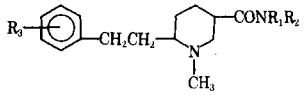
Table V—Dopa Response Potentiation



Number	R_3	NR_1R_2	Oral, mg./kg.	Motor Activity
III*a*	3,4-$(OCH_3)_2$	$N(C_2H_5)_2$	25	1+
			100	1+
III*b*	3,4-$(OCH_3)_2$	$N(C_2H_5)_2$	25	3+
			100	3+
III*c*	3,4,5-$(OCH_3)_3$	$N(C_2H_5)_2$	25	2+
			100	2+
III*d*	H	C_4H_8NO[a]	25	2+
			100	3+
III*e*	3,4-$(OCH_3)_2$	C_4H_8NO[a]	25	3+
			100	2+
III*f*	3,4,5-$(OCH_3)_3$	C_4H_8NO[a]	25	1+
			100	2+
Amitriptyline			20	3+

[a] Morpholino.

(3 × 50 ml.). After drying over anhydrous magnesium sulfate and evaporation of the solvent, the product was purified by elution chromatography, using neutral alumina I and anhydrous ether as the eluent.

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Chemistry and Biological Activity of N^1-Acyl-4-arylazopyrazoles

H. G. GARG*▲ and VEENA ARORA

Abstract □ The preparation of N^1-acyl-4-arylazopyrazole derivatives by cyclization of 3-arylhydrazono-2,3,4-pentanetriones or 2-arylhydrazonopropane-1,3-diphenyl-1,2,3-triones with acetylhydrazine or 4-sulfamoylbenzoylhydrazine is presented. The structure was assigned on the basis of elemental analysis and IR data. No significant activity was observed against Gram-positive and Gram-negative bacteria, fungi, and *Trichomonas foetus* P-1005.

Keyphrases □ N^1-Acyl-4-arylazopyrazoles—synthesis, screened for pharmacological activity □ Pyrazole derivatives—synthesis of N^1-acyl-4-arylazopyrazoles, screened for pharmacological activity

In continuation of work on the synthesis of pyrazoles as potential biologically active agents, preparation of N^1-acyl analogs was undertaken since heterocyclics having a $—CONH_2$ group possess various activities (1).

N^1-Acetyl-3,5-diphenyl-4-arylazo-, N^1-acetyl-3,5-dimethyl-4-arylazo-, and N^1-sulfamoylbenzoyl-3,5-dimethyl-4-arylazopyrazoles were prepared by the cyclization of 2-arylhydrazonopropane-1,3-diphenyl-1,2,3-triones (2) and 3-arylhydrazono-2,3,4-pentanetriones (3) with acetylhydrazine (4) or 4-sulfamoylbenzoylhydrazine (5). The yields ranged from 45 to 65%.

The IR (KBr) spectrum revealed bands characteristic of the acetyl group, the —N=N— grouping, and the C=C—NH—N= grouping in the regions 1684–1709, 1400–1540, and 1556–1565 $cm.^{-1}$, respectively, which are in good agreement with the assigned structures.

UV spectra of N^1-sulfamoyl-3,5-dimethyl-4-(2,4-

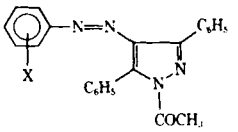

Table I—Characteristics of N^1-Acetyl-3,5-diphenyl-4-arylazopyrazoles

Number	X	Yield, %	Melting Point	Color[a]	Formula	Analysis, % Calc.	Found
1	H—	60	155°	OSp	$C_{23}H_{18}N_4O$	C 75.41	75.38
						H 4.92	4.95
						N 15.30	15.26
2	2-Br—	55	230°	PeYSp	$C_{23}H_{17}BrN_4O$	N 17.98	18.00
						Br 12.58	12.62
3	2,5-$(Me)_2$	65	195°	ON	$C_{25}H_{22}N_4O$	N 14.21	14.25
4	2,6-$(Me)_2$	50	171°	GP	$C_{25}H_{22}N_4O$	N 14.21	14.26
5	2-Et	55	193°	YN	$C_{25}H_{22}N_4O$	N 14.21	14.25
6	2,4-$(Me)_2$	55	150°	OYN	$C_{25}H_{22}N_4O$	N 14.21	14.23
7	2,3-$(Me)_2$	60	232°	GYN	$C_{25}H_{22}N_4O$	N 14.21	14.25
8	2,5-$(MeO)_2$	65	174°	BP	$C_{25}H_{22}N_4O_3$	N 13.14	13.18
9	2,5-$(EtO)_2$	55	172°	ON	$C_{27}H_{26}N_4O_3$	N 12.33	12.35
10	2,4-$(Cl)_2$	50	222°	GN	$C_{23}H_{16}Cl_2N_4O$	N 12.87	12.90
						Cl 16.32	16.28
11	4-Cl; 2,5-$(MeO)_2$	55	184°	DYN	$C_{25}H_{21}ClN_4O_3$	N 12.16	12.12
						Cl 7.71	7.74

[a] O = orange, Sp = specks, Pe = pale, Y = yellow, N = needles, G = golden, B = brown, D = dark, M = mustard, and Br = bright.

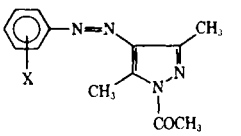

Table II—Characteristics of N^1-Acetyl-3,5-dimethyl-4-arylazopyrazoles

Number	X	Yield, %	Melting Point	Color[a]	Formula	Analysis, % Calc.	Found
1	2-Me	55	196°	GP	$C_{14}H_{16}N_4O$	C 65.63	65.60
						H 6.30	6.34
						N 21.88	21.90
2	3-MeO	60	170°	MSp	$C_{14}H_{16}N_4O_2$	N 20.59	20.63
3	3,4-$(Me)_2$	55	195°	BrYN	$C_{15}H_{18}N_4O$	N 20.74	20.70
4	2,3-$(Cl)_2$	40	201°	ON	$C_{13}H_{12}Cl_2N_4O$	N 18.01	17.96
						Cl 22.83	22.85

[a] See footnote of Table I.

dichlorophenylazo)pyrazoles and N^1-sulfamoylbenzoyl-3,5-dimethyl-4-(2-methoxyphenylazo)pyrazoles showed maxima at 242/360 and at 244/330 nm., respectively.

PHARMACOLOGY

The compounds prepared in this study were tested for antibacterial activity *in vitro*, using the agar diffusion method. Five mice were given a single oral dose equivalent to 500 mg./kg. Pooled 5-hr. urine was then tested for activity using the agar diffusion method. Filter paper disks (6.3 mm.) were dipped in a 20-mg./ml. suspension of the test compound and tested for activity.

EXPERIMENTAL[1]

3-Arylhydrazono-2,3,4-pentanetriones (2) and 2-arylhydrazono-propane-1,3-diphenyl-1,2,3-triones (3) were prepared by earlier described procedures.

[1] Analyses were done at C.D.R.I., Lucknow, India. Melting points were determined on a Kofler hot-stage apparatus and are uncorrected. IR spectra were recorded on a Perkin-Elmer Infracord in the KBr phase. UV spectra were measured for solutions in EtOH.

Acetylhydrazine—This hydrazine was synthesized by treating acetyl chloride with hydrazine hydrate in equimolar quantities and keeping the mixture overnight at 0°. The resultant solid was recrystallized from ethanol (m.p. 67°).

4-Sulfamoylbenzoylhydrazine—*p*-Toluenesulfonamide was oxidized according to the method of Kamm and Mathews (6). The acid obtained was esterified, and the ester formed was treated with hydrazine hydrate to yield the solid hydrazide, which was finally recrystallized from boiling water (m.p. 238°).

N^1-Acetyl-3,5-diphenyl-4-arylazopyrazoles—A solution of acetylhydrazine (0.005 mole) in alcohol (15 ml.) containing a few drops of concentrated H_2SO_4 was added to the appropriate 2-arylhydrazono-propane-1,3-diphenyl-1,2,3-trione (0.005 mole) dissolved in an alcohol–acetic acid mixture. The resultant solution was boiled under reflux for several hours and then cooled. The reaction mixture was diluted with water, and the crystals which separated were collected and recrystallized from ethanol or acetic acid. The characteristics of N^1-acetyl-3,5-diphenyl-4-arylazopyrazoles are listed in Table I.

N^1-Acetyl-3,5-dimethyl-4-arylazopyrazoles—These were obtained from acetylhydrazine (0.005 mole) and 3-arylhydrazono-2,3,4-pentanetrione (0.005 mole) by the same procedure as was used for N^1-acetyl-3,5-diphenyl-4-arylazopyrazoles. The yields and physical constants of these pyrazoles are listed in Table II.

N^1-4-Sulfamoylbenzoyl-3,5-dimethyl-4-arylazopyrazoles—Treatment of 3-arylhydrazono-2,3,4-pentanetrione (0.005 mole) with 4-sulfamoylbenzoylhydrazine under conditions similar to those used

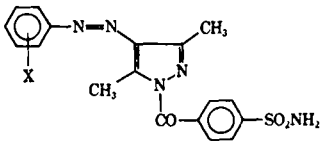

Table III—Characteristics of N^1-(4′-Sulfamoylbenzoyl)-3,5-dimethyl-4-arylazopyrazoles

Number	X	Yield, %	Melting Point	Color[a]	Formula	Analysis, % Calc.	Found
1	H—	55	245° dec.	BN	$C_{18}H_{17}N_5O_3S$	C 56.40 H 4.44 N 18.28 S 5.35	56.38 4.48 18.30 5.34
2	2-Me	55	188°	MSp	$C_{19}H_{19}N_5O_3S$	N 17.63 S 8.06	17.65 8.08
3	3-MeO	50	160°	GP	$C_{19}H_{19}N_5O_4S$	N 16.94 S 7.75	16.95 7.78
4	4-MeO	60	250°	DBP	$C_{19}H_{19}N_5O_4S$	N 16.94 S 7.75	16.90 7.76
5	3,4-$(Me)_2$	55	240°	YSp	$C_{20}H_{21}N_5O_3S$	N 17.03 S 7.79	17.05 7.78
6	2,4-$(Cl)_2$	45	250°	DYSp	$C_{18}H_{15}Cl_2N_5O_3S$	N 15.45 S 7.06	15.48 7.08
7	2,3-$(Cl)_2$	50	250°	MN	$C_{18}H_{15}Cl_2N_5O_3S$	N 15.45 S 7.06	15.44 7.08
8	2,6-$(Cl)_2$	55	189°	BP	$C_{18}H_{15}Cl_2N_5O_3S$	N 15.45 S 7.06	15.46 7.04
9	5-Cl; 2,4-$(MeO)_2$	55	235°	MYSp	$C_{20}H_{20}ClN_5O_5S$	N 13.65 S 6.24	13.68 6.22

[a] See footnote of Table I.

in other cases gave pyrazoles, whose characteristics are listed in Table III.

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