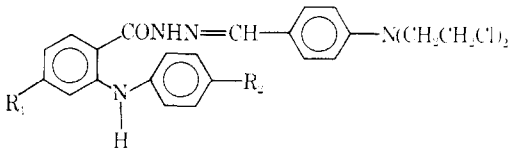
Table I



Cmpd[a]	R_1	R_2	% Yield	Mp, °C	Formula[c]
1	Cl	Cl	70	196–198	$C_{24}H_{22}Cl_4N_4O$
2	H	OCH_3	80	215–217	$C_{25}H_{26}Cl_2N_4O_2$
3	H	Cl	80	194–196	$C_{24}H_{23}Cl_3N_4O$
4[b]	H	Br	85	198–199.5	$C_{24}H_{23}BrCl_2N_4O$

[a] All compounds were recrystallized from EtOH unless otherwise noted. [b] Recrystallization from MeCN. [c] All compounds were analyzed for C, H, N.

idene Hydrazides.—In a typical reaction, 3.06 g (0.01 mol) of *N*-(4-bromophenyl)anthranilic acid hydrazide, 2.46 g (0.01 mol) of *p*-*N*,*N*-bis(2-chloroethyl)aminobenzaldehyde in 40 ml of EtOH containing 1 drop of HOAc were refluxed for 4 hr. The reaction mixture was cooled, the precipitate filtered to yield 5.1 g of crude material, mp 195–199°. Recrystallization from MeCN raised the melting point to 198–199.5°.

Some Substituted [*p*-(*p*-Ethoxyphenyl)anilino]acetamides

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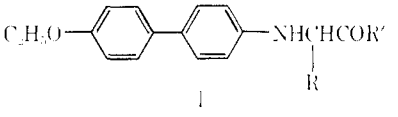
Received November 24, 1969

In further search for pharmacologically active arylaminoacylamide derivatives[1] we have synthesized a series of compounds of the general formula I. However, none of the compounds described here (see Table I) was active when screened for analgetic or antiinflammatory activity.



I

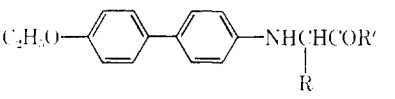
Experimental Section[2]

General Procedure.—A solution of 0.1 mol of *p*-(*p*-ethoxyphenyl)aniline and 0.1 mol of the appropriate halogenoacylamide in 200 ml of *n*-PrOH was refluxed in the presence of an excess of $NaHCO_3$ for 3–4 days. The cooled reaction mixture was concentrated, diluted (H_2O), and filtered. The solid obtained was recrystallized till the compound was chromatographically pure.

Ethyl Ester of *N*-[*p*-(*p*-Ethoxyphenyl)phenyl]glycine.—*p*-(*p*-Ethoxyphenyl)aniline (30 g), 24 g (16 ml) of ethyl bromoacetate, and 15 g of $NaHCO_3$ in 200 ml of *n*-PrOH, were refluxed for 4 days. The cooled reaction mixture was filtered and the solid residue was partitioned (Et_2O–H_2O). The Et_2O layer was separated, dried (Na_2SO_4), and concentrated to dryness (26 g, yield 58%). A sample recrystallized from EtOH had mp 137–139°. *Anal.* ($C_{18}H_{21}NO_3$) C, H, N.

[*p*-(*p*-Ethoxyphenyl)anilino]acetyl(*N*-methyl)piperazide.—A mixture of 5.5 g of *N*-[*p*-(*p*-ethoxyphenyl)phenyl]glycine ethyl ester and 4.4 ml of freshly distilled *N*-methylpiperazine was refluxed for 4 days. The reaction mixture was then treated with EtOAc and filtered (see Table I).

Table I



R	R′	Mp, °C	Recrystn solvent[a]	Formula[b]
H	EtNH	152–154	A	$C_{18}H_{22}N_2O_2$
H	*n*-PrNH	159–161	A	$C_{19}H_{24}N_2O_2$
H	*i*-PrNH	150–151	A	$C_{19}H_{24}N_2O_2$
H	*n*-BuNH	153–155	B	$C_{20}H_{26}N_2O_2$
H	*sec*-BuNH	113–115	A + D	$C_{20}H_{26}N_2O_2$
H	*i*-BuNH	165–167	A	$C_{20}H_{26}N_2O_2$
H	*t*-BuNH	129–131	A + D	$C_{20}H_{26}N_2O_2$
CH_3	*n*-PrNH	124–126	B	$C_{20}H_{26}N_2O_2$
H	Et_2N	151	C	$C_{20}H_{26}N_2O_2$
H	*n*-Pr_2N	124–125	C	$C_{22}H_{30}N_2O_2$[c]
H	Pyrrolidino	176–178	E	$C_{20}H_{24}N_2O_2$
H	Piperidino	169–171	A	$C_{21}H_{26}N_2O_2$
H	Morpholino	145–147	A	$C_{20}H_{24}N_2O_3$
H	*N*-Methylpiperazino	166–168	F	$C_{21}H_{27}N_3O_2$

[a] A, EtOAc; B, EtOH; C, 95° EtOH; D, petr ether (bp 40–68°); E, MeCN; F, dioxane. [b] All compounds were analyzed for C, H, N. The analytical results obtained are within ±0.3% of the theoretical values. [c] C: calcd, 74.54; found, 74.11.

Acknowledgment.—We are indebted to Dr. A. De Leonibus for the microanalyses and to Dr. M. L. Reviglio for the tlc.

Substituted Chroman-6-ylureas and Thioureas

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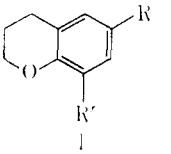
Received November 24, 1969

In connection with our interest in pharmacological properties of 6-aminochroman derivatives[1] we have synthesized compounds of structure I where R represents an alkyl or arylurea, or thiourea moiety; and



I

R′ can be H, Cl or Me. These compounds are related to the pharmacologically active 2,3-dihydro-2-methylbenzofuranyl analogs.[2]

Experimental Section[3]

***N*-Methyl-6-aminochromane.**—A mixture of 6-aminochroman[4] (9 g) and 90% HCO_2H (3 ml) was boiled for 90 min.

(1) A. Larizza and G. Brancaccio, U.S. Patent 3,264,349; G. Brancaccio, A. Larizza, G. Lettieri, and R. Viterbo, *Farmaco Ed. Sci.*, **22**, 930 (1967); and the references indicated therein.

(2) Melting points were determined in capillary tubes in a heated copper block and are uncorrected. Tlc was carried out on silica gel using PhH–MeAc–petr ether (1:1:1) as the solvent system.

(1) G. Lettieri, G. Brancaccio, A. Larizza, R. Viterbo, and G. C. Perri, *Farmaco Ed. Sci.*, **24**, (1970), in press.

(2) David R. Herbst, U. S. 3,252,999 [*Chem. Abstr.*, **65**, 3835 (1966)].

(3) Melting points were determined in open capillary tubes and are uncorrected.

(4) V. Hach, *Collect. Czech. Chem. Commun.*, **24**, 3136 (1959).