Synthesis and Activity of 1-Alkyl-2-aryl-2,3-dihydro-4(1H)-quinazolinones

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Only one 1-alkyl-2-aryl-2,3-dihydro-4(1H)-quinazolinone has previously been reported, 1-methyl-2-phenyl-2,3-dihydro-4(1H)-quinazolinone (1). We have prepared a series of such novel quinazolinones and tested them for analgesic and sedative activity. These substances were obtained by reaction of the appropriate *o*-alkylaminobenzamide with an aromatic aldehyde in ethanol containing a small amount of hydrochloric acid according to the scheme

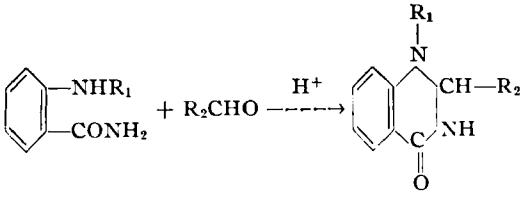


Table I summarizes the physical properties of these substances.

EXPERIMENTAL

1-Alkyl-2-aryl-2,3-dihydro-4(1H)-quinazolinones.—As a general procedure, 0.038 mole of the *o*-alkylaminobenzamide was mixed with 0.050 mole of aldehyde in 30 ml. of ethanol containing one drop of concentrated hydrochloric acid. The mixture was then refluxed for 36 hours. Removal of the solvent was carried out at reduced pressure and the residual solid was recrystallized from toluene. Substituted *o*-alkylaminobenzamides were obtained by reaction of the corresponding isatic anhydrides with ammonia.[1]

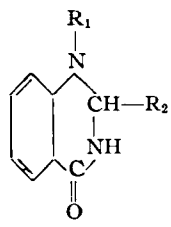
PHARMACOLOGICAL DATA[2]

None of the compounds tested showed any significant analgesic, sedative, or muscle relaxant activity in mice at levels up to 100 mg./Kg. when dosed intravenously using propylene glycol–water suspensions. Prostration and decreased activity were observed in the test animals when compounds IV, V, VI, and VII were administered at levels of 100–300 mg./Kg.

REFERENCES

(1) Böhme, H., and Böeing, H., *Arch. Pharm.*, **283**, 1011 (1960); through *Chem. Abstr.*, **55**, 7420d(1961).

TABLE I.—2-SUBSTITUTED-1-ALKYL-2,3-DIHYDRO-4(1H)-QUINAZOLINONES



Compd. No.	R_1	R_2	Yield, %	M.p., (corrected)	Formula	Analyses[a] Calcd. N	Calcd. S	Found N	Found S
I	Methyl	2-Furyl	73.5	184.2 to 185.6	$C_{13}H_{12}N_2O_2$	12.29	...	12.18	...
II	Methyl	3-Indolyl	56.4	217–220	$C_{17}H_{15}N_3O$	15.15	...	15.03	...
III	Methyl	2-Thienyl	90.0	178.8 to 181.2	$C_{13}H_{12}N_2OS$	11.46	13.11	11.00	12.82
IV	Methyl	Phenyl	62.9	206 to 207.5 (uncorrected)	$C_{15}H_{14}N_2O$	11.76	...	11.79	...
V	*n*-Propyl	2-Furyl	53.2	150.5 to 152.0	$C_{15}H_{16}N_2O_2$	10.91	...	10.30	...
VI	*n*-Propyl	Phenyl	49.0	120–121	$C_{17}H_{18}N_2O$	10.52	...	10.82	...
VII	*n*-Propyl	2-Thienyl	48.9	146–148	$C_{15}H_{16}N_2OS$	10.28	11.74	10.03	11.70
VIII	Ethyl	Phenyl	72.5	141 to 143.5	$C_{16}H_{16}N_2O$	11.10	...	10.95	...
IX	Isopropyl	Phenyl	52.2	122–125	$C_{17}H_{18}N_2O$	10.50	...	10.52	...
X	*n*-Butyl	Phenyl	85.8	111 to 112.5	$C_{18}H_{20}N_2O$	10.00	...	9.94	...
XI	*n*-Pentyl	Phenyl	85.5	123.5 to 126	$C_{19}H_{22}N_2O$	9.51	...	10.12	...

[a] Analyses were carried out by Spang Microanalytical Laboratories, Ann Arbor, Mich.

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[1] *o*-Alkylaminobenzamides were prepared by C. Baumann in this laboratory (unpublished work).

[2] Tests carried out by Woodard Research Corp., Herndon, Va.