FABAD J. Pharm. Sci., 36, 189-195, 2011

RESEARCH ARTICLE

Studies on Synthesis and Anthelmintic Activities of Some N-Benzylidenepyridin-2-amines

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Studies on Synthesis and Anthelmintic Activities of Some N-Benzylidenepyridin-2-amines

Summary

*A series of N-benzylidenepyridin-2-amines (**1a-j**) were synthesized by heating 2-aminopyridine with different substituted aromatic aldehydes in the presence of toluene. The structures of the synthesized compounds were confirmed on the basis of IR, ^{1}H NMR, ^{13}C NMR and mass spectral data. The compounds **1a-j** were screened for anthelmintic activity. Test results revealed that the compounds showed paralysis time of 0.27 to 1.52 min and death time of 0.42 to 4.42 min, whereas the standard drugs albendazole and piperazine citrate showed paralysis time of 0.54 and 0.58 min and death time of 2.16 and 2.47 min, respectively at the same concentration of 1% (m/V). Five compounds, N- (2-hydroxybenzylidene) pyridin-2-amine (**1e**), N- (4-bromobenzylidene) pyridin-2-amine (**1g**), N- (4-nitrobenzylidene) pyridin-2-amine (**1h**), N- (4-hydroxybenzylidene) pyridin-2-amine (**1i**) and N- (4-methoxybenzylidene) pyridin-2-amine (**1j**) showed the highest anthelmintic activity.*

***Key Words:** N-benzylidenepyridin-2-amines, 2-aminopyridine, N-benzylideneanilines, anthelmintic, antiparasitic*

Bazı N-Benzilidenpiridin-2-aminlerin Sentezleri ve Antihelmintik Aktiviteleri Üzerine Çalışmalar

Özet

*Bir seri N-benzilidenpiridin-2-amin türevi (**1a-j**), 2-aminopiridinin farklı sübstitüentler taşıyan aromatic aldehitlerle toluene içerisinde ısıtılmasıyla sentezlendi. Sentezlenen bileşiklerin yapıları IR, ^{1}H-NMR, ^{13}C-NMR and mass spectrum verileri ile aydınlatıldı. Bileşiklerin **1a-j**, anthelmintik aktiviteleri tarandı. Bileşiklerin 0.27 ile 1.52 dakikalar arasında paraliz, 0.42 ile 4.42 dakikalar arasında ölüme neden oldukları belirlendi. Standart olarak kullanılan albendazol ve piperazine sitrat aynı konsantrasyonda %1 (m/V), sırasıyla 0.54 ve 0.58 dakikada paraliz, ve 2.16 ve 2.47 dakikada ölüme denen olmuştur. Beş adet bileşik, N-(2-hidroksibenziliden) piridin-2-amin (**1e**), N-(4-bromobenziliden)piridin-2-amin (**1g**), N-(4-nitrobenziliden)piridin-2-amin (**1h**), N-(4-hidroksibenziliden)piridin-2-amin (**1i**) ve N-(4-metoksibenziliden)piridin-2-amin (**1j**) en yüksek antihelmintik aktiviteye sahip bulundu.*

***Anahtar Kelimeler:** N-benzilidenpiridin-2-amin, 2-aminopiridin, N-benzilidenanilin, antihelmintik, antiparazitik*

Received: 01.10.2012
Revised: 09.01.2013
Accepted: 11.02.2013

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INTRODUCTION

In coordination chemistry, Schiff bases have a significant role as ligands still a century after their discovery (1,2). The Schiff bases and their metal complexes are important as biochemical (3), electrochemical (4), analytical (5), antifungal and antibacterial activities (6-9), redox catalysts (10,11). The synthesis and assaying of biological activity of *N*-benzylideneanilines have received considerable interest in recent decades. Due to the presence of the carbon-nitrogen double bond, *N*-benzylideneanilines provide a potential site for chemical (12-14) as well as biological activity (15). The effect of the nature of the substituent and its position (16) on the aromatic rings of these compounds on their biological activity has been thoroughly investigated. The extent of conjugation in the molecule and the length of spacer between two phenyl rings (17) play a vital role in determining biological activity. *N*-benzylideneanilines show biological activities including antibacterial (18-20), antifungal (21,22), anticancer (23-25) and herbicidal (26) activities. In view of the above observations, the synthesis of N-benzylideneaniline derivatives have been developed starting from various substituted benzylidene anilines with the aim of investigating their anthelmintic activities.

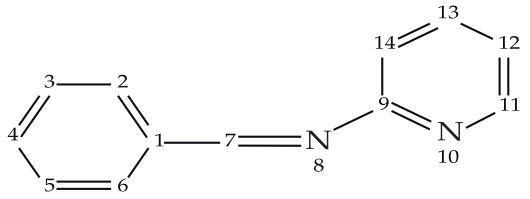
MATERIALS and METHODS

Chemistry

The chemicals and solvents used for the experimental work were commercially procured from E. Merck, India, CDH, s.d. Fine Chem, India and Qualigens, India. Silica gel G used for TLC was obtained from E. Merck. Melting points were determined in an open glass capillary using a Kjeldahl flask containing paraffin and are uncorrected. The proton and carbon magnetic resonance spectra (^{1}H NMR, ^{13}C NMR) were recorded on a Bruker 300 MHz instrument (Bruker, Germany) in dimethyl sulfoxide-d_6 (DMSO-d_6) using tetramethylsilane as internal standard. Chemical shifts (δ) are expressed in ppm. The infrared spectra of compounds were recorded in KBr on a Fourier Transform FTIR-8400S (Shimadzu, Japan) infrared spectrophotometer. Mass spectra were recorded on a LC-MS/MS (API-4000 TM, Applied BioSystems, MDS SCIEX, Canada). Elemental analyses were performed on a Perkin-Elmer model 240c analyzer (Perkin Elmer, USA). The physicochemical data of the compounds are listed in **Table 1**. The spectral data of the synthesized compounds have been presented under the experimental part.

General Procedure for the Preparation of N-Benzylidenepyridin-2-amines (1a-j)

2-Aminopyridine (1.85 g, 0.0197 mol) in 20 mL toluene was added to a solution of substituted aromatic aldehyde (0.0197 mol). The reaction mixture was heated, stirring for 2 h at 60-70°C. The mixture was filtered and then the solvent was evaporated. The crude products were purified by crystallization from ethanol to give desired compounds **1a-j** (27).



***N*-benzylidenepyridin-2-amine (1a).** Yield: 2.45 g (68.43%). m.p.: 178-180°C (EtOH). R_f: 0.88. IR (KBr, cm^{-1}): 1625 (-CH = N-), 1570 (C-C aromatic) 3010 (C-H aromatic). ^{1}H NMR (DMSO-d$_6$; δ, ppm): 7.4 (d, 2H, H-3 & H-5), 7.3 (s, 3H, H-11, H-12 & H-13), 7.6 (t, 2H, H-10 & H-14), 8.6 (d, 1H, H-6) & 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d$_6$; δ, ppm): 160.7 (C-2), 137.3 (C-4), 150.4 (C-6), 160.1 (C-8), 133.8 (C-9), 129.2 (C-10 & C-14), 128.9 (C-11 & C-13). MS (FAB; *m/z*): 182. Elemental analysis Found for $C_{12}H_{10}N_2$, M. W.: 182 (%): C, 78.98; H, 5.41; N, 7.74; Anal. calcd. (%): C, 79.09; H, 5.53; N, 7.67.

***N*- (2-chlorobenzylidene) pyridin-2-amine (1b).** Yield: 3.6 g (84.50%). m.p.: 210-212°C (EtOH). R_f: 0.93. IR (KBr, cm^{-1}): 1632 (-CH = N-), 1568 (C-C aromatic), 3023 (C-H aromatic). ^{1}H NMR (DMSO-d$_6$; δ, ppm): 7.34 (d, 2H, H-3 & H-5), 8.2 (m, 4H, H-10, H-11, H-13 & H-14), 6.8 (t, 1H, H-4), 8.04 (d, 1H, H-6), 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d$_6$; δ, ppm): 157.3 (C-2), 116.2 (C-3), 139.3 (C-4), 147.4 (C-6), 160.1 (C-8), 132.4 (C-9), 130.8 (C-10 & C-14), 131.8 (C-11 & C-13). MS (FAB; *m/z*): 216.6. Elemental analysis Found for $C_{12}H_9N_2Cl$, M. W.:216.6 (%): C, 66.21; H, 4.11; N, 12.56; Anal. calcd. (%): C, 66.52; H, 4.19; N, 12.93.

Table 1. Anthelmintic activity of synthesized compounds

Compound	Time for paralysis (min) a				Time for death (min) a			
	Concentration (g / dl)				Concentration (g / dl)			
	0.1	0.2	0.5	1.0	0.1	0.2	0.5	1.0
1a	3.25 ±0.57	2.24 ±0.12	1.27 ±0.16	1.22 ±0.16	7.13 ±0.96	5.09 ±0.21	3.15 ±0.23	2.28 ±0.15
1b	4.44 ±0.30	3.15 ±0.40	2.08 ±0.20	1.52 ±0.26	11.21 ±0.54	9.29 ±0.98	4.57 ±0.41	4.42 ±0.08
1c	3.08 ±0.04	2.45 ±0.09	2.37 ±0.15	1.09 ±0.17	8.07 ±0.21	5.57 ±0.23	4.05 ±0.39	2.23 ±0.03
1d	2.39 ±0.26	2.08 ±0.18	1.51 ±0.03	1.18 ±0.10	6.15 ±0.27	4.32 ±0.09	3.25 ±0.10	2.45 ±0.08
1e	1.27 ±0.10	1.11 ±0.02	0.55 ±0.16	0.43 ±0.07	3.05 ±0.22	2.25 ±0.10	2.14 ±0.15	1.55 ±0.26
1f	4.55 ±0.36	3.12 ±0.40	2.25 ±0.09	1.28 ±0.09	9.45 ±0.66	7.07 ±1.39	5.28 ±0.13	3.07 ±0.37
1g	2.08 ±0.18	1.48 ±0.21	1.16 ±0.06	0.55 ±0.15	8.56 ±0.31	5.05 ±0.19	4.04 ±0.04	2.09 ±0.04
1h	1.26 ±0.19	1.08 ±0.18	0.35 ±0.03	0.27 ±0.06	4.16 ±0.29	2.34 ±0.48	1.16 ±0.06	1.05 ±0.17
1i	4.09 ±0.39	2.29 ±0.09	1.02 ±0.15	0.52 ±0.006	20.55 ±0.26	8.53 ±0.35	2.34 ±0.13	1.29 ±0.03
1j	1.32 ±0.08	0.38 ±0.02	0.32 ±0.01	0.35 ±0.009	5.39 ±0.21	1.44 ±0.06	1.08 ±0.04	0.42 ±0.006
Negative control (Dimethyl sulphoxide)	24.47 ±0.05	22.09 ± 0.11	20.13 ±0.02	17.19 ±0.21	38.09 ±0.09	37.12 ±0.22	34.23 ±0.17	30.09 ±0.11
Albendazole	1.36 ±0.06	1.31 ±0.09	1.05 ±0.03	0.54 ±0.02	4.11 ±0.21	4.02 ±0.24	3.58 ±0.23	2.16 ±0.03
Piperazine citrate	2.06 ±0.03	1.51 ±0.19	1.25 ±0.007	0.58 ±0.34	6.02 ±0.31	4.42 ±0.36	4.04 ±0.03	2.47 ±0.03

[a] Mean ±SEM, $n = 6$.

***N*- (2-bromobenzylidene) pyridin-2-amine (1c).** Yield: 4.8 g (93.56%). m.p.: 151-153°C (EtOH). R_f: 0.87. IR (KBr, cm^{-1}): 1628 (-CH = N-), 1563 (C-C aromatic), 3036 (C-H aromatic), 515 (C-Br). ^{1}H NMR (DMSO-d_6; δ, ppm): 7.6 (m, 1H, H-5), 6.6 (m, 2H, H-11 & H-13), 6.9 (d, 2H, H-10 & H-14), 6.8 (t, 1H, H-4), 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d_6; δ, ppm): 161.8 (C-2), 110.8 (C-3), 122.4 (C-5), 160.1 (C-8), 132.8 (C-9), 132.8 (C-10 &

C-14), 131.4 (C-11 & C-13), 125.4 (C-12). MS (FAB; *m/z*): 261. Elemental analysis Found for $C_{12}H_9N_2Br$, M. W.: 261 (%): C, 54.75; H, 3.31; N, 11.04; Anal. calcd. (%): C, 54.47; H, 3.25; N, 11.13.

***N*- (2-nitrobenzylidene) pyridin-2-amine (1d).** Yield: 3.7 g (82.95%). m.p.: 245-247°C (EtOH). R_f: 0.90. IR (KBr, cm^{-1}): 1638 (-CH = N-), 1350 (C-C aromatic), 3040 (C-H aromatic). ^1H NMR (DMSO-d_6; δ, ppm): 7.2 (d, 2H, H-3 & H-5), 7.4 (d, 3H, H-11, H-12 & H-13), 7.6 (t, 2H, H-10 & H-14), 8.53 (d, 1H, H-6) & 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d_6; δ, ppm): 160.2 (C-2), 137.4 (C-4), 148.8 (C-6), 160.1 (C-8), 132.8 (C-9), 129.7 (C-10 & C-14), 130.4 (C-11 & C-13), 131.1 (C-12). MS (FAB; *m/z*): 227. Elemental analysis Found for $C_{12}H_9N_3O_2$, M. W.: 227 (%): C, 63.78; H, 4.20; N, 18.84; Anal. calcd. (%): C, 63.47; H, 4.23; N, 18.70.

***N*- (2-hydroxybenzylidene) pyridin-2-amine (1e).** Yield: 2.5 g (64.26%). m.p.: 127-130°C (EtOH). R_f: 0.82. IR (KBr, cm^{-1}): 1650 (-CH = N-), 1570 (C-C aromatic), 3030 (C-H aromatic), 3210 (OH). ^1H NMR (DMSO-d_6; δ, ppm): 7.4 (t, 2H, H-3 & H-5), 7.1 (m, 4H, H-10, H-11, H-13 & H-14), 7.3 (d, 1H, H-4), 8.42 (d, 1H, H-6), 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d_6; δ, ppm): 161.8 (C-2), 110.2 (C-3), 113.3 (C-5), 152.6 (C-6), 160.1 (C-8), 132.8 (C-9), 131.4 (C-10 & C-14), 131.8 (C-11 & C-13). MS (FAB; *m/z*): 198. Elemental analysis Found for $C_{12}H_{10}N_2O$, M. W. 198: (%): C, 73.01; H, 4.33; N, 13.89;. Anal. calcd. (%): C, 73.11; H, 4.27; N, 13.74.

***N*- (4-chlorobenzylidene) pyridin-2-amine (1f).** Yield: 4.1 g (96.24%). m.p.: 191-193°C (EtOH). R_f: 0.95. IR (KBr, cm^{-1}): 1632 (-CH = N-), 1578 (C-C aromatic), 3033 (C-H aromatic). ^1H NMR (DMSO-d_6; δ, ppm): 7.6 (d, 2H, H-3 & H-5), 7.1 (d, 4H, H-10, H-11, H-13 & H-14), 7.9 (t, 1H, H-4), 8.5 (d, 1H, H-6), 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d_6; δ, ppm): 159.2 (C-2), 112.5 (C-3), 138.8 (C-4), 160.1 (C-8), 132.8 (C-9), 131.4 (C-10 & C-14), 131.8 (C-11 & C-13), 131.1 (C-12). MS (FAB; *m/z*): 216.6. Elemental analysis Found for $C_{12}H_9N_2Cl$, M. W.:216.6 (%): C, 66.43; H, 3.69; N, 13.21; Anal. calcd. (%): C, 66.34; H, 3.57; N, 13.26.

***N*- (4-bromobenzylidene) pyridin-2-amine (1g).** Yield: 4.7 g (91.62%). m.p.: 186-188°C (EtOH). R_f: 0.91. IR (KBr, cm^{-1}): 1630 (-CH = N-), 1563 (C-C aromatic), 3049 (C-H aromatic), 510 (C-Br). ^1H NMR (DMSO-d_6; δ, ppm): 7.4 (d, 2H, H-3 & H-5), 7.5 (m, 4H, H-10, H-11, H-13 & H-14), 7.8 (t, 1H, H-4), 8.6 (d, 1H, H-6), 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d_6; δ, ppm): 160.6 (C-2), 115.8 (C-3), 137.3 (C-4), 150.8 (C-6), 160.1 (C-8), 132.8 (C-9), 131.4 (C-10 & C-14), 131.8 (C-11 & C-13). MS (FAB; *m/z*): 261. Elemental analysis Found for $C_{12}H_9N_2Br$, M. W.:261 (%): C, 55.59; H, 3.82; N, 10.51; Anal. calcd. (%): C, 55.38; H, 3.79; N, 10.46.

***N*- (4-nitrobenzylidene) pyridin-2-amine (1h).** Yield: 3.4 g (76.23%). m.p.: 99-101°C (EtOH). R_f: 0.89. IR (KBr, cm^{-1}): 1646 (-CH = N-), 1361 (C-C aromatic), 3030 (C-H aromatic). ^1H NMR (DMSO-d_6; δ, ppm): 6.6 (m, 1H, H-5), 7.65 (d, 2H, H-11 & H-13), 7.7 (d, 2H, H-10 & H-14), 7.44 (t, 1H, H-4), 8.1 (s, 1H, H-8). ^{13}C NMR (DMSO-d_6; δ, ppm): 158.7 (C-2), 116.6 (C-3), 136.6 (C-4), 151.7 (C-6), 160.1 (C-8), 131.4 (C-9), 132.2 (C-10 & C-14), 130.3 (C-11 & C-13). MS (FAB; *m/z*): 227. Elemental analysis Found for $C_{12}H_9N_3O_2$, M. W.: 227 (%): C, 63.84; H, 4.21; N, 18.08; Anal. calcd. (%): C, 63.73; H, 4.25; N, 18.13.

***N*- (4-hydroxybenzylidene) pyridin-2-amine (1i).** Yield: 3.1 g (79.69%). m.p.: 107-109°C (EtOH). R_f: 0.97. IR (KBr, cm^{-1}): 1648 (-CH = N-), 1559 (C-C aromatic), 3052 (C-H aromatic), 3210 (OH). ^1H NMR (DMSO-d_6; δ, ppm): 6.8 (d, 2H, H-11 & H-13), 7.4 (t, 4H, H-3, H-5, H-10 & H-14), 7.8 (t, 1H, H-4), 8.6 (d, 1H, H-6), 8.1 (s, 1H, H-8), 5.1 (s, 1H, OH). ^{13}C NMR (DMSO-d_6; δ, ppm): 160.3 (C-2), 137.3 (C-4), 120.4 (C-5), 148.0 (C-6), 160.1 (C-8), 126.4 (C-9), 130.6 (C-10 & C-14), 116.0 (C-11 & C-13), 160.8 (C-12). MS (FAB; *m/z*): 198. Elemental analysis Found for $C_{12}H_{10}N_2O$, M. W.: 198 (%): C, 73.22; H, 5.46; N, 13.78; Anal. calcd. (%): C, 73.18; H, 5.43; N, 13.69.

***N*- (4-methoxybenzylidene) pyridin-2-amine (1j).** Yield: 3.4 g (81.53%). m.p.: 95-98°C (EtOH). R_f: 0.86. IR (KBr, cm^{-1}): 1640 (-CH = N-), 1569 (C-C aromatic), 3023 (C-H aromatic), 1100 (OCH_3). ^1H NMR (DMSO-d_6; δ, ppm): 6.6 (m, 1H, H-5), 6.65 (m, 2H, H-11 & H-13), 6.95 (d, 2H, H-10 & H-14), 7.44 (t, 1H, H-4), 8.1 (s, 1H, H-8), 3.6 (s, 1H, OCH3). ^{13}C NMR (DMSO-d_6; δ, ppm): 158.6 (C-2), 109.9 (C-3), 138.3 (C-4), 148.2 (C-6), 160.1 (C-8), 134.0 (C-9), 128.0 (C-10 & C-14), 114.1 (C-11 & C-13), 158.7 (C-12), 55.7 (C-16). MS (FAB; *m/z*): 212.

Elemental analysis Found for $C_{13}H_{12}N_2O$, M. W.:212 (%): C, 73.78; H, 6.27; N, 12.97; Anal. calcd. (%): C, 73.69; H, 6.21; N, 12.93.

Anthelmintic Activity

The newly synthesized compounds were tested for anthelmintic activity, according to the method described by Kuppast and Nayak (28). *Pheretima posthuma* (earth worms) were obtained from Shibpur Botanical Garden, Kolkata, India) of nearly equal size (6 ±1 cm) were selected randomly for present study. The worms were acclimatized to the laboratory conditions before experimentation. The earthworms were divided into four groups of six earth worms in each group. Albendazole and piperazine citrate diluted with normal saline solution to obtain 0.1, 0.2, 0.5 and 1% (*m/V*) served as standards and were poured into Petri dishes. The synthesized compounds were dissolved in minimal quantities of ethanol and diluted to prepare the same concentrations as above for each compound. Normal saline served as control. The mean paralysis time and mean lethal time for each compound was calculated (each reading was taken in triplicate). The time taken for worms to become motionless was noted as paralysis time and to ascertain death, each worm was frequently applied with external stimuli which stimulates and induce movement in the earth worms, if alive.

RESULTS and DISCUSSION

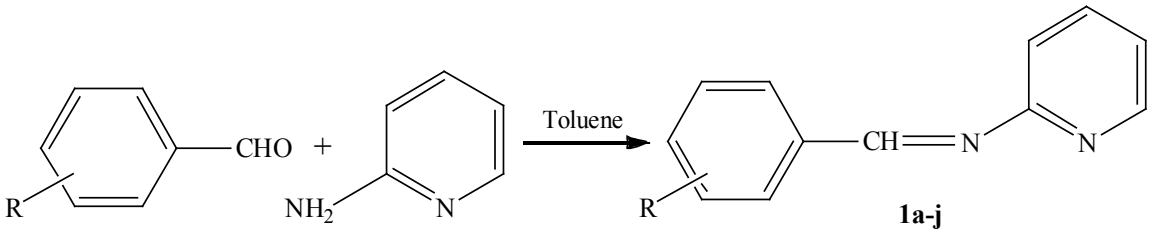
Chemistry

N-Benzylidenepyridin-2-amines (**1a-j**) were synthesized by heating 2-aminopyridines with different substituted aromatic aldehydes in the presence of toluene. The synthetic pathway is presented in Scheme 1. The IR spectra of compounds **1a-j** revealed the presence of absorption bands from 1625 to 1650 cm^{-1} that indicate the presence of azomethinic (-CH = N-) linkage, from 1350 to 1578 cm^{-1} for C-C aromatic, and from 3010 to 3052 cm^{-1} for C-H aromatic stretching vibrations. In addition to the proton signals of the functional groups and both aromatic ring present in the respective molecule ^1H NMR spectra of these compounds contained one proton singlet at δ 8.1 ppm which was assigned to azomethenic proton. The ^1H NMR spectra of compounds **1a-j** showed singlets, doublets, triplets and multiplets from δ 6.6 to 8.6 ppm for aromatic protons, one singlet at δ 5.1 ppm and δ 3.6 ppm for -OH and $-OCH_3$ proton of compound **1i** and **1j** respectively confirming the formation of compounds **1a-j**. The ^{13}C NMR spectra of compounds **1a-j** showed peaks from δ 109.9 ppm to 161.8 ppm for aromatic protons, δ 55.7 ppm for $-OCH_3$ carbon of compound **1j**, confirming the formation of compounds **1a-j**. The mass spectra of compounds **1a-j** showed molecular ion peaks M^+ at *m/z* corresponding to their respective molecular masses, which is in consistency with their respective molecular formulas (Tables 1 and 2) .

Anthelmintic Activity

The anthelmintic activities of all compounds were examined using reported procedures (19). The anthelmintic evaluation of the compounds **1a-j** in earth worm is summarized in Table III together with standard drug albendazole and piperazine citrate. A closer inspection of the data from the table indicates that compounds **1e, 1g, 1h, 1i** and **1j** have higher activity than other compounds which was confirmed from their paralysis time (0.43, 0.55, 0.27, 0.52 and 0.35 min, respectively) and death time (1.55, 2.09, 1.05, 1.29 and 0.42 min, respectively) whereas the standard drugs albendazole and piperazine citrate showed paralysis time of 0.54 and 0.58 min and

Scheme 1. Schematic representation of the synthesized compounds.



1a-j

R = H (1a), 2-Cl (1b), 2-Br (1c), 2-NO_2 (1d), 2-OH (1e), 4-Cl (1f), 4-Br (1g), 4-NO_2 (1h), 4-OH (1i), 4-OCH_3 (1j)

death time of 2.16 and 2.47 min, respectively at the same concentration of 1% (*m/V*) .

Compounds with hydroxy substituent in *ortho* and *para* position of the phenyl ring of *N*-benzylidenepyridin-2-amine (compounds **1e** and **1i**) led to considerable increase in the activities. Again, compound with methoxy substituent in *para* position of *N*-benzylidenepyridin-2-amine (compound **1j**) led to considerable increase in the anthelmintic activities. The electron withdrawing nitro group at *para* position of *N*-benzylidenepyridin-2-amine resulted in an increase in activity of the compound **1h**. The effect of *p*-bromo substitution on *N*-benzylidenepyridin-2-amine gives the anthelmintic activity of the compound **1g**. Hence there is no significant role of both electron withdrawing and donating group on anthelmintic activity.

CONCLUSIONS

Various *N*-benzylidenepyridin-2-amine derivatives were prepared with the objective of developing better anthelmintic molecules. The compounds bearing 2-hydroxy, 4-bromo, 4-nitro, 4-hydroxy and 4-methoxy of *N*-benzylidenepyridin-2-amine were found to have improved activity compared to albendazole and piperazine citrate.

Acknowledgements

The author is thankful to IIMT College of Medical Sciences (Meerut) for providing research facilities to pursue this work.

REFERENCES

1. Ayad MI, Sallam ASh, Mabrouk HE. Characterization and thermal behaviour of Cu (II) chelates of Schiff bases derived from aminopyridines. *Thermochim. Acta*. 189, 65-73, 1991; DOI: 10.1016/0040-6031 (91) 87100-B.
2. Temel H, Cakir U, Ugras HI. Synthesis and characterization of Zn (II), Cu (II) and Ni (II) complexes with bidentate Schiff base ligands: Complexation studies and the determination of stability constant (Ke)[1]. *Russian Journal of Inorganic Chemistry.* 46, 1846-1850, 2001.
3. Johnson DK, Murphy TB, Rose NJ, Goodwin WH. Cytotoxic chelators and chelates 1. Inhibition of DNA synthesis in cultured rodent and human cells by aroylhydrazones and by a copper (II) complex of salicylaldehyde benzoyl hydrazine. *Inorg. Chim. Acta.* 67, 159-165, 1982; DOI: 10.1016/S0020-1693 (00) 85058-6.
4. Yildirim LT, Emregul KC, Kurtaran R, Atakol O. Structure and electrochemical behavior of bis [*N*- (4-methylphenyl) salicylaldimine] copper (II) *N*,*N*′dimethylformamide solvate. *Cryst. Res. Technol.* 37, 1344-1351, 2002; DOI: 10.1002/crat.200290012.
5. Hao Y, Shen H. Application of aluminium (III) complex with salicylidene-*o*-aminophenol to the fluorometric determination of nucleic acids. *Spectrochim. Acta A*. 56, 1013-1020, 2000; DOI: 10.1016/S1386-1425 (99) 00286-3.
6. Miniyar PB, Makhija SJ. Synthesis and antibacterial activity of 5-methylpyrazine-2-carbohydrazide derivatives. *Int. J. Drug Dev. Res.* 1, 19-26, 2009.
7. Bulut H, Karatepe M, Temel H, Sekerci M, Koparir M. Studies on the antiviral and cytotoxic activity of Schiff bases derived from 1,2-bis- (*o*- and *p*-aminophenoxy) ethane and salicylaldehyde. *Asian J. Chem.* 17, 2793-2796, 2005.
8. Cukurovali A, Yilmaz I, Gur S, Kazaz C. Synthesis, antibacterial and antifungal activity of some new thiazolylhydrazone derivatives containing 3-substituted cyclobutane ring. *Eur. J. Med. Chem.* 41, 201-207, 2006; DOI: 10.1016/j.ejmech.2005.01.013.
9. Ispir E. The synthesis, characterization, electrochemical character, catalytic and antimicrobial activity of novel azo-containing Schiff bases and their metal complexes. *Dyes Pigments* 82, 13-19, 2009; DOI: 10.1016/j.dyepig.2008.09.019.
10. Tsuchida E, Oyaizu K. Oxovanadium (III-V) mononuclear complexes and their linear assemblies bearing tetradentate Schiff base ligands: structure and reactivity as multielectron redox catalysts. *Coord. Chem. Rev.* 237, 213-228, 2003; DOI: 10.1016/S0010-8545 (02) 00251-5.
11. Kwiatkowski E, Romanowski G, Nowicki W, Kwiatkowski M, Suwinska K. Dioxovanadium (V) Schiff base complexes of *N*-methyl-1,2- diaminoethane and 2-methyl-1,2-diaminopropane with aromatic ohydroxyaldehydes and *o*-hydroxyketones: synthesis, characterisation, catalytic

properties and structure. *Polyhedron.* 22, 1009-1018, 2003; DOI: 10.1016/S0277-5387 (03) 00041-X.

12. Chen G -M, Brown HC. An efficient synthesis of *N*-unsubstituted imines as organoborane adducts stable at room temperature: new promising intermediates for synthesis. *J. Am. Chem. Soc.* 122, 4217-4218, 2000; DOI: 10.1021/ja993965v.
13. Sidhu A, Rai M. Reaction of ethyl cyanoacetate with benzal-4-acetylanilines: An unexpected result. *Indian J. Chem.* 47B, 778-780, 2008.
14. Hothi HS, Makkar A, Sharma JR, Manrao MR. Synthesis and antifungal potential of Co (II) complexes of 1- (2'-hydroxyphenyl) ethylideneanilines. *Eur. J. Med. Chem.* 41, 253-255, 2006; DOI: 10.1016/j.ejmech.2005.07.016.
15. Sandhar RK, Sharma JR, Manrao MR. Synthesis and fungitoxicity of aldimines and 4-thiazolidinones derived from 4-bromoaniline. *J. Indian Chem. Soc.* 85, 220-223, 2008.
16. Rai M, Khera V, Kaul VK, Sharma JR. Schiff bases of toluidines: Synthesis and effect of position of methyl group on biological potential. *J. Indian Chem. Soc.* 83, 208-209, 2006.
17. Rani N, Sharma JR, Kaul VK, Manrao MR. Secondary amines: Synthesis and effect of length of spacer linking two phenyl rings on biological activity, *J. Indian Chem. Soc.* 85, 1041-1044, 2008.
18. Karia FD, Parsania PH. Synthesis, biological and thermal properties of Schiff bases of bisphenol-C, *Asian J. Chem.*, 11 (3), 991-995, 1999.
19. More PG, Bhalvankar RB, Pattar SC. Schiff bases derived from substituted 2-aminothiazole and substituted salicylaldehyde and 2-hydroxy napthaldehyde exhibits antimicrobial and antifungal activity, *J. Indian Chem. Soc.*, 78 (9), 474-475, 2001.
20. El-masry AH, Fahmy HH, Abdelwahed SHA. Synthesis and antimicrobial activity of some new benzimidazole derivatives, *Molecules*, 5, 1429-1438, 2000; DOI: 10.3390/51201429.
21. Pandeya SN, Sriram D, Nath G, De Clercq E. Synthesis and antimicrobial activity of Schiff and Mannich bases of isatin and its derivatives with pyrimidine, *IL Farmaco*, 54, 624-628, 1999; DOI: 10.1016/S0014-827X (99) 00075-0.
22. Singh WM, Dash BC. Synthesis of some new Schiff bases containing thiazole and oxazole nuclei and their fungicidal activity, *Pesticides*, 22, 33-37, 1988.
23. Hodnett EM, Dunn WJ. Structure-antitumor activity correlation of some Schiff bases, *J. Med. Chem.*, 13, 768-770, 1970.
24. Desai SB, Desai PB, Desai KR. Synthesis of some Schiff bases, thiazolidones, and azetidinones derived from 2,6-diaminobenzo [1,2-d:4,5-d'] bisthiazole and their anticancer activities, *Heterocycl. Commun.*, 7, 83-90, 2001.
25. Pathak P, Jolly VS, Sharma KP. Synthesis and biological activities of some new substituted arylazo Schiff bases, *Orient. J. Chem.*, 16, 161-162, 2000.
26. Samadhiya S, Halve A. Synthetic utility of Schiff bases as potential herbicidal agents, *Orient. J. Chem.*, 17, 119-122, 2001.
27. Hania MM. Synthesis of some imines and investigation of their biological activity. *E-J. Chem.* 6, 629-632, 2009; DOI: 10.1155/2009/104058.
28. Kuppast IJ, Nayak PV. Anthelmintic activity of fruits of *Cordia dichotoma*. *Indian J. Nat. Prod.* 19, 27-29, 2003.