

## SPECTRAL ANALYSIS FOR HETEROCYCLIC STRUCTURE OF THE PYRROLOPYRIDAZINE ADDUCT

### UTILIZAREA ANALIZEI SPECTRALE PENTRU DOVEDIREA STRUCTURII HETEROCICLICE A UNUI DERIVAT DE PIRIDAZINĂ

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**Abstract.** By [3+2] cycloaddition reaction, between pyridazine and an alkene in alkaline medium ( $Et_3N$ ), were obtained in situ a pyrrolopyridazine adduct. The structure of the compound was proved by spectral analysis, using the following spectral methods: IR,  $^1H$  NMR,  $^{13}C$  NMR and MS. Taking into account the chemical shifts, the coupling constants and signal splitting in the spectra, the only reasonable structure for the cycloadduct is that one presented.

**Key words:** pyridazine, cycloadduct, chemical structure, spectral analysis.

**Rezumat.** Printr-o reacție de cicloadiție [3+2] dipolară între heterociclul de piridazinic și o alchenă, în mediul alcalin ( $Et_3N$ ) s-a obținut in situ un cicloadduct de pirolpiridazinic. Structura compusului a fost dovedită prin analiză spectrală și au fost utilizate următoarele metode spectrale: IR,  $^1H$  RMN,  $^{13}C$  RMN și MS. Luând în considerare deplasările chimice, constantele de cuplare și divizările semnalului în spectre, singura structură rezonabilă pentru cicloadduct este cea prezentată.

**Cuvinte cheie:** piridazină, produs de cicloadiție, structură chimică, analiză spectrală.

## INTRODUCTION

To obtain a new diazine heterocycle (**b**), by [3+2] cycloaddition reaction, a pyrrolo ring with acetophenone skeleton (**I**) was introduced at the pyridazine (**a**).

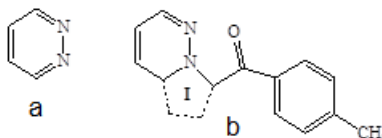


Fig. 1. Pyridazine (**a**) and the pyrrolopyridazine adduct (**b**)

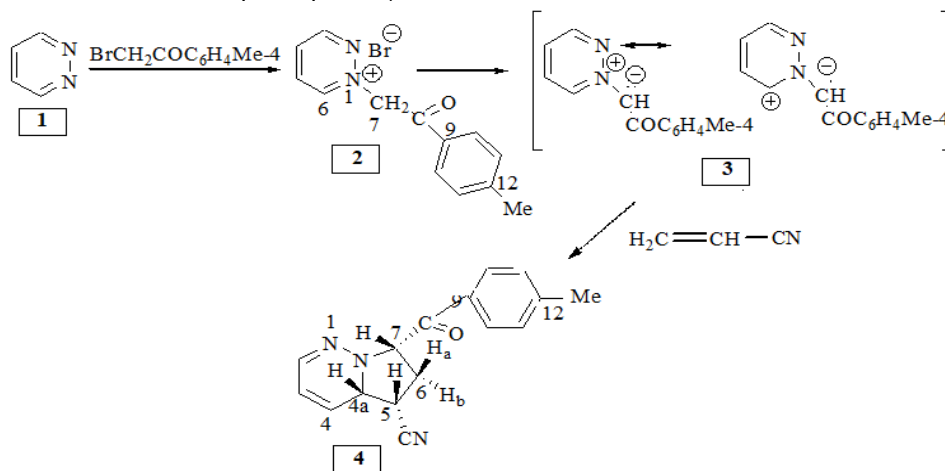
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A facile way to obtain the condensed pyridazines (**b**) is to use ylide as intermediate. So, first were obtained the corresponding cycloimmonium salt (**2**) which in alkaline medium ( $\text{Et}_3\text{N}$ ) generated the ylide (**3**) *in situ*.

Pyridazinium ylide (**3**), generated *in situ* from the salts (**2**) in alkaline medium by triethylamine ( $\text{Et}_3\text{N}$ ) react *via* a Huisgen 3+2 dipolar cycloaddition reaction with non-symmetrically substituted alkene, leading to the corresponding pyridazine cycloadduct (**4**), (Scheme 1) (Padwa, 1984).

## MATERIAL AND METHOD

The reaction of ylide (**3**) with non-symmetrical dipolarophiles (acrylonitrile) involves additional regiochemical problems (Butnariu *et al.*, 2007; Butnariu *et al.*, 2009; Caproșu *et al.*, 2005). No matter what conditions we used (different solvents, temperature, time), the reaction of ylide (**3**) with acrylonitrile leads to a single isomer, the tetrahydropyrrolopyridazine adduct (**4**) (Scheme 1). This means that one bond is formed between the ylide carbon and the non-substituted carbon atom of the dipolarophile and the second bond between the positively charged carbon of the ylide and the substituted carbon of the dipolarophile. This is in accordance with the usual electronic effects in dipolarophiles (.



**Scheme 1.** Cycloaddition reaction of pyridazinium ylides (**3**) to acrylonitrile.

Because a single regioisomer is obtained, the reaction is regioselective being under charge control (Tucaliuc *et al.*, 2013; Zbancioc *et al.*, 2022).

The synthesis was performed both under conventional thermal heating (TH) and nonconventional methods using microwave (MW) technology. The literature data (Amariuca-Mantu *et al.*, 2021, Tucaliuc, 2008; Zbancioc, 2007) indicate that the use of MW in chemical reactions has some undeniable advantages compared with conventional TH such as shorter reaction times, higher yields, spectacular accelerations of chemical reactions, higher product purities, and, in many cases, being

environmentally friendly (using small amounts or no organic solvents, having milder reaction conditions, having no side reactions).

Having in view these considerations, the consumed energy decreases considerably, reaction time decrease dramatically and yield is higher. Taking into consideration these aspects, the authors claim that these reactions could be considered environmentally friendly.

## RESULTS AND DISCUSSIONS

The main spectral data for the tetrahydropyrrolopyridazine adduct (**4**) confirm the proposed structure. The following spectral methods were used: IR,  $^1\text{H}$  NMR,  $^{13}\text{C}$  NMR and MS.

The IR spectra was recorded on an FT-IR Shimadzu Prestige 8400s spectrophotometer in KBr.

The  $^1\text{H}$  and  $^{13}\text{C}$  NMR spectra were recorded on a Bruker Avance 400 DRX spectrometer at 400/100 MHz in DMSO-d<sub>6</sub>.

The MS spectra was recorded on a Bruker APEX-Q-IV-7T spectrometer, using electrospray method (ES). The signals [M+Z] provided, represent the sum of the mass of the molecule (M) and the absorption ion (Z).

In IR spectrum (fig. 2) the most important signals are the band from 2229  $\text{cm}^{-1}$  (with medium intensity, appropriate to the valence vibration for cyan group) and the intense band from 1683  $\text{cm}^{-1}$  (appropriate to the valence vibration for carbonyl group).

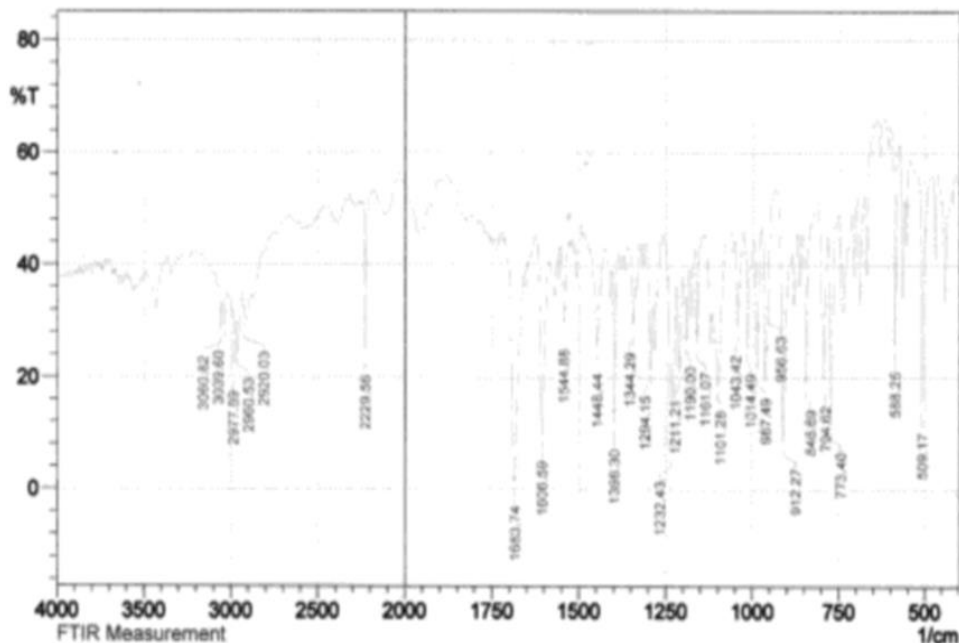


Fig. 2. The IR spectrum for compound 4.

In  $^1\text{H}$  NMR spectrum (figure 3) the most important signals are those of the H-5, H-6a, H-6b, H-7 and H-4a atoms. H-7 appears at 5.54-5.51 ppm (dd). It has two different coupling constants [ $J(7,6a) = 8.4$  Hz,  $J(7,6b) = 2.8$  Hz], which prove the *trans* configuration to H-6b and *cis* to H-6a.

The H-6a (dtd) proton has three different coupling constants [ $J(6a,6b) = 19.8$  Hz,  $J(6a,7) = 8.4$  Hz,  $J(6a,5) = 7.0$  Hz] which proves the *cis* configuration with respect to H-7 and H-5.

The H-4a (t) proton has two different coupling constants [ $J(4a,5) = 11.6$  Hz,  $J(4a,4) = 6.0$  Hz], which prove the *cis* configuration to H-5.

Additional evidence for the assigned structures is the great chemical shifts difference between H-7 (*ca.* 5.50 ppm) and H-4a (*ca.* 4.0 ppm), H-5 (*ca.* 3.25 ppm), H-6a (*ca.* 2.80 ppm) and H-6b (*ca.* 2.15 ppm).

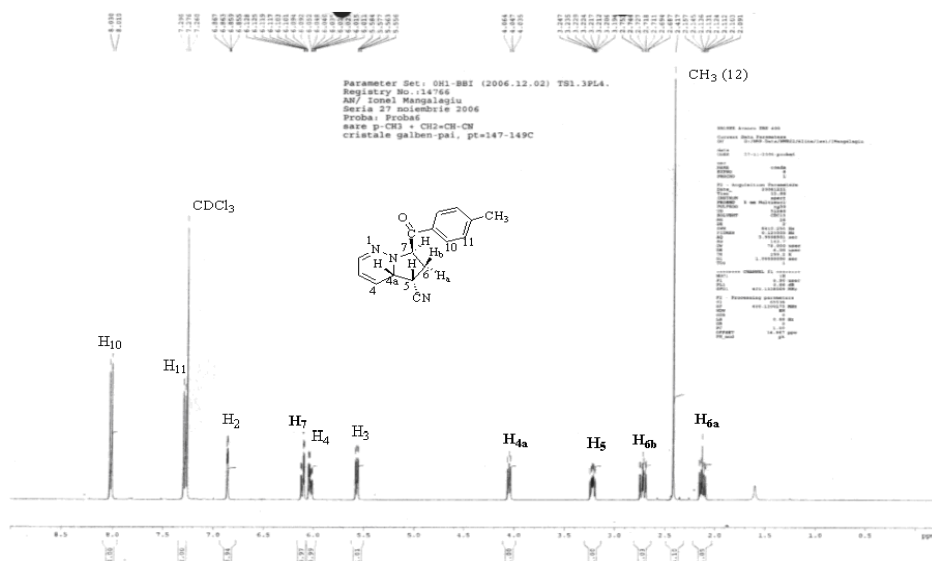


Fig. 3. The  $^1\text{H}$  NMR spectrum for compound 4.

In the  $^{13}\text{C}$  NMR spectra carbons (Figure 4), the most important signals are for the carbonyl-ketonic group (195,31 ppm), cyan group (120,48 pp) and C-4a, C-5, C-6 and C-7.

The chemical shifts are in accordance with the saturated structure proposed for adduct (4) (C-4a at 55.83 ppm, C-5 at 35.25 ppm, C-6 at 28.06 ppm and C-7 at 70.44 ppm). The low chemical shifts of these carbon atoms are further evidence in favour of the structure.

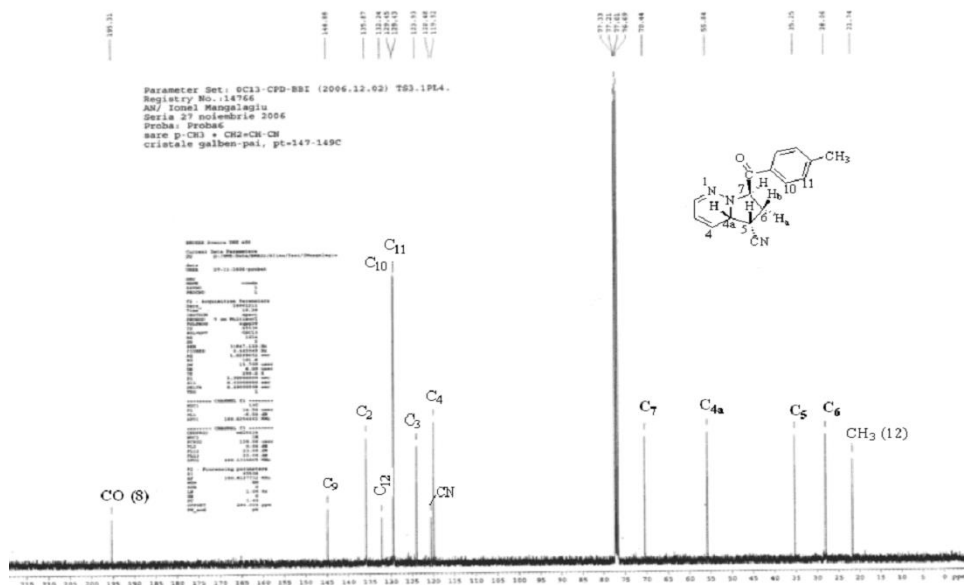


Fig. 4. The  $^{13}\text{C}$  NMR spectrum for compound 4.

In the MS spectrum (Figure 5), the most important signals are at 288 nm ( $\text{M}+\text{Na}^+$ ) and 553 nm ( $2\text{M}+\text{Na}^+$ ).

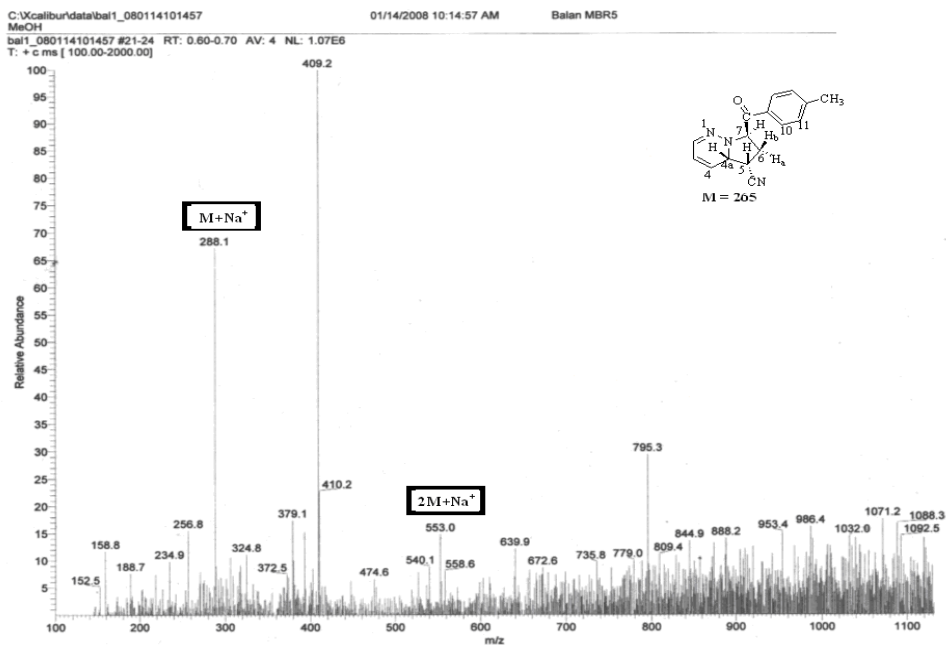


Fig. 5. The MS spectrum for compound 4.

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## CONCLUSIONS

1. By [3+2] cycloaddition reaction between pyridazine and an alkene in alkaline medium (Et<sub>3</sub>N) were obtained *in situ* a pyrrolopyridazine adduct.
2. The reactions were performed both using conventional thermal heating and microwave irradiation.
3. The structure of the compound was proved by spectral analysis. The following spectral methods were used: IR, <sup>1</sup>H NMR, <sup>13</sup>C NMR and MS.
4. Taking into account the chemical shifts, the coupling constants and signal splitting in the IR, NMR and MS spectra, the only reasonable structure for the cycloadduct is that one presented.
5. The results obtained suggest that the research for synthesis of pyridazine derivatives should be continued.

## REFERENCES

1. Amariuca-Mantu D., Mangalagiu V., Mangalagiu I.I., 2021 - [3 + n] Cycloaddition Reactions: A Milestone Approach for Elaborating Pyridazine of Potential Interest in Medicinal Chemistry and Optoelectronics. *Molecules*, 26, p. 3359.
2. Butnariu R., Caprosu M., Bejan V., Ungureanu M., Poiata A., Tuchilus C., Florescu M., Mangalagiu I.I., 2007 - Pyridazine and Phthalazine Derivatives with Potential Antimicrobial Activity. *J.Het.Chem*, 44, p. 1149-1152.
3. Butnariu R., Mangalagiu I.I., 2009 - New pyridazine derivatives: synthesis, chemistry and biological activity. *Bioorg. Med. Chem.*, 17, p. 2823-2829.
4. Caproșu M., Butnariu R., Mangalagiu I., 2005 - Synthesis and antimicrobial activity of some new pyridazine derivatives. *Heterocycles*, 65 (8), p. 1871-1879.
5. Padwa A., 1984 - *1,3-Dipolar Cyloaddition Chemistry*, J. Wiley, New York.
6. Tucaliuc R., 2008 – *Obținerea de compuși 1,2-diazinici cu potențiale aplicații practice prin metode convenționale și nonconvenționale*, Teză de doctorat.
7. Tucaliuc R.; Cotea V.; Niculaua M.; Tuchilus C.; Mantu D.; Mangalagiu, I.I., 2013 - New pyridazine-fluorine derivatives: synthesis, chemistry and biological activity. *Part II. Eur. J. Med. Chem.*, 67, p. 367-372.
8. Zbancioc Gh., 2007 – *Studiul unor 1,2-diazinii ilide și derivați prin metode convenționale și neconvenționale (cu ajutorul microundelor)*, Teză de doctorat.
9. Zbancioc Ghe., Mangalagiu I.I., Moldoveanu C., 2022 - A review on the synthesis of fluorescent five- and six- membered ring azaheterocycles. *Molecules*, 27, p. 6321.