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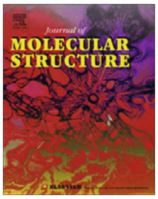

Conformational analysis of polymethine dyes derived from the 2-azaazulene

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ABSTRACT

A systematic investigation of the conformational structure was performed for the series of symmetrical and unsymmetrical mono-, tri-, pentamethine cyanines, and styryl dyes bearing 2-azaazulenium terminal group. The rotation energy barriers of terminal groups were determined *via* the dynamic variable temperature NMR experiments. The conformational transformation energy was calculated by quantum chemical methods (B3LYP and M05-2X) both for the cases of considering the solvent influence and not tacking it into account. Based on the comparison of theoretical and experimental data, relative electron-donating abilities and geometrical features of the heterocyclic terminal groups in 2-azaazulenium dyes were estimated. The arrangement of certain heterocyclic nuclei in order of basicity by considering the results of the dynamic NMR investigations was proposed. Influence of the conjugated chain length and the solvent nature on the conformational lability of the investigated dye molecules was discussed.

1. Introduction

Considerable attention is paid to the investigation of cyanine dyes due to their usefulness in different fields of science and industry [1,2]. These compounds have found numerous applications such as photographic sensitizers [3], nonlinear optical materials [4], fluorescent probes for the biomolecular labelling [5]. They are able to interact with biomolecules *via* the covalent and noncovalent coupling. Thus, suitable fluorophores can be bound to the double-stranded DNA molecules, resulting in the significant enhancement of the fluorescence properties of the latter [6]. To study interactions and structure of the complexes, different physicochemical methods of analysis including X-ray, NMR, and FRET were applied [7]. Depending on the structure, terminal groups and the length of the polymethine chain the dye can bind DNA in several ways [8]. Sterical effects of the terminal groups are very important for the *J*-aggregation of symmetrical cyanines with DNA [9,10].

The molecular structure of the cyanine dye and the asymmetry of its electronic structure (the differences in the electron-donating properties of the terminal groups) are crucial for the process of interaction with biomolecules (DNA), and hence for the spectral properties of the formed complexes [11]. Therefore, study of the peculiarities of the structure and physicochemical properties of the cyanines is important for the prediction and analysis of their bimolecular labelling properties.

The dependence of the dye spectral properties on the electronic nature of terminal groups was examined for an extensive series of symmetrical and asymmetrical cyanines in the middle of the 20th century by Brooker [12]. The concept of the absorption maximum “deviation” and the corresponding scale of basicity were introduced. The dependence of the positions of the absorption maxima in the UV spectra on the differences of the electron-donating properties (basicity) of terminal groups was reported in [13]. Quantum-chemical analysis method of terminal heterocyclic groups’ basicity was developed by Dyadusha and Kachkovskii [14]. On the basis of these studies one can draw conclusions regarding the influence of the asymmetry of the polymethines electronic structure on their physical properties.

However, optical methods are not the only option for the estimation of the electronic asymmetry of the cyanines. NMR spectroscopy is found to be one of the most useful instruments for the investigation of the molecular electronic structure and conformations of the cyanine dye molecules [15,16]. Influence of the sterical hindrance from the terminal groups on the trimethine cyanines conformations was investigated [17]. The dependence of the conformational transformations energy barriers (*cis*-*trans*-isomerization) on the terminal groups and the chromophore chain length was determined experimentally by means of dynamic NMR [18].

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Detailed data on the variable-temperature ^1H NMR conformational analysis for the series of trimethine cyanines derivatives of benzoxazole, benzothiazole, etc. is presented in the literature [19]. This method was also successfully applied to the study of the photoisomerization of trimethine cyanines [20].

According to the X-ray diffraction data and the quantum-chemical analysis of the constitution of polymethine cyanines, in the absence of the sterical hindrance dye chromophores adopt *all-trans* conformation [18]. Quantum-chemical calculations within the AM1 approximation were applied to determine the conformational transformations energy barriers for the cyanines and other linear conjugated systems [21].

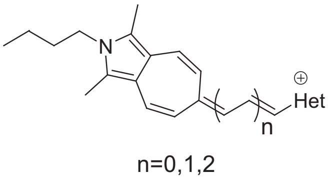
Earlier we have synthesized the series of monomethine [22] and trimethine [23] cyanines bearing 2-azaazulenium moiety and studied it using spectral and quantum-chemical methods. In our previous paper [24] we presented the investigation results of the conformational features of the unsymmetrical monomethine cyanine dye 2-[(2-butyl-1,3-dimethylcyclohepta[*c*]pyrrol-6(2*H*)-ylidene)methyl]-3-ethyl-1,3-benzothiazol-3-ium perchlorate. It was studied both in solution by means of NMR spectroscopy and in the solid state by X-ray diffraction. Due to the data obtained, it was proved that the dye molecule is practically planar in crystalline state. We described the effect of the intramolecular rotation of molecular fragments around the $C_{heterocycle}$—$C_{methine}$ bond, which is slow on the NMR time scale. Both the bond order of the cyanine dye, around which rotation occurs, and the energy barrier of this process were assumed to depend on the electron-donating nature of the terminal groups. The results of the quantum-chemical calculations supported the experimental data. In the work presented below we show that this approach can be used to draw a certain scale of the electron-donating properties of different terminal groups on the basis of the rotation energy derived by the dynamic NMR experiments. Thus, we studied the dependence of the conformational transformations energy barriers on the nature of the terminal groups and on the chromophore chain length for the polymethine dyes derivatives of the 2-azaazulenium.

2. Experimental

2.1. General methods

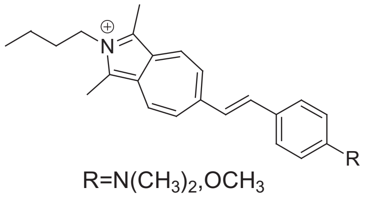
All starting materials and solvents for the synthesis and spectroscopic measurements were supplied by Aldrich Chemical Co. and were used as received without further purification. UV/Vis absorption spectra were recorded on a Shimadzu UV-3100 spectrophotometer. The melting points were measured with a melting point apparatus (Kleinfeld GmbH) and are uncorrected.

We chose representatives of the following groups of 2-azaazulene derivatives as objects of our research: unsymmetrical mono-, tri-, and pentamethine cyanines **AAz-*n*-Het** (Het is second terminal group, see Table 1) and styryl (methoxystyryl) dyes **AAz-St**.



n=0,1,2

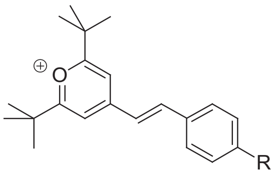
AAz-n-Het



R=N(CH3)2,OCH3

AAz-St(R)

We also investigated styryl/methoxystyryl dyes derivatives of 2,6-di(terbutyl)-pyrylium **OPy-St(R)**:



R=N(CH3)2,OCH3

OPy-St(R)

2.2. Synthesis

The synthesis, UV/Vis spectral characteristics, ^1H and ^{13}C NMR data of 2-azaazulene monomethine cyanines **AAz-0-AAz**, **AAz-0-BIn**, **AAz-0-BO**, **AAz-0-BT**, **AAz-0-4Q** have been described in [22], the synthesis and properties of the corresponding trimethine cyanines – **AAz-1-AAz**, **AAz-1-BIn**, **AAz-1-In**, **AAz-1-BT**, **AAz-1-4Q**, **AAz-1-2Q**, **AAz-1-BIm**, **AAz-1-NPy** – in [23]. The corresponding new monomethine **AAz-0-OPy** and trimethines **AAz-1-OPy** and **AAz-1-BO** have been synthesized in a similar way. The symmetrical (**AAz-2-AAz**) and asymmetrical (**AAz-2-OPy**) pentamethine cyanines as well as styryl dyes (**AAz-St(R)** and **OPy-St(R)**) were synthesized according to the general approaches described in [25]. All compounds were purified by column chromatography and/or recrystallized before use, and their structures were confirmed by NMR.

2.2.1. 2-Butyl-6-[(2,6-di-tert-butyl-4H-pyran-4-ylidene)methyl]-1,3-dimethylcyclohepta[c]pyrrolium tetrafluoroborate *AAz-0-OPy*

Triethylamine (0.1 mL) was added to the solution of 2-butyl-1,3-dimethyl-6-(methylthio)cyclohepta[c]pyrrolium iodide (0.175 g, 0.5 mmol) and 2,6-di-*tert*-butyl-4-methylpyrylium tetrafluoroborate (0.147 g, 0.5 mmol). The solution was refluxed for 5 min, and was then allowed to cool to room temperature. After adding of diethyl ether the dye was precipitated, filtered off, and purified by chromatography on silica gel column eluting with a mixture chloroform: methanol (50:1). Yield 0.1 g (39.6%); mp 225 °C (decomposition). λ_{max} = 580 nm, ε = 63,400 M^{-1} cm^{-1} (in acetonitrile). ^1H NMR ($CDCl_3$, 400 MHz) δ: 7.86 (d, *J* = 11.3 Hz, 2H, 4-H 8-H AAz), 7.05 (d, *J* = 11.3 Hz, 2H, 5-H 7-H AAz), 6.86–6.81 (br. s, 2H, Ar OPy), 6.23 (s, 1H, C_{AAz}—CH), 4.17–4.06 (m, 2H, NCH_2), 2.58 (s, 6H, AAz—CH_3), 1.82–1.54 (m, 2H, NCH_2CH_2), 1.48–1.45 (m, 2H, CH_2CH_3), 1.31 (s, 18H, *t*-Bu), 0.92 (t, *J* = 7.3 Hz, 3H, CH_2CH_3). Calcd. for $C_{29}H_{40}BF_4NO$ (505.44): C 68.91, H 7.98, N 2.77%; found: C 68.73; H 7.71; N 2.85%.

2.2.2. 2-Butyl-6-[3-(2,6-di-tert-butyl-4H-pyran-4-ylidene)prop-1-en-1-yl]-1,3-dimethylcyclohepta[c]pyrrolium tetrafluoroborate *AAz-1-OPy*

Triethylamine (0.1 mL) was added to a solution of 6-(2-anilinovinyl)-2-butyl-1,3-dimethylcyclohepta[c]pyrrolium tetrafluoroborate (0.160 g, 0.38 mmol) and 2,6-di-*tert*-butyl-4-methylpyrylium