SYNTHESIS AND FLUORESCENCE OF 1-[7-(4-NITROBENZOYL)-3-(BIPHENYL-4-YL)PYRROLO[1,2-C]PYRIMIDIN-5-YL]ETHANONE

Marian-Laurențiu TATU1, Emilian GEORGESCU2, Cristian BOSCORNEA3, Marcel-Mirel POPOA4, Eleonora-Mihaela UNGUREANU5

This work is devoted to the synthesis and spectral characterization of 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethanone. The investigations were performed by absorbance and fluorescence. Following spectrophotometric analysis the molar extinction coefficient, quantum yield and Stokes shifts have been calculated.

Keywords: 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethanone, absorbance, fluorescence, Stokes shift, quantum yield

1. Introduction

Pyrrolo[1,2-c]pyrimidine system is the core of several bioactive synthetic [1 - 5] or natural [6 - 10] compounds and the investigation on synthesis and properties of this system is an active research area.

Different synthetic procedures for pyrrolo[1,2-c]pyrimidine system, starting from both pyrrole [11, 12] or pyrimidine [13 - 16] derivatives have been reported. One of them, namely the 1,3-dipolar cycloaddition of the pyrimidinium-N-ylides with acetylenic or olefinic dipolarophiles, is one of the most versatile procedure, leading to substituted pyrrolo[1,2-c]pyrimidines, unavailable by other methods. The classical multistep procedure starts with the preparation of pyrimidinium salts. In the second step, this procedure led directly to pyrrolo[1,2-c]pyrimidine [17 - 20], by means of the reaction with electron-deficient alkynes or alkenes, in the presence of an organic or inorganic base, with the role of

1 PhD.Stud, Faculty of Applied Chemistry and Material Sciences, University POLITEHNICA of Bucharest, Romania
2 researcher, Research Center Olchim, Bucharest, Romania
3 PhD., Faculty of Applied Chemistry and Material Sciences, University POLITEHNICA of Bucharest, Romania
4 PhD Eng., “C.D. Nenitzescu” Centre of Organic Chemistry, Romanian Academy, Bucharest, Romania
5 Prof., Faculty of Applied Chemistry and Material Sciences, University POLITEHNICA of Bucharest, Romania
generating pyrimidinium-N-ylide in situ. In order to avoid the formation of inactivation products of the pyrimidinium-N-ylides, by 3+3 cycloaddition reaction of two molecules of pyrimidinium-N-ylide [18, 19], a new synthetic protocol to a library of pyrrolo[1,2-c]pyrimidines via one-pot, a three component procedure has been developed. This synthetic protocol starts from pyrimidine derivatives, substituted 2-bromo-acetophenones, and electron deficient alkynes, in the presence of an epoxide, which acts both as reaction medium, and acid scavenger [21]. A microwave-assisted synthesis of a library of pyrrolo[1,2-c]pyrimidines based on the one-pot, the three component procedure starting from various pyrimidines, substituted 2-bromoacetophenones, and electron deficient non-symmetrical alkynes in the presence of 1,2-epoxybutane was also reported [22].

Investigation of biological activities, fluorescence and electric properties of indolizines is still an active research area. They present biological activities and have been studied for their psychotropic activities, as well for their anti-microbial, anti-tubercular, anti-fungal, anti-cancer, anti-histamine activities [23]. The indolizines are used in pharmacological industry.

It has been recently discovered that indolizine derivatives show also remarkable optical properties: blue emissions with high quantum yields, electron-transporting properties, and sufficiently high triplet energy (ET) levels. These properties recommend the indolizines to be used as new compounds in organic light-emitting diodes (OLED) technology. This application could be very useful nowadays, as OLED technology began to be worldwide used. Materials are vital components of OLEDs. In 2006, Forrest et al. proposed a hybrid fluorescent/phosphorescent route to realize efficient white organic light-emitting diodes (WORLDs) [23]. In this design, the emitting layer should not only show highly efficient blue fluorescence, but also sensitize the green, red or yellow-orange phosphors [23]. Once the OLED technology developed, the materials used have become of major importance, in order to involve a long lifetime [24 - 26].

In our group have been studied the properties of different pyrrolo[1,2-c]pyrimidine derivatives, we noticed that some of them exhibited green luminescence when exposed on UV light. This observation prompted us to investigate the fluorescence properties of several pyrrolo[1,2-c]pyrimidine derivatives. Herein, we report the results of our investigations on the synthesis and spectral properties of 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethaneone (I). Thus, the UV/VIS and fluorescence properties of compound I were investigated, as some indolizines and biindolizines with related structure are highly fluorescent (some of the biindolizines having a remarkably high quantum yield) [27].
Synthesis and fluorescence of 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethanone

Fig. 1. Structure of 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethanone (I)

2. Experimental

All reagents used for synthesis were commercially available products. Acetonitrile and chloroform (Fluka) were used as received as solvents. Quinine sulphate (Buchler) was used as reference to calculate the quantum yield.

Melting points were determined on a Boëtius hot plate microscope. The elemental analysis was carried out on a COSTECH Instruments EAS32 apparatus. The IR spectra were recorded on a Nicolet Impact410 spectrometer, with KBr pellets. The NMR spectra were recorded on a Varian Gemini 300 BB instrument, operating at 300 MHz for $^1$H-NMR and 75 MHz for $^{13}$C-NMR. Supplementary evidence was given by HETCOR and COSY experiments. The absorption spectra have been recorded at room temperature (23°C) with JASCO V550 spectrophotometer. The fluorescent spectra were measured with Jasco FP6500 spectrofluorimeter, with reading at an angle of 90°. The refractive indexes were measured at room temperature, using a refractometer (Abbe from CETI Belgium).

For spectral studies, a stock solution (~0.43mM) of I in a mixture of solvents acetonitrile and chloroform (1:1) has been prepared. Then, solutions of different concentrations (from $10^{-6}$ mole/L to $5 \times 10^{-6}$ mole/L) have been prepared by dilution. UV-vis spectra were recorded for the diluted solutions using as reference the acetonitrile:chloroform (1:1) solvent mixture. A more diluted stock solution (of $3.5 \times 10^{-5}$ mole/L) of I in the mixture acetonitrile:chloroform (1:1) was prepared and measured, in order to determine the fluorescence spectra.

3. Results and Discussion

1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethanone (I) has been obtained via 1,3-dipolar cycloaddition reaction of a 4 biphenyl pyrimidinium-N-ylide with 3-butyn-2-one in 1,2-epoxybutane at reflux.
temperature, by the one-pot, three-component procedure, according to the previously presented method[21].

A mixture of 4-biphenylypyrimidine (1mmole), 2-bromo-4'-nitroacetophenone (1 mmole) and 3-butyn-2-one (1mmole) in 20 mL of 1,2-epoxybutane was heated at reflux temperature for 24 hours. The solvent was partly removed under vacuum, 2 mL of MeOH was added under gentle stirring, and the mixture was left over night in the refrigerator. The solid formed was filtered off and recrystallized from CHCl₃/MeOH giving I as orange crystals, mp 295-297°C (0.3 g, yield 65%).

FT-IR (KBr, cm⁻¹): 3094, 3066, 1654, 1623, 1599, 1515, 1485, 1472, 1419, 1346, 1332, 1222, 1194, 1090.

¹H-NMR (CDCl₃+TFA, 300 MHz, δ): 2.76 (s, 3H, CH₃); 7.45-7.54 (m,3H, 3H-Ph); 7.67-7.70 (m,2H, 2H-Ph); 7.87-8.09 (m , 7H, H-2, H-2’, H-3’, H-5’, H-6’, H-2”, H-6”); 8.47 (d, J = 8.8 Hz, 2H, H-3”, H-5”); 9.04 (d, J = 1.1 Hz, 1H, H-8); 11.32 (d, J = 1.1 Hz, 1H, H-5).

¹³C-NMR (CDCl₃+TFA, 75 MHz, δ): 27.7 (Me); 112.5 (C-8); 116.7 (C-1); 124.6, 127.3, 128.1, 128.7, 128.8, 130.1, 133.6 (C-2”, C-4”, C-5”, C-6”, C-2’, C-3’, C-5’, C-6’, 5C-Ph); 123.8, 133.6, 139.3, 142.3, 143.9, 145.9, 150.5, 153.2 (C-3, C-8a, C-7, C-1’, C-4’, C-1”, C-4”, Cq-Ph); 130.5 (C-2); 140.7 (C-5); 184.6 (COAr), 197.9 (COMe);


The UV-vis spectra for solutions of I were first recorded (Fig. 2), in order to get the fluorescence characterization of I, using a mixture of solvents – acetonitrile:chloroform (1:1) as reference. The spectrum has two absorption peaks at the wavelengths λmax₁ and λmax₂. Maximum values of absorbances were plotted depending on the concentration (C) of the compound (Fig.3). The extinction coefficients (ε₁, ε₂) have been calculated from the slopes of the line. The results are summarized in Table 1. Fig. 2 shows the absorbance linearly increases with concentration. The equations for the linear dependences are given in Table 2 as well.

<table>
<thead>
<tr>
<th>Peak</th>
<th>1</th>
<th>2</th>
</tr>
</thead>
<tbody>
<tr>
<td>λmax (nm)</td>
<td>381</td>
<td>260</td>
</tr>
<tr>
<td>A = f ([I])*</td>
<td>A = 44950.[I] + 0.0155</td>
<td>A = 40740.[I] + 0.0131</td>
</tr>
<tr>
<td>ε (L<em>mole⁻¹</em>cm⁻¹)</td>
<td>44950</td>
<td>40740</td>
</tr>
</tbody>
</table>

* Equation of absorbance (A) at λmax vs 1 concentration [I] in mole/L
Fig. 2. Spectra of I in acetonitrile:chloroform (1: 1) for increasing concentrations of I:
$10^{-6}$ (a), $2 \times 10^{-6}$ (b), $3 \times 10^{-6}$ (c), $4 \times 10^{-6}$ (d), $5 \times 10^{-6}$ (e)

Fig. 3  Dependences of the peaks absorbances on concentration (C) for I in acetonitrile:chloroform (1:1)

Emission and excitation spectra of compound I are shown in Fig.4. One can observe that the fluorescence intensity (Int.) is influenced by concentration of I in solution. Fluorescence intensity increases when the concentration decreases.
Stokes shifts ($\Delta \nu$) of the absorption maximum at each concentration were been calculated using data obtained from emission (maximum wavelength - $\lambda_{\text{max, em}}$) and excitation (maximum wavelength - $\lambda_{\text{max, exc}}$), according to formula (1). The values calculated by this equation is apparent and could give errors of 5-20% [27].

$$\Delta \nu = \frac{1}{\lambda_{\text{max excitation}}} - \frac{1}{\lambda_{\text{max emission}}} \quad (1)$$

A plot of the peak emission and absorbance vs concentration has been made, in order to observe the evolution of Stokes shifts with concentration (Fig. 5). The absorption and excitation peaks and the corresponding Stokes shifts are shown in Table 2.

### Table 2.

<table>
<thead>
<tr>
<th>[I] (mole/L)</th>
<th>$\lambda_{\text{max, abs}}$ (nm)</th>
<th>$\lambda_{\text{max, emission}}$ (nm)</th>
<th>Intensity of excitation</th>
<th>Intensity of emission</th>
<th>Stokes shift $\Delta \nu$ ($\text{cm}^{-1}$)</th>
</tr>
</thead>
<tbody>
<tr>
<td>$5.8 \times 10^{-4}$</td>
<td>329</td>
<td>478</td>
<td>316.1</td>
<td>35.0</td>
<td>9860</td>
</tr>
<tr>
<td>$2.9 \times 10^{-4}$</td>
<td>336</td>
<td>474</td>
<td>722.8</td>
<td>334.4</td>
<td>8660</td>
</tr>
<tr>
<td>$1.4 \times 10^{-4}$</td>
<td>347</td>
<td>473</td>
<td>848.7</td>
<td>680.7</td>
<td>7670</td>
</tr>
<tr>
<td>$7.2 \times 10^{-5}$</td>
<td>358</td>
<td>472</td>
<td>992.4</td>
<td>742.0</td>
<td>6740</td>
</tr>
</tbody>
</table>

The data from Table 2 show high Stokes shifts for the investigated compound. It can be seen that Stokes shift becomes smaller when the concentration decreases.
Synthesis and fluorescence of 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2- c]pyrimidin…55

Fig. 5. Maximum wavelength of excitation $\lambda_{\text{max, exc}}$ and emission $\lambda_{\text{max, em}}$ dependences on $I$ concentration

The quantum yield (QY) was calculated using formula (2), in order to measure the fluorescence of compound I. Quinine sulphate was used as fluorescence standard [28].

$$QY = QY_{\text{ref}} \times \frac{I}{A} \times \frac{A_{\text{ref}}}{I_{\text{ref}}} \times \frac{n}{n_{\text{ref}}}$$  (2)

where $QY_{\text{ref}}$ - quantum yield of the standard, $A$ - absorbance value of the studied compound, $A_{\text{ref}}$ - absorbance value of the standard, $I$ - area of the emission peak of the studied compound, $I_{\text{ref}}$ - area of the emission peak of the standard, $n$ - refractive index of the compound under study, $n_{\text{ref}}$ - refractive index of the standard.

Quantum yield was calculated using as standard a quinine sulfate solution with the concentration of $10^{-6}$ mole / L in 0.5 M H$_2$SO$_4$ which has a quantum yield of 0.6 [29]. The emission spectra for both I and standard are given in Fig. 6. The following data are used: $A = 0.06906$, $A_{\text{ref}} = 0.02$, $I = 10784.5$, $I_{\text{ref}} = 16463.6$, $n = 1.3942$, $n_{\text{ref}} = 1.3390$. It results: $QY = 0.1185$
Fig. 6 shows that the fluorescence intensity of the compound I is smaller, but has the same order of magnitude as the fluorescence intensity of quinine sulphate. However, the quantum yield calculation shows that the quantum yield of compound I is much lower being about five times lower than that for quinine sulphate. That is why the calculation of the quantum yield for applications is essential. The investigated compound has a good fluorescence compared to other organic compounds, and can be tested in applications, such as OLED technology.

4. Conclusion

We have successfully synthesized 1-[7-(4-nitrobenzoyl)-3-(biphenyl-4-yl)pyrrolo[1,2-c]pyrimidin-5-yl]ethanone in good yield via 1,3-dipolar cycloaddition reaction of 4-biphenylpyrimidinium-N-ylides with 3-butyln-2-one in the 1,2-epoxybutane at reflux temperature, by the one-pot, three-component procedure. The formation of dipyrimidino-pyrazinic dimers was avoided, leading directly to the fully aromatic compound.

Fluorescence characterization of I has been performed by absorbance and fluorescence studies. The molar extinction coefficient, quantum yield and Stokes shift have been calculated. The investigated compound has an important fluorescence, being as well a candidate in OLED technology.

Acknowledgement

Marcel Popa greatly acknowledges financial support through POSDRU/159/1.5/S/134398.
REFERENCES


24. Yasuhiro, S; Masayori, H; Naoko, M; Bo-Cheng, W; Yoshinori, T. Theoretical interpretations of electronic and fluorescence spectra of new 2(H)-pyridone derivatives in solution and solid state. Dyes and Pigments 99 (2013) 940-949
25. Yaroslav, P; Oleksiy, D; Lucinda, V; Paulo, F. New unsymmetrical squaraine dyes derived from imidazo[1,5-a]pyridine. Dyes and Pigments 96 (2013) 554-562
27. Rotaru, A; Druta, I; Avram, E; Danac, R. Synthesis and properties of fluorescent 1,3-substituted mono and biindolizines ARKIVOC 2009 (xiii) 287-299