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# The modification of phenyl – pyridine compounds under UV irradiation: FTIR investigation

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Phenyl-pyridine compounds present a high interest for Photodynamic Therapy due to their important anti-inflammatory and anti-tumor properties. In this study, two phenyl-pyridine compounds were investigated BG204 (3-amino, 9-thio [2-N-N-diethylaminoethyl] acridine) and BG 1120 (4,5 bis [thio(2-N-N-diethylaminoethyl)], 9methyl 1,8-diazantracene), because they present modification during UV irradiation. In order to elucidate these modifications FTIR spectroscopy was used. BG204 and BG1120 were UV irradiated using a Xe lamp, with a power density of 11mW/cm$^2$, for 1 hour, and 3 hours, respectively. The FTIR spectra, in the range of 4000 cm$^{-1}$ – 400 cm$^{-1}$, were performed by a Nicolet Magna IR 550 spectrometer. The results of the analyzed samples showed that these molecules are photo-reactive, and their therapeutic effects can be improved by UV irradiation.

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*Keywords*: Phenyl – pyridine compounds, FTIR spectroscopy, UV irradiation

## 1. Introduction

The phenyl pyridine compounds are known as compounds with antibacterial, antifungal and anticancer properties [1,2]. The study regarding the anticancer activity of the phenyl pyridine compounds started in 1920, a various number of natural and synthetic compounds were tested. The common property of all these compounds is their intercalation in the DNA structure. The acridine or the anthracene rest inside the phenyl pyridine compounds ensure a planar structure of the molecule that allows the intercalation of the molecule in the DNA, resulting the disabling of the DNA replication property [3-5].

Also the acridine compounds obstruct the activity of telomerasis and topopizomerasis and disturb the protein metabolism [2]. It has been proved that the anticancer activity is more efficient using phenyl – pyridine structures with lateral catena [2, 9]. Some studies observed the behaviour of the substances during irradiation, and lead to the conclusion that if absorption of the incident light by the phenyl–pyridine compounds has as result their photo-transformation, then the molecule is photo-reactive [11].

The purpose of this study was to characterize by FTIR spectroscopy the modifications of the phenyl pyridine compounds after UV irradiation.

## 2. Materials and methods

The substances used during this study were: 3 –amino, 9 thio [2 NN diethylaminoethyl] acridine or BG 204 and 4, 5 bis [thio (2 NN diethylaminoethyl)] 9 methyl 1, 8 diazantracene or BG 1120 (Fig. 1). The materials were supplied by Faculté de Farmacie, Université de la Mediteranée, Marseille, France.

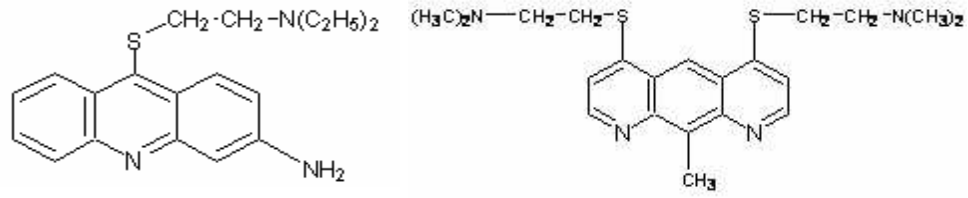


*Fig. 1. a) BG 204, b) BG 1120.*

Aqueous solutions of phenyl – pyridine compounds, at concentrations of $5 \times 10^{-5}$ M, were prepared. The samples were exposed to UV light; using a Xe lamp, the exposure times were 1 and 3 hours. The Xe lamp used is characterised by a spectral range of 320 to 480 nm and a power density of 11 mW/cm$^2$. In order to perform the FTIR spectra, the solutions were poured on KBr crystals and let to dry for 1 day. The resulted solid sample is then grounded in an agate mortar and subjected to a pressure of about $1.575 \times 10^5$ kg cm$^{-2}$. The obtained pellet was then used for FTIR study. The FTIR spectra were acquired using a Nicolet Magna – IR 550 spectrometer in the spectral range of 4000 – 400 cm$^{-1}$.

## 3. Results

### 3.1 BG 204

Three spectra of the BG 204 sample were obtained: non – irradiated, 1 hour irradiated and 3 hours irradiated. By superposing the three spectra, it can clearly be observed some important modification of the spectra's structure after sample irradiation (Fig. 2).

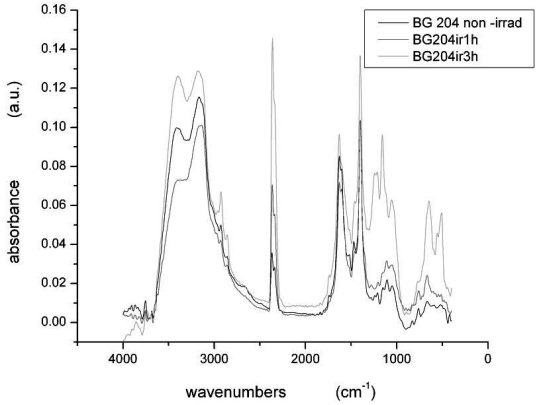


*Fig. 2. Superimposed FTIR spectra of the non – irradiated BG 204, irradiated 1 h and irradiated 3 h.*

For three hours irradiated sample, notable modifications of FTIR spectrum are observed in the regions of 500 – 650 and 1000 – 1300 $cm^{-1}$ (Fig. 3).

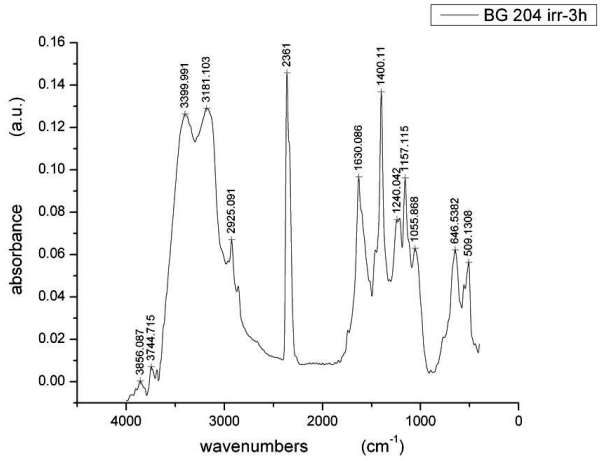


*Fig. 3. BG 204 irradiated 3 h FTIR spectra.*

The strong peak centred between 550 and 500 $cm^{-1}$ could be assigned to the S–S bound, while the peak situated in the range of 670 – 640 $cm^{-1}$ can be attributed to the C – S stretching vibrations in sulphides. These observations suggest that a break of the lateral catena of the molecule occurred; S remained bounded to the acridinic rest. These modifications make possible the formation of thiols and disulphides (Fig. 4).

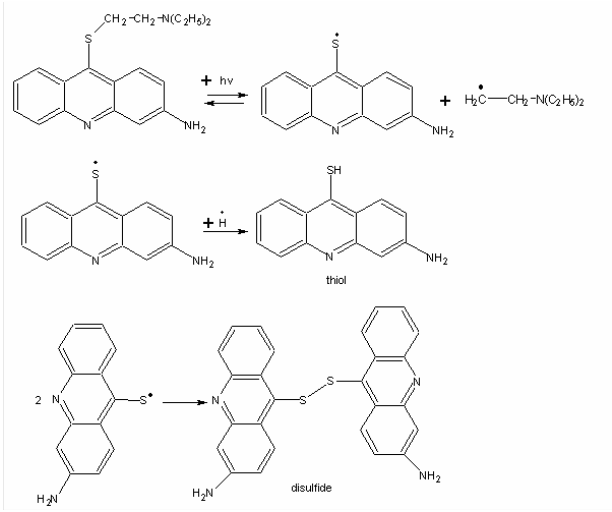


*Fig. 4. Suggested chemical transformation process of BG204.*

In the region 1300 – 100 $cm^{-1}$, the absorption bands could be assigned to substituted tertiary amine or to $CH_2$ – S group. It is worth noticing the presence of bands due to the C=S stretching vibrations (1230 – 1030 cm - 1), which could suggest that after irradiation the equilibrium was shifted to the lactam form (Fig. 5).

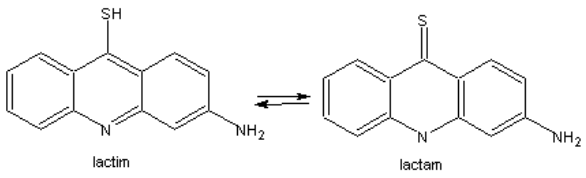


*Fig. 5. Tautomerization process of the antracenic rest.*

From the resulted data and the observations done it can be concluded that the tautomeric forms and the dimmers coexist.

To mention also that these are regions in the spectra where no major modifications due to the irradiation of the substance were observed. The band corresponding to N – H bending vibration of primary amines localized at 1630 $cm^{-1}$ does not modify too much as well as the bands corresponding to alkyl groups: 2850 $cm^{-1}$ attributed to alkyl $\nu_s$ $CH_2$ groups and 2925 $cm^{-1}$ alkyl $\nu_s$ ($CH_3$ + $CH_2$). Very strong absorption bands could be observed at 1400 $cm^{-1}$ and in the region 3100 -3500 $cm^{-1}$, both assigned to N – H stretching vibrations of ammonium ion formed by amine.

$$R_3N + HOH \leftrightarrow R_3NH^+ + OH^-$$

### 3.2 BG 1120

Regarding BG 1120, by superimposing the 3 spectra, of the non – irradiated, irradiated for 1 h and irradiated for

3 h sample, the differences between the structures of the three spectra suggest that major modification in the structure of the molecule has occurred after irradiation (Fig. 6).

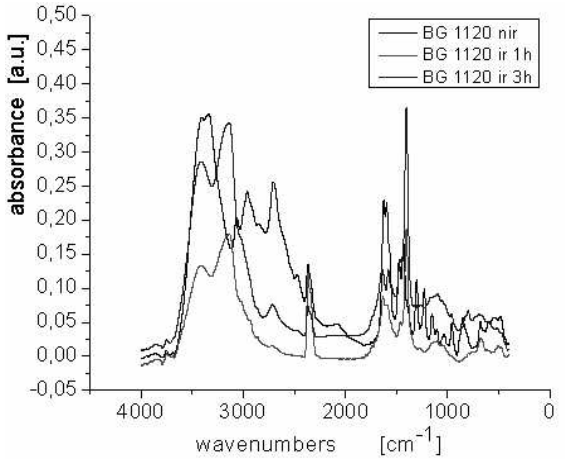


*Fig .6. Superimposed FTIR spectra of the non – irradiated, 1 h irradiated and 3 h irradiated BG 1120 Sample.*

For practical reasons the analyzed spectrum is that of BG 1120 irradiated for three hours. The modifications suffered in the structure of the molecule are more obvious after a longer irradiation exposure (Fig. 7).

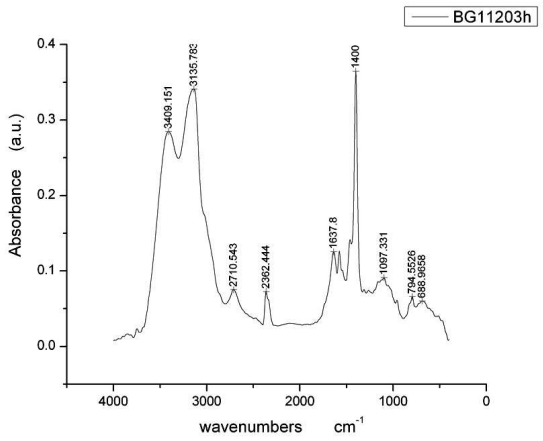


*Fig. 7. BG 1120 irradiated 3 h FTIR spectra.*

Beside the very strong and sharp signal localized at 1400 $cm^{-1}$, attributed to the ring stretching mode in thiols, the spectrum has another weak and broad signal at 680 $cm^{-1}$, which corresponds to the in-plane C – S - H bending. The absorption bands present especially in the spectrum corresponding to 3 h irradiated sample, suggest the mechanism of broken bond S – C with tertiary amine and the formation of a tertiary amine and dithiols (Fig. 8).

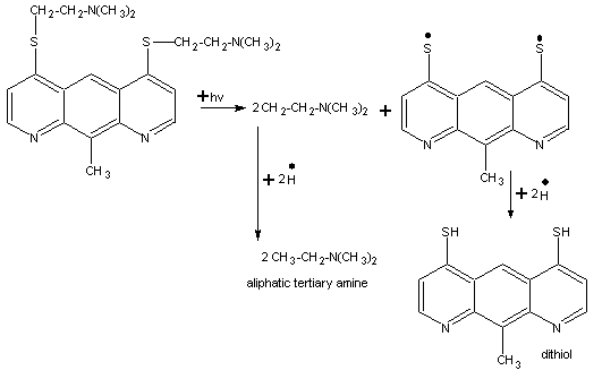


*Fig. 8. Breaking process of the lateral catena and possible related combinations.*

Further analysis of the spectra allows to observe the presence of a broad band situated at 1098 $cm^{-1}$, corresponding to compounds that contain a thiocarbonyl group (C=S) and two sharp medium signals localized at 1638 $cm^{-1}$ and 1579 $cm^{-1}$ that correspond to the vibrations of the C=S bond met in lactam form of aromatic rest. The two atoms of S that bond to the azaantracenic rest unstabilize the molecule, therefore a complex process of tautomerization could take place. The rest of the molecule transforms in one of the three tautomeric forms: bis – lactim, lactim –lactam or bis – lactam (Fig. 9).


*Fig. 9. Tautomeric forms of the diazaantracenic rest.*

The band from 1400 $cm^{-1}$ could be assigned to C–C ring stretch in thiols (SH) and to N–H bending vibration in $NH_4^+$ ion (completely ionized hydroxide formed by amine in aqueous solution). The broad band localized at 2710 $cm^{-1}$ was attributed to – $CH_2$ stretching mode in $CH_2$ – N group from tertiary amine.

$$(CH_3)_2N - C_2H_5 + HOH \leftrightarrow (CH_3)_2 \overset{\oplus}{N} H - C_2H_5 + HO^-$$

The bands in the region 3500 – 3100 $cm^{-1}$ are attributed to NH stretching vibrations in $NH_4$ ion and are met in all the spectra.

## 4. Discussion

The analyzed substances are used in the study of new anticancer compounds. The aim of this study was to observe if the phenyl–pyridine compounds modify under UV irradiation and what could be these modifications.

All the observations lead to the conclusion that irradiation causes important modifications in the structure

of the molecules. First, a brake, localized at the S atom, between the aromatic rest and the lateral catena occurs in both situations and then a process of tautomerization of the molecules could be observed.

The presence of $NH_4$ ions can suggest the existence of $HO^{\cdot}$ radicals, which are considered to induce tumour necrosis.

The photo-transformation of the analyzed samples show that molecules are photo-reactive and their therapeutic effect can be improved by UV irradiation.

**Acknowledgement**

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## References

[1] J. Millet, M. Torrentino- Mdamet, S. Alibert, C. Rogier, C. Santelli-Rouvier, J. Mosnier, E. Baret, J. Barbe, D. Parzy, B. Pradines, Antimicrobial Agents and Chemotherapy, July 2004, p 2753- 2756.

[2] M. Mallea, A. Mahamoud, J. Chevalier, S. Alibert – Franco, P. Brouant, J. Barbe, J.-M. Pages, Biochem. J. **376**, 801 (2003).

[3] M. L. Pascu, M. Brezeanu, L. Voicu, B. Carstocea, R. A. Pascu, In Vivo **19**, 215 (2005).

[4] M. L. Pascu, L. Voicu, M. Brezeanu, A. Staicu, B. Carstocea, D. M. Gazdaru, "Anticancer Research" **24**, 2925 (2004)

[5] O. Keskin, I. Bahar, R. L. Jernigan Anti-Cancer Drug Design **15**, 79 (2000).

[6] DiCesare N, Lakowicz JR. Anal. Biochem, Jul.15, **294**(2), 154 (2001).

[7] M. Brezeanu, D. M Gazdaru, L. Voicu, R. Morarescu J. Optoelectron. Adv. Mater. **6**(4), 1305 (2004).

[8] W. Obexer, C. Schmid, J. Barbe, J. P. Galy, R. Brun, Trop Med Parasitol. **46**(1), 49 (1995).

[9] Sham M. Sondhi, Gurudas Bhattacharjee, Rafid K. Jameel Rakesh Shukla CEJC **2**(1), 1 (2004 ).

[10] Hongtao Yu, Jian Yan, Yuguo Jiao, Peter P. Fu, Int. J. Environ. Res. Public Health, **2**(1), 114 (2005).

[11] Dabestani Reza, Ivanov Ilia N., Photochemistry and Photobiology, July 1999.

[12] Martine Demeunynck, Franck Charmantray, Alain Martinelli, Current Pharmaceutical Design, **7**, 1703 (2001).

[13] Shiming Dong, Shuguang Wang, Gernerique Stewart, Huey-Min Hwang, Peter P. Fu, Hongtao Yu, Int. J. Mol. Sci. **3**, 937 (2002).

[14] Chanan Sluszny, Valery Bulatov, Vladimir V. Gridin and Israel Schechter, Photochemistry and Photobiology **74**(6), 780 (2001).

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