

Synthesis and Photophysical Properties of Bispsoralen Derivatives Linked by a Bisamide-polymethylene Chain

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New bispsoralen derivatives **5-10**, 8-MOP-NIICO(CH₂)_nCONH-8-MOP (BPSBA-C_n, *n* = 0, 1, 2, 3, 4 and 5) in which 5 position of an 8-methoxypsoralen (8-MOP) is linked by various lengths of bisamide polymethylene chain to 5 position of the other 8-MOP, have been synthesized by the amidation of 5-amino-8-methoxypsoralen (**12**) with α,ω -alkanoyl dichloride. Photophysical properties of their derivatives including π - π stacking interaction between the two aromatic moieties were investigated by UV absorption and fluorescence emission spectra. Efficient ring-ring stacking interactions have been observed in BPSBA-C₄ (**9**) from the percent hypochromism (%II) of the models.

Key Words : 8-Methoxypsoralen, Bispsoralen derivatives, UV absorption, Fluorescence emission spectra, Ring-ring stacking interaction

Introduction

Psoralens (Ps) are widely used as dermal photosensitizing agents for the treatment of various skin diseases, such as vitiligo, psoriasis, mycosis fungoides, chronic leukemia, and some infections connected with AIDS and as chemical tools for the study of nucleic acid structure-function relationship.¹⁻⁵ A large number of studies on the mechanism of the photochemical reactions between psoralen and DNA bases *in vivo* or with thymine derivatives have been carried out. These studies involved intermolecular processes leading generally to a mixture of several photoproducts. Binding of psoralens to DNA^{6,7} is generally the consequence of two successive events: (a) intercalation of the psoralens between the base pairs of nucleic acids in the ground state; (b) [2+2] type photoaddition of the complexed psoralens to pyrimidine bases of DNA. The 3,4-pyrone and/or 4',5'-furan double bonds of the psoralen molecules add to pyrimidine 5,6 double bond.⁸ The formation of the intercalated complex between psoralens and DNA is an important step, which markedly affects the successive covalent photobinding to the macromolecule leading to site specificity in addition. The psoralen derivatives are used as a chemical tool to study the relationship between the structure of nucleic acid and the ability to bind psoralen recently based on this site specificity.⁹⁻¹¹

To investigate these two processes in the absence of complicating factors associated with hydrogen bonding or the usual carbohydrate and phosphodiester linkages, Lhomme

and Decout¹²⁻¹⁵ prepared a series of model compounds (**3**) starting from 8-hydroxypsoralen (**2**) and showed that the polymethylene bridges control the intramolecular ring-ring stacking of the two chromophores in the molecules. Castellan *et al.*¹⁶ also investigated the interactions and the photoreactions of synthetic psoralens containing psoralen and thymine rings, two psoralen rings, or two thymine rings. Recently, because of the importance of interaction between the 8-methoxypsoralen and purine base pairs in DNA, Yoo *et al.* reported preparation of some 8-methoxypsoralen-adenine (MOPCH₂OCnAd) model compounds, the bifunctional psoralen derivatives containing an adenine as electron donor linked by a varying length of polymethylene bridges starting from **1**, and studied some photophysical properties including intramolecular ring-ring stacking interactions between the two aromatic moieties.¹⁷

It seemed to be of great significance in relation to previous works to study new bispsoralen analogs whose structures allow cross-linking of DNA. Hence, in this paper, synthetic models BPSBA-C_n (**5-10**) in which the psoralens are linked by a bisamide-polymethylene chain to psoralens, thymine, and adenine were devised. Photophysical properties of new models **5-10** including π - π stacking interaction between the two aromatic moieties were also reported.

Experimental Section

Materials and instruments. All the reactions were carried out under a dry nitrogen atmosphere, unless otherwise stated. The solvents were reagent grade or high-performance liquid chromatography (HPLC) grade and purified according to the literature procedures.¹⁸ Most of the chemical reagents were purchased from Aldrich chemical Co. and were used as received without further purification in most cases. 8-MOP (**1**) was obtained from Sigma chemical Co. and purified by recrystallization from methanol. Merck precoated silica gel plates (Art. 5554) with fluorescent

Abbreviations: DMF, *N,N*-dimethylformamide; EI, electron impact; FTIR, Fourier transform infrared; HRMS, high resolution mass spectroscopy; HPLC, high-performance liquid chromatography; 8-MOP, 8-methoxypsoralen; PBSBA-C₂, 8-MOP-NHCOCH₂CH₂; BPSBA-C_n, Bispsoralen bisamide polymethylene (8-MOP-NHCO(CH₂)_nCONH-8-MOP); NMR, nuclear magnetic resonance; PL, photoluminescence; Ps, psoralen; PUVA, psoralen + UVA; THF, tetrahydrofuran; TMS, tetramethylsilane; UV, ultraviolet; UVA, 320-400 nm radiation.

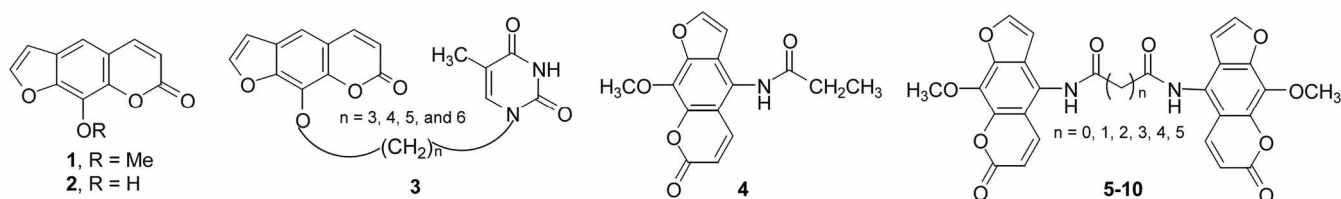


Figure 1. Chemical structures of 8-MOP (**1**), 8-hydroxypsoralen (**2**), model compounds **3** of Lhomme and Decout, PSBA-C2 (**4**), and BPSBA-Cn (**5-10**).

indicator were used as analytical TLC. Gravity column chromatography and flash chromatography were carried out on a silica gel column (230-400 mesh from Merck).

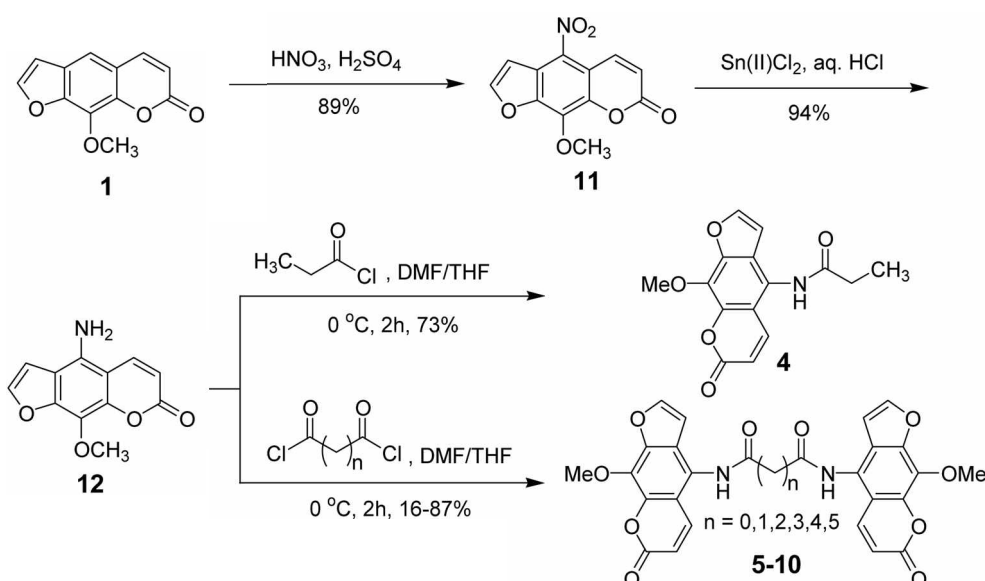
The ¹H nuclear magnetic resonance (NMR) and ¹³C NMR spectra were recorded on Bruker AM-400 MHz and AM-300 MHz spectrometers. Proton chemical shifts (δ) were reported in ppm downfield from tetramethylsilane (TMS), and ¹³C resonances were recorded using the 39.5 ppm DMSO-d₆ resonance peak of the solvent as internal reference and reported in ppm downfield from TMS. Infrared spectra (IR) spectra were recorded on a Bomem MB-100 Series FT-IR spectrophotometer. Mass spectra were determined at 70 eV with V.G. AutoSpec Ultima by the electron impact (EI) method. Elemental analysis (EA) data were recorded on EA 1110-Fisons elemental analyzers. Melting points were determined in capillary tubes on a Thomas Hoover capillary melting point apparatus. UV-visible spectra were recorded on a Shimadzu UV-3100S spectrophotometer. Fluorescence spectra were recorded on a Perkin-Elmer LS-50 luminescence spectrometer with a gated photomultiplier tube detector at room temperature (excitation source at 350 nm).

Synthesis. Individual new bispsoralen and reference compounds were synthesized as follows: 8-MOP-NO₂ (**11**, 5-nitro-8-methoxypsoralen) was obtained from 8-MOP (**1**) in 89% yield by the known procedure.¹⁹ Reduction of 8-

MOP-NO₂ (**11**) with Sn(II)Cl₂ and aqueous HCl solution afforded 8-MOP-NH₂ (**12**, 5-amino-8-methoxypsoralen) in 94% yield. The reference molecule (**4**) was prepared in 73% yield by the amidation of **12** with propionyl chloride in ice-bath.²⁰ The model compounds (BPSBA-Cn, **5-10**) were directly prepared by the amidation of **12** in DMF with α,ω -alkanoyl dichloride in THF at 0 °C (Scheme 1).

Preparation of PSBA-C2 (4). To a stirred solution of 8-MOP-NH₂ (**12**, 0.20 g, 0.87 mmol) in DMF (3 mL) under argon gas was added propionyl chloride (80.0 mg, 0.87 mmol) in THF (50 mL) dropwise at 0 °C for 2 h. The reaction mixture was filtered, washed with methanol and dried *in vacuo* to give compound **4** (0.18 g, 73%); mp 223-224 °C; ¹H NMR (400 MHz, DMSO-d₆) δ 1.15 (t, 3H, *J* = 7.6 Hz), 2.50 (t, 2H, *J* = 7.6 Hz), 4.15 (s, 3H), 6.42 (d, 1H, *J* = 9.8 Hz), 6.87 (d, 1H, *J* = 2.2 Hz), 7.98 (d, 1H, *J* = 9.8 Hz), 8.07 (d, 1H, *J* = 2.2 Hz), 10.08 (s, 1H); ¹³C NMR (100 MHz, DMSO-d₆) δ 9.72, 28.63, 61.11, 106.35, 111.92, 113.38, 121.72, 122.82, 130.19, 141.92, 142.65, 146.90, 147.03, 159.44, 172.80; IR (cm⁻¹) 3431, 3246, 3133, 3102, 2980, 2949, 2903, 1723, 1656, 1592, 1517, 1481, 1381, 1227, 1165, 1138, 1082, 1049, 1035, 940, 852, 755; Mass (*m/e*, %) 287 (42), 230 (54), 216 (100), 159 (11), 57 (58); HRMS calcd for C₁₅H₁₃NO₃: 287.0794, found: 287.0799.

Preparation of BPSBA-C0 (5). Reaction of 8-MOP-NH₂ (**12**, 0.30 g, 1.30 mmol) in DMF (2 mL) with oxalyl chloride



Scheme 1. Synthesis of the reference, PSBA-C2 (**4**) and the model compounds, BPSBA-Cn (**5-10**).

(82.0 mg, 0.65 mmol) in THF (70 mL) was carried out as described for the preparation of **4** to obtain compound **5** (0.29 g, 87%): mp 326–327 °C; ^1H NMR (300 MHz, DMSO- d_6) δ 4.19 (s, 6H), 6.45 (d, 2H, $J=9.8$ Hz), 7.10 (d, 2H, $J=2.2$ Hz), 8.11 (d, 2H, $J=2.2$ Hz), 8.19 (d, 2H, $J=9.8$ Hz), 11.19 (s, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 61.33, 106.87, 112.75, 113.71, 120.36, 123.66, 131.08, 142.01, 142.71, 146.97, 147.36, 159.42, 159.68; IR (cm^{-1}) 3437, 3367, 3270, 3123, 3037, 2955, 2892, 1735, 1686, 1591, 1500, 1423, 1383, 1315, 1207, 1158, 1045, 949, 827, 752; Mass (m/e , %) 516 (26), 313 (12), 257 (18), 231 (70), 216 (60), 117 (49), 111 (37), 97 (57), 84 (65), 71 (73), 66 (65), 57 (100); Anal. Calcd. for $\text{C}_{26}\text{H}_{16}\text{N}_2\text{O}_{10}$: C (60.47%), H (3.12%), N (5.43%). Found: C (60.02%), H (3.09%), N (5.45%).

Preparation of BPSBA-C1 (6). Reaction of 8-MOP-NH₂ (**12**, 0.20 g, 0.87 mmol) in DMF (2 mL) with malonyl dichloride (61.0 mg, 0.43 mmol) in THF (70 mL) was carried out as described for the preparation of **4** to obtain compound **6** (36.5 mg, 16%): mp 271–273 °C; ^1H NMR (300 MHz, DMSO- d_6) δ 3.78 (s, 2H), 4.18 (s, 6H), 6.45 (d, 2H, $J=9.8$ Hz), 6.96 (d, 2H, $J=2.2$ Hz), 8.09 (d, 2H, $J=2.2$ Hz), 8.13 (d, 2H, $J=9.8$ Hz), 10.46 (s, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 30.65, 61.14, 106.26, 112.25, 113.77, 121.04, 123.16, 130.55, 141.19, 142.64, 146.97, 147.16, 159.42, 166.77; IR (cm^{-1}) 3441, 3243, 3120, 3103, 3001, 2953, 2862, 1733, 1641, 1587, 1510, 1473, 1412, 1389, 1201, 1165, 1132, 1051, 1039, 963, 948, 829, 751; Mass (m/e , %) 530 (2), 446 (2), 257 (52), 232 (61), 231 (98), 217 (67), 216 (100), 188 (68), 170 (46), 160 (35), 132 (36), 120 (56), 104 (30), 80 (54), 77 (27), 52 (32); HRMS calcd for $\text{C}_{27}\text{H}_{18}\text{N}_2\text{O}_{10}$: 530.0962, found: 530.0978.

Preparation of BPSBA-C2 (7). Reaction of 8-MOP-NH₂ (**12**, 0.20 g, 0.87 mmol) in DMF (3 mL) with succinyl chloride (67.0 mg, 0.43 mmol) in THF (70 mL) was carried out as described for the preparation of **4** to obtain compound **7** (0.12 g, 50%): mp 332–334 °C; ^1H NMR (300 MHz, DMSO- d_6) δ 2.86 (s, 4H), 4.15 (s, 6H), 6.34 (d, 2H, $J=9.8$ Hz), 6.86 (d, 2H, $J=2.2$ Hz), 8.02 (d, 2H, $J=2.2$ Hz), 8.05 (d, 2H, $J=9.8$ Hz), 10.23 (s, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 30.80, 30.90, 61.26, 106.86, 112.00, 113.15, 122.13, 123.03, 130.19, 141.97, 142.74, 146.83, 147.13, 159.62, 171.73; IR (cm^{-1}) 3437, 3251, 3167, 3142, 3037, 2947, 2868, 1724, 1647, 1592, 1520, 1481, 1424, 1380, 1320, 1141, 1050, 975, 950, 829, 754; Anal. Calcd. for $\text{C}_{28}\text{H}_{20}\text{N}_2\text{O}_{10}$: C (61.76%), H (3.70%), N (5.15%). Found: C (61.71%), H (3.80%), N (5.11%).

Preparation of BPSBA-C3 (8). Reaction of 8-MOP-NH₂ (**12**, 0.27 g, 1.18 mmol) in DMF (3 mL) with glutaryl dichloride (99.7 mg, 0.59 mmol) in THF (80 mL) was carried out as described for the preparation of **4** to obtain compound **8** (0.25 g, 76%): mp 338–339 °C; ^1H NMR (300 MHz, DMSO- d_6) δ 1.98–2.07 (m, 2H), 2.64 (t, 4H, $J=6.8$ Hz), 4.10 (s, 6H), 6.33 (d, 2H, $J=9.8$ Hz), 6.93 (d, 2H, $J=1.8$ Hz), 8.03 (d, 2H, $J=1.8$ Hz), 8.08 (d, 2H, $J=9.8$ Hz), 10.84 (s, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 20.98, 34.79, 61.10, 106.43, 111.90, 113.31, 121.59, 122.83,

130.23, 141.40, 142.63, 146.86, 147.01, 159.39, 171.59; IR (cm^{-1}) 3440, 3248, 3150, 3121, 3009, 2951, 2865, 1735, 1662, 1592, 1518, 1481, 1383, 1210, 1164, 1137, 1062, 1030, 952, 845, 824, 749; Anal. Calcd. for $\text{C}_{29}\text{H}_{22}\text{N}_2\text{O}_{10}$: C (62.37%), H (3.97%), N (5.02%). Found: C (62.84%), H (4.04%), N (5.10%).

Preparation of BPSBA-C4 (9). Reaction of 8-MOP-NH₂ (**12**, 0.15 g, 0.65 mmol) in DMF (2 mL) with adipoyl chloride (59.4 mg, 0.32 mmol) in THF (50 mL) was carried out as described for the preparation of **4** to obtain compound **9** (81.0 mg, 44%): mp 329–330 °C; ^1H NMR (300 MHz, DMSO- d_6) δ 1.78 (s, 4H), 2.58 (s, 4H), 4.13 (s, 6H), 6.36 (d, 2H, $J=9.9$ Hz), 6.88 (d, 2H, $J=2.2$ Hz), 8.02 (d, 2H, $J=9.9$ Hz), 8.05 (d, 2H, $J=2.2$ Hz), 10.43 (s, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 24.88, 35.17, 61.13, 106.52, 111.83, 113.28, 121.78, 122.77, 130.17, 141.52, 142.67, 146.85, 147.04, 159.45, 171.98; IR (cm^{-1}) 3440, 3245, 3133, 3104, 3007, 2947, 2867, 1729, 1649, 1591, 1517, 1479, 1423, 1380, 1208, 1163, 1138, 1054, 1031, 972, 951, 828, 753; Mass (m/e , %) 572 (9), 356 (56), 342 (15), 328 (39), 314 (11), 286 (24), 272 (22), 257 (12), 244 (20), 232 (40), 231 (91), 230 (31), 217 (26), 216 (100), 201 (10), 188 (17), 170 (12), 120 (8). HRMS calcd for $\text{C}_{30}\text{H}_{24}\text{N}_2\text{O}_{10}$: 572.1431, found: 572.1480.

Preparation of BPSBA-C5 (10). Reaction of 8-MOP-NH₂ (**12**, 0.27 g, 1.17 mmol) in DMF (3 mL) with pimeloyl chloride (0.12 g, 0.58 mmol) in THF (80 mL) was carried out as described for the preparation of **4** to obtain compound **10** (0.18 g, 52%): mp 283–285 °C; ^1H NMR (300 MHz, DMSO- d_6) δ 1.44–1.53 (m, 2H), 1.68–1.82 (m, 4H), 2.48 (t, 4H, $J=1.4$ Hz), 4.13 (s, 6H), 6.29 (d, 2H, $J=7.4$ Hz), 6.81 (d, 2H, $J=1.5$ Hz), 7.91 (d, 2H, $J=7.4$ Hz), 7.99 (d, 2H, $J=1.5$ Hz), 10.13 (s, 2H); ^{13}C NMR (75 MHz, DMSO- d_6) δ 24.96, 28.36, 35.39, 61.12, 106.37, 111.89, 113.35, 121.62, 122.83, 130.24, 141.28, 142.64, 146.86, 147.03, 159.40, 172.10; IR (cm^{-1}) 3439, 3252, 3143, 3119, 3008, 2946, 2860, 1731, 1659, 1592, 1519, 1480, 1423, 1382, 1318, 1208, 1163, 1140, 1052, 974, 951, 823, 751; Mass (m/e , %) 586 (42), 342 (26), 339 (32), 328 (36), 327 (52), 254 (69), 253 (100), 236 (52), 235 (99), 231 (59), 230 (90), 224 (40), 216 (94), 160 (40), 130 (45), 120 (64), 105 (39), 77 (39); HRMS calcd for $\text{C}_{31}\text{H}_{26}\text{N}_2\text{O}_{10}$: 586.1587, found: 586.1578.

Determination of the percent of hypochromism (%H). All UV spectra were measured under the same condition: 2.5×10^{-5} M, 20 °C, 100% DMF. The percent of hypochromism (%H) corresponds to an integrated hypochromic effect. The hypochromic effect is defined by the percent of hypochromism (%H) = $[1 - f(\text{BPSBA-Cn})/2f(\text{PSBA-C2})] \times 100$, where f is the oscillator strength of the transition, *i.e.* a measure of the intensity of absorption $f = 4.32 \times 10^{-9} \epsilon(\lambda)/\lambda^2 d\lambda$, where $\epsilon(\lambda)$ is the molar absorption coefficient. The f values were obtained from optical densities measured at every 2.5 nm by application of the Simpson's rule, as described in precedent publications.^{21,22} The percent hypochromism (%H) reflects the stacking of the two chromophores in the molecules and its value is generally considered as a measure of the interactions.

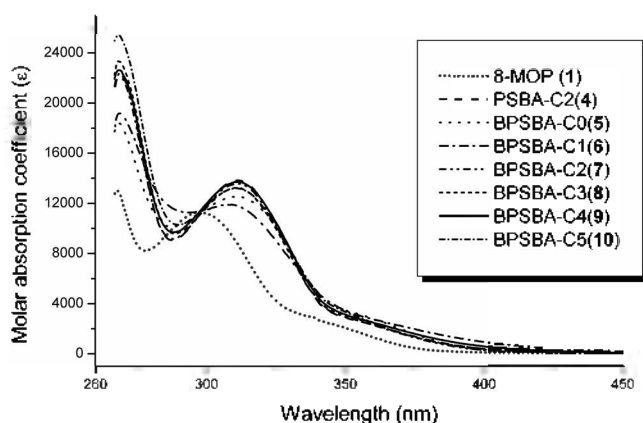


Figure 2. Ultraviolet absorption spectra of BPSBA-C_n (5-10), PSBA-C2 (4), 8-MOP (1). All the spectra were measured under the same conditions: 2.5×10^{-5} M, 20 °C in DMF.

Results and Discussion

UV absorption spectra. UV absorption spectra of the model BPSBA-C_n (5-10) and two reference compounds 8-MOP (1) and PSBA-C2 (4) are shown in Figure 2 and Table 2. All the spectra were obtained under the same condition in DMF at 20 °C. The concentrations of the solutions were kept low enough (*ca.* 25 μM) to avoid any intermolecular contribution.¹³ The most striking feature characterizing the relationships between BPSBA-C_n (5-10) and 8-MOP (1) is that absorption maximum of BPSBA-C_n (5-10) (*ca.* 269 and 313 nm) having two aromatic moieties tends to move toward longer wavelengths than 8-MOP (1) (265 and 299 nm). BPSBA-C_n shows red-shifted but similar UV absorption pattern as 8-MOP in the range of 310-380 nm, at which psoralen + UVA(PUVA) therapy is conducted.

Percent hypochromism (%H). The %H values calculated in six different regions of the spectra for the six models 5-10 are summarized in Table 1. The table indicates that all the systems prepared show appreciable hypochromism which is indicative of substantial intramolecular ring-ring stacking. An interesting point, which needs further investigation, is raised by the comparison of %H for the six models 5-10 possessing chains of different lengths. All values are important and remain in the same order. The results clearly indicate that the model compounds 5-10 are in equilibrium of folded or stacked and unfolded conformations. The variation of %H values showed a significant difference between three and four atoms in bridging methylene chain, but a slight difference in the linker with more than four atoms as shown in Table 1. These variations probably reflect a decrease of the proportion of folded or stacked conformations as the length of the linker is decreased or/and the geometrical overlap of the chromophores in the folded or stacked conformations. For BPSBA-C3 (8) and BPSBA-C4 (9), the magnitudes of %H determined for the whole spectrum are quite different, suggesting incomparable degrees of stacking for the two compounds. The large differences observed in the values calculated for the different

Table 1. Percent hypochromism values (%H) determined for model 5-10 between different wavelength ranges. Spectra measured at 20 °C in DMF. Relative precision of %H is $\pm 0.5\%$

Model Wave- length Range (nm)	5 (n=0)	6 (n=1)	7 (n=2)	8 (n=3)	9 (n=4)	10 (n=5)
450-310	-6.3	8.1	12.3	13.9	18.3	15.9
450-300	-4.0	8.2	12.3	13.8	19.2	16.3
450-290	-4.3	8.5	12.4	14.0	19.7	16.6
450-270	0.0	9.3	13.3	14.2	20.6	16.4
340-290	-0.9	8.9	12.3	13.6	21.3	16.9
340-270	-2.9	8.2	13.4	14.0	21.8	16.7

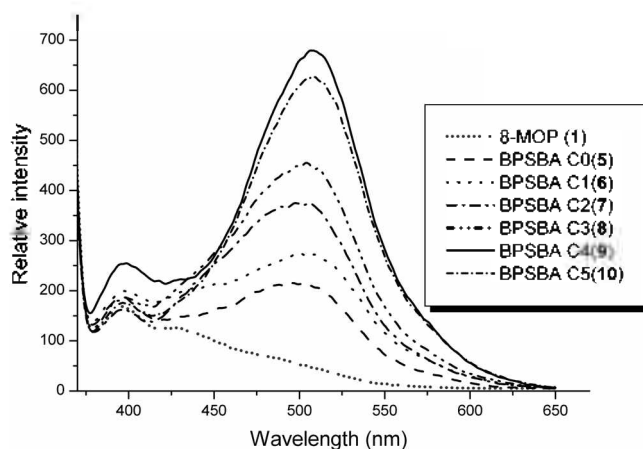


Figure 3. Fluorescence spectra of BPSBA-C_n in DMF at room temperature (excitation at 350 nm).

spectrum portions probably reflect variations in the geometrical overlap of the chromophores in the folded or stacked conformations. This suggests that the complexes adopt different preferred geometries according to the chain length. The model 9 showed the highest value of %H, which allowed the most efficient ring-ring stacking between two aromatic units linked by bisamide-four methylene chain.

We compared the percent hypochromism value (%H) of the model compound BPSBA-C4 (9) with that of previously reported 8-methoxypsoralen-adenine (MOPCH₂OC_nAd) model compounds^{17a} to study the correlation of %H with molecular structures. The maximum %H values of MOPCH₂OC₂Ad were 10.4-18.2, while those of BPSBA-C4 (9) were 18.3-21.8 as shown in Table 1. The results indicate that the model compounds, bis-8-methoxypsoralen systems show more efficient π - π stacking interaction than the 8-methoxypsoralen-adenine pair.

Fluorescence emission spectra. A particular folded or stacked conformation was intended to portray not necessarily a preferred overlap but rather any stacked conformation.²³ BPSBA-C_n could have a number of conformations including unstacked or unfolded and stacked or folded forms. The fluorescence emission spectra of 8-MOP (1) and BPSBA-C_n (5-10) in DMF at room temperature were measured at the same excitation wavelength (350 nm) shown in

Table 2. The electronic absorption and fluorescence maximum (λ_{max}) of 8-MOP (**1**) and BPSBA-Cn (**5-10**)

Entry	Compounds	UV (nm)		PL (nm)	
		265	299	396	–
1	8-MOP (1)	265	299	396	–
2	BPSBA-C0 (5)	267	310	397	503
3	BPSBA-C1 (6)	267	307	397	500
4	BPSBA-C2 (7)	267	309	398	500
5	BPSBA-C3 (8)	268	311	398	504
6	BPSBA-C4 (9)	269	313	399	509
8	BPSBA-C5 (10)	268	312	398	507

Figure 3 and Table 2. Although the spectral shapes for all samples were similar having two maximum intensities around 399 and 509 nm, the intensity of all model compounds **5-10** was much stronger than that of 8-MOP (**1**). Two aromatic units linked by flexible polymethylene bridge could adopt folded and unfolded conformations in solution and the position of the folded \rightleftharpoons unfolded conformational equilibrium was a measure of the intramolecular ring-ring stacking interaction as reported earlier.^{17a} Interestingly, the model **9** ($n = 4$) showed much stronger fluorescence than the other compounds (**5**, **6**, **8**, **10** and 8-MOP) in agreement with the percent hypochromism (%H) values. The results indicate that two aromatic units in the compound **9** were well stacked due to strong π - π stacking interactions resulting in the rigid conformation and consequently, the nonradiative decay paths like internal conversion or intersystem crossing were slowed down leading to strong fluorescence compared to those in the short linker models ($n < 3$). On the other hand, the compounds (**5**, **6**, **7** and **8**) having the short linker were probably less stacked due to the diminishing folded conformation resulted from reducing flexibility by two amide bonds.

In conclusion, we have prepared new bifunctional bispsoralen derivatives (BPSBA-Cn, **5-10**) allowing the π - π stacking interactions between two 8-methoxypsoralens. UV absorption and fluorescence emission spectra were obtained and the percent hypochromism studies indicated the most efficient ring-ring stacking interactions in BPSBA-C4 (**9**). Additionally the model bis-8-methoxypsoralen systems showed more efficient ring-ring stacking interaction than the 8-methoxypsoralen-adenine pair.

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