Synthesis of 1- (5-nitro-benzimidazol-2´-yl-sulphonyl-acetyl)-4-aryl-thiosemicarbazide with biological potential

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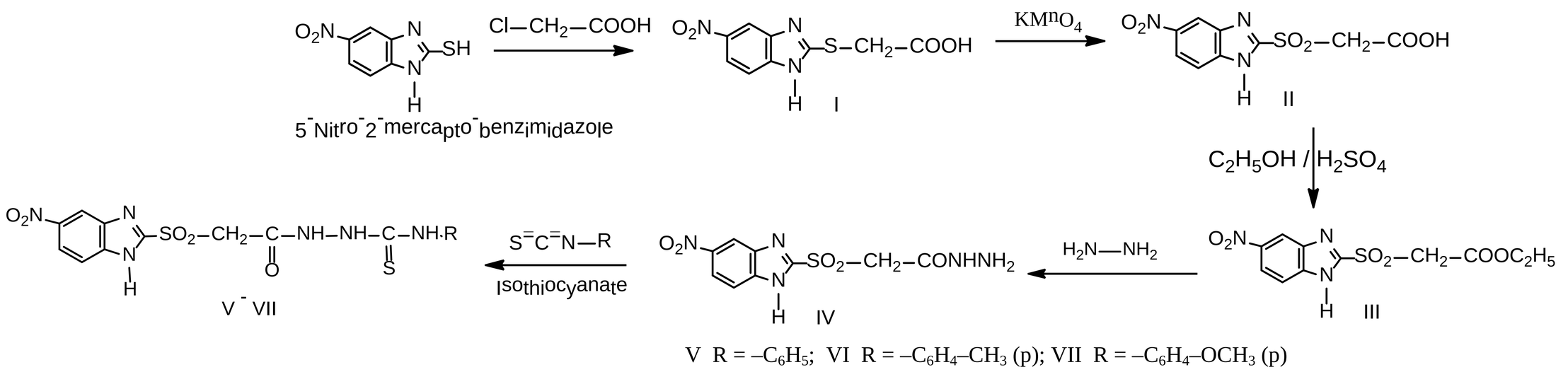
INTRODUCTION

Thiosemicarbazides present increasing interest due to their various pharmacological applications, the antibacterial [1], anticonvulsant [2], antifungal [3], cytostatic, anti-oxidant [4] activity, among which, tuberculostatic activity [5] are worth to be mentioned.

Considering the well known biological potential of the thiosemicarbazides, this work is focused on developing a new method of synthesizing of 1- (5-nitro-benzimidazol-2´-yl-sulphonyl-acetyl)-4-aryl-thiosemicarbazide

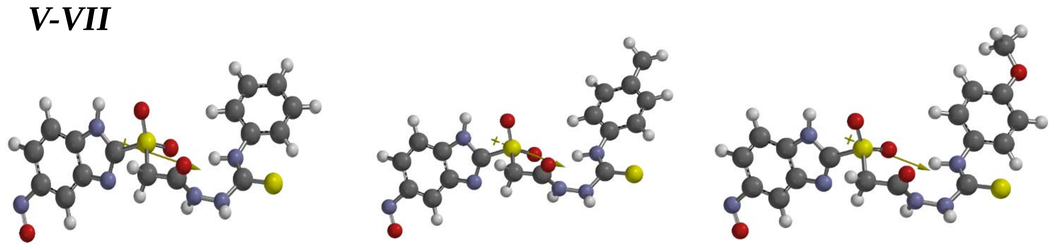
RESULTS AND DISCUSSIONS

This paper presents the synthesis of new thiosemicarbazides whose active group has as support the rest of the ethyl ester of 5-nitrobenzimidazol-2-yl-sulfonyl-acetic acid. A number of intermediates are required to obtain such combinations (Scheme 1)



Scheme 1. Synthesis of 1-(5´-nitrobenzimidazole-2´-yl-sulphonyl-acetyl) -4-aryl-thiosemicarbazides V-VII

QUANTUM CHEMICAL ANALYSIS OF THE THIOSEMICARBAZIDES V-VII



V VI VII

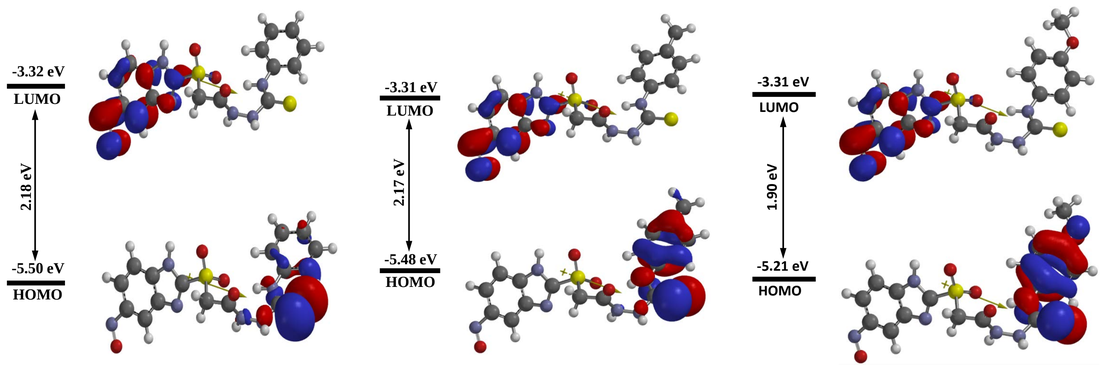
Fig. 1. Optimized molecular structures of compounds V-VII

Some molecular parameters computed by Spartan Program are listed in Table 1

Table 1. Molecular parameters of the compounds V-VII.

Nr.	Molecular parameter	V	VI	VII
1	Formula	$C_{16}H_{14}N_6O_4S_2$	$C_{17}H_{16}N_6O_4S_2$	$C_{17}H_{16}N_6O_5S_2$
2	Weight (amu)	418.46	432.49	448.48
3	Energy (au)	-2043.00	-2082.28	-2157.46
4	Energy(aq)(au)	-2043.04	-2082.32 au	-2157.50
5	Solvation E (kJ/mol)	-106.27	-103.38	-112.60
6	E HOMO (eV)	-5.50	-5.48	-5.21
7	E LUMO (eV)	-3.32	-3.31	-3.31
8	Dipole Moment (D)	7.67	7.67	8.85
9	Area (Å^2)	393.69	413.47	424.41
10	Volume (Å^3)	362.52	380.81	389.46
11	PSA (Å^2)	125.37	125.06	133.00
12	Ovality	1.60	1.63	1.65
13	Polarizability (Å^3)	70.27	71.67 Å^3	72.52 Å^3

From Fig. 2 one results that the electronic transition between HOMO and LUMO take place by an intramolecular charge transfer (ICT) between the ending parts of these molecules



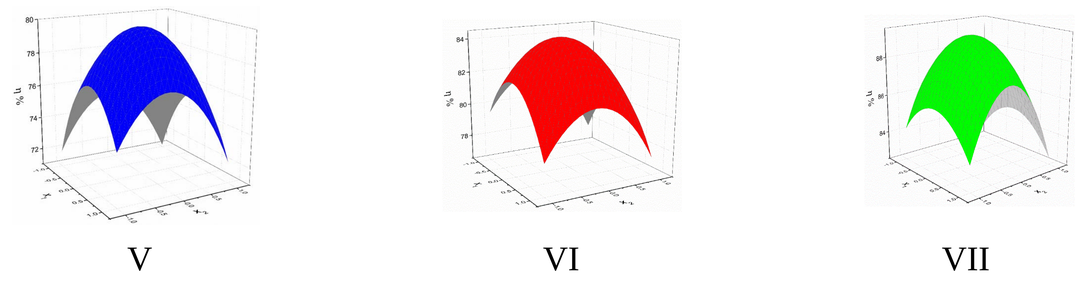
ICT for molecule V ICT for molecule VI ICT for molecule VII

Fig. 2. Electronic transition HOMO-LUMO

We computed the favorable conditions for the chemical reactions in which the substances V-VII can be obtained. These conditions are listed in the table 2

Table 2. Favorable conditions for the chemical reactions in which the substances V-VII can be obtained

Compound	$x_1; T(^0C)$	$x_2; t(h)$	η (%)
V	0.11 (64^0 33' 20")	-0.09 (3h 57min 18s)	79.83%
VI	-0.05 (64^0 28' 30")	0.114 (3h 33min 25s)	84.22%
VII	- 0.05 ($64^0$28' 30")	-0.07 (3h 57 min 54s)	89.24%



V VI VII

Fig. 3. Yields of optimized reactions for obtaining the substances V-VII

The method of the selective sulphonation of 5-nitrobenzimidazole-2-yl-mercapto-acetic acid and the method of forming 5-nitrobenzimidazole-2-yl-sulphonyl-acetic acid ester have been developed.

5-Nitrobenzimidazole-2-yl-sulphonyl-acetic acid hydrazide was prepared, and by its addition to some aromatic isothiocyanates the corresponding series of heterocyclic acyl-sulphonyl-thiosemicarbazides was obtained.

The synthesized intermediates and final products were characterized using elemental and spectral analysis (FT-IR, ^{1}H-NMR).

The experimental conditions corresponding to the maximum yields of reactions were established.

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