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Note

Synthesis of Some Derivatives of *p*-(1,1-Dioxotetrahydro-2--thiazinyl) benzenesulfonamide*

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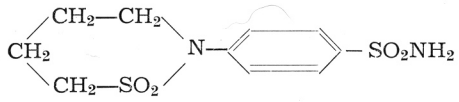
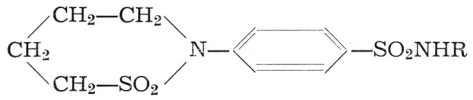
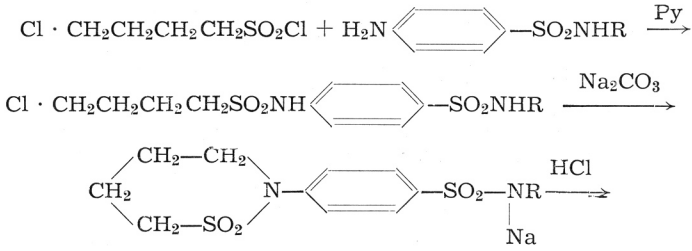
The anticonvulsant drug *p*-(1,1-dioxotetrahydro-2-thiazinyl) benzenesulfonamide (I)[1], although structurally different from classical anticonvulsant drugs, was found to be active in psychomotor seizures or epileptic equivalents.[2]



We thought it of interest to prepare further substances of this general structure substituted at N^1 with heterocyclic substituents. Similar compounds have also been synthesized by Kalman Harsanyi *et al.*[3].



A series of compounds of this structure (II—X, see table I) were prepared by slightly modifying general methods used for the preparation of *N*-arylsultams[1,4–7]. N^1-Substituted sulphanylamides were condensed with 4-chloro-1--butanesulphonyl chloride in pyridine and the intermediates so obtained cyclised in aqueous sodium carbonate solution. The resulting sodium salts were neutralised with dilute hydrochloric acid. The reaction scheme is:

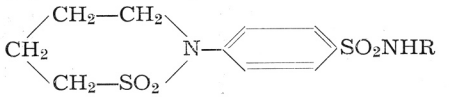


* Yug. Pat. Applic. 442/64

** Taken from the thesis submitted by A. Junašević-Holjevac in partial fulfilment of the requirements for the degree of Doctor of Chemistry at the University of Zagreb.

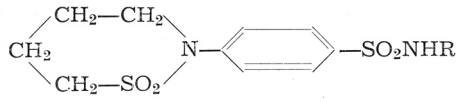
TABLE I

Derivatives of p-*(1,1-Dioxotetrahydro-2-thiazinyl) benzenesulfonamide*



Compound	R	Yield of crude prod. %	m. p.*	Formula	Calc'd. C	Calc'd. H	Calc'd. N	Found C	Found H	Found N
II	3-(5-methylisoxazolyl)	81	185° *a*	$C_{14}H_{17}N_3O_5S_2$	45.27	4.61	11.31	45.42	4.41	11.43
III	5-(1-phenylpirazolyl)	97.5	201° *a*	$C_{19}H_{20}N_4O_4S_2$	52.76	4.66	12.95	52.65	4.58	12.70
IV	2-thiazolyl	53.7	236° *b*	$C_{13}H_{15}N_3O_4S_3$	41.81	4.04	11.25	41.95	3.86	11.09
V	2-pyrimidyl	56	261° *c*	$C_{14}H_{16}N_4O_4S_2$	45.64	4.37	15.21	45.68	4.10	14.97
VI	2-(4-methylpyrimidyl)	99.5	246° *c*	$C_{15}H_{18}N_4O_4S_2$	47.10	4.74	14.65	47.16	4.54	14.73
VII	2-(5-methoxypyrimidyl)	22	270° *c*	$C_{15}H_{18}N_4O_5S_2$	45.21	4.55	14.06	44.98	4.52	13.82
VIII	2-(4,6-dimethylpyrimidyl)	31	212° *a, d*	$C_{16}H_{20}N_4O_4S_2$	48.47	5.09	14.13	48.47	4.80	13.91
IX	4-(2,6-dimethoxypyrimidyl)	75	175° *a*	$C_{16}H_{20}N_4O_6S_2$	44.85	4.71	13.08	44.88	4.64	13.29
X	5-(3,4-dimethylisoxazolyl)	25	168° *e*	$C_{15}H_{19}N_3O_5S_2$	46.74	4.96	10.90	46.82	4.64	10.95

* After crystallization
a. Recrystallized from methanol
b. Recrystallized from dioxane
c. Recrystallized from dimethylformamide + water (1 : 1)
d. Reported m. p. 20° C[3]
e. Recrystallized from benzene



The tested compounds did not exhibit any anticonvulsant activity.

EXPERIMENTAL

All melting points are uncorrected. All analytical samples were dried *in vacuo* under phosphorus pentoxide for 5 hours. Samples of pure commercial N^1-substituted sulphanilamides were used as starting materials. 4-Chloro-1-butanesulphonyl chloride was prepared according to B. Helferich and K. G. Kleb.[7]

General procedure for the preparation of p-*(1,1-Dioxotetrahydro-2-thiazinyl) benzenesulfonamide derivatives*

0.05 mole of the sulphanylamide derivative was dissolved in 30—200 ml. of pyridine, cooled to 15° C, and 0.05 mole of 4-chloro-1-butanesulphonyl chloride (b. p. 112—120° C/1.5 mm.) added dropwise at 15—20° C with stirring. The reaction mixture was stirred for an additional 12 hours at room temperature and then poured into 300 ml. of dilute hydrochloric acid (1 : 3). The separated solid product was collected by filtration, washed with water until the washings were neutral, and heated under reflux for one hour with 100 ml. of 15% sodium carbonate solution. The reaction mixture was then cooled, diluted with an equal volume of water, and acidified with dilute hydrochloric acid. The crystals obtained were collected by filtration, washed with water and dried. The crude products were isolated in yields ranging from 22—99.5%. By this method new compounds were prepared and presented in Table I.

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IZVOD

Sinteza nekih derivata *p*-(1,1-dioksotetrahidro-2-tiazinil) benzensulfonamida

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Priređeni su neki derivati *p*-(1,1-dioksotetrahidro-2-tiazinil) benzensulfonamida reakcijom 4-klorbutansulfoklorida s odgovarajućim N^1 supstituiranim sulfonamidima u piridinu i naknadnom ciklizacijom tako dobivenih intermedijernih N^1 supstituiranih N^4-(4-klorbutilsulfonil) sulfanilamida. Dobiveni spojevi navedeni su u tabeli I.

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