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## Synthesis of Novel Azo Dyes Derived from 8-Hydroxyquinoline

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### ABSTRACT

The novel azo dyes derived from the 7-substituted 8-Hydroxyquinoline (8HQ) presented in this work were synthesized by a coupling reaction with 8HQ derivatives using a primary aromatic amine. These new azo dyes were obtained with quantitative yields varying between 75 and 90% with a predominance of the trans-isomer. They may have potential biological properties compared to similar compounds.

The structure of the new heterocyclic compounds obtained not yet described in the literature was confirmed on the basis of the <sup>1</sup>H NMR (300MHz) and <sup>13</sup>C NMR (75MHz) spectroscopic parameters.

**Keywords:** Azo Dyes, Coupling Reaction, Heterocyclic compound, 8-Hydroxyquinoline

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### INTRODUCTION

This work is a part of the continuing research undertaken in our laboratory to synthesize new products based on 8-hydroxyquinoline (8HQ) [1-8].

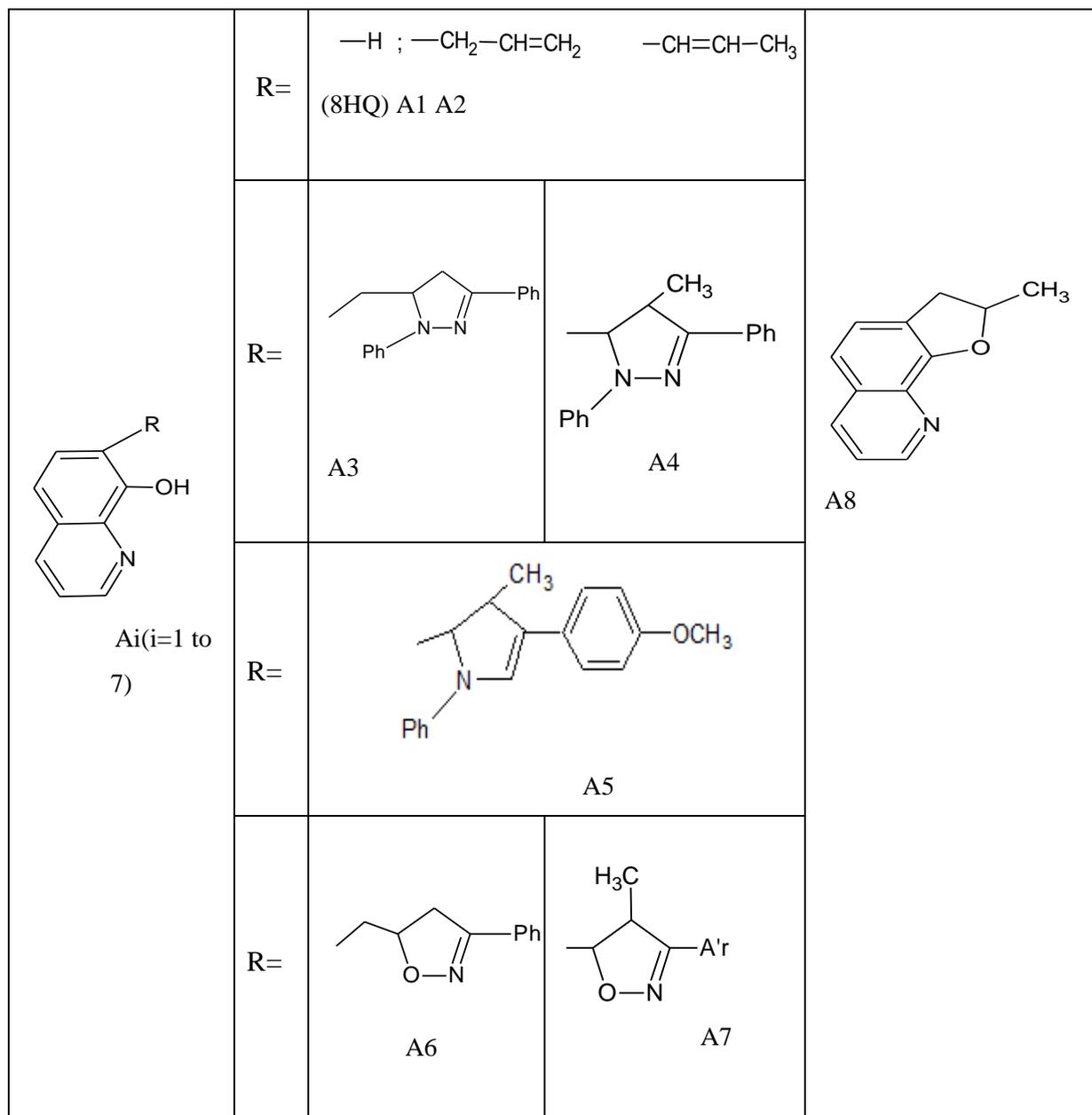
Thus, we have adopted a particular research strategy involving the synthesis of new azo dyes Ai derivatives from 8HQ substituted in position 7.

Indeed, the synthesis of these compounds is a coupling reaction with 8HQ's derivatives Ai by means of an aromatic primary amine. We adopted the method recommended by several researchers [9-11] with a change in the stoichiometry of the coupling reaction [12].

The Precursors Ai (i=1 to 8) are leading to the new coupling products Bi (i=1 to 8) (Scheme 1) which are derivatives of 8HQ substituted in position 7, so as to make the coupling reaction specific and quantitative.

The remaining in this position is composed first by an allelic group A1 or ethylenic group A2, or second by a pyrazolinic cycle (A3, A4, A5) or isoxazolinic (A6, A7), or third by a furan ring A8.

We note that the A3 to A7 precursors were synthesized for the first time in our laboratory via a 1,3-dipolar cycloaddition reaction [1]. Some of these precursors have been tested as having antileishmanial activities and applied in hydrometallurgy field to extract metals [1,13].



Scheme 1: Precursors Ai: 8HQ substituted in the position 7

As for the product A8 which has a benzofuranic form, it has been already prepared by Pène *et al.*; Fiedler *et al.* [13,14] who highlighted allyl cyclisation A1 under acidic conditions.

We also synthesized A8 in this work; according to an original method by distilling to 15 mmHg through allyl ether A'1 formed *in situ* (Scheme 2) [15].

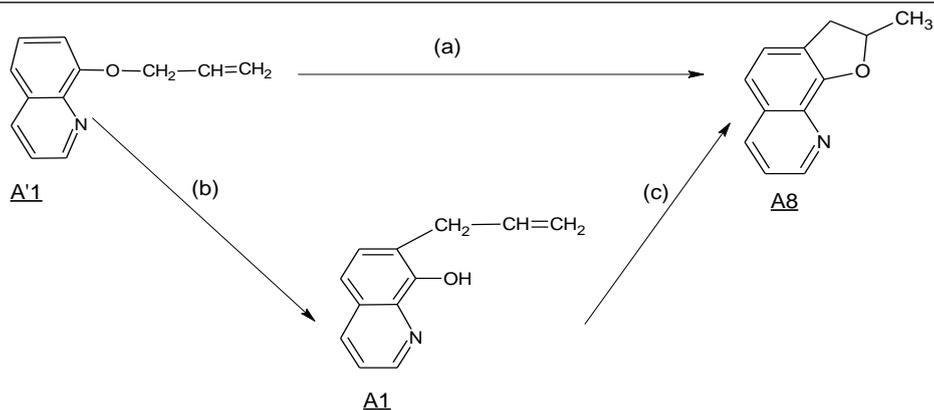
### Coupling reaction

The preparation of azo colorants Bi is done in two stages

The first step is the diazotization of para methyl aniline: which is a reaction of the para methyl aniline with sodium nitrite ( $\text{NaNO}_2$ ) under the action of hydrochloric acid (HCl) at  $0^\circ\text{C}$ . The product obtained is a diazonium salt [16-20].

The second step results from a diazo coupling reaction of the diazonium salt on the precursor Ai involving an electrophilic substitution reaction which is quantitatively on the para position of the phenol nucleus site 8HQ [21] and leads to azo colorants as Bi two cis and Trans isomers with a predominance of the Trans isomer (Scheme 3).

The reaction yields vary between 75 and 90% (Table 1).



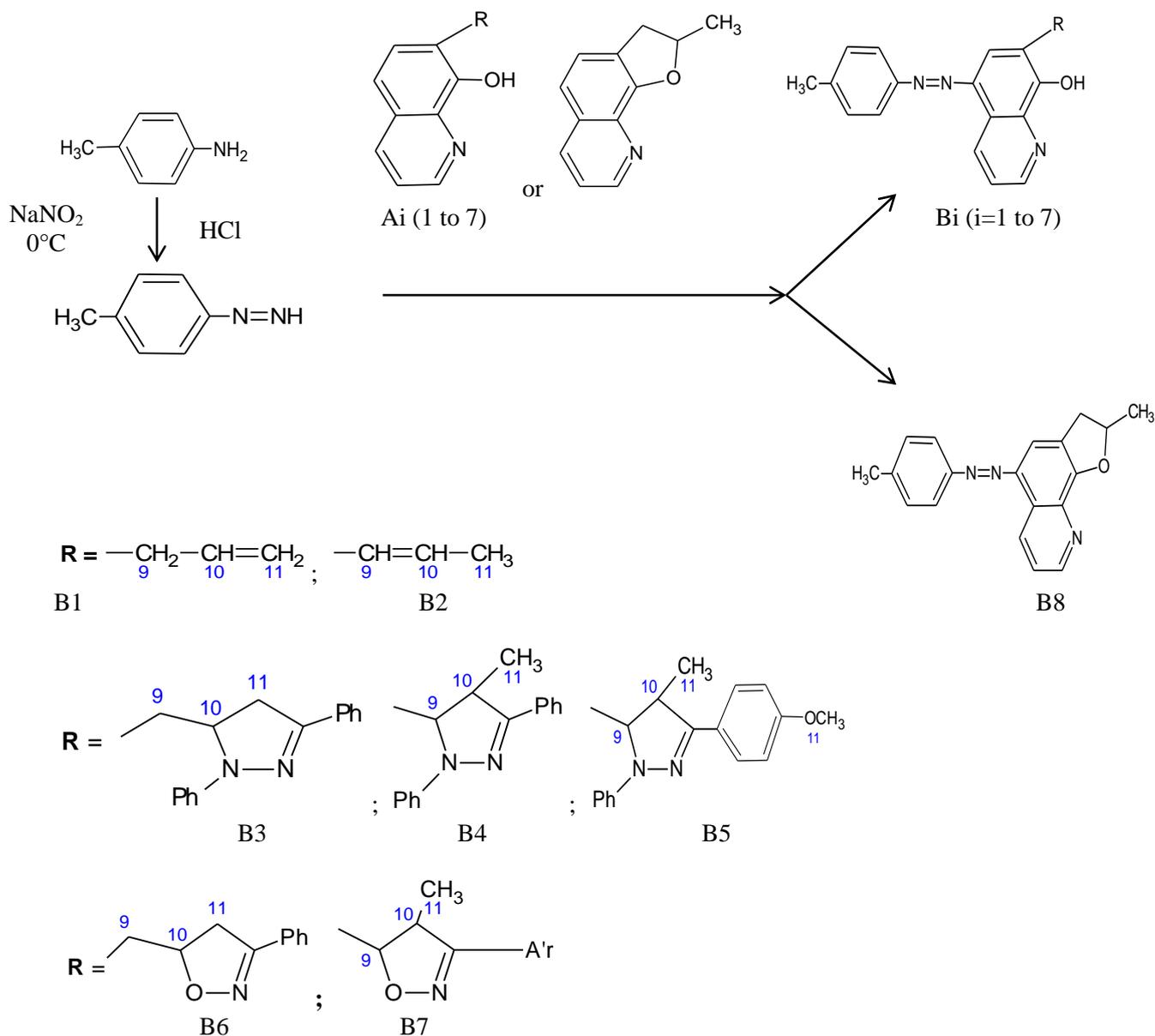
**Scheme 2: Synthesis of compound A8 by different methods  
whose (a) is original to this work**

(a) Original method (this work):

- 1) Heating at 200°C, N<sub>2</sub>, 30 mn;
- 2) Distillation at 15 mmHg;

(b) 1) Heating at 200°C, N<sub>2</sub>, 30 mn;  
2) Distillation at 5 mmHg;

(c) Fielder's Method using the APP or method of Pène et al. using H<sub>2</sub>SO<sub>4</sub>.



**Scheme 3: General scheme of Bi dyes synthesis**

Table 1: Yields and physical characteristics of Bi's dyes

Precursors A	A1	A2	A3	A4	A5	A6	A7	A8
Products B	B1	B2	B3	B4	B5	B6	B7	B8
F°C (A)	42	86	214	192	160	122	163	113
F°C (B)	116	196	207	197	254	260	244	> 260
Solid's color B	Red	Red	Brown	Orange	Yellow	Orange	Yellow	Red
Yield (%)	90	90	85	80	80	78	88	75

## MATERIALS AND METHODS

### Preparation of precursors A1, A2, A8

A refluxed mixture of 0.2 mole of (8HQ) and 0.3 mole of potassium carbonate in a 500 ml Bicol equipped with a condenser fitted with a CaCl<sub>2</sub> tube. After 15 min, 0.2 mole of allyl bromide is added and continued the reflux for 24 h. After cooling the solid obtained is filtered and then washed three times with acetone. We washed with a solution of KOH (5%) then with water until neutral. Dried over anhydrous Na<sub>2</sub>SO<sub>4</sub>. The oil obtained after evaporation of the solvent, being A'1 raw allyl ether.

<sup>1</sup>H NMR of the allyl ether of A'1: 4.84 ppm (d, 2H), 5.34 ppm (dd, 1H), 5.40 ppm (dd, 1H), 6.20 ppm (Octuplet, 1H). We proceed to a Claisen rearrangement by heating the ether A'1 to 160°C under a dry nitrogen atmosphere in a sand bath. The reaction is exothermic and reached 200°C. The Distillation of the residue at 165-170°C under 5 mmHg leads to a yellowish oil which crystallized from heptane (A1: F°C=42, Yield=80%). Then a distillation under 15 mmHg affords the compound A8 (white crystals, F°C=113, Yield=53%). The A2 product is prepared from allyl A1 by refluxing for four hours a mixture of 20 g of A1 and 34 g of KOH in 200 ml of butanol. After distillation of butanol, we neutralize the solution with 6 N HCl, extracted with ether, washed with water and dried on anhydrous sodium sulphate. After solvent evaporation, we get A2 in the form of a yellow solid which is recrystallized in ethanol (F°C=86, yield=72%).

	<sup>1</sup> H NMR characteristics (300 MHz)	Caractéristiques RMN- <sup>13</sup> C (75 MHz) <sup>13</sup> C NMR characteristics (75 MHz)
A'1	<sup>1</sup> H NMR of allyl ether part of A'1 : 4,84 ppm (d, 2H), 5,34 ppm (dd, 1H), 5,40 ppm (dd,1H), 6,20 ppm (octuplet, 1H).	--
A1	<sup>1</sup> H NMR of allyl part: 3,68 ppm (d, 2H), 5,10 ppm (dd, 1H), 5,18 ppm (dd,1H), 6,10 ppm (multiplet, 1H).	<sup>13</sup> C NMR allylic part: 34 ppm, 116 ppm, 136 ppm.
A2	<sup>1</sup> H NMR of the ethylene part: 2,00 ppm (dd, 3H), 6,40 ppm (octuplet, 1H), 6,95 ppm (octuplet, 1H).	<sup>1</sup> H NMR of the ethylenic part: 19 ppm, 125 ppm, 126 ppm.
A8	<sup>1</sup> H NMR of the furan part: 1,65 ppm (d, 3H), 3,05 ppm (dd, 1H), 3,57 ppm (dd,1H), 5,20 ppm (multiplet, 1H).	<sup>13</sup> C NMR of the furan part: 22 ppm, 38 ppm, 81 ppm.

### Preparation of precursors Ai (i=3-7)

#### Obtaining A3, A4, A5

They are prepared according to a general procedure described in the literature [1 and cited references] involving dipolar cycloaddition of 1,3-diarylnitilimines (DANI) reaction applied to the ethylenic site which taken as dipolarophile of A1 and A2 compounds.

#### Obtaining A6, A7

We synthesize them using a dipolar cycloaddition reaction of 1,3-arylnitriloydes (OAA) also applied to the ethylenic sites of A1 and A2 compounds [1 and cited references].

### Synthesis of coupling compounds Bi (i=1-8)

10 ml of 37% hydrochloric acid are added slowly to aniline (5.00 g; 54 moles) previously dispersed in 15 ml of water in a flask. The above mixture is cooled to 0°C before adding dropwise 25 mL of aqueous sodium nitrite (4.07 g; 1.1 eq). The diazonium solution generated is then coupled with the precursor Ai (7.79 g; 1 eq) previously dissolved in 50 ml of 1.2 N sodium hydroxide between 0 and 4°C.

This coupling is associated immediately a yellow-orange color of the reaction mixture. After one hour under stirring at 0 ° C followed by a gradual return to room temperature, the suspension obtained was acidified with dilute hydrochloric acid and the precipitate formed is collected by filtration and washed with water and CH<sub>2</sub>Cl<sub>2</sub>.

The obtained crude product is recrystallized from CHCl<sub>3</sub>/EtOH 50:50. Yields vary between 75 and 90%. After drying, the final product Bi is in the form of a colored powder (Table 1).

## RESULTS AND DISCUSSION

For example, the NMR  $^1\text{H}$  spectrum of compound B6 in DMSO $_d6$  (Table 2 and Figures 1-3) has 2 multiplets.

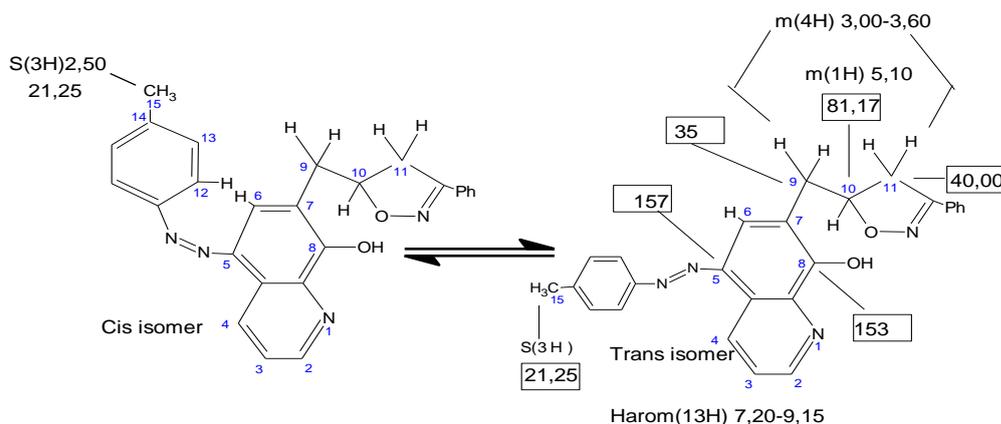


Figure 1: Chemical shift, Characteristic of NMR  $^1\text{H}$  and  $^{13}\text{C}$  in DMSO $_d6$  of B6 product

We attributed the multiplet centered at 5.12 ppm to the carbon-bonded C10 proton adjacent to the hetero atom (O). Another very intense multiplet between 3.00 and 3.60 ppm is attributed to the proton carried by the carbon C9 and C11. These allocations have been shown in our previous work and compared to related structures [2,22].

In addition, it is observed on all the spectra of the isolated products that two distinct signals to 2.34 ppm and 2.50 ppm, all of them incorporating three protons of the methyl group bonded to carbon 15.

This observation confirms in one hand, that the coupling reaction was held showing the existence of CH $_3$  protons relatively not deshielded as linked to an aromatic ring.

On the other hand, and wherein the structure of the isolated products can oscillate between two cis and trans geometric configurations due to the unsaturation between the two nitrogen atoms, the singlet at 2.34 ppm corresponds to the cis isomer and one at 2.50 ppm is due to the trans isomer with respective proportions of 23 and 77%.

We Note that the CH $_3$  protons are more deshielded in the Trans isomer, the more stable, than cis isomer, because of the high voltage of the rings which are attached to nitrogen atoms that are causing a deshielding of protons attached to carbons C6 and C12.

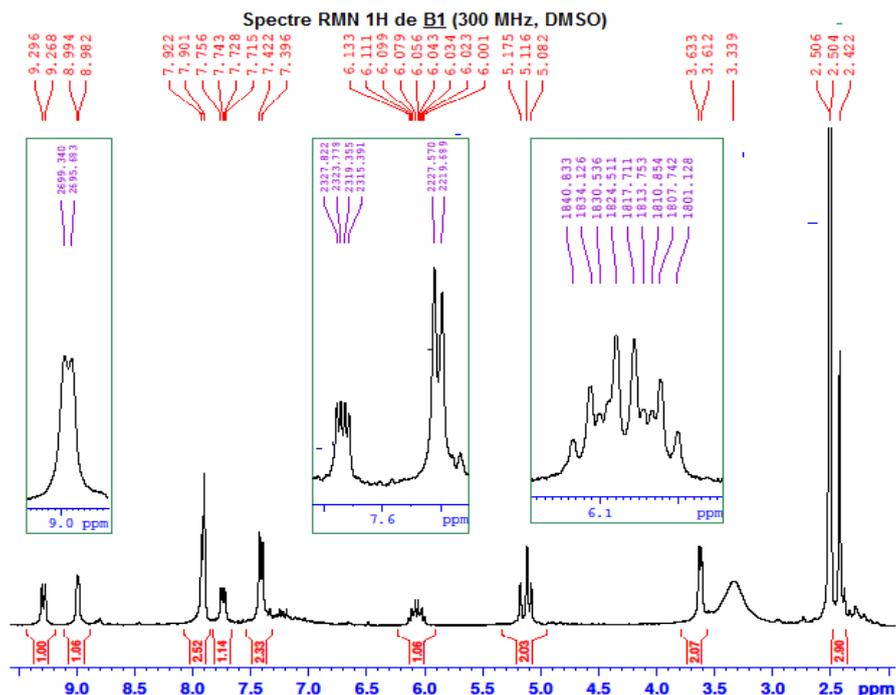
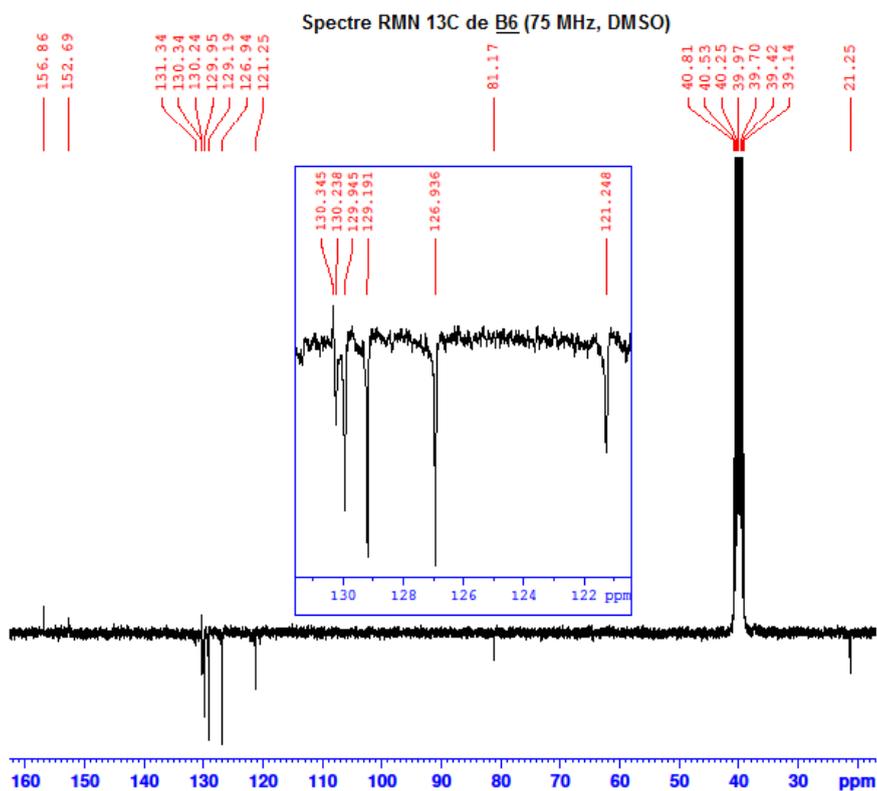
Deshielded of signals between 7.20 and 9.15 ppm are attributable to aromatic protons. These protons have larger chemical shifts due to the circular diamagnetic current.

The structure of compound B6 was also confirmed after review of  $^{13}\text{C}$  NMR parameters (75 MHz) DMSO in which we specify the characterized signals:

- A peak at 21.25 ppm due to carbon C15 of CH $_3$  group. The DEPT (Distortion less Enhancement by Polarization Transfer) spectrum confirms its inversion because the C15 carbon is odd.
- A peak at 81.17 ppm, which corresponds to C10 carbon bonded to an odd number of proton and adjacent to an oxygen atom. The DEPT spectrum also confirms its reversal.
- Two very intense signals observed at 35 and 40 ppm respectively are due to C9 and C11 carbons that are even and thus undergo no effect using the DEPT spectral technique.
- A peak corresponds to 153 ppm quaternary carbon C8 related to OH group.
- A peak corresponding to 157 ppm quaternary carbon C5 linked to the diazo group -N=N-.

Table 2: Spectroscopic characteristics of  $^1\text{H}$ -NMR and  $^{13}\text{C}$  of new products Bi: \* Solvent DMSO $_d6$ ; \*\* Solvent CDCl $_3$

Bi	$^1\text{H}$ NMR (300 MHz), $\delta$ in ppm					$^{13}\text{C}$ NMR (75 MHz), $\delta$ in ppm						
	H9	H10	H11	H15 Cis	H15 Trans	C5	C7	C8	C9	C10	C11	C15
B1**	3,71 (d,2H)	6,145 (m, 1H)	5,10-5,25 (m, 2H)	2,45 (s, 3H) 09%	2,50 (s, 3H) 91%	153	122	151	34,1	143, 4	--	21,5
B2*	6,95 (m,1H)	6,40 (m, 1H)	2,00 (dd, 3H)	2,35 (s, 3H)	2,52 (s, 3H)	153	122	148	126	125	19	21,2
B3*	2,75-3,90 (m,2H)	4,85 (m,1H)	2,75-3,50 (m, 2H)	2,30 (s, 3H)	2,50 (s, 3H)	155	120	148	32,5	59,2	37,4	21,4
B4**	5,60 (d,2H)	3,55 (m, 1H)	1,55 (d, 3H)	2,30 (s, 3H)	2,51 (s, 3H)	156	120	151	65,3	49,6	19,1	21,3
B5**	5,57 (d,2H)	3,54 (m, 1H)	1,55 (d, 3H) -OCH $_3$ : 3,83 (s, 3H)	2,34 (s, 3H)	2,52 (s, 3H)	156	120	150	65,4	49,7	19,1	21,7 -OCH $_3$ : 55,2
B6*	3,00-3,60 (m,2H)	5,12 (m, 1H)	3,00-3,60 (m, 2H)	2,34 (s, 3H)	2,50 (s, 3H)	157	122	153	35	81,2	40	21,3
B7**	5,95 (d,2H)	3,70 (m, 1H)	1,60 (d, 3H)	2,36 (s, 3H)	2,50 (s, 3H)	154	122	149	86	52	18,9	21,2
B8**	3,05-3,57 (m,2H)	5,20 (m, 1H)	1,65 (d, 3H)	2,40 (s, 3H)	2,50 (s, 3H)	154	122	155	37,9	81	21,8	21,5

Figure 2: <sup>1</sup>H NMR spectrum of B1 (300 MHz, DMSO)Figure 3: <sup>13</sup>C NMR spectrum of B6 (75MHz, DMSO)

### CONCLUSION

The Copulation of 8HQ derivatives, Ai by means of an aromatic primary amine p-methyl phenyl amine, is a specific and quantitative reaction. The aspects of reaction's compounds are significant and clearly confirm the production of dyes with quantitative yields. The structure of the new heterocyclic resulting compounds and not yet disclosed in the literature, was hereby confirmed on the basis of spectroscopic parameters <sup>1</sup>H NMR (300 MHz) and <sup>13</sup>C NMR (75 MHz). The compounds obtained in the working processes not yet described in the literature are likely to have the characteristics of the azo dyes and also to present probable biological properties with respect to their lower homologues mentioned in this work.

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