CCA-441 615.778.2:547.58.024
Note

N^4-Acylsulphonamides. I. Derivatives of p-(2-Ethoxybenzamido) benzenesulphamide*

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N-Substituted derivatives of the established analgetic 2-ethoxybenzamide[1], with analgetic[2], local anesthetic[3] or insect repellent[4,5] activity, have been previously prepared and tested.

In view of obtaining new compounds derived from this pharmacologically active grouping we have now prepared new N^4-2-ethoxybenzoyl derivatives of classical sulphonamides presented in Table 1.

The preparation of these compounds was performed by condensing 2-ethoxybenzoyl chloride with the corresponding sulphonamide in pyridine, applying the slightly modified method given for the preparation of 4-succinimidobenzenesulphonamide by Miller *et. al.*[6]

The prepared compounds have been tested in rats for analgetic activity. Only N^1-(6-methoxy-3-pyridazinyl)-N^4-(2-ethoxybenzamido) benzenesulphamide (V) produced, 2 hr. after *s. c.* injection in a »hot plate« test, an analgetic effect similar to the effect of phenacetine. A detailed report of these tests will be published elsewhere.

EXPERIMENTAL

General procedure for the preparation of substituted p-*(2-ethoxybenzamido) benzenesulphamides*

To a solution of 0.01 mole of a N^1-substituted sulphanylamide in a 30—40 ml. of pyridine 1.34 g. (0.01 mole) of *o*-ethoxybenzoyl chloride was added portionwise during 5 min. at room temperature. After standing for 20 hrs. under the same conditions, the reaction mixture was cooled to 0° and acidified with hydrochloric acid to pH 1. The separated solid products were filtered off and washed with water to pH 7. The crude products were crystallized from 96% ethanol.

By this method the new compounds I—XI were prepared (see Table I).

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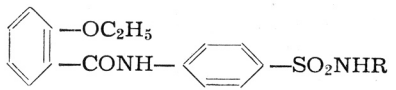
* Yug. pat. appl. P-1134/66

TABLE I

Derivatives of p-*(2-Ethoxybenzamido) benzenesulphamide*



Compound	R	Yield of crude prod. %	m. p* °C	Formula	Calc'd			Found		
					C	H	N	C	H	N
I	H	74	210—211	$C_{15}H_{16}N_2O_4S$	56.25	5.04	8.75	56.01	4.80	8.98
II	5-(1-phenylpyrazolyl)	87	193—194	$C_{24}H_{22}N_4O_4S_4$	62.33	4.88	12.12	62.10	4.60	12.25
III	2-(thiazolyl)	77	224—225	$C_{18}H_{17}N_3O_4S_2$	53.60	4.25	10.42	53.40	4.00	10.41
IV	5-(3,4-dimethylisoxazolyl)	86.8	181—182	$C_{20}H_{21}N_3O_5S$	57.83	5.10	10.12	57.83	4.89	10.24
V	3-(6-methoxypyridazinyl)	91	198—200	$C_{20}H_{20}N_4O_5S$	56.07	4.71	13.08	56.35	4.75	13.15
VI	-guanyl	61	271—273	$C_{16}H_{18}N_4O_4S$	53.03	5.01	15.46	53.23	4.80	15.16
VII	2-(4,6-dimethylpyrimidyl)	71	214.5—216	$C_{21}H_{22}N_4O_4S$	59.15	5.20	13.14	59.15	5.00	13.28
VIII	2-(5-methoxypyrimidyl)	65	244—245	$C_{20}H_{20}N_4O_5S$	56.07	4.71	13.08	56.26	4.42	13.25
IX	4-(2,6-dimethoxypyrimidyl)	87.5	202—203	$C_{21}H_{22}N_4O_6S$	55.02	4.84	12.22	55.11	4.58	12.26
X	2-pyrimidyl	86.8	241—242	$C_{19}H_{18}N_4O_4S$	57.28	4.55	14.07	57.10	4.30	14.35
XI	2-(4-methylpyrimidyl)	80	228—229	$C_{19}H_{20}N_4O_4S$	56.99	5.04	13.99	57.18	5.00	13.97

* After crystallization. All melting points are uncorrected.

IZVOD

N^4-Acilsulfonamidi. I. Derivati *p*-(2-etoksibenzamido) benzensulfamida

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Kondenzacijom klorida 2-etoksibenzojeve kiseline i poznatih sulfonamida u piridinu pripravljeno je 11 novih *p*-(2-etoksibenzamido) benzensulfamida. Prilikom ispitivanja na analgetsko djelovanje testom na »vrućoj ploči« samo je spoj V pokazao djelovanje slično djelovanju fenacetina.

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