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NOTE

Synthesis and Antifungal Activity of Some Substituted Pyrazolo[4,5-e]pyrimidines Derivatives

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1-Aroyl-5-aryl-4-oxo-6-thio-pyrazolo[4,5-e]pyrimidines have been synthesized. The newly synthesized compounds showed antifungal activity against *Aspergillus niger* and *Aspergillus flavus*.

Key Words: Pyrazolo[4,5-e]pyrimidines derivatives, Antifungal activities, Synthesis.

Pyrimidines derivatives have been reported as antihypertensive drugs[1-3], herbicides[4], pesticides[5], antitumor[6,7], antimalarial[8], antiviral[9] and anti-inflammatory[10] agents. Similarly pyrazolo derivatives with antimicrobial, antiviral and anticancer properties have been reported[11].

Melting points were determined in open capillaries and are uncorrected. IR (KBr) spectra were recorded on a Perkin-Elmer 1800 (FTIR) spectrometer and ^{1}H NMR spectra ($CDCl_3$) were recorded on a DRX-300 (300 MHz) spectrometer using TMS as internal standard. The purity of synthesized compounds was chekced by TLC using silica gel-G and spots were exposed in iodine vapour.

Synthesis of 1-(4-chlorobenzoyl)-4-carboethoxy-5-amino-pyrazolone (1a): A mixture of ethyl-2-cyano-3-ethoxy acrylate (0.05 mol, 8.45 g), hydrazide ($RCONHNH_2$) (0.05 mol, 8.5 g), were refluxed in methanol for 4 h. Upon cooling solid product obtained. It was filtered, washed, dried and crystallized by acetone, m.p. 135 ºC (yield 69 %); ^{1}H NMR ($CDCl_3$): δ 1.3 (t, 3H, OCH_2CH_3), 4.2 (q, 2H, OCH_2-), 7.4-8.5 (m, 5H, ArH), IR (KBr, ν_{max}, cm^{-1}): 3300 (N-H str.) 1687 (C=O ester), 1606 (C=O benzoyl), 1480, 1560, 1597 (C=C aromatic). Anal. calcd. for $C_{13}H_{12}N_3O_3Cl$: C, 53.24; H, 4.09; N, 14.33; Found: C, 53.20; H, 4.05; N, 14.30. Similarly compounds **1b-g** were prepared by the same method.

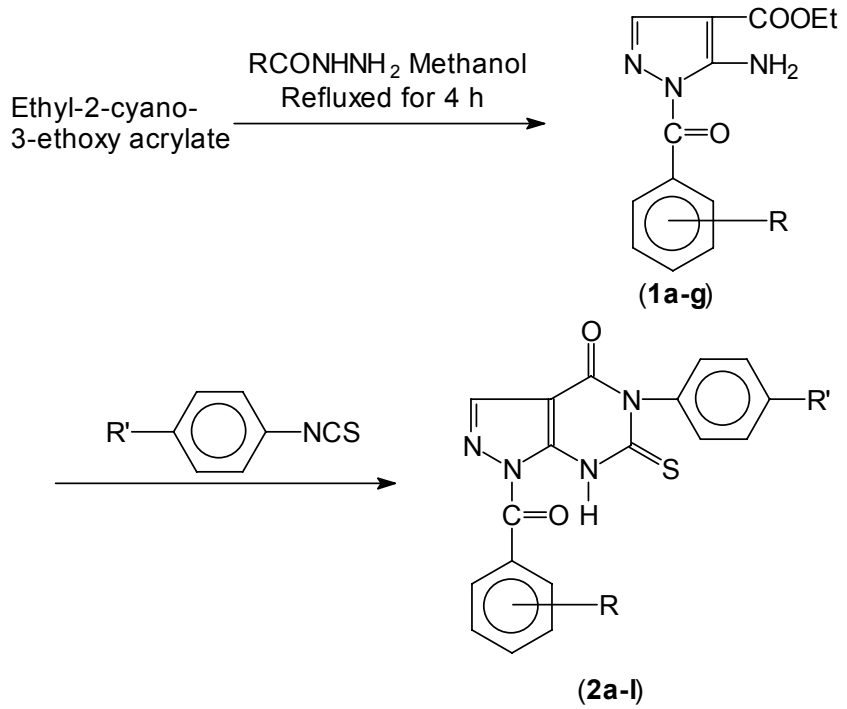
Synthesis of 1-(4-chlorobenzoyl)-5-phenyl-4-oxo-6-thiopyrazolo-[4,5-e]pyrimidines (2a): The requisite **1a** (0.01 mol, 2.9 g) and phenyl-iso-thiocyanate (0.01 mol, 1.19 mL) in 1:1 molar ratio in methanol were refluxed for 5 h. On cooling, the mass was poured in cold water. The product thus obtained was filtered, washed, dried and crystallized from acetone,

m.p. 220 ºC (yield 71 %); IR (KBr, ν_{max}, cm^{-1}): 3292 (N-H str), 1687 (C=O ester), 1637 (C=O, benzoyl), 1483, 1562, 1598 (C=C, ArH), 1344 (C-N str), 1228 (C=S str), ^1H NMR ($CDCl_3$): δ = 1.2 (t, 3H, OCH_2CH_3), 4.3 (q, 2H, OCH_2-), 7.9-8.2 (m, 5H, Arh), 8.7 (s, 1H, NH). Anal. calcd. for $C_{18}H_{11}N_4O_2SCl$: C, 56.24, H, 2.87; N, 14.65; Found: C, 56.50; H, 2.84; N, 14.62, Similarly, compounds **2b-l** were synthesized. The analytical data are given in Table-1.

TABLE-1
PHYSICAL AND ELEMENTAL ANALYSIS
DATA OF COMPOUNDS **2b-l**

Compd.	m.p. (ºC)	Yield (%)	m.f.	Analysis (%), Found (Calcd.)		
				C	H	N
2b	130	70	$C_{18}H_{11}N_4O_2SCl$	56.50 (56.54)	2.83 (2.87)	14.62 (14.65)
2c	105	72	$C_{18}H_{10}N_4O_2SCl_2$	51.89 (51.92)	2.36 (2.40)	13.42 (13.47)
2d	200	73	$C_{19}H_{14}N_4O_2S$	62.93 (62.98)	3.83 (3.86)	15.40 (15.46)
2e	180	74	$C_{19}H_{12}N_4O_3SCl_2$	52.50 (52.53)	2.73 (2.76)	12.86 (12.90)
2f	120	75	$C_{19}H_{14}N_4O_3S$	60.28 (60.31)	3.65 (3.70)	14.80 (14.81)
2g	200	76	$C_{20}H_{15}N_4O_2SCl$	58.50 (58.53)	3.60 (3.65)	13.62 (13.65)
2h	125	74	$C_{20}H_{15}N_4O_2SCl$	58.50 (58.53)	3.60 (3.65)	13.62 (13.65)
2i	97	73	$C_{20}H_{14}N_4O_2SCl_2$	54.00 (54.05)	3.09 (3.15)	12.59 (12.61)
2j	185	69	$C_{21}H_{18}N_4O_2S$	56.47 (56.50)	4.00 (4.03)	12.50 (12.55)
2k	150	68	$C_{21}H_{16}N_4O_3SCl_2$	53.12 (53.16)	3.34 (3.37)	11.79 (11.81)
2l	125	71	$C_{22}H_{18}N_4O_3S$	63.09 (63.15)	4.28 (4.30)	13.35 (13.39)

Antifungal activity: All the synthesized 4-oxo-6-thio-pyrazolo[4,5-e] pyrimidines (**2a-l**) were tested *in vitro* antifungal activities against *A. niger* and *A. flavus* by the paper disc diffusion method[12]. Salicylic acid was used as reference compounds in antifungal activity. Among the synthesized pyrazolo-[4,5-e]pyrimidines, **2a**, **2c**, **2d**, **2e** and **2i** showed promising antifungal activity.



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