water. After stirring for several hours the oil was extracted into ether and the extract washed with water, 4 *N* hydrochloric acid, water, saturated bicarbonate solution, and water. After drying over sodium sulfate the solvent was distilled to yield 0.17 g. (70%) of amber sirup which could not be crystallized from 2-propanol; $[\alpha]^{19}D$ was $-23.9°$ (chloroform; *c*, 33.3).

Anal. Calcd. for $C_{24}H_{32}O_{11}S$: C, 54.5; H, 6.10. Found: C, 55.3; H, 6.24.

Summary

1. Alkyl and aryl polyacetyl-β-D-thioglycosides have been shown to be readily oxidized to the corresponding alkyl or aryl polyacetyl-β-D-glycosyl sulfones by action of either potassium permanganate or 30% hydrogen peroxide. Partial deacetylation apparently attends the latter oxidation in acetic acid medium. A number of examples of these oxidations are given, and several members of this new class of sulfones are described.

2. Two phenyl polyacetyl-β-D-glycosyl sulfones have been deacetylated using ammoniacal methanol, and the deacetylation products have been described.

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[CONTRIBUTION FROM THE DEPARTMENT OF CHEMISTRY, UNIVERSITY OF TEXAS]

5-Alkyl (or 5-Phenyl)-5-propoxymethylhydantoins[1]

BY HENRY R. HENZE, JOE W. MELTON[2] AND EUGENE O. FORMAN

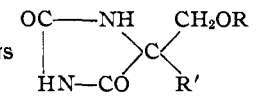
Some time ago, Henze and Rigler[3] prepared 5-ethoxymethyl-5-phenylhydantoin which later was shown to possess considerable anticonvulsant activity.[4] This behavior is in contrast to that of 5-ethyl-5-isoamyoxymethylhydantoin[3] which shows no anticonvulsant activity even in far larger doses,[4] and is, in fact, an unsatisfactory soporific. To obtain additional compounds, suitable for subsequent pharmacological testing for activity, we converted seventeen keto ethers, previously reported,[5] into the corresponding 5-alkyl (or 5-phenyl)-5-propoxymethylhydantoins. The latter have proved to be potent anticonvulsants,[4] the most active being 5-isopropoxymethyl-5-phenylhydantoin which compares favorably with 5,5-diphenylhydantoin in this respect and has merited clinical study.

Experimental

The hydantoins were obtained by warming a mixture of 1 part of keto ether, 1.1 parts of potassium cyanide and 3 parts of ammonium carbonate (U. S. P. cubes) in sufficient 50% alcohol at 58–60° for periods up to twenty-four hours. After the period of interaction, the solutions were evaporated to about half volume, acidified with hydrochloric acid and boiled to remove hydrogen cyanide. Usually, at this point, the hydantoins

TABLE I

5-ALKYL (OR 5-PHENYL)-5-PROPOXYMETHYLHYDANTOINS



—R	—R′	M. p., °C. (cor.)	Yield, %	Carbon, % Calcd.	Carbon, % Found	Hydrogen, % Calcd.	Hydrogen, % Found	Nitrogen, % Calcd.	Nitrogen, % Found
C_3H_7-*n*	—CH_3	85.0	42	51.60	51.39	7.58	7.51	15.05	15.38
C_3H_7-iso	—CH_3	136.5	49	51.60	51.35	7.58	7.71	15.05	15.10
C_3H_7-*n*	—CH_2CH_3	96.0	51	53.98	54.04	8.05	7.92	13.99	14.05
C_3H_7-iso	—CH_2CH_3	143.5	34	53.98	54.14	8.05	8.23	13.99	14.11
C_3H_7-*n*	—$(CH_2)_2CH_3$	113.0	54	56.05	55.91	8.47	8.30	13.08	13.32
C_3H_7-iso	—$(CH_2)_2CH_3$	166.5	66	56.05	56.08	8.47	8.76	13.08	13.38
C_3H_7-iso	—$CH(CH_3)_2$	182.0	54	56.05	56.20	8.47	8.47	13.08	13.07
C_3H_7-*n*	—$(CH_2)_3CH_3$	141.5	35	57.87	57.87	8.83	8.83	12.27	12.58
C_3H_7-iso	—$(CH_2)_3CH_3$	175.8	74	57.87	57.83	8.83	9.03	12.27	12.44
C_3H_7-iso	—$CH_2CH(CH_3)_2$	221.7	65	57.87	57.78	8.83	8.95	12.27	12.52
C_3H_7-iso	—$CH(CH_3)CH_2CH_3$	180.2	64	57.87	57.73	8.83	8.86	12.27	12.51
C_3H_7-*n*	—$(CH_2)_4CH_3$	130.0	60	59.48	59.65	9.15	9.08	11.56	11.67
C_3H_7-iso	—$(CH_2)_4CH_3$	165.4	85	59.48	59.79	9.15	9.34	11.56	11.68
C_3H_7-*n*	—$(CH_2)_2CH(CH_3)_2$	180.0	45	59.48	59.70	9.15	9.24	11.56	11.63
C_3H_7-iso	—$(CH_2)_2CH(CH_3)_2$	218.2	78	59.48	59.56	9.15	9.37	11.56	11.45
C_3H_7-*n*	—C_6H_5	133.0	75	62.89	62.67	6.50	6.33	11.28	11.42
C_3H_7-iso	—C_6H_5	162.0	78	62.89	62.89	6.50	6.34	11.28	11.52

(1) From the M. A. thesis of J. W. M. (August, 1940) and of E. O. F. (June, 1941).

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(3) Rigler with Henze, THIS JOURNAL, **58**, 474 (1936).

(4) Merritt, Putnam and Bywater, *J. Pharmacol.*, **84**, 67 (1945).

(5) Henze, Duff, Matthews, Melton and Forman, THIS JOURNAL, **64**, 1222 (1942).

separated as white, crystalline solids; some, of lower m.p., separated as liquids which crystallized upon contact with ice. Recrystallization was effected in most cases by use of diluted alcohol or of a mixture of benzene and petroleum ether. The hydantoins can be dissolved in cold 10% solution of alkali and are reprecipitated unchanged upon acidification. Data for melting points and analyses are listed in Table I.

Summary

Seventeen new 5-alkyl (or 5-phenyl)-5-alkoxyalkylhydantoins have been prepared from the corresponding alkyl (or phenyl) *n*- or iso-propoxymethyl ketones. Of these, the 5-isopropoxymethyl-5-phenylhydantoin exhibits outstanding activity as an anticonvulsant.

AUSTIN, TEXAS RECEIVED APRIL 12, 1948

[CONTRIBUTION FROM THE ORGANIC DEPARTMENT OF THE ABBOTT RESEARCH LABORATORIES]

Organic Thio-antimonials in Schistosomiasis

BY LEROY W. CLEMENCE AND MARLIN T. LEFFLER[1]

Organic antimony compounds have been used for a number of years in the treatment of protozoan diseases, but with certain drawbacks such as toxicity and a high relapse rate. It was felt that oil soluble antimonials would tend to overcome these difficulties because of slower and more prolonged absorption. A series of compounds has been prepared in which each compound is either an oil or a low melting solid and is soluble in vegetable oils. The general structure is $(RS-)_3Sb$ where R is *n*-alkyl (C_8-C_{18}), aralkyl (phenylethyl or naphthylethyl), cycloalkyl (cyclohexylethyl, cyclohexylamyl, tetralylbutyl, decalylbutyl), and heteroalkyl (pyridylethyl).

The compounds were prepared by the action of antimony trichloride on the appropriate mercaptan in chloroform. They were tested in experimental schistosomiasis[2] and preliminary results indicate some promise. Further animal investigation is under way and the results will be published elsewhere.

Experimental

The procedures described below were used for the preparation of the isothiouronium bromides, mercaptans and antimony compounds. Table I gives the physical constants and analytical data of previously undescribed compounds in the two former groups; Table II gives the data on the antimony compounds.

ω-Cyclohexylamyl Bromide.[3]—To 227 g. (1.33 moles) of cyclohexylamyl alcohol[3] (prepared by hydrogenation of ethyl ω-cyclohexylvalerate[3] at 250°, 3600 lb. pressure and copper chromite catalyst; b. p. 106–107° at 3 mm., $n^{25}D$ 1.4634) cooled to −10° in a 500-cc. flask fitted with stirrer, dropping funnel and thermometer, was added dropwise, 144 g. (0.44 mole + 20% excess) of phosphorus tribromide, keeping the temperature below 0°. This

TABLE I

R—	Isothiouronium bromides Yield, %	M. p., °C.	N Analyses, % Calcd.	Found	Mercaptans Yield, %	B. p., °C.	$n^{25}D$	Analyses C Calcd.	Found	Hydrogen Calcd.	Found
β-Cyclohexylethyl-	90	115–116[a]	10.48	10.35	56	50–52.5	1.4910	66.66	67.00	11.23	11.11
ω-Cyclohexylamyl-	68	140–141[b]	9.06	8.92	87	89.5–91	1.4820	70.96	71.06	11.82	11.78
ω-(β-Tetralyl)-butyl-	89	112–113[a]	8.16	8.10	72	143	1.5569	76.36	76.19	9.09	8.89
ω-(β-Decalyl)-butyl-	56	123–124[c]	8.02	8.00	62	124[d]	1.5072	74.33	74.52	11.49	11.29

[a] Recrystallized from alcohol. [b] Recrystallized from water. [c] Recrystallized from alcohol and ether. [d] Distilled at 0.5 mm. pressure.

TABLE II

TRI-(R-MERCAPTO)-S-ANTIMONOUS ACIDS, $(R-S-)_3Sb$

R—	Anal. Sb Calcd.	Found
n-Octyl	21.9	22.14[a]
n-Decyl	19.07	18.85[a]
n-Undecyl	17.83	17.14[a]
n-Dodecyl	16.8	16.85[a,b]
n-Tetradecyl	15.05	15.40[c,d]
n-Hexadecyl	13.68	13.43[c,e]
n-Octadecyl	12.4	12.62[c,f]
β-Phenylethyl	22.85	22.9[a]
β-(1-Naphthylethyl)	17.83	17.8[a]
β-(*p*-Diisobutylphenoxyethoxy)-ethyl	11.60	11.6[a]
β-Cyclohexylethyl	22.10	21.85[a]
ω-Cyclohexylamyl	18.00	18.33[a]
ω-(β-Tetralyl)-butyl	15.63	15.52[a]
ω-(β-Decalyl)-butyl	15.22	15.30[a]
β-(2-Pyridyl)-ethyl	22.72	21.4[g]

[a] Oil. [b] Solidified on cooling, recrystallized from Skelly C, m. p. 38–40°. [c] Solid; recrystallized from Skelly C. [d] M. p. 50–51°. [e] M. p. 51–52°. [f] M. p. 58–59°. [g] Resin.

(1) Presented at the 112th meeting of the American Chemical Society, Division of Medicinal Chemistry, at New York, N. Y., September, 1947.

(2) These compounds were submitted to the Chemotherapy Center for Tropical Diseases, National Research Council, and were screened by Drs. Maxwell Schubert and Arthur DeGraff.

(3) Hiers and Adams, THIS JOURNAL, **48**, 2385 (1926); Katsnelson and Dubinin, *Compt. rend. Acad. Sci. (U. R. S. S.)*, [N. S.] **4**, 405 (1936).