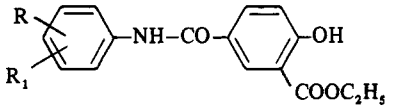
Table I.



No.	R	R_1	Mp, °C	Recrystallization solvent[a]	Formula	Analgetic activity (mice)[b,c]	Probability[d] $P \leq$
1	H	H	159-160	B	$C_{16}H_{15}NO_4$	37.1	<0.001
2	2Cl	H	154-155	A	$C_{16}H_{14}ClNO_4$	52.5	<0.001
3	3Cl	H	143-144	A	$C_{16}H_{14}ClNO_4$	56.4	≤0.001
4	4Cl	H	195-196	A	$C_{16}H_{14}ClNO_4$	32	<0.005
5	2Cl	3Cl	157-158	C	$C_{16}H_{13}Cl_2NO_4$	64.1	<0.001
6	2Cl	4Cl	164-165	C	$C_{16}H_{13}Cl_2NO_4$	74.3	<0.001
7	2Cl	5Cl	203-204	C	$C_{16}H_{13}Cl_2NO_4$	70.5	<0.001
8	2Cl	6Cl	200-201	C	$C_{16}H_{13}Cl_2NO_4$	62.8	<0.01
9	3Cl	4Cl	194-195	C	$C_{16}H_{13}Cl_2NO_4$	61.5	<0.01
10	3Cl	5Cl	185-186	C	$C_{16}H_{13}Cl_2NO_4$	67.9	<0.001
11	$2CH_3$	H	149-150	B	$C_{17}H_{17}NO_4$	55.1	<0.001
12	$3CH_3$	H	125-126	B	$C_{17}H_{17}NO_4$	51.2	<0.001
13	$4CH_3$	H	170-171	B	$C_{17}H_{17}NO_4$	37.1	<0.05
14	$2CH_3$	$3CH_3$	167-168	C	$C_{18}H_{19}NO_4$	46.1	≤0.01
15	$4OCH_3$	H	163-164	C	$C_{17}H_{17}NO_5$	44.8	<0.001
16	$4OC_2H_5$	H	165-166	C	$C_{18}H_{19}NO_5$	47.4	<0.001
17	$2CF_3$	H	160-161	B	$C_{17}H_{14}F_3NO_4$	42.3	≤0.001
18	$2CH_3$	5Cl	181-182	B	$C_{17}H_{16}ClNO_4$	46.1	<0.05
19	$2CH_3$	4Cl	178-179	B	$C_{17}H_{16}ClNO_4$	41	<0.001
20	$2CH_3$	3Cl	188-189	B	$C_{17}H_{16}ClNO_4$	41	<0.01
4HHA						48.7	<0.001

[a] A, MeOH; B, *i*-PrOH; C, AcOH. [b] Increase of reaction time % 3 hr after treatment. [c] Doses were of 30 mg/kg for each group of 10 mice. [d] The hot plate test counts were analyzed statistically by means of the Student *t* test. *P* was compared to controls.

0.05 mole of substituted anilines. The reaction mixture was refluxed for 2 hr and then diluted with cold H_2O, and the crystalline reaction product was filtered off. It was washed with 5% $NaHCO_3$ and recrystallized.

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Substituted Thiazolidones as Anticonvulsants†

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In continuation of our interest[1,2] in thiazolidones, some new 2-arylimino-3-(3,4-dimethoxyphenethyl)thiazolid-4-ones have been synthesized and tested for their anticonvulsant activity against pentylenetetrazol-induced seizures in albino mice.

Anticonvulsant activity was detd[2] by injecting the thiazolidone ip in a 5% aqueous suspension of gum acacia in groups of 10 mice of either sex. Pentylenetetrazol (80 mg/kg) was injected 4 hr after the administration of thiazolidones and the mice were then observed for 60 min for the occurrence of seizures. Animals devoid of even a threshold convulsion were considered protected. Anticonvulsant activity shown by substituted thiazolidones at 100 mg/kg is given in Table II. Compd 2 having an *o*-tolyl group at position 2 afforded the maximum protection of 70%, while administration in doses above or below 100 mg/kg caused lesser anticonvulsant activity. The low toxicity of this compound was reflected by its approximate LD_{50} (>2000 mg/kg).

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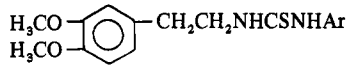
‡Junior Research Fellow of I.C.M.R., New Delhi.

Table I. Substituted Thiocarbamides



No.	Ar	Mp,[a] °C	Yield, %	Molecular formula[b]
1	C_6H_5	125	85	$C_{17}H_{20}N_2O_2S$
2	o-$CH_3C_6H_4$	112	65	$C_{18}H_{22}N_2O_2S$
3	m-$CH_3C_6H_4$	122	78	$C_{18}H_{22}N_2O_2S$
4	p-$CH_3C_6H_4$	92	85	$C_{18}H_{22}N_2O_2S$
5	3,4-$(CH_3)_2C_6H_3$	125	82	$C_{19}H_{24}N_2O_2S$
6	o-$OCH_3C_6H_4$	108	62	$C_{18}H_{22}N_2O_3S$
7	p-$OCH_3C_6H_4$	120	72	$C_{18}H_{22}N_2O_3S$
8	p-ClC_6H_4	114	80	$C_{17}H_{19}ClN_2O_2S$
9	p-BrC_6H_4	135	80	$C_{17}H_{19}BrN_2O_2S$
10	α-$C_{10}H_7$	166	68	$C_{21}H_{22}N_2O_2S$

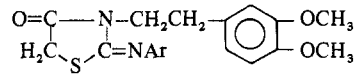
[a] Melting points were taken in open capillary tubes. [b] All compds were analyzed for C, H, and N and analyses were found within 0.4% of theory.

Experimental Section

1-Aryl-3-(3,4-dimethoxyphenethyl)thiocarbamide. 3,4-Dimethoxyphenethylamine (0.01 mole) was mixed with a suitable aryl isothiocyanate (0.01 mole) in 15 ml of dry PhH and was refluxed on a steam bath for 2 hr. The reaction mixt was concd under reduced pressure. The solid mass which sepd on cooling was filtered, washed (Et_2O, dil HCl), dried, and recrystd from EtOH. All thiocarbamides were characterized by their sharp melting points and elemental analyses (Table I).

2-Arylimino-3-(3,4-dimethoxyphenethyl)thiazolid-4-ones. A mixt of 1-aryl-3-(3,4-dimethoxyphenethyl)thiocarbamide (0.01 mole), $ClCH_2COOH$ (0.01 mole), and anhyd NaOAc (0.015 mole) in 15 ml of glacial AcOH was refluxed for 5–6 hr. The reaction mixt was poured into H_2O and refrigerated overnight. The sepd crude product was filtered, washed several times (H_2O), and recrystd from EtOH (Table II).

Table II. Substituted 4-Thiazolidones and Their Anticonvulsant Activity



No.	Ar	Mp,[a] °C	Yield, %	Molecular formula[b]	Protection, %	Mortality after 24 hr, %
1	C_6H_5	117	62	$C_{19}H_{20}N_2O_3S$	30	60
2	o-$CH_3C_6H_4$	126	55	$C_{20}H_{22}N_2O_3S$	70	20
3	m-$CH_3C_6H_4$	118	60	$C_{20}H_{22}N_2O_3S$	30	40
4	p-$CH_3C_6H_4$	160	64	$C_{20}H_{22}N_2O_3S$	40	50
5	3,4-$(CH_3)_2C_6H_3$	175	62	$C_{21}H_{24}N_2O_3S$	10	70
6	o-$OCH_3C_6H_4$	90	54	$C_{20}H_{22}N_2O_4S$	50	30
7	p-$OCH_3C_6H_4$	147	62	$C_{20}H_{22}N_2O_4S$	10	60
8	p-ClC_6H_4	150	60	$C_{19}H_{19}ClN_2O_3S$	60	50
9	p-BrC_6H_4	153	62	$C_{19}H_{19}BrN_2O_3S$	30	60
10	α-$C_{10}H_7$	128	58	$C_{23}H_{22}N_2O_3S$	50	40

[a,b] See footnotes to Table I.

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Synthesis of N′-Substituted Arylsulfonylpyrazoles, Their Anthelmintic Activity, and the Cytotoxicity of Some Hydrazides†

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Our continued interest in the synthesis of biological active heterocycles has led us to study the synthesis and anthelmintic activity of N′-substituted arylsulfonyl-3,5-dimethyl-4-arylazopyrazoles. These compounds displayed anthelmintic and cytotoxicity activities of different magnitudes. All are apparently nontoxic to mice at the dosages used.

Experimental Section

Melting points, taken with a Kofler hot-stage apparatus, are uncorr. Where analyses are indicated only by symbols of the elements, analytical result obtd for those elements were within ±0.4% of the calcd values.

2,3,4-Pentanetrione-3-arylhydrazons,[1] cinnamic acids, and hydrazides,[2] 3-nitro-4-methoxybenzenesulfonylhydrazide,[3] 3-chloro-4-methoxybenzenesylfonylhydrazide,[3] and 2,5-dichlorobenzenesulfonylhydrazide[4] were prepd by standard procedures.

2-Methoxy-3,5-dimethyl- and 2-Chloro-5-carboxybenzenesulfonyl Hydrazide. A soln of 2-methoxy-3,5-dimethyl- and 2-chloro-5-carboxybenzenesulfonyl chloride in EtOH was treated with NH_2NH_2-H_2O (98%) at 0°. It was left at room temp for several hr, when crystals of the hydrazide were obtd. Recrystn from EtOH gave a colorless product, mp 116–117°. 2-MeO-3,5-Me_2 deriv. *Anal.* ($C_9H_{14}N_2O_3S$) C, H, N. 2-Cl-5-CO_2H deriv, mp 87°. *Anal.* ($C_7H_7ClN_2O_4S$) C, H, N.

N′-Substituted Arylsulfonyl-3,5-dimethyl-4-arylazopyrazoles. A hot soln of arylsulfonylhydrazide (0.01 mole) in EtOH (30 ml)

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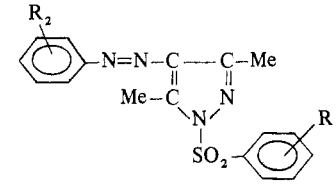
Table I. N^1-Arylsulfonyl-3,5-dimethyl-4-arylazopyrazoles



No.	R_1	R_2	Yield, %	Mp, °C	Color[a]	Formula[b]
1	3-NO_2-4-OMe	2-Cl	65	168–169	Ly	$C_{18}H_{16}ClN_5O_5S$
2	3-NO_2-4-OMe	4-OMe	95	194–195	y	$C_{19}H_{19}N_5O_6S$
3	3-NO_2-4-OMe	4-NO_2	80	167–168	O	$C_{18}H_{16}N_6O_7S$
4	3-Cl-4-OMe	2-Cl	65	150–151	Y	$C_{18}H_{16}Cl_2N_4O_3S$
5	3-Cl-4-OMe	2-NO_2	76	224–225	R	$C_{18}H_{16}ClN_5O_5S$
6	3-Cl-4-OMe	4-OMe	70	161–162	Y	$C_{19}H_{19}ClN_4O_4S$
7	2-OMe-5-Cl	2-NO_2	80	200–201	R	$C_{18}H_{16}ClN_5O_5S$
8	2,5-Cl	2-NO_2	90	190–191	DBn	$C_{17}H_{13}Cl_2N_5O_4S$
9	2-Cl-5-COOH	2-NO_2	96	220–221	BR	$C_{18}H_{14}ClN_5O_6S$
10	2-OMe-3,5-Me	4-OMe	96	154–155	Py	$C_{21}H_{24}N_4O_4S$

[a] B, brick; Bn, brown; D, dark; L, light; O, orange; P, pale; R, red; Y, yellow. [b] All compds were analyzed for C, H, N, S.

Table II. Biological Activities of N^1-Arylsulfonylpyrazoles

	% activity at highest tested dosage[b]							
	In Vivo				*In Vitro*			
	Mice				Manure			
No.[a]	Tg	N	C	O	R/Lv/Ad	Hc/Ts	F	Dose, ppm
1		0	0	60	75/0/0	100/100	0	100
2	0	0	0	0				400 mg/kg
3	0	0	0	0	50/0/0	100/100	0	100 mg/kg
4		0		0	0/0/0	60/90	0	100
5	0	0	0	0	0/0/0	0/50	0	100, 400 mg/kg
6	0	0	0	50				400 mg/kg
7	0				0/0/0	50/50	0	100
8	0				0/0/0	0/50	0	100
9	0	0	0	50				400 mg/kg
10	0	0	0	0				100

[a] Same as Table I. [b] Tg, *Toxoplasma gondii*–RH strain in mice prevention (of mortality); N, nematodes (*trichostrongyles* in mice); C, cestoses (tapeworms in mice); O, oxyurids (in mice); R, % repellency (of face fly oviposition); Lv, % contact activity on face fly larvae (prevention of pupation); Ad, % kill of adult face flies and/or pupae which fail to hatch; Hc, % inhibition of *Haemonchus contorus* larvae development; Ts, % inhibition of *Trichostorgylus spp.* larvae development; F, % inhibition of fungus growth.