Full Paper

Synthesis and Biological Evaluation of Some Pyrazolinylpyridines and Pyrazolylpyridines

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Various new 2-(1′-acetyl-5′-substituted-aryl-2′-pyrazolin-3′-yl)aminopyridines (**3a** – **3e**) and 2-(1′-phenyl 5′-substituted aryl-2′-pyrazol-3′-yl)aminopyridines (**4a** – **4e**) have been derived from 2-(substituted benzylidenylacetyl)aminopyridines (**2a** – **2e**). The structure of these compounds have been elucidated by elemental and spectral (IR, ^{1}H-NMR, mass) analysis. Furthermore, above said compounds were evaluated for their insecticidal, antifungal, and antibacterial activities. Compound **4b** 2-[1′-phenyl-5′-(*o*-chlorophenyl)-2′-pyrazol-3′-yl]aminopyridine, when compared for insecticidal and antifungal activities with parathion and fluconazole, respectively, was found to be the most potent one in this series. It also possessed remarkable antibacterial properties.

Keywords: Pyrazolinylpyridines / Pyrazolylpyridines / Insecticidal / Antifungal; Antibacterial

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Introduction

Insecticides are agents of chemical or biological origin that produce lethal effects on insects. Imidacloprid, acetamprid (nicotinoids) [1, 2] derivatives of pyridine, act on the central nervous system (CNS) of insects causing irreversible blockage of post-synaptic nicotenergic acetylcholine receptor and fipronil (fiproles) [3] pyrazole derivative blocks the g-aminobutyric acid (GABA) regulated chloride channel in neurons, thereby antagonizing the calming effects of GABA. It has been found in the literature that pyridine derivatives have been synthesized as insecticidal [4, 5], antifungal [6], antibacterial [7], herbicidal [8] agents, and the substitution pattern for the pyridine nucleus at the 2- or 3-position by different heterocyclic moieties markedly modulates its biological properties. Furthermore, pyrazole and pyrazoline congeners have also been found to exhibit insecticidal [9 – 12], antifungal [13, 14], antibacterial [15, 16] activities. These findings prompted us to synthesize a new series of pyridine derivatives by incorporating pyrazole and pyrazoline moieties at its 2-position, with a hope to get a better insecticidal potential along with additional, antifungal and antibacterial, biological activities.

Results and discussion

Chemistry

For the synthesis of the target heterocycles, the reaction sequences outlined in Scheme 1 were followed. Thus, the reaction of 2-aminopyridine with acetyl chloride in the presence of dry benzene yielded the desired 2-acetylaminopyridine **1**, which on condensation with proper aromatic aldehydes resulted in the formation of 2-(substituted benzylidenylacetyl)aminopyridines **2a** – **2e**. Cyclization of the **2a** – **2e** with hydrazine hydrate and a few drops of glacial acetic acid afforded compounds 2-(1′-acetyl-5′substitutedaryl-2′-pyrazolin-3′-yl)aminopyridines **3a** – **3e**. Furthermore, **2a** – **2e** were converted into their corresponding pyrazole congeners i.e. 2-(1′-phenyl-5′-substituted aryl-2′-pyrazol-3′-yl)aminopyridines **4a** – **4e** on treatment with pyridine-bromine complex and phenylhydra-

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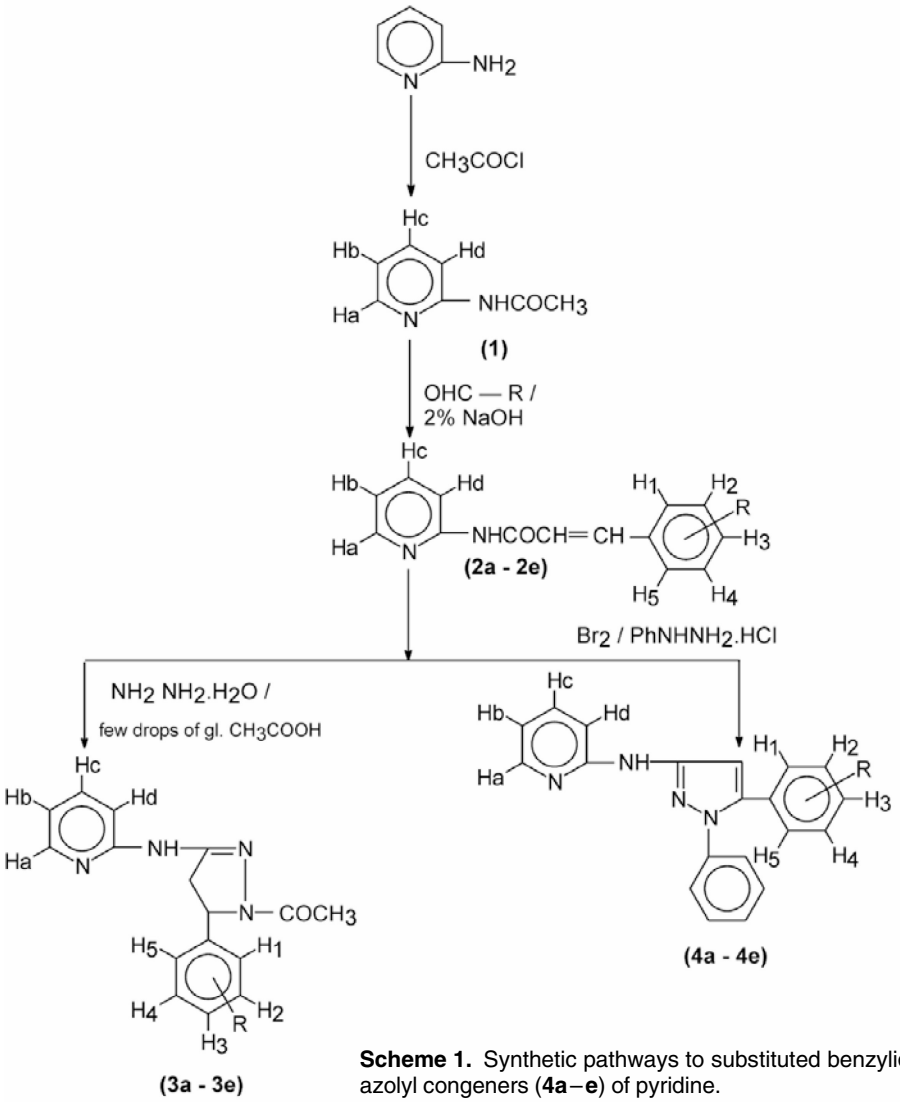


Scheme 1. Synthetic pathways to substituted benzylidenyl (**2a**–**e**), pyrazolinyl (**3a**–**e**), and pyrazolyl congeners (**4a**–**e**) of pyridine.

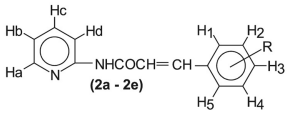
zine hydrochloride. The structures of above said compounds were established by their elemental (C, H, N) and spectral (IR, ^{1}H-NMR, mass) analysis.

Biological studies

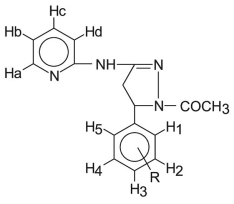
All the compounds **2a**–**2e**, **3a**–**3e,** and **4a**–**4e** along with reference drug parathion were assayed for their insecticidal activity against *Periplaneta americana* at a concentration of 5 g/L. These compounds demonstrated a greater level of activity in comparison to parathion (Table 1). Out of fifteen compounds tested, compound **4b** was found to be the most active insecticidal agent. Considering its potentiality, we examine this compound together with parathion at two more concentrations, i.e. 10 g/L and 20 g/L for its insecticidal activity. After that experiment, compound **4b** showed maximal activity than the standard at all doses tested (Figure 1). Above mentioned compounds were also screened *in vitro* for antifungal and antibacterial activities at a concentration of 250 mg/mL. Several of the compounds tested produced varying degrees of inhibition of growth of different strains of fungi and bacteria (Table 1).

Biological results are illustrated in Table 1. All the compounds have shown statistically significant activity. Out of the five compounds **2a**–**2e**, compound **2b** substituted with *o*-chlorophenyl was found to be most active. Among the compounds **2a**–**2e**, only compounds **2a**, **2b,** and **2c** displayed antifungal activity against various strains of fungi used except *C. krusei G03*. On the other hand, compounds **2a, 2c,** and **2b** showed inhibition against both bacteria tested, while compound **2d** inhibited the growth of *E. coli ESS 2231* only. It is tempting to speculate from the above results that compound **2b** gave outstanding control of insects, fungi, and bacteria.

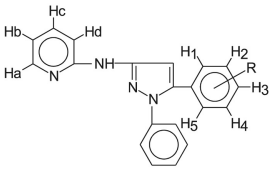
Table 1. Insecticidal, antifungal, and antibacterial data of compounds **2a**–**2e**, **3a**–**3e**, and **4a**–**4e**.



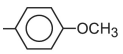
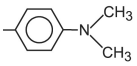
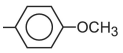
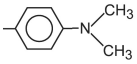
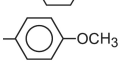
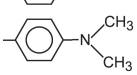
(2a - 2e)



(3a - 3e)



(4a - 4e)

Compound	R	Insecticidal activity against *Periplaneta americana*		Antifungal activity[a] Diameter of the inhibition zone [mm]					Antibacterial activity[a] Diameter of the inhibition zone [mm]	
		Conc. [g/L]	Mean killing time [min] ± S.E.	*Aspergillus fumigatus*	*Candida albicans* ATCC 2091	*Candida albicans* ATCC 10231	*Candida krusei* G03	*Candida glabrata* H05	*S. aureus* 209P	*E. coli* ESS 2231
Control		0.02 mL	720 ± 10.29							
Parathion		5 g/L	280 + 4.74[b]							
		10 g/L	247 + 9.29[c]							
		20 g/L	231 ± 1.75[d]							
Fluconazole				–	29	25	19	15		
Chloroamphenicol									20	20
2a		5 g/L	204 ± 8.22**	10	14	11	–	09	08	10
2b		-do-	178.6 ± 6.38*	11	12	13	–	10	10	11
2c		-do-	214.2 ± 5.80*	08	11	10	–	10	08	10
2d		-do-	245.4 ± 6.37**	–	–	–	–	–	–	08
2e		-do-	233.4 ± 5.33*	–	–	–	–	–	–	–
3a		-do-	175 ± 5.70**	12	16	12	10	11	11	12
3b		-do-	140 ± 6.33*	13	18	15	12	11	13	13
3c		-do-	162.6 ± 6.20*	10	12	11	–	10	–	12
3d		-do-	180 ± 5.0*	–	12	10	–	09	–	10
3e		-do-	200.6 ± 5.84*	10	08	08	–	–	10	–
4a		-do-	142.4 ± 5.26*	16	24	20	16	13	14	12
4b		5 g/L 10 g/L 20 g/L	98 ± 5.38*** 67 ± 7.40** 53 ± 5.23**	20	33	28	21	17	16	15
4c		5 g/L	139 ± 5.78*	15	20	17	15	13	10	12
4d		-do-	166.6 ± 5.34**	14	18	13	13	10	–	10
4e		-do-	182 ± 6.03**	12	13	10	14	15	10	–

n = 5.

a) Concentration was 250 mg/mL, – denotes no inhibition.

b) $P < 0.01$, c) $P < 0.001$ in comparison to control, d) $P < 0.05$. *$P < 0.05$, **$P < 0.01$, ***$P < 0.001$ in comparison to standard.

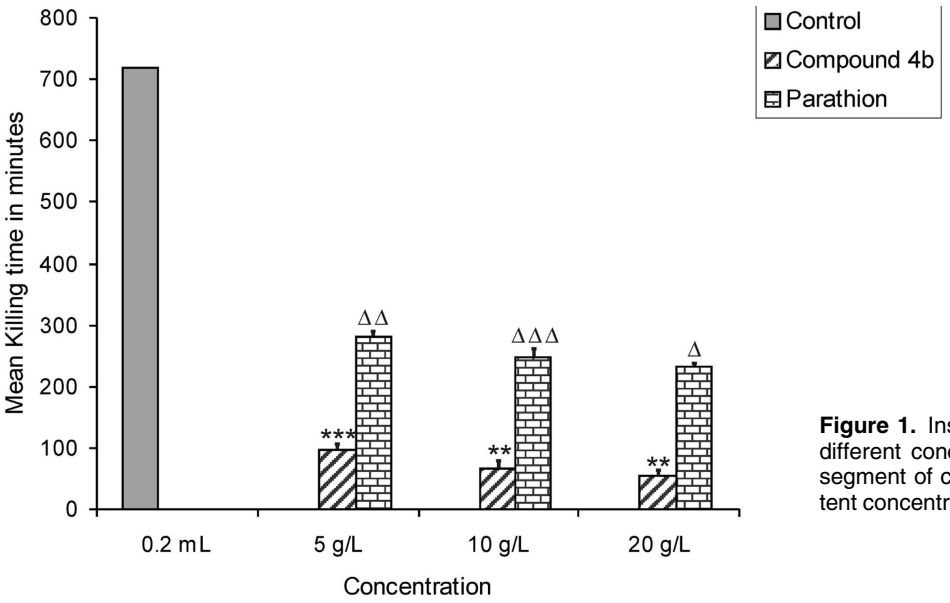


Figure 1. Insecticidial activity of compound **4b** at different concentrations injected in the 4th and 5th segment of cockroaches in comparison to equipotent concentrations of parathion.

= 5, *P <0.05, **P <0.01, ***P <0.001 in comparison to standard, parathion; ΔP <0.05, ΔΔP <0.01, ΔΔΔP <0.001 in comparison to control.

Furthermore, the effects of pyrazoline and pyrazole rings at the 2-position of the pyridine nucleus were next examined. Results indicated that the presence of pyrazoline and pyrazole rings in compounds **3a**–**3e** and **4a**–**4e**, respectively, enhanced insecticidal, antifungal, and antibacterial profiles of the compounds as compared to their parent compounds **2a**–**2e**. However, pyrazole congeners **4a**–**4e** exhibited superiority over pyrazoline derivatives **3a**–**3e** in terms of the biological properties. It is significant to note from the observations that when compounds **3a** and **4a** bearing *p*-chlorophenyl group as a substitutent they showed appreciable activities, whereas substitution with *o*-chlorophenyl groups, as seen in compounds **3b** and **4b**, produced most potent insecticidal, antifungal, and antibacterial activities. The *o*-hydroxyphenyl substituent in compounds **3c** and **4c** yielded less but still adequate biological properties. Out of sixteen compounds synthesized, **4b** was found to be the most potent compound of the present study. It exhibited better insecticidal and antifungal activities than the standards parathion and fluconazole, respectively, and the other compounds of this series. It displayed promising antibacterial activity but less than the standard chloroamphenicol.

Hence, it may be concluded that: Cyclization of benzylidene congener **2a**–**2e** into pyrazolines **3a**–**3e** and pyrazoles **4a**–**4e** increases the insecticidal, antifungal, and antibacterial activities. Pyrazole derivatives were found to be more efficacious than pyrazoline congener **3a**–**3e**. Presence of *para*-chlorophenyl or *ortho*-chlorophenyl as a substituent elicits a remarkable increase in activities. However, *ortho*-chloro substitution showed better activities. Presence of an electronegative atom e.g. Cl may play a pivotal role in the modulation of insecticidal activity.

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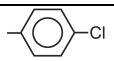
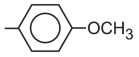
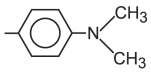
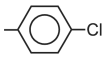
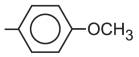
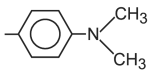
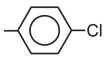
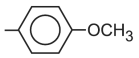
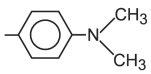
Experimental

General

All reagents and anhydrous solvents were generally used as received from the commercial supplier. Reaction was routinely performed in oven-dried glassware. Melting points were determined with an electrothermal melting point apparatus (Campbell Electronic, Mumbai, India), and are uncorrected. The homogeneity of all newly synthesized compounds was checked by thin layer chromatography (TLC) on silica gel-G coated plates. Eluent was a mixture of benzene and acetone/methanol in different proportions, and spots were visualized in an Iodine chamber. Infrared (IR) spectra (KBr) were recorded on a Brucker – IFS – 66 FTIR instrument (Bruker, Rheinstetten, Germany); the wave number (ν) was recorded in cm^{-1}. ^{1}H-NMR spectra were

Table 2. Physical data of compounds **2a**, **2c**–**2e**, **3a**, **3c**–**3e**, and **4a**, **4c**–**4e**.

Compound	R	Mp. [°C]	Yield [%]	Crystallization Solvent	Molecular Formula
2a		79–80	70	B	$C_{14}H_{11}N_2OCl$
2c		159–160	63	D	$C_{14}H_{12}N_2O$
2d		154-155	68	E	$C_{15}H_{14}N_2O_2$
2e		89–90	61	C–W	$C_{16}H_{17}N_3O$
3a		119–120	58	F	$C_{16}H_{15}N_4OCl$
3c		101–102	48	C–W	$C_{16}H_{16}N_4O_2$
3d		179–180	52	D	$C_{17}H_{18}N_4O_2$
3e		189–190	46	C–W	$C_{18}H_{21}N_5O$
4a		124–125	52	E	$C_{20}H_{15}N_4Cl$
4c		199–200	48	B	$C_{20}H_{16}N_4O$
4d		69–70	46	F	$C_{21}H_{18}N_4O$
4e		109–110	51	D	$C_{22}H_{21}N_5$

B – Benzene, C – Methanol, D – Ethanol, E – Acetone, F – Acetic acid, W – Water.

recorded on a JEOL GSX-400 FT NMR instrument (Jeol, Tokyo, Japan) in $CDCl_3$ or DMSO-d_6 unless otherwise specified; chemical shifts (δ) are reported in ppm relative to tetramethylsilane as an internal standard. Mass spectra were determined from GC-Mass Spec Finnigan Mat 8230 MS (Thermo Electron Corporation, Bremen, Germany). Elemental analysis (C, H, N) of all the compounds was performed on Carlo Erba-1108 elemental analyzer. Satisfactory analysis for C, H, N was obtained for all the compounds with ±0.4% of the theoretical values. All chemicals used were obtained from Sisco Research Laboratories (SRL), Mumbai, India; Qualigens Fine Chemicals, Mumbai, India; E. Merck Ltd., New Delhi, India.

Chemistry

2-Acetylaminopyridine ***1***

To a solution of 2-aminopyridine (83.5 g, 0.887 mol) in dry benzene (220 mL), acetylchloride (126.13 mL, 1.77 mol) was slowly added with constant stirring at a temperature of 0–5°C. This reaction mixture was stirred for further 4 h at room temperature and then refluxed for 6 h. The excess of solvent was distilled off. The contents were cooled, poured onto crushed ice, and crystallized with benzene-petroleum ether (40–60°C) to furnish compound **1**: mp. 164–167°C; yield 73%; molecular formula $C_7H_8N_2O$; IR (KBr) ν in cm^{-1}: 3350 (N–H), 3050 (C–H aromatic),

2915 (C–H aliphatic), 1678 (C=O), 1575 (C…C of aromatic ring); ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.42 (brs, 1H, NHCO), 8.32 (d, *J* = 2.2 Hz, 1H, Ha), 7.67 (dd, *J* = 8.4/2.2 Hz, 1H, Hb), 7.46 (d, *J* = 8.0 Hz, 1H, Hd), 7.33 (dd, *J* = 8.4/2.2 Hz, 1H, Hc), 2.45 (s, 3H, $COCH_3$),); MS: $[M]^+$ m/z 136.

2-(o-Chlorobenzylidenylacetyl)aminopyridine ***2b***

A solution of compound **1** (12 g, 0.0465 mol) in methanol (100 mL) with *o*-chlorobenzaldehyde (5.25 mL, 0.0465 mol) in the presence of few drops of 2% NaOH solution (dissolved in water) was refluxed for 10 h, while progress and completion of the reaction was monitored by TLC. The reaction mixture was distilled off, cooled, then poured onto crushed ice, and filtered. The solid mass thus separated out was crystallized from methanol-water giving compound **2b**. By this procedure, compounds **2a, 2c, 2d,** and **2e** were obtained starting from *p*-chlorobenzaldehyde, salicyldehyde, anisaldehyde, and *p*-aminodimethylbenzaldehyde, respectively. The physical data of these compounds are given in Table 2. Compound **2b**: mp. 204–205°C; yield 67%; molecular formula $C_{14}H_{11}N_2OCl$; IR (KBr) ν in cm^{-1}: 3356 (N–H), 3030 (C–H aromatic), 2933 (C–H aliphatic), 1676 (C=O), 1582 (C…C of aromatic ring), 1115 (C–N), 790 (C–Cl); ^{1}H-NMR (DMSO-d_6) δ in ppm: 8.44 (brs, 1H, NHCO), 8.28 (d, *J* = 2.6 Hz, 1H, Ha), 8.14 (d, *J* = 3.5 Hz, 1H, Ar-H_2), 7.68 (dd, *J* = 8.0/2.1 Hz, 1H, Hb), 7.46 (d, *J* = 8.4 Hz, 1H, Hd), 7.39 (dd, *J* = 8.0/2.2 Hz, 1H, Hc), 6.96-7.05 (m, 3H, Ar-H), 6.86 (d, *J* = 3.5 Hz, 1H, CH-Ar), 6.18 (d, *J* = 8.2 Hz, 1H, CHCO); MS: $[M]^+$ at m/z 258.

2-[1′-Acetyl-5′-(o-chlorophenyl)-2′-pyrazolin-3′-yl)]aminopyridine ***3b***

To a solution of compound **2b** (2.81 g, 0.011 mol) in absolute ethanol (60 mL), hydrazine hydrate 99% (1.07 mL; 0.022 mol) was added followed by a few drops of glacial acetic acid and then refluxed for 12 h. Excess of solvent was distilled off. Remnant of the reaction mixture was cooled and poured on to crushed ice, filtered, then dried, and finally crystallized from ethanol-water to give compound **3b**. By employing this identical procedure, compounds **3a, 3c, 3d,** and **3e** were synthesized from compounds **2a, 2c, 2d,** and **2e**, respectively. Their physical data are listed in Table 2. Compound **3b**: mp. 241–243°C; yield 54%; molecular formula $C_{16}H_{15}N_4OCl$; IR (KBr) ν in cm^{-1}: 3368 (N–H), 3030 (C–H aromatic), 2920 (C–H aliphatic), 1712 (C=O), 1610 (C=N), 1562 (C…C of aromatic ring), 1165 (C–N), 793 (C–Cl); ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.30 (d, *J* = 2.4 Hz, 1H, Ha), 8.11 (d, *J* = 7.6 Hz, 1H, Ar-H_2), 7.65 (dd, *J* = 7.7/2.4 Hz, 1H, Hb), 7.55 (d, *J* = 8.0 Hz, 1H, Hd), 7.31 (dd, *J* = 8.2/2.2 Hz, 1H, Hc), 6.83-7.10 (m, 3H, Ar-H), 6.60 (t, *J* = 7.2 Hz, 1H, CH-Ar), 5.76 (d, *J* = 11.0 Hz, 2H, CH_2 of pyrazoline ring), 5.12 (s, 1H, NH), 2.50 (s, 3H, $COCH_3$); MS: $[M]^+$ at m/z 314.

2-[1′-Phenyl-5′-(o-chlorophenyl)-2′-pyrazol-3′-yl]aminopyridine ***4b***

Pyridine-bromine complex was prepared by addition of pure bromine (2.5 mL, 0.049 mol) to pyridine (20 mL, 0.247 mol) at 0–5°C temperature. The complex was added to a solution of compound **2b** (3.70 g, 0.0143 mol) and phenylhydrazine hydrochloride (4.14 g, 0.0286 mol) in pyridine (100 mL). The resulting mixture was refluxed for 4 h, cooled, poured in cold water, and washed with 30% acetic acid to remove pyridine and the gummy product triturated with glacial acetic acid to get an amorphous powder, which was crystallized from methanol-water to yield compound **4b**. By this procedure, compounds **4a, 4c, 4d**, and **4e** were procured from compounds **2a, 2c, 2d,** and **2e**, respectively. The physical data of compounds **4a, 4c, 4d,** and **4e** are shown in Table 2. Compound **4b**: mp. 182-183 0C; yield 54%; molecular formula $C_{20}H_{15}N_4Cl$; IR (KBr) ν in cm^{-1}: 3352 (N–H), 3033 (C–H aromatic), 1611 (C=N), 1565 (C…C of aromatic ring), 1120 (C–N), 791 (C–Cl); ^{1}H-NMR ($CDCl_3$) δ in ppm: 8.33 (d, *J* = 2.4 Hz, 1H, Ha), 8.16 (d, *J* = 7.2 Hz, 1H, Ar-H_2), 7.64 (dd, *J* = 7.7/2.4 Hz, 1H, Hb), 7.52 (d, *J* = 8.4 Hz, 1H, Hd), 7.38 (dd, *J* = 8.0/2.2 Hz, 1H, Hc), 6.73–7.22 (m, 8H, Ar-H), 6.22 (s, 1H, CH of pyrazole ring), 5.12 (s, 1H, NH).

The general mass fragmentation pathway of compound **4b** along with m/z values and relative intensities of different fragments is illustrated in Scheme 2. On electron impact, the molecular ion $[M]^+$ was observed at m/z 346. Three modes of fragmentation have been observed. According to route I, fragment $[a]^+$ with m/z 52 was found on disintegration of the pyridine nucleus [17]. Route II, splitting across the pyrazole ring occurred, yielded fragment $[b]^+$ at m/z 227 as a base peak [18]. Further, chloride radical was ejected from fragment $[b]^+$ to give ion $[c]^+$ with m/z 192. This fragment exhibited cleavage at two sites to yield the phenyl radical $[d]^+$ and ion $[e]^+$ with m/z 77 and 116, respectively, Fragment $[e]^+$ finally decomposed to give ion $[f]^+$ at m/z 39. Route III showed another type of splitting across the pyrazole ring, as shown by Singh et al. [19, 20] to produce radical ion $[g]^+$ with m/z 210, which on ejection of the phenyl radical gave ion $[h]^+$ at m/z 133. This fragment on expulsion of the pyridine radical afforded ion $[i]^+$ with m/z 55, and ion $[i]^+$ finally eliminated the NH radical to give rise of fragment $[j]^+$ at m/z 40 (Scheme 2).

Biology

Biological evaluation

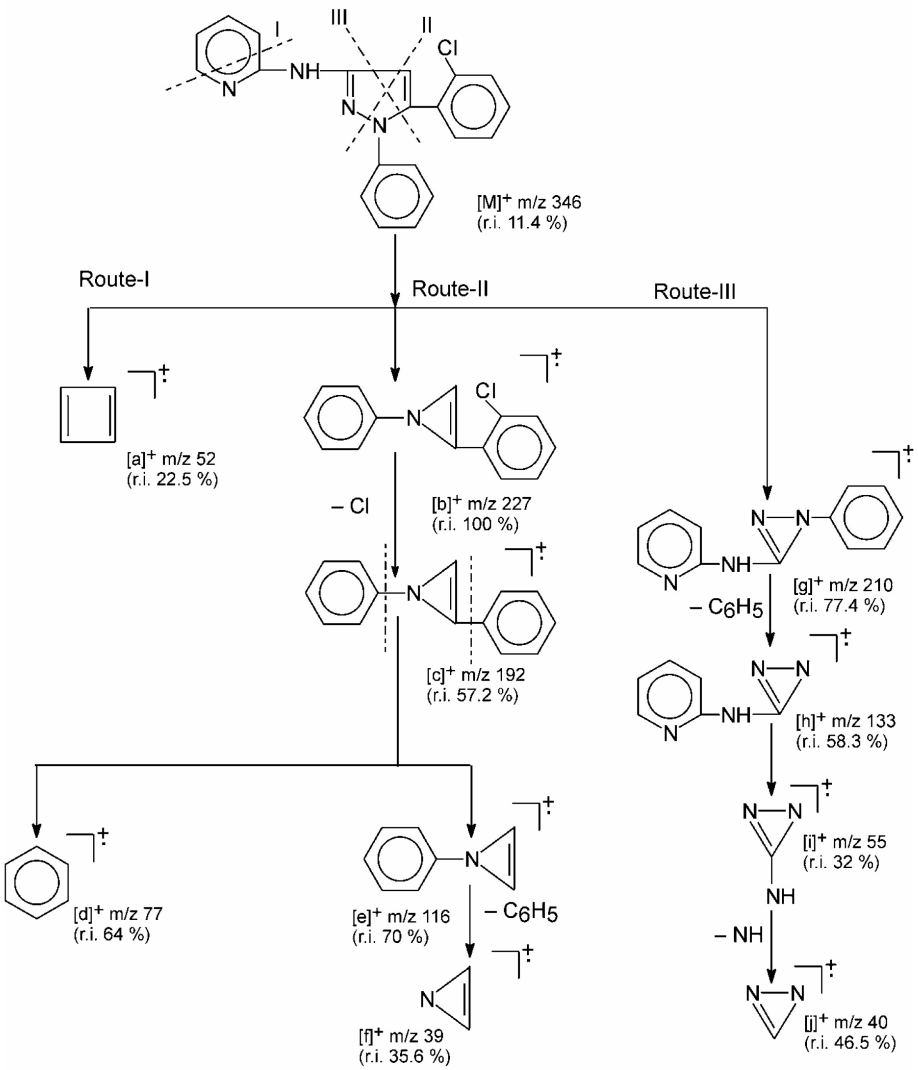
Compounds **2a–2e**, **3a–3e,** and **4a–4e** have been evaluated *in vivo* for insecticidal activity against male or female cockroaches (*Periplaneta americana*). These compounds were also assayed in *vitro* for their antifungal activity against *Aspergillus fumigatus*, *Candida albicans ATCC 2091*, *Candida krusei GO3*, *Candida albicans ATCC 10231*, *Candida glabrata HO5* and antibacterial activity against *Eschericia coli ESS 2231*, *Staphylococcus aureus 209P*.

Insecticidal activity

The insecticidal activity was determined according to the method of Joshi and Tholia [21]. Each experimental group consisted of five cockroaches of each sex. An acetone solution (0.02 mL of 5 g/L) of standard insecticide, parathion, and different test compounds were injected on the ventral side of the insect between the fourth and fifth abdominal segment with the help of micrometer syringe. Insects receiving 0.02 mL of acetone by the same route served as control. The treated cockroaches were kept under observation to record the time taken to die (till 100% mortality). During this period, no food was given. In another set of experiments, test compound **4b**, 0.02 mL of 10 g/L and 20 g/L solution in acetone, were also injected to other groups of insects and compared with the identical doses of parathion regarding the killing time. The statistical significance of the difference between the data of standard and test compound was calculated by employing student's t-test.

Antifungal activity

The agar diffusion technique was followed by the method of Goulding et al. [22]. A solution of the test compounds dissolved in acetone was given to a final concentration of molten sterile Czapek-Dox agar medium at 45°C. The resultant solution was



Scheme 2. The general mass fragmentation pattern of compound **4b**.

thoroughly mixed and approximately 20 mL were poured into each of 9 cm sterile glass Petri dish and allowed to set. The resulting agar plates were inoculated with 5 mm plugs of fungi cut from freshly prepared actively growing inoculum cultures and incubated at 18°C in the dark. Three replicates were used for each compound. For each test organisms control cultures, also comprising three replicates, received an equivalent amount of the solvent used to dissolve the test compounds. The average inhibition was calculated using the equation:

$$\text{Inhibition } [\%] = (C - T) \times 100,$$

C is the diameter of the fungal colony (in mm) in the test Petri dishes. The reference drug used is fluconazole.

Antibacterial activity

The antibacterial activity was determined *in vitro* by an agar plate diffusion technique described by Varma et al [23]. The medium consisting of agar (15 g/L), sodium chloride (5 g/L), glucose (5 g/L), and peptone (25 g/L) at pH 7.0 was inoculated with 1 mL of a 24 h-old culture of the test bacteria at 35°C. Filter paper discs (Whatman filter paper, 41, 5 mm diameter), saturated with ethanolic solution of the test compounds (10 mg/mL) in acetone, were dried in air and then placed on the nutrient agar. The plates were incubated at 37 °C and the zones of inhibition around the disc were measured after 24 h. Chloroamphenicol was used as standard drug.

References

[1] A. Elbert, H. Overbeck, K. Iwaya, S. Tsuboi, in *Proc Brighton Crop Protect Conf. – Pests Diseases, BCPC, Farnham, Surrey, U.K.* **1990**, 21 – 28.

[2] T. Yamada, H. Takahashi, R. Hatano, "*Nicotinoid Insecticides and the Nicotine Acetylcholine Receptor*" (Eds.: I. Yamamoto, J. E. Casida) Springer–Verlag, Hong Kong, **1999**, 149 – 176.

[3] G. Balanca, M. M. de Visscher, *Crop. Prot.* **1997**, *16*, 553 – 564.

[4] S. Kagabu, A. Azuma, K. Nishimura, *J. Pestic. Sci.* **2002**, *27*, 267 – 271.

[5] H. Nishiwaki, Y. Nakagawa, T. Ueno, S. Kagabu, K. Nishimura, *Pest. Manag. Sci.* **2001**, *57*, 810 – 814.

[6] M. P. P. Raj, J. T. Rao, *Asian J. Chem.* **2003**, *25*, 492 – 496.

[7] D. B. Reddy, T. Seshamma, B. Seenaiah, *Indian J. Chem.* **1991**, *30B*, 46 – 51.

[8] A. D. Kennedy, A. L. Summers, *J. Heterocyclic. Chem.* **1981**, *18*, 409 – 410.

[9] Y. Shiga, I. Okada, Y. Ikeda, E. Takizawa, T. Fukuchi, *J. Pestic. Sci.* **2003**, *28*, 313 – 314.

[10] B. P. S. Khambay, I. Denholm, G. R. Carlson, R. M. Jacobson, T. S. Dhadialla, *Pest. Manag. Sci.* **2001**, *57*, 761 – 763.

[11] S. F. McCann, G. D. Annis, R. Shapiro, D. W. Piotrowski, G. P. Lahm, J. K. Long, K. C. Lee, M. M. Hughes, B. J. Myers, S. M. Griswold, B. M. Reeves, R. W. March, P. L. Sharpe, P. Lowder, W. E. Barnette, K. D. Wing, *Pest. Manag. Sci.* **2001**, *57*, 153 – 164.

[12] K. Nishimura, T. Tada, R. Shimizu, A. Ohoka, *Pestic. Sci*. **1999**, *55*, 446 – 451.

[13] J. Mohan, *Indian. J. Chem.* **2003**, *42B*, 1460 – 1462.

[14] M. Shah, P. Patel, S. Korgaokar, H. Parekh, *Indian J. Chem.* **1996**, *35B*, 1282 – 1286.

[15] S. D. Srivastava, N. J. Guru, *Indian Chem. Soc.* **2000**, *77*, 400 – 401.

[16] B. S. Holla, M. K. Shivananda, P. M. Akberali, M. S. Shenoy, *Indian J. Chem.* **2000**, *39B*, 440 – 447.

[17] S. T. Lin, L. L. Tien, Y. H. Kuo, K. S. Shih, *Org. Mass Spectrom.* **1991**, *26*, 583 – 586.

[18] S. P. Singh, R. K. Vaid, *Org. Mass Spectrom.* **1986**, *21*, 77 – 79.

[19] S. P. Singh, R. K. Vaid, *Org. Mass Spectrom.* **1985**, *20*, 484 – 485.

[20] S. P. Singh, R. K. Vaid, P. Diwakar, L. Singh, *Org. Mass Spectrom.* **1988**, *23*, 140 – 144.

[21] K. C. Joshi, M. K. Tholia, *Pestic. Sci.* **1973**, *4*, 701 – 705.

[22] K. H. Goulding, K. M. Yung, A. M. Hall, R. J. W. Cremlyn, *Pestic. Sci.* **1983**, *14*, 158 – 166.

[23] R. S. Varma, S. A. Imam, W. L. Nobles, *J. Pharm. Sci.* **1973**, *62*, 140 – 142.

