

Aggregating tendencies of some *N*-alkylcarbazoles

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Aggregation of some nitrogen-containing heterocyclic compounds have been investigated by means of fluorescence spectroscopy in aqueous or aquiorgano binary mixtures of different Φ values for the first time. The aggregators studied are *N*-butylcarbazole (CBZ-4), *N*-octylcarbazole (CBZ-8), *N*-dodecylcarbazole (CBZ-12), and *N*-hexadecylcarbazole (CBZ-16). Their aggregating tendencies have been evaluated by measuring their critical aggregate concentration values (CAgC's). Our results indicate that the *N*-alkylcarbazoles, just like the anthracene derivatives with different chain-lengths, can also be used as fluorescence probes for evaluating aggregating tendencies or CAgC values.

Keywords Aggregation, hydrophobic-lipophilic interaction, *N*-alkylcarbazoles

Hydrophobic-lipophilic interaction (HLI), together with Nature's other forces, creates aggregates (Ag's), micelles, vesicles, and living cells from organic molecules in aggregating media.¹ Organic molecules which tend to aggregate in solvents with solvent aggregating power (SAgP) were named as aggregators (Agr's).^{2,3} Ag's of electrically neutral organic molecules are formed almost solely by HLI.^{4,5} The aggregating tendencies of aggregators are generally evaluated by measuring their critical aggregate concentrations (CAgC's) in aqueous solutions or in aquiorgano binary mixtures of different Φ values, where Φ is the volume fraction of the organic component of the mixtures. CAgC is the concentration of the Agr at the onset of aggregation. Under similar conditions, a smaller CAgC value signifies a greater aggregating tendency. In general, in the absence of pronounced shape effect and on the basis of roughly estimated Rekker's Σf values for hydrophobicity,⁶ the more hydrophobic a particular Agr molecule is, the greater will be its aggregating tendency.

In the past, CAgC's of naphthalene Agr's and anthracene Agr's have been evaluated by plotting their I_e/I_m ratios against their initial concentrations ($[Agr]_i$) by means of fluorescence spectroscopy,^{4,7} where I_e is the fluorescence intensity of the excimer formed by the probe after the occurrence of aggregation, I_m is the fluorescence intensity of the excited monomer. However, all these previously studied simple Agr's are either carboxylates or some phosphorous-containing and sulfur-containing compounds.^{8,9} We have now extended our study to the aggregation behavior of some nitrogen-containing heterocyclic compounds in the dioxane (DX)-H₂O binary solvent system, namely, *N*-alkylcarbazoles.

The *N*-alkylcarbazoles studied are, namely, *N*-butylcarbazole (CBZ-4), *N*-octylcarbazole (CBZ-8), *N*-dodecylcarbazole (CBZ-12), as well as *N*-hexadecylcarbazole (CBZ-16) in DX-H₂O binary mixtures or in aqueous solution at 35°C. These carbazoles were prepared by reactions as shown in Scheme 1.¹⁰

Experimental

Apparatus

¹H NMR spectra were obtained at 90 MHz on a Varian FX-90Q spectrometer with TMS as the internal standard. Flash column chromatography was performed on silica gel with petroleum ether-ethyl acetate (EtOAc) as the eluent.

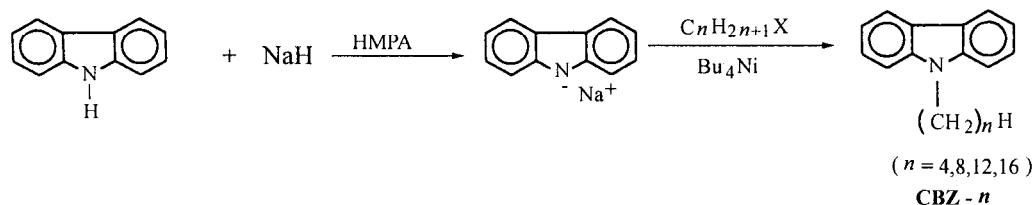
Reagents and substrates

All target compounds were prepared in this laboratory and identified later by elemental analysis and ¹H

NMR spectra. They were purified by flash column chromatography on silica gel with petroleum ether-ethyl ac-

etate as the eluent. They all possess the strongest UV-Vis absorption λ_{\max} at 235 nm in cyclohexane.

Scheme 1



Electronic spectra

All aqiorgano solutions used for spectroscopic measurements were prepared from deionized water and dioxane (DX) which was purified by a standard procedure.¹¹ Fluorescence emission spectra in aqueous or aqiorgano solutions (DX-H₂O) of **CBZ-n** were recorded by a Perkin-Elmer LS-50 spectrometer at 35°C. The relative fluorescence intensity measurements were determined at the emission maximum 353 nm for the monomer and 410 nm for the excimer of **CBZ-n**^{*}; an excitation wavelength of 315 nm was used. The wavelengths of fluorescence peaks in the emission of excited **CBZ-n** were somewhat red-shifted as compared with those reported for the solvent cyclohexane¹² because of the polarity of the DX-H₂O solution. The error in the fluorescence intensity measurements was less than $\pm 5\%$. UV-Vis spectra were recorded on a Perkin-Elmer 559 spectrometer.

Preparation and identification of the *N*-alkylcarbazoles (**CBZ-n**)

General procedure

A solution of carbazole (3.34 g, 0.02 mol) in 15 mL DMSO (or HMPA) in a three-necked flask was flushed with nitrogen and then chilled to 0°C. To this solution was added sodium hydride (0.48 g, 0.02 mol) with stirring over a period of 10 min. The mixture was then stirred at room temperature for 5 h. At this point the solution was rechilled to 0°C, C_nH_{2n+1}Br (0.02 mol) was rapidly added, and the resulting mixture was

allowed to come to room temperature overnight with stirring. The mixture was then diluted with water (25 mL) and extracted with ether (3 \times 25 mL). The combined ethereal extracts were washed with water (3 \times 40 mL) and dried with anhydrous magnesium sulfate. The crude *N*-alkylcarbazole was purified by crystallization from ethanol or by flash column chromatography on silica gel with petroleum ether-ethyl acetate as the eluent to afford the pure compound.

N-Butylcarbazole (**CBZ-4**) White solid. mp 62–63°C. λ_{\max} (cyclohexane): 235, 262, 287, 293, 328, 343 nm. δ_{H} (benzene-*d*₆): 0.1–1.1 (m, 7H), 3.2 (t, 2H), 6.6–6.9 (m, 6H), 7.5 (d, 2H). Anal. C₁₆H₁₇N. Calcd: C, 86.09; H, 7.62; N, 6.28. Found: C, 85.98; H, 7.77; N, 6.22.

N-Octylcarbazole (**CBZ-8**) Yellowish liquid. λ_{\max} (cyclohexane): 235, 259, 287, 293, 329, 343 nm. δ_{H} (benzene-*d*₆): 0.2–1.1 (m, 15H), 3.3 (t, 2H), 6.7–6.9 (m, 6H), 7.6 (d, 2H). Anal. C₂₀H₂₅N. Calcd: C, 86.07; H, 8.96; N, 5.01. Found: C, 86.06; H, 9.39; N, 4.64.

N-Dodecylcarbazole (**CBZ-12**) White solid. mp: 38–39°C. λ_{\max} (cyclohexane): 235, 259, 287, 293, 328, 344 nm. δ_{H} (benzene-*d*₆): 0.2–1.1 (m, 23H), 3.2 (t, 2H), 6.5–6.9 (m, 6H), 7.5 (d, 2H). Anal. C₂₄H₃₃N. Calcd: C, 85.97; H, 9.85; N, 4.18. Found: C, 85.79; H, 10.04; N, 4.00.

N-Hexadecylcarbazole (**CBZ-16**) White sol-

id. mp: 51—52°C. λ_{\max} (cyclohexane): 235, 260, 287, 293, 328, 344 nm. δ_{H} (CDCl₃): (in comparison with the chemical shifts of the sample in benzene-*d*₆, these values appear downfield in CDCl₃): 0.7—1.8 (m, 31H), 4.3(t, 2H), 7.4(d, 6H), 8.2(d, 2H). Anal. C₂₈H₄₁N. Calcd: C, 85.93; H, 10.49; N, 3.58. Found: C, 86.21; H, 10.73; N, 3.63.

Preparation of the carboxylates (A-*n*)

Carboxylates esters A-*n* were prepared by previously reported procedures.^{13,14} All of them were also identified by elemental analysis, UV-Vis and ¹H NMR.

Results and discussion

The target molecule CBZ-*n* in the present study is an excellent fluorescence probe.¹³ In order to investigate the aggregating tendencies of CBZ-*n* in the DX-H₂O system, we selected the fluorescence methodology for evaluating their CA_gC values. In the fluorescence spectra, the peak of CBZ-*n* excimer at 410 nm was formed with increasing CBZ-*n* concentration as a consequence of coaggregation of CBZ-*n** with CBZ-*n* (see Fig. 1). Therefore, I_e at 410 nm and I_m at 353 nm can be measured independently. The ratio I_e/I_m represents the fluorescence intensity of the total amount of excimer

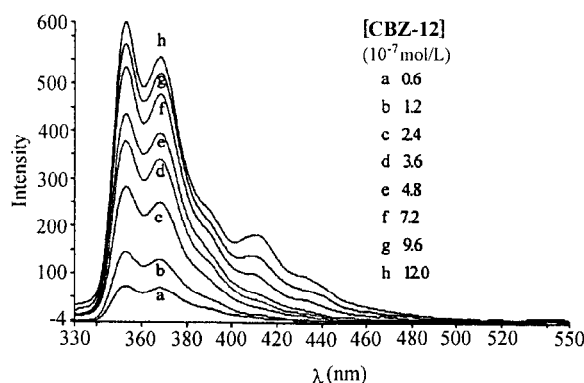


Fig. 1 Concentration effect on the fluorescence spectra of CBZ-12* in $\Phi = 0.30$ DX-H₂O at 35°C.

formed at 410 nm relative to the fluorescence intensity of the monomer at 353 nm. When the concentration of CBZ-12 is below CA_gC (see Fig. 2), the I_e/I_m ratio appeared to be a constant within experimental uncertainty ($\pm 10\%$), when above CA_gC. The I_e/I_m vs. [CBZ-

n] plot increases linearly with graded concentrations of CBZ-*n*, the CA_gC value is then determined at the crossing point of the curves.

In a particular aggregating binary solvent of constant composition Φ , the degree of aggregation of the Agr increases with its concentration.^{4b,14} CBZ-*n* exists only in a monomeric state when their concentrations are below their CA_gC values. The fluorescence spectra (see Fig. 1) show that there is only a monomeric emission band of CBZ-12* in the $\Phi = 0.30$ DX-H₂O system when the concentration is 0.60×10^{-7} mol/L, *i. e.*, below its CA_gC value, with a emission maximum at 353 nm. The intensities of monomeric emission increase with the graded concentrations of CBZ-12 and an emission peak emerges at the wavelength of 410 nm when the concentration of CBZ-12 is higher than CA_gC at this Φ value. This peak can be used to monitor the excimer formation of CBZ-12 brought about by aggregation.

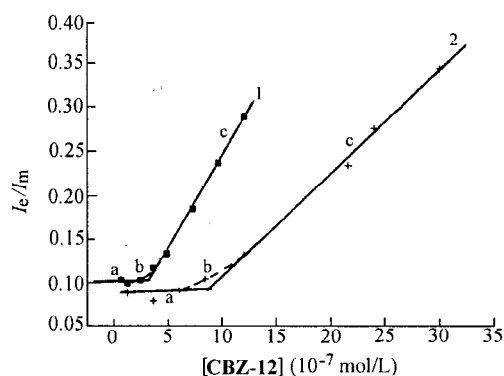


Fig. 2 Plot of I_e/I_m vs. [CBZ-12] (10^{-7} mol/L) in DX-H₂O with $\Phi_1 = 0.30$ for curve 1, $\Phi_2 = 0.35$ for curve 2 at 35°C.

The I_e/I_m values of Agr's in the DX-H₂O mixture of graded Φ values at various initial substrate concentrations were measured and plotted against initial substrate concentrations ($[Agr]_i$), for each Agr and solvent system a figure with curves corresponding to different Φ values can be obtained, and CA_gC values can be determined by the crossing point in these curves. As exemplified by Fig. 2, the relationship between the initial concentration of CBZ-12 and I_e/I_m values at different Φ values has been investigated. As illustrated by curve 1, the horizontal phase "a" shows that there is a monomeric region in which no aggregation of the target molecule (CBZ-12) occurs. After a transition phase "b" (dashed

line),¹⁵ the fluorescence intensities of excited fluorescence probe increase with its concentration linearly. In this ascending phase "c" the fluorescence intensities of excimer increase with the concentration of the target molecule. The CAgC value of target molecule can be evaluated to be $3.17 \pm 0.31 \times 10^{-7}$ mol/L for **CBZ-12** in the $\Phi = 0.30$ system, and $9.06 \pm 0.33 \times 10^{-7}$ mol/L in the $\Phi = 0.35$ system (Curve 2). These results also show that the occurrence of aggregation of the target molecule depends on the concentration of **CBZ-*n*** and the Φ value of the medium. This observation is very similar to observations on the behavior of the carboxylates.¹⁵ Other Agr's, *i. e.*, **CBZ-4**, **CBZ-8**, and **CBZ-16** all have similar curves, in other words, all these data indicate that the occurrence of aggregation depend on the substrate concentration ($[Agr]_i$) and solvent aggregation power (SAGP) of the medium, because the SAGP of one specified solvent system is directly related to the Φ values.¹⁶

The CAgC values of **CBZ-4**, **CBZ-8**, **CBZ-12**, and **CBZ-16** in the H₂O or DX-H₂O system with graded Φ values are listed in Table 1. Examination of Table 1 reveals the following observations: As expected, CAgC values increase with increasing Φ values for **CBZ-8**, **CBZ-12**, and **CBZ-16** in the DX-H₂O system. Another interesting result found for the first time is that even the "short-chained" **CBZ-4** molecule can also aggregate in H₂O (see Fig. 3). The CAgC value of **CBZ-4** has been found to be $22.6 \pm 1.74 \times 10^{-7}$ mol/L, because four-carbon chain compounds of carboxylates, phosphonates, phosphinates and alkylsulfonates in H₂O solution do not undergo aggregation in the above-mentioned concentration range. Zhu *et al.* reported that neutral organic molecules even with only a three carbon chain can show some aggregating tendencies, thus Agr's are formed by a stepwise process.¹⁵ Our results might also imply that simple aggregates are formed by a stepwise process.

Table 1 CAgC values (10^{-7} mol/L) of **CBZ-*n*** in DX-H₂O system of different Φ values at 35°C

Agr	Φ (DX-H ₂ O)						
	0	0.20	0.25	0.30	0.35	0.40	0.45
CBZ-4	22.6 ± 1.74						
CBZ-8		8.00 ± 0.78	26.0 ± 0.89				
CBZ-12				3.17 ± 0.31	9.06 ± 0.33		
CBZ-16						7.17 ± 0.76	16.8 ± 0.05

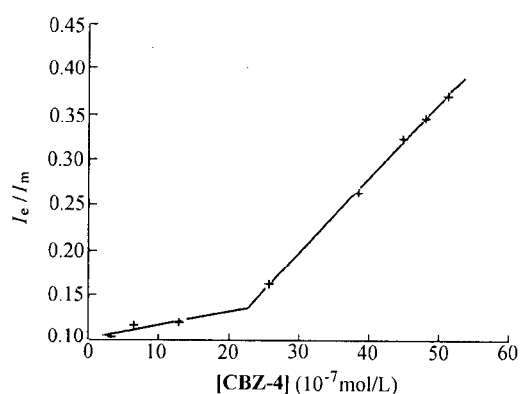


Fig. 3 Plots of I_e/I_m vs. $[CBZ-4]$ (10^{-7} mol/L) in H₂O at 35°C.

Figs. 4 and 5 showed that there was a chain-length effect on the aggregation tendencies of **CBZ-8**, **CBZ-12** and **CBZ-16** in $\Phi = 0.30$, 0.35 DX-H₂O systems. As previously mentioned, there could be three phases (a, b and c) for the I_e/I_m vs. $[Agr]_i$ plots. In Figs. 4 and

5, the plots for **CBZ-12** show all these three phases in the concentration range of **CBZ-*n***, however, the plot for **CBZ-16** shows only phase "c" while that for **CBZ-8** shows only the phase "a". Based on the results of the Φ value effect on the aggregating tendencies of **CBZ-*n***, we can legitimately say that there is only a monomeric region for **CBZ-8** in the $\Phi = 0.35$ DX-H₂O system, therefore, the order of increasing aggregating tendency in the $\Phi = 0.35$ DX-H₂O system is **CBZ-8** < **CBZ-12** < **CBZ-16**. In the meanwhile, in the $\Phi = 0.30$ solvent system, the order is the same for **CBZ-*n***. It demonstrates once again that the aggregation tendencies of **CBZ-*n*** depend on alkyl chain-length. Our results are the first evidence for aggregation phenomena of **CBZ-*n*** in DX-H₂O system driven by HLI.

Conclusions

Finally, we may draw the following conclusions: 1) **CBZ-8**, **12** and **16** form simple aggregates in the solu-

tion with SAgP and their aggregation behaviors are rather similar to carboxylates, phosphonates, phosphinates and alkylsulfonates with similar chain lengths. 2) Besides the above-mentioned observations, there is also an interesting aggregation behavior for **CBZ-4**, namely, even the "short-chained" **CBZ-4** molecule can aggregate in H_2O , and its CAgC value is $22.6 \pm 1.74 \times 10^{-7}$ mol/L. 3) The nitrogen-containing heterocyclic carbazole group can now be considered as a useful fluorescence probe group for studying the aggregation behavior of organic compounds.

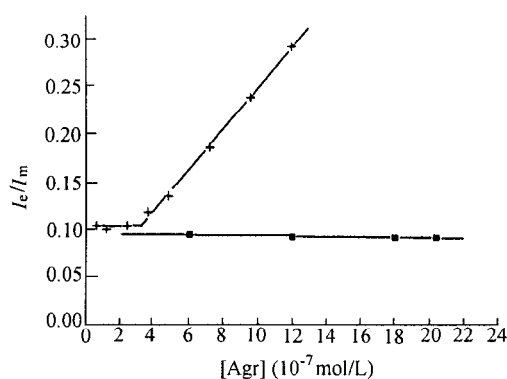


Fig. 4 Plots of I_e/I_m vs. (+) [CBZ-12] and (■) [CBZ-8] (10^{-7} mol/L) in $\Phi = 0.30$ DX- H_2O at $35^\circ C$.

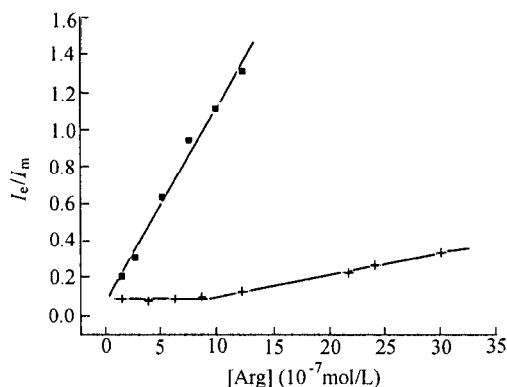


Fig. 5 Plots of I_e/I_m vs. (+) [CBZ-12] and (■) [CBZ-16] (10^{-7} mol/L) in $\Phi = 0.35$ DX- H_2O at $35^\circ C$.

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