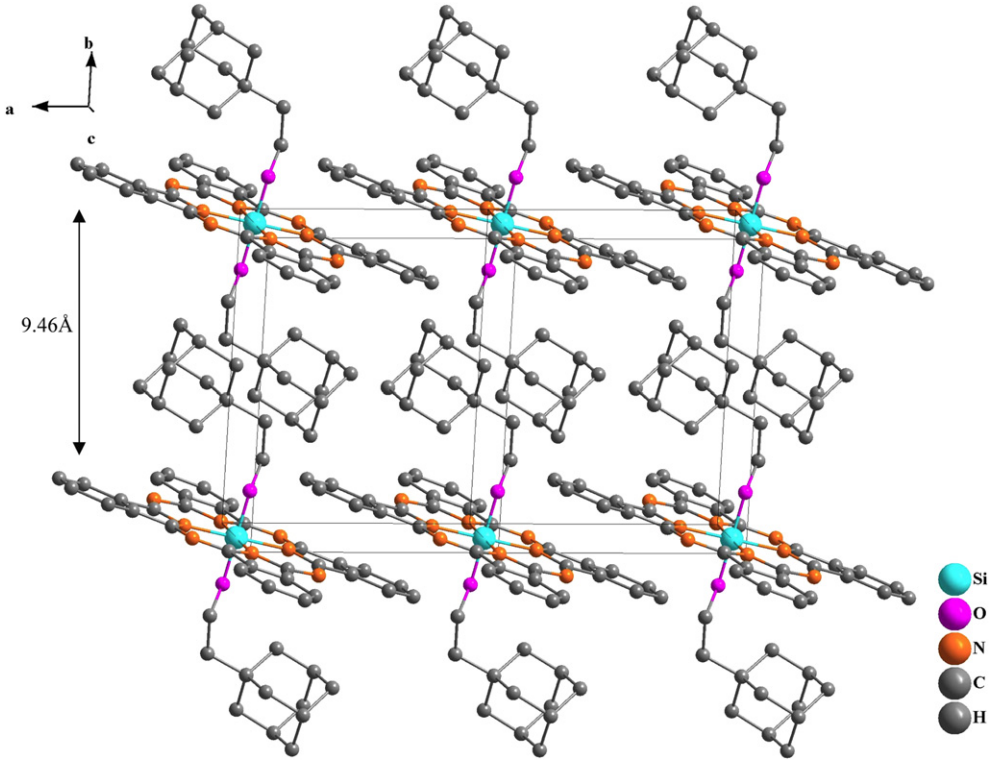


Fig. 2. Phthalocyanine stacking in the crystal packing of **2**.

2.3. Absorption and fluorescence spectroscopic properties

As shown in Fig. 3, the electronic absorption spectra of compounds **1** and **2** in *N*,*N*-dimethylformamide (DMF) were typical for non-aggregated phthalocyanines, showing a B (or Soret) bond at 354 nm, an intense and sharp Q band at 672–673 nm, together with two vibronic bands at 605 nm and 643 nm. For both compounds, the Q band strictly followed the Lambert–Beer law, indicating that two compounds are essentially free from aggregation in DMF. Monomeric spectra were also observed for these SiPcs in MeOH or tetrahydrofuran (THF).

2.4. Photochemical properties

To evaluate the photostabilities of the silicon phthalocyanines axially functionalized with adamantine moieties, the photodegradation behaviors of compounds **1** and **2** were analyzed in DMF by measuring the decrease of the intensity of the Q band over time by irradiation with red light under air. For comparison, the ZnPc and two other SiPcs (**3** and **4**) were also involved in this test. Compounds **3** and **4** (see Fig. 5) are silicon phthalocyanines containing the *N*-methylated acetylpiperzaine phenoxys or 4-hydroxyphenylacetamide as the axial substituent, which have been reported by us previously.[6d,g]

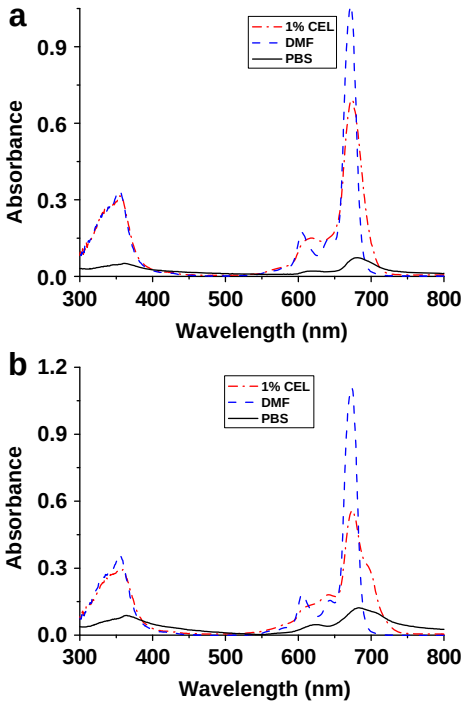


Fig. 3. Electronic absorption spectra of 5 μM of **1** (a) and **2** (b) in DMF, 1% CEL, and PBS. 1% CEL: a PBS solution containing 1% Cremophor EL (1 g in 100 mL of PBS).

Table 2
Electronic absorption and photophysical data for compounds **1** and **2**

Compound	Solvent	λ_{max} (nm)	λ_{em} (nm)[a]	Stokes shift (nm)	ε_{max} (10^5 cm^{-1} mol^{-1} L)	Φ_F[b]
1	DMF	672	679	7	2.08	0.46
	1% CEL[c]	674	682	8	1.36	0.24
2	DMF	673	680	7	2.30	0.50
	1% CEL	674	681	7	1.12	0.22

[a] Excited at 610 nm.
[b] Using unsubstituted zinc(II) phthalocyanine (ZnPc) in DMF as the reference[17] (Φ_F=0.28).
[c] A PBS solution containing 1% Cremophor EL (1 g in 100 mL of PBS).

The results are shown in Fig. 6 and Table 3. It can be seen that only a tiny decomposition was taken place for both **1** and **2**, while a substantial degradation was occurred to the ZnPc under the same condition. The decay of the absorbance maxima of the Q band for all three phthalocyanines obeyed first-order kinetics as shown in the insets of Fig. 6. The corresponding photodegradation first-order constants K for **1** and **2** are found to be $3.25-3.67\times10^{-4}$ min^{-1}, which is lower 100 times than that of ZnPc (2.30×10^{-2} min^{-1}). Smaller values of K mean higher photooxidative stability. In a word, compounds **1** and **2** are more than 100 times stable than ZnPc under the same irradiation condition. On the other hand, the SiPcs **1** and **2** containing adamantane moieties also show obviously higher photostabilities than other SiPcs **3** and **4** (see Table 3).

To evaluate the photosensitizing efficiencies of phthalocyanines **1** and **2**, their single oxygen quantum yields (Φ_Δ) were determined in DMF by a steady-state method using 1,3-diphenylisobenzofuran (DPBF) as the scavenger.[18] The concentration of the quencher was monitored spectroscopically at 411 nm over time, from which the Φ_Δ values were determined by the previously described method.[19] During the determination, the photodegradation of phthalocyanines was not observed as shown in Fig. 7, where there were not decreases in the Q band or formation of new bonds. Both phthalocyanines **1** and **2** are efficient single oxygen generator with the Φ_Δ of 0.40–0.43, although, which is a little lower than that of zinc phthalocyanine (ZnPc) (Table 3).

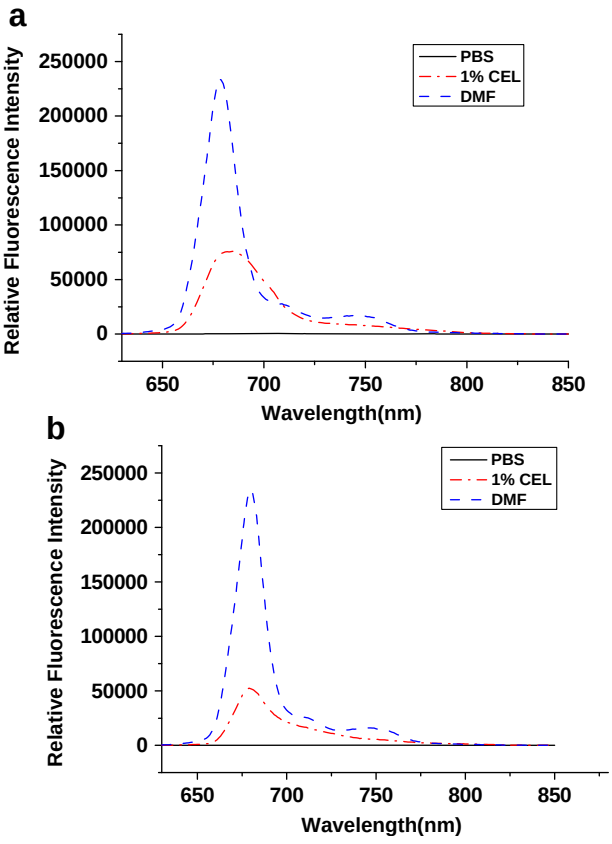


Fig. 4. Fluorescence spectra of 1.5 μM of **1**(a) and **2**(b) in DMF, 1% CEL, and PBS.

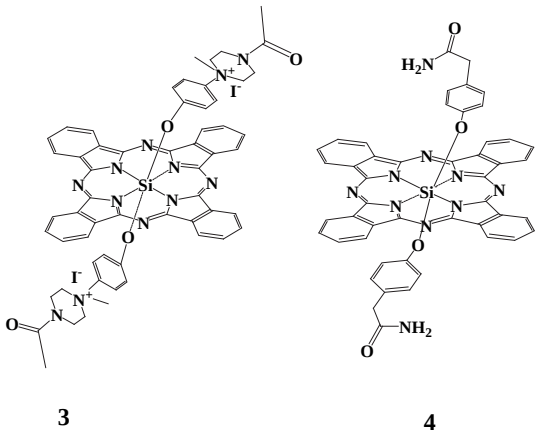


Fig. 5. Structures of silicon phthalocyanines **3** and **4**.

Under light irradiation, the ROS generated by the photosensitizer is known to be responsible for the decomposition of photosensitizer itself.[4] SiPcs **1** and **2** have the comparative singlet oxygen quantum yields compared with ZnPc and SiPc **3** (Table 3), but exhibit a remarkably higher photostability. It is believed that degradation of silicon phthalocyanine ring generally resulted from the attack of ROS on the silicon center.[4] Due to having rigid and large hindrance, the adamantanes at the axial position of silicon may efficiently prevent the ROS close the silicon and hence enhance the photostabilities of the corresponding silicon phthalocyanines. The very high photostabilities of compounds designed in this work

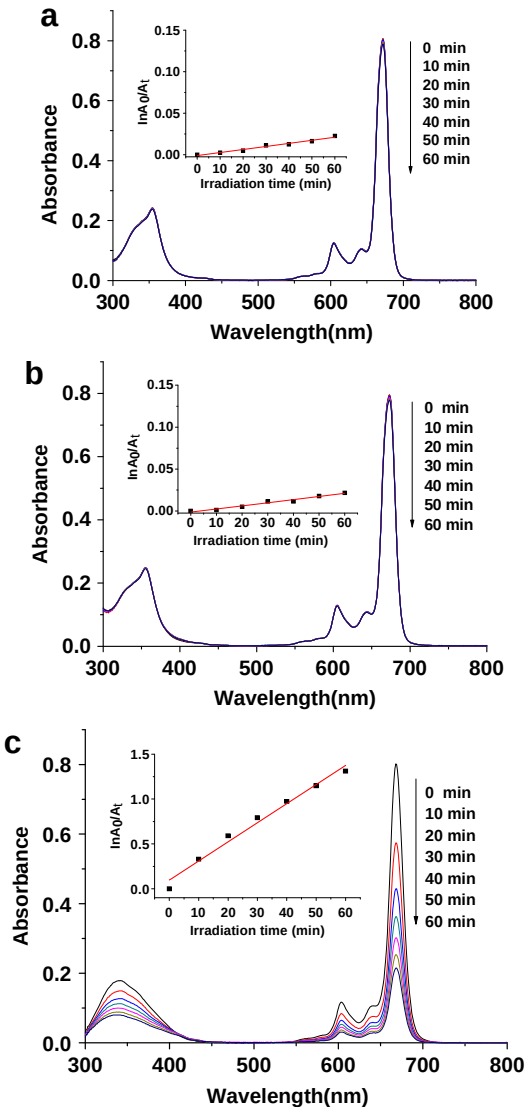


Fig. 6. Absorption spectra changes of **1** (a), **2** (b), and ZnPc (c) in DMF at 10 min intervals under irradiation with red light. The insets are the first-order plots for the photodegradation of phthalocyanines in DMF. The concentration of the samples is ca. 3.6 μM.

Table 3
Photochemical data for compounds **1** and **2** in DMF

Compound	**1**	**2**	**3**	**4**	ZnPc
K (min^{-1})	3.67×10^{-4}	3.25×10^{-4}	2.23×10^{-3}	1.34×10^{-3}	2.30×10^{-2}
Φ_Δ[a]	0.43	0.40	0.49[6d]	0.18[6g]	0.56

[a] Using ZnPc as the reference (singlet oxygen quantum yield Φ_Δ=0.56 in DMF).[18]

prove the feasibility of our idea that the photodecomposition of silicon phthalocyanines should be reduced by the axial adamantanes.

2.5. Interaction and conjugation with BSA

To further enhance the biocompatibilities of these silicon phthalocyanine-based photosensitizers for application in photodynamic therapy of cancer, attempts were made to prepare the bovine serum albumin (BSA) conjugates of these compounds. Being the most abundant serum protein in human, albumin has been used as carrier for targeted delivery of various anti-cancer drugs

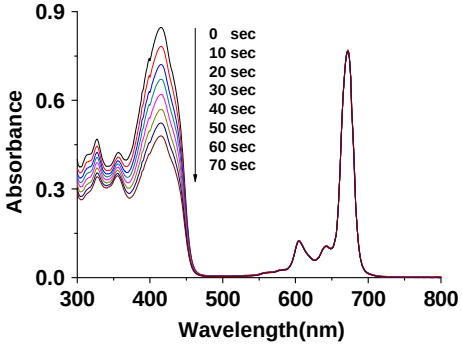


Fig. 7. The typical electronic absorption spectra for the measurement of singlet oxygen quantum yield of compound **1** in DMF ([**1**]=4 μM).

including doxorubicin, methotrexate, and mitomycin C.[20] Conjugation of photosensitizers to albumins has also been briefly studied.[21–23]

We first analyzed the interaction of compounds **1** and **2** with BSA by a fluorescence quenching method.[23] Fig. 8(a) shows the change of fluorescence emission spectra of BSA upon titration with **1**. With the increasing of concentration of **1**, the intrinsic emission band of BSA at 340 nm decreases in intensity and shifts gradually to 336 nm. The quenching data follow the Stern–Volmer equation as show in the inset of Fig. 7, giving a quenching constant (K_{sv}) of 5.32×10^4 M^{-1}. Compound **2** also exhibited a similar effect on the fluorescence of BSA (Fig. 8(b)), giving the K_{sv} of 4.57×10^4 M^{-1}. The

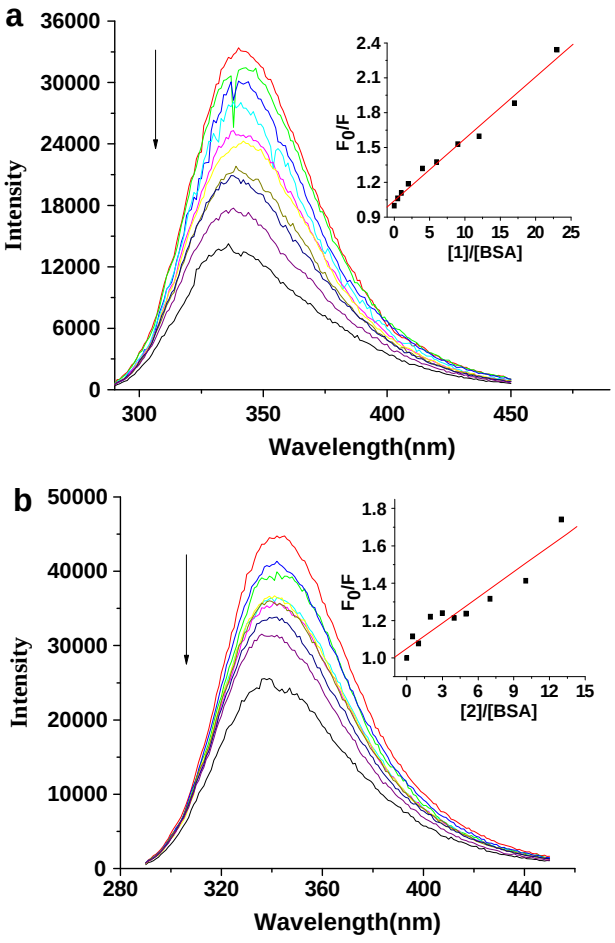


Fig. 8. Change in fluorescence spectrum of BSA (2 μM, excited at 280 nm) in PBS upon titration with **1** (a) or **2** (b). The inset shows the corresponding Stern–Volmer plot.

high K_{sv} values suggest that there are strong interactions between these two phthalocyanines and the protein.

In view of the strong interactions between these phthalocyanines and BSA, attempts were made to prepare their non-covalent conjugates according to the literature procedure.[23] The conjugates were obtained by stirring a mixture of **1** (or **2**) and BSA (with a molar ratio of 5) in PBS at ambient temperature overnight, followed by gel chromatography on a G-100 Sephadex column using PBS as eluent. The conjugates collected as the first blue fraction were then characterized by absorption spectrum and Bio-Rad protein assay kit. The molar ratio of phthalocyanine to BSA was found to be 4.5:1 for **1**–BSA and 3:1 for **2**–BSA conjugates.

As shown in Fig. 9, **1**–BSA exhibits a sharper Q-band at 689 nm than free **1** in PBS, and a band at 280 nm, which is the typical absorption of BSA. The spectra of **2**–BSA is very similar to that of **1**–BSA. The considerable sharp and intense Q-band absorption suggests that two silicon phthalocyanines **1** and **2** are relatively non-aggregated in albumin conjugates, which is an important desirable property for the PDT application.[2,4]

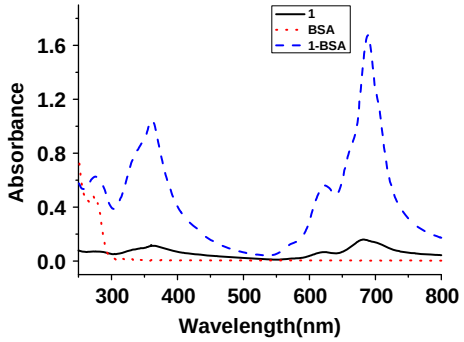


Fig. 9. Electronic absorption spectra of **1**, BSA and **1**-BSA in PBS ([1]=ca. 10 μM).

3. Conclusion

Two new silicon(IV) phthalocyanines axially substituted with adamantane moieties have been designed and synthesized. Both compounds are efficient photosensitizers with a singlet-oxygen quantum yield of 0.40–0.43. As expected, they are high photostable, exhibiting about 100 times more stable than zinc phthalocyanine, which may be attributed to the introducing of the axial rigid spherical adamentane substituents. Moreover, the rigid bulky axial ligands can efficiently isolate the chromophoric phthalocyanine ring as reflected by the crystal structure of compound **2**. As the result, these two compounds show typical monomeric absorption spectra in common organic solvents. In additional, two compounds can be successfully conjugated into BSA. Both **1** and **2** are mainly non-aggregated in albumin conjugates, which is an important desirable characteristic for the use in PDT. Future studies are in progress to evaluate the real application performances of these two high photostable SiPcs and their BSA conjugates.

4. Experimental

4.1. General

Reactions were performed under an atmosphere of nitrogen. Toluene was distilled from sodium. Cremophor EL and unsubstituted zinc(II) phthalocyanine (ZnPc) were obtained from Sigma–Aldrich. Chromatographic purifications were performed on silica gel columns (100–200 mesh, Qingdao Haiyang Chemical Co., Ltd, China) with the indicated eluents. All other solvents and reagents were of reagent grade and used as received. Silicon phthalocyanine dichloride was prepared according to literature procedures.[24]

^{1}H NMR spectra were recorded on a Bruker DPX 300 spectrometer (300 MHz) in $CDCl_3$. Chemical shifts were relative to internal $SiMe_4$ (δ=0 ppm). Mass spectra were recorded on a Finnigan LCQ Deca xpMAX mass spectrometer. Elemental analyses were performed by Element Vario EL III equipment. IR spectra were recorded on a Perkin–Elmer SP2000 FT-IR spectrometer, using KBr disks. Electronic absorption spectra were measured on a Perkin–Elmer Lambda 900 UV–vis–NIR spectrophotometer. Fluorescence spectra were taken on an Edinburgh FL900/FS900 spectrofluorometer.

4.2. Synthesis

*4.2.1. Silicon phthalocyanine **1**.* Silicon(IV) phthalocyanine dichloride (61 mg, 0.1 mmol) was treated with 1-adamantanemethanol (166 mg, 1 mmol) and NaH (24 mg, 1 mmol) in toluene (30 mL). After evaporating the solvent in vacuo, the residue was washed with water, followed by chromatography on a silica gel column using ethyl acetate as eluent to give compound **1** as a blue solid (57 mg, 65%). IR (KBr, cm^{-1}): 1591, 1429, 1335, 1292, 1166, 1124, 1082, 911, 760 (Pc ring); 2921, 2851, 1472 (CH_2); 1007 (Si–O). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 9.66–9.63 (m, 8H, Pc-H_α); 8.35–8.32 (m, 8H, Pc-H_β); 0.74–0.71 (m, 12H, CH_2); 0.33–0.30 (m, 6H, CH); −1.36 to −1.35 (m, 12H, CH_2); −2.62 (s, 4H, CH_2). MS (ESI) m/z 871.1$[M+H]^+$. Anal. Calcd for $C_{54}H_{50}N_8O_2Si$: C, 74.45; H, 5.79; N, 12.86. Found: C, 73.89; H, 5.47; N, 12.39.

*4.2.2. Silicon phthalocyanine **2**.* By using the above procedure, silicon(IV) phthalocyanine dichloride (61 mg, 0.1 mmol) was treated with 1-adamantaneethanol (180 mg, 1 mmol) and NaH (24 mg, 1 mmol) in toluene (30 mL) to give the product **2** as a blue solid (50 mg, 56%). IR (KBr, cm^{-1}): 1614, 1520, 1428, 1336, 1289, 1164, 1123, 1081, 910, 759, 736 (Pc ring); 2896, 2844, 1472 (CH_2); 999 (Si–O). ^{1}H NMR (300 MHz, $CDCl_3$, ppm): δ 9.64 (m, 8H, Pc-H_α); 8.31 (m, 8H, Pc-H_β); 1.031 (m, 12H, CH_2); 0.879 (m, 6H, CH); 0.79 (s, 12H, CH_2); −0.69 (s, 4H, CH_2); −1.98(s, 4H, CH_2). MS (ESI) m/z 898.4 $[M]^+$. Anal. Calcd for $C_{56}H_{54}N_8O_2Si$: C, 74.80; H, 6.05; N, 12.46. Found: C, 74.46; H, 6.29; N, 11.38.

4.3. X- ray crystallographic analysis

The X-ray intensity data were collected at 293(2) K on a Rigaku R-AXIS RAPID X-ray diffractometer system with graphite-monochromated Mo K_α radiation (0.71073 Å), using the u and x-scan technique. The structure was solved by direct methods using the SHELXTL 6.1 bundled software package.[25] Absorption corrections were applied with SADABS. All non-hydrogen atoms were refined anisotropically. The hydrogen atoms were placed in geometrically idealized positions and refined as riding atoms, with U_{iso}(H)= 1.2U_{eq}(N). Crystallographic data and the processing parameters are given in Table 4. The crystallographic information file is deposited in the Cambridge Crystallographic Data Center as CCDC 743601.

4.4. Photophysical and photochemical properties

4.4.1. Fluorescence quantum yield. The fluorescence quantum yields (Φ_F) were determined are measured by the equation: $\Phi_{F(sample)}=(n^2_{sample}/n^2_{ref})\cdot(F_{sample}/F_{ref})\cdot(A_{ref}/A_{sample})\cdot\Phi_{F(ref)}$, where F, A, and n are the measured fluorescence (area under the emission peak), the absorbance at the excitation position (610 nm), and the refractive index of the solvent, respectively. Unsubstituted zinc(II)

Table 4
Crystallographic data and final refinement parameters for compound **2**

Empirical formula	$C_{56}H_{54.32}N_8O_{2.16}Si_1$
Molecular weight	902.22
T (K)	123(2) K
Crystal system	Triclinic
Space group	P-1
a (Å)	8.657(2)
b (Å)	11.255(2)
c (Å)	11.789(2)
α (°)	76.19
β (°)	81.16
γ (°)	88.66
V (Å^3)	1102.0(4)
Z	1
F(000)	478
D_{calcd} (g cm^{-3})	1.359
μ (mm^{-1})	0.110
Crystal size (mm^3)	0.26×0.16×0.06
T_{min}/T_{max}	0.91/1.00
Reflections collected/unique/observed	8653/4948/4209
R(int)	0.0203
Refinement on	F^2
Data/restraints/parameters	4948/0/308
Final R_1/R_2 indices [$I>2\sigma(I)$]	$R1$=0.0429, $wR2$=0.1196
Largest diff. peak and hole	0.486 and −0.492 e Å^3
Goodness-of-fit on F^2	1.124

phthalocyanine (ZnPc) in DMF was used as the reference [$\Phi_{F\,(ref)}$=0.28].[17]

4.4.2. Photostability. The photostabilities of phthalocyanines were determined by the decay of the intensity of the Q band after exposure to red light.[26] The light source consisted of a 150 W halogen lamp, a water tank for cooling, and a color glass filter cut-on 610 nm. Measurements were carried out under air in DMF. The photodegradation rate constants k were calculated by the equation: $\ln A_0/A_t=kt$, where t, A_0, A_t are the irradiation time, absorbance at t=0, absorbance at different time, respectively.

4.4.3. Singlet oxygen yield. The singlet oxygen quantum yields (Φ_Δ) were determined by a steady-state method using DPBF (1,3-diphenylisobenzofuran) as the scavenger in DMF.[18] The DMF solution of phthalocyanine (ca. 4 μM) containing DPBF (35 μM) was prepared in the dark and irradiated with red light, then DPBF degradation at 411 nm was monitored along with irradiated time. The singlet oxygen quantum yields (Φ_Δ) is calculated by the equation: $\Phi_{\Delta(sample)}=(k_{sample}/k_{ref})\cdot(A_{ref}/A_{sample})\cdot\Phi_{\Delta(ref)}$, where $\Phi_{\Delta(ref)}$ is the singlet oxygen quantum yield for the reference (unsubstituted ZnPc) in DMF ($\Phi_{\Delta(ref)}$=0.56),[18] k_{sample} and k_{ref} are the DPBF photobleaching rates in the presence of the samples and reference, respectively; A_{ref} and A_{sample} are the absorbance at Q band (area under the absorption spectra in 610–750 nm) of the samples and reference, respectively. The light source is similar to that described above, but the fluence of light was adjusted to about 10% of that used in the determination of the photostability.

4.5. Silicon phthalocyanine–BSA conjugate

A solution of **1** or **2** in tetrahydrofuran (THF) (1.0 mM) was added dropwise to a solution of bovine serum albumin (BSA) (30 mM) in PBS (phosphate buffer solution, pH=7.4). The molar ratio of phthalocyanine to BSA in the mixture was adjusted to 5:1. This mixture was stirred at ambient temperature overnight, then chromatographed on a G-100 Sephadex column (Sigma, dry bead diameter=40–120 μm) (1.8×19 cm) using PBS as eluent. The conjugates collected as the first blue fraction were then characterized. The protein content was determined with the Bio-Rad protein assay kit using BSA as standard.[27] The phthalocyanine concentration was calculated from the Q band absorbance in a diluted DMF solution with reference to the corresponding molar absorptivity.

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Supplementary data

Supplementary data associated with this article can be found in the online version, at doi:10.1016/j.tet.2010.09.007. These data include MOL files and InChIKeys of the most important compounds described in this article.

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