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CONTRIBUTION TO SYNTHESES OF SOME AZOMETHINES OF 5-AMINO-1-METHYL-2-PHENYLINDOLE SERIES

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SUMMARY

Ten azomethines of 5-amino-1-methy-2-phenyllindole series have been synthesized by reaction between these amines and substituted benzaldehyde. The structures of obtained compounds have been confirmed by using spectroscopic methods, such as IR, mass, ^{1}H-NMR, ^{13}C-NMR spectra with two-dimensional experiments (HSQC and HMBC).

I - INTRODUCTION

As known that the azomethines were paid special attention to study due to their significant chemical and biological properties, such as the activities: antibacterial, anti-inflammation, growth stimulus, etc… [1]. Some studies recently reported about the high corrosion inhibition properties of azomethines [2, 3]. In some previous articles [4 - 9] we communicated about the syntheses of several azomethines of 5-amino-l-ethyl-2-methylindole and 5-amino-2-methylindole. Continuing our previous works in the field of synthesis and study of the azomethines containing indole ring [4 - 9], now in the present article, some another azomethines of analogous series have been synthesized from 5-amino-1-methyl-2-phenylindole.

II - EXPERIMENT

Melting points of the synthesized compounds were measured by using Thiele's apparatus in capillary and uncorrected. The IR-spectra were recorded on FTS 6000 FT-IR Spectrometer (BIORAD, USA) in form of mixing with KBr tablet. The mass spectra were recorded on MS Engine 5989B Spectrometer (Hewlet Packard, USA). The ^{1}H-NMR, ^{13}C-NMR{1H} spectra were recorded on AVANCE Spectrometer (BRUKER, German) at 500 MHz, using DMSO-d6 as solvent and TMS as internal reference.

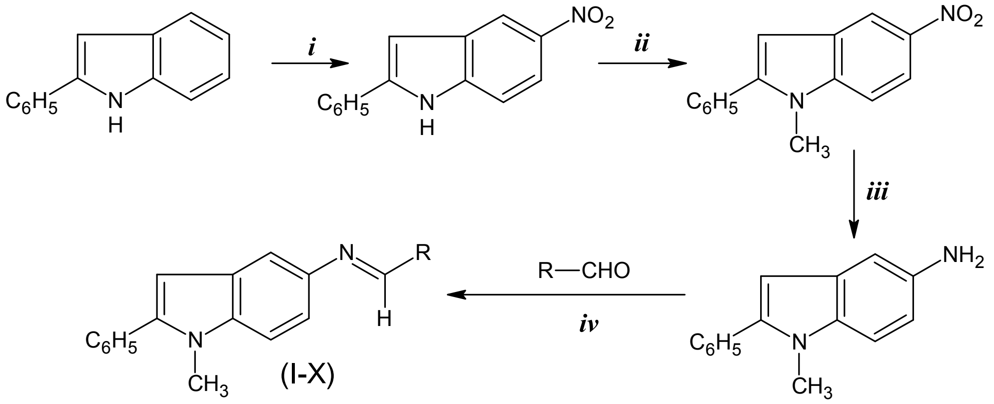
General method for synthesis of azomethines of 5-amino-1-methyl-2-phenylindole

To 50-ml. round-bottomed flask equipped with a reflux condenser was added a mixture of 6 mmol of substituted benzaldehyde and 5 mmol of substituted 5-amino-1-methyl-2-phenylindole in absolute ethanol (25 ml). Some drops of piperidine were added in the mixture. The obtained solution was stirred with reflux in 3 - 4 hrs. Then the reaction mixture was cooled, filtered the separated precipitate, washed two times with cold methanol. Recrystallized from 95% ethanol or methanol. The synthesized azomethines were represented in table 1.

III - RESULTS AND DISCUSSION

Starting from 2-phenylindole, some

azomethines of 5-amino-1-methyl-2-phenylindole series have been synthesized in this research through several transformations as follows: Nitration of 2-phenylindole using nitration mixture of KNO_3 or $NaNO_3$ and concentrated sulfuric acid at low temperature (0 - 5°C) produced 5-nitro derivative and then methylation of this compound lead to form N-methyl-5-nitro-2-phenylindole which have been undergone a reduction to form 5-amino corresponding compound using 80% hydrazine hydrate in ethanol solution in the present of Raney's porous nickel powder. That synthesis has been performed as describing in our previous article [5]. Obtained 5-amino-1-methyl-2-phenylindole have been transformed into different azomethines by reaction this amine with substituted benzaldehydes and furan-2-aldehyde. Piperidine and triethylamine were used as catalyst. The yields were 69 - 86%. The obtained azomethines were the solid substances with high melting points, dissolved in some common organic solvents (ethanol, methanol, acetone, etc…) (see table 1). These processes could be represented in figure 1 below.



(i) KNO_3 or $NaNO_3/H_2SO_4$, 0 - 5°C; (ii) $(CH_3)_2SO_4$, NaOH, acetone; (iii) 80% hydrazine hydrate; Raney's Nickel powder, ethanol 96%; (iv) absolute ethanol, piperidine, reflux 2-4 hrs.

where, R = C_6H_5(I); p-Cl-C_6H_4 (II); *m*-$NO_2C_6H_4$ (III); *p*-$CH_3OC_6H_4$(IV); *p*-$(CH_3)_2NC_6H_4$ (V); *p*-HOC_6H_4 (VI); 4-HO-3-$CH_3OC_6H_4$ (VII); *o*-HOC_6H_4 (VIII); m-HOC_6H_4 (IX); 3,4-$O_2CH_2C_6H_3$ (X); *p*-$(CH_3)_2CHC_6H_4$ (XI); *p*-FC_6H_4(XII); 1-napthyl (XIII).

Figure 1: Synthesis of some azomethines of 5-amino-1-methyl-2-phenylindole series

Table 1: Some azomethines of 5-amino-1-methyl-2-phenylindole series

No.	Compound, R	Melting point, °C	Yield, %	IR spectra, cm^{-1}		Mass spectra	
				νC=N	νc-X	M^+	$(M+1)^+$
(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
1	C_6H_5-	140.4 - 141.2	78	1624	-	310	311
2	*m*-$NO_2C_6H_4$-	134.9 - 135.6	87	1601	1351νNO_2	355	356
3	*o*-HOC_6H_4-	198.7 - 200.3	69	1605	3655 (νOH)	326	327
4	*p*-HOC_6H_5-	224.7 - 225.0	70	1604	3617 (νOH)	326	327
5	*p*-ClC_6H_4-	165.1 - 166.3	84	1595	760(νCl)	344	346
6	*p*-$(CH_3)_2NC_6H_4$	163.8 - 164.5	70	1591	1356(νC-N)	353	354

(1)	(2)	(3)	(4)	(5)	(6)	(7)	(8)
8	3,4-$O_2CH_2C_6H_3$	124.2 - 124.5	80	1596	1261 (νO-C)	354	-
9	*p*-HO, *m*-$CH_3OC_6H_3$	187.9 - 188.3	85	1588	3597 (νOH)	356	-
10	*p*-$(CH_3)_2CHC_6H_4$-	129.0 - 130.5	77	1600	-	352	-
12	*p*-FC_6H_4-	148.0 - 150.0	86	1597	1091(νF)	328	-
13	*m*-HOC_6H_4	104.5 - 105.0	71	1622	3610(νOH)	326	-
14	1-napthyl	108.0 - 108.5	79	1599	-	360	-

The structure of these azomethines have been confirmed by using spectroscopic methods (infrared, mass, and NMR spectra), including the two-dimensional experiments (such as HSQC and HMBC spectral experiments). The analysis and the discursion of these spectroscopic properties will be mentioned in another article, so in this one there were some summaries as follows [10].

In the IR spectra, there were the absorption band in regions 1588 - 1624 cm^{-1} [4 - 9] characterized the stretching vibrations of the azomethine bond –CH=N–. In addition, there were some absorption bands in IR spectra that belonged to the substituents on aldehyde component of azomethine molecules, such as band νC-Cl at 760 cm^{-1} of *p*-chlorobenzylidene-5-amino-1-methyl-2-phenylidole, band νNO_2 at 1351 cm^{-1} and 1526 cm^{-1} of *m*-nitrobenzylidene-5-amino-1-methyl-2-phenylindole, band νOH at 3655 cm^{-1} and 3617 cm^{-1} of *p*- and *o*-hydroxybenzylidene-5-amino-1-methyl-2-phenylidole, bands νC-O-C at 1250 cm^{-1} and 1261 cm^{-1} of *p*-methoxybenzylidene-5-amino-1-methyl-2-phenylindole and piperonyl-5-amino-2-phenylindole.

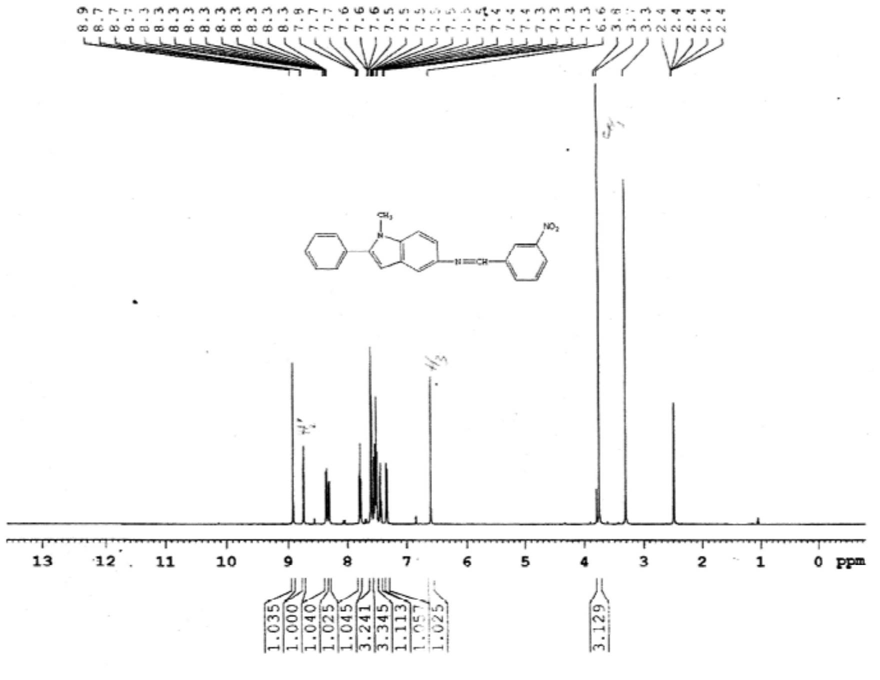


Figure 2: ^{1}H-NMR of *m*-nitrobenzylidene-5-amino-1-methyl-2-phenylindole

In the ^{1}H-NMR spectra of these above azomethines, proton on the azomethine bond had the resonance signal in the region of 8.512 - 9.353 ppm (singlet) [4]; this signal had no coupling interaction with any other protons in molecular system. Besides, there were other resonance signals of protons presented in different substituents of azomethine molecules, for examples, protons in methyl group on position 1 of indole ring had chemical shifts in the regions of 3.704 - 3.788 ppm; proton of hydroxyl group had resonance signals at δ = 10.009 ppm and δ = 10.005 ppm in *para-* and *ortho*-hydroxybenzylidene-5-amino-1-methyl-2-phenylidole, respectively; protons of methyl in N,N-dimethylamino- and methoxy-groups had chemical shifts at about 3.007 ppm. The ^{1}H- and ^{13}C-NMR of *m*-nitrobenzylidene-5-amino-1-methyl-2-phenylindole have been shown in figures 2 and 3, respectively [4 - 9].

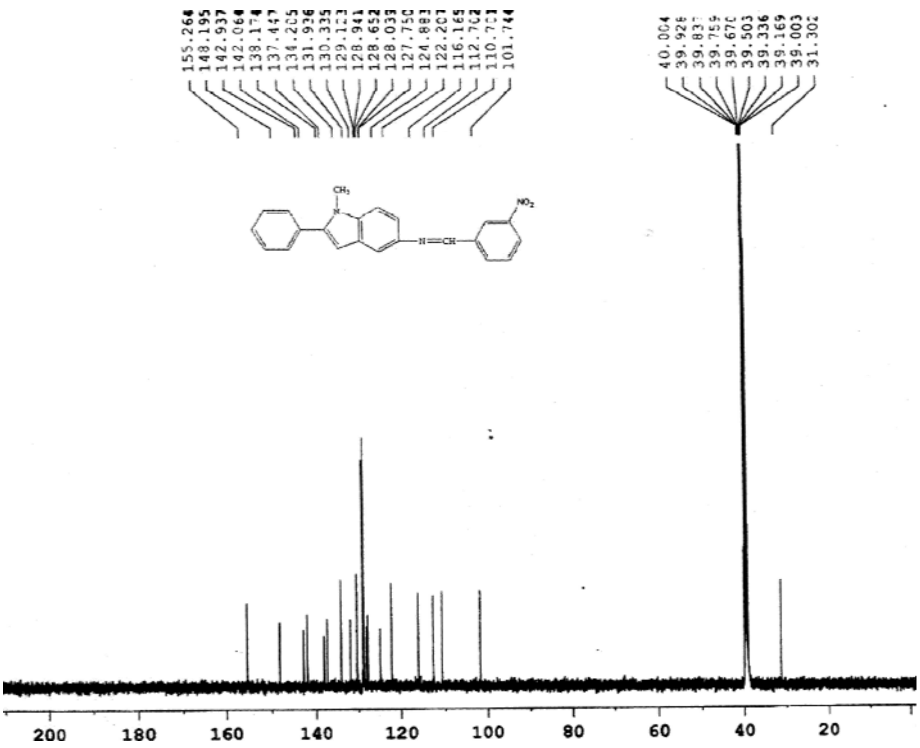


Figure 3: ^{13}C-NMR of *m*-nitrobenzylidene-5-amino-1-methyl-2-phenylindole

In ^{13}C-NMR spectra, carbon atom of azomethine bond had chemical shifts in low-field region of 152.460 - 160.238 ppm. The resonance signals of aromatic and aromatic heterocyclic carbons appeared in medium-field region at 99.039 - 139.042 ppm. Protons in aliphatic groups had chemical shifts in high-field regions from 60 ppm. Amount of carbon atoms in provided formulae of azomethines accorded with the amount of resonance signals in ^{13}C-NMR spectra.

The long and short C–H interactions can be shown in the NMR spectra with two-dimensional experiment, HSQC and HMBC respectively. In the HSQC spectrum of azomethine III (R = *m*-NO_2), it's indicated that the short-range C–H interactions in each C–H bond, as following pairs: C3–H3; $C_{azomethine}$–$H_{azomethine}$, C4–H4, C2" and C6" with H2" and H6"; C4"–H4"; C2' and C6' with H2' and H6'. The HMBC spectrum of this azomethine that is represented in figure 3 indicated some longrange C–H interactions in azomethine molecules.

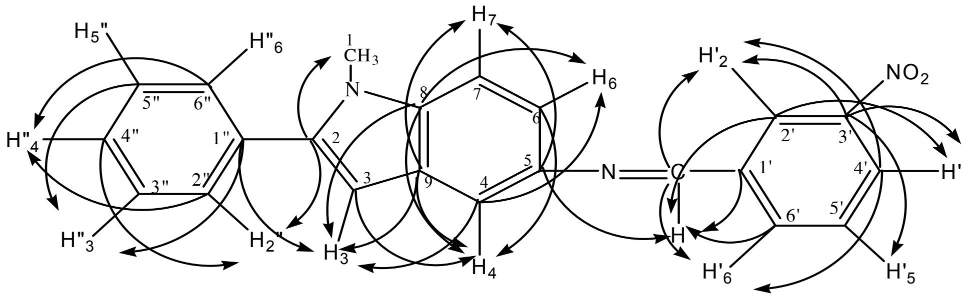


Figure 3: The C-H interactions in HMBC spectrum of *m*-nitrobenzylidene-5-amino-1-methyl-2-phenylindole

In the mass spectra of these azomethines, the molecular ion peaks appeared with significant intensities. The molecular ions M^+ had lost hydrogen radical $H^\bullet$ and given the $[M-1]^+$ peaks with remarkable intensity [4 - 9]. Simultaneously, amount of nitrogen atoms in each azomethine molecule have been obeyed the nitrogen rule: azomethine which molecular ion M^+ was the odd m/z had odd number of nitrogen atom, and if its molecular ion M^+ was the even m/z had even number of nitrogen atom. On the other hand, the m/z values of these peaks have been corresponded with molecular weight of appropriate azomethine (see table 1).

It has shown that there were some tendencies in fragmentation of these above azomethines, such as a cleavage of C–N bond between indole ring and azomethine bond –CH=N–, a cleavage of C–C bond between benzene ring of aldehyde component and the rest of azomethine molecule lead to form fragment ion at m/z 233, a loss of proton from azomethine bond lead to form ion $[M-H]^+$, a cleavage of substituents out of the aldehyde benzene ring lead to form fragment ions $[M–R]^+$ (R=substituent) and cleavage of phenyl group out of azomethine molecule lead to form fragment ions $[M-C_6H_5]^+$.

IV - CONCLUSIONS

Ten azomethines of 5-amino-1-methy-2-phenyllindole series have been synthesized by reaction between these amines and substituted benzaldehyde. The structures of obtained compounds have been confirmed by using spectroscopic methods, such as IR, mass, ^{1}H-NMR, ^{13}C-NMR spectra with two-dimensional experiments (HSQC and HMBC).

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