PYRROLOPYRIDAZINE DERIVATIVES: SYNTHESIS AND FLUORESCENT PROPRIETIES

DERIVAȚI PIROLOPIRIDAZINICI: SINTEZĂ ȘI STUDIUL PROPRIETĂȚILOR FLUORESCENTE

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Abstract. *Recent studies proved that 1,2-diazines derivatives are invaluable materials in the fields of medicine (such as anti-HIV, antiviral and anticancer, antibacterial and antifungus medicines), opto-electronics (compounds with liquid crystal properties and highly fluorescent derivatives: sensors and biosensors, electroluminescent materials, lasers) and agriculture (herbicidal activity and the grow up factor for plants). 1,3-Dipolar cycloaddition is one the most important methods of constructing the pyrrolopyridazine. For some pyrrolopyridazine derivatives was studied the absorption and emission spectra, in ethanol, chloroform and cyclohexane solutions at room temperature.*

Key words: pyrolopiridazine derivatives, fluorescence, 3+2 dipolar cycloadditions.

Rezumat. *Studii recente au demonstrat faptul că derivații 1,2-diazinici sunt compuși cu proprietăți deosebite în medicină (cum ar fi anti-HIV, medicamente antivirale şi împotriva cancerului, proprietăți antibacteriene şi antifungice), proprietăți opto-electronice (compuși cu proprietăți de cristale lichide şi produse derivate foarte fluorescente: senzori și biosenzori materiale electroluminiscente, lasere) și în agricultură (compuși cu activitate erbicidă și stimulatori în creșterea și dezvoltarea plantelor). Reacțiile de cicloadiție 1,3-dipolare sunt cea mai accesibilă metodă în sinteza derivaților pirolopiridazinici. Spectre de absobție și emisie au fost înregistrate, pentru diferiți derivați piridazinici, în etanol, cloroform şi ciclohexan la temperatura camerei.*

Cuvinte cheie: derivați pirolopiridazinici, fluorescență, cicloadiții 3+2 dipolare.

INTRODUCTION

Literature describes a large variety of pyridazine compounds with different biological activities: anticancer, antituberculosis, antimicrobial, antihypertensive etc (Mangalagiu, 2011).

1,2-diazines are also reviewed for their applications in opto-electronics, with a focus on highly fluorescent derivatives (with potential as sensors and biosensors, electroluminescent materials, lasers and other semiconductor devices) and compounds with liquid crystal properties. Herbicidal activity and grow up factor for plants are also reviewed (Mitsumori et al., 2005; Valeur, 2002).

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In a preliminary communication (Zbancioc et al., 2006) is presented the synthesis and spectral analysis of pyrrolopyridazine derivatives. The aim of this work was to study the relationship between optical properties and structure (the effect of substituents and conjugation).

MATERIAL AND METHOD

The strategies adopted for construction of fluorescent derivatives, are depicted in figure 1. The preparation of all derivatives (**11-16)** involves two steps: initially N-alkylation of the pyridazine, followed by a 3 +2 dipolar cycloaddition of diazinium ylides (**8a-8b)** (generated *in situ* from the corresponding salts) to the corresponding dipolarophiles (activated alkenes nonsymmetrical substitued: **9 and 10 -** acrylonitrile and methyl propiolate).

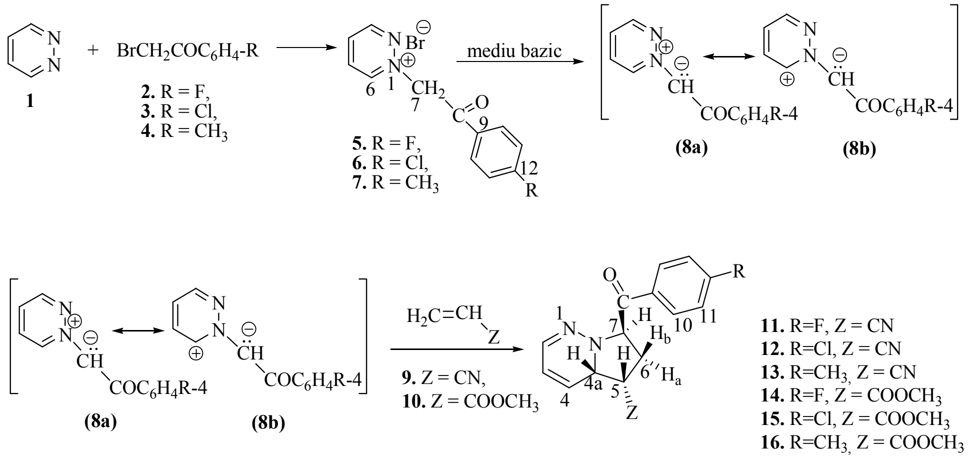

Fig. 1 - Synthesis of pyridazine derivatives.

The 3+2 cycloaddition occurs with high stereospecificity and no formation of other isomers was observed (Butnariu et al., 2009).

All reagents and solvents employed were of the best grade available and were used without further purification.

The structure of the compounds was proved by spectral analysis: the 1H NMR and 13C NMR spectra and two-dimensional experiments 2D-COSY, 2D-HETCOR(HMQC), long range 2D-HETCOR (HMBC) were recorded on a Bruker Avance 400 DRX spectrometer at 400/100 MHz. Chemical shifts are given in parts per million (δ-scale), coupling constants (J) in hertz and downfield shift from internal tetramethylsilane (δ 0.00 ppm). The IR spectra were recorded on an FT-IR Shimadzu Prestige 8400s spectrophotometerin KBr. Melting points were determined using an electrothermal apparatus and are uncorrected. Flash chromatography was performed with Aldrich 230e400 mesh silica gel. TLC was carried out on Merck silica gel 60-F-254 plates.

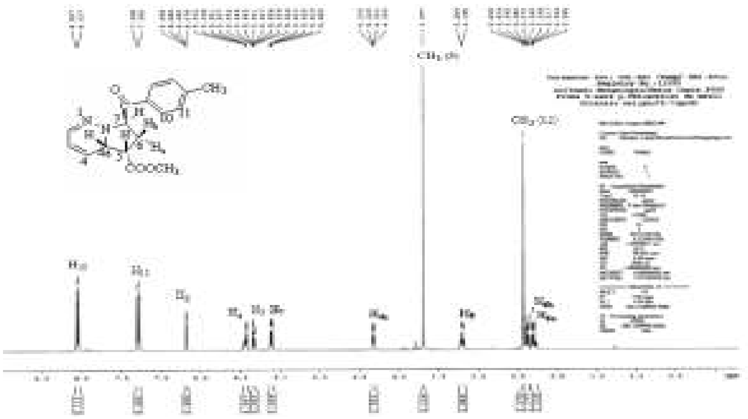

Fig. 2 - 1H-NMR spectrum for compound **16**.

In the next stage of our work, we studied the absorption and emission spectra of the obtained compounds. The spectra of all the compounds were recorded in ethanol, chloroform and cyclohexane solutions at room temperature.

The fluorescence spectra were recorded with a Turner Bio Systems fluorimeter using FluoOpticalKitID PN: 9300-043 SN: F2000000BB5A4C2D SIG: UV with λ_{ex} = 365 nm and λ_{em} = 410–460 nm.

Relative quantum yields were determined by using anthracene in ethanol (□ = 0,27 at 25° C) (Parker C. A., 1986). Although, compounds are relatively similar in molecular structure, exhibit clear differences in their experimental absorption and emission spectra, as summarised in table 1.

Table 1

λmax (nm) of absorption spectra and relative quantum yields (%) of piridazine derivatives (11-16)

Comp.	Fluorescence (λ_{max}, nm) (quantum yield %)			Absorption (λ_{max}, nm)		
	Etanol	Cloroform	Ciclohexan	Etanol	Cloroform	Ciclohexan
11	425 (3)	421 (2)	Insolubile	320	318	Insolubile
12	423 (2)	420 (2)	Insolubile	320	319	Insolubile
13	438 (2)	429 (2)	Insolubile	323	320	Insolubile
14	456 (3)	453 (3)	Insolubile	335	330	Insolubile
15	458(4)	455 (3)	Insolubile	336	330	Insolubile
16	461(4)	459 (4)	Insolubile	338	335	Insolubile

RESULTS AND DISCUSSIONS

As shown in Table 1, the compounds (**11-16**) are blue emitters (λ_{max} of fluorescence around 423-461 nm, λ_{max} of absorption around 320-338 nm) and have low quantum yield.

The comparative analysis of the obtained data (table 1) leads to the conclusion: the compounds (**14-16**) which possess a carbomethoxy group, in 5-position, have a higher fluorescence.

The effect of conjugation and the presence of double bonds in azaheterocycles compounds determine fluorescence and quantum yields of the analyzed compounds (fig. 3).

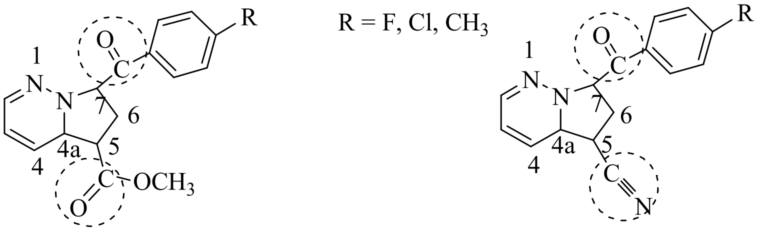

Fig. 3 – The detailed structure for compounds **14-16**.

If pyrroloderivatides were fully aromatized, then the quantum yield was extremely high (Zbancioc et al., 2010).

CONCLUSIONS

1. We report a fast, efficient and straightforward method for preparation of fluorescent derivatives containing the piridazine ring.

2. The compounds obtained and tested posses fluorescent proprieties (λ_{max} of fluorescence is around 423-461 nm, λ_{max} of absorption is around 320-338 nm).

3. A certain influence of the substituents concerning absorption and fluorescent properties were observed: the subtituent from the position 5 being important for fluorescence.

Acknowledgments: *This work was co-financed from the European Social Fund Sectoral Operational Human Resources Development 2007-2013, project number POSDRU/I.89/1.5/S62371 „Postdoctoral School in Agriculture and Veterinary Medicine area".*

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