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Synthesis of Some New Pyridine-2-yl-Benzylidene-Imines

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Abstract

A series of new Schiff bases derived from 2-aminopyridenes and various aromatic aldehydes have been synthesized and thoroughly investigated by ^{1}H and ^{13}C NMR spectroscopy. The imines were found to exist as only a single E-isomer at ambient temperature. Interestingly, ^{1}H- and ^{13}C-NMR chemical shifts of the (CH=N) amino group are affected by the type of substituent group (X) on the aryl ring. Furthermore UV and IR Spectra of some of the title compounds are also reported.

Keywords

Schiff's Bases, ^{1}H, ^{13}C-NMR, Pyridine-2-yl-Benzylidene, E-Z-Isomers, Azomethane Group

1. Introduction

Schiff bases appear to be an important intermediate in a number of enzymatic reactions involving interaction of an enzyme with an amino or a carbonyl group of the substrate. One of the most important types of catalytic mechanism is the biochemical process which involves the condensation of a primary amine in an enzyme usually that of a lysine residue, with a carbonyl group of the substrate to form an imine, or Schiff base. Many studies have been carried out on various rings such as triazoles, pyrazoles, oxadiazoles, and imidazoles to develop new antibacterial agents. In view of these reports, the synthesis of a new series of substituted 2-aminopyridine derivatives is reported here since pyridine derivatives continue to attract great interest due to the wide variety of interesting biological activities observed in these compounds, such as anticancer, analgesic, antimicrobial, and antidepressant, activities [1]-[8].

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2. Experimental

2.1. Materials and Methods

2-Aaminopyridine and its substituents andbenzaldehyde and its substituents were procured from Lancaster Synthesis Ltd and were used without any further purification.

2.2. Instruments

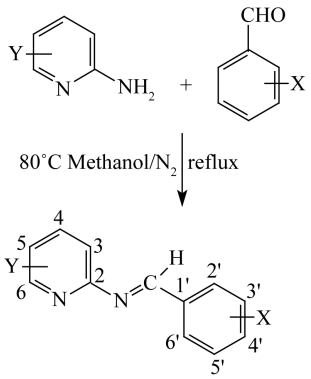
IR spectra were measured using Nexus, 470-670-760 spectrophotometer FT IR, spectrometer spectrum 8400 s, using KBr pellets for solid compounds and neat liquid compounds between KBr plates. NMR spectra were measured at 24˚C on a Jeol 400 MHz spectrometer using deuterium locking $^{13}C(^{1}H)$-NMR observation frequency 100 MHz, ^{1}H-NMR,observation frequencies, 400 MHz.

2.3. Synthesis of Schiff's Bases

The Schiff bases were prepared by mixing equivalent amounts of substituted aryl aldehydes and 2-aminopyridine derivatives in 80 ml. methanol. This mixture was boiled under reflux with stirring for 9 h at 80˚C in an oil bath, and then concentrated by rotary evaporation to give yellow liquid. This was treated with n-hexane to precipitate the crude product, which was recrystallized in dichloromethane and with n-hexane to give yellow precipitate, dried. Yield 70% - 90%, (**Scheme 1**, **Table 1**).

The microanalytical data and m.pts. Data are listed in **Table 2**, for the synthesized Schiff bases.

^{1}H-NMR (400 MHz, $CDCl_3$, δ ppm), compound **1**, 7.31 (H-3-arom.), 7.24 (H-4, arom.), H-5 (7.81, arom., H-6 (8.49, arom.), H-3' (7.43, arom.), H-4' (7.34 arom.), H-5' (6.69, arom.), H-6' (7.58, arom.), -OH (13.48), HC=N (9.44); compound **2**, H-5 (6.60, arom.), H-6 (8.04, arom.), H-2' (7.30, arom.), H-6' (6.82, arom.), -OH (12.60), HC=N (9.15); compound **3**, H-5 (6.71, arom.), H-6 (8.45, arom.), H-3' (6.28, arom.), H-4' (7.93, arom.), H-5' (6.16, arom.), -OH (12.37), HC=CN (9.42); compound **4**, H-5 (6.62, arom.), H-6 (8.54), H-2' (7.50, arom.), H-3'



Scheme 1. Synthesis of Schiff bases.

Table 1. Schiff bases compounds.

Compound No.	X	Y	Compound No.	X	Y
1	2-OH	H	8	4-NO_2	4-Me
2	H	3-Me	9	4-Br	4-Me
3	2-OH	3-Me	10	H	5-Cl
4	4-NO_2	3-Me	11	2-OH	5-Cl
5	4-Br	3-Me	12	4-NO_2	5-Cl
6	H	4-Me	13	4-Br	5-Cl
7	2-OH	4-Me			

Table 2. Microanalytical data and M.P. data for the synthesized Schiff bases.

No.	X	M.p. (˚C)	M.F.	Calculated (%)			Found (%)		
				C	H	N	C	H	N
1	2-OH	73	$C_{12}H_{10}N_2O$	72.71	5.08	14.13	72.38	4.98	14.05
2	H	88	$C_{13}H_{12}N_2O$	79.56	6.16	14.27	77.98	6.31	13.64
3	2-OH	110	$C_{13}H_{12}N_2O$	73.56	5.69	13.19	73.63	5.82	13.34
4	4-NO_2	130	$C_{13}H_{11}N_3O_2$	64.72	5.59	17.41	64.35	3.91	16.55
5	4-Br	77	$C_{13}H_{11}Br_{N2}$	57.15	4.02	10.18	57.43	4.13	9.81
6	H	84	$C_{13}H_{12}N_2$	79.56	6.16	14.27	78.28	6.31	17.64
7	2-OH	100	$C_{13}H_{12}N_2O$	73.56	5.69	13.19	73.63	5.82	13.34
8	4-NO_2	140	$C_{13}H_{11}N_3O_2$	64.72	5.59	17.41	64.35	3.91	15.55
9	4-Br	98	$C_{13}H_{11}Br_{N2}$	57.15	4.02	10.18	57.43	4.13	12.81
10	H	106	$C_{12}H_9ClN_2$	66.51	4.15	12.93	65.68	4.13	12.32
11	2-OH	94	$C_{12}H_9ClN_2O$	61.93	3.87	12.01	61.84	3.78	12.12
12	4-NO_2	203	$C_{12}H_8ClN_3O_2$	55.06	3.05	16.06	55.80	3.04	15.89
13	4-Br	180	$C_{12}H_8BrClN_2$	48.74	2.70	9.47	47.31	2.51	10.67

(7.71, arom.), H-5' (7.71, arom.), H-6' (7.5, arom.), -OH (12.55), HC=N (9.25); compound **5**, H-5 (6.60, arom.), H-6 (8.45), H-2' (7.50, arom.), H-3' (6.81, arom.), H-5' (6.81, arom.), H-6' (7.5, arom.), -OH (12.50), HC=N (9.25); compound **6**, H-6 (8.34), H-2' (7.80, arom.), H-6' (7.00, arom.), HC=N (9.15); compound **7**, H-3 (6.80, arom.), H-6 (7.67), H-2' (6.96, arom.), H-6' (6.94, arom.), -OH (13.59), HC=N (9.43); compound **8**, H-3 (6.80, arom.), H-6 (8.80), H-2' (7.50, arom.), H-6' (6.33, arom.), HC=N (9.26); compound **9**, H-3 (6.80, arom.), H-6 (8.35), H-2' (7.80, arom.), H-6' (7.03, arom.), HC=N (9.11); compound **10**, H-3 (7.48, arom.), H-4 (7.35, arom.) H-6 (8.42), H-1' (7.93, arom.), H-6' (7.27, arom.), HC=N (9.12); compound **11**, H-3 (7.51, arom.), H-4 (7.10, arom.), H-6 (8.45), H-1' (7.76, arom.), H-6'(6.95 arom.), HC=N (9.41), -OH (13.24); compound **12**, H-3 (8.14, arom.), H-4 (8.12, arom.) H-6 (8.44), H-1' (8.32, arom.), H-6' (7.30, arom.), HC=N (9.26); compound **13**, H-3 (7.26, arom.), H-4 (7.84, arom.) H-6 (8.42), H-1' (7.26, arom.), H-6' (7.84, arom.), HC=N (9.08); ^{13}C-NMR (400 MHz, $CDCl_3$, δ ppm), compound **1**, C-2 (155.20), C-3 (119.50), C-4 (138.80), C-5 (123.40), C-6 (149.20), C-1' (118.20), C-2' (161.20), C-3' (119.20), C-4' (133.40), C-5' (118.10), C-6' (132.90), C=N (163.50); compound **6**, C-4 (138.00), C-1' (135.00), C-2' (129.26), C-3' (128.58), C-4' (131.69), C-5' (128.58), C-6' (129.260), -CH_3 (20.97); compound **7**, C-2 (156.69), C-3 (121.98), C-4 (138.37), C-5 (121.98), C-6 (157.88), C-1' (118.93), C-2' (161.62), C-3' (117.09), C-4' (133.22), C-5' (118.87), C-6' (133.45), C=N (164.15), -CH_3 (24.38); compound **8**, C-2 (159.16), C-3 (125.49), C-4 (137.00), C-5 (125.49), C-6 (149.20), C-1' (137.16), C-2' (129.33), C-3' (134.40), C-4' (148.05), C-5' (134.40), C-6' (129.33), C=N (159.39), -CH_3 (20.93); compound **9**, C-2 (148.33), C-3 (134.01), C-4 (136.56), C-5 (134.01), C-6 (149.39), C-1' (134.67), C-2' (130.57), C-3' (131.88), C-4' (120.56), C-5' (131.88), C-6' (130.87), C=N (161.13), -CH_3 (20.97); compound **10**, C-2 (159.39), C-3 (120.85), C-4 (137.51), C-5 (137.58), C-6 (157.07), C-1' (137.88), C-2' (129.88), C-3' (132.26), C-4' (129.66), C-5' (132.26), C-6' (128.90), C=N (163.46); compound **11**, C-2 (161.59), C-3 (133.45), C-4 (137.96), C-5 (130.24), C-6 (147.57), C-1' (121.60), C-2' (155.64), C-3' (117.14), C-4' (133.99), C-5' (119.22), C-6' (133.45), C=N (164.97); compound **12**, C-1 (158.47), C-2 (131.00), C-4 (138.04), C-5 (130.14), C-6 (149.85), C-1' (141.14), C-2' (130.98), C-3' (124.08), C-4' (147.85), C-5' (124.04), C-6' (130.18), C=N (160.52); compound **13**, C-2 (158.95), C-3 (134.64), C-4 (137.95), C-5 (130.13), C-6 (147.41), C-1' (137.958), C-2' (132.23), C-3' (130.94), C-4' (121.09), C-5' (130.94), C-6' (132.23), C=N (162.00).

3. Results and Discussion

In the present work, the new 2-(X-benzylidine)-Y-pyridins (Schiff's bases) were obtained from the reaction of

X-benzaldehydes with 2-amino-Y-pyridines. The products were solids and the yields were 70% - 90%, reasonably high which indicates greater reactivity of these carbonyl compounds.

3.1. The Stereochemistry of the Schiff's Bases

The stereochemistry of the free imines was determined on the basis of their ^{1}H and ^{13}C-NMR spectral data. The ^{1}H-NMR spectrum (in $CDCl_3$), shows that there is only one set of isomer signals, exist mainly in E-imine form.

3.2. IR, ^{1}H and ^{13}C-NMR Spectra

The infrared spectra show that the absorption of the C=N group for imines 1 - 13 (**Table 1**) occurred in the region (v1590 - 1620 cm^{-1}) as one band for each imine. In addition to the absorption of proton of (^{1}H-C=N) group, occurred in the region (δ 9.01 - 9.43 ppm) as one single peak for each imine. Inspection of the region 700 - 900 cm^{-1}, where C-H out of plane bending vibrations of the aromatic ring is expected, did not result in the observation of mixtures of E- and Z-diastereoisomers [9].

The IR results are in good agreement with an earlier study of some imines derived from some thiophene and furfural derivatives which have been reported to exist exclusively in the E-form [10]-[12]. Further evidence of formation of imine is the absence of absorption of C=O group at (1695 - 1700 cm^{-1}) and absence of absorption of NH_2 group at ca. 3300 cm^{-1} for symmetric stretching frequency and unsymmetric frequency at 3450 cm^{-1}. In addition, further evidence comes from the absorption of C=C (stretching), at v1500 - 1600 cm^{-1}. infrared spectrum of compound (1), in which v-C=N absorption appear at 1608.63 cm^{-1} and v-OH at 3440 - 3485 cm^{-1}, as broad band compared with the absorption of v-C=N at 1600.92 cm^{-1} for compound 9, which are affected by both (X) and (Y) substituents. The substituent of electron withdrawing group (-NO_2) para to -C=N, shift the absorption of v-C=N to higher frequency as a result of decrease in electron density on C=N bond, induced by electron withdrawing NO_2 group.

IR spectrum of compound (9), shows (C=C-H), for aromatic ring, stretching frequency, abdsorbed at 3039.81 cm^{-1}, v 2964.59 cm^{-1}, and CH_3 stretching vibration appear at v 2864.59 cm^{-1}. These results are in agreement with published results [13] [14].

The ^{1}H NMR spectra of imines having CH_3-substituents (imines, 1 - 9) in pyridine ring, the CH_3 and =C-H groups of this imines appear as a single peak at δ (2.37 - 2.60) ppm for CH_3 groups, and at δ (9.01 - 9.43) ppm as a single peak for C-H protons. These results indicate that only one diasterioisomeris present in the solution for these imines.

The ^{1}H-NMR spectra of imines (7) has been chosen as a model in order to simplify the NMR spectra. In $CDCl_3$ solution, the Ar-CH_3 group resonates at δ 2.59 ppm (single peak) and -OH group resonates at δ 13.59 ppm (single peak). The H-C= Proton resonate at δ 9.43 ppm (single peak). The aromatic protons appear as (ABA'B') pattern. The pyridine proton, H6 of imine (7) resonate at δ 7.67 ppm (doublet of doublet) at low field, and so the H3 and H5, and due to the absorption of pyridine protons and aromatic ring protons absorb in the same region, a complicated and observed as an overlap spectra.

The ^{13}C-NMR spectra of imine (7) has been chosen model in order to simplify the ^{13}C-NMR spectra. The quaternary carbon in pyridine and aromatic rings and imine group C=N, are readily identified since they are less intense compared with other signals as a result of long relaxation times of the quaternary carbons [15] [16]. The ^{13}C spectrum (in $CDCl_3$), shows signals at δ 164.15 ppm and single peak at δ 24.38 ppm for pyridine -CH_3 group. The C-2' (attached to OH group) show signal at δ 161.62 ppm. The total numbers of carbons in both rings and C=N group are 12 carbons, this is demonstrated in the experimental part.

Further evidence comes from imine spectrum of compound (13). The proton NMR spectrum shows signal at δ 9.08 ppm (single peak) for ^{1}H-C=N proton, and another signal at δ 8.42 ppm assigned for C_6-H. The ^{1}H-NMR signals C_3-H, C_4-H (on pyridine ring) and aromatic protons signals shown at δ 7.26 - 7.84 ppm together. But the case will be different by studying the ^{13}C-NMR of imine (13). The numbers of ^{13}C are 10 carbons. The quaternary carbon is less intense compared with other carbon signals. The assignments of the chemical shifts of the backbone carbons are based either on spin-lattice relaxation or on the study of substituent effects in benzene derivatives [17] [18].

The ^{13}C chemical shifts of imines are listed in the experimental part. It is worth noting that the carbon −13 chemical shifts for isomethine group (imines) (HC=N) carbons are affected by both (X) and (Y) substituent's on aromatic and pyridine rings respectively. When (X)-NO_2 group substituted at C-4, the C=N, singleresonance

Table 3. δ ^{1}H-CH=N and δ ^{13}C=N for Schiff bases (1 - 13).

Complex No.	δ ^{13}C=N (ppm)	δ ^{1}H-CH=N (ppm)	Complex No.	δ ^{13}C=N (ppm)	δ ^{1}H-CH=N (ppm)
1	163.50	9.44	8	159.39	9.26
2	164.11	9.15	9	161.13	9.11
3	146.24	9.42	10	163.46	9.12
4	159.25	9.25	11	164.97	9.41
5	161.02	9.01	12	160.52	9.26
6	164.65	9.15	13	162.00	9.08
7	164.15	9.43			

appear at δ 159.39 ppm, the more electron withdrawing group, the more shielding effect. The substitution at pyridine ring shows less effect on δ C=N absorption (**Table 3**).

4. Conclusion

The new pyridine imines derivatives have been characterized by elemental analysis, UV, IR, ^{1}H, and ^{13}C-NMR spectroscopy. Interestingly, the carbon-13 chemical shifts for azomethine group (imines) (CH=N) carbons which are affected by both (X) and (Y) substituents. The stereochemistry of the imines was determined through their NMR spectral data. The imines were found to exist in solution as only a single E-isomer at ambient temperature.

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