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Dedicated to professor Gh. Marcu at his 80th anniversary

BIS-PHENOTHIAZINYL-PHENYL-METHANE DERIVATIVES

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ABSTRACT. The synthesis of some *bis*-(phenothiazin-3-yl)-phenylmethane derivatives by the condensation of phenothiazine with aromatic aldehydes was investigated. The structural assignments for the new compounds were based on NMR, IR and UV-Vis spectroscopy.

INTRODUCTION:

The chemical reactivity of phenothiazine towards electrophilic substitution reactions was demonstrated in numerous examples of N- or C- substituted derivatives preparations. The transmission of the electronic effects between the two heteroatoms and the two benzene rings is very efficient and electrophilic substitution occurs easily. Rather mild electrophiles can be used to accomplish the substitution reaction in position 10 (N-alkylphenothiazines [1], N-acylphenothiazines [2]) or in positions 3 and 7 (C-halogenophenothiazines [3-5], C-nitrophenothiazines [6.] C-alkylphenothiazines [7,8]). Dyes formation by the condensation of phenothiazine with aromatic ketones (such as Michler's ketone) was also reported [9].

The paper presents the condensation reaction of phenothiazine with aromatic aldehydes in the presence of acid catalysts.

RESULTS AND DISCUSSIONS

The condensation reaction of phenothiazine **1** with aromatic aldehydes (benzaldehyde, *o-, m-* and *p*-nitrobenzaldehyde) in acid media was performed. The mild electrophile generated by the aldehyde in the presence of methanesulfonic acid determines the substitution of the phenothiazine ring in position 3 (activated by the electron donor effect of the nitrogen heteroatom). In boiling ethanol solvent the reaction product **4** has a low solubility and easily separates from the reaction mixture. Scheme 1 presents an overview of the chemical reactions involved.

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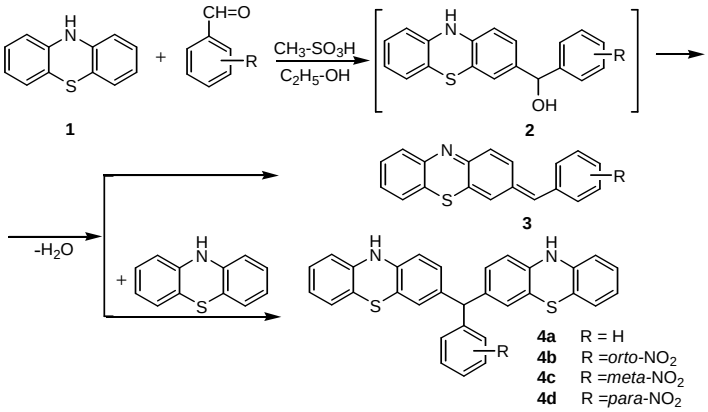
* Part I [1]



Scheme 1.

The structure assignment for compounds **4a-d** was performed by H-NMR, FTIR and UV-Vis spectroscopy.

The IR spectroscopic investigations of the reaction products showed that the alcohol intermediate **2** was not separated under the reaction conditions employed (no characteristic absorption bands due to C-O and O-H bonds stretching vibrations were recorded for the separated reaction product).

During the reaction progress, a green color appears in to the reaction mixture, possibly due to the competing elimination reaction generating the compounds **3 (**characterized by a fully conjugated π electrons system). The compounds **3** are soluble in ethanol.

The *bis*-(phenothiazin-3yl)-phenylmethane **4a** and its nitro-substituted derivatives **4b-d** separated from the boiling reaction mixture as precipitates which were filtered. The H-NMR spectra, showed for the aliphatic proton a characteristic chemical shift situated in the range of 5.1-5.8 ppm. The most deshielded aliphatic proton appears in the structure of the *orto*-nitro-substituted derivative **4b** (δ=5.8 ppm), while the signal of the same proton in the structure **4a** is situated at 5.1 ppm. Intermediate values (5.4 ppm) were recorded for the compounds **4c-d** containing a nitro group situated in position *meta* or *para.*

EXPERIMENTAL:

The chemical reagents and the solvents were purchased from Merck (for synthesis purity)

The IR spectra were recorded on a FTIR Bruker Vector 22 spectrometer.

The UV-Vis spectra were recorded on a UNICAM Helios β spectrometer.

The H-NMR spectra were recorded on a Bruker Avance 300 MHz spectrometer.

General procedure for the condensation of phenothiazine with aromatic aldehydes.

Phenothiazine (2g, 1 mmol) was solved in ethanol (120 mL), methanesulphonic acid (0.5 mL) and an ethanolic solution of the aromatic aldehyde (0.5 mmol) were added to the clear phenothiazine solution. The reaction mixture was heated under

vigorous stirring to reflux for several hours. During the reaction progress, a green color appears and a precipitate starts to accumulate.

The reaction mixture thus obtained was cooled down at room temperature, the precipitate was filtered out and then washed several times with cool ethanol. The reaction product is a grey-green powder highly insoluble in toluene, acetone and chloroform, soluble in THF.

***Bis*-(phenothiazin-3-yl)-phenylmethane 4a**

Reaction time: 12 hours, green powder , m.p. 251 ^{o}C, yield 60 %.

IR [cm^{-1}]: 3400, 3100, 1600, 1462, 1300, 803, 741, 604

UV [nm]: 248, 320.

H-RMN (300 MHz, DMSO-d_6) δ: 7.3-6.1 ppm, m 19H (phenyl and phenothiazine unit), 5.1 ppm, s, 1H (CH)

***Bis*-(phenothiazin-3-yl)-2-nitrophenylmethane 4b**

Reaction time: 40 hours, grey powder , m.p. 278 ^{o}C, yield 48%.

IR [cm^{-1}] 3400, 3100, 1514, 1339, 810, 742, 650

UV [nm]: 248, 320.

H-RMN (300 MHz, DMSO-d_6) δ: 8.1-6.6 ppm, m 18H (*o*-phenylene and phenothiazine unit, 5.8 ppm, s, 1H (CH).

***Bis*-(phenothiazin-3-yl)-3-nitrophenylmethane 4c**

Reaction time: 20 hours, brown powder, m.p. 264 ^{o}C, yield 55 %.

H-RMN (300 MHz, DMSO-d_6) δ: 8ppm, d, 2H, 7.4 m 2H, (*m*-phenylene unit), 6.1ppm, m, 14 H (phenothiazine unit), 5.3 ppm, s, 1H (CH).

***Bis*-(phenothiazin-3-yl)-4-nitrophenylmethane 4d**

Reaction time: 15 hours, grey powder , m.p. 255 ^{o}C, yield 61%.

IR: [cm^{-1}]: 3400, 3100, 1600, 1514, 1339, 809, 742, 690.

UV: 250 nm, 324 nm

H-RMN (300 MHz, DMSO-d_6) δ: 8.6 ppm s, 2H (NH), 7.34 d 2H, 8.1, d, 2H (*p*-phenylene unit), 6.6–6.9 ppm, m, 14 H (phenothiazine unit), 5.4 ppm, s, 1H (CH).

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