Sensitivity of the phenoxy derivatives of 2,4-dihydro-5\textit{H}-[1,2,3]triazolo[4,5-\textit{d}]pyrimidin-5-ones to acidic and basic stimuli

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Abstract

Herein we report the research on the sensitivity of six hydroxy derivatives of dihydrotriazolopyrimidines (HO-DTP) to acids and bases. The UV/Vis and fluorescence spectra of these compounds were investigated with the addition of the acids and bases. Spectral data revealed the strong red shifts for emission and absorption maxima in the presence of KOH and NaOH. Moreover, two DTPs demonstrated strengthening of the emission intensity. The obtained results and data published in our previous paper demonstrated the strong and selective sensory response of DTPs to the acids and bases and elucidated relationships between the structure and sensitivity to the environment. This finding allowed us to manage these properties by introducing the combination of substituents and functionalities into the heterocyclic core. Thus, investigations demonstrated the potential of the application of DTPs as chemo- and fluorosensors for selective detection of acids and bases.

Keywords: dihydrotriazolopyrimidines, acids, bases, fluorescence response, chemosensor

1. Introduction

Fluorophores sensitive to external stimuli are attractive compounds owing to their application in contaminant analysis environment, electrochemical sensors, biosensing, and detection of toxins [1]. Extensive studies have been directed for development of new fluorescent sensory organic materials which are able to respond on the external stimuli via changes of their absorption or fluorescence characteristics. These stimuli may include temperature, scattered light, pH, and even nature of solvent [2].

Monitoring the pH levels in high alkaline media is of wide importance for many industrial processes, in gas scrubbers, wastewater monitoring, treatment of the plants and concrete structures [3, 4]. The sensing materials suitable for measurement of high alkali media are very limited. In recent years, a few fluorescent sensors in an alkaline pH region have been reported [5-7].

Recently we reported the synthesis and photophysical properties of new blue and blue-green fluorophores derived on dihydro-1,2,3-triazolopyrimidine core (DTP) [8]. These fluorophores exhibited multifunctional properties and showed good fluorescence in solutions (with QY up to 88%, Stokes shift (SS) ~151 nm and \( \lambda_{em} \) up to 534 nm). We suggested and developed synthetic procedure providing various DTPs with different electronic structures (A-\( \pi \)-D and D-\( \pi \)-A). These compounds showed selective reversible acidochromism in solution and in a solid state in the presence of HCl vapor. \(^1\)H NMR investigation showed that the pyrimidine and N-\textit{tert}-cycloalkylamine moieties are the binding sites responsible for specific sensory response to the acids.

Current research is focused on the investigation of the photophysical characteristics of the phenoxyderivatives of triazolopyrimidines (OH-DTPs) bearing OH-functionality in the different positions of the molecule and studies of their response to the different acids and bases as external stimuli.

Hydroxy group is very attractive from a biological point of view. Numerous biocompounds include OH-functionalities in their structure (alkaloids, flavonoids, isoflavonoids, terpenoids, lipids, fatty acids, amino acids etc.) [9, 10]. Bioluminescent molecule (luciferin) and different synthetic fluorophores bearing this substituent are well known [11-19]. Introduction of hydroxy groups usually causes the changes in electronic properties owing to its strong electron-donating nature and increases the intramolecular charge transfer (ICT) effect. Moreover, hydroxy...
group can strengthen the fluorophore participation in intra- and intermolecular noncovalent bonding to enhance the molecule rigidity and take part in self-organization. Finally, hydroxy groups [20] can be transformed into the salts, which are more soluble in water. Deprotonation of hydroxy group may influence the optical properties of the resulted salts.

2. Experimental

UV-Vis absorption spectra were recorded on a Perkin-Elmer Lambda 35 UV-Vis spectrophotometer (Shelton, CT USA). Fluorescence of the sample solutions was measured using a Hitachi F-7000 spectrophotometer (Tokyo, Japan). The excitation wavelength was at the absorption maxima. Atmospheric oxygen contained in solutions was not removed. Concentration of the compounds in the solution was 5.0·10⁻⁵ M and 5.0·10⁻⁶ M for absorption and fluorescence measurements, respectively. The relative fluorescence quantum yields (QY) were determined using quinine sulfate in 0.1 M H₂SO₄ as a standard (QY = 0.546). Absolute quantum yield study was performed on Horiba FluoroMax 4 Spectrofluorometer (Kyoto, Japan) with Quanta-φ integrating sphere using FluorEssence 3.5 Software.

DTPs 1a-e, 2a-c and 3a-b were prepared according to procedures reported in the literature and their spectral characteristics were identical to the published data [8, 21].

3. Results and Discussion

2-(Hydroxyphenyl)-4-(4-trifluoromethylphenyl)-2,4,5H-[1,2,3]triazolo[4,5-d]pyrimidines (HO-DTPs) 2a-c and 3a-b were prepared via the demethylation of their methoxy congeners by using BBr₃ solution in dichloromethane with special temperature profile regime (Scheme 1).

The spectral and analytical data of DTPs 2a-d and 3a, b were consistent with the published data [21]. Absorption and emission spectra recorded earlier showed insignificant difference in long wavelength maxima positions compared to the corresponding MeO-DTPs derivatives. At the same time HO-DTPs quantum yields (QY) of were in 6-40-fold lower. Only HO-DTP 2a demonstrated good QY compared to QY of DTP 1a in DMSO (40.1% and 39.4%, respectively) (Table 1). However, in the other solvents QYs of HO-DTP 2a decreased significantly.

The preliminary investigation of the influence of the different acids and bases on the optical properties of the HO-DTP solutions in DMSO showed the absence of any effect. Therefore, we included only trifluoroacetic acid (TFA) into further consideration. Absorption and emission spectral data of the HO-DTPs 2a-d and 3a, b in the presence of different organic bases, alkalis and TFA are collected in Table 1. Analysis of the Table 1 data showed that addition of the KOH (5% water solution) caused red shift of the absorption and emission maxima by 20-121 and 22-169 nm, respectively, and for the most HO-DTP QYs were decreased. Addition of TFA did not affect the photophysical properties for the most compounds, except the DTP 2b. In this case, the maxima of absorption and emission bands were redshifted for 30 nm and 11 nm accordingly. Unlike most acids, the addition of KOH solution caused dramatic changes in the photophysical properties of DTPs 2a-d, 3a, b. Thus, in fluorescence spectra a strong bathochromic shift of the emission maxima of 57-169 nm was observed
Table 1 Absorption and emission data for DTPs 2a-d, 3a,b solution (c = 5·10^{-6} M) in DMSO before and after the addition of 500 eq. of TFA or KOH (5% solution in water)

| Entry | Compound | Acid/Base | λ_{abs}, nm | λ_{em}, nm | SS, nm/cm^2 | QY, % |
|-------|-----------|-----------|-------------|-------------|-------------|-------|
| 1     | 2a        | -         | 347         | 441         | 94/6143     | 40.1  |
| 2     | 2a        | TFA       | 347         | 441         | 94/6143     | 18.2  |
| 3     | 2a        | KOH       | 375         | 498         | 123/6586    | 19.8  |
| 4     | 2b        | -         | 296         | 419         | 123/9917    | 0.4   |
| 5     | 2b        | TFA       | 326         | 408         | 82/6165     | 0.6   |
| 6     | 2b        | KOH       | 364         | 503         | 139/7592    | 7.5   |
| 7     | 2c        | -         | 340         | 416         | 76/9903     | 0.5   |
| 8     | 2c        | TFA       | 331         | 414         | 83/6057     | 0.8   |
| 9     | 2c        | KOH       | 360         | 500         | 140/7778    | 5.9   |
| 10    | 2d        | -         | 356         | 472         | 116/8903    | 1.1   |
| 11    | 2d        | TFA       | 360         | 450         | 90/5556     | 0.6   |
| 12    | 2d        | KOH       | 418         | 530         | 110/5056    | 0.6   |
| 13    | 3a        | -         | 347         | 432         | 85/5670     | 0.6   |
| 14    | 3a        | TFA       | 347         | 420         | 74/5092     | 0.6   |
| 15    | 3a        | KOH       | 423         | 500         | 77/3641     | -     |
| 16    | 3b        | -         | 341         | 416         | 75/5287     | 0.3   |
| 17    | 3b        | TFA       | 339         | 404         | 65/4746     | 0.2   |
| 18    | 3b        | KOH       | 492         | 585         | 93/3231     | -     |

along with the QY decrease for the most DTPs, with the exception for 2b and 2c. DTPs 2b and 2c, bearing hydroxy group at ortho- and meta-position of aromatic ring A showed the large increase of their QYs from 0.4 and 0.5% (in pure DMSO) to 7.5 and 5.9%, respectively. Thus, hydroxyl DTP derivatives display different sensitivity to the alkali media depending on their structure.

These results inspired us to check the influence of the set of bases on the photophysical properties of DTP 2b (Fig. 1) under the same conditions. These data indicated a significant effect of bases on both the absorption and the emission of DTP 2b. In all the cases, the absorption and emission maxima were redshifted in range 68-110 nm and 19-62 nm, respectively. The effect of TEA stimulus deviates from common trend and consists in slight blue shifting (4 nm) (Fig. 1). The most effective were alkalis (NaOH and KOH), whose addition to the HO-DTPs 2b solution in DMSO led to large redshifts (61-62 nm) and substantial (in 9-10 folds) increasing of emission intensity. Visual emission change from colorless to green was observed for the DTPs 2b solution after the addition of 50 eq of NaOH solution, which further developed to bright green-yellow emission (Fig. 2).

Further, we studied changes in absorption and emission spectra of HO-DTP 2c induced by NaOH (Fig. 3). HO-DTP 2c was almost non-fluorescent in DMSO solution (c = 5·10^{-6} M), while the addition of NaOH caused an appearance of a new fluorescence maximum at 504 nm (Fig. 3b). The intensity of this new maximum was enhanced drastically upon the increasing amounts of NaOH and reached the saturation at 300 eq. Changes in absorption were also registered. In this case new maximum was located at 395 nm when 25 eq. of NaOH solution were added, and further NaOH addition led to increasing of this

![Fig. 1 UV-Vis absorption (left) and emission (right) spectra of DTP 2b after addition of different bases (for absorption and emission c = 5·10^{-6} M)](image-url)
maximum intensity and simultaneous appearance of the new maximum at 368 nm. Isosbestic points in absorption spectra emerged at 325 and 425 nm and this suggests a reactive equilibrium between these two components.

4. Conclusions

In conclusion, we reported the results of the investigation of the optical properties of hydroxy substituted DTPs in the presence of different acids or bases. Hydroxy-DTPs demonstrated a pronounced fluorescence response in alkaline environment, which resulted in strong bathochromic shift of the absorption and emission maxima along with enhancement of the intensity of the fluorescence. However, they did not display any noticeable perceptible response to organic or mineral acids. Thus, introducing of the OH group onto the dihydro-1,2,3-triazole structure led to the sharp change in response of these compounds to basic/alkali stimuli. These results together with our recent ones demonstrated that acid/base sensitivity of the DTPs can be adjusted by varying the substituents and functionalities attached to the dihydropyrimidine core.

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