Medicinal Chemistry Research (2018) 27:1478–1484
https://doi.org/10.1007/s00044-018-2166-0

MEDICINAL CHEMISTRY RESEARCH

ORIGINAL RESEARCH

Optimal axial alkylpyridinium-bonded tricationic P-porphyrin in photodynamic inactivation of *Escherichia coli*

Jin Matsumoto[1] · Masahide Yasuda[1]

Received: 21 December 2017 / Accepted: 5 March 2018 / Published online: 28 March 2018

Abstract
Alkylpyridinium (Apy)-bonded porphyrins have received considerable attention as singlet-oxygen ($^1O_2$) sensitizers for photodynamic inactivation (PDI). It is expected that the introduction of Apy makes porphyrins water-soluble and enhances the affinity of porphyrins to DNA. Here, we focused on Apy-bonded P-porphyrins that were prepared through the modification of axial ligands of *meso*-tetraphenylporphyrinatophosphorus by the Apy's group and linkers. These water-soluble porphyrins (**1**) were applied to sensitize the inactivation of *Escherichia coli* under visible-light irradiation, since there are only few $^1O_2$ sensitizers that can efficiently inactivate *E. coli* at low concentrations. The PDI activities were evaluated using the half-life ($T_{1/2}$ in min) of *E. coli* and the minimum effective concentrations ([*P*]) of the porphyrin sensitizers. It was found that the PDI activity towards *E. coli* depends on the alkyl chain length of Apy. The [*P*] value for *E. coli* was optimized to be 0.25 μM of bis[5-(3- ethyl-1-pyridinio)-3-oxapentyloxo]tetraphenylporphyrinatophosphorus dibromide chloride (**1b**). Since the previous results on the optimized [*P*] value for *S. cerevisiae* was 50 nM for **1b**, it was found that the [*P*] value for *E. coli* was larger than that for *S. cerevisiae*.

Keywords Photoinactivation · P-porphyrins · Alkylpyridinium · *Escherichia coli*

Introduction

Photodynamic inactivation (PDI) of bacteria has received considerable attention as a methodology leading to the medical application such as photodynamic therapy for tumor cells. PDI refers to the use of a visible-light source, oxidizing agents (e.g., O_2), and photosensitizers. Photosensitizers absorb light energy that causes an energy transfer to O_2, which leads to the formation of reactive oxygen such as singlet oxygen ($^1O_2$), thereby inactivating cells and bacteria. Preliminary studies on the photodynamic action for biological systems started in 1930s by the PDI of phages using methylene blue (Clifton 1931; Perdrau and Todd 1933). Among the large variety of photosensitizers developed for PDI over the last 60 years, porphyrins and metalloporphyrins become attractive sensitizers owing to their strong absorption band in the visible-light region (Pandey and Zheng 2000; Nyman and Hynninen 2004; Shiragami et al. 2005; Ethirajan et al. 2011).

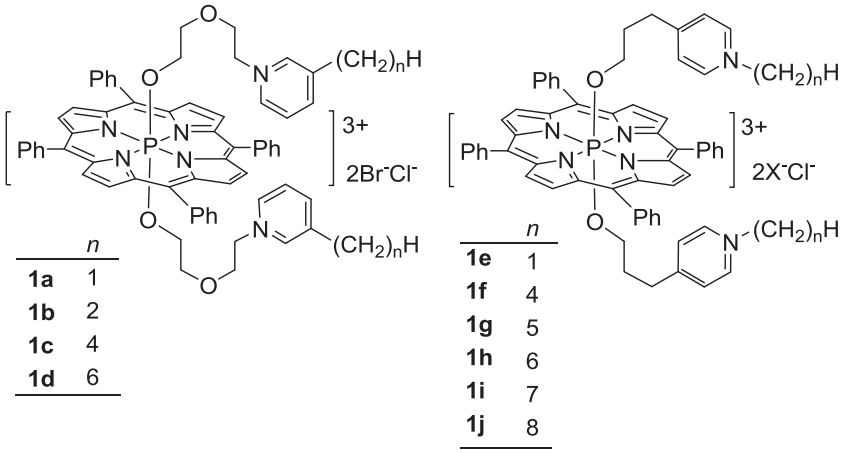
For biological applications of porphyrins, their water solubility is an important characteristic for handling the aqueous solution. However, in general, porphyrin derivatives have poor water-solubility. The introduction of cationic groups into porphyrins is the most popular method to enhance the water solubility of porphyrins. In particular, the introduction of an alkylpyridinium (Apy) group into porphyrins is a convenient method to make porphyrins water-soluble (Kalyanasundaram 1984; Girek and Sliwa 2013). A typical Apy-bonded porphyrin is represented by *meso*-tetra [4-(1-methylpyridinium)]porphyrin (TMP). The first application of TMP to PDI was reported by Ben Amor et al. in 1998 (Ben Amor et al. 1998). For the last two decades, a variety of Apy-bonded porphyrins have been prepared and studied for PDI (Kano et al. 2000; Kubát et al. 2000; Trommel and Marzilli 2001; Lang et al. 2004; Banfi et al. 2006; Haeubl et al. 2009; Batinic-Haberle et al. 2012). We have interested in axially Apy-bonded tricationic P-porphyrins (**1**, Scheme 1) (Matsumoto et al. 2013;

✉ Jin Matsumoto
jmatsu@cc.miyazaki-u.ac.jp

✉ Masahide Yasuda
yasuda@cc.miyazaki-u.ac.jp

[1] Department of Applied Chemistry, Faculty of Engineering, University of Miyazaki, Gakuen-Kibanadai Nishi, Miyazaki 889-2192, Japan

Scheme 1 Tricationic P-porphyrins bonded to alkylpyridinium (Apy) (**1a**−**1j**)



	n
1a	1
1b	2
1c	4
1d	6

	n
1e	1
1f	4
1g	5
1h	6
1i	7
1j	8

Matsumoto et al. 2016; Matsumoto et al. 2017a). It is advantageous that the water solubilization is easily achieved through the modification of the axial ligands. Recently we have reported the PDI of *E. coli* using several kinds of axially Apy-bonded P-porphyrins (**1e**–**1j**) (Matsumoto et al. 2017a). Here, to develop more efficient $^1O_2$ sensitizers than **1e**–**1j**, we assessed the potential of another type of Apy-bonded P-porphyrins (**1a**–**1d**) in the PDI of *E. coli*.

Materials and methods

Instruments

^{1}H nuclear magnetic resonance (NMR) (400 MHz) and ^{13}C NMR (100 MHz) spectra were obtained with a Bruker AV 400 M spectrometer in CD_3OD solutions using $SiMe_4$ as an internal standard. High-resolution mass spectra (HRMS) were measured on a Thermo Scientific Q Exactive mass spectrometer equipped with an electrospray ionization source. The molar absorption coefficients (ε) of **1** at the Soret and Q bands were determined from the visible spectra measured in MeOH using a JASCO V-550 spectrophotometer. The fluorescence spectra of solutions were measured on a Shimadzu RF-5300PC spectrometer. Time-resolved fluorescence lifetime were measured via time-correlated single photon counting using a lifetime fluorescence spectrometer (Horiba, DeltaFlex) equipped with a PPD detector and a pulsed laser diode (Horiba, DeltaDiode DD-415L, peak wavelength: 419 nm, pulse width: 70 ps). Fluorescence at 595 nm emitted from MeOH solution of **1** under aerated conditions was collected with a monochrometer on the spectrometer.

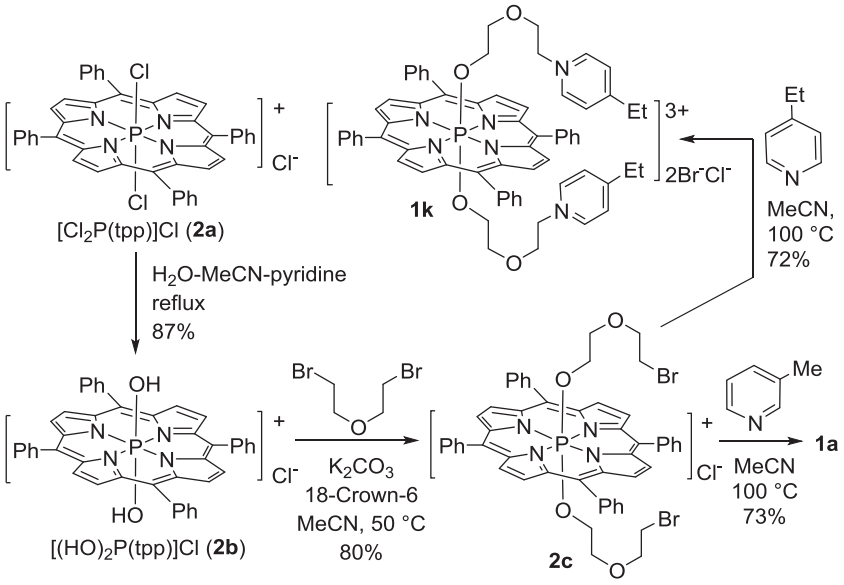
General procedure for the preparation of Apy-bonded tricationic P-porphyrins (1a–1d)

As we have described in previous reports (Matsumoto et al. 2013), [$(HO)_2$P(tpp)]Cl (**2b**, tpp = tetraphenylporphyrino), which was prepared by hydrolysis of [Cl_2P(tpp)]Cl (**2a**; 300 mg) by refluxing in a mixed solvent of MeCN (160 mL) with pyridine (60 mL) and H_2O (60 mL), was used as starting material (Scheme 2). Bis(5-bromo-3-oxa-pentyloxo)tetraphenylporphyrinatophosphorus(V) chloride (**2c**) was synthesized by the alkylation of **2b** (80 mg) with di(2-bromoethyl) ether (1 mL) in the presence of K_2CO_3 (19 mg) and 18-crown-6 ether (4.2 mg) in MeCN (5 mL) at 50 °C. The compound bis[5-(3-methyl-1-pyridinio)-3-oxa-pentyloxo]tetraphenylporphyrinatophosphorus(V) dibromide, chloride (**1a**) was prepared via the reaction of **2c** (51 mg) with 3-methylpyridine (1.0 mL) in dry MeCN (10 mL) at 100 °C for 20 h. Similarly bis[5-(4-ethyl-1-pyridinio)-3-oxapentyloxo]tetraphenylporphyrinatophosphorus(V) dibromide chloride (**1k**) was prepared via the reaction of **2c** (63 mg) with 4-ethylpyridine (1.0 mL) in dry MeCN (10 mL) at 100 °C for 20 h. Spectroscopic characterizations of **1b**−**1d** have been reported in previous studies (Matsumoto et al. 2013; Matsumoto et al. 2017b). The spectral data of newly prepared 3-methyl analog (**1a**) and 4-ethyl analog (**1k**) are provided as follows.

Bis[5-(3-methyl-1-pyridinio)-3-oxapentyloxo]tetraphenylporphyrinatophosphorus(V) dibromide chloride (1a)

Yield 73% from [$(HO)_2$P(tpp)]Cl. ^{1}H NMR (400 MHz, CD_3OD): δ −2.20 (dt, $J_{P-H} = 11.1$ Hz, $J = 4.6$ Hz, 4H, P–OC$\underline{H}_2$CH_2O–), 0.70 (brs, 4H, P–OCH_2C$\underline{H}_2$O–), 2.25 (s, 6H, CH_3), 2.43 (t, $J = 4.7$ Hz, 4H, –OC$\underline{H}_2$CH_2N–), 3.84 (t, $J = 4.7$ Hz, 4H, –OCH_2C$\underline{H}_2$N–), 7.46 (dd, $J = 8.0$, 6.0 Hz, 2H, H-5 of C_5H_4N), 7.74 (d, $J = 6.0$ Hz, 2H, H-4 of C_5H_4N), 7.80–7.86 (m, 12H, H-3, H-4, and H-5 of C_6H_5), 7.99–8.01 (m, 8H, H-2, and H-6 of C_6H_5), 8.04 (s, 2H, H-2 of C_5H_4N), 8.20 (d, $J = 8.0$ Hz, 2H, H-6 of C_5H_4N), 9.18 (d, $J_{P-H} = 2.9$ Hz, 8H, pyrrole β); ^{13}C NMR (100 MHz, CD_3OD): δ 18.31 (CH_3), 60.85 (–O$\underline{C}H_2$CH_2N), 61.68 (d, $J_{P-C} = 13.9$ Hz, P–OCH_2C$\underline{H}_2$O–), 68.25 (d, $J_{P-C} = 18.9$ Hz, –O$\underline{C}H_2$CH_2N), 68.74 (–OCH_2C$\underline{H}_2$N), 117.63 (*meso*),

Scheme 2 Preparation of tricationic P-porphyrins (**1a** and **1k**)



127.73 (C-5 of C_5H_4N), 129.6 (C-3 of C_6H_5), 131.0 (C-4 of C_6H_5), 134.6 (d, $J_{P-C} = 5.1$ Hz, pyrrole β), 134.7 (C-2 of C_6H_5), 136.7 (C-1 of C_6H_5), 140.4 (C-4 of C_5H_4N), 140.5 (pyrrole α), 142.6 (C-2 of C_5H_4N), 145.1 (C-3 of C_5H_4N), 147.2 (C-6 of C_5H_4N); HRMS calcd for $C_{64}H_{58}N_6O_4P^{3+}$ [M^{3+}]: 1005.4241, *m/z* 335.1414. Found: 335.1415.

Bis[5-(4-ethyl-1-pyridinio)-3-oxapentyloxo]tetraphenylporphyrinatophosphorus(V) dibromide chloride (1k)

Yield 72% from [$(HO)_2$P(tpp)]Cl. ^{1}H NMR (400 MHz, CD_3OD): δ −2.18 (dt, $J_{P-H} = 10.3$ Hz, $J = 5.1$ Hz, 4H, P–OC$\underline{H}_2$CH_2O–), 0.72 (brs, 4H, P–OCH$_2$C$\underline{H}_2$O–), 1.26 (t, $J = 7.5$ Hz, 6H, CH_3), 2.41 (t, $J = 4.5$ Hz, 4H, –OC$\underline{H}_2$CH$_2$N), 2.84 (q, $J = 7.5$ Hz, 4H, –C$\underline{H}_2$CH$_3$), 3.80 (t, $J = 4.5$ Hz, 4H, –OCH$_2$C$\underline{H}_2$N), 7.50 (d, $J = 6.2$ Hz, 4H, H-3 of C_5H_4N), 7.82–7.86 (m, 12H, H-3, H-4, and H-5 of C_6H_5), 7.87 (d, $J = 6.2$ Hz, 4H, H-2 of C_5H_4N), 8.00–8.02 (m, 8H, H-2 and H-6 of C_6H_5), 9.17 (d, $J_{P-H} = 2.7$ Hz, 8H, pyrrole β); ^{13}C NMR (100 MHz, CD_3OD): δ 13.83 (–CH$_2$C$\underline{H}_3$), 29.71 (–C$\underline{H}_2$CH$_3$), 60.27 (–OC$\underline{H}_2$CH$_2$N), 62.00 (brs, P–OC$\underline{H}_2$CH$_2$O–), 68.44 (brs, P–OCH$_2$C$\underline{H}_2$O–), 68.94 (–OCH$_2$C$\underline{H}_2$–N), 117.78 (brs, *meso*), 127.98 (C-3 of C_5H_4N), 129.70 (C-3 of C_6H_5), 131.04 (C-4 of C_6H_5), 134.62 (d, $J_{P-C} = 3.5$ Hz, pyrrole β), 134.83 (C-2 of C_6H_5), 136.80 (C-1 of C_6H_5), 140.60 (pyrrole α), 144.82 (C-1 of C_5H_4N), 166.19 (C-4 of C_5H_4N); HRMS Calcd for $C_{66}H_{62}N_6O_4P^{3+}$ [M^{3+}]: 1033.4554, *m/z* 344.4851. Found: 344.4845. Molar absorption coefficients of **1k** in MeOH were much smaller than that of **1b**, because of broadening of Soret and Q bands in UV–Vis absorption spectra due to aggregation of porphyrin chromophores (Fig. 1). As a results, **1k** did not show clear ^{13}C NMR spectrum and the

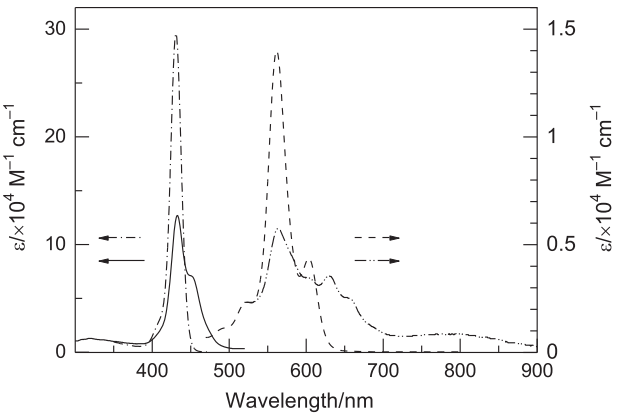


Fig. 1 UV–Vis absorption spectra of **1b** (botted line) and **1k** (solid line) in MeOH

doublet peak for the carbons at P–OC$\underline{H}_2$C$\underline{H}_2$O–, *meso* position, and pyrrole-β.

Photoinactivation of *E.coli*

E. coli K-12 (IFO 3335) was cultured aerobically at 30°C for 8 h in a basal medium (pH 6.5) consisting of bactotryptone (10 g L^{-1}), yeast extract (5 g L^{-1}), and NaCl (10 g L^{-1}). After centrifugation of the cultured broth at 12,000 rpm for 10 min, the harvested cells were washed with physiological saline (NaCl, 7 g L^{-1}) and then suspended in physiological saline, resulting in a cell suspension of *E. coli* (6.4×10^4 cells mL^{-1}). The cell concentrations were determined using a calibration curve and turbidity quantified by the absorbance measured at 600 nm on a UV −Vis spectrometer.

A phosphate buffer (0.1 M, pH 7.6) was prepared by dissolving Na_2HPO_4 (2.469 g) and NaH_2PO_4 (0.312 g) in 100 mL of water. The suspension of *E. coli* cells (1×10^5 cells mL^{-1}, 1.0 mL), an aqueous solution of **1a**−**1d** and **1k** (40–200 μM, 0.1 mL), and the phosphate buffer (0.1 M, pH 7.6, 8.9 mL) were introduced into L-type glass tubes, resulting in buffer solution (10 mL) containing *E.coli* (1×10^4 cells mL^{-1}) and **1a**−**1d** and **1k** (0.25−1.0 μM). The L-type glass tubes were set on a reciprocal shaker and shaken at 160 rpm at room temperature for 2 h under dark conditions (Matsumoto et al. 2017a). Irradiation was performed using a fluorescent lamp (Panasonic FL-15ECW, Japan; λ = 400–723 nm; the maximum intensity: 545 nm; 10.5 W cm^{-2}) on a reciprocal shaker for 2 h at room temperature. A portion of the reaction mixture (0.1 mL) was taken at 20-min intervals and plated on an agar medium.

The amount of the living cells (B) was defined as the average number of *E. coli* colonies that appeared after an incubation period of 30 h at 30 °C in three replicate plates. The B values for **1a**–**1d** and **1k** were recorded at each irradiation times, as summarized in Table 1.

Results and discussion

Axially Apy-bonded P-porphyrins

The values of water solubility (C_W) of **1a**–**1k** are listed in Table 2. In addition, Table 2 lists the coefficient (ε) of Soret band around 431 nm and Q-band at 562 nm. Effect of Apy group on the physicochemical properties of porphyrin was examined using $[(MeO)_2P(tpp)]Cl$ (**3a**, Scheme 3) as a reference porphyrins without Apy. The absorption coefficient (ε) of **3a** was determined to be $3.12 \times 10^5\ M^{-1}\ cm^{-1}$ for Soret band (λ_{max} = 424 nm) and $1.82 \times 10^4\ M^{-1}\ cm^{-1}$ for Q band (554 nm). The reduction potential ($E_{1/2}^{red}$ vs. Ag/$AgNO_3$) of **3a** was measured to be −0.82 V. The fluorescence of **3a** was observed at 610 nm under excitation at 550 nm. The fluorescence quantum yield (Φ_F) and fluorescence lifetime (τ_F) of **3a** was 0.0388 and 4.64 ns, respectively. In contrast, **1d** with Apy group has $E_{1/2}^{red}$ (−0.85 V), Φ_F (0.0350), and τ_F (4.91 ns) (Matsumoto et al. 2015). These physicochemical values were similar to those of **3a**. Thus, the introduction of the Apy on axial ligands does not affect the physicochemical parameters of the P(tpp) moiety. Moreover, the **1** could sensitize $^1O_2$ formation in high efficiency. The quantum yields for the formation of $^1O_2$ were measured to be 0.87 for **1d** (Matsumoto et al. 2017a). The reduction potentials of the P-porphyrins shifted to positive compared with the free-base porphyrins due to more positive pentavalent phosphorus. Therefore, they are expected to have abilities of electron transfer sensitizer in addition to energy transfer sensitizer.

PDI activity of 1a−1d and 1k

The PDI of *E. coli* was performed by irradiation of buffer solution (10 mL) containing *E.coli* (1×10^4 cells mL^{-1}) and **1a**−**1d** and **1k** (0.25−1.0 μM) for 2 h using a fluorescent lamp at 545 nm. Based on Table 1, the survival ratios were calculated as $100B/B_0$ where B_0 is the initial amount of *E. coli*. From the time-course plots of survival ratios, the half-life ($T_{1/2}$ in min), i.e., the time required to reduce B from B_0 to $0.5B_0$, was measured. The minimum concentrations of the sensitizer ([P]) were adjusted such that $T_{1/2}$ attained values between 20 and 120 min. Thus, the bactericidal activity (A_F in $\mu M^{-1}\ h^{-1}$) was evaluated using the following equation: $A_F = 60/([P] \times T_{1/2})$. Table 2 summarizes [$P$], $T_{1/2}$, and A_F values of **1a**–**1d** and **1k** along with those of **1e**–**1j**.

Table 1 The amount of living cells (B) in PDI of *Escherichia coli* using **1**

NO.	1	[P]/μM[a]	Amount of bacteria (B)/10^2 cell mL^{-1} [b]						
			$t = 0$[c]	20	40	60	80	100	120
1	**1a**	1.00	29 ± 6.4	16 ± 4.2	12 ± 5.6	10 ± 1.0	13 ± 2.3	6.7 ± 2.1	6.7 ± 1.5
2	**1b**	0.25	167 ± 14	141 ± 18	59 ± 9.0	5.7 ± 0.6	1.7 ± 1.5	0.3 ± 0.6	0
3	**1c**	0.25	145 ± 11	123 ± 7.6	92 ± 7.5	63 ± 4.6	33 ± 8.4	6.7 ± 4.9	4.7 ± 0.6
4	**1d**	0.25	213 ± 10	213 ± 9.5	176 ± 16	166 ± 6.8	140 ± 8.2	132 ± 12	97 ± 4.4
5	**1k**	0.50	139 ± 14	85 ± 13	88 ± 16	62 ± 6.0	42 ± 8.7	32 ± 7.0	33 ± 1.5

PDI was performed for the aqueous solution (10 mL) containing bacteria (approximately 1×10^4 cell mL^{-1}) and **1** (0.25−1.00 μM). Under dark conditions, no PDI occurred

[a][P]: Minimum effective concentration of **1**

[b]The amount of living cells (B) was defined as the average number of the colonies of *E. coli* that appeared on an agar medium after incubation for 24 h in three replicate plates

[c]Reaction time (t) in min

Table 2 The PDI of *E. coli* by porphyrins (**1a**–**1j**)

1	Yield /%[a]	R	*n*	ε[b]/10^4 M^{-1} cm^{-1}		C_W[c] /mM	[*P*][d]/μM	$T_{1/2}$[e] /min	A_F[f] /μM^{-1} h^{-1}
				Soret	Q				
1a	73	3-Me	1	28.2	1.36	>120	1.00	40	1.5
1b	58	3-Et	2	29.6	1.40	>120	0.25	32	7.5
1k	72	4-Et	2	12.7[g]	0.57[g]	>120	0.50	50	2.4
1c	44	3-Bu	4	25.3	1.29	112	0.25	53	4.5
1d	44	3-Hex	6	24.7	1.22	64	0.25	120	2.0
1e	95	*N*-Me	1	26.9	1.38	3.4	2.00	66	0.5
1f	93	*N*-Bu	4	23.1	1.18	6.1	2.00	27	1.1
1g	32	*N*-Pent	5	27.2	1.32	3.8	0.50	29	4.1
1h	91	*N*-Hex	6	31.3	1.45	5.8	0.50	31	3.9
1i	32	*N*-Hep	7	26.7	1.26	6.0	0.40	24	6.3
1j	48	*N*-Oct	8	18.7	0.97	3.8	0.50	63	1.9

The data for **1e**–**1j** were referred from Matsumoto et al. 2017b

[a]Isolated yields of **1** for the preparation from the precursors

[b]Molar absorption coefficient for the Soret and Q bands in the MeOH solution. Absorption maxima of Soret and Q band appeared at 431 nm 562 nm, respectively

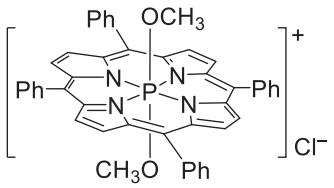
[c]C_W: Water solubility in mM

[d][*P*]: Minimum effective concentrations of the porphyrins adjusted to obtain the value of $T_{1/2}$ between 20 and 120 min

[e]$T_{1/2}$: Half-life in min

[f]A_F = The PDI activity in μM^{-1} h^{-1} = 60/([*P*] × $T_{1/2}$)

[g]Broadening of UV spectra occurred



3a

Scheme 3 Structure of [$(MeO)_2$P(tpp)]Cl (**3a**)

Optimization of carbon atoms (*n*) in the alkyl group on the APy group

As shown in Table 2, the A_F values varied by the number of carbon atoms (*n*) in the alkyl group on the APy group in a series of **1a**−**1d** and **1k**. Figure 2 shows the dependence of the A_F values on *n*. The maximum value of A_F appeared at *n* = 2 (**1b**) whose [*P*] value for *E. coli* was 0.25 μM. Therefore, the optimized A_F and [*P*] values of **1b**, which was 3-ethyl analog, were compared with that of 4-ethyl analog (**1k**). It was found that the A_F value of **1k** was lower than that of **1b**. As shown in Fig. 1, broadening of Soret and Q bands occurred due to aggregation of porphyrin chromophores. It is suggested that aggregation caused to lower the A_F value of **1k**. As has reported previously in a series of **1e**−**1j** (Matsumoto et al. 2017a), the optimized [*P*] value in PDI of *E. coli* was 0.40 μM in **1i** whose *n* was 7. Thus, the optimum [*P*] value for *E. coli* was 0.25 μM of **1b** (*n* = 2) among **1a**–**1k** totally.

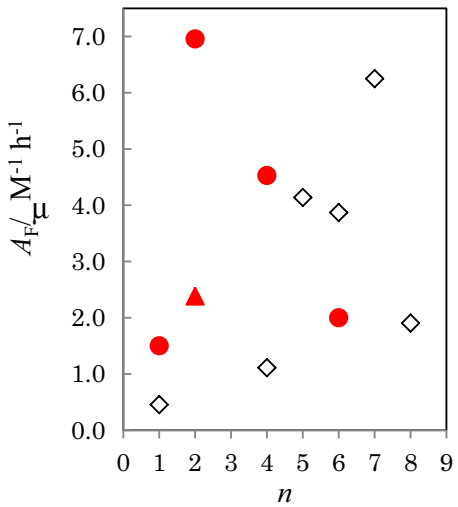


Fig. 2 Relationship between the A_F values and number of carbon atoms (*n*) in alkyl group on the alkylpyridinium (Apy) in **1a**−**1d** (●), **1e**−**1j** (◇), and **1k** (▲)

The [*P*] value (0.25 μM) of **1b** for *E.coli* was larger than the reported [*P*] value (50 nM) of **1b** for *S. cerevisiae* (Matsumoto et al. 2016). In general, gram-negative bacteria, such as *E. coli*, have complex cell wall structures comprising

phospholipids, lipopolysaccharides, lipoteichoic acids and lipoproteins, which pose an impermeable barrier to antimicrobial agents (Alves et al. 2014). Therefore, the present results are accord with these features already known.

Conclusion

Apy-bonded tricationic P-porphyrins (**1**) could photoinactivate *E. coli*. The [*P*] value for *E. coli* was optimized at bis[5-(3-ethyl-1-pyridinio)-3-oxapentyloxo]tetraphenylporphyrinatophosphorus dibromide, chloride (**1b**). Polycationic porphyrins have strong binding affinities to DNA (Pasternack et al. 2001; Sirish et al. 2002; Marczak et al. 2007; Haeubl et al. 2009; Tada-Oikawa et al. 2009; Kim et al. 2013) and proteins (Gyulkhandanyan et al. 2013). Alkyl chains might result in moderate hydrophobicity to take advantage of passing through cell wall. Therefore, it is important to provide the porphyrins with both polycationic character and hydrophobicity for an efficient PDI of *E. coli*.

Acknowledgements This research was supported by a Grant-in-Aid for Scientific Research (C) (16K05847) from the Japan Society for the Promotion of Science (JSPS).

Compliance with ethical standards

Conflict of interest The authors declare that they have no conflict of interest.

References

Alves E, Faustino MAF, Neves MGPMS, Cunha T, Nadais H, Almeida A (2014) Potential applications of porphyrins in photodynamic inactivation beyond the medical scope. J Photochem Photobiol C 22:34–57

Banfi S, Caruso E, Buccafurni L, Battini V, Zazzaron S, Barbieri P, Orlandi V (2006) Antibacterial activity of tetraaryl-porphyrin photosensitizers: an in vitro study on Gram negative and Gram positive bacteria. J Photochem Photobiol B 85(1):28–38

Batinic-Haberle I, Spasojevic I, Tse HM, Tovmasyan A, Rajic Z, Clair DKS, Vujaskovic Z, Dewhirst MW, Piganelli JD (2012) Design of Mn porphyrins for treating oxidative stress injuries and their redox-based regulation of cellular transcriptional activities. Amino Acids 42(1):95–113

Ben Amor T, Bortolotto L, Jori G (1998) Porphyrins and related compounds as photoactivatable insecticides. 2. Phototoxic activity of meso-substituted porphyrins. Photochem Photobiol 68 (3):314–318

Clifton CE (1931) Photodynamic action of certain dyes on the inactivation of Staphylococcus bacteriophage. Proc Soc Exp Biol Med 28(7):745–746

Ethirajan M, Chen Y, Joshi P, Pandey RK (2011) The role of porphyrin chemistry in tumor imaging and photodynamic therapy. Chem Soc Rev 40(1):340–362

Girek B, Sliwa W (2013) Porphyrins functionalized by quaternary pyridinium units. J Porphyr Phthalocyanines 17(12):1139–1156

Gyulkhandanyan A, Gyulkhandanyan L, Ghazaryan R, Fleury F, Angelini M, Gyulkhandanyan G, Sakanyan V (2013) Assessment of new cationic porphyrin binding to plasma proteins by planar microarray and spectroscopic methods. J Biomol Struct Dyn 31 (4):363–375

Haeubl M, Reith LM, Gruber B, Karner U, Müller N, Knör G, Schoefberger W (2009) DNA interactions and photocatalytic strand cleavage by artificial nucleases based on water-soluble gold(III) porphyrins. J Biol Inorg Chem 14(7):1037–1052

Kalyanasundaram K (1984) Photochemistry of water-soluble porphyrins: comparative study of isomeric tetrapyridyl- and tetrakis(*N*-methylpyridiniumyl)porphyrins. Inorg Chem 23 (16):2453–2459

Kano K, Fukuda K, Wakami H, Nishiyabu R, Pasternack RF (2000) Factors influencing self-aggregation tendencies of cationic porphyrins in aqueous solution. J Am Chem Soc 122(31):7494–7502

Kim YH, Jung SD, Lee MH, Im C, Kim YH, Jang YJ, Kim SK, Cho DW (2013) Photoinduced reduction of manganese(III) *meso*-tetrakis(1-methylpyridinium-4-yl)porphyrin at AT and GC base pairs. J Phys Chem B 117(33):9585–9590

Kubát P, Lang K, Anzenbacher Jr P, Jursíková K, Král V, Ehrenberg B (2000) Interaction of novel cationic *meso*-tetraphenylporphyrins in the ground and excited states with DNA and nucleotides. J Chem Soc Perkin Trans 1(6):933–941

Lang K, Mosinger J, Wagnerová DM (2004) Photophysical properties of porphyrinoid sensitizers non-covalently bound to host molecules; models for photodynamic therapy. Coord Chem Rev 248 (3–4):321–350

Marczak R, Sgobba V, Kutner W, Gadde S, D'Souza F, Guldi DM (2007) Langmuir-Blodgett films of a cationic zinc porphyrin - Imidazole- functionalized fullerene dyad: formation and photoelectronchemical studies. Langmuir 23(4):1917–1923

Matsumoto J, Kai Y, Yokoi H, Okazaki S, Yasuda M (2016) Assistance of human serum albumin to photo-sensitized inactivation of *Saccharomyces cerevisiae* with axially pyridinio-bonded P-porphyrins. J Photochem Photobiol B 161:279–283

Matsumoto J, Kubo T, Shinbara T, Matsuda N, Shiragami T, Fujitsuka M, Majima T, Yasuda M (2013) Spectroscopic analysis of the interaction of human serum albumin with tricationic phosphorus porphyrins bearing axial pyridinio groups. Bull Chem Soc Jpn 86 (11):1240–1247

Matsumoto J, Shiragami T, Hirakawa K, Yasuda M (2015) Water-solubilization of P(V) and Sb(V) porphyrins and their photobiological application. Int J Photoenergy. https://doi.org/10.1155/2015/148964

Matsumoto J, Suemoto Y, Kanemaru H, Takemori K, Shigehara M, Miyamoto A, Yokoi H, Yasuda M (2017a) Alkyl substituent effect on photosensitized inactivation of *Escherichia coli* by pyridinium- bonded P-porphyrins. J Photochem Photobiol B 168:124–131

Matsumoto J, Suzuki K, Uezono H, Watanabe K, Yasuda M (2017b) Additive effect of heparin on the photoinactivation of *Escherichia coli* using tricationic P-porphyrins. Bioorg Med Chem Lett 27:5258–5261

Nyman ES, Hynninen PH (2004) Research advances in the use of tetrapyrrolic photosensitizers for photodynamic therapy. J Photochem Photobiol B 73(1–2):1–28

Pandey RK, Zheng G (2000) Porphyrins as photosensitizers in photodynamic therapy. In: Kadish KM, Smith KM, Guilluy R (ed) The porphyrin handbook. vol 6. Academic Press, San Diego, pp 157–230

Pasternack RF, Ewen S, Rao A, Meyer AS, Freedman MA, Collings PJ, Frey SL, Ranen MC, De Paula JC (2001) Interactions of copper(II) porphyrins with DNA. Inorg Chim Acta 317 (1–2):59–71

Perdrau JR, Todd C (1933) The photodynamic action of methylene blue on bacteriophage. Proc R Soc Lond Ser B 112(777):277–287

Shiragami T, Matsumoto J, Inoue H, Yasuda M (2005) Antimony porphyrin complexes as visible-light driven photocatalyst. J Photochem Photobiol C 6(4):227–248

Sirish M, Chertkov VA, Schneider HJ (2002) Porphyrin-based peptide receptors: syntheses and NMR analysis. Chem Eur J 8 (5):1181–1188

Tada-Oikawa S, Oikawa S, Hirayama J, Hirakawa K, Kawanishi S (2009) DNA damage and apoptosis induced by photosensitization of 5,10,15,20-tetrakis (*N*-methyl-4-pyridyl)- 21*H*,23*H*-porphyrin via singlet oxygen generation. Photochem Photobiol 85 (6):1391–1399

Trommel JS, Marzilli LG (2001) Synthesis and DNA binding of novel water-soluble cationic methylcobalt porphyrins. Inorg Chem 40 (17):4374–4383