59.5 Gm. (0.5 mole) of propargyl bromide (Aldrich Chemical Co.). The mixture was stirred at reflux for 12 hours. The ether solution was decanted from the oily amine hydrobromide layer, and the latter was extracted three times with ether. The ether was evaporated from the combined ether extracts and the residue was fractionated at reduced pressure (see Table I). The hydrochloride salts were prepared by passing dry hydrogen chloride through ether solutions of the amines. The precipitated salts were collected on a filter, washed with ether and were recrystallized (see Table I).

C. Aminoalkynyltetrahydroquinolines

To 0.18 mole of a freshly distilled 1,2,3,4-tetrahydroquinoline in 35 ml. of isopropyl alcohol was added 10.7 Gm. (0.09 mole) of propargyl bromide over a period of 30 minutes with stirring. The reaction mixture was refluxed 2 hours, then the mixture was cooled to 4° and was allowed to stand for 12 hours. The precipitate of the 1,2,3,4-tetrahydroquinoline hydrobromide was removed by filtration, and the filtrate was subjected to fractional distillation (see Table I).

The hydrochloride salts were prepared by passing dry hydrogen chloride through an ether solution of the amine. The precipitated salts were collected on a filter, washed with ether, and were recrystallized (see Table I).

D. 2-(3-Butynyl)quinoline

2-(Lithio methyl)-quinoline was synthesized by the method of Cannon (6) for the preparation of 1-(lithio methyl) isoquinoline. To the ethereal solution containing 0.1 mole of 2-(lithio methyl)-quinoline was added, in a slow stream and with stirring, a solution of 11.9 Gm. (0.1 mole) of propargyl bromide in 100 ml. of anhydrous ether. The solution turned a deep purple color and a moderate boiling ensued. As additional organic halide was added the purple color became fainter and finally disappeared. Stirring was continued overnight at room temperature, during which time a brown precipitate formed. Stirring was continued while 100 ml. of distilled water was slowly added. The aqueous layer was removed and discarded and the ethereal solution which also contained a considerable quantity of a brown precipitate was filtered and washed several times with water. After drying with anhydrous magnesium sulfate and filtering, the ether was removed from the filtrate on a steam bath and the brown-black oily residue was distilled under reduced pressure (see Table I). $\lambda_{max.\mu}^{film}$ 3.05 (=CH stretching), m 4.70 (—C≡C— stretching.)

E. Fungicidal Activity

Fungicidal activity was evaluated by a serial dilution procedure, utilizing Sabouraud's medium. The tubes were incubated at 25°; turbidimetric and growth readings were taken after 48 hours.

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Some 1,2,3,4-Benzothiatriazine 1,1-Dioxides

By SCOTT J. CHILDRESS

1,2,3,4-Benzothiatriazine 1,1-dioxide analogs of chlorothiazide have been prepared and tested for diuretic activity.

NOVELLO and Sprague (1) in 1957 reported the synthesis and diuretic activity of 6-chloro-7-sulfamyl-1,2,4-benzothiadiazine 1,1-dioxide (chlorothiazide). Since then numerous analogs have been described (2). There are no specific structural requirements for activity except for the presence of a sulfamyl group and even this can be substituted (3). It seemed to be of interest to prepare some substituted 1,2,3,4-benzothiatriazine 1,1-dioxides and examine them for diuretic activity.

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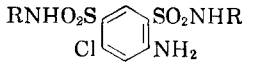
In order to isolate stable compounds, it was necessary to have an alkyl group in the 2-position. For convenience in synthesis, the 7-sulfamyl group was also substituted by an alkyl group. It did not seem that such substitution would destroy any potential activity in the benzothiatriazine 1,1-dioxides, for 5-chloro-2,4-bis-(methylsulfamyl)aniline, an intermediate, is reported to have diuretic properties (4). Also, methyl and isopropyl substituents in sulfamyl groups are removed metabolically in some cases (5).

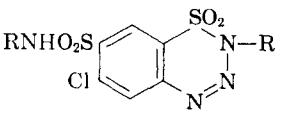
The desired benzothiatriazine 1,1-dioxides were prepared by treatment of the appropriate 5-chloro-2,4-bis-(alkylsulfamyl)aniline with nitrous acid (6). The intermediates are listed in Table I and the products in Table II. The benzothiatriazine 1,1-dioxides proved to have statistically significant diuretic activity in rats (7).

TABLE I.—INTERMEDIATES FOR BENZOTHIATRIAZINE 1,1-DIOXIDES



R	M.P., °C.	Formula	Analysis, % Calcd. C	H	N	Found C	H	N
CH_3—	181–182	$C_8H_{12}ClN_3O_4S_2$	30.62	3.85	13.39	30.55	3.83	13.28
i-C_3H_7—	232–234	$C_{12}H_{20}ClN_3O_4S_2$	38.96	5.45	11.36	39.34	5.46	11.24
$C_6H_5CH_2$—	146–147	$C_{20}H_{20}ClN_3O_4S_2$	51.55	4.33	9.02	51.85	4.41	8.91
Cyclo-C_6H_{11}—	192–194	$C_{18}H_{28}ClN_3O_4S_2$	48.04	6.27	9.34	48.20	6.25	9.18

TABLE II.—BENZOTHIATRIAZINE 1,1-DIOXIDES



R	M.P., °C.	Formula	Analysis, % Calcd. C	H	Cl	S	Found C	H	Cl	S
CH_3—	176 (decompn.)	$C_8H_9ClN_4O_4S_2$	29.58	2.79	10.92	19.75	30.04	2.77	11.10	19.57
i-C_3H_7—	134 (decompn.)	$C_{12}H_{17}ClN_4O_4S_2$	37.84	4.50	9.31	16.84	37.68	4.54	9.38	16.70
$C_6H_5CH_2$—	158 (decompn.)	$C_{20}H_{17}ClN_4O_4S_2$	50.36	3.59	7.43	13.76	50.38	3.71	7.61	13.92
Cyclo-C_6H_{11}—	165 (decompn.)	$C_{18}H_{23}ClN_4O_4S_2$	46.89	5.47	7.69	13.91	47.13	5.67	7.81	13.98

EXPERIMENTAL

5-Chloro-2,4-bis-(alkylsulfamyl)anilines.—The required intermediates, 5-chloro-2,4-bis-(alkylsulfamyl)anilines (Table I), were prepared by treating an alcoholic or aqueous solution of 4 equivalents of the appropriate amine with crude 5-chloro-2,4-bis-(chlorosulfonyl)aniline prepared by the method of Novello (8). The products were recrystallized from alcohol.

2-Benzyl-7-benzylsulfamyl-6-chloro-1,2,3,4-benzothiatriazine 1,1-Dioxide.—A suspension of 7.8 Gm. of 5-chloro-2,4-bis-(benzylsulfamyl)aniline in 22 ml. of acetic acid and 1 ml. of water was treated with a solution of 1.2 Gm. of sodium nitrite in 9 ml. of sulfuric acid, keeping the temperature below 20°. The mixture was filtered and the filtrate was diluted with water. The gummy precipitate was washed with alcohol and recrystallized from acetone by addition of water, affording 5.5 Gm. of cream-colored crystals.

The other compounds (Table II) were prepared similarly. They showed positive diazo coupling tests with alkaline β-naphthol. Dumas nitrogen analyses were erratic.

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