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Synthesis and photochemistry of novel bromo substituted stilbene derivatives as triplet state sensitizers for the generation of singlet oxygen

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Abstract

We have presented the synthesis and characterization of three new bromo substituted stilbene derivatives, p-3,4,5-trimethoxy-p′-2,3,4,5,6-pentabromo stilbene (**C1**), p-N,N-dimethylamino-p′-2,3,4,5,6-pentabromo stilbene (**C2**) and p-N,N-diphenylamino-p′-2,3,4,5,6-pentabromo stilbene (**C3**) in this letter. The UV/vis absorption and photoluminescence were investigated in various solvents. The maximal absorption wavelength of **C1** exhibited blue-shift to those of **C2** and **C3** in different solvents. No florescence emission could be detected for these compounds at room temperature. Singlet oxygen could be efficiently produced with these sensitizers under near-ultraviolet and visible light irradiation.

Keywords: Synthesis; Photochemistry; Triplet state; Bromo substitution; Singlet oxygen

Numerous efforts have been devoted to the chemistry and biochemistry of singlet oxygen ($^1O_2$) since its discovery in the 1960s [1], which was applied a wide range of fields, such as photodynamic therapy, photooxygenation of organic compounds, and photodegradation of some polymers. Of particular interest for chemists was that singlet oxygen had synthetic ability because it could undergo selective reactions with a wide variety of electron-rich molecules such as olefins [2], conjugated dienes [3], polycyclic aromatic hydrocarbons [4], phenols [5], sulfides [6], and heterocycles [7]. Generally, a sensitizing molecule absorbs visible or near ultraviolet light so that singlet oxygen can be produced through energy transfer at the triplet state of sensitizer and molecular oxygen. More recently, the development of new dyes with large upconverted fluorescence became the focus of the research and it has opened up a myriad of application [8]. Some molecules showed strong upconverted fluorescence, other molecules were demonstrated to exhibit strong upconverted phosphorescence [9]. These two-photon-absorbing molecules could act as efficient triplet sensitizers – singlet oxygen sensitizers. Consequently, they could play important role on the cytotoxicity and photodynamic therapy studies in biological tissues. Unfortunately, this technique has never reached its full potential due to the lack of suitable dyes. As a result, the full utility of two-photon-absorbing materials has not been realized, especially in two-photon photodynamic therapy. In this letter, we designed and synthesized three new bromo substituted molecules with conjugated structures in order to increase spin–orbit coupling of the compounds.

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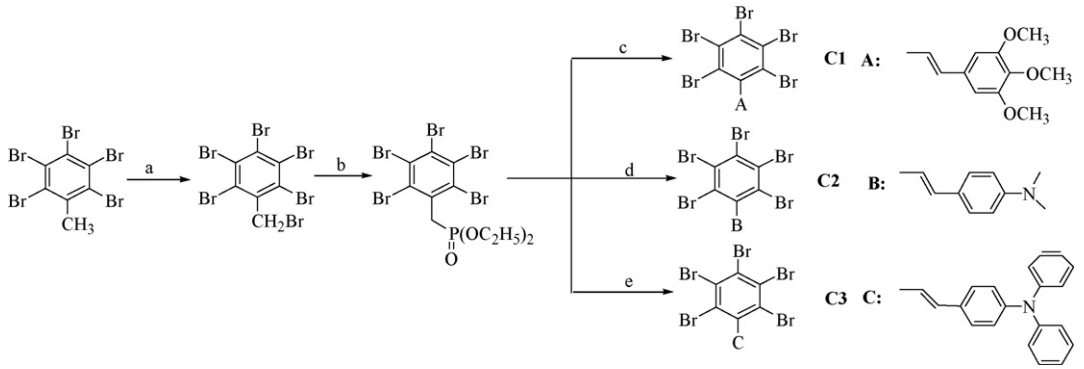

Scheme 1. Synthesis routes of compounds **1–3**. (a) NBS, AIBN, CCl_4, reflux; (b) $P(OC_2H_5)_3$, 130–160 °C; (c) 3,4,5-trimethoxybenzaldehyde, CH_3CH_2ONa, THF; (d) 4-(dimethylamino)benzaldehyde, CH_3CH_2ONa, THF; (e) N,N-diphenylformamide, CH_3CH_2ONa, THF.

They could act as efficient triplet sensitizers which included p-3,4,5-trimethoxy-p′-2,3,4,5,6-pentabromo stilbene (**C1**), p-N,N-dimethylamino-p′-2,3,4,5,6-pentabromo stilbene (**C2**) and p-N,N-diphenylamino-p′-2,3,4,5,6-pentabromostilbene (**C3**).

1. Experimental

The chemical structures and synthesis routes of **C1** to **C3** were presented in Scheme 1. These compounds were synthesized with similar routes. 1-Bromomethyl-2,3,4,5,6-pentabromobenzene was obtained from the reaction of 1-methyl-2,3,4,5,6-pentabromobenzene and N-bromosuccinimide (NBS) in CCl_4 under reflux. The compound was purified with recrystallization in petroleum ether. 1-Benzylphosphonate-2,3,4,5,6-pentabromobenzene was prepared from triethyl phosphite and 1-bromomethyl-2,3,4,5,6-pentbromobenzene and it was used in the next step without further purification. The compounds **C1** to **C3** were prepared from 1-benzylphosphonate-2,3,4,5,6-pentabromobenzene and 3,4,5-trimethoxylbenzaldehyde, p-N,N-dimethylaminobenzaldehyde, and 4-formyl-triphenylamino respectively in THF with catalyst sodium ethoxide. After filtration of solid materials and evaporation of THF in vacuum, the reactant mixture was dissolved in chloroform and washed by water. The organic layer was dried over magnesium sulfate. After evaporated in vacuum, the compounds were separated with column chromography using benzene as eluent. The compounds were further purified with recrystallization in the mixture of benzene and cyclohexane (3:1). The chemical structures of **C1** to **C3** were characterized with ^1H NMR and elemental analysis. **C1**, yield: 34.2%, color, light yellow, m.p. 192–193 °C, ^1H NMR ($CDCl_3$, 500 Hz, δ ppm): 6.832–6.865 (d, 1H, J = 16.5 Hz, 1H, Ar–*CH*=CH), 6.741 (s, 2H, J = 7.5 Hz, Ar–H), 6.609–6.642 (d, 1H, J = 16.5 Hz, Ar–*CH*=CH), 3.925 (s, 6H, $-OCH_3$), 3.878 (s, 3H, $-OCH_3$). Anal. Calcd. for $C_{17}H_{13}Br_5O_3$: C, 30.71; H, 1.97; O, 7.22; Br, 60.10. Found: C, 30.83; H, 1.91. **C2**, yield: 30.5%, color, light yellow, m.p. 229–230 °C, ^1H NMR ($CDCl_3$, 500 Hz, δ ppm): 7.825–7.842 (d, 2H, J = 8.5 Hz, Ar–H), 7.436–7.419 (d, 1H, J = 8.5 Hz, Ar–*CH*=CH), 6.725–6.801 (m, 2H, Ar–H), 6.634–6.667 (d, 1H, J = 16.5 Hz, Ar–*CH*=CH), 3.012 (s, 6H, $-N-CH_3$). Anal. Calcd. for $C_{16}H_{12}Br_5N$: C, 31.11; H, 1.96; N, 2.27; Br, 64.67. Found: C, 31.23; H, 1.90; N, 2.19. **C3**, yield: 41.1%, color, yellow, m.p. 199–201 °C, ^1H NMR ($CDCl_3$, 500 Hz, δ ppm): 7.367–7.389 (d, 2H, J = 11 Hz, Ar–H), 7.253–7.288 (m, 4H, Ar–H), 7.112–7.127 (d, 2H, J = 7.5 Hz, Ar–H), 7.062–7.073 (m, 2H, Ar–H), 7.035–7.056 (m, 4H, Ar–H), 6.809–6.842 (d, 1H, J = 16.5 Hz, Ar–*CH*=CH), 6.636–6.669 (d, 1H, J = 16.5 Hz, Ar–*CH*=CH). Anal. Calcd. for $C_{26}H_{16}Br_5N$: C, 42.09; H, 2.17; N, 1.89; Br, 53.85. Found: C, 42.16; H, 2.09; N, 1.93.

2. Results and discussion

The UV/vis absorption spectroscopy of **C1**, **C2** and **C3** was investigated in various solvents. Some typical absorption spectral data of compounds **1–3** were shown in Table 1. Obviously, the maximal absorption wavelength of the compounds **1–3** displayed remarkable difference in various solvents. Fig. 1 showed typical absorption spectroscopy of **C1**, **C2** and **C3** in methylchloride. The maximal absorption wavelength of **C1** was blue-shift to those of **C2** and **C3** in different solvents. This demonstrated that the UV–vis spectroscopy of the compounds had a

Table 1
Typical absorption spectral data of compounds **1–3** in various solvents.

Solvents	**C1**		**C2**		**C3**	
	λ_{max}	ε	λ_{max}	ε	λ_{max}	ε
Cyclohexane	306	0.113	344	0.173	362	0.192
Benzene	311	0.198	356	0.188	366	0.223
Acetonitrile	303	0.173	353	0.139	361	0.228

λ_{max}: nm; ε: (1×10^5) L/mol cm.

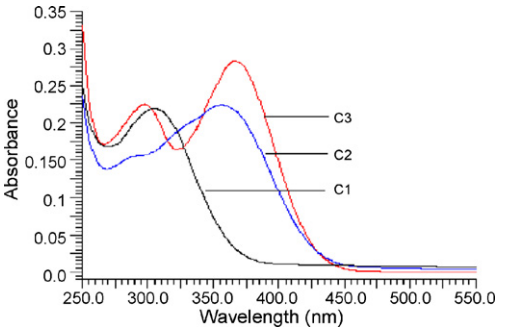

Fig. 1. Typical absorption spectroscopy of compounds **1–3** in methyl chloride ($C = 1 \times 10^{-5}$ mol/L).

correlationship with electron-donating properties of substituent groups. The stronger electron-donating effects of dimethylamino and diphenylamino groups led to the red-shift of the maximal absorption wavelength of **C2** and **C3**. No fluorescence emission could be determined for these compounds in various solvents at room temperature. This strongly demonstrated that the introduction of heavy atom Br into molecule could increase the spin–orbit coupling, and thus the intersystem crossing coefficients from the S_1 state to the lowest excited triplet state, T_1 was greatly enhanced [10].

The production of singlet oxygen by these sensitizers under near-ultraviolet and visible light was performed in a pyrex glass cell. Oxygen was continuously bubbled into the cell containing the solutions of the sensitizers and substrates. Efficient photooxidation reaction occurred between the produced singlet oxygen and the substrates in various solvents. The photooxidation products were successfully detected with GC–MS. Typical photooxidation reaction of 2,3-dimethyl-2-butene with singlet oxygen was presented in Fig. 2. It clearly showed that singlet oxygen was efficiently produced from the dye-sensitization process. The basic process could be expressed as shown in Fig. 2.

The singlet oxygen quantum yields of these sensitizers were determined with photobleaching method of 9,10-diphenylanthracence due to the photooxidation [11]. This method in turn confirmed the production of singlet oxygen by these new sensitizers. Table 2 listed some typical data of singlet oxygen quantum yields of **C1**, **C2** and **C3** in acetonitrile. It clearly showed that they exhibited remarkably high singlet oxygen quantum yields, which was close to that of 9,10-dicyanoanthracence [12], a representative singlet oxygen sensitizer.

We have further employed electron spin resonance (ESR) technique to detect the photosensitized production of singlet oxygen by these compounds using 2,2,6,6-tetramethyl piperidine (TEMP) as substrate under 355 nm and 532 nm laser irradiation. Characteristic triplet ESR signal of nitrooxide radial (TEMPO) was successfully determined due to its long lifetime. Typical ESR results of **C3** were presented in Fig. 3. From the UV/vis absorption spectroscopy, it was easily understood that dye-sensitized production of singlet oxygen could be achieved by 355 nm. Because compounds **1–3** did not have any absorption above 500 nm wavelength, ESR detection have confirmed that the

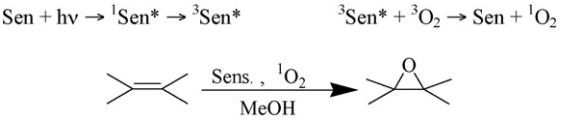

Fig. 2. Photooxidation reaction of 2,3-dimethyl-2-butene with singlet oxygen.

Table 2
Singlet oxygen quantum yields of the compounds **1–3** in acetonitrile.

Compounds	Φ
C1	0.73
C2	0.74
C3	0.68

Φ: the quantum yields of singlet oxygen.

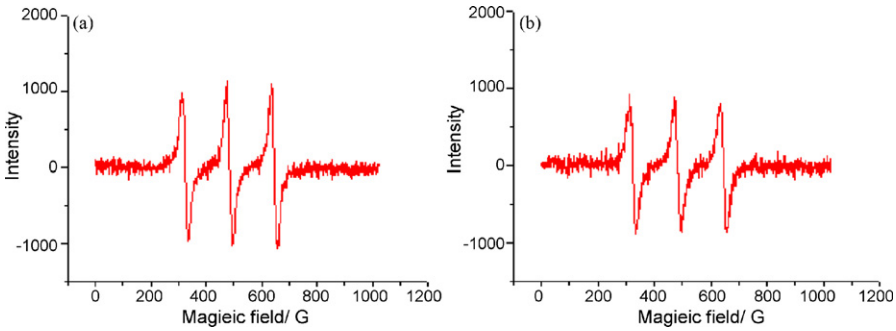

Fig. 3. ESR Spectrum produced after 5 min irradiation of a solution containing 0.01 mol/L **C3** and 10 mmol/L TEMP: (a) 355 nm laser and (b) 532 nm laser.

photosensitized production of singlet oxygen by these compounds with 532 nm laser was definitely resulted from two-photon photochemistry.

To summarize, this paper presented the synthesis of a series of new stilbene derivatives with bromo atoms. The exited states of these compounds displayed remarkable heavy atom effects, and the triplet states were thus efficiently formed. We presented strong evidences that singlet oxygen could be efficiently produced with these new sensitizers.

Acknowledgments

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