Synthesis of Covalently Linked Chlorin-Fullerene Dyads

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Recently, some electron donor-acceptor (DA) system that employs porphyrins or chlorins as electron donors and fullerene as electron acceptor have already prepared and examined for the mimicry of photosynthetic reaction centers.[1] And also such compounds have potential applications in photodynamic therapy (PDT). In particular, the chlorin linked systems would be of great interest,[2] since the excitation possibility at the chlorin long-wavelength Q-band, which is missing from the electronic spectrum of fully conjugated porphyrins, enables the achievement of higher quantum yields in solar energy conversions. The chlorins are known to possess a variety of photophysical and electrochemical properties, which provide an opportunity to tune the energetics of photoinduced charge separation. Therefore, they have well characterized photophysical properties. In this respect, photoinduced electron transfer systems comprising fullerene seems to be excellent combinations for revealing basic photophysical properties of donor linked fullerene system.

Many research groups have reported biological application of fullerene and fullerene derivatives.[3] In terms of biological activity the formation of singlet oxygen is crucial because it can be applied for the cleavage of biomolecules. Efficient formation of $^3C_{60}$ was seen in porphyrin-C_{60} dyads under certain conditions, indicating that singlet oxygen can be generated efficiently by selecting the linkage and solvents.[4] In addition, the increase of the absorption cross section by both porphyrin and C_{60} chromophores is also advantageous. Therefore, C_{60} linked porphyrin or chlorin compounds will provide a new opportunity for the design of photodynamic agents in cancer or viral therapy.

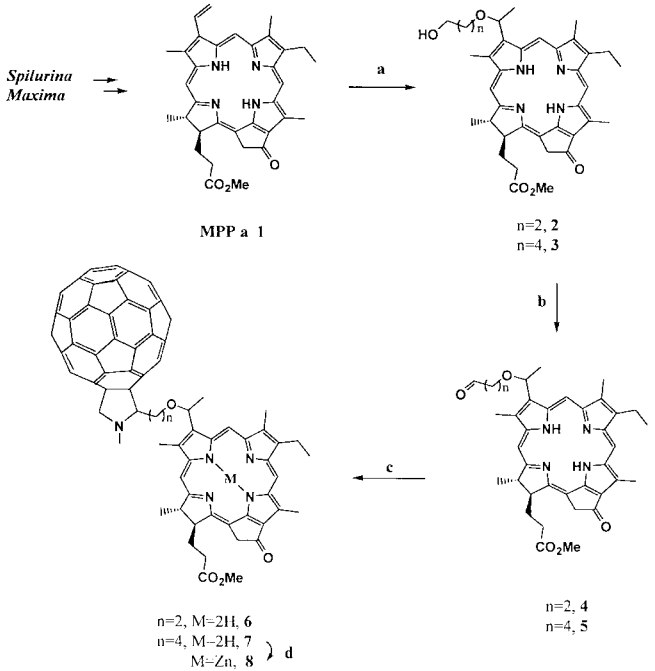
Now we are reporting the synthesis of covalently linked chlorin-fullerene dyads. The novel chlorin-fullerene dyads have great potential for preparing not only promising models for photosynthetic reaction centers, but also for constructing a wide variety of chlorin-based compounds of biological significance.

Methyl pyropheophorbide *a* (MPPa) **1** which was extracted from the alga[5] *Spilurina maxima* was reacted with 30% hydrobromic acid in acetic acid followed by treatment with an appropriate diol to give alcohols **2** and **3** as diastereomeric mixtures.[6] Oxidation of alcohols with sulfur trioxide-pyridine complex, DMSO and triethylamine produced aldehydes **4** and **5**.[7] The coupling reaction of aldehydes with *N*-methylglycine and C_{60} in toluene at reflux gave the pyrrolidine-linked chlorin-fullerene dyads **6** and **7**.[8] respectively.

The structures of all compounds were determined by spectroscopic analysis such as ^{1}H NMR, IR, UV-Vis, and Fluorescence spectroscopy. MALDI-TOF MS spectra exhibited the corresponding M^- ion peak (m/z) 1371 for **6** and 1398 for **7**.[9]

To a great extent the absorption spectrum of dyads is a simple superposition of the spectra of chlorin and C_{60}. Small perturbations in the spectrum of the dyads indicate a weak electronic interaction between the chlorin and the fullerene chromophores in the ground state. Whereas dyads **6-8** containing the fullerene moieties showed a remarkable decrease in fluorescence, which indicates a rapid quenching of the chlorin excited singlet state by fullerene.

Conformational studies and detailed photophysical studies, such as fluorescence lifetime measurements, time-resolved



Scheme 1. (a) (i) 30% HBr in acetic acid, (ii) 1,3-propanediol or 1,5-pentanediol, MC, K_2CO_3 (**2**: 53%, **3**: 58%, two steps); (b) SO_3·pyridine, DMSO, triethylamine (quantitative); (c) C_{60}, sarcosine, toluene, reflux (**6**: 41%, **7**: 40%); (d) $Zn(OAc)_2$·$2H_2O$, MC, reflux (quantitative).

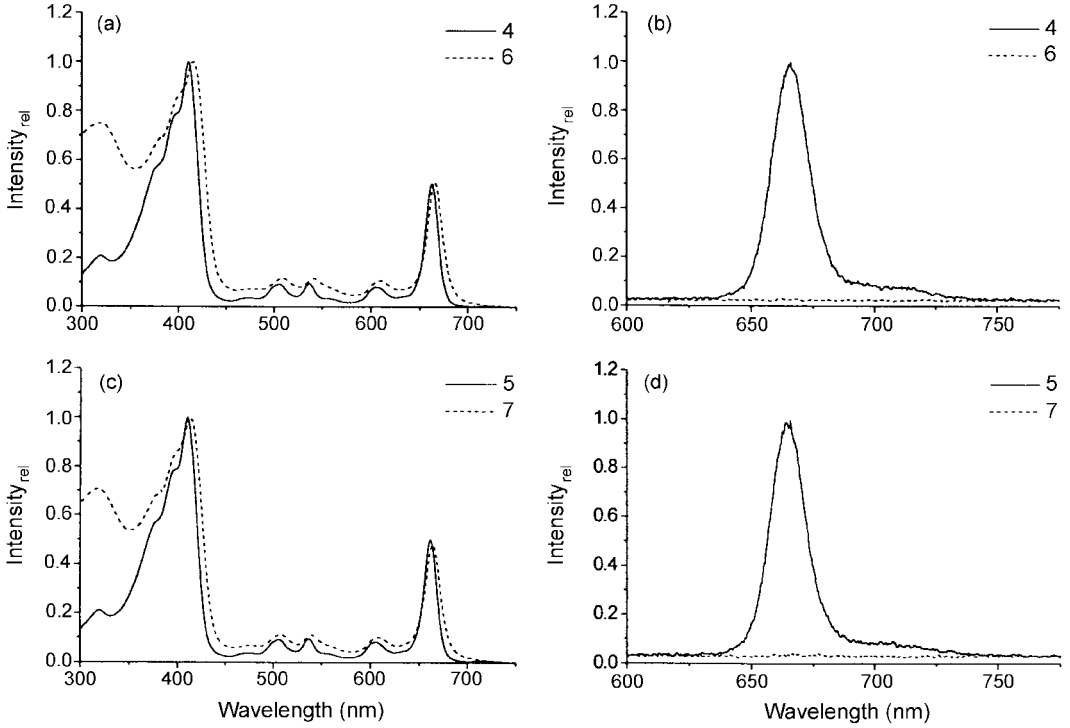


Figure 1. UV-Vis spectra (a, c), and Fluorescence spectra (b, d) in $CHCl_3$.

transient absorption spectroscopy, singlet oxygen quantum yield, are under investigation.

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References

1. (a) Wedel, M.; Montforts, F.-P. *Tetrahedron Lett.* **1999**, *40*, 7071-7074. (b) Imahori, H.; Hagiwara, K.; Aoki, M.; Akiyama, T.; Taniguchi, S.; Okada, T.; Shirakawa, M.; Sakata, Y. *J. Am. Chem. Soc.* **1996**, *118*, 11771-11782. (c) Schuster, D. I.; Cheng, P.; Wilson, S. R.; Prokhorenko, V.; Katterle, M.; Holzwartz, A. R.; Braslavsky, S. E.; Klihm, G.; Williams, R. M.; Luo, C. *J. Am. Chem. Soc.* **1999**, *121*, 11599-11600.
2. (a) Tkachenko, N. V.; Rantala, L.; Tauber, A. Y.; Helaja, J.; Hynninen, P. H.; Lemmetyinen, H. *J. Am. Chem. Soc.* **1999**, *121*, 9378-9387. (b) Zheng, G.; Dougherty, T. J.; Pandey, R. K. *J. Chem. Soc., Chem. Commun.* **1999**, 2469-2470.
3. Jensen, A. W.; Wilson, S. R.; Schster, D. I. *Bioorg. & Med. Chem.* **1996**, *4*, 767-779.
4. Schuster, D. I.; Cheng, P.; Wilson, S. R.; Prokhorenko, V.; Katterle, M.; Holzwartz, A. R.; Braslavsky, S. E.; Klihm, G.; Williams, R. M.; Luo, C. *J. Am. Chem. Soc.* **1999**, *121*, 11599-11600.
5. Smith, K. M.; Goff, D. A.; Simpson, D. J. *J. Am. Chem. Soc.* **1985**, *107*, 4946-4954.
6. Pandey, R. K.; Sumlin, A. B.; Constantine, S.; Aoudia, M.; Potter, W. R.; Bellnier, D. A.; Henderson, B. W.; Rodgers, M. A.; Smith, K. M.; Dougherty, T. J. *Photochem. Photobio.* **1996**, *64*(1), 194-204.
7. Hamada, Y.; Shioiri, T. *Chem. Pharm. Bull.* **1982**, *30*(5), 1921-1924.
8. Maggini, M.; Scorrano, G.; Prato, M. *J. Am. Chem. Soc.* **1993**, *115*, 9798-9799.
9. Spectral data for selected compounds are as follows. **6**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.92, 9.40 and 8.40 (each s, 1H, meso-H), 5.81 (q, 1H, J = 6.9 Hz, CH_3CHO), 5.18 (dd, 2H, CH_2CO), 5.09 (m, 1H, CH_2N), 4.45 (m, 1H, CHN), 4.33 (m, 1H, $CHCH_3$), 4.10 (m, 1H, CH_2N), 3.95 (m, 1H, $CHCH_2$), 3.73 (s, 3H, CH_3), 3.57-3.53 (m, 7H, CO_2CH_3, CH_2CH_3 and OCH_2CH_2), 3.40 (s, 3H, CH_3), 3.20 (s, 3H, CH_3), 3.13 (s, 3H, NCH_3), 2.40-2.65 (m, 2H, CH_2CO), 2.20-2.35 (m, 2H, CH_2CH_2CO), 2.12 (d, 1H, J = 6.9 Hz, CH_3CH), 1.79 (d, 3H, J = 7.3 Hz, $CHCH_3$), 1.55 (m, 5H, CH_3CH_2 and CH_2CH_2CH), -2.07 (br s, 2H, NH); MALDI-TOF-MS *m/z* calcd for $C_{99}H_{47}N_5O_4$ 1371, obsd 1371; UV/Vis (CH_2Cl_2) λ_{max} (rel absorbance) 319 nm (0.766), 415 (1.000), 508 (0.121), 541 (0.120), 608 (0.110), 664 (0.524). **7**: ^{1}H NMR (300 MHz, $CDCl_3$) δ 9.83, 9.43 and 8.42 (each s, 1H, meso-H), 5.85 (q, 1H, J = 6.6 Hz, CH_3CHO), 5.25 (m, 1H, CH_2N), 5.07 (dd, 2H, CH_2CO), 4.48 (m, 1H, CHN), 4.41 (m, 1H, $CHCH_3$), 4.28 (m, 1H, CH_2N), 4.21 (m, 1H, $CHCH_2$), 3.70 (s, 3H, CH_3), 3.67-3.56 (m, 7H, CO_2CH_3, CH_2CH_3 and OCH_2CH_2), 3.46 (s, 3H, CH_3), 3.31 (s, 3H, CH_3), 3.21 (s, 3H, NCH_3), 2.75-2.55 (m, 2H, CH_2CO), 2.40-2.31 (m, 2H, CH_2CH_2CO), 2.10 (d, 1H, J = 6.6 Hz, CH_3CH), 2.05 (m, 2H, CH_2CH_2CH), 1.79 (m, 7H, $CHCH_3$ and CH_2 CH_2CH_2CH), 1.62 (t, 3H, J = 7.6 Hz, CH_3CH_2), -1.81 (br s, 2H, NH); MALDI-TOF-MS *m/z* calcd for $C_{101}H_{51}N_5O_4$ 1398, obsd 1398; UV/Vis (CH_2Cl_2) λ_{max} (rel absorbance) 326 nm (0.929), 414 (1.000), 507 (0.125), 539 (0.121), 607 (0.106), 663 (0.480).