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.

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

Organic Thio-antimonials in Schistosomiasis

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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).

addition required three hours. The reaction mixture was stirred until room temperature was reached, allowed to stand overnight, heated at 100° for several hours, then cooled and poured into 1000 cc. of ice and water with good agitation. The heavy oily layer was dissolved in ether, the ether layer washed several times with water then with sodium carbonate solution, again with water, then dried over magnesium sulfate and evaporated. On distillation in vacuum, the fraction boiling at 89.5–90.5° at 1 mm., $n^{24}D$ 1.4784, was collected; yield 271 g. (87%). *Anal.* Calcd. for $C_{11}H_{21}Br$: C, 56.65; H, 9.01. Found: C, 56.87; H, 9.14.

ω-Cyclohexylamyl Isothiouronium Bromide.—To 23.3 g. (0.1 mole) of the above bromide was added a hot, filtered solution of 7.6 g. (0.1 mole) of thiourea in 125 cc. of absolute alcohol. The mixture was refluxed for thirty-six hours, then cooled and stirred until the whole mass became a crystalline mush. The solid was filtered, washed with a little acetone and dried. The yield was 22.6 g., m. p. 138–141°. After recrystallization of this material from 250 cc. of boiling water using a small amount of norite, the yield was 20.9 g. (68%), m. p. 140–141°. *Anal.* Calcd. for $C_{12}H_{24}N_2S \cdot HBr$: N, 9.06. Found: N, 8.92.

ω-Cyclohexylamyl Mercaptan.—Seventy-eight grams (0.25 mole) of the isothiouronium compound described above was added to a solution of 50 g. (1.25 moles) of sodium hydroxide dissolved in 325 cc. of water. The mixture was heated to boiling and refluxed for ten minutes, then cooled quickly and made acid to congo red by addition of concd. hydrochloric acid. It was extracted with ether and dried over anhydrous sodium sulfate, then evaporated. The residual oil was distilled in vacuum. The main fraction boiled at 93–94.5° at 1.2 mm. It was redistilled, b. p. 89.5–91° at 1 mm., $n^{25}D$ 1.4820, yield 41 g. (87%). *Anal.* Calcd. for $C_{11}H_{22}S$: C, 70.96; H, 11.82. Found: C, 71.06; H, 11.78.

Tri-[ω-cyclohexylamylmercapto]-S-antimonous Acid.—A solution of 7.61 g. (0.033 mole) of antimony trichloride in 50 cc. of warm chloroform was filtered and added to a solution of 18.6 g. (0.1 mole) of ω-cyclohexylamyl mercaptan in 50 cc. of chloroform. The clear solution was evaporated in vacuum to remove the solvent, then placed in a vacuum desiccator over solid sodium hydroxide for forty-eight hours to remove the last traces of hydrochloric acid. A quantitative yield of almost colorless oil was obtained. It was insoluble in water, soluble in chloroform, ether, benzene and vegetable oils. *Anal.* Calcd. for $C_{33}H_{66}S_3Sb$: Sb, 17.99. Found: Sb, 18.33.

The *n*-alkyl mercaptans, except the undecyl, were obtained from the Connecticut Hard Rubber Company. This was prepared by converting undecyl alcohol to the bromide and following the above procedure. β-(*p*-Diisobutylphenoxyethoxy)-ethyl mercaptan was obtained from Rohm & Haas Company; 2-pyridylethyl mercaptan was obtained from Reilly Tar and Chemical Corporation.

The intermediates, for conversion to the remaining mercaptans by the above procedures, were obtained as follows. Phenylethyl bromide was obtained from Columbia Organic Chemicals Company. β-(1-Naphthyl)-ethyl alcohol was prepared by method of Ruzicka.[4] β-Cyclohexylethyl alcohol,[3] b. p. 78–80° at 5 mm., $n^{25}D$ 1.4629, was prepared by catalytic hydrogenation of ethyl cyclohexylacetate.

The following alcohols were previously undescribed. ω-(β-Tetralyl)-butyl alcohol was obtained by hydrogenation of ethyl ω-(β-tetralyl)-butyrate[5] at 250°, 3600 lb. pressure with copper chromite catalyst; b. p. 167° at 5 mm., $n^{25}D$ 1.5391. *Anal.* Calcd. for $C_{14}H_{20}O$: C, 82.32; H, 9.81. Found: C, 82.03; H, 9.98. ω-(β-Decalyl)-butyl alcohol was obtained by further hydrogenation of the above alcohol at 200°, 3500 lb. pressure with Raney nickel catalyst; b. p. 148–149° at 6 mm., $n^{25}D$ 1.4919. *Anal.* Calcd. for $C_{14}H_{26}O$: C, 80.00; H, 12.38. Found: C, 80.64; H, 12.33.

The bromides obtained from the alcohols were slightly impure and were converted to the corresponding isothiouronium bromides without redistillation.

An attempt was made to purify one of the antimony compounds (*n*-dodecyl-) by molecular distillation but decomposition occurred. Tri-[(β-(2-pyridyl)-ethylmercapto]-S-antimonous acid was a resinous material only slightly soluble in olive oil.

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Summary

1. A series of thio-antimony compounds has been prepared, which are either oils or low melting solids soluble in vegetable oils.

2. Several new alcohols, isothiouronium bromides and mercaptans have been prepared.

3. The antimony compounds show some promise in experimental schistosomiasis and further investigation is being carried out.

(4) Ruzicka, *Helv. Chim. Acta*, **16**, 836 (1933).

(5) Newman and Zahm, THIS JOURNAL, **65**, 1099 (1943), described the preparation of the corresponding methyl ester.

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