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NOTES

Synthesis and Antitumor Activity of N^1-(3-Pyridoyl)-3-Methyl-4-(Substituted Azo) Pyrazol-5-Ones

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A series of N^1-(3-pyridoyl)-3-methyl-4-(substituted azo) pyrazol-5-ones have been synthesised by the reaction of substituted azo ethyl-3-oxobutyrates with 3-pyridoylhydrazine, using glacial acetic acid as condensing agent. All compounds were evaluated against the *Lymphoid leukemia* L-1210 tumor system in mice. Some of them showed significant antitumor activity.

In recent years, pyrazol-5-ones have been reported to possess antimicrobial,[1] antidiuretics,[2] antipyretic,[3], antirheumatics,[4] antibacterial,[5] antifungals,[6] and antituberculosis[7] activities. Sulphadrugs are well known chemotherapeutic agents. It has been reported that an arylazo grouping is of interest in promoting antitumor activity.[8,9] In view of these observations, it was thought to synthesise N^1-(3-pyridoyl)-3-methyl-4-(substituted azo) pyrazol-5-ones by the condensation of substituted azo ethyl-3-oxobutyrates[10,11] with 3-pyridoyl hydrazine and to study their antitumor activity.

All the chemicals used are either BDH or E. Merck grade. The substituted sulphonamides[12–15] and 3-pyridoyl hydrazine[16] were prepared by standard methods and melting points were taken in open capillaries. The homogeneity and purity of the compounds were checked through TLC. IR spectra in KBr were recorded on a Perkin Elmer grating spectrophotometer. The spectra of title compounds exhibit characteristic peaks at 780 cm^{-1} (aromatic ring); 1575 cm^{-1} (N = N); 1695 cm^{-1} (C = O) cyclic; 1280 cm^{-1} (C = N); 1562 cm^{-1} (heterocyclic five membered pyrazol-5-one ring) and 1350 cm^{-1} (C—F).

Synthesis of N^1-(3-pyridoyl)-3-methyl-4-(substituted azo) pyrazol-5-ones

3-pyridoyl hydrazine (0.05 mole) and substituted azo ethyl-3-oxobutyrate (0·05 mole) were dissolved in glacial acetic acid and contents were refluxed on a water bath for 6 hrs. The coloured product which separated out was filtered off, washed well with water, dried and recrystallised from glacial acetic acid/methanol. By adopting similar procedure, a few substituted pyrazol-5-ones have been synthesized and their characteristics are recorded in Table 1.

All the synthesised compounds were screened for their antitumor activity on *Lymphoid leukemia* L-1210 in mice. The compounds **1,5**

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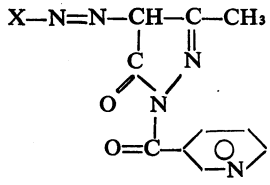
TABLE 1

CHARACTERISTICS OF N¹-(-3-PYRIDOYL)-3-METHYL-4-(X)-AZOPYRAZOL-5-ONES[a]



X	M. pt. (°C)	Colour[b]	Yield %	R_f^c Value
4-Chlorophenyl	225	SON	70	0.93
2-Nitrophenyl	194	SRF	75	0.80
4-Methylphenyl	205	DY	72	0.77
2-Methoxyphenyl	165	SON	65	0.84
3-Fluorophenyl	246	PY	78	0.95
4-Sulphonamidobenzene	260	SOF	80	0.86
4-N¹-2-pyrimidyl sulphono-amidobenzene	220	DO	75	0.97
4.N¹-2-guanyl sulphonamido benzene	250	LY	85	0.71
4-N¹-2-acetylsulphonamido benzene	198	SBF	65	0.90
4-N¹-2-(4,6-dimethyl) pyrimi-dyl-sulphonamido benzene	230	GDY	80	0.65
4-N¹-2-thiazolyl sulphonamido benzene	146	PY	70	0.79
2,3-Dimethyl-1-phenylpyrazolone	168	SPYN	82	0.82

a. All compounds had satisfactory analysis of Nitrogen.

b. F = Flakes, S = Shining, B = Brown, O = Orange, P = Pale, Y = Yellow, D = Dark, N = Needles, G = Golden, R = Red and L = Light.

c. The R_f values for all the compounds on silica gel-G plates (thickness 0.5 mm) with developer as acetic acid/dimethyl formamide (2: 1) in saturated chambers at room temperature (20 ± 1°C).

and 7, namely, N¹-(3-pyridoyl)-3-methyl-4-(4-chlorophenyl azo)-4-(3-fluorophenyl azo)-, and -4-(4-N¹-2-pyrimidylsulphonamidobenzeneazo) pyrazol-5-ones showed promising antitumor activity and their screening data are given in Table 2.

TABLE 2

ANTITUMOR ACTIVITY DATA

Compound No.	Dose mg/kg	Survivors	Animal Wt. diff*(T.C.)	Average test**	Evaluation control***	T/C****
1	200	6/6	−0.2	9.0	9.0	100
	100	6/6	−0.3	8.5	9.0	94
	50	6/6	−0.1	9.8	9.0	108
5	200	6/6	−I.2	8.5	8.8	96
	100	6/6	−0.2	8.5	8.8	100
7	400	5/6	−0.2	9.0	9.2	97
	200	6/6	−0.1	10.0	9.2	108

*Average weight change of test group minus average weight change of control animals in grams.

**Measure of response in treated animals (Survivals time, tumor weight etc.)

***Measure of tumor progression in untreated animals (Survival time; tumor weight etc,)

****Ratio of mean survival time of test animals (T) to control animals (C).

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