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Synthesis and termiticidal activity of pyrazolo pyrimidine derivatives: N^1-nicotinoyl-4'- (sulpha/substituted phenylazo)-1,2-diazole-4, 6-dimethyl pyrimidine-5-one

Y Singh*, S S Nayal, B S Rawat & Mahesh Pal

Building Pests & Mycology Laboratory, Central Building Research Institute, Roorkee 247 667, India

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A novel series of fused heterocycle pyrazolo pyrinmidine namely N^1-nicotinoyl- 4'- (sulpha/substituted phenylazo)-1, 2-diazole-4, 6-dimethyl pyrimidine-5-one has been synthesized. The structure of the synthesized compounds is supported by elemental analysis, IR and NMR spectra data. The homogeneity and purity of the compounds are checked through TLC. The compounds have been screened for termiticidal activity against termites (*Odentotermes obesus*) at different concentrations. It is compared with Chlorpyriphos and mortality is expressed in terms of LC_{50} value of compounds. A few compounds have shown excellent activity against termites.

Pyrimidine and its derivatives have been extensively studied for their close association with life process. Barbiturates, the most common derivatives of pyrimidine are well known for their CNS activity[1-4]. A number of their derivatives are also used as herbicides[5], insecticides[6] and antimicrobials[7,8]. It has been studied that the introduction of aromatic amine/sulpha drugs at position 5 of 1,3-dimethyl barbituric acid exhibit broad spectrum of biological activity[9]. Similarly diazoles and their derivatives are known to have wide variety of biological activity such as antiprotozoal, orthopodicidal and nematicidal activity[10]. Few diazoles have pesticidal as well as fungicidal activity[11-16]. Keeping these facts in view and in continuation of our earlier work on fused heterocyclic system[17-23], we have synthesized few pyrazolopyrimidine derivatives namely N^1-nicotinoyl-4'-(sulpha/substituted phenylazo)-1,2-diazole-4, 6-dimethyl pyrimidine –5-one by condensation of sulpha/substituted phenylazo 1,3-dimethyl-2,4,6- pyrimidine trione with nicotinic acid hydrazide using Glacial acetic acid/DMF as condensing agent (**Scheme I**). They were tested for their termiticidal activity and are reported in this paper.

Experimental Section

General. The melting points of the synthesized compounds were determined in open capillaries in a Ganson electrical melting point apparatus and are uncorrected. The homogeneity and purity of the compounds were checked over thin layer chromatoplates coated with Silica Gel. G (Thickness 0.5 mm), developing solvent acetone /DMF (3:1) non-saturated chamber at room temp. (20±1°C). Infrared spectra (in cm^{-1}) were determined in KBr on a Perkin Elmer 577 spectrophotometer and ^1H NMR spectra were recorded on Bruker WM-400 spectrophotometer at 300 MHz in $CDCl_3$+DMSO-d_6 using TMS as an internal reference (Chemical shift in δ ppm). Elemental (CHN) analysis were carried out on Heraeus CHN-rapid analyser.

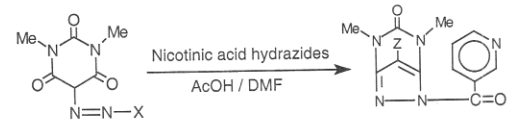
Termiticidal activity

The termite mortality was determined using filter paper method and data is summarized in **Table I** in

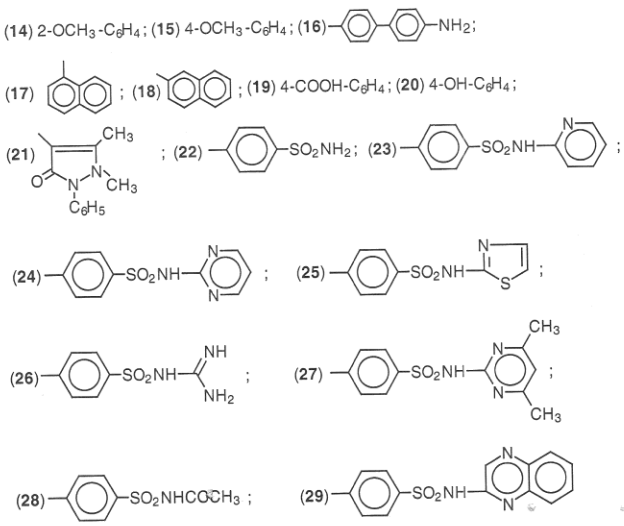
Table I — LC_{50} values for termiticidal activity against *Odentotermes obesus.*

Compd	Hetero-geneity X^2=	Regression equation Y=	LC_{50}	Fiducial limits
6	0.6658	1.972x+1.990	0.03360	0.02175 0.05192
7	0.7011	2.470x+1.270	0.03226	0.02261 0.04603
10	4.3950	1.707x+2.661	0.02346	0.01736 0.02939
22	1.3170	2.222x+1.793	0.02776	0.01862 0.04140
25	0.6493	2.065x+1.923	0.03091	0.02110 0.04528
26	1.6448	2.987x+1.576	0.01401	0.01118 0.01756
28	0.6271	2.360x+1.805	0.02259	0.01736 0.02939
Chlorpyriphos	0.6268	2.349x+1.798	0.02238	0.01729 0.02435

Y = Probit kill, × = Log concentration, LC_{50} = Concentration to give 50 % mortality.



X = (**1**) C_6H_5; (**2**) 2-Cl-C_6H_4; (**3**) 3-Cl-C_6H_4; (**4**) 4-Cl-C_6H_4;
(**5**) 2,4,6-$(Br)_3$-C_6H_2; (**6**) 3-F-C_6H_4; (**7**) 2-Cl-4-NO_2-C_6H_3;
(**8**) 2-NO_2-C_6H_4; (**9**) 3-NO_2-C_6H_4; (**10**) 4-NO_2-C_6H_4;
(**11**) 3-NO_2-4-CH_3-C_6H_3; (**12**) 2-CH_3-C_6H_4; (**13**) 4-CH_3-C_6H_4;



Scheme I

the form of LC_{50} value. All the synthesized compounds were screened for their termiticidal activity against *Odentotermes obesus* at various concentrations. It was compared with pesticide chlorpyriphos (20 EC). Termite mortality was observed at 24 hr after compounds application. Mortality was converted to percentages, subjected to probit analysis[24] and LC_{50} values were determined. Percent mortalities in control were corrected by Abott's formula[25]. The compounds **6**, **7**, **10**, **22**, **25**, **26**, and **28** exhibited significant activity. The nature of substituent at C -4 in pyrazole nucleus is very important in confirming drug activity as it not only contributes to the lipid solubility but governs the *p*Ka value of the molecule as well. Marked mortality was observed in compounds bearing 3-fluorophenyl, 2-chloro-4-nitrophenyl, 4-nitrophenyl, N^1-2-sulfon-amidobenzene, N^1–2–thiazolylsulfon-amidobenzene, N^1-2–guanylsulfonamidobenzene and N^1-2-acetyl-sulfon-amidobenzene in all the classes of compounds.

N^1-nicotinoyl-4'(sulpha/substitutedphenylazo)-1,2-diazoles-4,6-dimethyl pyrimidine-5-one. A mixture of sulpha/substituted phenylazo-1, 3-dimethyl-2, 4, 6-pyrimidine trione (0.05 mole) and nicotinic acid hydrazide (0.05 mole) was refluxed in gl.acetic acid/DMF for 6 hr, and contents were left overnight. The

coloured solid mass was filtered, washed with water and dried. It was crystallized from DMF to furnish shining crystals. By analogous procedure, several substituted - 1,2-diazole have been synthesized. Their characterisation are recorded in **Table II**.

The structure of the synthesized compounds were supported by IR spectra. The parent compound showed peak at 690 - 830 cm^{-1} (substituted phenyl) and a sharp peak at 1420 as the [N-CH_3] group is present. A number of peaks were obtained at 1535,

Table II — Characterization data of compounds of N^1-nicotinoyl-4'- (**10**) azo 1,2-diazole 4, 6- dimethyl pyrimidine- 5-one

Compd	Yield (%)	m.p. (°C)	Mol. Formula	Nitrogen (%) Found	Calcd	^{1}H NMR (δppm)
1	65	279	$C_{18}H_{15}N_7O_2$	26.10	27.14	3.20 (s, 6H, 2 × N-CH_3); 7.52-7.98 (m, 4H, ArH); 8.6 (s, 1H, Pyr.C_2-H); 8.3 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
2	60	268	$C_{18}H_{14}N_7O_2Cl$	23.72	24.77	3.18 (s, 6H, 2x N-CH_3); 7.41-7.72 (m, 4H, ArH); 8.8 (s, 1H, Pyr.C_2-H); 8.65 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.6Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
3	69	258	$C_{18}H_{14}N_7O_2Cl$	23.00	24.77	3.20 (s, 6H, 2x N-CH_3); 7.47-7.75 (m, 4H, ArH); 8.7 (s, 1H, Pyr.C_2-H); 8.62 (d, 1H, *J*=8.3Hz, Pyr.C_6-H); 7.7 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
4	71	265	$C_{18}H_{14}N_7O_2Cl$	23.15	24.77	3.24 (s, 6H, 2 × N-CH_3); 7.20 (d, 4H, ArH, *J*=8Hz); 8.4 (s, 1H, Pyr.C_2-H); 8.6 (d, 1H, *J*=8.5Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
5	62	295	$C_{18}H_{12}N_7O_2Br_3$	15.40	16.38	3.23 (s, 6H, 2 × N-CH_3); 8.72 (s, 1H, Pyr.C_2-H); 8.3 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.7 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3-7.5(m, 3H, ArH&Pyr.C_5-H)
6	70	255	$C_{18}H_{14}N_7O_2F$	24.36	25.78	3.20 (s, 6H, 2x N-CH_3); 7.95-7.21 (m, 4H, ArH); 8.7 (s, 1H, Pyr.C_2-H); 8.62 (d, 1H, *J*=8.8Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.2Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
7	70	280	$C_{18}H_{13}N_8O_4Cl$	24.36	25.42	3.21 (s, 6H, 2x N-CH_3); 7.12-7.28 (m, 3H, ArH); 8.79 (s, 1H, Pyr.C_2-H); 8.63 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
8	65	265	$C_{18}H_{14}N_8O_4$	26.50	27.58	3.24 (s, 6H, 2x N-CH_3); 7.64-7.79 (m, 4H, ArH); 8.72 (s, 1H, Pyr.C_2-H); 8.3 (d, 1H, *J*=8.2Hz, Pyr.C_6-H); 7.5 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
9	58	252	$C_{18}H_{14}N_8O_4$	26.41	27.58	3.22 (s, 6H, 2x N-CH_3); 7.52-7.68 (m, 4H, ArH); 8.7 (s, 1H, Pyr.C_2-H); 8.63 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.2 Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
10	50	273	$C_{18}H_{14}N_8O_4$	26.43	27.58	3.27 (s, 6H, 2x N-CH_3); 7.57-7.81 (m, 4H, ArH); 8.79 (s, 1H, Pyr.C_2-H); 8.54 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.7(d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
11	68	245	$C_{19}H_{16}N_8O_4$	25.30	26.66	3.25 (s, 6H, 2x N-CH_3); 2.27 (s, 3H, Ar-CH_3); 8.7 (s, 1H, Pyr.C_2-H); 8.64 (d, 1H, *J*=8.6Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3-7.7(m, 4H, ArH &Pyr.C_5-H)
12	70	292	$C_{19}H_{17}N_7O_2$	25.10	26.13	3.25 (s, 6H, 2x N-CH_3); 2.30 (S, 3H, Ar-CH_3); 8.7 (s, 1H, Pyr.C_2-H); 8.65 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.3-7.7 (m, 5H, ArH&Pyr.C_5-H)
13	72	280	$C_{19}H_{17}N_7O_2$	25.10	26.13	3.25 (s, 6H, 2x N-CH_3); 2.32 (s, 3H, Ar-CH_3); 8.7 (s, 1H, Pyr.C_2-H); 8.68(d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.5 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.5-7.9 (m, 5H, ArH&Pyr.C_5-H)
14	72	265	$C_{19}H_{17}N_7O_3$	24.00	25.06	3.25 (s, 6H, 2x N-CH_3); 3.68 (s, 3H, Ar-OCH_3); 8.7 (s, 1H, Pyr.C_2-H); 8.69(d, 1H, *J*=8.2Hz, Pyr.C_6-H); 7.5 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.5-7.9 (m, 5H, ArH&Pyr.C_5-H)
15	72	270	$C_{19}H_{17}N_7O_3$	24.01	25.06	3.20 (s, 6H, 2x N-CH_3); 3.68 (s, 3H, Ar-OCH_3) 8.8 (s, 1H, Pyr.C_2-H); 8.69 (d, 1H, *J*=8.4Hz, Pyr.C_6-H); 7.7 (d, 1H, *J*=8.6Hz, Pyr.C_4-H) 7.3(m, 1H, Pyr.C_5-H)
16	80	276	$C_{24}H_{20}N_8O_2$	23.71	24.77	3.28 (s, 6H, 2x N-CH_3);; 6.4(s, 2H, NH_2) 8.7 (s, 1H, Pyr.C_2-H); 8.3 (d, 1H, *J*=8.7Hz, Pyr.C_6-H); 7.9 (d, 1H, *J*=8.7Hz, Pyr.C_4-H) 7.38-7.98(m, 9H, ArH&Pyr.C_5-H)

— Contd.

encouraging termiticidal activity in compounds no. **6**, **7**, **10**, **22**, **25**, **26**, and **28**. These compounds have therefore good potential for use as pesticides for soil treatment to control termite.

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