Synthesis and Photochemistry of Diphenylchlorin and Diphenylbacteriochlorin

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Abstract: Diphenylchlorin (DPC) and diphenylbacteriochlorin (DPBC) were synthesized for the first time from reduction of 5,10-diphenylporphyrin (DPP). As photosensitizers they have sizable absorption in the red region of the visible spectrum. The high yield of DPC-photosensitized generation of $^1O_2$, and the EPR studies in homogenerous solution showed that the photodynamic action of DPP-based photosensitizers may proceed *via* type I and type II machanisms.

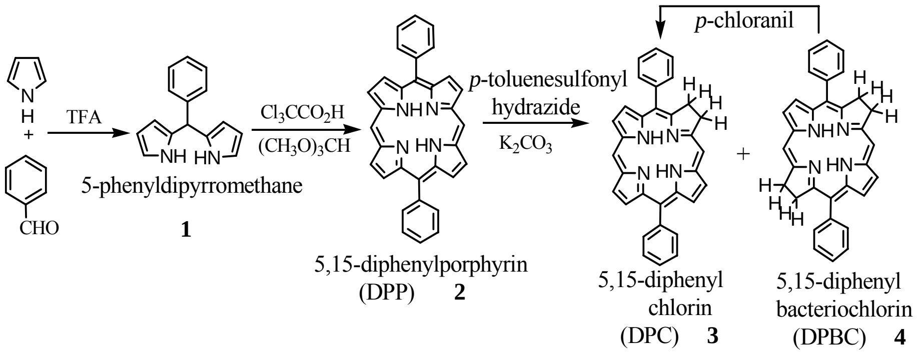
Keywords: Diphenylchlorin, diphenylbacteriochlorin, synthesis, photochemistry.

5, 15-Diphenylporphyrin (DPP), a novel porphyrin model compound, was always inaccessible in quantities suitable for study[1] because the difficulty of synthesis. So that the characteristic of this molecule had not been explored until a novel method developed for the preparation of DPP recently[2]. Therefore it will be possible for the synthesis of DPP-based photosensitizers, and investigation of their photodynamic properties. Here we reported the synthesis of novel photosensitizers 5, 15-diphenylchlorin (DPC) and 5, 15-diphenylbacteriochlorin (DPBC) from reduction of 5, 10-diphenylporphyrin (DPP), and the studies of photodynamic actions. The results of these initial researches made us believe that DPP-based photosensitizers have great potential for using as photodynamic therapy (PDT) agent, and the extensive investigation is undergoing.

The synthesis of DPC and DPBC are summarized in **scheme 1**. DPP was prepared as described in the literatures[1,2] with an improvement of work-up procedures. According to the methods of literatures, the resulting mixture of DPP was concentrated under high vacuum over night to get rid of pyridine before further purification by column chromatography. The modification of work-up procedures was addition of water into the mixture in the course of evaporating CH_2Cl_2. Thus when the whole CH_2Cl_2 was removed, pyridine dissolved in water, simply filtration and air-drying could get DPP appropriate for chromatography.

The porphyrin was reduced with di-imide using the method of Whitlock *et al.*[3,4]. When DPC was the target compound, this reaction requires 4h, which is faster than the synthesis of meso-tetraphenylchlorin (TPC)[3] with the same manner. The synthesis of DPBC is much difficult which requires longer reaction time and a great deal of *p*-toluenesulfonylhydrazine.

Scheme 1



Separation of the pigments from one another is facilitated by their differing partition coefficients between benzene and phosphoric acid. Since the basicity of DPP is higher than TPP[1], a more diluted aqueous phosphoric acid was needed to extract DPC and DPBC from DPP, compared with the separation of TPC and meso-tetraphenylbacterichlorin (TPBC) from TPP[3]. The structures were fully characterized by MS, ^{1}H NMR, IR and elemental analysis[5]. The UV-vis and Fluorescence spectral data of DPC and DPBC are summed in **Table 1**. DPC and DPBC all have strong light absorption in the red spectral region, which is the ideal wavelength for PDT.

Electron paramagnetic resonance (EPR) measurement was used to investigate the photogeneration of active oxygen species (O_2^{-}, $^1O_2$) and photosensitizer anion radicals (sens^{-}) by DPC and DPBC in the present or absent of oxygen[6]. Superoxide anion radical (O_2^{-}) was studied by means of spin trap of DMPO (5, 5-dimethyl-1-pyrroline-N-oxide) (**Figure 1a**)[7]. Photosensitizer anion radical (sens^{-}) was investigated by EPR method with TEMPO (2, 2, 6, 6-tetramethyl-4-piperidone-N-oxyl radical) as spin trap (**Figure 1b**)[8]. Singlet oxygen ($^1O_2$) was also detected by EPR method with TEMP (2, 2, 6, 6-tetramethyl- 4-piperidone) as spin trap (**Figure 1c**)[9].

A xenon arc lamp (150W) with an intensity of 3.6W/cm^2 was used as the light source equipped with UV and IR cut-off filters (transmittance 470-750nm).

Table 1 Spectral data of DPC and DPBC

	DPC	DPBC
λ_{max}, (log ε) in benzene	363 nm (4.53), 409 nm (5.21), 505 nm (4.11), 532 nm (3.72), 593 nm (3.62), 645 nm (4.63)	349 nm (5.07), 373 nm (5.16), 506 nm (4.66), 734 nm (5.11)
F_{max} (nm), in benzene	646	737
Φ_F in N_2-benzene	0.18	0.14
Φ_F in air-benzene	0.15	0.12

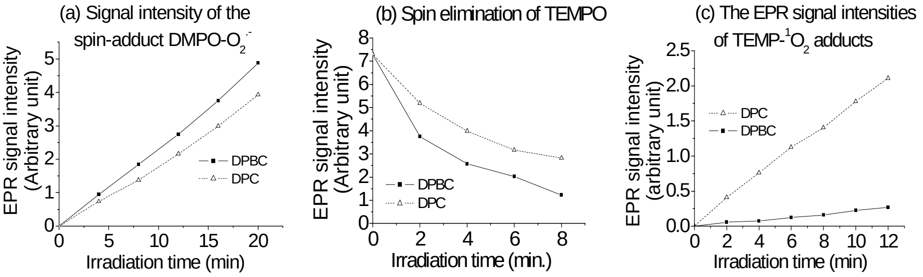
Figure 1

$$(a)\quad \mathrm{DMPO} + O_2^{\cdot -} \longrightarrow \mathrm{DMPO\text{-}}O_2^{\cdot -}$$

$$(b)\quad \mathrm{TEMPO} + \mathrm{Sen}^{\cdot -} \xrightarrow{H^+} \mathrm{TEMPOH} + \mathrm{Sen}$$

$$(c)\quad \mathrm{TEMP} + {}^1O_2 \xrightarrow{H^+} \mathrm{TEMP\text{-}}{}^1O_2 + H_2O$$

Figure 2



(a) Illumination of oxygen-saturated CH_3CN (5% $CHCl_3$) solution of photosensitizers (0.1 mM) and DMPO (50 mM); (b) Illumination of TEMPO (0.05mM) and photosensitizer (0.1mM) in anaerobic CH_3CN (5% $CHCl_3$); (c) Illumination on $CHCl_3$ solution of photosensitizers (0.1 mM) and TEMP (10 mM).

The transformation of EPR signal intensity as a function of illumination time was shown in **Figure 2**. DPC, DPBC could photosensitize the generation of O_2^- with fine effectiveness. They were also efficient for the spin elimination of TEMPO in the absent of oxygen, and the relative efficiency of them was corresponding to the capability of photoproduction of superoxide anion radicals by DPC and DPBC in oxygen-saturated solution.

DPC is a very competent photosensitizer for the photoproduction of $^1O_2$ in $CHCl_3$. However DPBC photosensitizes the generation of $^1O_2$ with much lower efficiency (**Figure 2c**). The reason of this is not well understood, presumably due to the energy of DPBC′s triplet states was not high enough to yield $^1O_2$[10].

The $^1O_2$ quantum yield of DPC was determined to be 0.72 in benzene using the 9,10-diphenyl-anthracene (DPA)-bleaching method[11a] with meso-tetraphenylporphyrin (TPP) as reference (Φ_Δ=0.58)[11b].

In summary, our results show that DPC is a very effective $^1O_2$ sensitizer with high quantum yield (0.72). DPC and DPBC are also efficient in photoproduction of O_2^- under aerobic condition and sens$^-$ under anaerobic condition. DPP-based photosensitizers must have great potential for using as PDT agent, and should be given extensive investigation.

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5. **DPC**: Yield 51%; mp. >300℃; ^{1}H NMR (200MHz, CDCl$_3$): δ -1.8 (brs, 2H, 2NH), 4.38 (t, 2H, J=3.8Hz, CH$_2$), 4.69 (t, 2H, J=3.8Hz, CH$_2$), 7.77 (m, 6H, 6phenyl-H), 7.96 (m, 2H, 2phenyl-H), 8.21 (d, 1H, J=4.5Hz, CH), 8.33 (d, 1H, J=4.5Hz, CH), 8.51 (m, 2H, 2phenyl-H), 8.89 (m, 2H, 2CH), 9.11 (d, 1H, J=4.5Hz, CH), 9.35 (d, 1H, J=4.5Hz, CH), 9.97 (s, 1H, meso-CH), 10.78 (s, 1H, meso-CH). FAB-MS: *m/z* 465 (M+1); IR (KBr) cm^{-1}: 3380, 2923, 2849, 1606, 1440, 1417; *Anal.* calcd. for C$_{32}$H$_{24}$N$_4$: C, 82.73; H, 5.21; N, 12.06. Found: C, 82.80; H, 5.37; N, 11.94. **DPBC**: Yield 19%; mp. >300°C; ^{1}H NMR (200 MHz, CDCl$_3$): δ -1.53 (brs, 2H, 2NH), 4.39 (t, 4H, J=4.0Hz, 2CH$_2$), 4.67 (t, 4H, J=4.0Hz, 2CH$_2$), 7.67 (m, 6H, 6phenyl-H), 7.86 (m, 4H, 4phenyl-H), 8.19 (d, J=4.6Hz, 2H, 2CH), 8.81 (d, J=4.6Hz, 2H, 2CH), 9.97 (s, 2H, 2meso-CH); FAB-MS: *m/z* 467 (M+1$^+$); IR (KBr) cm^{-1}: 3372, 2925, 2851, 1606, 1440, 1419; *Anal.* calcd. for C$_{32}$H$_{26}$N$_4$: C, 82.38; H, 5.62; N, 12.01. Found: C, 82.19; H, 5.61; N, 11.97.
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